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GENERIC DRUG NAME: Tofacitinib

PROTOCOL NO.: A3921021

PROTOCOL TITLE: A Multicenter, Phase 2, Open-Label, Controlled, Extension Study for Stage 1 Subjects of Study A3921009 to Evaluate the Long Term Safety and Efficacy of CP-690,550 Versus Tacrolimus, When Co-Administered with Mycophenolate Mofetil in Renal Allograft Recipients

Study Center(s): Thirteen centers in the United States (US) took part in the study.

Study Initiation Date and Primary Completion or Final Completion Dates:
Study Initiation Date: 07 December 2005 (First Subject First Visit)

Primary Completion Date: 06 January 2014

Study Completion Date: 13 June 2014 (Last Subject Last Visit)

Phase of Development: Phase 2

Study Objective(s):

Primary Objective

To evaluate the long term safety of tofacitinib including adverse events (AEs), safety laboratory tests, common calcineurin inhibitor (CNI)-related toxicities, clinically significant infections, and neoplasms (including post-transplant lymphoproliferative disease [PTLD]), and estimates of glomerular filtration rate [GFR].

Secondary Objectives:

- To evaluate the long term efficacy of tofacitinib including biopsy-proven acute rejection (BPAR), graft loss, death, rejection (defined as BPAR, antibody-mediated rejection or suspicious for acute rejection, ie, combined Banff categories 2-4), efficacy failure (defined as BPAR, death or graft loss), and treatment failure (defined as BPAR, death, graft loss or premature discontinuation of trial medication for any reason).

- To evaluate the effect of tofacitinib on lymphocyte subsets, peripheral blood gene expression, β-cell function and insulin resistance.

- To evaluate the effect of tofacitinib on Patient Reported Outcomes (PROs) including health status and healthcare resource utilization.

- To explore relationships between tofacitinib concentrations and safety, efficacy, and pharmacodynamic endpoints.

METHODS

Study Design: This was a multicenter, Phase 2, open-label, parallel group, active comparator controlled study designed to provide extended treatment of renal transplant recipients. Subjects who had been enrolled in Stage 1 of Study A3921009 and had completed 6 months of treatment with tofacitinib or tacrolimus were eligible for this extension study.

It was planned that subjects would continue study medications (tofacitinib or tacrolimus) for 90 months in the extension study, ie, through 8 years post-transplant. Following implementation of Protocol Amendment 4, (for administrative reasons, and not for safety concerns), the tacrolimus active comparator group was discontinued from the extension study.

Treatment assignment in the extension study was carried forward from the prior treatment assignment in Study A3921009. Treatment with study medications in the extension study began immediately following completion of the 6-month treatment period in Study A3921009. Assignment to tacrolimus versus tofacitinib 15-10-5 mg twice daily (BID) or tofacitinib 30-15-10 mg BID was open to the investigators, the subjects and the Pfizer study team. If necessary, (eg, due to AEs), dosing of tofacitinib was temporarily withheld. Thereafter, the subject resumed the original tofacitinib regimen.

Subjects who completed Stage 1 of Study A3921009 (6 month treatment) who elected to participate in the extension study were evaluated at Month 6 (subject's last visit for A3921009 and first visit for A3921021). Subjects returned to the study site for outpatient visits for safety and other evaluations at Months 9, 12, 15, 18, 24, 30, 36, 42, 48, 54, 60, 66, 72, 78, 84, 90, 96, and 98 (non-treatment follow-up) post-transplant. For those subjects who discontinued study treatment early prior to study completion, a follow-up visit was conducted 2 months following the discontinuation of the study treatment. Schedules of activities up to and including Month 24, and after Month 24, are presented in Table 1 and Table 2, respectively.

Table 1. Schedule of Activities for all Visits up to and Including Month 24

Protocol Activities	Time Post-transplant (There was a window of ±7 days for all visits up to and including Month 24)					
	Month 6	Month 9	Month 12	Month 15	Month 18	Month 24
Determination of enrollment eligibility/Sign new Informed Consent Form[a]	X					X
Full physical exam			X			
Limited physical exam		X			X	X
Supine vital signs		X	X	X	X	X
Oral body temperature		X	X	X	X	X
Subject weight		X	X	X	X	X
12 lead ECG			X			X
Safety laboratory tests		X	X	X	X	X
Urinalysis with microscopy		X	X	X	X	X
Pregnancy test (urine)		X	X	X	X	X
OGTT[b]	X		X			X
HbA1c	X		X			X
EBV DNA PCR		X	X	X	X	X
Plasma BKV DNA PCR[c]		X	X	X	X	X
FACS			X			X
Gene expression analysis sample (mRNA)			X			X
PK sample (predose) for tofacitinib subjects only[d]		X	X		X	X
Tacrolimus levels (predose) for tacrolimus subjects only		X	X		X	X
AE assessment		X	X	X	X	X
Concomitant medication assessment		X	X	X	X	X
Patient reported outcomes measures			X		X	X
Treatment assignment	X					
Dosing	X	→	→	→	→	X

Abbreviations: AE = adverse event; BKV = BK virus; EBV = Epstein Barr Virus; ECG = electrocardiograms; FACS = fluorescence activated cell sorting; HbA1c = glycosylated hemoglobin; OGTT = oral glucose tolerance tests; PCR = polymerase chain reaction; PK = pharmacokinetic.

a. Further extensions of the treatment period via protocol amendments required provision of separate informed consent from study subjects.

b. OGTT was only performed on eligible subjects. Prior to the OGTT, the subject had an overnight fast of 8 to 16 hours, during which water could have been consumed. Coffee and smoking were prohibited in the morning of the OGTT. Fasting blood samples were collected at the beginning of the OGTT (pre) to measure fasting serum glucose, insulin, and proinsulin and at 30, 60, 90, and 120 minutes after glucose ingestion to measure serum glucose and insulin. OGTT at any given visit was performed within ± 14 days of the specified visit date.

c. Plasma BKV DNA PCR was performed on tofacitinib-treated subjects only.

d. In addition to the predose sample, 2 samples were collected at approximately 30 (±10) and 60 (±10) minutes postdose at the study visit prior to reducing the subject's tofacitinib dose and at the next study visit after the tofacitinib dose reduction. On these visits, subjects were given their morning dose in the clinic.

→ indicates dosing was ongoing in this period.

Table 2. Schedule of Activities Beyond Month 24

	Time post-transplant (There was a window of ± 14 days for all visits after Month 24) Month												
Protocol activities	30	36	42	48	54	60	66	72	78	84	90	96	98 Follow-up
Sign new Informed Consent Form[a]				X									
Limited physical exam		X		X		X		X		X		X	X
Supine vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X
Oral body temperature	X	X	X	X	X	X	X	X	X	X	X	X	X
Subject weight	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead ECG		X		X		X		X		X		X	
Safety laboratory tests	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinalysis[b]	X	X	X	X	X	X	X	X	X	X	X	X	
Pregnancy test (urine)	X	X	X	X	X	X	X	X	X	X	X	X	X
Random urine for protein/ creatinine ratio		X		X		X		X		X		X	
HbA1c		X		X		X		X		X		X	
EBV DNA PCR	X	X	X	X	X	X	X	X	X	X	X	X	
Plasma BKV DNA PCR[c]	X	X	X	X	X	X	X	X	X	X	X	X	
PK sample (predose) for tofacitinib subjects only[d]	X	X	X	X	X	X	X	X	X	X	X	X	
Tacrolimus levels (predose) for tacrolimus subjects only[e]	X	X	X	X		X		X		X		X	
AE assessment	X	X	X	X	X	X	X	X	X	X	X	X	X

Table 2. Schedule of Activities Beyond Month 24

	Time post-transplant (There was a window of ± 14 days for all visits after Month 24) Month												
Protocol activities	30	36	42	48	54	60	66	72	78	84	90	96	98 Follow-up
Concomitant medication assessment	X	X	X	X	X	X	X	X	X	X	X	X	X
Dosing	X	→	→	→	→	→	→	→	→	→	→	→	X
Drug dispensing and accountability	X	X	X	X	X	X	X	X	X	X	X	X	

Abbreviations: AE = adverse event; BKV = BK virus; EBV = Epstein Barr Virus; ECG = electrocardiograms; FACS = fluorescence activated cell sorting; HbA1c = glycosylated hemoglobin; OGTT = oral glucose tolerance tests; PCR = polymerase chain reaction; PK = pharmacokinetic.

a. Further extensions of the treatment period via protocol amendments required provision of separate informed consent from study subjects.

b. Urine microscopy was not performed after Month 24 Visit (urinalysis only).

c. Plasma BKV DNA PCR was performed on tofacitinib-treated subjects only.

d. In addition to the predose sample, 2 samples were collected at approximately 30 (±10) and 60 (±10) minutes postdose at the study visit prior to reducing the subject's tofacitinib dose and at the next study visit after the tofacitinib dose reduction. On these visits, subjects were given their morning dose in the clinic.

e. Tacrolimus levels were collected at appropriate study visits until the individual subject was discontinued per Amendment #4.

→ indicates dosing was ongoing in this period.

Number of Subjects (Planned and Analyzed): This study planned to enroll approximately 54 subjects. Overall, 45 subjects were screened in the US, all of whom were entered into the study. Of these, 18 subjects received tacrolimus, 14 subjects received tofacitinib 15-10-5 mg BID and 13 subjects received tofacitinib 30-15-10 mg BID.

Diagnosis and Main Criteria for Inclusion: Subjects who were willing and able to provide written informed consent who had received a primary renal allograft from a cadaveric donor, a living related donor, or a living unrelated donor; been enrolled in Stage 1 of Study A3921009 and completed 6 months of treatment with study drugs (tofacitinib or tacrolimus), and with no known contraindications to the continued administration of tofacitinib, tacrolimus, mycophenolate mofetil (MMF) or corticosteroids.

Study Treatment: Tofacitinib was provided as 5 mg tablets and was administered orally, BID, approximately 12 hours apart. Tacrolimus was provided as 0.5 mg and 1.0 mg capsules and was administered orally according to standard institutional practice; no special preparation for tacrolimus was required. It was planned that subjects would continue study drug administration for 90 months in this extension study, ie, through 8 years post-transplant.

In treatment group 1, tacrolimus dosage was adjusted to achieve pre-determined target predose (trough) tacrolimus levels in whole blood.

In treatment group 2, upon entry into the extension study, subjects reduced tofacitinib dosage from 15 mg BID to 10 mg BID. Within the window of Month 12 to 24, subjects were to taper their tofacitinib dosage from 10 mg BID to 5 mg BID over 4 weeks (ie, 5 mg in the morning and 10 mg in the evening for 4 weeks, then 5 mg BID thereafter) and remain on 5 mg BID through the duration of this extension study. If the subject developed evidence of over immunosuppression (eg, moderate/severe clinically significant infection) during this extension study, the subject's immunosuppressive regimen could be reduced. If the subject had been receiving MMF >1 g daily, the subject's MMF could be reduced to 1 g daily (eg, 500 mg BID). If the subject continued to exhibit evidence of over immunosuppression despite an MMF regimen of 1 g daily, MMF could have been further reduced or discontinued after discussion with the sponsor.

In treatment group 3, upon entry into the extension study, the tofacitinib dosage was tapered from 30 mg BID to 15 mg BID over 4 weeks, eg, 25 mg BID for 2 weeks, then 20 mg BID for 2 weeks, then 15 mg BID thereafter. Within the window of Month 12 to 24, subjects should reduce their tofacitinib dosage from 15 mg BID to 10 mg BID and remain on 10 mg BID through the duration of the extension study. Subjects in treatment group 3 did not receive concomitant MMF. If clinically indicated, a subject assigned to treatment group 3 could convert to a tofacitinib-MMF regimen as described for treatment group 2, after discussion and agreement with the sponsor.

If necessary, further adjustments (increases or decreases in dose) of the study drug regimen in treatment groups 2 and 3 were determined after discussion between the investigator(s) and the sponsor.

Safety Endpoints:

Safety assessments were conducted at time points specified in Table 1 and Table 2.

The primary safety endpoints were as follows:

- GFR calculated using Modification of Diet in Renal Disease [MDRD] equation
- Serum creatinine levels
- Time to first clinically significant infection
- CNI-related toxicities, including but not limited to:
    - New onset diabetes mellitus-1 (NODM-1), defined as an event experienced by subjects who were non-diabetic prior to transplantation and now require treatment with oral hypoglycemic agents, anti-diabetic agents, and/or insulin for ≥30 days
    - Hypercholesterolemia, defined as a value of total serum cholesterol >240 mg/dL at each visit
    - Hypertriglyceridemia, defined as a value >200 mg/dL.

The following secondary safety variables were analyzed:

- GFR calculated by the Nankivell and Cockroft-Gault equations and reciprocal of serum creatinine (1/sCr)
- Adverse events (AEs)
- Serious infections
- CNI-related toxicities, including but not limited to:
    - New onset diabetes mellitus-2 (NODM-2), defined as an event experienced by a transplanted subject who met any of the following criteria:
        - NODM-1; or
        - Symptoms of diabetes plus 2 casual serum glucose levels ≥200 mg/dL separated by at least approximately 24 hours. Casual was defined as any time of day without regard to time since last meal; or
        - Fasting serum glucose ≥126 mg/dL on 2 different occasions separated by at least approximately 24 hours. Fasting was defined as no caloric intake for at least 8 hours; or

        - 2-hour serum glucose ≥200 mg/dL during an Oral Glucose Tolerance Test (OGTT).

    - Fasting serum glucose levels

    - Total serum cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels

    - The levels of serum triglycerides

    - Supine systolic and diastolic blood pressure

    - Any usage of lipid-lowering agents collected during the visit window

    - Any usage of antihypertensive agents during the visit window

    - Any usage of oral hypoglycemics, anti-diabetic agents or insulin during the visit window

- Epstein-Barr virus (EBV) DNA levels by polymerase chain reaction (PCR; number of copies/500 ng deoxyribonucleic acid [DNA])

- BK virus (BKV) DNA levels by PCR (number of copies/20 µL plasma)

- Cytomegalovirus (CMV) disease, defined as an AE associated with the signs and/or symptoms characteristic of CMV infection (eg, fever, new-onset or increased malaise, leucopenia, neutropenia, elevation of hepatic transaminases to more than twice the upper limit of normal), confirmed by evidence of CMV replication in blood (by PCR, antigen assay or culture) or histological evidence of CMV infection in a tissue specimen, and attributed to CMV by the investigator.

Additional safety evaluations included other safety laboratory tests, electrocardiograms and vital signs data.

Efficacy endpoints:

Efficacy assessments were conducted at time points specified in Table 1 and Table 2.

The following key efficacy endpoints were analyzed:

- Time to first BPAR (Banff category 4)

- Time to treatment failure (defined as the first BPAR, death, graft loss or premature discontinuation of trial medication for any reason)

The following non-key efficacy endpoints were analyzed:

- Time to first biopsy proven chronic allograft nephropathy (BPCAN; Banff category 5)

- Ordered categorical severity of first BPAR (5 categories: IA, IB, IIA, IIB and III) and first BPCAN (3 categories: Grades I, II and III) according to the Banff Classification

- Time to efficacy failure (defined as the first BPAR, death or graft loss)

- Time to graft loss (defined as graft nephrectomy, retransplantation, return to dialysis for ≥6 consecutive weeks, or subject death)

- Time to subject death

- Time to rejection (first occurrence of BPAR, antibody mediated rejection (category 2 of Banff), or suspicious for acute rejection (category 3 of Banff).

Pharmacodynamic endpoints:

Pharmacodynamic assessments were conducted at time points specified in Table 1 and Table 2. The following secondary pharmacodynamics endpoints were analyzed:

- Flow cytometry of Lymphocyte Subsets: absolute cell counts for $CD4^+$ (helper T-lymphocytes), $CD8^+$ (cytotoxic T-lymphocytes), $CD3^-CD56^+$ (natural killer cells) and $CD19^+$ (B-lymphocytes).

- Hemoglobin A1c (HbA1c)

- β-cell function and insulin resistance using the homeostatic model assessment (HOMA):

  - β-cell function (HOMA-%B)

  - Insulin resistance (IR)

  - Ratio of fasting serum proinsulin:insulin

  - Areas under the curve (AUC) of serum glucose measured during OGTT (time points: 0 (prior to glucose ingestion), 30, 60, 90 and 120 minutes after glucose ingestion)

  - AUC of serum insulin measured during OGTT (time points: 0 (prior to glucose ingestion), 30, 60, 90 and 120 minutes after glucose ingestion).

Pharmacokinetic endpoints:

Pharmacokinetic assessments were conducted at time points specified in Table 1 and Table 2.

- Trough levels of tacrolimus (ng/mL) by Visit

- Trough levels of tofacitinib by visit (ng/mL).

Outcomes research endpoints:

Outcomes research assessments were conducted at time points specified in Table 1 and Table 2. The following patient reported outcomes were analyzed:

- Short Form (36) health survey (SF-36) v2 Standard
- End Stage Renal Disease Symptom Checklist Transplantation Module (ESRD-SCL)
- Healthcare Resource Utilization Questionnaire (HCRUQ).

Statistical Methods:

The Full Analysis Set (FAS) included all subjects who received at least 1 dose of study drug in study A3921021. The Safety Analysis Set was defined as those subjects who received at least 1 dose of the study drug in study A3921021. The efficacy analyses were performed for the FAS.

For all time-to-event endpoints, the time was from the first day of dosing in Study A3921009 to that when the event occurred. The time unit was days. For time-to-event data, Kaplan-Meier survival curves were fitted. Cumulative proportions, standard errors (SEs), and confidence intervals (CIs) were estimated from the fitted curves for each treatment at scheduled visits. Comparisons in proportions between each of the tofacitinib dose regimens and tacrolimus were made (difference in proportions, SE, and CI) at each scheduled visit. P-values using Wald test statistics for treatment comparisons were provided. The p-values from the Log-Rank test were reported to compare the curves between each of the tofacitinib dose regimens (treatment groups) and tacrolimus as supportive tests. The estimates were computed at the protocol scheduled day for each visit. Data collected up to the follow-up visit were included in the analysis. If no event occurred, the time was censored at the last available visit, or Day 2980 (the maximum scheduled day for follow-up, approximately 98 month post-transplant), whichever came earliest.

For each vital signs endpoint, descriptive statistics (number of subjects [N], mean, median, coefficient of variation [CV], standard deviation [SD], minimum [Min], first quartile [Q1], third quartile [Q3] and maximum [Max]) were produced for each time point including baseline for each treatment group, as well as for change from baseline to each time point. For electrocardiogram (ECG) endpoints, descriptive statistics (N, mean, median, CV, SD, Min, Q1, Q3 and Max) were produced for each time point including baseline for each treatment group, as well for change from baseline to each time point. The ECG values and changes from baseline were also descriptively summarized using Pfizer QT standard. Numbers and percentages of subjects meeting the categorical criteria during any postdose period were provided.

Descriptive summary statistics were reported for all other study endpoints by treatment group and visit based on the available observed data. Safety data were summarized per Pfizer standards.

RESULTS

Subject Disposition and Demography:

Subject disposition is summarized in Table 3; subject demographics are summarized in Table 4.

In all, 28 subjects completed the study (12 [85.7%] subjects on tofacitinib 15-10-5 mg BID, 6 [46.2%] subjects on tofacitinib 30-15-10 mg BID and 10 [55.6%] subjects on tacrolimus) and 17 subjects discontinued the study. The primary reason for discontinuation was AE (related to study drug; 5 subjects in total: tofacitinib 15-10-5 mg BID 1 subject, tofacitinib 30-15-10 mg BID 4 subjects, tacrolimus 0 subjects).

Demographic characteristics at the time of enrollment in the parent study (Study A3921009) were similar across the 3 groups. The majority of the subjects were male (28 subjects, 62.2%) and the most frequent race reported was white (25 subjects, 55.6%). The age ranges of subjects were 27 to 56 years in the tacrolimus group, 35 to 61 years in the tofacitinib 15-10-5 mg BID group and 20 to 60 years in the tofacitinib 30-15-10 mg BID group. The ranges of weight were 47.6 to 134.5 kg in the tacrolimus group, 56.5 to 113.0 kg in the tofacitinib 15-10-5 mg BID group and 56.6 to 100.9 kg in the tofacitinib 30-15-10 mg BID group.

Table 3. Subject Disposition (All Subjects) in Study A3921021

	Number (%) subjects		
	Tacrolimus	**Tofacitinib 15-10-5 mg BID**	**Tofacitinib 30-15-10 mg BID**
Assigned to Study Treatment	18	14	13
Treated, n (%)	18 (100)	14 (100)	13 (100)
Completed, n (%)	10 (55.6)	12 (85.7)	6 (46.2)
Discontinued, n (%)	8 (44.4)	2 (14.3)	7 (53.8)
Analyzed for Safety	18	14	13
Adverse events, n (%)	18 (100)	14 (100)	13 (100)
Laboratory data, n (%)	18 (100)	14 (100)	13 (100)
Reason for discontinuation, n			
Subject died	0	0	1
Relation to study drug not defined:	7	1	2
Lost to follow-up	1	1	0
No longer willing to participate in study	3	0	1
Other	3	0	1
Adverse event (related to study drug)	0	1	4
Adverse event (not related to study drug)	1	0	0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis.
Included are data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
Tacrolimus subjects who were discontinued from treatment due to Protocol Amendment 4 were considered as completed.
Discontinued referred to discontinued from study. One subject discontinued in the postdose follow-up period and was included in the discontinued category. Other reasons for discontinuation included recurrence of primary disease and on dialysis, per principal investigator discretion, non-compliant with study visits and decided to pursue pregnancy. Death resulting in discontinuation during active treatment phase was included.
Abbreviations: BID = twice daily; n = number of subjects in each category.

Table 4. Summary of Demographic Characteristics – Safety Analysis Set

	Tacrolimus N=18			Tofacitinib 15-10-5 mg BID N=14			Tofacitinib 30-15-10 mg BID N=13		
	Male n=11	**Female** n=7	**Total** n=18	**Male** n=7	**Female** n=7	**Total** n=14	**Male** n=10	**Female** n=3	**Total** n=13
Age (years), n (%)									
18-44	6 (54.5)	4 (57.1)	10 (55.6)	2 (28.6)	3 (42.9)	5 (35.7)	4 (40.0)	0	4 (30.8)
45-64	5 (45.5)	3 (42.9)	8 (44.4)	5 (71.4)	4 (57.1)	9 (64.3)	6 (60.0)	3 (100.0)	9 (69.2)
Mean (SD)	40.5 (9.0)	38.3 (10.3)	39.6 (9.3)	50.3 (8.1)	45.9 (7.6)	48.1 (7.9)	41.8 (12.6)	53.3 (5.1)	44.5 (12.2)
Range	27-56	28-52	27-56	38-61	35-56	35-61	20-60	49-59	20-60
Race, n (%)									
White	3 (27.3)	5 (71.4)	8 (44.4)	4 (57.1)	4 (57.1)	8 (57.1)	6 (60.0)	3 (100.0)	9 (69.2)
Black	3 (27.3)	0	3 (16.7)	0	1 (14.3)	1 (7.1)	1 (10.0)	0	1 (7.7)
Asian	2 (18.2)	1 (14.3)	3 (16.7)	0	0	0	1 (10.0)	0	1 (7.7)
Hispanic	3 (27.3)	1 (14.3)	4 (22.2)	3 (42.9)	2 (28.6)	5 (35.7)	2 (20.0)	0	2 (15.4)
Weight (kg)									
Mean (SD)	88.9 (23.8)	77.6 (21.9)	84.5 (23.2)	85.3 (18.4)	80.9 (21.3)	83.1 (19.3)	82.0 (14.8)	76.8 (5.4)	80.8 (13.2)
Range	51.2-134.5	47.6-109.0	47.6-134.5	62.0-113.0	56.5-112.0	56.5-113.0	56.6-100.9	73.4-83.0	56.6-100.9
Height (cm)									
Mean (SD)	177.3 (10.2)	159.5 (5.7)	170.4 (12.3)	177.9 (12.2)	160.7 (4.2)	169.3 (12.5)	174.3 (8.3)	163.3 (6.3)	171.8 (9.1)
Range	165.0-198.1	152.0-168.0	152.0-198.1	157.0-192.0	156.0-168.0	156.0-192.0	163.0-185.4	157.4-170.0	157.4-185.4

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis; includes data from both A3921009 and A3921021 and only from subjects enrolled in A3921021.
Abbreviations: BID = twice daily; N = number of subjects in Safety Analysis Set; n = number of subjects in each category; SD = standard deviation.

Safety Results:

Primary Endpoints:

GFR calculated using MDRD equation: Descriptive statistics for GFR (mL/minute/1.73 m^2) calculated using the MDRD equation are summarized by visit for the Safety Analysis Set in Table 5.

From Month 18 through Month 72, mean estimated GFR calculated by the MDRD equation was highest in the tacrolimus group (ranging from 72.81 to 89.80 mL/minute/1.73 m^2), followed by the tofacitinib 15-10-5 mg BID group (ranging from 66.91 to 71.55 mL/minute/1.73 m^2), and then by the tofacitinib 30-15-10 mg BID group (ranging from 61.72 to 67.30 mL/minute/1.73 m^2).

Table 5. Descriptive Statistics of Glomerular Filtration Rate (mL/minute/1.73 m^2) Calculated by the MDRD Equation Over Time (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	67.06	19.79	29.51	38.7	55.4	64.3	71.5	122.5
	Tofacitinib 15-10-5 mg BID	14	65.99	12.46	18.88	50.4	55.8	61.6	76.9	89.0
	Tofacitinib 30-15-10 mg BID	12	67.05	13.63	20.33	40.0	58.0	69.5	74.9	87.4
Month 12	Tacrolimus	16	64.97	25.10	38.64	33.9	47.1	57.1	86.4	128.7
	Tofacitinib 15-10-5 mg BID	14	65.16	11.90	18.26	49.2	55.0	65.6	73.0	82.7
	Tofacitinib 30-15-10 mg BID	12	63.50	12.01	18.91	41.5	56.4	62.1	72.8	83.3
Month 15	Tacrolimus	16	66.22	15.10	22.81	43.1	52.3	67.9	75.6	94.8
	Tofacitinib 15-10-5 mg BID	14	67.86	9.33	13.75	52.6	62.5	66.3	76.0	81.9
	Tofacitinib 30-15-10 mg BID	12	65.71	9.44	14.36	47.9	59.6	65.1	72.8	82.7
Month 18	Tacrolimus	18	72.81	23.09	31.72	39.1	55.7	70.9	82.0	127.7
	Tofacitinib 15-10-5 mg BID	14	66.91	12.19	18.21	42.2	59.3	69.5	75.9	86.6
	Tofacitinib 30-15-10 mg BID	12	64.71	12.10	18.70	40.5	58.8	65.7	72.2	81.8
Month 24	Tacrolimus	17	77.05	28.23	36.63	38.4	57.4	71.1	94.3	156.3
	Tofacitinib 15-10-5 mg BID	14	68.45	10.47	15.29	54.2	62.0	65.8	75.3	93.0
	Tofacitinib 30-15-10 mg BID	12	66.29	8.72	13.16	46.6	61.1	68.9	72.0	79.2
Month 30	Tacrolimus	14	79.89	29.56	37.01	42.3	54.8	73.4	110.5	127.9
	Tofacitinib 15-10-5 mg BID	14	71.55	7.33	10.25	63.5	66.1	70.4	74.2	90.5
	Tofacitinib 30-15-10 mg BID	10	64.04	10.24	15.99	54.5	55.6	59	73.2	83.4
Month 36	Tacrolimus	15	79.87	30.20	37.81	31.5	54.1	73.0	106.9	125.9
	Tofacitinib 15-10-5 mg BID	14	70.44	13.65	19.38	47.4	59.6	70.5	79.9	101.4
	Tofacitinib 30-15-10 mg BID	9	61.72	15.84	25.67	37.6	54.0	62.4	74.9	86.0
Month 42	Tacrolimus	15	77.95	29.77	38.18	27.5	56.9	76.3	101.7	140.8
	Tofacitinib 15-10-5 mg BID	14	70.77	16.05	22.69	40.4	57.1	70.0	84.2	93.3
	Tofacitinib 30-15-10 mg BID	9	65.25	8.71	13.35	55.8	59.3	62.5	70.1	81.6
Month 48	Tacrolimus	15	76.23	30.34	39.80	19.1	56.9	71.0	102.3	142.2
	Tofacitinib 15-10-5 mg BID	14	70.36	14.36	20.40	37.0	62.9	72.1	81.8	89.0
	Tofacitinib 30-15-10 mg BID	10	65.50	10.19	15.56	51.7	52.9	69.6	73.2	78.4
Month 54	Tacrolimus	14	78.10	32.27	41.32	9.8	55.1	77.1	103.3	120.4
	Tofacitinib 15-10-5 mg BID	14	69.98	15.18	21.7	39.4	64.1	70.9	80.8	96.4
	Tofacitinib 30-15-10 mg BID	10	61.99	9.54	15.39	40.7	56.4	64.5	68.4	74.3

Table 5. Descriptive Statistics of Glomerular Filtration Rate (mL/minute/1.73 m^2) Calculated by the MDRD Equation Over Time (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 60	Tacrolimus	13	82.86	33.72	40.69	35.3	61.5	78.5	93.8	164.1
	Tofacitinib 15-10-5 mg BID	13	70.10	18.01	25.69	38.2	59.1	70.1	79.8	97.2
	Tofacitinib 30-15-10 mg BID	10	67.30	9.37	13.92	49.6	61.4	67.9	72.5	82.2
Month 66	Tacrolimus	12	89.80	36.51	40.65	23.9	66.7	89.0	121.0	140.3
	Tofacitinib 15-10-5 mg BID	14	69.69	18.23	26.16	38.9	59.6	68.2	85.6	97.1
	Tofacitinib 30-15-10 mg BID	10	64.98	15.95	24.55	32.2	60.2	66.9	75.7	84.0
Month 72	Tacrolimus	9	76.61	20.99	27.40	42.3	62.5	74.8	84.8	109.6
	Tofacitinib 15-10-5 mg BID	13	67.89	11.61	17.10	43.1	62.6	69.4	72.9	92.4
	Tofacitinib 30-15-10 mg BID	8	61.96	8.15	13.16	50.4	56.3	62.8	65.9	75.2
Month 78	Tofacitinib 15-10-5 mg BID	13	69.95	14.40	20.59	45.4	60.7	67.2	79.3	98.9
	Tofacitinib 30-15-10 mg BID	8	68.64	6.15	8.96	61.8	62.7	68.1	73.9	77.9
Month 84	Tofacitinib 15-10-5 mg BID	12	69.24	13.80	19.92	42.3	61.1	68.4	78.2	95.8
	Tofacitinib 30-15-10 mg BID	8	68.77	4.90	7.13	60.8	65.9	68.8	71.6	76.6
Month 90	Tofacitinib 15-10-5 mg BID	12	65.28	14.19	21.74	39.0	58.3	64.0	69.9	94.5
	Tofacitinib 30-15-10 mg BID	7	69.46	6.23	8.97	60.3	61.2	71.5	74.2	75.4
Month 96	Tofacitinib 15-10-5 mg BID	11	64.94	14.01	21.58	35.8	57.9	62.5	73.1	90.7
	Tofacitinib 30-15-10 mg BID	6	70.33	14.22	20.21	54.7	59.8	66.1	86.4	88.8
Follow-up	Tacrolimus	6	42.29	19.87	46.99	7.6	35.2	45.2	57.0	63.5
	Tofacitinib 15-10-5 mg BID	12	63.25	14.07	22.25	34.8	55.9	62.8	69.1	86.9
	Tofacitinib 30-15-10 mg BID	8	60.41	24.43	10.44	14.3	45.3	66.9	77.4	89.7

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; CV = coefficient of variation; Max = maximum; MDRD = modification of diet in renal disease; Min = minimum; N = number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Serum creatinine levels: Descriptive statistics for creatinine (mg/dL) are summarized by visit for the Safety Analysis Set in Table 6. Mean serum creatinine levels were generally similar across the 3 treatment groups.

Table 6. Descriptive Statistics of Serum Creatinine Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	1.26	0.30	23.42	0.9	1.1	1.1	1.4	2.0
	Tofacitinib 15-10-5 mg BID	14	1.19	0.26	21.93	0.7	1.0	1.2	1.4	1.6
	Tofacitinib 30-15-10 mg BID	12	1.28	0.31	24.38	0.8	1.1	1.3	1.4	2.0
Month 12	Tacrolimus	16	1.34	0.30	22.57	0.9	1.1	1.3	1.5	2.1
	Tofacitinib 15-10-5 mg BID	14	1.21	0.30	25.06	0.8	1.0	1.2	1.4	1.7
	Tofacitinib 30-15-10 mg BID	12	1.33	0.32	23.89	0.8	1.1	1.4	1.6	1.9
Month 15	Tacrolimus	16	1.24	0.32	25.42	0.8	1.0	1.2	1.4	2.0
	Tofacitinib 15-10-5 mg BID	14	1.13	0.20	17.87	0.8	1.0	1.2	1.2	1.5
	Tofacitinib 30-15-10 mg BID	12	1.28	0.29	22.96	0.8	1.1	1.3	1.5	1.8
Month 18	Tacrolimus	18	1.18	0.30	25.14	0.8	0.9	1.2	1.3	1.9
	Tofacitinib 15-10-5 mg BID	14	1.15	0.23	19.81	0.8	1.0	1.1	1.4	1.5
	Tofacitinib 30-15-10 mg BID	12	1.29	0.29	22.74	0.8	1.2	1.2	1.5	2.0
Month 24	Tacrolimus	17	1.15	0.29	24.93	0.7	1.0	1.2	1.3	1.9
	Tofacitinib 15-10-5 mg BID	14	1.11	0.18	16.03	0.8	0.9	1.1	1.3	1.3
	Tofacitinib 30-15-10 mg BID	12	1.23	0.22	18.08	0.9	1.1	1.2	1.4	1.7
Month 30	Tacrolimus	14	1.14	0.36	31.21	0.6	0.9	1.1	1.2	1.9
	Tofacitinib 15-10-5 mg BID	14	1.06	0.16	14.71	0.9	0.9	1.0	1.2	1.3
	Tofacitinib 30-15-10 mg BID	10	1.24	0.22	17.91	0.8	1.1	1.3	1.4	1.5
Month 36	Tacrolimus	15	1.18	0.43	36.13	0.5	0.9	1.1	1.5	2.1
	Tofacitinib 15-10-5 mg BID	14	1.08	0.22	19.98	0.8	0.9	1.1	1.3	1.4
	Tofacitinib 30-15-10 mg BID	9	1.33	0.30	22.19	1.1	1.1	1.3	1.4	2.0
Month 42	Tacrolimus	15	1.19	0.42	35.02	0.8	0.9	1.1	1.4	2.2
	Tofacitinib 15-10-5 mg BID	14	1.09	0.27	24.73	0.7	0.9	1.1	1.3	1.5
	Tofacitinib 30-15-10 mg BID	9	1.17	0.12	10.50	10	1.1	1.1	1.2	1.4
Month 48	Tacrolimus	15	1.23	0.47	38.42	0.8	0.9	1.1	1.4	2.5
	Tofacitinib 15-10-5 mg BID	14	1.08	0.27	24.98	0.7	0.9	1.0	1.2	1.6
	Tofacitinib 30-15-10 mg BID	10	1.20	0.11	8.78	1.0	1.2	1.2	1.2	1.4
Month 54	Tacrolimus	14	1.38	1.04	75.13	0.7	0.8	1.1	1.4	4.8
	Tofacitinib 15-10-5 mg BID	14	1.10	0.26	23.38	0.7	0.9	1.2	1.3	1.5
	Tofacitinib 30-15-10 mg BID	10	1.25	0.14	10.83	1.0	1.2	1.3	1.4	1.4

Table 6. Descriptive Statistics of Serum Creatinine Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 60	Tacrolimus	13	1.17	0.40	34.10	0.7	0.8	1.1	1.3	2.0
	Tofacitinib 15-10-5 mg BID	13	1.12	0.35	31.24	0.7	0.9	1.0	1.2	2.0
	Tofacitinib 30-15-10 mg BID	10	1.16	0.13	11.64	1.0	1.0	1.2	1.2	1.4
Month 66	Tacrolimus	12	1.12	0.50	44.67	0.5	0.8	1.0	1.3	2.3
	Tofacitinib 15-10-5 mg BID	14	1.14	0.33	29.02	0.7	0.9	1.1	1.3	1.9
	Tofacitinib 30-15-10 mg BID	10	1.24	0.27	21.57	0.9	1.0	1.3	1.3	1.8
Month 72	Tacrolimus	9	1.12	0.26	23.48	0.8	0.8	1.2	1.3	1.5
	Tofacitinib 15-10-5 mg BID	13	1.09	0.21	18.91	0.7	1.0	1.1	1.2	1.4
	Tofacitinib 30-15-10 mg BID	8	1.29	0.21	16.31	1.0	1.2	1.3	1.4	1.7
Month 78	Tofacitinib 15-10-5 mg BID	13	1.09	0.21	18.86	0.7	1.0	1.1	1.2	1.4
	Tofacitinib 30-15-10 mg BID	8	1.16	0.14	12.11	1.0	1.1	1.2	1.3	1.4
Month 84	Tofacitinib 15-10-5 mg BID	12	1.10	0.21	18.99	0.7	1.0	1.1	1.3	1.4
	Tofacitinib 30-15-10 mg BID	8	1.15	0.15	13.15	0.9	1.1	1.2	1.2	1.4
Month 90	Tofacitinib 15-10-5 mg BID	12	1.16	0.25	21.92	0.7	1.0	1.2	1.4	1.5
	Tofacitinib 30-15-10 mg BID	7	1.16	0.19	16.44	0.9	1.0	1.2	1.2	1.5
Month 96	Tofacitinib 15-10-5 mg BID	11	1.15	0.25	21.69	0.8	0.9	1.1	1.4	1.6
	Tofacitinib 30-15-10 mg BID	6	1.10	0.14	12.86	0.9	1.0	1.1	1.2	1.3
Follow-up	Tacrolimus	6	2.36	2.11	89.78	1.1	1.3	1.5	2.1	6.6
	Tofacitinib 15-10-5 mg BID	12	1.16	0.27	23.12	0.7	1.0	1.2	1.3	1.6
	Tofacitinib 30-15-10 mg BID	8	1.50	0.84	56.23	0.9	1.0	1.2	1.7	3.4

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; CV = coefficient of variation; Max = maximum; Min = minimum; N = number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Time to clinically significant infections: Percentages of subjects with clinically significant infections (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Safety Analysis Set in Table 7

Comparisons in proportions of subjects with clinically significant infections at various time points showed no statistically significant differences between tofacitinib 15-10-5 mg BID and tacrolimus ($p>0.05$ at all time points).

Comparisons in proportions of subjects with clinically significant infections at various time points showed significantly higher rates in the tofacitinib 30-15-10 mg BID group compared with tacrolimus at Month 3 ($p=0.0255$), Month 6 ($p=0.0035$), Month 9 ($p=0.0125$), Month 12 ($p=0.0342$), and Month 15 through to Month 30 visits ($p=0.0203$, at each visit).

Table 7. Percent of Subjects with Clinically Significant Infections estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Day 1	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0	0	0	0		
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	0	0	0	0		
Month 1	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	-3.42	10.46	-16.83	9.99	0.7439	
Month 3	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	6	7	46.15	13.83	28.43	63.87	35.04	15.69	14.94	55.14	0.0255	
Month 6	Tacrolimus	4	14	22.22	9.80	9.66	34.78						
	Tofacitinib 15-10-5 mg BID	2	12	14.29	9.35	2.30	26.27	-7.94	13.55	-25.30	9.42	0.5579	
	Tofacitinib 30-15-10 mg BID	9	4	69.23	12.80	52.83	85.64	47.01	16.12	26.35	67.67	0.0035	
Month 9	Tacrolimus	5	13	27.78	10.56	14.25	41.31						
	Tofacitinib 15-10-5 mg BID	3	11	21.43	10.97	7.37	35.48	-6.35	15.22	-25.86	13.16	0.6766	
	Tofacitinib 30-15-10 mg BID	9	4	69.23	12.80	52.83	85.64	41.45	16.59	20.19	62.72	0.0125	
Month 12	Tacrolimus	6	12	33.33	11.11	19.09	47.57						
	Tofacitinib 15-10-5 mg BID	5	9	35.71	12.81	19.30	52.13	2.38	16.95	-19.35	24.11	0.8883	
	Tofacitinib 30-15-10 mg BID	9	4	69.23	12.80	52.83	85.64	35.90	16.95	14.17	57.62	0.0342	
Month 15	Tacrolimus	7	11	38.89	11.49	24.16	53.61						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	3.97	17.52	-18.48	26.42	0.8208	
	Tofacitinib 30-15-10 mg BID	10	3	76.92	11.69	61.95	91.90	38.03	16.39	17.03	59.04	0.0203	
Month 18	Tacrolimus	7	10	38.89	11.49	24.16	53.61						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	3.97	17.52	-18.48	26.42	0.8208	
	Tofacitinib 30-15-10 mg BID	10	3	76.92	11.69	61.95	91.90	38.03	16.39	17.03	59.04	0.0203	

Table 7. Percent of Subjects with Clinically Significant Infections estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 24	Tacrolimus	7	10	38.89	11.49	24.16	53.61						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	3.97	17.52	-18.48	26.42	0.8208	
	Tofacitinib 30-15-10 mg BID	10	3	76.92	11.69	61.95	91.90	38.03	16.39	17.03	59.04	0.0203	
Month 30	Tacrolimus	7	9	38.89	11.49	24.16	53.61						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	3.97	17.52	-18.48	26.42	0.8208	
	Tofacitinib 30-15-10 mg BID	10	3	76.92	11.69	61.95	91.90	38.03	16.39	17.03	59.04	0.0203	
Month 36	Tacrolimus	8	8	45.68	12.05	30.23	61.13						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	-2.82	17.89	-25.76	20.11	0.8747	
	Tofacitinib 30-15-10 mg BID	10	3	76.92	11.69	61.95	91.90	31.24	16.79	9.73	52.76	0.0627	
Month 42	Tacrolimus	8	8	45.68	12.05	30.23	61.13						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	-2.82	17.89	-25.76	20.11	0.8747	
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.69	61.95	91.90	31.24	16.79	9.73	52.76	0.0627	
Month 48	Tacrolimus	8	7	45.68	12.05	30.23	61.13						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	-2.82	17.89	-25.76	20.11	0.8747	
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.69	61.95	91.90	31.24	16.79	9.73	52.76	0.0627	
Month 54	Tacrolimus	8	7	45.68	12.05	30.23	61.13						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	-2.82	17.89	-25.76	20.11	0.8747	
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.69	61.95	91.90	31.24	16.79	9.73	52.76	0.0627	
Month 60	Tacrolimus	8	7	45.68	12.05	30.23	61.13						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	-2.82	17.89	-25.76	20.11	0.8747	
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.69	61.95	91.90	31.24	16.79	9.73	52.76	0.0627	
Month 66	Tacrolimus	8	7	45.68	12.05	30.23	61.13						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	-2.82	17.89	-25.76	20.11	0.8747	
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.69	61.95	91.90	31.24	16.79	9.73	52.76	0.0627	

Table 7. Percent of Subjects with Clinically Significant Infections estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

		Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
Visit	Treatment	Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 72	Tacrolimus	8	4	45.68	12.05	30.23	61.13						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	-2.82	17.89	-25.76	20.11	0.8747	
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.69	61.95	91.90	31.24	16.79	9.73	52.76	0.0627	
Month 78	Tacrolimus	8	0										
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81						
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.69	61.95	91.90						
Month 84	Tacrolimus	8	0										
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81						
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.59	61.95	91.90						
Month 90	Tacrolimus	8	0										
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81						
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.59	61.95	91.90						
Month 96	Tacrolimus	8	0										
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81						0.8883
	Tofacitinib 30-15-10 mg BID	10	2	76.92	11.59	61.95	91.90						0.0291

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
Abbreviations: BID = twice daily dosing; CI = confidence interval; Cum.=cumulative; Diff. = difference; N = number of subjects; No. = number; SE = standard error.

CNI-related toxicities, including but not limited to NODM-1, hypercholesterolemia and hypertriglyceridemia: Percentages of subjects with NODM-1 events (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Safety Analysis Set in Table 8.

There was 1 NODM-1 event in the tacrolimus group (between Month 18 and Month 24) and no event in either of the tofacitinib groups. The incidence of events was low and precluded any comparisons between treatment groups.

Percentages of subjects with hypercholesterolemia and hypertriglyceridemia are presented by visit for the Safety Analysis Set in Table 9 and Table 10, respectively.

The proportion of subjects with hypercholesterolemia was similar between the tofacitinib 15-10-5 mg BID group or tofacitinib 30-15-10 mg BID and tacrolimus groups at various time points.

Comparisons in proportions of subjects with hypertriglyceridemia at scheduled visits showed significantly higher rates for tofacitinib 15-10-5 mg BID compared with tacrolimus at Month 9 (p=0.0169), Month 12 (p=0.0127), Month 15 (p=0.0127), and Month 18 (p=0.0328). Comparisons in proportions of subjects with hypertriglyceridemia at scheduled visits showed significantly higher rates for tofacitinib 30-15-10 mg BID compared with tacrolimus at Month 12 (p=0.0493), Month 15 (p=0.0172), and Month 18 (p=0.0493).

Table 8. Percent of Subjects with NODM-1 estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 18	Tacrolimus	0	16	0.00	0.00	0.00	9.57						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	9	0.00	0.00	0.00	16.37	0.00	0.00	0.00	0.00		
Month 24	Tacrolimus	1	15	6.25	6.05	0.00	14.01						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
	Tofacitinib 30-15-10 mg BID	0	9	0.00	0.00	0.00	16.37	-6.25	6.05	-14.01	1.51	0.3017	
Month 30	Tacrolimus	1	13	6.25	6.05	0.00	14.01						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
	Tofacitinib 30-15-10 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
Month 36	Tacrolimus	1	13	6.25	6.05	0.00	14.01						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
	Tofacitinib 30-15-10 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
Month 42	Tacrolimus	1	13	6.25	6.05	0.00	14.01						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
	Tofacitinib 30-15-10 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
Month 48	Tacrolimus	1	12	6.25	6.05	0.00	14.01						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
	Tofacitinib 30-15-10 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
Month 54	Tacrolimus	1	12	6.25	6.05	0.00	14.01						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
	Tofacitinib 30-15-10 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
Month 60	Tacrolimus	1	11	6.25	6.05	0.00	14.01						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
	Tofacitinib 30-15-10 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	

Table 8. Percent of Subjects with NODM-1 estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 66	Tacrolimus	1	11	6.25	6.05	0.00	14.01						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
	Tofacitinib 30-15-10 mg BID	0	7	0.00	0.00	0.00	20.54	-6.25	6.05	-14.01	1.51	0.3017	
Month 72	Tacrolimus	1	6	6.25	6.05	0.00	14.01						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	-6.25	6.05	-14.01	1.51	0.3017	
	Tofacitinib 30-15-10 mg BID	0	7	0.00	0.00	0.00	20.54	-6.25	6.05	-14.01	1.51	0.3017	
Month 78	Tacrolimus	1	0										
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22						
	Tofacitinib 30-15-10 mg BID	0	6	0.00	0.00	0.00	23.53						
Month 84	Tacrolimus	1	0										
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22						
	Tofacitinib 30-15-10 mg BID	0	6	0.00	0.00	0.00	23.53						
Month 90	Tacrolimus	1	0										
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22						
	Tofacitinib 30-15-10 mg BID	0	6	0.00	0.00	0.00	23.53						
Month 96	Tacrolimus	1	0										
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22						0.4795
	Tofacitinib 30-15-10 mg BID	0	6	0.00	0.00	0.00	23.53						0.4533

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
Subjects who had a history of diabetics at transplant were not included in the Kaplan-Meier analysis.
NODM-1 was defined as an event experienced by subjects who were non-diabetic prior to transplantation and now required treatment with oral hypoglycemic agents, anti-diabetic agents, and/or insulin for ≥30 days.
If event did not occur, it was censored to last visit day or day 2980, whichever was earlier. If event occurred after day 2980, it was censored to day 2980.
Abbreviations: BID = twice daily dosing; CI = confidence interval; Cum.=cumulative; Diff. = difference; N = number of subjects; No. = number; NODM-1=new onset diabetes mellitus-1; SE = standard error.

Table 9. Percent of Subjects with Hypercholesterolemia (>240 mg/dL or 6.2 mmol/L) by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 9	Tacrolimus	18	2 (11.1)	
	Tofacitinib 15-10-5 mg BID	14	5 (35.7)	0.1002
	Tofacitinib 30-15-10 mg BID	13	2 (15.4)	0.7304
Month 12	Tacrolimus	18	1 (5.6)	
	Tofacitinib 15-10-5 mg BID	14	4 (28.6)	0.0800
	Tofacitinib 30-15-10 mg BID	12	1 (8.3)	0.7689
Month 15	Tacrolimus	18	1 (5.6)	
	Tofacitinib 15-10-5 mg BID	14	5 (35.7)	0.0328
	Tofacitinib 30-15-10 mg BID	12	0	0.4142
Month 18	Tacrolimus	18	1 (5.6)	
	Tofacitinib 15-10-5 mg BID	14	1 (7.1)	0.8563
	Tofacitinib 30-15-10 mg BID	12	1 (8.3)	0.7689
Month 24	Tacrolimus	17	2 (11.8)	
	Tofacitinib 15-10-5 mg BID	14	1 (7.1)	0.6700
	Tofacitinib 30-15-10 mg BID	12	2 (16.7)	0.7110
Month 30	Tacrolimus	15	1 (6.7)	
	Tofacitinib 15-10-5 mg BID	14	1 (7.1)	0.9604
	Tofacitinib 30-15-10 mg BID	11	1 (9.1)	0.8222
Month 36	Tacrolimus	15	1 (6.7)	
	Tofacitinib 15-10-5 mg BID	14	0	0.3340
	Tofacitinib 30-15-10 mg BID	11	1 (9.1)	0.8222
Month 42	Tacrolimus	15	1 (6.7)	
	Tofacitinib 15-10-5 mg BID	14	3 (21.4)	0.2577
	Tofacitinib 30-15-10 mg BID	10	0	0.4142
Month 48	Tacrolimus	15	3 (20.0)	
	Tofacitinib 15-10-5 mg BID	14	1 (7.10)	0.3242
	Tofacitinib 30-15-10 mg BID	10	1 (10.0)	0.5127
Month 54	Tacrolimus	14	2 (14.3)	
	Tofacitinib 15-10-5 mg BID	14	3 (21.4)	0.6280
	Tofacitinib 30-15-10 mg BID	10	1 (10.0)	0.7593
Month 60	Tacrolimus	13	1 (7.7)	
	Tofacitinib 15-10-5 mg BID	14	0	0.2994
	Tofacitinib 30-15-10 mg BID	10	2 (20.0)	0.3955
Month 66	Tacrolimus	12	2 (16.7)	
	Tofacitinib 15-10-5 mg BID	14	2 (14.3)	0.8693
	Tofacitinib 30-15-10 mg BID	10	0	0.1859
Month 72	Tacrolimus	9	1 (11.1)	
	Tofacitinib 15-10-5 mg BID	13	2 (15.4)	0.7790
	Tofacitinib 30-15-10 mg BID	8	1 (12.5)	0.9314
Month 78	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	1 (7.7)	
	Tofacitinib 30-15-10 mg BID	8	1 (12.5)	

Table 9. Percent of Subjects with Hypercholesterolemia (>240 mg/dL or 6.2 mmol/L) by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 84	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	1 (7.7)	
	Tofacitinib 30-15-10 mg BID	8	0	
Month 90	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	1 (8.3)	
	Tofacitinib 30-15-10 mg BID	8	0	

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Hypercholesterolemia was defined as a value of total serum cholesterol greater than 240 mg/dL or 6.2 mmol/L.
P-values were obtained using Mantel-Haenszel Chi Square.
Abbreviations: BID = twice daily dosing; N = number of subjects in Safety Analysis Set per visit; n = number of subjects with hypercholesterolemia.

Table 10. Percent of Subjects with Hypertriglyceridemia (>200 mg/dL or 2.3 mmol/L) by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 9	Tacrolimus	18	2 (11.1)	
	Tofacitinib 15-10-5 mg BID	14	7 (50.0)	0.0169
	Tofacitinib 30-15-10 mg BID	13	5 (38.5)	0.0771
Month 12	Tacrolimus	18	1 (5.6)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.0127
	Tofacitinib 30-15-10 mg BID	12	4 (33.3)	0.0493
Month 15	Tacrolimus	18	1 (5.6)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.0127
	Tofacitinib 30-15-10 mg BID	12	5 (41.7)	0.0172
Month 18	Tacrolimus	18	1 (5.6)	
	Tofacitinib 15-10-5 mg BID	14	5 (35.7)	0.0328
	Tofacitinib 30-15-10 mg BID	12	4 (33.3)	0.0493
Month 24	Tacrolimus	17	3 (17.6)	
	Tofacitinib 15-10-5 mg BID	14	3 (21.4)	0.7942
	Tofacitinib 30-15-10 mg BID	12	4 (33.3)	0.3394
Month 30	Tacrolimus	15	2 (13.3)	
	Tofacitinib 15-10-5 mg BID	14	4 (28.6)	0.3199
	Tofacitinib 30-15-10 mg BID	11	4 (36.4)	0.1769
Month 36	Tacrolimus	15	3 (20.0)	
	Tofacitinib 15-10-5 mg BID	14	2 (14.3)	0.6892
	Tofacitinib 30-15-10 mg BID	11	3 (27.3)	0.6698
Month 42	Tacrolimus	15	3 (20.0)	
	Tofacitinib 15-10-5 mg BID	14	5 (35.7)	0.3525
	Tofacitinib 30-15-10 mg BID	10	2 (20.0)	1
Month 48	Tacrolimus	15	3 (20.0)	
	Tofacitinib 15-10-5 mg BID	14	5 (35.7)	0.3525
	Tofacitinib 30-15-10 mg BID	10	3 (30.0)	0.5741
Month 54	Tacrolimus	14	1 (7.1)	
	Tofacitinib 15-10-5 mg BID	14	5 (35.7)	0.0704
	Tofacitinib 30-15-10 mg BID	10	4 (40.0)	0.0558
Month 60	Tacrolimus	13	2 (15.4)	
	Tofacitinib 15-10-5 mg BID	14	0	0.1345
	Tofacitinib 30-15-10 mg BID	10	3 (30.0)	0.4100
Month 66	Tacrolimus	12	2 (16.7)	
	Tofacitinib 15-10-5 mg BID	14	2 (14.3)	
	Tofacitinib 30-15-10 mg BID	10	2 (20.0)	0.8693
				0.8437
Month 72	Tacrolimus	9	1 (11.1)	
	Tofacitinib 15-10-5 mg BID	13	3 (23.1)	0.4846
	Tofacitinib 30-15-10 mg BID	8	4 (50.0)	0.0884
Month 78	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	1 (7.7)	
	Tofacitinib 30-15-10 mg BID	8	2 (25.0)	

Table 10. Percent of Subjects with Hypertriglyceridemia (>200 mg/dL or 2.3 mmol/L) by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 84	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	1 (7.7)	
	Tofacitinib 30-15-10 mg BID	8	3 (37.5)	
Month 90	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	1 (8.3)	
	Tofacitinib 30-15-10 mg BID	8	4 (50.0)	

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Hypertriglyceridemia was defined as a value of triglycerides >200 mg.dL or 2.3 mmol/L.
P-values were obtained using Mantel-Haenszel Chi Square.
Abbreviations: BID = twice daily dosing; N = number of subjects in Safety Analysis Set per visit; n = number of subjects with hypercholesterolemia.

Secondary Endpoints:

GFR calculated by the Nankivell and Cockroft-Gault equations and reciprocal of serum creatinine: Descriptive statistics for GFR (minute/mL) calculated using the Nankivell equation and the Cockroft-Gault equation are summarized by visit for the Safety Analysis Set in Table 11 and Table 12, respectively. Descriptive statistics for the reciprocal of serum creatinine (mg/dL) are summarized by visit for the Safety Analysis Set in Table 13.

From Month 18 through Month 72, mean estimated GFR was highest in the tacrolimus group (ranging from 98.68 to 118.60 min/mL) when calculated by the Cockcroft-Gault equation and also highest (except at Month 48) when calculated by the Nankivell equation (ranging from 82.77 to 98.72 min/mL).

Mean reciprocal values of creatinine were generally similar across the 3 treatment groups.

Table 11. Descriptive Statistics of Glomerular Filtration Rate (min/mL) Calculated by the Nankivell Equation By Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	77.98	11.29	14.48	55.0	71.9	78.7	83.9	98.8
	Tofacitinib 15-10-5 mg BID	14	80.15	9.74	12.15	65.0	74.4	79.9	85.5	104.0
	Tofacitinib 30-15-10 mg BID	12	81.39	9.77	12.01	65.0	74.3	81.8	88.5	99.4
Month 12	Tacrolimus	16	73.64	15.23	20.68	49.6	63.1	71.7	84.2	96.6
	Tofacitinib 15-10-5 mg BID	14	80.02	9.39	11.73	64.0	73.8	80.0	85.2	96.3
	Tofacitinib 30-15-10 mg BID	12	79.31	11.71	14.77	67.5	69.9	76.6	85.1	102.5
Month 15	Tacrolimus	16	80.92	12.79	15.80	50.6	74.3	81.1	87.5	106.0
	Tofacitinib 15-10-5 mg BID	14	83.06	6.99	8.42	74.1	77.5	80.5	91.0	96.6
	Tofacitinib 30-15-10 mg BID	12	81.18	10.61	13.06	64.7	73.8	78.9	88.5	99.3
Month 18	Tacrolimus	18	82.77	14.14	17.08	54.1	74.8	84.0	96.8	100.1
	Tofacitinib 15-10-5 mg BID	14	81.72	10.35	12.66	58.8	78.1	82.2	84.8	104.6
	Tofacitinib 30-15-10 mg BID	12	80.03	10.82	13.51	65.1	71.0	78.8	87.0	98.9
Month 24	Tacrolimus	17	84.93	14.36	16.91	58.4	75.8	87.5	93.4	108.7
	Tofacitinib 15-10-5 mg BID	14	82.62	10.15	12.29	64.0	76.3	82.0	87.2	105.0
	Tofacitinib 30-15-10 mg BID	12	81.66	8.20	10.04	69.8	75.7	82.8	86.6	98.0
Month 30	Tacrolimus	14	88.61	16.59	18.73	60.3	76.6	89.7	99.7	118.1
	Tofacitinib 15-10-5 mg BID	14	86.35	7.12	8.24	73.8	81.7	86.1	89.7	104.6
	Tofacitinib 30-15-10 mg BID	10	79.87	9.74	12.20	66.7	70.5	79.4	86.5	98.9
Month 36	Tacrolimus	15	89.08	24.53	27.54	45.0	72.5	86.9	99.9	155.0
	Tofacitinib 15-10-5 mg BID	14	86.05	12.76	14.83	67.7	77.0	86.0	93.4	115.2
	Tofacitinib 30-15-10 mg BID	9	76.38	15.14	19.82	47.2	68.2	75.6	84.3	97.6
Month 42	Tacrolimus	15	86.95	17.96	20.66	36.5	78.5	90.6	99.0	111.2
	Tofacitinib 15-10-5 mg BID	14	86.07	13.13	15.25	61.5	78.3	84.5	96.3	105.5
	Tofacitinib 30-15-10 mg BID	9	81.89	7.03	8.58	72.1	77.9	81.8	84.4	92.2
Month 48	Tacrolimus	15	85.59	21.32	24.91	24.4	75.9	87.8	99.6	111.8
	Tofacitinib 15-10-5 mg BID	14	86.47	13.32	15.40	55.6	83.0	88.4	93.3	103.9
	Tofacitinib 30-15-10 mg BID	10	82.06	8.68	10.58	65.40	78.0	82.2	85.4	97.9

Table 11. Descriptive Statistics of Glomerular Filtration Rate (min/mL) Calculated by the Nankivell Equation By Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 54	Tacrolimus	14	88.08	27.63	31.37	6.3	74.5	95.2	109.3	111.6
	Tofacitinib 15-10-5 mg BID	14	85.35	12.99	15.22	60.0	79.9	85.1	93.4	105.9
	Tofacitinib 30-15-10 mg BID	10	79.98	10.36	12.96	56.2	78.2	80.3	82.8	98.8
Month 60	Tacrolimus	13	93.01	19.88	21.37	49.5	86.0	97.2	108.8	122.8
	Tofacitinib 15-10-5 mg BID	13	85.75	15.79	18.41	54.7	78.8	87.2	98.7	104.9
	Tofacitinib 30-15-10 mg BID	10	85.36	10.01	11.73	65.5	79.0	84.7	90.7	99.0
Month 66	Tacrolimus	12	98.72	33.70	34.13	34.6	88.7	97.7	105.5	177.0
	Tofacitinib 15-10-5 mg BID	14	84.26	16.14	19.15	57.9	72.6	84.1	99.1	110.6
	Tofacitinib 30-15-10 mg BID	10	82.21	17.48	21.26	44.0	78.3	82.8	86.7	111.1
Month 72	Tacrolimus	9	90.60	17.58	19.41	57.0	83.8	85.6	99.6	114.6
	Tofacitinib 15-10-5 mg BID	13	83.80	10.92	13.04	62.1	77.2	82.0	92.7	104.4
	Tofacitinib 30-15-10 mg BID	8	81.46	7.94	9.75	70.0	75.9	81.3	87.2	93.1
Month 78	Tofacitinib 15-10-5 mg BID	13	83.94	10.95	13.05	66.2	78.2	80.5	90.6	105.2
	Tofacitinib 30-15-10 mg BID	8	87.44	8.72	9.97	76.4	80.3	87.9	91.5	103.8
Month 84	Tofacitinib 15-10-5 mg BID	12	84.21	12.50	14.85	62.3	77.7	82.4	92.4	110.7
	Tofacitinib 30-15-10 mg BID	8	88.53	5.40	6.10	82.5	83.8	87.6	92.9	97.0
Month 90	Tofacitinib 15-10-5 mg BID	12	81.09	12.75	15.72	58.7	74.1	80.2	86.9	110.2
	Tofacitinib 30-15-10 mg BID	7	88.91	6.31	7.10	79.30	82.4	90.3	91.0	98.7
Month 96	Tofacitinib 15-10-5 mg BID	11	79.46	12.35	15.54	54.6	71.4	80.9	90.2	96.8
	Tofacitinib 30-15-10 mg BID	6	88.20	8.93	10.13	79.7	83.1	96.1	89.0	105.1
Follow-up	Tacrolimus	6	52.35	28.37	54.19	1.9	35.7	66.1	67.6	76.7
	Tofacitinib 15-10-5 mg BID	12	81.06	12.76	15.74	54.7	74.4	81.0	89.4	103.2
	Tofacitinib 30-15-10 mg BID	8	76.41	29.81	39.01	18.2	62.6	78.9	102.4	105.5

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; CV = coefficient of variation; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 12. Descriptive Statistics of Glomerular Filtration Rate (min/mL) Calculated by the Cockroft-Gault Equation by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	92.82	19.95	21.49	51.1	79.2	94.6	110.3	117.5
	Tofacitinib 15-10-5 mg BID	14	86.74	15.70	18.10	71.2	75.1	83.2	97.0	129.4
	Tofacitinib 30-15-10 mg BID	12	92.35	10.45	11.31	72.5	85.9	92.0	97.6	115.3
Month 12	Tacrolimus	16	87.05	19.95	22.92	56.0	69.8	85.8	106.3	112.9
	Tofacitinib 15-10-5 mg BID	14	87.29	17.83	20.43	59.7	79.9	85.2	95.2	133.9
	Tofacitinib 30-15-10 mg BID	12	90.36	18.79	20.80	74.3	77.1	88.0	92.6	144.2
Month 15	Tacrolimus	16	98.39	22.67	23.04	47.4	84.8	98.4	115.5	138.0
	Tofacitinib 15-10-5 mg BID	14	92.69	15.97	17.23	67.5	79.3	93.8	101.5	124.4
	Tofacitinib 30-15-10 mg BID	12	92.79	15.98	17.23	73.2	80.7	93.3	96.9	135.6
Month 18	Tacrolimus	18	98.68	24.03	24.35	47.8	80.0	101.3	112.4	138.3
	Tofacitinib 15-10-5 mg BID	14	90.61	16.53	18.25	61.7	83.5	87.5	102.1	123.8
	Tofacitinib 30-15-10 mg BID	12	91.31	18.19	19.92	70.6	81.8	87.4	90.2	137.6
Month 24	Tacrolimus	17	100.46	21.65	21.55	53.1	87.3	96.4	116.0	140.3
	Tofacitinib 15-10-5 mg BID	14	89.62	24.06	26.85	47.1	73.4	93.6	104.0	129.3
	Tofacitinib 30-15-10 mg BID	12	94.67	16.46	17.39	78.3	82.0	93.7	97.6	136.9
Month 30	Tacrolimus	14	102.29	21.29	20.81	69.4	91.5	101.6	115.6	149.7
	Tofacitinib 15-10-5 mg BID	14	95.79	20.38	21.28	66.2	82.2	93.7	110.1	128.9
	Tofacitinib 30-15-10 mg BID	10	88.19	13.32	15.11	60.4	82.3	89.2	94.9	113.1
Month 36	Tacrolimus	15	101.92	33.77	33.13	49.6	76.9	102.5	118.4	183.8
	Tofacitinib 15-10-5 mg BID	14	94.67	23.12	24.42	56.5	77.8	98.6	106.8	134.9
	Tofacitinib 30-15-10 mg BID	9	86.32	22.76	26.36	42.3	76.3	87.1	93.9	126.1
Month 42	Tacrolimus	15	102.79	27.15	26.41	39.4	82.2	99.0	118.2	157.7
	Tofacitinib 15-10-5 mg BID	14	92.13	19.39	21.04	64.8	76.8	91.4	105.9	125.8
	Tofacitinib 30-15-10 mg BID	9	91.96	14.62	15.90	63.3	90.6	91.4	94.5	120.3
Month 48	Tacrolimus	15	100.77	27.37	27.16	29.2	86.5	98.9	119.0	142.0
	Tofacitinib 15-10-5 mg BID	14	92.78	23.60	25.43	57.6	75.8	91.4	107.5	144.6
	Tofacitinib 30-15-10 mg BID	10	93.23	19.62	21.05	54.5	84.7	90.1	103.0	131.3

Table 12. Descriptive Statistics of Glomerular Filtration Rate (min/mL) Calculated by the Cockroft-Gault Equation by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 54	Tacrolimus	14	106.65	33.50	31.41	15.6	96.5	109.6	123.7	155.5
	Tofacitinib 15-10-5 mg BID	14	89.96	19.19	21.34	63.0	74.3	89.9	102.5	134.2
	Tofacitinib 30-15-10 mg BID	10	91.90	21.03	22.88	50.2	81.4	93.0	101.0	134.4
Month 60	Tacrolimus	13	113.73	31.33	27.55	66.4	83.2	106.7	135.8	165.3
	Tofacitinib 15-10-5 mg BID	13	87.89	21.20	24.12	47.3	78.1	89.8	100.7	118.0
	Tofacitinib 30-15-10 mg BID	10	98.94	21.29	21.52	56.8	84.7	105.5	107.6	132.9
Month 66	Tacrolimus	12	118.60	42.38	35.73	44.6	95.4	110.2	149.8	195.0
	Tofacitinib 15-10-5 mg BID	14	86.74	20.14	23.22	53.0	69.7	90.0	105.9	110.3
	Tofacitinib 30-15-10 mg BID	10	94.80	32.99	34.80	37.5	79.7	92.5	100.3	161.2
Month 72	Tacrolimus	9	113.23	30.03	26.52	74.2	88.3	115.8	134.4	154.4
	Tofacitinib 15-10-5 mg BID	13	86.00	17.77	20.66	59.9	71.0	93.9	96.8	112.2
	Tofacitinib 30-15-10 mg BID	8	93.33	18.12	19.41	63.1	84.9	92.4	104.1	120.8
Month 78	Tofacitinib 15-10-5 mg BID	13	85.10	16.99	19.97	51.5	74.4	94.6	98.1	106.4
	Tofacitinib 30-15-10 mg BID	8	100.93	20.40	20.22	78.9	86.4	95.9	111.6	140.9
Month 84	Tofacitinib 15-10-5 mg BID	12	85.54	19.31	22.57	58.1	69.4	85.4	103.6	109.9
	Tofacitinib 30-15-10 mg BID	8	102.36	14.46	14.12	78.8	94.0	101.7	111.9	125.0
Month 90	Tofacitinib 15-10-5 mg BID	12	80.73	19.03	23.57	56.3	64.9	75.9	99.8	107.3
	Tofacitinib 30-15-10 mg BID	7	103.59	16.99	16.41	72.0	99.0	105.7	108.8	129.4
Month 96	Tofacitinib 15-10-5 mg BID	11	79.02	18.97	24.01	52.9	62.5	74.2	98.0	106.4
	Tofacitinib 30-15-10 mg BID	6	100.89	14.55	14.43	89.2	90.9	95.2	107.8	126.9
Follow-up	Tacrolimus	6	63.95	35.17	55.00	10.9	42.5	66.8	83.8	112.9
	Tofacitinib 15-10-5 mg BID	12	82.26	17.32	21.05	61.7	66.5	80.1	99.6	107.6
	Tofacitinib 30-15-10 mg BID	8	89.79	40.28	44.86	20.4	66.5	90.7	121.8	140.1

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; CV = coefficient of variation; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 13. Descriptive Statistics of the Reciprocal of Serum Creatinine (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	0.83	0.17	20.16	0.5	0.7	0.9	0.9	1.1
	Tofacitinib 15-10-5 mg BID	14	0.88	0.22	25.08	0.6	0.7	0.8	1.0	1.4
	Tofacitinib 30-15-10 mg BID	12	0.83	0.20	24.38	0.5	0.7	0.8	0.9	1.3
Month 12	Tacrolimus	16	0.78	0.17	21.25	0.5	0.7	0.8	0.9	1.1
	Tofacitinib 15-10-5 mg BID	14	0.88	0.22	24.95	0.6	0.7	0.9	1.0	1.3
	Tofacitinib 30-15-10 mg BID	12	0.80	0.21	26.66	0.5	0.6	0.7	0.9	1.3
Month 15	Tacrolimus	16	0.85	0.19	22.73	0.5	0.7	0.8	1.0	1.3
	Tofacitinib 15-10-5 mg BID	14	0.91	0.17	19.09	0.7	0.8	0.9	1.0	1.3
	Tofacitinib 30-15-10 mg BID	12	0.82	0.20	23.75	0.6	0.7	0.8	1.0	1.3
Month 18	Tacrolimus	18	0.89	0.20	22.92	0.5	0.8	0.9	1.1	1.3
	Tofacitinib 15-10-5 mg BID	14	0.90	0.18	19.89	0.7	0.7	0.9	1.0.	1.3
	Tofacitinib 30-15-10 mg BID	12	0.81	0.18	22.44	0.5	0.7	0.8	0.9	1.3
Month 24	Tacrolimus	17	0.92	0.22	24.34	0.5	0.8	0.8	1.0	1.4
	Tofacitinib 15-10-5 mg BID	14	0.93	0.16	17.25	0.8	0.8	0.9	1.1	1.3
	Tofacitinib 30-15-10 mg BID	12	0.83	0.15	17.42	0.6	0.7	0.8	0.9	1.1
Month 30	Tacrolimus	14	0.95	0.29	30.32	0.5	0.8	0.9	1.1	1.7
	Tofacitinib 15-10-5 mg BID	14	0.96	0.14	14.15	0.8	0.8	1.0	1.1	1.1
	Tofacitinib 30-15-10 mg BID	10	0.83	0.18	21.10	0.7	0.7	0.8	0.9	1.3
Month 36	Tacrolimus	15	0.96	0.38	39.11	0.5	0.7	0.9	1.1	2.0
	Tofacitinib 15-10-5 mg BID	14	0.96	0.20	20.26	0.7	0.8	1.0	1.1	1.3
	Tofacitinib 30-15-10 mg BID	9	0.78	0.14	18.55	0.5	0.7	0.8	0.9	0.9
Month 42	Tacrolimus	15	0.92	0.25	27.01	0.5	0.7	0.9	1.1	1.3
	Tofacitinib 15-10-5 mg BID	14	0.97	0.24	25.07	0.7	0.8	0.9	1.1	1.4
	Tofacitinib 30-15-10 mg BID	9	0.87	0.09	10.00	0.7	0.8	0.9	0.9	1.0
Month 48	Tacrolimus	15	0.91	0.27	29.83	0.4	0.7	0.9	1.1	1.3
	Tofacitinib 15-10-5 mg BID	14	0.98	0.23	23.48	0.6	0.8	1.0	1.1	1.4
	Tofacitinib 30-15-10 mg BID	10	0.84	0.08	9.01	0.7	0.8	0.8	0.8	1.0
Month 54	Tacrolimus	14	0.91	0.33	36.07	0.2	0.7	0.9	1.3	1.4
	Tofacitinib 15-10-5 mg BID	14	0.96	0.24	24.71	0.7	0.8	0.9	1.1	1.4
	Tofacitinib 30-15-10 mg BID	10	0.81	0.09	11.53	0.7	0.7	0.8	0.8	1.0

Table 13. Descriptive Statistics of the Reciprocal of Serum Creatinine (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 60	Tacrolimus	13	0.94	0.29	30.69	0.5	0.8	0.9	1.3	1.4
	Tofacitinib 15-10-5 mg BID	13	0.97	0.26	26.95	0.5	0.8	1.0	1.1	1.4
	Tofacitinib 30-15-10 mg BID	10	0.87	0.10	11.58	0.7	0.8	0.8	1.0	1.0
Month 66	Tacrolimus	12	1.05	0.42	39.80	0.4	0.8	1.0	1.3	2.0
	Tofacitinib 15-10-5 mg BID	14	0.95	0.26	27.37	0.5	0.8	0.9	1.1	1.4
	Tofacitinib 30-15-10 mg BID	10	0.84	0.17	20.10	0.6	0.8	0.8	1.0	1.1
Month 72	Tacrolimus	9	0.94	0.24	25.57	0.7	0.8	0.8	1.3	1.3
	Tofacitinib 15-10-5 mg BID	13	0.95	0.20	20.63	0.7	0.8	0.9	1.0	1.4
	Tofacitinib 30-15-10 mg BID	8	0.79	0.12	15.63	0.6	0.7	0.8	0.9	1.0
Month 78	Tofacitinib 15-10-5 mg BID	13	0.95	0.21	21.79	0.7	0.8	0.9	1.0	1.4
	Tofacitinib 30-15-10 mg BID	8	0.87	0.10	11.80	0.7	0.8	0.9	1.0	1.0
Month 84	Tofacitinib 15-10-5 mg BID	12	0.94	0.20	21.58	0.7	0.8	0.9	1.1	1.4
	Tofacitinib 30-15-10 mg BID	8	0.88	0.12	13.85	0.7	0.8	0.8	1.0	1.1
Month 90	Tofacitinib 15-10-5 mg BID	12	0.91	0.23	24.87	0.7	0.7	0.9	1.1	1.4
	Tofacitinib 30-15-10 mg BID	7	0.88	0.14	16.04	0.7	0.8	0.8	1.0	1.1
Month 96	Tofacitinib 15-10-5 mg BID	11	0.90	0.20	21.78	0.6	0.7	0.9	1.1	1.3
	Tofacitinib 30-15-10 mg BID	6	0.92	0.12	13.14	0.8	0.8	0.9	1.0	1.1
Follow-up	Tacrolimus	6	0.61	0.27	43.80	0.2	0.5	0.7	0.8	0.9
	Tofacitinib 15-10-5 mg BID	12	0.91	0.23	24.89	0.6	0.8	0.8	1.1	1.4
	Tofacitinib 30-15-10 mg BID	8	0.80	0.28	35.02	0.3	0.6	0.9	1.0	1.1

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

Abbreviations: BID = twice daily; CV = coefficient of variation; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Serious infections: Percentages of subjects with clinically significant infections (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Safety Analysis Set in Table 14.

The overall comparison of the Kaplan-Meier curve of tofacitinib 15-10-5 mg BID or tofacitinib 30-15-10 mg BID with tacrolimus showed no statistically significant differences (p=0.2579 or p=0.3531, respectively). However, the proportion of subjects in the tofacitinib groups with serious infections was numerically higher compared with the tacrolimus group at each time point. At Month 6, compared with the tacrolimus group, the rate of serious infection was higher in the tofacitinib 15-10-5 mg BID group by 1.6%, and in the tofacitinib 30-15-10 mg BID group by 17.5%. At Month 60, the cumulative serious infection rate was 11.5% for tacrolimus, 42.9% for tofacitinib 15-10-5 mg BID (rate difference 31.4%), and 30.8% for tofacitinib 30-15-10 mg BID (rate difference 19.3%).

Table 14. Summary of Percent of Subjects with Serious Infections Estimated Using Kaplan-Meier Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Cumulative Number of Events	Number of Subjects Remaining at Risk	Estimated Rate (%)				Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
Month				Rate	SE	Lower	Upper	Rate difference	SE	Lower	Upper	P value[a]	P value[b]
1	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	-5.56	5.40	-12.47	1.36	0.3035	
6	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	3	10	23.08	11.69	8.10	38.05	17.52	12.87	1.02	34.02	0.1735	
12	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	2	12	14.29	9.35	2.30	26.27	8.73	10.80	-5.11	22.57	0.4188	
	Tofacitinib 30-15-10-mg BID	3	10	23.08	11.69	8.10	38.05	17.52	12.87	1.02	34.02	0.1735	
24	Tacrolimus	2	15	11.46	7.63	1.67	21.24						
	Tofacitinib 15-10-5 mg BID	4	10	28.57	12.07	13.10	44.04	17.11	14.28	-1.19	35.42	0.2309	
	Tofacitinib 30-15-10 mg BID	3	10	23.08	11.69	8.10	38.05	11.62	13.96	-6.27	29.51	0.4052	
48	Tacrolimus	2	13	11.46	7.63	1.67	21.24						
	Tofacitinib 15-10-5 mg BID	5	9	35.71	12.81	19.30	52.13	24.26	14.91	5.15	43.36	0.1038	
	Tofacitinib 30-15-10 mg BID	4	8	30.77	12.80	14.36	47.17	19.31	14.90	0.21	38.41	0.1951	
60	Tacrolimus	2	12	11.46	7.63	1.67	21.24						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	31.40	15.27	11.83	50.97	0.0398	
	Tofacitinib 30-15-10 mg BID	4	8	30.77	12.80	14.36	47.17	19.31	14.90	0.21	38.41	0.1951	

Table 14. Summary of Percent of Subjects with Serious Infections Estimated Using Kaplan-Meier Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Cumulative Number of Events	Number of Subjects Remaining at Risk	Estimated Rate (%)				Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
Month				Rate	SE	Lower	Upper	Rate difference	SE	Lower	Upper	P value[a]	P value[b]
66	Tacrolimus	3	11	18.84	9.94	6.09	31.58						
	Tofacitinib 15-10-5 mg BID	6	8	42.86	13.23	25.91	59.81	24.02	16.55	2.81	45.23	0.1466	
	Tofacitinib 30-15-10 mg BID	5	6	39.42	13.82	21.71	57.13	20.59	17.03	-1.23	42.41	0.2266	
96	Tacrolimus	4	0										
	Tofacitinib 15-10-5 mg BID	7	6	51.02	13.62	33.56	68.48						0.2579
	Tofacitinib 30-15-10 mg BID	5	6	39.42	13.82	21.71	57.13						0.3531

Per site-specific Protocol Amendment 1, the data collected for Subject 10191006 was excluded from this analysis. Included data from both Study A3921009 and Study A3921021, and only from subjects enrolled in Study A3921021; serious infection was a serious adverse event associated with the infections and infestations system organ class or from significant infections page. If event did not occur, it was censored to last visit day or day 2980, whichever came earlier. If the event occurred after day 2980, it was censored to day 2980.

Abbreviations: BID = twice daily; CI = confidence interval; SE = standard error

a. P-value for comparing rate difference between Tofacitinib and Tacrolimus using Wald test.

b. P-value for comparing survival curves between Tofacitinib and Tacrolimus based on Log-Rank test.

CNI-related toxicities, including but not limited to NODM-2, fasting serum glucose levels, total serum, cholesterol, LDL and HDL levels, levels of serum triglycerides, usage of lipid-lowering agents, usage of antihypertensive agents, and usage of oral hypoglycemics:

Percentages of subjects with NODM-2 events (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Safety Analysis Set in Table 15.

The number of subjects with NODM-2 events was low in each of the 3 treatment groups and precluded comparisons between the groups.

Descriptive statistics for fasting serum glucose, total serum cholesterol, LDL cholesterol and HDL cholesterol levels (mg/dL) are summarized by visit for the Safety Analysis Set in Table 16, Table 17, Table 18 and Table 19, respectively.

Mean fasting serum glucose values were generally similar across the 3 treatment groups. Overall, total serum cholesterol, LDL cholesterol and HDL cholesterol levels, were similar across the 3 treatment groups at various time points.

Descriptive statistics for the ratio of total serum cholesterol to serum HDL cholesterol, and for the ratio of serum LDL cholesterol to serum HDL cholesterol, are summarized by visit for the Safety Analysis Set in Table 20 and Table 22, respectively. Comparisons of percentages of subjects with a ratio of total serum cholesterol to serum HDL cholesterol <5, and of percentage of subjects with a ratio of serum LDL cholesterol to serum HDL cholesterol, are summarized by visit for the Safety Analysis Set in Table 21 and Table 23, respectively.

Overall, the ratio of total serum cholesterol to serum HDL cholesterol was similar across the 3 treatment groups at various time points; comparisons in proportions of subjects with a ratio of total serum cholesterol to serum HDL cholesterol <5 showed no differences between each of the tofacitinib treatments and tacrolimus.

Overall, the ratio of serum LDL cholesterol to serum HDL cholesterol was similar across the 3 treatment groups at various time points; comparisons in proportions of subjects with a ratio of serum LDL cholesterol to serum HDL cholesterol <3.5 showed no differences between each of the tofacitinib treatments and tacrolimus.

Descriptive statistics for levels of serum triglycerides are summarized by visit for the Safety Analysis Set in Table 24.

The mean serum triglycerides levels were higher in the tofacitinib groups compared with the tacrolimus group at the Month 9, 12, 15, and 18 visits.

Percentages of subjects requiring lipid-lowering agents, antihypertensive medication, and diabetes agents are summarized by visit for the Safety Analysis Set in Table 25, Table 26 and Table 27, respectively.

The use of lipid-lowering medications was common. From Month 9 through Month 66, no fewer than 38% of subjects in each of the treatment groups received lipid-lowering

medications. There was a trend towards more frequent use of lipid-lowering medications among the tofacitinib treatment groups than tacrolimus, with the difference being statistically significant ($p<0.05$) between the tofacitinib 30-15-10 mg BID group and tacrolimus group at Months 42 and 48. At Month 66, the percentages of subjects receiving lipid-lowering medications were 46.2% in the tacrolimus group, 64.3% in the tofacitinib 15-10-5 mg BID group, and 80.0% in the tofacitinib 30-15-10 mg BID group.

The use of antihypertensive medications was common. From Month 9 through Month 66, no fewer than 69% of subjects in each of the treatment groups received antihypertensive medications. From the Month 9 visit through the Month 72 visit and the follow-up visit, no significant difference in antihypertensive drug usage was observed in the tofacitinib 15-10-5 mg BID group or the tofacitinib 30-15-10 mg BID group, when compared with tacrolimus.

Although the number of subjects was limited, a numerically higher percentage of subjects in both tofacitinib groups were using concomitant anti-diabetic medications when compared with tacrolimus from Month 9 through Month 66, and was highest in the tofacitinib 15-10-5 mg BID group. At Month 66, the percentages of subject receiving anti-diabetic medications were 15.4% in the tacrolimus group, 42.9% in the tofacitinib 15-10-5 mg BID group, and 30.0% in the tofacitinib 30-15-10 mg BID group.

Table 15. Percent of Subjects with NODM-2 estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 6	Tacrolimus	0	17	0.00	0.00	0.00	9.03						
	Tofacitinib 15-10-5 mg BID	0	8	0.00	0.00	0.00	18.22	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	9	0.00	0.00	0.00	16.37	0.00	0.00	0.00	0.00		
Month 9	Tacrolimus	1	16	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	0	9	0.00	0.00	0.00	16.37	-5.88	5.71	-13.20	1.43	0.3026	
Month 12	Tacrolimus	1	16	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	0	9	0.00	0.00	0.00	16.37	-5.88	5.71	-13.20	1.43	0.3026	
Month 15	Tacrolimus	1	16	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	0	9	0.00	0.00	0.00	16.37	-5.88	5.71	-13.20	1.43	0.3026	
Month 18	Tacrolimus	1	15	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	0	9	0.00	0.00	0.00	16.37	-5.88	5.71	-13.20	1.43	0.3026	
Month 24	Tacrolimus	1	15	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	0	9	0.00	0.00	0.00	16.37	-5.88	5.71	-13.20	1.43	0.3026	
Month 30	Tacrolimus	1	13	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
Month 36	Tacrolimus	1	13	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	

Table 15. Percent of Subjects with NODM-2 estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 42	Tacrolimus	1	13	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
Month 48	Tacrolimus	1	12	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
Month 54	Tacrolimus	1	12	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
Month 60	Tacrolimus	1	11	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
Month 66	Tacrolimus	1	11	5.88	5.71	0.00	13.20						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
	Tofacitinib 30-15-10 mg BID	1	6	12.50	11.69	0.00	27.48	6.62	13.01	-10.06	23.29	0.6110	
Month 72	Tacrolimus	2	6	14.44	9.67	2.05	26.83						
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48	-1.94	15.17	-21.38	17.51	0.8983	
	Tofacitinib 30-15-10 mg BID	1	6	12.50	11.69	0.00	27.48	-1.94	15.17	-21.38	17.51	0.8983	
Month 78	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48						
	Tofacitinib 30-15-10 mg BID	1	5	12.50	11.69	0.00	27.48						
Month 84	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48						
	Tofacitinib 30-15-10 mg BID	1	5	12.50	11.69	0.00	27.48						

Table 15. Percent of Subjects with NODM-2 estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 90	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48						
	Tofacitinib 30-15-10 mg BID	1	5	12.50	11.69	0.00	27.48						
Month 96	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	7	12.50	11.69	0.00	27.48						0.9591
	Tofacitinib 30-15-10 mg BID	1	5	12.50	11.69	0.00	27.48						0.9233

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis.
*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
Subjects who had a history of diabetics at transplant were not included in the Kaplan-Meier analysis.
NODM-2 was defined as an event experienced by a transplanted subject who met any of the following criteria: (a) NODM-1; or (b) Symptoms of diabetes plus 2 casual serum glucose levels ≥200 mg/dL separated by at least approximately 24 hours (casual was defined as any time of day without regard to time since last meal); or (c) Fasting serum glucose ≥126 mg/dL on 2 different occasions separated by at least approximately 24 hours (fasting was defined as no caloric intake for at least 8 hours); or (d) 2-hour serum glucose ≥200 mg/dL during an Oral Glucose Tolerance Test.
If event did not occur, it was censored to last visit day or day 2980, whichever was earlier. If event occurred after day 2980, it was censored to day 2980.
Abbreviations: BID = twice daily dosing; CI = confidence interval; Cum.=cumulative; Diff. = difference; N = number of subjects; No. = number; NODM-2=new onset diabetes mellitus-2; SE = standard error.

Table 16. Descriptive Statistics of Fasting Serum Glucose Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	96.89	18.78	19.39	72.0	86.0	93.0	101.0	155.0
	Tofacitinib 15-10-5 mg BID	14	115.14	42.16	36.62	71.0	84.0	99.0	139.0	200.0
	Tofacitinib 30-15-10 mg BID	10	97.90	19.44	19.86	76.0	83.0	91.5	113.0	138.0
Month 12	Tacrolimus	17	103.00	26.25	25.49	47.0	96.0	99.0	108.0	173.0
	Tofacitinib 15-10-5 mg BID	14	133.79	51.07	38.17	76.0	101.0	115.5	179.0	233.0
	Tofacitinib 30-15-10 mg BID	12	102.75	35.70	34.74	43.0	75.0	105.5	134.0	150.0
Month 15	Tacrolimus	17	95.41	20.99	22.00	68.0	85	910	102.0	166.0
	Tofacitinib 15-10-5 mg BID	13	128.08	85.36	66.65	62.0	84	920	127.0	377.0
	Tofacitinib 30-15-10 mg BID	11	99.18	33.34	33.62	71.0	79	90.0	96.0	183.0
Month 18	Tacrolimus	18	94.72	21.38	22.57	63.0	88	95.0	102.0	165.0
	Tofacitinib 15-10-5 mg BID	14	117.93	51.81	43.94	72.0	88	95.0	138.0	267.0
	Tofacitinib 30-15-10 mg BID	12	112.50	48.45	43.06	43.0	89	94.5	124.5	210.0
Month 24	Tacrolimus	17	113.71	32.54	28.62	66.0	90.0	106.0	131.0	184.0
	Tofacitinib 15-10-5 mg BID	14	115.64	45.68	39.50	58.0	81.0	101.5	148.0	225.0
	Tofacitinib 30-15-10 mg BID	12	122.25	33.94	27.77	88.0	91.5	115.0	142.5	195.0
Month 30	Tacrolimus	14	102.50	29.02	28.31	81.0	87.0	91.5	103.0	188.0
	Tofacitinib 15-10-5 mg BID	14	137.86	77.07	55.91	73.0	92.0	99.0	158.0	325.0
	Tofacitinib 30-15-10 mg BID	10	140.00	79.88	57.06	78.0	93.0	120.0	150.0	353.0
Month 36	Tacrolimus	15	108.20	39.01	36.05	79.0	86.0	97.0	103.0	228.0
	Tofacitinib 15-10-5 mg BID	14	128.00	54.34	42.45	80.0	89.0	102.5	143.0	248.0
	Tofacitinib 30-15-10 mg BID	9	143.33	76.69	53.51	85.0	93.0	113.0	159.0	325.0
Month 42	Tacrolimus	15	104.47	30.92	29.60	77.0	86.0	96.0	113.0	197.0
	Tofacitinib 15-10-5 mg BID	14	113.71	47.34	41.63	52.0	84.0	91.5	136.0	208.0
	Tofacitinib 30-15-10 mg BID	9	109.56	34.93	31.89	78.0	85.0	103.0	118.0	192.0
Month 48	Tacrolimus	15	112.93	49.35	43.70	73.0	94.0	95.0	113.0	247.0
	Tofacitinib 15-10-5 mg BID	14	123.29	77.74	63.06	61.0	88.0	97.0	126.0	369.0
	Tofacitinib 30-15-10 mg BID	10	98.00	13.80	14.08	740	89.0	99.5	104.0	124.0
Month 54	Tacrolimus	12	126.58	81.04	64.02	78.0	88.5	403.5	115.0	373.0
	Tofacitinib 15-10-5 mg BID	14	119.21	50.15	42.06	52.0	89.0	94.5	138.0	229.0
	Tofacitinib 30-15-10 mg BID	10	116.30	69.12	59.44	54.0	80.0	93.0	115.0	290.0

Table 16. Descriptive Statistics of Fasting Serum Glucose Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 60	Tacrolimus	12	107.08	22.95	21.43	74.0	96.0	104.5	116.0	155.0
	Tofacitinib 15-10-5 mg BID	12	136.17	68.68	50.44	81.0	89.5	108.5	151.0	303.0
	Tofacitinib 30-15-10 mg BID	10	111.70	34.86	31.21	75.0	90.0	100.0	134.0	190.0
Month 66	Tacrolimus	10	111.90	36.39	32.52	79.0	94.0	102.5	114.0	205.0
	Tofacitinib 15-10-5 mg BID	13	143.77	103.15	71.75	79.0	92.0	105.0	146.0	466.0
	Tofacitinib 30-15-10 mg BID	10	112.90	48.43	42.90	55.0	88.0	92.0	171.0	198.0
Month 72	Tacrolimus	9	100.44	39.41	39.23	68.0	78.0	100.0	102.0	198.0
	Tofacitinib 15-10-5 mg BID	13	117.69	61.22	52.01	81.0	85.0	103.0	117.0	314.0
	Tofacitinib 30-15-10 mg BID	7	127.43	74.82	58.71	88.0	89.0	92.0	148.0	290.0
Month 78	Tofacitinib 15-10-5 mg BID	12	131.67	66.25	50.31	79.0	91.0	102.5	147.5	307.0
	Tofacitinib 30-15-10 mg BID	8	98.50	30.07	30.52	72.0	84.0	92.5	96.5	170.0
Month 84	Tofacitinib 15-10-5 mg BID	12	139.50	86.88	62.28	76.0	88.5	103.0	162.5	388.0
	Tofacitinib 30-15-10 mg BID	6	112.50	50.12	44.55	79.0	84.0	93.5	113.0	212.0
Month 90	Tofacitinib 15-10-5 mg BID	11	114.55	33.39	29.15	85.0	88.0	96.0	149.0	170.0
	Tofacitinib 30-15-10 mg BID	7	96.43	16.83	17.45	80.0	88.0	89.0	109.0	129.0
Month 96	Tofacitinib 15-10-5 mg BID	11	154.64	115.73	74.84	79.0	89.0	98.0	150.0	411.0
	Tofacitinib 30-15-10 mg BID	6	100.33	15.65	15.60	87.0	87.0	97.0	106.0	128.0
Follow-up	Tacrolimus	6	112.17	42.96	38.30	69.0	82.0	95.0	161.0	171.0
	Tofacitinib 15-10-5 mg BID	10	126.30	75.84	60.04	82.0	90.0	105.5	121.0	336.0
	Tofacitinib 30-15-10 mg BID	7	98.86	31.73	32.09	56.0	88.0	88.0	108.0	160.0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

Abbreviations: BID = twice daily; CV = coefficient of variation; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 17. Descriptive Statistics of Total Serum Cholesterol Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	187.94	44.81	23.84	119.0	167.0	176.5	200.0	331.0
	Tofacitinib 15-10-5 mg BID	14	233.71	71.97	30.79	135.0	191.0	216.0	285.0	424.0
	Tofacitinib 30-15-10 mg BID	12	198.58	40.95	20.62	130.0	181.0	193.5	214.0	281.0
Month 12	Tacrolimus	16	180.31	46.99	26.06	88.0	155.5	178.0	203.0	298.0
	Tofacitinib 15-10-5 mg BID	14	228.57	64.34	28.15	122.0	179.0	223.0	260.0	382.0
	Tofacitinib 30-15-10 mg BID	12	210.08	44.32	21.10	140.0	187.5	205.5	225.5	320.0
Month 15	Tacrolimus	16	171.06	40.13	23.46	110.0	150.5	161.0	193.0	264.0
	Tofacitinib 15-10-5 mg BID	14	208.79	50.90	24.38	121.0	174.0	214.0	246.0	279.0
	Tofacitinib 30-15-10 mg BID	12	198.58	30.80	15.51	145.0	172.5	200.0	228.5	237.0
Month 18	Tacrolimus	18	173.28	41.76	24.10	106.0	145.0	170.5	201.0	275.0
	Tofacitinib 15-10-5 mg BID	14	185.21	45.99	24.83	110.0	157.0	182.5	202.0	305.0
	Tofacitinib 30-15-10 mg BID	12	192.00	42.14	21.95	107.0	159.5	198.0	221.0	256.0
Month 24	Tacrolimus	17	185.53	62.85	33.88	89.0	160.0	172.0	197.0	381.0
	Tofacitinib 15-10-5 mg BID	14	188.64	40.29	21.36	109.0	166.0	195.0	207.0	266.0
	Tofacitinib 30-15-10 mg BID	12	201.58	47.21	23.42	140.0	184.5	192.5	208.0	305.0
Month 30	Tacrolimus	14	175.43	44.91	25.60	102.0	149.0	164.5	210.0	276.0
	Tofacitinib 15-10-5 mg BID	14	185.71	37.82	20.36	101.0	162.0	184.0	212.0	250.0
	Tofacitinib 30-15-10 mg BID	10	198.30	36.42	18.37	145.0	173.0	194.0	224.0	268.0
Month 36	Tacrolimus	15	175.80	42.49	24.17	91.0	151.0	166.0	217.0	253.0
	Tofacitinib 15-10-5 mg BID	14	174.86	34.82	19.92	109.0	151.0	180.0	194.0	237.0
	Tofacitinib 30-15-10 mg BID	9	202.22	31.25	15.45	154.0	179.0	204.0	224.0	253.0
Month 42	Tacrolimus	15	179.87	40.82	22.70	127.0	147.0	166.0	206.0	267.0
	Tofacitinib 15-10-5 mg BID	14	206.29	78.76	38.18	116.0	162.0	188.5	220.0	424.0
	Tofacitinib 30-15-10 mg BID	9	187.67	22.57	12.03	150.0	167.0	194.0	202.0	217.0
Month 48	Tacrolimus	15	188.87	64.11	33.95	130.0	142.0	165.0	205.0	377.0
	Tofacitinib 15-10-5 mg BID	14	195.79	45.97	23.48	103.0	170.0	201.5	227.0	275.0
	Tofacitinib 30-15-10 mg BID	10	180.10	38.08	21.14	127.0	151.0	170.5	203.0	252.0
Month 54	Tacrolimus	14	184.86	43.06	23.30	113.0	160.0	169.0	214.0	267.0
	Tofacitinib 15-10-5 mg BID	14	201.79	51.39	24.47	90.0	176.0	197.5	237.0	283.0
	Tofacitinib 30-15-10 mg BID	10	183.7	42.500	23.14	132.0	149.0	170.5	207.0	263.0

Table 17. Descriptive Statistics of Total Serum Cholesterol Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 60	Tacrolimus	13	178.77	50.2	28.08	116.0	149.0	171.0	185.0	309.0
	Tofacitinib 15-10-5 mg BID	13	184.23	34.67	18.82	97.0	174.0	193.0	202.0	228.0
	Tofacitinib 30-15-10 mg BID	10	189.10	56.48	29.87	122.0	148.0	186.5	236.0	296.0
Month 66	Tacrolimus	12	188.25	46.65	24.78	114.0	166.0	171.0	212.5	287.0
	Tofacitinib 15-10-5 mg BID	14	185.64	46.49	25.04	90.0	168.0	180.5	203.0	261.0
	Tofacitinib 30-15-10 mg BID	10	172.20	36.33	21.10	109.0	156.0	166.5	193.0	234.0
Month 72	Tacrolimus	9	177.22	43.21	24.38	135.0	146.0	165.0	196.0	263.0
	Tofacitinib 15-10-5 mg BID	12	186.42	44.88	24.07	103.0	165.0	180.0	214.0	269.0
	Tofacitinib 30-15-10 mg BID	8	200.25	57.28	28.60	121.0	162.5	200.0	216.5	282.0
Month 78	Tofacitinib 15-10-5 mg BID	13	191.85	41.96	21.87	97.0	174.0	191.0	217.0	275.0
	Tofacitinib 30-15-10 mg BID	8	195.00	48.57	24.91	120.0	162.5	200.0	216.5	282.0
Month 84	Tofacitinib 15-10-5 mg BID	12	192.42	42.02	21.84	96.0	175.0	194.5	218.5	258.0
	Tofacitinib 30-15-10 mg BID	8	204.00	36.43	17.86	136.0	183.5	210.5	235.0	238.0
Month 90	Tofacitinib 15-10-5 mg BID	12	185.92	51.46	27.68	98.0	145.5	189.5	213.5	291.0
	Tofacitinib 30-15-10 mg BID	7	189.86	30.62	16.13	153.0	162.0	185.0	220.0	239.0
Month 96	Tofacitinib 15-10-5 mg BID	11	183.27	38.74	21.14	96.0	172.0	186.0	205.0	248.0
	Tofacitinib 30-15-10 mg BID	6	188.00	18.89	10.05	165.0	181.0	184.0	192.0	222.0
Follow-up	Tacrolimus	6	191.83	41.84	21.81	158.0	165.0	175.0	209.0	269.0
	Tofacitinib 15-10-5 mg BID	12	185.58	56.08	30.22	95.0	154.5	177.0	213.5	323.0
	Tofacitinib 30-15-10 mg BID	8	213.13	40.70	19.10	170.0	179.5	215.0	224.5	297.0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

Abbreviations: BID = twice daily; CV = coefficient of variation; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 18. Descriptive Statistics of Serum LDL Cholesterol Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	107.11	37.14	34.67	56.0	80.0	109.0	120.0	202.0
	Tofacitinib 15-10-5 mg BID	12	138.83	65.33	47.06	84.0	93.5	122.0	156.5	314.0
	Tofacitinib 30-15-10 mg BID	11	109.82	32.60	29.69	64.0	89.0	107.0	128.0	164.0
Month 12	Tacrolimus	16	102.75	32.98	32.10	44.0	85.0	92.5	123.0	173.0
	Tofacitinib 15-10-5 mg BID	14	130.21	50.51	38.79	75.0	95.0	119.0	158.0	259.0
	Tofacitinib 30-15-10 mg BID	12	119.42	39.38	32.98	64.0	83.5	127.5	139.0	202.0
Month 15	Tacrolimus	16	95.13	28.34	29.79	57.0	71.5	98.5	105.5	159.0
	Tofacitinib 15-10-5 mg BID	14	117.29	39.80	33.94	41.0	84.0	121.5	157.0	167.0
	Tofacitinib 30-15-10 mg BID	11	106.64	26.98	25.30	72.0	81.0	99.0	137.0	146.0
Month 18	Tacrolimus	18	95.94	34.55	36.01	50.0	64.0	74.0	118.0	158.0
	Tofacitinib 15-10-5 mg BID	14	95.14	37.28	39.19	39.0	79.0	88.0	99.0	198.0
	Tofacitinib 30-15-10 mg BID	12	104.42	39.30	37.64	45.0	72.5	96.5	137.5	170.0
Month 24	Tacrolimus	17	101.82	48.27	47.41	44.0	78.0	91.0	110.0	237.0
	Tofacitinib 15-10-5 mg BID	14	99.29	26.75	26.94	43.0	87.0	105.0	120.0	136.0
	Tofacitinib 30-15-10 mg BID	12	114.00	38.82	34.05	61.0	86.5	108.0	132.0	188.0
Month 30	Tacrolimus	14	97.93	37.96	38.76	58.0	72.0	81.5	121.0	194.0
	Tofacitinib 15-10-5 mg BID	14	96.86	26.09	26.94	54.0	81.0	98.0	119.0	136.0
	Tofacitinib 30-15-10 mg BID	10	115.50	33.45	28.96	67.0	93.0	116.0	140.0	173.0
Month 36	Tacrolimus	15	94.20	34.49	36.62	40.0	75.0	90.0	105.0	165.0
	Tofacitinib 15-10-5 mg BID	14	90.29	26.07	28.87	50.0	72.0	84.0	105.0	137.0
	Tofacitinib 30-15-10 mg BID	9	112.00	27.83	24.85	75.0	96.0	103.0	119.0	167.0
Month 42	Tacrolimus	15	100.27	34.56	34.47	56.0	75.0	92.0	129.0	184.0
	Tofacitinib 15-10-5 mg BID	13	99.69	36.08	36.19	63.0	74.0	85.0	122.0	187.0
	Tofacitinib 30-15-10 mg BID	9	102.11	24.94	24.43	66.0	80.0	100.0	124.0	138.0
Month 48	Tacrolimus	15	110.13	55.46	50.36	54.0	70.0	90.0	143.0	269.0
	Tofacitinib 15-10-5 mg BID	14	107.07	29.03	27.11	63.0	89.0	104.5	126.0	156.0
	Tofacitinib 30-15-10 mg BID	10	99.70	34.56	34.66	64.0	75.0	92.0	102.0	182.0
Month 54	Tacrolimus	14	108.36	40.27	37.17	59.0	83.0	95.0	131.0	184.0
	Tofacitinib 15-10-5 mg BID	13	109.08	32.78	30.06	52.0	87.0	109.0	127.0	173.0
	Tofacitinib 30-15-10 mg BID	10	96.50	41.04	42.53	40.0	70.0	86.0	136.0	171.0

Table 18. Descriptive Statistics of Serum LDL Cholesterol Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 60	Tacrolimus	13	105.62	42.86	40.58	50.0	81.0	106.0	113.0	215.0
	Tofacitinib 15-10-5 mg BID	13	101.00	24.15	23.91	58.0	81.0	101.0	111.0	144.0
	Tofacitinib 30-15-10 mg BID	10	98.60	44.67	45.30	53.0	69.0	85.5	126.0	179.0
Month 66	Tacrolimus	12	109.83	44.59	40.59	54.0	81.0	104.0	132.0	213.0
	Tofacitinib 15-10-5 mg BID	13	100.92	33.67	33.37	52.0	81.0	94.0	115.0	170.0
	Tofacitinib 30-15-10 mg BID	10	91.90	33.14	36.06	47.0	74.0	86.0	107.0	158.0
Month 72	Tacrolimus	9	102.89	43.96	42.72	56.0	74.0	85.0	128.0	186.0
	Tofacitinib 15-10-5 mg BID	12	100.00	28.63	28.63	60.0	85.5	87.5	114.0	165.0
	Tofacitinib 30-15-10 mg BID	8	114.25	46.57	40.76	57.0	83.5	103.5	140.5	202.0
Month 78	Tofacitinib 15-10-5 mg BID	12	103.25	31.13	30.15	58.0	90.0	94.0	115.5	165.0
	Tofacitinib 30-15-10 mg BID	8	111.13	41.46	37.31	55.0	80.0	113.5	129.5	188.0
Month 84	Tofacitinib 15-10-5 mg BID	12	103.92	37.55	36.13	55.0	75.0	104.0	131.0	170.0
	Tofacitinib 30-15-10 mg BID	8	117.88	32.73	27.77	69.0	97.0	116.0	137.5	173.0
Month 90	Tofacitinib 15-10-5 mg BID	12	101.92	41.67	40.88	53.0	67.5	91.5	131.5	189.0
	Tofacitinib 30-15-10 mg BID	7	99.00	23.93	24.17	80.0	83.0	89.0	106.0	149.0
Month 96	Tofacitinib 15-10-5 mg BID	11	93.82	28.22	30.08	54.0	69.0	92.0	99.0	142.0
	Tofacitinib 30-15-10 mg BID	6	99.83	30.30	30.35	75.0	75.0	89.0	120.0	151.0
Follow-up	Tacrolimus	6	110.00	49.37	44.88	52.0	80.0	97.5	142.0	191.0
	Tofacitinib 15-10-5 mg BID	12	102.42	46.08	44.99	46.0	75.0	95.5	117.5	221.0
	Tofacitinib 30-15-10 mg BID	8	129.38	39.71	30.69	82.0	105.0	130.0	133.5	216.0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

Abbreviations: BID = twice daily; CV = coefficient of variation; LDL = low-density lipoprotein; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 19. Descriptive Statistics of Serum HDL Cholesterol Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	54.83	14.92	27.20	33.0	43.0	52.0	70.0	80.0
	Tofacitinib 15-10-5 mg BID	14	59.93	14.38	23.99	34.0	47.0	59.0	73.0	85.0
	Tofacitinib 30-15-10 mg BID	12	52.58	16.32	31.04	31.0	38.0	52.5	66.0	83.0
Month 12	Tacrolimus	16	51.81	18.82	36.32	16.0	38.0	49.0	65.0	86.0
	Tofacitinib 15-10-5 mg BID	14	62.07	17.68	28.48	31.0	49.0	67.0	70.0	90.0
	Tofacitinib 30-15-10 mg BID	12	56.00	16.99	30.34	35.0	44.0	47.5	68.0	89.0
Month 15	Tacrolimus	16	51.31	16.08	31.33	31.0	38.5	47.5	62.5	89.0
	Tofacitinib 15-10-5 mg BID	14	59.79	16.37	27.38	29.0	48.0	59.0	68.0	89.0
	Tofacitinib 30-15-10 mg BID	12	53.08	16.72	31.51	33.0	40.0	47.0	64.5	84.0
Month 18	Tacrolimus	18	52.67	17.07	32.42	29.0	40.0	49.0	60.0	89.0
	Tofacitinib 15-10-5 mg BID	14	59.29	17.03	28.73	26.0	44.0	58.5	73.0	90.0
	Tofacitinib 30-15-10 mg BID	12	52.92	15.17	28.66	31.0	42.0	52.5	65.0	77.0
Month 24	Tacrolimus	17	53.76	18.60	34.60	26.0	44.0	50.0	67.0	91.0
	Tofacitinib 15-10-5 mg BID	14	60.07	17.09	28.46	30.0	49.0	60.5	73.0	92.0
	Tofacitinib 30-15-10 mg BID	12	55.17	17.78	32.23	31.0	42.5	49.0	66.0	85.0
Month 30	Tacrolimus	14	51.21	16.83	32.85	27.0	35.0	51.5	60.0	83.0
	Tofacitinib 15-10-5 mg BID	14	59.29	15.03	25.34	31.0	49.0	62.0	70.0	82.0
	Tofacitinib 30-15-10 mg BID	10	50.40	9.29	18.43	39.0	45.0	49.0	56.0	69.0
Month 36	Tacrolimus	15	53.13	16.92	31.84	28.0	41.0	53.0	61.0	96.0
	Tofacitinib 15-10-5 mg BID	14	55.14	15.42	27.96	30.0	39.0	55.5	71.0	76.0
	Tofacitinib 30-15-10 mg BID	9	56.44	13.51	23.94	42.0	47.0	56.0	61.0	87.0
Month 42	Tacrolimus	15	52.27	14.40	27.56	27.0	41.0	53.0	64.0	76.0
	Tofacitinib 15-10-5 mg BID	14	56.57	12.69	22.43	29.0	51.0	59.5	66.0	72.0
	Tofacitinib 30-15-10 mg BID	9	57.33	12.23	21.33	40.0	53.0	55.0	68.0	74.0
Month 48	Tacrolimus	15	49.67	16.56	33.35	30.0	33.0	48.0	55.0	82.0
	Tofacitinib 15-10-5 mg BID	14	57.71	17.73	30.71	29.0	48.0	54.5	70.0	100.0
	Tofacitinib 30-15-10 mg BID	10	50.10	10.63	21.22	27.0	47.0	49.0	596.0	68.0
Month 54	Tacrolimus	14	46.64	13.28	28.46	27.0	42.0	43.5	54.0	73.0
	Tofacitinib 15-10-5 mg BID	14	60.07	16.36	27.24	27.0	52.0	58.0	72.0	85.0
	Tofacitinib 30-15-10 mg BID	10	52.80	12.27	23.24	40.0	43.0	49.0	61.0	79.0

Table 19. Descriptive Statistics of Serum HDL Cholesterol Levels (mg/dL) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 60	Tacrolimus	13	45.23	11.89	26.29	25.0	41.0	47.0	53.0	68.0
	Tofacitinib 15-10-5 mg BID	13	58.23	15.69	26.94	27.0	45.0	62.0	74.0	76.0
	Tofacitinib 30-15-10 mg BID	10	58.30	28.33	48.59	29.0	44.0	47.0	57.0	124.0
Month 66	Tacrolimus	12	49.75	15.72	31.60	28.0	38.0	47.5	59.0	78.0
	Tofacitinib 15-10-5 mg BID	14	56.57	19.03	33.64	26.0	44.0	57.0	64.0	91.0
	Tofacitinib 30-15-10 mg BID	10	51.40	13.92	27.09	31.0	43.0	49.0	56.0	78.0
Month 72	Tacrolimus	9	46.67	12.40	26.57	28.0	38.0	44.0	57.0	68.0
	Tofacitinib 15-10-5 mg BID	12	62.67	15.25	24.33	32.0	57.5	66.0	73.0	83.0
	Tofacitinib 30-15-10 mg BID	8	48.38	14.06	29.07	33.0	40.0	47.5	49.5	80.0
Month 78	Tofacitinib 15-10-5 mg BID	12	65.58	18.75	28.59	29.0	54.5	65.0	84.0	91.0
	Tofacitinib 30-15-10 mg BID	8	49.38	14.79	29.96	30.0	43.0	46.0	53.0	81.0
Month 84	Tofacitinib 15-10-5 mg BID	12	63.00	17.79	28.23	29.0	51.0	66.0	72.0	96.0
	Tofacitinib 30-15-10 mg BID	8	46.38	10.16	21.90	35.0	40.0	44.0	50.5	67.0
Month 90	Tofacitinib 15-10-5 mg BID	12	61.17	14.94	24.43	31.0	56.0	59.0	70.0	88.0
	Tofacitinib 30-15-10 mg BID	7	49.57	9.43	19.03	34.0	46.0	49.0	52.0	66.0
Month 96	Tofacitinib 15-10-5 mg BID	11	65.36	18.78	28.73	31.0	50.0	60.0	83.0	90.0
	Tofacitinib 30-15-10 mg BID	6	52.00	10.97	21.10	40.0	45.0	48.0	64.0	67.0
Follow-up	Tacrolimus	6	55.67	10.95	19.67	39.0	53.0	53.5	64.0	71.0
	Tofacitinib 15-10-5 mg BID	12	56.25	15.78	28.06	28.0	42.5	59.0	70.0	75.0
	Tofacitinib 30-15-10 mg BID	8	45.38	12.64	27.85	29.0	34.0	46.5	54.0	65.0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

Abbreviations: BID = twice daily; CV = coefficient of variation; HDL = high-density lipoprotein; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 20. Descriptive Statistics of Ratio of Total Serum Cholesterol to Serum HDL Cholesterol Levels by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	3.62	1.05	29.09	2.1	2.5	3.6	4.4	6.0
	Tofacitinib 15-10-5 mg BID	14	4.09	1.47	35.94	2.2	2.7	3.8	5.0	6.6
	Tofacitinib 30-15-10 mg BID	12	4.08	1.34	32.93	2.2	2.9	3.7	5.4	6.1
Month 12	Tacrolimus	16	3.72	0.94	25.29	2.4	3.1	3.7	4.1	5.6
	Tofacitinib 15-10-5 mg BID	14	3.92	1.40	35.65	2.1	2.7	4.0	4.3	7.4
	Tofacitinib 30-15-10 mg BID	12	4.03	1.34	33.31	2.2	3.0	3.7	5.0	6.5
Month 15	Tacrolimus	16	3.48	0.78	22.41	2.3	3.0	3.5	4.1	5.0
	Tofacitinib 15-10-5 mg BID	14	3.66	1.04	28.38	2.1	2.7	3.9	4.3	5.7
	Tofacitinib 30-15-10 mg BID	12	4.08	1.33	32.60	2.0	3.0	4.1	5.3	5.8
Month 18	Tacrolimus	18	3.50	1.01	28.89	1.9	2.9	3.5	3.8	5.7
	Tofacitinib 15-10-5 mg BID	14	3.32	1.03	31.02	2.2	2.5	3.1	3.8	5.4
	Tofacitinib 30-15-10 mg BID	12	3.88	1.29	33.15	2.1	2.8	3.8	5.1	5.8
Month 24	Tacrolimus	17	3.69	1.28	34.75	1.9	2.5	3.8	4.1	6.4
	Tofacitinib 15-10-5 mg BID	14	3.35	1.06	31.67	2.1	2.5	3.0	4.1	5.4
	Tofacitinib 30-15-10 mg BID	12	3.97	1.43	36.09	2.1	3.0	3.3	5.3	6.3
Month 30	Tacrolimus	14	3.70	1.30	35.27	2.1	2.9	3.3	4.5	6.3
	Tofacitinib 15-10-5 mg BID	14	3.30	0.99	30.05	2.2	2.4	3.1	4.1	5.3
	Tofacitinib 30-15-10 mg BID	10	4.03	0.89	22.22	2.7	3.2	3.9	5.0	5.1
Month 36	Tacrolimus	15	3.54	1.23	34.60	2.2	2.5	3.4	4.2	6.2
	Tofacitinib 15-10-5 mg BID	14	3.35	0.89	26.56	2.2	2.5	3.3	4.1	5.0
	Tofacitinib 30-15-10 mg BID	9	3.68	0.61	16.68	2.6	3.6	3.9	4.0	4.4
Month 42	Tacrolimus	15	3.63	1.00	27.67	2.1	2.9	3.6	4.0	5.6
	Tofacitinib 15-10-5 mg BID	14	3.85	1.82	47.44	2.2	2.6	3.4	4.0	9.0
	Tofacitinib 30-15-10 mg BID	9	3.35	0.50	14.99	2.6	3.0	3.4	3.7	4.2
Month 48	Tacrolimus	15	3.95	1.04	26.27	2.3	3.1	3.9	4.7	6.0
	Tofacitinib 15-10-5 mg BID	14	3.59	1.09	30.48	2.3	2.5	3.7	4.1	6.2
	Tofacitinib 30-15-10 mg BID	10	3.76	1.20	31.89	2.4	3.0	3.4	4.6	6.3

Table 20. Descriptive Statistics of Ratio of Total Serum Cholesterol to Serum HDL Cholesterol Levels by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 54	Tacrolimus	14	4.17	1.22	29.33	2.3	3.4	3.8	5.0	6.2
	Tofacitinib 15-10-5 mg BID	14	3.52	1.14	32.29	2.1	2.7	3.3	4.0	6.1
	Tofacitinib 30-15-10 mg BID	10	3.64	1.23	33.87	2.2	2.9	3.6	4.0	6.6
Month 60	Tacrolimus	13	4.12	1.18	28.55	2.2	3.3	4.0	5.1	6.0
	Tofacitinib 15-10-5 mg BID	13	3.32	0.87	26.11	2.3	2.7	2.9	4.0	5.1
	Tofacitinib 30-15-10 mg BID	10	3.59	1.20	33.51	1.9	2.6	3.7	4.4	5.2
Month 66	Tacrolimus	12	3.99	1.00	25.08	2.2	3.5	3.9	4.9	5.3
	Tofacitinib 15-10-5 mg BID	14	3.51	1.08	30.85	2.1	2.8	3.3	4.5	5.7
	Tofacitinib 30-15-10 mg BID	10	3.50	0.93	26.69	2.4	2.8	3.4	4.3	5.1
Month 72	Tacrolimus	9	3.97	1.08	27.18	2.2	3.6	3.7	4.6	5.8
	Tofacitinib 15-10-5 mg BID	12	3.05	0.62	20.49	2.1	2.6	3.0	3.5	4.3
	Tofacitinib 30-15-10 mg BID	8	4.30	1.31	30.38	2.4	3.7	4.0	5.3	6.3
Month 78	Tofacitinib 15-10-5 mg BID	12	3.06	0.96	31.42	2.2	2.3	2.7	3.4	4.9
	Tofacitinib 30-15-10 mg BID	8	4.06	0.89	21.83	2.7	3.6	3.9	4.6	5.6
Month 84	Tofacitinib 15-10-5 mg BID	12	3.22	0.99	30.68	2.1	2.5	2.8	3.7	5.2
	Tofacitinib 30-15-10 mg BID	8	4.50	0.96	21.35	3.5	3.6	4.4	5.5	5.5
Month 90	Tofacitinib 15-10-5 mg BID	12	3.14	0.89	28.46	2.2	2.3	2.9	4.0	4.6
	Tofacitinib 30-15-10 mg BID	7	3.91	0.74	18.90	2.8	3.3	3.9	4.6	4.8
Month 96	Tofacitinib 15-10-5 mg BID	11	2.97	0.92	31.09	2.1	2.3	2.5	3.7	5.0
	Tofacitinib 30-15-10 mg BID	6	3.72	0.69	18.42	2.9	2.9	4.0	4.1	4.4
Follow-up	Tacrolimus	6	3.57	1.06	29.85	2.4	2.9	3.3	4.2	5.4
	Tofacitinib 15-10-5 mg BID	12	3.45	1.07	31.15	2.3	2.5	3.3	4.3	5.8
	Tofacitinib 30-15-10 mg BID	8	4.95	1.27	25.63	3.1	3.9	5.1	6.0	6.6

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; CV = coefficient of variation; HDL = high-density lipoprotein; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 21. Percent of Subjects with Ratio of Total Serum Cholesterol to Serum HDL Cholesterol <5 and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 9	Tacrolimus	18	17 (94.4)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.0800
	Tofacitinib 30-15-10 mg BID	12	8 (66.7)	0.0493
Month 12	Tacrolimus	16	14 (87.5)	
	Tofacitinib 15-10-5 mg BID	14	12 (85.7)	0.8878
	Tofacitinib 30-15-10 mg BID	12	9 (75.0)	0.4013
Month 15	Tacrolimus	16	15 (93.8)	
	Tofacitinib 15-10-5 mg BID	14	13 (92.9)	0.9234
	Tofacitinib 30-15-10 mg BID	12	8 (66.7)	0.0690
Month 18	Tacrolimus	18	16 (88.9)	
	Tofacitinib 15-10-5 mg BID	14	13 (92.9)	0.7069
	Tofacitinib 30-15-10 mg BID	12	9 (75.0)	0.3255
Month 24	Tacrolimus	17	15 (88.2)	
	Tofacitinib 15-10-5 mg BID	14	12 (85.7)	0.8376
	Tofacitinib 30-15-10 mg BID	12	8 (66.7)	0.1652
Month 30	Tacrolimus	14	11 (78.6)	
	Tofacitinib 15-10-5 mg BID	14	13 (92.9)	0.2888
	Tofacitinib 30-15-10 mg BID	10	7 (70.0)	0.6398
Month 36	Tacrolimus	15	13 (86.7)	
	Tofacitinib 15-10-5 mg BID	14	14 (100.0)	0.1641
	Tofacitinib 30-15-10 mg BID	9	9 (100.0)	0.2627
Month 42	Tacrolimus	15	13 (86.7)	
	Tofacitinib 15-10-5 mg BID	14	11 (78.6)	0.5709
	Tofacitinib 30-15-10 mg BID	9	9 (100.0)	0.2627
Month 48	Tacrolimus	15	13 (86.7)	
	Tofacitinib 15-10-5 mg BID	14	13 (92.9)	0.5909
	Tofacitinib 30-15-10 mg BID	10	8 (80.0)	0.6625
Month 54	Tacrolimus	14	11 (78.6)	
	Tofacitinib 15-10-5 mg BID	14	12 (85.7)	0.6280
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.4684
Month 60	Tacrolimus	13	9 (69.2)	
	Tofacitinib 15-10-5 mg BID	13	12 (92.3)	0.1432
	Tofacitinib 30-15-10 mg BID	10	8 (80.0)	0.5685
Month 66	Tacrolimus	12	10 (83.3)	
	Tofacitinib 15-10-5 mg BID	14	13 (92.9)	0.4575
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.6576
Month 72	Tacrolimus	9	8 (88.9)	
	Tofacitinib 15-10-5 mg BID	12	12 (100.0)	0.2482
	Tofacitinib 30-15-10 mg BID	8	6 (75.0)	0.4670
Month 78	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	12 (100.0)	
	Tofacitinib 30-15-10 mg BID	8	7 (87.5)	

Table 21. Percent of Subjects with Ratio of Total Serum Cholesterol to Serum HDL Cholesterol <5 and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 84	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	11 (91.7)	
	Tofacitinib 30-15-10 mg BID	8	4 (50.0)	
Month 90	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	12 (100.0)	
	Tofacitinib 30-15-10 mg BID	7	7 (100.0)	
Month 96	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	11	11 (100.0)	
	Tofacitinib 30-15-10 mg BID	6	6 (100.0)	
Follow-up	Tacrolimus	6	6 (100.0)	
	Tofacitinib 15-10-5 mg BID	12	11 (91.7)	0.4795
	Tofacitinib 30-15-10 mg BID	8	4 (50.0)	0.0483

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Hypercholesterolemia was defined as a value of total serum cholesterol greater than 240 mg/dL or 6.2 mmol/L.
P-values were obtained using Mantel-Haenszel Chi Square.
Abbreviations: BID = twice daily dosing; HDL = high-density lipoprotein; N = number of subjects in Safety Analysis Set per visit; n = number of subjects with ratio of total serum cholesterol to serum HDL cholesterol <5.

Table 22. Descriptive Statistics of Ratio of Serum LDL Cholesterol to Serum HDL Cholesterol Levels by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	2.09	0.84	40.23	0.8	1.3	2.1	2.8	3.6
	Tofacitinib 15-10-5 mg BID	12	2.42	1.25	51.72	1.1	1.4	2.1	3.2	4.9
	Tofacitinib 30-15-10 mg BID	11	2.17	0.82	37.85	1.1	1.6	1.9	2.9	3.6
Month 12	Tacrolimus	16	2.14	0.71	33.25	1.1	1.8	2.1	2.5	3.8
	Tofacitinib 15-10-5 mg BID	14	2.24	0.98	43.66	1.0	1.4	2.2	2.5	4.6
	Tofacitinib 30-15-10 mg BID	12	2.31	0.99	42.94	1.0	1.6	2.0	3.1	4.1
Month 15	Tacrolimus	16	1.97	0.62	31.68	0.9	1.6	2.0	2.4	3.2
	Tofacitinib 15-10-5 mg BID	14	2.07	0.81	39.31	0.9	1.3	2.2	2.6	3.6
	Tofacitinib 30-15-10 mg BID	11	2.11	0.74	35.32	0.9	1.5	2.2	2.6	3.3
Month 18	Tacrolimus	18	1.98	0.86	43.59	0.7	1.3	2.0	2.3	3.7
	Tofacitinib 15-10-5 mg BID	14	1.74	0.80	45.93	0.7	1.1	1.6	2.2	3.2
	Tofacitinib 30-15-10 mg BID	12	2.10	0.93	44.23	0.9	1.3	1.8	3.0	3.7
Month 24	Tacrolimus	17	2.04	0.94	45.96	0.8	1.3	2.0	2.4	4.2
	Tofacitinib 15-10-5 mg BID	14	1.78	0.69	38.42	0.8	1.3	1.7	2.3	2.9
	Tofacitinib 30-15-10 mg BID	12	2.25	0.98	43.76	0.9	1.6	1.9	3.3	4.0
Month 30	Tacrolimus	14	2.09	0.99	47.08	0.9	1.5	1.8	2.5	3.9
	Tofacitinib 15-10-5 mg BID	14	1.76	0.69	39.36	0.8	1.2	1.7	2.3	2.9
	Tofacitinib 30-15-10 mg BID	10	2.36	0.78	33.20	1.1	1.9	2.0	3.2	3.3
Month 36	Tacrolimus	15	1.93	0.92	47.54	0.6	1.2	1.8	2.4	4.0
	Tofacitinib 15-10-5 mg BID	14	1.75	0.64	36.25	0.7	1.2	1.7	2.2	3.0
	Tofacitinib 30-15-10 mg BID	9	2.03	0.49	23.97	1.4	1.8	2.0	2.1	2.9
Month 42	Tacrolimus	15	2.06	0.87	42.41	0.8	1.5	1.9	2.7	3.9
	Tofacitinib 15-10-5 mg BID	13	1.85	0.81	43.93	1.0	1.2	1.6	2.6	3.4
	Tofacitinib 30-15-10 mg BID	9	1.82	0.44	24.41	1.2	1.6	1.8	2.0	2.6
Month 48	Tacrolimus	15	2.27	0.85	37.60	0.9	1.6	2.0	3.3	3.6
	Tofacitinib 15-10-5 mg BID	14	1.99	0.73	36.76	1.1	1.2	2.2	2.4	3.6
	Tofacitinib 30-15-10 mg BID	10	2.07	0.80	38.45	1.3	1.5	1.9	2.4	3.6

Table 22. Descriptive Statistics of Ratio of Serum LDL Cholesterol to Serum HDL Cholesterol Levels by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 54	Tacrolimus	14	2.48	1.08	43.59	0.8	1.8	2.1	3.7	4.3
	Tofacitinib 15-10-5 mg BID	13	1.92	0.81	42.28	0.9	1.5	1.7	2.1	4.0
	Tofacitinib 30-15-10 mg BID	10	1.92	1.02	53.38	0.9	1.2	1.7	2.2	4.3
Month 60	Tacrolimus	13	2.45	0.99	40.41	0.9	1.7	2.2	3.5	3.9
	Tofacitinib 15-10-5 mg BID	13	1.86	0.67	36.23	1.1	1.3	1.7	2.4	3.3
	Tofacitinib 30-15-10 mg BID	10	1.92	0.98	51.07	0.7	1.4	1.7	2.9	3.7
Month 66	Tacrolimus	12	2.34	0.91	38.98	0.7	1.8	2.1	2.9	3.9
	Tofacitinib 15-10-5 mg BID	13	1.96	0.85	43.18	0.9	1.3	2.0	2.5	3.8
	Tofacitinib 30-15-10 mg BID	10	1.88	0.83	44.11	1.2	1.3	1.5	2.4	3.7
Month 72	Tacrolimus	9	2.32	1.00	43.02	0.8	1.7	2.1	2.9	4.1
	Tofacitinib 15-10-5 mg BID	12	1.66	0.50	30.31	1.0	1.2	1.6	2.0	2.6
	Tofacitinib 30-15-10 mg BID	8	2.46	1.04	42.24	1.1	1.7	2.3	3.3	4.0
Month 78	Tofacitinib 15-10-5 mg BID	12	1.72	0.77	45.04	0.9	1.1	1.5	2.1	3.3
	Tofacitinib 30-15-10 mg BID	8	2.30	0.80	34.96	1.4	1.7	2.0	2.8	3.8
Month 84	Tofacitinib 15-10-5 mg BID	12	1.80	0.83	46.42	0.6	1.2	1.6	2.3	3.3
	Tofacitinib 30-15-10 mg BID	8	2.58	0.69	26.84	1.8	2.0	2.6	3.0	3.7
Month 90	Tofacitinib 15-10-5 mg BID	12	1.74	0.74	42.51	0.8	1.1	1.6	2.5	2.9
	Tofacitinib 30-15-10 mg BID	7	2.04	0.50	24.53	1.3	1.8	2.0	2.4	2.9
Month 96	Tofacitinib 15-10-5 mg BID	11	1.56	0.66	42.65	0.7	1.1	1.2	2.1	2.8
	Tofacitinib 30-15-10 mg BID	6	1.98	0.69	34.79	1.3	1.4	1.8	2.6	3.0
Follow-up	Tacrolimus	6	2.09	1.05	50.48	0.70	1.5	1.8	3.0	3.6
	Tofacitinib 15-10-5 mg BID	12	1.91	0.82	42.89	0.70	1.2	2.0	2.3	3.6
	Tofacitinib 30-15-10 mg BID	8	3.03	1.15	37.88	1.80	2.1	2.7	4.0	4.8

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; CV = coefficient of variation; HDL = high-density lipoprotein; LDL = low-density lipoprotein; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 23. Percent of Subjects with Ratio of Serum LDL Cholesterol to Serum HDL Cholesterol <3.5 and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 9	Tacrolimus	18	17 (94.4)	
	Tofacitinib 15-10-5 mg BID	12	9 (75.0)	0.1313
	Tofacitinib 30-15-10 mg BID	11	10 (90.9)	0.7202
Month 12	Tacrolimus	16	15 (93.8)	
	Tofacitinib 15-10-5 mg BID	14	12 (85.7)	0.4718
	Tofacitinib 30-15-10 mg BID	12	10 (83.3)	0.3865
Month 15	Tacrolimus	16	16 (100.0)	
	Tofacitinib 15-10-5 mg BID	14	13 (92.9)	0.2850
	Tofacitinib 30-15-10 mg BID	11	11 (100.0)	
Month 18	Tacrolimus	18	17 (94.4)	
	Tofacitinib 15-10-5 mg BID	14	14 (100.0)	0.3778
	Tofacitinib 30-15-10 mg BID	12	11 (91.7)	0.7689
Month 24	Tacrolimus	17	16 (94.1)	
	Tofacitinib 15-10-5 mg BID	14	14 (100.0)	0.3642
	Tofacitinib 30-15-10 mg BID	12	11 (91.7)	0.8010
Month 30	Tacrolimus	14	11 (78.6)	
	Tofacitinib 15-10-5 mg BID	14	14 (100.0)	0.0719
	Tofacitinib 30-15-10 mg BID	10	10 (100.0)	0.1255
Month 36	Tacrolimus	15	14 (93.3)	
	Tofacitinib 15-10-5 mg BID	14	14 (100.0)	0.3340
	Tofacitinib 30-15-10 mg BID	9	9 (100.0)	0.4386
Month 42	Tacrolimus	15	14 (93.3)	
	Tofacitinib 15-10-5 mg BID	13	13 (100.0)	0.3519
	Tofacitinib 30-15-10 mg BID	9	9 (100.0)	0.4386
Month 48	Tacrolimus	15	14 (93.3)	
	Tofacitinib 15-10-5 mg BID	14	13 (92.9)	0.9604
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.7681
Month 54	Tacrolimus	14	10 (71.4)	
	Tofacitinib 15-10-5 mg BID	13	12 (92.3)	0.1709
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.2796
Month 60	Tacrolimus	13	10 (76.9)	
	Tofacitinib 15-10-5 mg BID	13	13 (100.0)	0.0710
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.4224
Month 66	Tacrolimus	12	10 (83.3)	
	Tofacitinib 15-10-5 mg BID	13	12 (92.3)	0.4991
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.6576
Month 72	Tacrolimus	9	8 (88.9)	
	Tofacitinib 15-10-5 mg BID	12	12 (100.0)	0.2482
	Tofacitinib 30-15-10 mg BID	8	6 (75.0)	0.4670
Month 78	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	12 (100.0)	
	Tofacitinib 30-15-10 mg BID	8	7 (87.5)	

Table 23. Percent of Subjects with Ratio of Serum LDL Cholesterol to Serum HDL Cholesterol <3.5 and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 84	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	12 (100.0)	
	Tofacitinib 30-15-10 mg BID	8	7 (87.5)	
Month 90	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	12 (100.0)	
	Tofacitinib 30-15-10 mg BID	7	7 (100.0)	
Month 96	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	11	11 (100.0)	
	Tofacitinib 30-15-10 mg BID	6	6 (100.0)	
Follow-up	Tacrolimus	6	6 (100.0)	
	Tofacitinib 15-10-5 mg BID	12	11 (91.7)	0.4795
	Tofacitinib 30-15-10 mg BID	8	6 (62.5)	0.1030

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Hypercholesterolemia was defined as a value of total serum cholesterol greater than 240 mg/dL or 6.2 mmol/L.
P-values were obtained using Mantel-Haenszel Chi Square.
Abbreviations: BID = twice daily dosing; HDL = high-density lipoprotein; LDL = low-density lipoprotein; N = number of subjects in Safety Analysis Set per visit; n = number of subjects with ratio of serum LDL cholesterol to serum HDL cholesterol <3.5.

Table 24. Descriptive Statistics of Levels of Serum Triglycerides by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	18	129.44	53.45	41.29	58.0	86.0	124.5	155.0	262.0
	Tofacitinib 15-10-5 mg BID	14	205.07	139.91	68.22	58.0	85.0	178.5	240.0	497.0
	Tofacitinib 30-15-10 mg BID	12	194.00	128.60	66.29	34.0	94.0	156.5	276.0	429.0
Month 12	Tacrolimus	16	129.19	49.86	38.60	62.0	91.0	108.5	167.0	240.0
	Tofacitinib 15-10-5 mg BID	14	181.86	107.49	59.11	46.0	80.0	173.5	273.0	327.0
	Tofacitinib 30-15-10 mg BID	12	173.00	99.25	57.37	53.0	90.5	141.5	263.5	343.0
Month 15	Tacrolimus	16	123.56	52.90	42.82	57.0	77.0	115.0	152.0	241.0
	Tofacitinib 15-10-5 mg BID	14	158.93	84.58	53.22	48.0	84.0	177.0	232.0	285.0
	Tofacitinib 30-15-10 mg BID	12	200.50	122.75	61.22	47.0	98.5	157.5	301.5	404.0
Month 18	Tacrolimus	18	123.44	53.83	43.60	54.0	98.0	117.0	140.0	296.0
	Tofacitinib 15-10-5 mg BID	14	153.79	79.29	51.56	64.0	88.0	122.5	225.0	293.0
	Tofacitinib 30-15-10 mg BID	12	173.08	101.81	58.82	56.0	116.0	135.5	224.5	387.0
Month 24	Tacrolimus	17	149.71	86.56	57.82	49.0	89.0	128.0	175.0	328.0
	Tofacitinib 15-10-5 mg BID	14	146.50	106.28	72.55	46.0	70.0	116.0	175.0	394.0
	Tofacitinib 30-15-10 mg BID	12	161.33	83.95	52.04	48.0	102.0	138.5	236.5	297.0
Month 30	Tacrolimus	14	131.07	52.76	40.25	49.0	90.0	127.0	177.0	214.0
	Tofacitinib 15-10-5 mg BID	14	147.71	84.28	57.06	56.0	86.0	118.0	204.0	318.0
	Tofacitinib 30-15-10 mg BID	10	162.30	55.08	33.94	73.0	128.0	153.0	207.0	251.0
Month 36	Tacrolimus	15	142.00	68.44	48.20	53.0	80.0	134.0	184.0	265.0
	Tofacitinib 15-10-5 mg BID	14	147.14	93.13	63.29	56.0	81.0	136.5	172.0	289.0
	Tofacitinib 30-15-10 mg BID	9	169.11	79.39	46.94	53.0	113.0	180.0	226.0	282.0
Month 42	Tacrolimus	15	136.60	52.91	38.74	43.0	116.0	133.0	153.0	228.0
	Tofacitinib 15-10-5 mg BID	14	195.71	156.42	79.92	55.0	86.0	152.5	268.0	628.0
	Tofacitinib 30-15-10 mg BID	9	141.22	63.76	45.15	45.0	115.0	128.0	168.0	242.0
Month 48	Tacrolimus	15	144.67	70.99	49.07	68.0	96.0	118.0	174.0	322.0
	Tofacitinib 15-10-5 mg BID	14	155.07	91.61	59.07	55.0	89.0	107.5	225.0	337.0
	Tofacitinib 30-15-10 mg BID	10	150.70	106.82	70.88	38.0	81.0	131.5	141.0	394.0

Table 24. Descriptive Statistics of Levels of Serum Triglycerides by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 54	Tacrolimus	14	150.14	47.64	31.73	62.0	116.0	172.0	176.0	217.0
	Tofacitinib 15-10-5 mg BID	10	158.43	115.94	73.18	45.0	71.0	99.5	234.0	425.0
	Tofacitinib 30-15-10 mg BID	10	170.90	83.72	48.99	44.0	88.0	167.0	243.0	296.0
Month 60	Tacrolimus	13	139.387	71.94	51.61	45.0	84.0	132.0	184.0	301.0
	Tofacitinib 15-10-5 mg BID	13	125.23	46.55	37.17	58.0	92.0	112.0	168.0	181.0
	Tofacitinib 30-15-10 mg BID	10	161.10	93.01	57.73	41.0	109.0	123.5	201.0	348.0
Month 66	Tacrolimus	12	143.42	54.70	38.14	42.0	105.0	152.5	182.0	231.0
	Tofacitinib 15-10-5 mg BID	14	140.00	117.56	83.97	42.0	80.0	114.0	159.0	509.0
	Tofacitinib 30-15-10 mg BID	10	145.30	75.77	52.15	36.0	94.0	131.5	167.0	295.0
Month 72	Tacrolimus	9	138.33	59.14	42.75	65.0	107.0	129.0	151.0	276.0
	Tofacitinib 15-10-5 mg BID	12	118.33	83.47	70.54	54.0	66.5	84.5	147.0	283.0
	Tofacitinib 30-15-10 mg BID	8	188.00	72.59	38.61	82.0	131.5	196.0	230.0	307.0
Month 78	Tofacitinib 15-10-5 mg BID	12	104.42	58.22	55.75	52.0	62.0	98.0	112.5	270.0
	Tofacitinib 30-15-10 mg BID	8	172.38	53.73	31.17	93.0	133.0	179.0	211.0	240.0
Month 84	Tofacitinib 15-10-5 mg BID	12	127.17	66.01	51.91	50.0	73.5	116.5	181.5	255.0
	Tofacitinib 30-15-10 mg BID	8	199.75	84.79	42.45	91.0	130.0	183.5	279.0	322.0
Month 90	Tofacitinib 15-10-5 mg BID	12	113.75	57.79	50.80	41.0	64.0	103.5	158.5	215.0
	Tofacitinib 30-15-10 mg BID	7	206.29	83.17	40.32	88.0	137.0	191.0	284.0	327.0
Month 96	Tofacitinib 15-10-5 mg BID	11	119.64	76.86	64.24	54.0	56.0	88.0	153.0	278.0
	Tofacitinib 30-15-10 mg BID	6	180.17	93.92	52.13	73.0	103.0	165.0	252.0	323.0
Follow-up	Tacrolimus	6	130.67	63.87	48.88	51.0	70.0	138.5	158.0	228.0
	Tofacitinib 15-10-5 mg BID	12	134.50	73.14	54.38	51.0	73.5	112.0	184.5	267.0
	Tofacitinib 30-15-10 mg BID	8	191.88	83.21	43.37	102.0	129.0	170.5	248.5	337.0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; CV = coefficient of variation; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 25. Percent of Subjects with Lipid-Lowering Drug Usage and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 9	Tacrolimus	18	7 (38.9)	
	Tofacitinib 15-10-5 mg BID	14	9 (64.3)	0.1606
	Tofacitinib 30-15-10 mg BID	13	7 (53.8)	0.4166
Month 12	Tacrolimus	18	8 (44.4)	
	Tofacitinib 15-10-5 mg BID	14	9 (64.3)	0.2721
	Tofacitinib 30-15-10 mg BID	13	7 (53.8)	0.6111
Month 15	Tacrolimus	18	8 (44.4)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.1330
	Tofacitinib 30-15-10 mg BID	12	6 (50.0)	0.7689
Month 18	Tacrolimus	18	8 (44.4)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.1330
	Tofacitinib 30-15-10 mg BID	12	5 (41.7)	0.8824
Month 24	Tacrolimus	17	8 (47.1)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.1783
	Tofacitinib 30-15-10 mg BID	12	7 (58.3)	0.5565
Month 30	Tacrolimus	15	7 (46.7)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.1837
	Tofacitinib 30-15-10 mg BID	11	7 (63.6)	0.4004
Month 36	Tacrolimus	15	7 (46.7)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.1837
	Tofacitinib 30-15-10 mg BID	11	8 (72.7)	0.1926
Month 42	Tacrolimus	15	7 (46.7)	
	Tofacitinib 15-10-5 mg BID	14	9 (64.3)	0.3489
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.0303
Month 48	Tacrolimus	15	7 (46.7)	
	Tofacitinib 15-10-5 mg BID	14	9 (64.3)	0.3489
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.0303
Month 54	Tacrolimus	14	6 (42.9)	
	Tofacitinib 15-10-5 mg BID	14	9 (64.3)	0.2643
	Tofacitinib 30-15-10 mg BID	10	7 (70.0)	0.1977
Month 60	Tacrolimus	13	5 (38.5)	
	Tofacitinib 15-10-5 mg BID	14	9 (64.3)	0.1879
	Tofacitinib 30-15-10 mg BID	10	8 (80.0)	0.0514
Month 66	Tacrolimus	13	6 (46.2)	
	Tofacitinib 15-10-5 mg BID	14	9 (64.3)	0.3525
	Tofacitinib 30-15-10 mg BID	10	8 (80.0)	0.1068
Month 72	Tacrolimus	9	4 (44.4)	
	Tofacitinib 15-10-5 mg BID	14	9 (64.3)	0.3596
	Tofacitinib 30-15-10 mg BID	9	8 (88.9)	0.0519
Month 78	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	8 (61.5)	
	Tofacitinib 30-15-10 mg BID	8	7 (87.5)	

Table 25. Percent of Subjects with Lipid-Lowering Drug Usage and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 84	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	8 (61.5)	
	Tofacitinib 30-15-10 mg BID	8	7 (87.5)	
Month 90	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	7 (58.3)	
	Tofacitinib 30-15-10 mg BID	8	7 (87.5)	
Month 96	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	7 (58.3)	
	Tofacitinib 30-15-10 mg BID	6	6 (100.0)	
Follow-up	Tacrolimus	7	0	
	Tofacitinib 15-10-5 mg BID	13	0	
	Tofacitinib 30-15-10 mg BID	11	1 (9.1)	0.4250

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
P-values were obtained using Mantel-Haenszel Chi Square.
Abbreviations: BID = twice daily dosing; N = number of subjects in Safety Analysis Set per visit; n = number of subjects with ratio of serum LDL cholesterol to serum HDL cholesterol <3.5.

Table 26. Percent of Subjects with Antihypertensive Drug Usage and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 9	Tacrolimus	18	15 (83.3)	
	Tofacitinib 15-10-5 mg BID	14	12 (85.7)	0.8563
	Tofacitinib 30-15-10 mg BID	13	12 (92.3)	0.4694
Month 12	Tacrolimus	18	15 (83.3)	
	Tofacitinib 15-10-5 mg BID	14	12 (85.7)	0.8563
	Tofacitinib 30-15-10 mg BID	13	12 (92.3)	0.4694
Month 15	Tacrolimus	18	15 (83.3)	
	Tofacitinib 15-10-5 mg BID	14	12 (85.7)	0.8563
	Tofacitinib 30-15-10 mg BID	12	11 (91.7)	0.5178
Month 18	Tacrolimus	18	15 (83.3)	
	Tofacitinib 15-10-5 mg BID	14	11 (78.6)	0.7361
	Tofacitinib 30-15-10 mg BID	12	11 (91.7)	0.5178
Month 24	Tacrolimus	17	14 (82.4)	
	Tofacitinib 15-10-5 mg BID	14	12 (85.7)	0.8033
	Tofacitinib 30-15-10 mg BID	12	11 (91.7)	0.4815
Month 30	Tacrolimus	15	11 (73.3)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.9103
	Tofacitinib 30-15-10 mg BID	11	9 (81.8)	0.6189
Month 36	Tacrolimus	15	11 (73.3)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.9103
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.3173
Month 42	Tacrolimus	15	11 (73.3)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.9103
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.3173
Month 48	Tacrolimus	15	11 (73.3)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.9103
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.3173
Month 54	Tacrolimus	14	10 (71.4)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	1
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.2796
Month 60	Tacrolimus	13	9 (69.2)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.9024
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.2417
Month 66	Tacrolimus	13	10 (76.9)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.7494
	Tofacitinib 30-15-10 mg BID	10	9 (90.0)	0.4224
Month 72	Tacrolimus	9	7 (77.8)	
	Tofacitinib 15-10-5 mg BID	14	10 (71.4)	0.7407
	Tofacitinib 30-15-10 mg BID	9	8 (88.9)	0.5388
Month 78	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	9 (69.2)	
	Tofacitinib 30-15-10 mg BID	8	7 (87.5)	

Table 26. Percent of Subjects with Antihypertensive Drug Usage and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 84	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	9 (69.2)	
	Tofacitinib 30-15-10 mg BID	8	6 (75.0)	
Month 90	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	8 (66.7)	
	Tofacitinib 30-15-10 mg BID	8	6 (75.0)	
Month 96	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	11	8 (72.7)	
	Tofacitinib 30-15-10 mg BID	7	5 (71.4)	
Follow-up	Tacrolimus	8	1 (12.5)	
	Tofacitinib 15-10-5 mg BID	13	0	0.2024
	Tofacitinib 30-15-10 mg BID	11	1 (9.1)	0.8160

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
P-values were obtained using Mantel-Haenszel Chi Square.
Abbreviations: BID = twice daily dosing; N = number of subjects in Safety Analysis Set per visit; n = number of subjects with ratio of serum LDL cholesterol to serum HDL cholesterol <3.5.

Table 27. Percent of Subjects with Oral Hypoglycemics, Anti-Diabetic Agents and Insulin Usage and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 9	Tacrolimus	18	1 (5.6)	
	Tofacitinib 15-10-5 mg BID	14	5 (35.7)	0.0328
	Tofacitinib 30-15-10 mg BID	13	4 (30.8)	0.0639
Month 12	Tacrolimus	18	1 (5.6)	
	Tofacitinib 15-10-5 mg BID	14	5 (35.7)	0.0328
	Tofacitinib 30-15-10 mg BID	12	4 (33.3)	0.0493
Month 15	Tacrolimus	18	1 (5.6)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.0127
	Tofacitinib 30-15-10 mg BID	12	4 (33.3)	0.0493
Month 18	Tacrolimus	18	2 (11.1)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.0429
	Tofacitinib 30-15-10 mg BID	12	4 (33.3)	0.1427
Month 24	Tacrolimus	17	2 (11.8)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.0528
	Tofacitinib 30-15-10 mg BID	12	4 (33.3)	0.1652
Month 30	Tacrolimus	15	2 (13.3)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.0807
	Tofacitinib 30-15-10 mg BID	11	3 (27.3)	0.3823
Month 36	Tacrolimus	15	2 (13.3)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.0807
	Tofacitinib 30-15-10 mg BID	10	3 (30.0)	0.3173
Month 42	Tacrolimus	15	2 (13.3)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.0807
	Tofacitinib 30-15-10 mg BID	10	3 (30.0)	0.3173
Month 48	Tacrolimus	15	2 (13.3)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.0807
	Tofacitinib 30-15-10 mg BID	10	3 (30.0)	0.3173
Month 54	Tacrolimus	14	2 (14.3)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.1003
	Tofacitinib 30-15-10 mg BID	10	3 (30.0)	0.3603
Month 60	Tacrolimus	13	2 (15.4)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.1253
	Tofacitinib 30-15-10 mg BID	10	3 (30.0)	0.4100
Month 66	Tacrolimus	13	2 (15.4)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.1253
	Tofacitinib 30-15-10 mg BID	10	3 (30.0)	0.4100
Month 72	Tacrolimus	9	1 (11.1)	
	Tofacitinib 15-10-5 mg BID	14	6 (42.9)	0.1143
	Tofacitinib 30-15-10 mg BID	8	2 (25.0)	0.4670
Month 78	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	5 (38.5)	
	Tofacitinib 30-15-10 mg BID	8	2 (25.0)	

Table 27. Percent of Subjects with Oral Hypoglycemics, Anti-Diabetic Agents and Insulin Usage and Treatment Comparisons by Visit (Safety Analysis Set)

Visit	Treatment	N	n (%)	Compared to Tacrolimus P-value
Month 84	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	13	5 (38.5)	
	Tofacitinib 30-15-10 mg BID	8	2 (25.0)	
Month 90	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	12	4 (33.3)	
	Tofacitinib 30-15-10 mg BID	8	2 (25.0)	
Month 96	Tacrolimus	0	0	
	Tofacitinib 15-10-5 mg BID	11	4 (36.4)	
	Tofacitinib 30-15-10 mg BID	6	1 (16.7)	
Follow-up	Tacrolimus	7	0	
	Tofacitinib 15-10-5 mg BID	13	0	
	Tofacitinib 30-15-10 mg BID	11	1 (9.1)	0.4250

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
P-values were obtained using Mantel-Haenszel Chi Square.
Abbreviations: BID = twice daily dosing; N = number of subjects in Safety Analysis Set per visit; n = number of subjects with ratio of serum LDL cholesterol to serum HDL cholesterol <3.5.

EBV DNA levels by PCR: Descriptive statistics for EBV DNA by PCR (number of copies/500 ng DNA), and percentages of subjects meeting cut-offs, are presented by visit for the Safety Analysis Set in Table 28 and Table 29, respectively.

Mean EBV DNA levels were higher in the tofacitinib groups than in the tacrolimus group at each visit.

Of those with detectable levels of EBV DNA in the tofacitinib groups, the majority had EBV DNA level of 1-50 copies/500 ng DNA. No subject had EBV DNA level >1000 copies/500 ng DNA. In the tofacitinib 15-10-5 mg BID group at the Month 18 and Month 30 visits, 1 subject had an EBV DNA level of 101-1000 copies/500 ng DNA. In the tofacitinib 30-15-10 mg BID group at the Month 30, Month 36, Month 72 and Month 78 visits, 1 subject had an EBV DNA level of 101-1000 copies/500 ng DNA.

In the tacrolimus group the majority of subjects had undetectable levels of EBV. Of those with detectable levels, 1 subject (Month 15) had EBV DNA level of 51-101 copies/500 ng DNA and the remaining subjects had EBV DNA levels of 1-50 copies/500 ng DNA.

Table 28. Descriptive Statistics of EBV DNA by PCR (number of copies/500 ng DNA) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tacrolimus	17	0.41	1.46	354.63	0.0	0.0	0.0	0.0	6.0
	Tofacitinib 15-10-5 mg BID	14	1.00	2.18	218.39	0.0	0.0	0.0	1.0	7.0
	Tofacitinib 30-15-10 mg BID	12	3.17	3.30	104.16	0.0	0.0	2.5	5.5	9.0
Month 12	Tacrolimus	17	0.12	0.49	412.31	0.0	0.0	0.0	0.0	2.0
	Tofacitinib 15-10-5 mg BID	14	4.07	11.89	291.96	0.0	0.0	0.0	3.0	45.0
	Tofacitinib 30-15-10 mg BID	12	8.42	18.46	219.28	0.0	0.0	2.0	5.5	65.0
Month 15	Tacrolimus	17	5.47	22.05	402.99	0.0	0.0	0.0	0.0	91.0
	Tofacitinib 15-10-5 mg BID	14	6.71	20.36	303.23	0.0	0.0	0.0	2.0	77.0
	Tofacitinib 30-15-10 mg BID	12	18.42	24.27	131.80	0.0	0.0	2.5	34.0	71.0
Month 18	Tacrolimus	17	0.59	2.18	370.79	0.0	0.0	0.0	0.0	9.0
	Tofacitinib 15-10-5 mg BID	13	21.92	56.56	257.99	0.0	0.0	0.0	2.0	201.0
	Tofacitinib 30-15-10 mg BID	12	21.50	32.52	151.26	0.0	0.0	1.0	44.5	90.0
Month 24	Tacrolimus	15	0.00	0	0.00	0.0	0.0	0.0	0.0	0.0
	Tofacitinib 15-10-5 mg BID	13	10.38	24.22	233.26	0.0	0.0	0.0	3.0	86.0
	Tofacitinib 30-15-10 mg BID	12	10.83	25.90	239.06	0.0	0.0	2.0	9.0	92.0
Month 30	Tacrolimus	13	2.15	7.19	333.64	0.0	0.0	0.0	0.0	26.0
	Tofacitinib 15-10-5 mg BID	14	13.57	31.74	233.88	0.0	0.0	2.5	5.0	115.0
	Tofacitinib 30-15-10 mg BID	10	23.80	39.60	166.38	0.0	0.0	8.0	27.0	128.0
Month 36	Tacrolimus	15	1.20	3.19	265.77	0.0	0.0	0.0	0.0	10.0
	Tofacitinib 15-10-5 mg BID	14	8.64	25.37	293.50	0.0	0.0	0.0	3.0	96.0
	Tofacitinib 30-15-10 mg BID	8	42.63	110.49	259.22	0.0	1.5	4.0	7.0	316.0
Month 42	Tacrolimus	14	0.57	2.14	374.17	0.0	0.0	0.0	0.0	8.0
	Tofacitinib 15-10-5 mg BID	12	15.50	19.10	123.23	0.0	0.0	5.0	28.5	56.0
	Tofacitinib 30-15-10 mg BID	9	17.00	26.98	158.69	0.0	1.0	2.0	20.0	83.0
Month 48	Tacrolimus	15	0.07	0.26	387.30	0.0	0.0	0.0	0.0	1.0
	Tofacitinib 15-10-5 mg BID	9	17.00	32.60	191.79	0.0	0.0	0.0	5.0	82.0
	Tofacitinib 30-15-10 mg BID	6	11.50	21.42	186.24	1.0	2.0	2.0	7.0	55.0

Table 28. Descriptive Statistics of EBV DNA by PCR (number of copies/500 ng DNA) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 54	Tacrolimus	14	0.64	1.08	168.28	0.0	0.0	0.0	1.0	4.0
	Tofacitinib 15-10-5 mg BID	14	13.86	26.40	190.55	0.0	0.0	1.0	11.0	93.0
	Tofacitinib 30-15-10 mg BID	10	6.3	12.10	192.09	0.0	0.0	2.5	6.0	40.0
Month 60	Tacrolimus	13	0.31	0.63	204.89	0.0	0.0	0.0	0.0	2.0
	Tofacitinib 15-10-5 mg BID	13	11.46	27.20	237.33	0.0	0.0	0.0	6.0	95.0
	Tofacitinib 30-15-10 mg BID	10	10.20	20.86	204.54	0.0	1.0	1.5	3.0	66.0
Month 66	Tacrolimus	10	0.40	0.97	241.52	0.0	0.0	0.0	0.0	3.0
	Tofacitinib 15-10-5 mg BID	13	17.38	26.83	154.34	0.0	0.0	1.0	35.0	79.0
	Tofacitinib 30-15-10 mg BID	9	31.11	32.92	105.82	1.0	1.0	8.0	62.0	71.0
Month 72	Tacrolimus	9	1.11	3.33	300.00	0.0	0.0	0.0	0.0	10.0
	Tofacitinib 15-10-5 mg BID	12	11.08	27.22	245.63	0.0	0.0	1.5	7.5	96.0
	Tofacitinib 30-15-10 mg BID	8	19.25	41.80	217.13	0.0	0.0	4.5	11.5	122.0
Month 78	Tofacitinib 15-10-5 mg BID	12	10.08	16.10	159.66	0.0	0.0	2.0	15.0	48.0
	Tofacitinib 30-15-10 mg BID	8	17.63	42.28	239.89	0.0	0.5	2.0	7.0	122.0
Month 84	Tofacitinib 15-10-5 mg BID	12	1.08	1.51	138.93	0.0	0.0	0.5	1.5	4.0
	Tofacitinib 30-15-10 mg BID	8	10.88	21.24	195.34	0.0	1.5	3.5	7.0	63.0
Month 90	Tofacitinib 15-10-5 mg BID	12	2.92	5.18	177.53	0.0	0.0	0.0	4.0	17.0
	Tofacitinib 30-15-10 mg BID	7	9.29	20.69	222.77	0.0	0.0	1.0	5.0	56.0
Month 96	Tofacitinib 15-10-5 mg BID	9	5.67	6.69	118.05	0.0	0.0	2.0	9.0	16.0
	Tofacitinib 30-15-10 mg BID	6	17.67	23.11	130.79	0.0	0.0	7.0	37.0	55.0
Follow-up	Tacrolimus	2	0.00	0.00		0.0	0.0	0.0	0.0	0.0
	Tofacitinib 15-10-5 mg BID	4	12.75	24.84	194.81	0.0	0.0	0.5	25.5	50.0
	Tofacitinib 30-15-10 mg BID	4	2.00	4.00	200.00	0.0	0.0	0	4.0	8.0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; CV = coefficient of variation; DNA = deoxyribonucleic acid; EBV = Epstein-Barr virus; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; PCR = polymerase chain reaction; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 29. Percent of Subjects with EBV DNA by PCR Meeting Cutoffs (in number of copies/PCR) by Visit (Safety Analysis Set)

			Subjects with EBV DNA by PCR									
			0		1-50		51-100		101-1000		>1000	
Visit	Treatment	N	n	%	n	%	n	%	n	%	n	%
Month 9	Tacrolimus	17	15	88.2	2	11.8	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	14	10	71.4	4	28.6	0	0	0	0	0	0
	Tofacitinib 30-15-10 mg BID	12	4	33.3	8	66.7	0	0	0	0	0	0
Month 12	Tacrolimus	17	16	94.1	1	5.9	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	14	9	64.3	5	35.7	0	0	0	0	0	0
	Tofacitinib 30-15-10 mg BID	12	4	33.3	7	58.3	1	8.3	0	0	0	0
Month 15	Tacrolimus	17	15	88.2	1	5.9	1	5.9	0	0	0	0
	Tofacitinib 15-10-5 mg BID	14	8	57.1	5	35.7	1	7.1	0	0	0	0
	Tofacitinib 30-15-10 mg BID	12	5	41.7	6	50.0	1	8.3	0	0	0	0
Month 18	Tacrolimus	17	15	88.2	2	11.8	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	13	7	53.8	4	30.8	1	7.7	1	7.7	0	0
	Tofacitinib 30-15-10 mg BID	12	5	41.7	5	41.7	2	16.7	0	0	0	0
Month 24	Tacrolimus	15	15	100.0	0	0	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	13	8	61.5	4	30.8	1	7.7	0	0	0	0
	Tofacitinib 30-15-10 mg BID	12	4	33.3	7	58.3	1	8.3	0	0	0	0
Month 30	Tacrolimus	13	11	84.6	2	15.4	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	14	6	42.9	7	50.0	0	0	1	7.1	0	0
	Tofacitinib 30-15-10 mg BID	10	3	30.0	6	60.0	0	0	1	10	0	0
Month 36	Tacrolimus	15	13	86.7	2	13.3	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	14	8	57.1	5	35.7	1	7.1	0	0	0	0
	Tofacitinib 30-15-10 mg BID	8	2	25.0	5	62.5	0	0	1	12.5	0	0
Month 42	Tacrolimus	14	13	92.9	1	7.1	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	12	4	33.3	7	58.3	1	8.3	0	0	0	0
	Tofacitinib 30-15-10 mg BID	9	2	22.2	6	66.7	1	11.1	0	0	0	0
Month 48	Tacrolimus	15	14	93.3	1	6.7	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	9	6	66.7	1	11.1	2	22.2	0	0	0	0
	Tofacitinib 30-15-10 mg BID	6	0	0	5	83.3	1	16.7	0	0	0	0

Table 29. Percent of Subjects with EBV DNA by PCR Meeting Cutoffs (in number of copies/PCR) by Visit (Safety Analysis Set)

			Subjects with EBV DNA by PCR									
			0		1-50		51-100		101-1000		>1000	
Visit	Treatment	N	n	%	n	%	n	%	n	%	n	%
Month 54	Tacrolimus	14	8	7.1	6	42.9	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	14	7	50.0	6	42.9	1	7.1	0	0	0	0
	Tofacitinib 30-15-10 mg BID	10	3	300	7	70.0	0	0	0	0	0	0
Month 60	Tacrolimus	13	10	76.9	3	23.1	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	13	8	61.5	4	30.8	1	7.7	0	0	0	0
	Tofacitinib 30-15-10 mg BID	10	1	10.0	8	80.0	1	10.0	0	0	0	0
Month 66	Tacrolimus	10	8	80.0	2	20.0	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	13	5	38.5	6	46.2	2	15.4	0	0	0	0
	Tofacitinib 30-15-10 mg BID	9	0	0	5	55.6	4	44.4	0	0	0	0
Month 72	Tacrolimus	9	8	88.9	1	11.1	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	12	5	41.7	6	50.0	1	8.3	0	0	0	0
	Tofacitinib 30-15-10 mg BID	8	3	37.5	4	50.0	0	0	1	12.5	0	0
Month 78	Tacrolimus	0	0		0		0		0		0	
	Tofacitinib 15-10-5 mg BID	12	5	41.7	7	58.3	0	0	0	0	0	0
	Tofacitinib 30-15-10 mg BID	8	2	25.0	5	62.5	0	0	1	12.5	0	0
Month 84	Tacrolimus	0	0		0		0		0		0	
	Tofacitinib 15-10-5 mg BID	12	6	50.0	6	50.0	0	0	0	0	0	0
	Tofacitinib 30-15-10 mg BID	8	1	12.5	6	750	1	12.5	0	0	0	0
Month 90	Tacrolimus	0	0		0		0		0		0	
	Tofacitinib 15-10-5 mg BID	12	7	58.3	5	41.7	0	0	0	0	0	0
	Tofacitinib 30-15-10 mg BID	7	3	42.9	3	42.9	1	14.3	0	0	0	0
Month 96	Tacrolimus	0	0		0		0		0		0	
	Tofacitinib 15-10-5 mg BID	9	3	33.3	6	66.7	0	0	0	0	0	0
	Tofacitinib 30-15-10 mg BID	6	2	33.3	3	50.0	1	16.7	0	0	0	0

Table 29. Percent of Subjects with EBV DNA by PCR Meeting Cutoffs (in number of copies/PCR) by Visit (Safety Analysis Set)

			Subjects with EBV DNA by PCR									
			0		1-50		51-100		101-1000		>1000	
Visit	Treatment	N	n	%	n	%	n	%	n	%	n	%
Follow-up	Tacrolimus	2	2	100.0	0	0	0	0	0	0	0	0
	Tofacitinib 15-10-5 mg BID	4	2	50.0	2	50.0	0	0	0	0	0	0
	Tofacitinib 30-15-10 mg BID	4	3	75.0	1	25.0	0	0	0	0	0	0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

Abbreviations: BID = twice daily; CV = coefficient of variation; DNA = deoxyribonucleic acid; EBV = Epstein-Barr virus; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; n = number of subjects in each category; PCR = polymerase chain reaction; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

BKV DNA levels by PCR: Descriptive statistics for BKV DNA by PCR (number of copies/PCR), and percentages of subjects meeting cut-offs, are presented by visit for the Safety Analysis Set in Table 30 and Table 29, respectively.

In the tofacitinib 15-10-5 mg BID group, mean BKV DNA levels ranged from 0 copies/PCR (Month 24, 2 subjects with a value) to 15.85 copies/PCR (Month 60, 13 subjects with a value).

In the tofacitinib 30-15-10 mg BID group, mean BKV DNA levels ranged from 0 copies/PCR (Month 24, Month 30, 1 subject with a value at each visit) to 6.75 copies/PCR (Month 36, 4 subjects with a value).

In both tofacitinib groups, no subject had BKV DNA level ≥200 copies/PCR in plasma at any visit.

Table 30. Descriptive Statistics of BKV DNA by PCR (number of copies/PCR) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Tofacitinib 15-10-5 mg BID	14	1.29	4.53	352.39	0.0	0.0	0.0	0.0	17.0
	Tofacitinib 30-15-10 mg BID	12	1.58	2.84	179.57	0.0	0.0	0.0	1.5	8.0
Month 12	Tofacitinib 15-10-5 mg BID	13	2.23	3.81	170.85	0.0	0.0	0.0	1.0	10.0
	Tofacitinib 30-15-10 mg BID	10	0.10	0.32	316.23	0.0	0.0	0.0	0.0	1.0
Month 15	Tofacitinib 15-10-5 mg BID	13	2.85	7.66	269.06	0.0	0.0	0.0	2.0	28.0
	Tofacitinib 30-15-10 mg BID	12	0.75	0.97	128.71	0.0	0.0	0.5	1.0	3.0
Month 18	Tofacitinib 15-10-5 mg BID	7	0.14	0.38	264.58	0.0	0.0	0.0	0.0	1.0
	Tofacitinib 30-15-10 mg BID	8	0.38	0.74	198.41	0.0	0.0	0.0	0.5	2.0
Month 24	Tofacitinib 15-10-5 mg BID	2	0.00	0.00		0.0	0.0	0.0	0.0	0.0
	Tofacitinib 30-15-10 mg BID	1	0.00			0.0	0.0	0.0	0.0	0.0
Month 30	Tofacitinib 30-15-10 mg BID	1	0.00			0.0	0.0	0.0	0.0	0.0
Month 36	Tofacitinib 15-10-5 mg BID	5	15.80	34.77	220.09	0.0	0.0	0.0	1.0	78.0
	Tofacitinib 30-15-10 mg BID	4	6.75	13.50	200.00	0.0	0.0	0.0	13.5	27.0
Month 42	Tofacitinib 15-10-5 mg BID	11	0.64	2.11	331.66	0.0	0.0	0.0	0.0	7.0
	Tofacitinib 30-15-10 mg BID	7	1.86	4.49	241.67	0.0	0.0	0.0	1.0	12.0
Month 48	Tofacitinib 15-10-5 mg BID	9	8.33	23.18	278.21	0.0	0.0	0.0	0.0	70.0
	Tofacitinib 30-15-10 mg BID	6	3.33	8.16	244.95	0.0	0.0	0.0	0.0	20.0
Month 54	Tofacitinib 15-10-5 mg BID	13	4.54	14.66	322.91	0.0	0.0	0.0	0.0	53.0
	Tofacitinib 30-15-10 mg BID	10	1.40	3.78	269.79	0.0	0.0	0.0	0.0	12.0
Month 60	Tofacitinib 15-10-5 mg BID	13	15.85	41.81	263.84	0.0	0.0	0.0	2.0	147.0
	Tofacitinib 30-15-10 mg BID	7	0.86	2.27	264.58	0.0	0.0	0.0	0.0	6.0
Month 66	Tofacitinib 15-10-5 mg BID	13	6.15	21.00	341.30	0.0	0.0	0.0	0.0	76.0
	Tofacitinib 30-15-10 mg BID	8	0.00	0.00		0.0	0.0	0.0	0.0	0.0
Month 72	Tofacitinib 15-10-5 mg BID	10	1.00	2.83	282.84	0.0	0.0	0.0	0.0	9.0
	Tofacitinib 30-15-10 mg BID	7	0.14	0.38	264.58	0.0	0.0	0.0	0.0	1.0
Month 78	Tofacitinib 15-10-5 mg BID	9	0.56	1.13	203.47	0.0	0.0	0.0	0.0	3.0

Table 30. Descriptive Statistics of BKV DNA by PCR (number of copies/PCR) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
	Tofacitinib 30-15-10 mg BID	7	0.14	0.38	264.58	0.0	0.0	0.0	0.0	1.0
Month 84	Tofacitinib 15-10-5 mg BID	10	0.60	1.90	316.23	0.0	0.0	0.0	0.0	6.0
	Tofacitinib 30-15-10 mg BID	7	0.14	0.38	264.58	0.0	0.0	0.0	0.0	1.0
Month 90	Tofacitinib 15-10-5 mg BID	9	0.56	1.67	300.00	0.0	0.0	0.0	0.0	5.0
	Tofacitinib 30-15-10 mg BID	4	0.00	0.00		0.0	0.0	0.0	0.0	0.0
Month 96	Tofacitinib 15-10-5 mg BID	9	1.11	2.67	240.00	0.0	0.0	0.0	0.0	8.0
	Tofacitinib 30-15-10 mg BID	3	0.00	0		0.0	0.0	0.0	0.0	0.0
Follow-up	Tofacitinib 15-10-5 mg BID	3	0	0.00		0.0	0.0	0.0	0.0	0.0
	Tofacitinib 30-15-10 mg BID	2	0.5	0.71	141.42	0	0.0	0.5	1.0	1.0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; BKV = BK virus; CV = coefficient of variation; DNA = deoxyribonucleic acid; Max = maximum; Min = minimum; N = number of subjects in Safety Analysis Set per visit with non-missing value; PCR = polymerase chain reaction; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Table 31. Percent of Subjects with EBV DNA by PCR Meeting Cutoffs (in number of copies/PCR) by Visit (Safety Analysis Set)

			Subjects with BKV DNA by PCR				
			0-199			≥200	
Visit	Treatment	N	n	%		n	%
Month 9	Tofacitinib 15-10-5 mg BID	14	14	100.0		0	0
	Tofacitinib 30-15-10 mg BID	12	12	100.0		0	0
Month 12	Tofacitinib 15-10-5 mg BID	13	13	100.0		0	0
	Tofacitinib 30-15-10 mg BID	10	10	100.0		0	0
Month 15	Tofacitinib 15-10-5 mg BID	13	13	100.0		0	0
	Tofacitinib 30-15-10 mg BID	12	12	100.0		0	0
Month 18	Tofacitinib 15-10-5 mg BID	7	7	100.0		0	0
	Tofacitinib 30-15-10 mg BID	8	8	100.0		0	0
Month 24	Tofacitinib 15-10-5 mg BID	2	2	100.0		0	0
	Tofacitinib 30-15-10 mg BID	1	1	100.0		0	0
Month 30	Tofacitinib 15-10-5 mg BID	0	0	100.0		0	0
	Tofacitinib 30-15-10 mg BID	1	1	100.0		0	0
Month 36	Tofacitinib 15-10-5 mg BID	5	5	100.0		0	0
	Tofacitinib 30-15-10 mg BID	4	4	100.0		0	0
Month 42	Tofacitinib 15-10-5 mg BID	11	11	100.0		0	0
	Tofacitinib 30-15-10 mg BID	7	7	100.0		0	0
Month 48	Tofacitinib 15-10-5 mg BID	9	9	100.0		0	0
	Tofacitinib 30-15-10 mg BID	6	6	100.0		0	0
Month 54	Tofacitinib 15-10-5 mg BID	13	13	100.0		0	0
	Tofacitinib 30-15-10 mg BID	10	10	100.0		0	0
Month 60	Tofacitinib 15-10-5 mg BID	13	13	100.0		0	0
	Tofacitinib 30-15-10 mg BID	7	7	100.0		0	0
Month 66	Tofacitinib 15-10-5 mg BID	13	13	100.0		0	0
	Tofacitinib 30-15-10 mg BID	8	8	100.0		0	0
Month 72	Tofacitinib 15-10-5 mg BID	10	10	100.0		0	0
	Tofacitinib 30-15-10 mg BID	7	7	100.0		0	0
Month 78	Tofacitinib 15-10-5 mg BID	9	9	100.0		0	0
	Tofacitinib 30-15-10 mg BID	7	7	100.0		0	0
Month 84	Tofacitinib 15-10-5 mg BID	10	10	100.0		0	0
	Tofacitinib 30-15-10 mg BID	7	7	100.0		0	0
Month 90	Tofacitinib 15-10-5 mg BID	9	9	100.0		0	0
	Tofacitinib 30-15-10 mg BID	4	4	100.0		0	0
Month 96	Tofacitinib 15-10-5 mg BID	9	9	100.0		0	0
	Tofacitinib 30-15-10 mg BID	3	3	100.0		0	0

Table 31. Percent of Subjects with EBV DNA by PCR Meeting Cutoffs (in number of copies/PCR) by Visit (Safety Analysis Set)

			Subjects with BKV DNA by PCR				
			0-199			≥200	
Visit	Treatment	N	n	%		n	%
Follow-up	Tofacitinib 15-10-5 mg BID	3	3	100.0		0	0
	Tofacitinib 30-15-10 mg BID	2	2	100.0		0	0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; BKV = BK virus; CV = coefficient of variation; DNA = deoxyribonucleic acid; Max = maximum; Min = minimum; N= number of subjects in Safety Analysis Set per visit with non-missing value; n = number of subjects in each category; PCR = polymerase chain reaction; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

CMV disease: Percentages of subjects with CMV disease (including CMV syndrome) are presented by visit in Table 32.

Only 2 subjects developed first CMV disease in Study A3921021 (1 subject in the tacrolimus group and 1 subject in the tofacitinib 15-10-5 mg BID group]).

Table 32. Percent of Subjects with CMV Disease (including CMV Syndrome) estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

		Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						90% CI				80% CI			
Visit	Treatment	Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Day 1	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	0.00	0.00	0.00	0.00		
Month 1	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	0.00	0.00	0.00	0.00		
Month 3	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	
Month 6	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	
Month 9	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	7.14	6.88	-1.68	15.96	0.2994	
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	
Month 12	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	7.14	6.88	-1.68	15.96	0.2994	
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	
Month 15	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	
Month 18	Tacrolimus	1	16	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	

Table 32. Percent of Subjects with CMV Disease (including CMV Syndrome) estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						90% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 24	Tacrolimus	1	16	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	
Month 30	Tacrolimus	1	14	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	11	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	
Month 36	Tacrolimus	1	14	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	11	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	
Month 42	Tacrolimus	1	14	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	10	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	
Month 48	Tacrolimus	1	13	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	10	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	
Month 54	Tacrolimus	1	13	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	10	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	
Month 60	Tacrolimus	1	12	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	10	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	
Month 66	Tacrolimus	1	12	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	9	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	

Table 32. Percent of Subjects with CMV Disease (including CMV Syndrome) estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Safety Analysis Set)

		Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						90% CI				80% CI			
Visit	Treatment	Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 72	Tacrolimus	1	5	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	1	8	7.69	7.39	0.00	17.16	2.14	9.15	-9.59	13.87	0.8154	
Month 78	Tacrolimus	1	0										
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	1	8	7.69	7.39	0.00	17.16						
Month 84	Tacrolimus	1	0										
	Tofacitinib 15-10-5 mg BID	1	12	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	1	8	7.69	7.39	0.00	17.16						
Month 90	Tacrolimus	1	0										
	Tofacitinib 15-10-5 mg BID	1	12	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	1	8	7.69	7.39	0.00	17.16						
Month 96	Tacrolimus	1	0										
	Tofacitinib 15-10-5 mg BID	1	12	7.14	6.88	0.00	15.96						0.8379
	Tofacitinib 30-15-10 mg BID	1	7	7.69	7.39	0.00	17.16						0.7950

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
Abbreviations: BID = twice daily dosing; CI = confidence interval; CMV = cytomegalovirus; Cum.=cumulative; Diff. = difference; N = number of subjects; No. = number; SE = standard error.

Non-serious treatment-emergent AEs (TEAEs): Non-serious TEAEs reported in ≥5% of subjects are presented in Table 33. The most frequently reported all-causality non-serious TEAEs were those coded to the Medical Dictionary for Regulatory Activities (MedDRA) System Order Class (SOC) of Infections and Infestations (31 subjects: 11 [61.1%] subjects on tacrolimus, 12 [86.5%] subjects on tofacitinib 15-10-5 mg BID and 8 [61.5%] subjects on tofacitinib 30-15-10 mg BID) and Gastrointestinal Disorders (30 subjects: 14 [77.8%] subjects on tacrolimus, 10 [71.4%] subjects on tofacitinib 15-10-5 mg BID and 6 [46.2%] subjects on tofacitinib 30-15-10 mg BID).

The most common non-serious TEAE (all-causality) by preferred term (PT) was diarrhea (16 subjects in total: 10 [55.6%] subjects on tacrolimus, 5 [35.7%] subjects on tofacitinib 15-10-5 mg BID and 1 [7.7%] subject on tofacitinib 30-15-10 mg BID), followed by upper respiratory tract infection (12 subjects in total: 2 [11.1%] subjects on tacrolimus, 5 [35.7%] subjects on tofacitinib 15-10-5 mg BID and 5 [38.5%] subjects on tofacitinib 30-15-10 mg BID).

Non-serious treatment-related TEAEs reported in ≥5% of subjects are presented in Table 34. The most frequently reported non-serious TEAEs considered to be treatment-related were those coded to the MedDRA SOCs of Infections and Infestations (20 subjects in total: 7 [38.9%] subjects on tacrolimus, 7 [50.0%] subjects on tofacitinib 15-10-5 mg BID, and 6 [46.2%] subjects on tofacitinib 30-15-10 mg BID) and Skin and Subcutaneous Tissue Disorders (13 subjects in total: 4 [22.2%] subjects on tacrolimus, 4 [28.6%] subjects on tofacitinib 15-10-5 mg BID, 5 [38.5%] subjects on tofacitinib 30-15-10 mg BID).

The most common non-serious TEAE (treatment-related) by PT was herpes zoster (5 subjects in total: 1 [5.6%] subjects on tacrolimus, 3 [21.4%] subjects on tofacitinib 15-10-5 mg BID and 1 [7.7%] subject on tofacitinib 30-15-10 mg BID), followed by anaemia, urinary tract infection and rash, which were each reported in a total of 4 subjects.

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
	n (%)	n1*	n2**	n (%)	n1*	n2**	n (%)	n1*	n2**
Number (%) of subjects with AEs	17 (94.4)			14 (100.0)			11 (84.6)		
Blood and lymphatic system disorders	7 (38.9)	10	2	1 (7.1)	1	1	4 (30.8)	5	3
Anaemia	3 (16.7)	4	1	1 (7.1)	1	1	2 (15.4)	2	2
Leukopenia	2 (11.1)	3	1	0	0	0	1 (7.7)	1	1
Lymphadenopathy	1 (5.6)	1	0	0	0	0	1 (7.7)	1	0
Neutropenia	1 (5.6)	1	0	0	0	0	1 (7.7)	1	0
Polycythaemia	1 (5.6)	1	0	0	0	0	0	0	0
Cardiac disorders	3 (16.7)	4	0	6 (42.9)	7	0	2 (15.4)	2	1
Arrhythmia	0	0	0	1 (7.1)	1	0	0	0	0
Atrial fibrillation	1 (5.6)	1	0	1 (7.1)	1	0	0	0	0
Bradycardia	0	0	0	0	0	0	1 (7.7)	1	0
Cardiac flutter	0	0	0	1 (7.1)	0	0	0	0	0
Hypertensive heart disease	1 (5.6)	1	0	0	0	0	0	0	0
Palpitations	1 (5.6)	1	0	0	0	0	1 (7.7)	1	1
Sinus bradycardia	0	0	0	4 (28.6)	4	0	0	0	0
Sinus tachycardia	1 (5.6)	1	0	0	0	0	0	0	0
Ventricular extrasystoles	0	0	0	1 (7.1)	1	0	0	0	0
Ear and labyrinth disorders	5 (27.8)	7	1	1 (7.1)	1	0	0	0	0
Cerumen impaction	0	0	0	1 (7.1)	1	0	0	0	0
Ear discomfort	1 (5.6)	1	0	0	0	0	0	0	0
Ear disorder	1 (5.6)	1	0	0	0	0	0	0	0
Ear pain	1 (5.6)	2	0	0	0	0	0	0	0
Hearing impaired	1 (5.6)	1	0	0	0	0	0	0	0
Hypoacusis	2 (11.1)	2	0	0	0	0	0	0	0
Eye disorders	2 (11.1)	2	0	5 (35.7)	5	0	2 (15.4)	2	0
Blepharitis	0	0	0	1 (7.1)	1	0	0	0	0
Cataract	0	0	0	1 (7.1)	1	0	0	0	0

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
	n (%)	n1*	n2**	n (%)	n1*	n2**	n (%)	n1*	n2**
Conjunctival haemorrhage	0	0	0	0	0	0	1 (7.7)	1	0
Eye swelling	0	0	0	0	0	0	1 (7.7)	1	0
Glaucoma	0	0	0	1 (7.1)	1	0	0	0	0
Hyphaema	1 (5.6)	1	0	0	0	0	0	0	0
Vision blurred	0	0	1 (7.1)	1	0		0	0	0
Visual acuity reduced	1 (5.6)	1	0	0	0	0	0	0	0
Visual impairment	0	0	0	1 (7.1)	1	0	0	0	0
Gastrointestinal disorders	14 (77.8)	26	2	10 (71.4)	27	2	6 (46.2)	14	4
Abdominal discomfort	1 (5.6)	1	0	0	0	0	0	0	0
Abdominal distension	1 (5.6)	1	0	0	0	0	0	0	0
Abdominal pain	1 (5.6)	1	0	2 (14.3)	2	0	2 (15.4)	2	0
Abdominal pain lower	2 (11.1)	2	0	1 (7.1)	1	0	1 (7.7)	1	0
Abdominal pain upper	2 (11.1)	2	0	2 (14.3)	2	0	0	0	0
Constipation	0	0	0	1 (7.1)	1	0	2 (15.4)	3	2
Diarrhoea	10 (55.6)	12	2	5 (35.7)	10	1	1 (7.7)	1	0
Dyspepsia	2 (11.1)	2	0	0	0	0	3 (23.1)	3	1
Dysphagia	1 (5.6)	1	0	0	0	0	0	0	0
Eructation	0	0	0	1 (7.1)	1	0	0	0	0
Food poisoning	0	0	0	1 (7.1)	1	1	0	0	0
Gastrointestinal disorder	0	0	0	1 (7.1)	1	0	0	0	0
Gastrooesophageal reflux disease	1 (5.6)	1	0	1 (7.1)	1	0	0	0	0
Gingival hypertrophy	1 (5.6)	1	0	0	0	0	0	0	0
Glossodynia	0	0	0	0	0	0	1 (7.7)	1	0
Inguinal hernia	1 (5.6)	1	0	0	0	0	0	0	0
Lip blister	0	0	0	1 (7.1)	1	0	0	0	0
Nausea	0	0	0	2 (14.3)	2	0	2 (15.4)	2	1
Toothache	0	0	0	1 (7.1)	1	0	0	0	0
Umbilical hernia	0	0	0	0	0	0	1	1	0
Vomiting	1 (5.6)	1	0	3 (21.4)	3	0	0	0	0

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
	n (%)	n1*	n2**	n (%)	n1*	n2**	n (%)	n1*	n2**
General disorders and administration site conditions	9 (50.0)	14	3	8 (57.1)	10	1	7 (53.8)	17	7
Asthenia	0	0	0	1 (7.1)	1	0	1 (7.7)	1	1
Chest pain	1 (5.6)	1	0	0	0	0	0	0	0
Fatigue	4 (22.2)	4	1	2 (14.3)	2	0	4 (30.8)	5	3
Gravitational oedem	1 (5.6)	1	0	0	0	0	0	0	0
Oedema	1 (5.6)	1	0	0	0	0	0	0	0
Oedema peripheral	2 (11.1)	2	0	5 (35.7)	5	1	3 (23.1)	3	0
Pain	1 (5.6)	1	1	0	0	0	0	0	0
Peripheral swelling	1 (5.6)	1	0	0	0	0	2 (15.4)	4	1
Pyrexia	2 (11.1)	2	1	2 (14.3)	2	0	2 (15.4)	4	2
Sluggishness	1 (5.6)	1	0	0	0	0	0	0	0
Hepatobiliary disorders	1 (5.6)	1	1	0	0	0	0	0	0
Biliary dyskinesia	1 (5.6)	1	0	0	0	0	0	0	0
Immune system disorders	3 (16.7)	4	0	1 (7.1)	0	0	2 (15.4)	3	1
Allery to arthropod bite	0	0	0	1 (7.1)	0	0	0	0	0
Kidney transplant rejection	1 (5.6)	1	0	0	0	0	0	0	0
Multiple allergies	0	0	0	0	0	0	1 (7.7)	1	0
Seasonal allergy	2 (11.1)	2	0	0	0	0	1 (7.7)	1	0
Transplant rejection	1 (5.6)	1	0	0	0	0	1 (7.7)	1	1
Infections and infestations	11 (61.1)	28	14	12 (86.5)	69	17	8 (61.5)	29	9
Acute sinusitis	0	0	0	1 (7.1)	1	0	0	0	0
BK virus infection	1 (5.6)	1	0	2 (14.3)	2	1	0	0	0
Bacterial vaginosis	0	0	0	2 (14.3)	1	0	0	0	0
Bronchitis	1 (5.6)	1	1	0	0	0	2 (15.4)	4	1
Bronchitis viral	0	0	0	0	0	0	1 (7.7)	1	1
Cellulitis	0	0	0	2 (14.3)	2	0	0	0	0
Chronic sinusitis	1 (5.6)	1	0	0	0	0	0	0	0

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
	n (%)	n1*	n2**	n (%)	n1*	n2**	n (%)	n1*	n2**
Conjunctivitis	0	0	0	1 (7.1)	1	1	0	0	0
Cystitis	0	0	0	1 (7.1)	8	1	0	0	0
Cytomegalovirus infection	1 (5.6)	1	1	1 (7.1)	1	1	1 (7.7)	1	1
Ear infection	1 (5.6)	1	0	1 (7.1)	4	0	0	0	0
Epstein-Barr virus infection	0	0	0	0	0	0	1 (7.7)	1	1
Folliculitis	1 (5.6)	3	1	0	0	0	0	0	0
Fungal infection	1 (5.6)	1	0	0	0	0	0	0	0
Gastroenteritis	0	0	0	0	0	0	1 (7.7)	1	0
Gastroenteritis viral	1 (5.6)	1	1	1 (7.1)	1	0	0	0	0
Herpes simplex	0	0	0	1 (7.1)	1	0	0	0	0
Herpes virus infection	0	0	0	1 (7.1)	1	0	0	0	0
Herpes zoster	1 (5.6)	1	1	5 (35.7)	12	6	1 (7.7)	1	1
Hordeolum	0	0	0	1 (7.1)	1	0	0	0	0
Incision site abscess	1 (5.6)	1	1	0	0	0	0	0	0
Infected cyst	0	0	0	0	0	0	1 (7.7)	1	1
Influenza	2 (11.1)	2	0	0	0	0	0	0	0
Localised infection	0	0	0	1 (7.1)	1	1	0	0	0
Nasopharyngitis	2 (11.1)	2	1	0	0	0	2 (15.4)	2	0
Oesophageal candidiasis	0	0	0	0	0	0	1 (7.7)	2	0
Onychomycosis	0	0	0	0	0	0	1 (7.7)	2	0
Oral candidiasis	1 (5.6)	1	1	0	0	0	1 (7.7)	1	0
Oral fungal infection	0	0	0	0	0	0	1 (7.7)	1	1
Oral herpes	0	0	0	3 (21.4)	3	0	0	0	0
Papilloma viral infection	0	0	0	1 (7.1)	1	0	0	0	0
Pharyngitis	0	0	0	0	0	0	1 (7.7)	1	0
Pneumonia	0	0	0	1 (7.1)	2	1	0	0	0
Pyelonephritis	1 (5.6)	1	0	0	0	0	0	0	0
Sinusitis	1 (5.6)	2	0	2 (14.3)	2	0	1 (7.7)	1	0
Skin candida	1 (5.6)	1	1	0	0	0	0	0	0
Subcutaneous abscess	0	0	0	1 (7.1)	1	0	0	0	0
Tinea cruris	0	0	0	0	0	0	1 (7.7)	1	0

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18) n (%)	 n1*	 n2**	Tofacitinib 15-10-5 (N=14) n (%)	 n1*	 n2**	Tofacitinib 30-15-10 (N=13) n (%)	 n1*	 n2**
Tinea versicolour	1 (5.6)	1	1	1 (7.1)	1	1	0	0	0
Tooth abscess	0	0	0	0	0	0	1 (7.7)	1	0
Tooth infection	0	0	0	1 (7.1)	1	0	0	0	0
Upper respiratory tract infection	2 (11.1)	2	1	5 (35.7)	6	0	5 (38.5)	7	2
Urinary tract infection	3 (16.7)	4	3	5 (35.7)	14	3	0	0	0
Urosepsis	0	0	0	1 (7.1)	1	1	0	0	0
Injury, poisoning and procedural complications	2 (11.1)	3	1	5 (35.7)	8	2	7 (53.8)	12	1
Chloracne	0	0	0	0	0	0	1 (7.7)	1	1
Complications of transplant surgery	0	0	0	0	0	0	1 (7.7)	1	0
Complications of transplanted kidney	1 (5.6)	1	1	1 (7.1)	2	2	0	0	0
Contusion	1 (5.6)	1	0	0	0	0	1 (7.7)	1	0
Fall	1 (5.6)	1	0	0	0	0	1 (7.7)	1	0
Foot fracture	0	0	0	1 (7.1)	1	0	2 (15.4)	3	0
Ligament rupture	0	0	0	0	0	0	1 (7.7)	2	0
Ligament sprain	0	0	0	0	0	0	1 (7.7)	1	0
Patella fracture	0	0	0	0	0	0	1 (7.7)	1	0
Post-traumatic neck syndrome	0	0	0	1 (7.1)	1	0	0	0	0
Repetitive strain injury	0	0	0	1 (7.1)	1	0	0	0	0
Road traffic accident	0	0	0	0	0	0	1 (7.7)	1	0
Scratch	0	0	0	1 (7.1)	1	0	0	0	0
Tendon rupture	0	0	0	2 (14.3)	2	0	0	0	0
Investigations	6 (33.3)	14	2	8 (57.1)	16	3	9 (69.2)	28	7
Alanine aminotransferase increased	0	0	0	1 (7.1)	1	1	2 (15.4)	2	0
Arterial bruit	1 (5.6)	1	0	0	0	0	0	0	0
Aspartate aminotransferase increased	0	0	0	1 (7.1)	1	1	3 (23.1)	3	1
Blood alkaline phosphatase increased	0	0	0	0	0	0	1 (7.7)	1	0

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
System Organ Class Preferred Term	**n (%)**	**n1***	**n2****	**n (%)**	**n1***	**n2****	**n (%)**	**n1***	**n2****
Blood calcium decreased	1 (5.6)	1	0	0	0	0	0	0	0
Blood cholesterol increased	0	0	0	0	0	0	1 (7.7)	1	0
Blood creatine phosphokinase increased	0	0	0	0	0	0	1 (7.7)	1	1
Blood creatinine increased	2 (11.1)	2	0	1 (7.1)	1	0	1 (7.7)	1	0
Blood culture positive	1 (5.6)	1	0	0	0	0	0	0	0
Blood glucose decreased	0	0	0	0	0	0	1 (7.7)	1	0
Blood glucose increased	0	0	0	0	0	0	2 (15.4)	2	0
Blood potassium decreased	1 (5.6)	1	0	0	0	0	0	0	0
Blood pressure decreased	0	0	0	1 (7.1)	1	0	0	0	0
Blood pressure increased	1 (5.6)	1	0	0	0	0	1 (7.7)	1	0
Blood triglycerides increased	0	0	0	1 (7.1)	1	1	1 (7.7)	1	0
Cardiac murmur	0	0	0	2 (14.3)	2	0	0	0	0
Culture urine positive	0	0	0	0	0	0	1 (7.7)	1	1
Electrocardiogram P wave abnormal	0	0	0	1 (7.1)	1	0	0	0	0
Gamma-glutamyltransferase increased	0	0	0	0	0	0	2 (15.4)	3	3
Glycosylated haemoglobin increased	0	0	0	1 (7.1)	1	0	2 (15.4)	2	0
Liver function test abnormal	0	0	0	0	0	0	1 (7.7)	1	0
Low density lipoprotein increased	0	0	0	0	0	0	1 (7.7)	2	0
QRS axis abnormal	1 (5.6)	1	0	1 (7.1)	1	0	0	0	0
Vascular resistance systemic increased	0	0	0	1 (7.1)	1	0	0	0	0
Viral test positive	1 (5.6)	2	2	1 (7.1)	1	0	1 (7.7)	1	1
Vitamin D decreased	1 (5.6)	1	0	0	0	0	0	0	0
Weight decreased	1 (5.6)	1	0	3 (21.4)	3	0	0	0	0
Weight increased	2 (11.1)	2	0	1 (7.1)	1	0	4 (30.8)	4	0
Metabolism and nutrition disorders	7 (38.0)	17	2	7 (50.0)	12	2	4 (30.8)	8	2
Abnormal loss of weight	0	0	0	1 (7.1)	1	0	0	0	0
Dehydration	2 (11.1)	2	0	0	0	0	0	0	0
Fluid retention	0	0	0	1 (7.1)	1	1	0	0	0
Hypercalcaemia	0	0	0	1 (7.1)	1	0	1 (7.7)	1	0

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
System Organ Class Preferred Term	**n (%)**	**n1***	**n2****	**n (%)**	**n1***	**n2****	**n (%)**	**n1***	**n2****
Hypercholesterolaemia	0	0	0	0	0	0	2 (15.4)	2	1
Hyperglycaemia	0	0	0	0	0	0	2 (15.4)	2	0
Hyperlipidaemia	3 (16.7)	3	0	1 (7.1)	1	1	1 (7.7)	2	1
Hypocalcaemia	1 (5.6)	1	0	1 (7.1)	1	0	0	0	0
Hypoglycaemia	0	0	0	2 (14.3)	2	0	0	0	0
Hypokalaemia	3 (16.7)	5	1	1 (7.1)	1	0	0	0	0
Hypomagnesaemia	2 (11.1)	2	0	0	0	0	0	0	0
Hypophosphataemia	1 (5.6)	2	1	0	0	0	0	0	0
Increased appetite	0	0	0	1 (7.1)	1	0	0	0	0
Lactic acidosis	0	0	0	1 (7.1)	1	0	0	0	0
Magnesium deficiency	1 (5.6)	1	0	0	0	0	0	0	0
Obesity	0	0	0	1 (7.1)	2	0	1 (7.7)	1	0
Type 2 diabetes mellitus	1 (5.6)	1	0	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	8 (44.4)	13	2	8 (57.1)	18	1	7 (53.8)	23	5
Arthralgia	2 (11.1)	2	0	1 (7.1)	2	0	4 (30.8)	5	2
Arthritis	0	0	0	1 (7.1)	2	0	1 (7.7)	1	1
Back pain	2 (11.1)	2	0	0	0	0	3 (23.1)	3	1
Bone metabolism disorder	0	0	0	1 (7.1)	1	0	1 (7.7)	1	0
Bone pain	0	0	0	0	0	0	1 (7.7)	1	1
Chondrocalcinosis pyrophosphate	0	0	0	1 (7.1)	2	0	0	0	0
Foot deformity	0	0	0	1 (7.1)	1	0	0	0	0
Groin pain	0	0	0	0	0	0	1 (7.7)	1	0
Muscle spasms	3 (16.7)	3	0	1 (7.1)	1	0	1 (7.7)	1	0
Musculoskeletal pain	0	0	0	0	0	0	2 (15.4)	2	0
Musculoskeletal stiffness	1 (5.6)	1	0	0	0	0	1 (7.7)	1	0
Myalgia	1 (5.6)	1	1	2 (14.3)	2	0	0	0	0
Neck pain	0	0	0	1 (7.1)	1	0	1 (7.7)	1	0
Osteoarthritis	1 (5.6)	1	0	1 (7.1)	1	0	1 (7.7)	1	0
Pain in extremity	2 (11.1)	2	0	0	0	0	4 (30.8)	4	0

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
	n (%)	n1*	n2**	n (%)	n1*	n2**	n (%)	n1*	n2**
Plantar fasciitis	0	0	0	2 (14.3)	2	1	1 (7.7)	1	0
Synovial cyst	0	0	0	1 (7.1)	1	0	0	0	0
Synovitis	1 (5.6)	1	1	0	0	0	0	0	0
Tendonitis	0	0	0	1 (7.1)	1	0	0	0	0
Tenosynovitis	0	0	0	1 (7.1)	1	0	0	0	0
Neoplasms benign, malignant and unspecified	4 (22.2)	4	2	3 (21.4)	4	0	3 (23.1)	6	4
Basal cell carcinoma	0	0	0	1 (7.1)	1	0	2 (15.4)	4	4
Bowen's disease	1 (5.6)	1	1	0	0	0	0	0	0
Melanocytic naevus	1 (5.6)	1	0	0	0	0	0	0	0
Skin papilloma	1 (5.6)	1	1	0	0	0	1 (7.7)	2	0
Squamous cell carcinoma of skin	0	0	0	1 (7.1)	2	0	0	0	0
Uterine leiomyoma	0	0	0	1 (14.3)	1	0	0	0	0
Vulval cancer stage 0	1 (5.6)	1	0	0	0	0	0	0	0
Nervous system disorders	4 (22.2)	5	2	4 (28.6)	9	1	7 (53.8)	13	1
Cervical radiculopathy	0	0	0	0	0	0	1 (7.7)	1	0
Dizziness	1 (5.6)	1	0	2 (14.3)	2	0	1 (7.7)	1	0
Dysgeusia	0	0	0	1 (7.1)	1	0	0	0	0
Headache	1 (5.6)	1	0	2 (14.3)	3	0	4 (30.8)	5	1
Hypoaesthesia	1 (5.6)	1	0	0	0	0	0	0	0
Hypogeusia	0	0	0	1 (7.1)	1	0	0	0	0
Migraine	0	0	0	1 (7.1)	1	0	0	0	0
Paraesthesia	0	0	0	0	0	0	1 (7.7)	1	0
Post herpetic neuralgia	0	0	0	1 (7.1)	1	1	0	0	0
Sciatica	0	0	0	0	0	0	1 (7.7)	1	0
Tarsal tunnel syndrome	0	0	0	0	0	0	1 (7.7)	3	0
Tremor	2 (11.1)	2	2	0	0	0	1 (7.7)	1	0

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
	n (%)	n1*	n2**	n (%)	n1*	n2**	n (%)	n1*	n2**
Psychiatric disorders	4 (22.2)	4	1	7 (50.0)	10	0	4 (30.8)	7	2
Anxiety	1 (5.6)	1	0	2 (14.3)	2	0	1 (7.7)	1	0
Confusional state	1 (5.6)	1	1	0	0	0	0	0	0
Depression	0	0	0	4 (28.6)	4	0	3 (23.1)	4	1
Insomnia	2 (11.1)	2	0	3 (21.4)	3	0	2 (15.4)	2	1
Mental status changes	0	0	0	1 (7.1)	1	0	0	0	0
Renal and urinary disorders	4 (22.2)	6	2	3 (21.4)	4	0	5 (38.5)	12	3
Dysuria	0	0	0	0	0	0	2 (15.4)	3	2
Glycosuria	0	0	0	1 (7.1)	1	0	0	0	0
Haematuria	2 (11.1)	2	1	0	0	0	0	0	0
Hydronephrosis	0	0	0	0	0	0	1 (7.7)	3	0
Kidney fibrosis	0	0	0	0	0	0	1 (7.7)	1	0
Nephrotic syndrome	1 (5.6)	1	0	0	0	0	0	0	0
Nocturia	1 (5.6)	1	0	1 (7.1)	1	0	0	0	0
Proteinuria	0	0	0	0	0	0	2 (15.4)	2	1
Renal cyst	1 (5.6)	1	1	1 (7.1)	1	0	0	0	0
Renal disorder	0	0	0	1 (7.1)	1	0	0	0	0
Renal hypertrophy	1 (5.6)	1	0	0	0	0	0	0	0
Urinary retention	0	0	0	0	0	0	2 (15.4)	2	0
Urine odour abnormal	0	0	0	0	0	0	1 (7.7)	1	0
Reproductive system and breast disorders	2 (11.1)	2	0	2 (28.6)	2	0	3 (23.1)	5	2
Breast mass	0	0	0	0	0	0	1 (7.7)	1	0
Breast tenderness	0	0	0	0	0	0	1 (7.7)	1	1
Erectile dysfunction	1 (9.1)	1	0	0	0	0	1 (10.0)	2	0
Gynaecomastia	0	0	0	0	0	0	1 (10.0)	1	1
Menorrhagia	0	0	0	1 (14.3)	1	0	0	0	0
Nipple exudate bloody	1 (5.6)	1	0	0	0	0	0	0	0
Ovarian cyst	0	0	0	1 (14.3)	0	0	0	0	0

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
System Organ Class Preferred Term	**n (%)**	**n1***	**n2****	**n (%)**	**n1***	**n2****	**n (%)**	**n1***	**n2****
Respiratory, thoracic and mediastinal disorders	6 (33.3)	10	2	7 (50.0)	14	1	7 (53.8)	11	1
Allergic sinusitis	0	0	0	0	0	0	1 (7.7)	1	1
Asthma	0	0	0	1 (7.1)	2	0	0	0	0
Cough	4 (22.2)	6	2	4 (28.6)	4	0	3 (23.1)	4	0
Dyspnoea	0	0	0	1 (7.1)	1	0	0	0	0
Dyspnoea exertional	0	0	0	0	0	0	1 (7.7)	1	0
Oropharyngeal pain	2 (11.1)	2	0	0	0	0	1 (7.7)	1	0
Pneumonitis	0	0	0	1 (7.1)	1	1	0	0	0
Productive cough	0	0	0	1 (7.1)	1	0	0	0	0
Pulmonary mass	0	0	0	1 (7.1)	1	0	0	0	0
Rales	0	0	0	1 (7.1)	1	0	0	0	0
Rhinitis allergic	0	0	0	1 (7.1)	1	0	0	0	0
Rhinorrhoea	0	0	0	1 (7.1)	1	0	0	0	0
Sinus congestion	1 (5.6)	1	0	1 (7.1)	1	0	0	0	0
Sleep apnoea syndrome	0	0	0	0	0	0	3 (23.1)	3	0
Sputum discoloured	1 (5.6)	1	0	0	0	0	0	0	0
Wheezing	0	0	0	0	0	0	1 (7.7)	1	0
Skin and subcutaneous tissue disorders	5 (27.8)	7	4	8 (57.1)	14	6	7 (53.8)	17	8
Acne	2 (11.1)	3	1	2 (14.3)	2	1	3 (23.1)	3	3
Alopecia	2 (11.1)	2	2	2 (14.3)	2	0	0	0	0
Dermal cyst	0	0	0	1 (7.1)	1	0	1 (7.7)	1	1
Dermatitis acneiform	0	0	0	1 (7.1)	1	1	0	0	0
Dry skin	0	0	0	0	0	0	1 (7.7)	1	0
Ecchymosis	1 (5.6)	1	0	0	0	0	0	0	0
Erythema	0	0	0	0	0	0	1 (7.7)	1	0
Hand dermatitis	0	0	0	0	0	0	1 (7.7)	1	0
Hyperhidrosis	0	0	0	1 (7.1)	1	0	0	0	0
Itching scar	0	0	0	0	0	0	1 (7.7)	1	0
Rash	1 (5.6)	1	1	4 (28.6)	5	3	2 (15.4)	4	2

Table 33. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
System Organ Class Preferred Term	**n (%)**	**n1***	**n2****	**n (%)**	**n1***	**n2****	**n (%)**	**n1***	**n2****
Rash generalised	0	0	0	0	0	0	1 (7.7)	1	1
Skin discolouration	0	0	0	0	0	0	1 (7.7)	1	0
Skin lesion	0	0	0	2 (14.3)	2	1	1 (7.7)	1	0
Skin ulcer	0	0	0	0	0	0	1 (7.7)	1	0
Swelling face	0	0	0	0	0	0	1 (7.7)	1	1
Vascular disorders	1 (5.6)	1	0	4 (28.6)	5	0	0	0	0
Hypertension	0	0	0	1 (7.1)	1	0	0	0	0
Hypotension	1 (5.6)	1	0	1 (7.1)	1	0	0	0	0
Raynaud's phenomenon	0	0	0	1 (7.1)	1	0	0	0	0
Thrombosed varicose vein	0	0	0	1 (7.1)	1	0	0	0	0
Varicose vein	0	0	0	1 (7.1)	1	0	0	0	0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

Except for 'n1' and 'n2', subjects were only counted once per treatment for each row.

Includes data up to 999 days after last dose of study drug.

Percentages of gender-specific events are calculated using the corresponding gender count as denominator.

MedDRA (version 17.1) coding dictionary applied.

MedDRA=Medical Dictionary for Regulatory Activities; N=number of subjects in the treatment group; n=number of subjects in this reporting group affected by any occurrence of this adverse event, all causalities; n1*=the number of occurrences of treatment-emergent all causality adverse events; n2**=the number of occurrences of treatment-emergent causally related to treatment adverse events.

Table 34. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class and Preferred Term (Treatment-Related, Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18) n(%)	Tofacitinib 15-10-5 (N=14) n(%)	Tofacitinib 30-15-10 (N=13) n(%)
Number (%) of subjects with AEs	11 (61.1)	10 (71.4)	11 (84.6)
Blood and lymphatic system disorders	2 (11.1)	1 (7.1)	2 (15.4)
Anaemia	1 (5.6)	1 (7.1)	2 (15.4)
Leukopenia	1 (5.6)	0	1 (7.7)
Cardiac disorders	0	0	1 (7.7)
Palpitations	0	0	1 (7.7)
Ear and labyrinth disorders	1 (5.6)	0	0
Ear disorder	1 (5.6)	0	0
Gastrointestinal disorders	2 (11.1)	2 (14.3)	2 (15.4)
Constipation	0	0	1 (7.7)
Diarrhoea	2 (11.1)	1 (7.1)	0
Dyspepsia	0	0	1 (7.7)
Food poisoning	0	1 (7.1)	0
Nausea	0	0	1 (7.7)
General disorders and administration site conditions	1 (5.6)	1 (7.1)	4 (30.8)
Asthenia	0	0	1 (7.7)
Fatigue	1 (5.6)	0	2 (15.4)
Local swelling	0	0	1 (7.7)
Oedema peripheral	0	1 (7.1)	0
Pain	1 (5.6)	0	0
Pyrexia	1 (5.6)	0	2 (15.4)
Immune system disorders	0	0	1 (7.7)
Transplant rejection	0	0	1 (7.7)

Table 34. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class and Preferred Term (Treatment-Related, Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18) n(%)	Tofacitinib 15-10-5 (N=14) n(%)	Tofacitinib 30-15-10 (N=13) n(%)
Infections and infestations	7 (38.9)	7 (50.0)	6 (46.2)
BK virus infection	0	1 (7.1)	0
Bronchitis	1 (5.6)	0	1 (7.7)
Bronchitis viral	0	0	1 (7.7)
Conjunctivitis	0	1 (7.1)	0
Cystitis	0	1 (7.1)	0
Cytomegalovirus infection	1 (5.6)	1 (7.1)	1 (7.7)
Epstein-Barr virus infection	0	0	1 (7.7)
Folliculitis	1 (5.6)	0	0
Gastroenteritis viral	1 (5.6)	0	0
Herpes zoster	1 (5.6)	3 (21.4)	1 (7.7)
Incision site abscess	1 (5.6)	0	0
Infected cyst	0	0	1 (7.7)
Localised infection	0	1 (7.1)	0
Nasopharyngitis	1 (5.6)	0	0
Oral candidiasis	1 (5.6)	0	0
Oral fungal infection	0	0	1 (7.7)
Pneumonia	0	1 (7.1)	0
Skin candida	1 (5.6)	0	0
Tinea versicolour	1 (5.6)	1 (7.1)	0
Upper respiratory tract infection	1 (5.6)	0	2 (15.4)
Urinary tract infection	2 (11.1)	2 (14.3)	0
Urosepsis		1 (7.1)	0
Injury, poisoning and procedural complications	1 (5.6)	1 (7.1)	1 (7.7)
Chloracne	0	0	1 (7.7)
Complications of transplanted kidney	1 (5.6)	1 (7.1)	0

Table 34. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class and Preferred Term (Treatment-Related, Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18) n(%)	Tofacitinib 15-10-5 (N=14) n(%)	Tofacitinib 30-15-10 (N=13) n(%)
Investigations	1 (5.6)	2 (14.3)	3 (23.1)
Alanine aminotransferase increased	0	1 (7.1)	0
Aspartate aminotransferase increased	0	1 (7.1)	1 (7.7)
Blood creatine phosphokinase increased	0	0	1 (7.7)
Blood triglycerides increased	0	1 (7.1)	0
Culture urine positive	0	0	1 (7.7)
Gamma-glutamyltransferase increased	0	0	2 (15.4)
Viral test positive	1 (5.6)	0	1 (7.7)
Metabolism and nutrition disorders	1 (5.6)	2 (14.3)	2 (15.4)
Fluid retention	0	1 (7.1)	0
Hypercholesterolaemia	0	0	1 (7.7)
Hyperlipidaemia	0	1 (7.1)	1 (7.7)
Hypokalaemia	1 (5.6)	0	0
Hypophosphataemia	1 (5.6)	0	0
Musculoskeletal and connective tissue disorders	2 (11.1)	1 (7.1)	2 (15.4)
Arthralgia	0	0	2 (15.4)
Arthritis	0	0	1 (7.7)
Back pain	0	0	1 (7.7)
Bone pain	0	0	1 (7.7)
Myalgia	1 (5.6)	0	0
Plantar fasciitis	0	1 (7.1)	0
Synovitis	1 (5.6)	0	0
Neoplasms benign, malignant and unspecified	2 (11.1)	0	2 (15.4)
Basal cell carcinoma	0	0	2 (15.4)
Bowen’s disease	1 (5.6)	0	0
Skin papilloma	1 (5.6)	0	0

Table 34. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class and Preferred Term (Treatment-Related, Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18) n(%)	Tofacitinib 15-10-5 (N=14) n(%)	Tofacitinib 30-15-10 (N=13) n(%)
Nervous system disorders	2 (11.1)	1 (7.1)	1 (7.7)
Headache	0	0	1 (7.7)
Post herpetic neuralgia	0	1 (7.1)	0
Tremor	2 (1.1)	0	0
Psychiatric disorders	1 (5.6)	0	2 (15.4)
Confusional state	1 (5.6)	0	0
Depression	0	0	1 (7.7)
Insomnia	0	0	1 (7.7)
Renal and urinary disorders	1 (5.6)	0	3 (23.1)
Dysuria	0	0	2 (15.4)
Haematuria	1 (5.6)	0	0
Proteinuria	0	0	1 (7.7)
Renal cyst	1 (5.6)	0	0
Reproductive system and breast disorders	0	0	1 (7.7)
Breast tenderness	0	0	1 (7.7)
Gynaecomastia	0	0	1 (10.0)
Respiratory, thoracic and mediastinal disorders	1 (5.6)	1 (7.1)	1 (7.7)
Allergic sinusitis	0	0	1 (7.7)
Cough	1 (5.6)	0	0
Pneumonitis	0	1 (7.1)	0
Skin and subcutaneous tissue disorders	4 (22.2)	4 (28.6)	5 (38.5)
Acne	1 (5.6)	1 (7.1)	3 (23.1)
Alopecia	2 (11.1)	0	0
Dermal cyst	0	0	1 (7.7)
Dermatitis acneiform	0	1 (7.1)	0
Rash	1 (5.6)	2 (14.3)	1 (7.7)
Rash generalised	0	0	1 (7.7)

Table 34. Treatment-Emergent Non-Serious Adverse Events Reported in ≥5% of Subjects by System Organ Class and Preferred Term (Treatment-Related, Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18) n(%)	Tofacitinib 15-10-5 (N=14) n(%)	Tofacitinib 30-15-10 (N=13) n(%)
Skin lesion	0	1 (7.1)	0
Swelling face	0	0	1 (7.7)

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

Includes data up to 999 days after last dose of study drug.

Percentages of gender-specific events are calculated using the corresponding gender count as denominator.

MedDRA (version 17.1) coding dictionary applied.

MedDRA=Medical Dictionary for Regulatory Activities; N=number of subjects in the treatment group; n=number of subjects in this reporting group affected by any occurrence of this adverse event, all causalities; n1*=the number of occurrences of treatment-emergent all causality adverse events; n2**=the number of occurrences of treatment-emergent causally related to treatment adverse events.

Serious Adverse Events (SAEs): All-causality SAEs are presented by SOC and PT for the Safety Population in Table 35. SAEs were reported for 25 subjects (7 subjects in the tacrolimus group, 10 subjects in the tofacitinib 15-10-5 mg BID group and 8 subjects in the tofacitinib 30-15-10 mg BID group).

The most frequently reported all-causality serious TEAEs were those coded to the MedDRA SOC of Infections and Infestations (14 subjects: 4 [22.2%] subjects on tacrolimus, 7 [50.0%] subjects on tofacitinib 15-10-5 mg BID and 3 [23.1%] subjects on tofacitinib 30-15-10 mg BID) and Gastrointestinal Disorders (5 subjects: 1 [5.6%] subject on tacrolimus, 2 [14.3%] subjects on tofacitinib 15-10-5 mg BID and 2 [15.4%] subjects on tofacitinib 30-15-10 mg BID).

The most frequently reported serious TEAEs considered to be treatment-related were those coded to the MedDRA SOC of Infections and Infestations (7 subjects: 1 [5.6%] subject on tacrolimus, 5 [35.7%] subjects on tofacitinib 15-10-5 mg BID and 1 [7.7%] subject on tofacitinib 30-15-10 mg BID).

The most common serious TEAE (both all-causality and treatment-related) by PT was urinary tract infection (3 subjects in total: 0 subjects on tacrolimus, 2 [14.3%] subjects on tofacitinib 15-10-5 mg BID and 1 [7.7%] subject on tofacitinib 30-15-10 mg BID).

Table 35. Treatment-Emergent Serious Adverse Events by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
	n (%)	n1*	n2**	n (%)	n1*	n2**	n (%)	n1*	n2**
Number with AEs	7 (38.9)			10 (71.4)			8 (61.5)		
Blood and lymphatic system disorders	0	0	0	2 (14.3)	2	0	1 (7.7)	2	0
Anaemia	0	0	0	0	0	0	1 (7.7)	1	0
Haemorrhagic anaemia	0	0	0	1 (7.1)	1	0	0	0	0
Lymphadenopathy	0	0	0	1 (7.1)	1	0	0	0	0
Thrombocytopenia	0	0	0	0	0	0	1 (7.7)	1	0
Cardiac disorders	1 (5.6)	3	0	1 (7.1)	3	0	2 (15.4)	2	0
Arrhythmia	0	0	0	0	0	0	1 (7.7)	1	0
Atrial fibrillation	1 (5.6)	3	0	0	0	0	0	0	0
Cardiac failure congestive	0	0	0	1 (7.1)	2	0	0	0	0
Diastolic dysfunction	0	0	0	1 (7.1)	1	0	0	0	0
Myocardial infarction	0	0	0	0	0	0	1 (7.7)	1	0
Congenital, familial and genetic disorders	0	0	0	1 (7.1)	1	0	0	0	0
Congenital cystic kidney disease	0	0	0	1 (7.1)	1	0	0	0	0
Gastrointestinal disorders	1 (5.6)	1	0	2 (14.3)	4	1	2 (15.4)	2	0
Diarrhoea	1 (5.6)	1	0	1 (7.1)	1	0	0	0	0
Diverticulum	0	0	0	0	0	0	1 (7.7)	1	0
Dysphagia	0	0	0	0	0	0	1 (7.7)	1	0
Gastrointestinal haemorrhage	0	0	0	1 (7.1)	1	0	0	0	0
Ileus	0	0	0	1 (7.1)	1	1	0	0	0
Inguinal hernia	0	0	0	1 (7.1)	1	0	0	0	0
General disorders and administration site conditions	0	0	0	1 (7.1)	1	0	2 (15.4)	2	0
Chest pain	0	0	0	0	0	0	1 (7.7)	1	0
Pyrexia	0	0	0	1 (7.1)	1	0	1 (7.7)	1	0

Table 35. Treatment-Emergent Serious Adverse Events by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
	n (%)	n1*	n2**	n (%)	n1*	n2**	n (%)	n1*	n2**
Immune system disorders	0	0	0	0	0	0	1 (7.7)	1	0
Transplant rejection	0	0	0	0	0	0	1 (7.7)	1	0
Infections and infestations	4 (22.2)	7	1	7 (50.0)	22	13	3 (23.1)	5	0
Bronchitis	0	0	0	2 (14.3)	2	1	0	0	0
Cellulitis	0	0	0	1 (7.1)	1	0	1 (7.7)	1	0
Gangrene	0	0	0	1 (7.1)	1	0	1 (7.7)	1	0
Herpes simplex	0	0	0	1 (7.1)	1	0	0	0	0
Herpes zoster	0	0	0	1 (7.1)	3	2	0	0	0
Histoplasmosis	0	0	0	1 (7.1)	1	1	0	0	0
Mastitis	0	0	0	1 (7.1)	1	0	0	0	0
Periorbital cellulitis	0	0	0	1 (7.1)	1	1	0	0	0
Peritonsillar abscess	0	0	0	1 (7.1)	1	0	0	0	0
Pneumonia	1 (5.6)	1	0	0	0	0	1 (7.7)	1	0
Pneumonia influenzal	0	0	0	0	0	0	1 (7.7)	1	0
Pyelonephritis	1 (5.6)	3	0	1 (7.1)	3	3	0	0	0
Renal cyst infection	1 (5.6)	1	0	0	0	0	0	0	0
Septic shock	1 (5.6)	1	1	1 (7.1)	1	1	0	0	0
Sinusitis	1 (5.6)	1	0	0	0	0	0	0	0
Upper respiratory tract infection	0	0	0	1 (7.1)	1	0	0	0	0
Urinary tract infection	0	0	0	2 (14.3)	2	2	1 (7.7)	1	1
Urosepsis	0	0	0	1 (7.1)	1	1	0	0	0
Viral infection	0	0	0	1 (7.1)	2	1	0	0	0
Injury, poisoning and procedural complications	1 (5.6)	1	0	1 (7.1)	1	0	1 (7.7)	1	0
Arteriovenous fistula thrombosis	0	0	0	1 (7.1)	1	0	0	0	0
Overdose	0	0	0	0	0	0	1 (7.7)	1	0
Rib fracture	1 (5.6)	1	0	0	0	0	0	0	0

Table 35. Treatment-Emergent Serious Adverse Events by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18)			Tofacitinib 15-10-5 (N=14)			Tofacitinib 30-15-10 (N=13)		
	n (%)	n1*	n2**	n (%)	n1*	n2**	n (%)	n1*	n2**
Investigations	1 (5.6)	1	0	1 (7.1)	1	0	1 (7.7)	1	1
Blood creatinine increased	1 (5.6)	1	0	0	0	0	1 (7.7)	1	0
Transaminases increased	0	0	0	1 (7.1)	1	0	0	0	0
Metabolism and nutrition disorders	0	0	0	1 (7.1)	1	0	1 (7.7)	2	0
Hypoglycaemia	0	0	0	1 (7.1)	1	0	0	0	0
Hyponataemia	0	0	0	0	0	0	1 (7.7)	2	0
Musculoskeletal and connective tissue disorders	0	0	0	1 (7.1)	2	0	0	0	0
Arthritis	0	0	0	1 (7.1)	1	0	0	0	0
Chondrocalcinosis pyrophosphate	0	0	0	1 (7.1)	1	0	0	0	0
Neoplasms benign, malignant and unspecified	1 (5.6)	1	0	1 (7.1)	1	1	1 (7.7)	1	0
Carcinoid tumour of the appendix	0	0	0	0	0	0	1 (7.7)	1	0
Lung squamous cell carcinoma metastatic	0	0	0	1 (7.1)	1	1	0	0	0
Oesophageal carcinoma	1 (5.6)	1	0	0	0	0	0	0	0
Nervous system disorders	1 (5.6)	1	0	0	0	0	1 (7.7)	1	0
Haemorrhage intracranial	0	0	0	0	0	0	1 (7.7)	1	0
Syncope	1 (5.6)	1	0	0	0	0	0	0	0
Renal and urinary disorders	2 (11.1)	3	0	1 (7.1)	1	1	1 (7.7)	1	1
Focal segmental glomerulosclerosis	1 (5.6)	1	0	0	0	0	0	0	0
Haematuria	1 (5.6)	1	0	0	0	0	0	0	0
Renal failure acute	1 (5.6)	1	0	0	0	0	0	0	0
Renal impairment	0	0	0	0	0	0	1 (7.7)	1	1
Renal tubular necrosis	0	0	0	1 (7.1)	1	1	0	0	0

Table 35. Treatment-Emergent Serious Adverse Events by System Organ Class, Preferred Term and Relationship to Treatment (Safety Analysis Set)

System Organ Class Preferred Term	Tacrolimus (N=18) n (%)	 n1*	 n2**	Tofacitinib 15-10-5 (N=14) n (%)	 n1*	 n2**	Tofacitinib 30-15-10 (N=13) n (%)	 n1*	 n2**
Respiratory, thoracic and mediastinal disorders	0	0	0	1 (7.1)	1	1	1 (7.7)	2	0
Pulmonary oedema	0	0	0	0	0	0	1 (7.7)	1	0
Respiratory disorder	0	0	0	0	0	0	1 (7.7)	1	0
Respiratory distress	0	0	0	1 (7.1)	1	1	0	0	0
Skin and subcutaneous tissue disorders	0	0	0	0	0	0	1 (7.7)	1	0
Skin ulcer	0	0	0	0	0	0	1 (7.7)	1	0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Except for 'n1' and 'n2', subjects were only counted once per treatment for each row.
Includes data up to 999 days after last dose of study drug.
Percentages of gender-specific events are calculated using the corresponding gender count as denominator.
MedDRA (version 17.1) coding dictionary applied.
MedDRA=Medical Dictionary for Regulatory Activities; N=number of subjects in the treatment group; n=number of subjects in this reporting group affected by any occurrence of this adverse event.

Table 36. Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (Treatment-Related, Safety Analysis)

System Organ Class Preferred Term	Tacrolimus (N=18) n(%)	Tofacitinib 15-10-5 (N=14) n(%)	Tofacitinib 30-15-10 (N=13) n(%)
Number with AEs	1 (5.6)	6 (42.9)	3 (23.1)
Gastrointestinal disorders	0	1 (7.1)	0
Ileus	0	1 (7.1)	0
Immune system disorders	0	0	1 (7.7)
Transplant rejection	0	0	1 (7.7)
Infections and infestations	1 (5.6)	5 (35.7)	1 (7.7)
Bronchitis	0	1 (7.1)	0
Herpes zoster	0	1 (7.1)	0
Histoplasmosis	0	1 (7.1)	0
Periorbital cellulitis	0	1 (7.1)	0
Pyelonephritis	0	1 (7.1)	0
Septic shock	1 (5.6)	1 (7.1)	0
Urinary tract infection	0	2 (14.3)	1 (7.7)
Urosepsis	0	1 (7.1)	0
Viral infection	0	1 (7.1)	0
Investigations	0	0	1 (7.7)
Blood creatinine increased	0	0	1 (7.7)
Neoplasms benign, malignant and unspecified	0	1 (7.1)	0
Lung squamous cell carcinoma metastatic	0	1 (7.1)	0
Renal and urinary disorders	0	1 (7.1)	1 (7.7)
Renal impairment	0	0	1 (7.7)
Renal tubular necrosis	0	1 (7.1)	0

Table 36. Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (Treatment-Related, Safety Analysis)

System Organ Class Preferred Term	Tacrolimus (N=18) n(%)	Tofacitinib 15-10-5 (N=14) n(%)	Tofacitinib 30-15-10 (N=13) n(%)
Respiratory, thoracic and mediastinal disorders	0	1 (7.1)	0
Respiratory distress	0	1 (7.1)	0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

Subjects were only counted once per treatment for each row.

MedDRA (version 17.1) coding dictionary applied.

MedDRA=Medical Dictionary for Regulatory Activities; N=number of subjects in the treatment group; n=number of subjects in this reporting group affected by any occurrence of this adverse event, all causalities; n1*=the number of occurrences of treatment-emergent all causality adverse events; n2**=the number of occurrences of treatment-emergent causally related to treatment adverse events.

Deaths:

A total of 2 fatal cases were reported within the reporting period of Study A3921021 as specified by the study protocol. One fatal case occurred in the tofacitinib 15-10-5 mg BID group; the subject was diagnosed with lung squamous cell carcinoma metastatic on Study Day 2164 and died on Study Day 2468. The event was considered related to tofacitinib. One fatal case occurred in the tofacitinib 30-15-10 mg BID group; the subject experienced haemorrhage intracranial and died on Study Day 2024. The event was considered not related to tofacitinib.

One additional death occurred in the tacrolimus group approximately 5 months after the subject had received their last dose of tacrolimus; the subject experienced septic shock and died due to septic shock and bacterial infection. The septic shock was considered related to tacrolimus.

Table 37 Summary of Deaths

System Organ Class Preferred Term	Tacrolimus (N=18)		Tofacitinib 15-10-5 (N=14)		Tofacitinib 30-15-10 (N=13)	
	n	n1*	n	n1*	n	n1*
Infections and infestations	1	1	0	0	0	0
Septic shock	1	1	0	0	0	0
Neoplasms benign, malignant and unspecified	0	0	1	1	0	0
Lung squamous cell carcinoma metastatic	0	0	1	1	0	0
Nervous system disorders	0	0	0	0	1	1
Haemorrhage intracranial	0	0	0	0	1	1
Total number of fatalities from AEs[a]	1		1		1	
Total number of deaths all causes[b]	1		1		1	

MedDRA v.17.0 coding dictionary applied.
AE=adverse event; MedDRA=Medical Dictionary for Regulatory Activities; n=the number of AEs associated with a fatality; N=number of subjects in the treatment group; n1*=the number of AEs associated with a fatality and thought to be associated or related to treatment.
A fatality can be associated with multiple events.
a Total number of deaths in this reporting group thought to be causally related to AEs.
b Total number of deaths(all causes) in this reporting group. This includes deaths not related to the trial

Discontinuations due to AEs:

A total of 6 subjects (tacrolimus 1 subject, tofacitinib 15-10-5 mg BID 1 subject, and tofacitinib 30-15-10 mg BID 4 subjects) discontinued the study due to AEs. There was no PT which resulted in permanent discontinuation in >1 subject overall.

Table 38 Summary of AEs Resulting in Discontinuation

System Organ Class Preferred Term	Tacrolimus (N=18)		Tofacitinib 15-10-5 (N=14)		Tofacitinib 30-15-10 (N=13)	
	n	n1*	n	n1*	n	n1*
Immune system disorders	0	0	0	0	1	1
Transplant rejection	0	0	0	0	1	1
Infections and infestations	0	0	0	0	1	1
Human polyomavirus infection	0	0	0	0	1	1
Investigations	0	0	0	0	1	1
Blood creatinine increased	0	0	0	0	1	1
Neoplasms benign, malignant and unspecified	1	0	1	1	0	0
Oesophageal carcinoma	1	0	0	0	0	0
Lung squamous cell carcinoma metastatic	0	0	1	1	0	0
Renal and urinary disorders	0	0	0	0	1	1
Renal impairment	0	0	0	0	1	1
Respiratory, thoracic and mediastinal disorders	0	0	1	1	0	0
Pneumonitis	0	0	1	1	0	0
Skin and subcutaneous tissue disorders	0	0	0	0	1	1
Acne	0	0	0	0	1	1

Table only includes data from extension study A3921021.
MedDRA v.17.0 coding dictionary applied.
AE=adverse event; MedDRA=Medical Dictionary for Regulatory Activities; n=the number of AEs associated with a discontinuation; N=number of subjects in the treatment group; n1*=the number of AEs associated with a discontinuation and thought to be associated or related to treatment.

Efficacy Results:

Time to first BPAR: Percentages of subjects with first BPAR (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Full Analysis Set in Table 39.

Overall, first BPAR episodes occurred in 2 subjects in the tacrolimus group and in 2 subjects in the tofacitinib 30-15-10 mg BID group in the parent study A3921009. No first BPAR episodes occurred during Study A3921021. As a result, the Kaplan-Meier estimated rates were unchanged from Month 9 onwards in Study A3921021. At Month 12, the estimated rate was 11.1% for the tacrolimus group, 0.0% for the tofacitinib 15-10-5 mg BID group and 15.4% for the tofacitinib 30-15-10 mg BID group.

Comparing the Kaplan-Meier curves (based on Log-Rank test) for first BPAR between tofacitinib 15-10-5 mg BID or tofacitinib 30-15-10 mg BID and tacrolimus through Month 96 showed no statistically significant difference (p=0.2058 and p=0.7294, respectively).

Table 39. Percent of Subjects with First BPAR estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

		Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
Visit	Treatment	Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Day 1	Tacrolimus	0	18	0	0	0	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86	0	0	0	0		
	Tofacitinib 30-15-10 mg BID	0	13	0	0	0	11.64	0	0	0	0		
Month 1	Tacrolimus	1	17	5.56	5.40	0	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	0	13	0	0	0	11.64	-5.56	5.40	-12.47	1.36	0.3035	
Month 3	Tacrolimus	1	17	5.56	5.40	0	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	9.83	11.37	-4.74	24.04	0.3873	
Month 6	Tacrolimus	1	17	5.56	5.40	0	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	9.83	11.37	-4.74	24.40	0.3873	
Month 9	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 12	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 15	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 18	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	

Table 39. Percent of Subjects with First BPAR estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 24	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 30	Tacrolimus	2	14	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	10	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 36	Tacrolimus	2	14	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	10	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 42	Tacrolimus	2	14	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 48	Tacrolimus	2	13	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 54	Tacrolimus	2	13	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 60	Tacrolimus	2	12	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 66	Tacrolimus	2	12	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	8	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	

Table 39. Percent of Subjects with First BPAR estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 72	Tacrolimus	2	5	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86	-11.11	7.41	-20.6	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	7	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 78	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	0	14	0	0	0	10.86						
	Tofacitinib 30-15-10 mg BID	2	6	15.38	10.01	2.56	28.21						
Month 84	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	0	13	0	0	0	11.64						
	Tofacitinib 30-15-10 mg BID	2	6	15.38	10.01	2.56	28.21						
Month 90	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	0	13	0	0	0	11.64						
	Tofacitinib 30-15-10 mg BID	2	6	15.38	10.01	2.56	28.21						
Month 96	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	0	12	0.00	0.00	0.00	12.55						0.2058
	Tofacitinib 30-15-10 mg BID	2	6	15.38	10.01	2.56	28.21						0.7294

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis.
*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
If event did not occur, it was censored to last visit day or Day 2980, whichever was first. If event occurred after Day 2980, it was censored to Day 2980.
Abbreviations: BID = twice daily dosing; BPAR = biopsy proven acute rejection; CI = confidence interval; Cum.=cumulative; Diff. = difference; N = number of subjects; No. = number; SE = standard error.

Time to treatment failure: Percentages of subjects with treatment failure (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Full Analysis Set in Table 40.

From Month 30 onwards, statistically significant differences were observed between tofacitinib 15-10-5 mg BID and tacrolimus. At Month 66, there were no cumulative events (estimated rate 0.0% [SE 0.00]) in the tofacitinib 15-10-5 mg BID group compared with 7 cumulative events (estimated rate 38.9% [SE 11.49]) in the tacrolimus group (Month 66, estimated rate difference -38.9%, p=0.0007).

No statistically significant differences in the proportion of subjects with treatment failure were shown between tofacitinib 30-15-10 mg BID and tacrolimus at each scheduled visit. At Month 66 there were 5 cumulative events (estimated rate 38.5% [SE 13.49]) in the tofacitinib 30-15-10 mg BID group compared with 7 cumulative events (estimated rate 38.9% [SE 11.49]) in the tacrolimus group (Month 66, estimated rate difference -0.4%, p=0.9808).

Comparing Kaplan-Meier curves between tofacitinib and tacrolimus (based on Log-Rank test) through Month 96, a statistically significant difference was shown between tofacitinib 15-10-5 mg BID and tacrolimus (Log-Rank p=0.0072) but not between tofacitinib 30-15-10 mg BID and tacrolimus (Log-Rank p=0.8090).

Table 40. Percent of Subjects with Treatment Failure estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Day 1	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	0.00	0.00	0.00	0.00		
Month 1	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	-5.56	5.40	-12.47	1.36	0.3035	
Month 3	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	9.83	11.37	-4.74	24.40	0.3873	
Month 6	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	9.83	11.37	-4.74	24.40	0.3873	
Month 9	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 12	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	3	10	23.08	11.69	8.10	38.05	11.97	13.84	-5.77	29.70	0.3871	
Month 15	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	3	10	23.08	11.69	8.10	38.05	11.97	13.84	-5.77	29.70	0.3871	
Month 18	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	3	10	23.08	11.69	8.10	38.05	11.97	13.84	-5.77	29.70	0.3871	

Table 40. Percent of Subjects with Treatment Failure estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 24	Tacrolimus	3	15	16.67	8.78	5.41	27.92						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-16.67	8.78	-27.92	-5.41	0.0578	
	Tofacitinib 30-15-10 mg BID	3	10	23.08	11.69	8.10	38.05	6.41	14.62	-12.32	25.15	0.6610	
Month 30	Tacrolimus	4	14	22.22	9.80	9.66	34.78						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-22.22	9.80	-34.78	-9.66	0.0233	
	Tofacitinib 30-15-10 mg BID	4	9	30.77	12.80	14.36	47.17	8.55	16.12	-12.11	29.21	0.5960	
Month 36	Tacrolimus	4	14	22.22	9.80	9.66	34.78						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-22.22	9.80	-34.78	-9.66	0.0233	
	Tofacitinib 30-15-10 mg BID	5	8	38.46	13.49	21.17	55.75	16.24	16.68	-5.13	37.61	0.3301	
Month 42	Tacrolimus	4	14	22.22	9.80	9.66	34.78						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-22.22	9.80	-34.78	-9.66	0.0233	
	Tofacitinib 30-15-10 mg BID	5	8	38.46	13.49	21.17	55.75	16.24	16.68	-5.13	37.61	0.3301	
Month 48	Tacrolimus	5	13	27.78	10.56	14.25	41.31						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-27.78	10.56	-41.31	-14.25	0.0085	
	Tofacitinib 30-15-10 mg BID	5	8	38.46	13.49	21.17	55.75	10.68	17.13	-11.27	32.64	0.5329	
Month 54	Tacrolimus	5	13	27.78	10.56	14.25	41.31						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-27.78	10.56	-41.31	-14.25	0.0085	
	Tofacitinib 30-15-10 mg BID	5	8	38.46	13.49	21.17	55.75	10.68	17.13	-11.27	32.64	0.5329	
Month 60	Tacrolimus	6	12	33.33	11.11	19.09	47.57						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-33.33	11.11	-47.57	-19.09	0.0027	
	Tofacitinib 30-15-10 mg BID	5	8	38.46	13.49	21.17	55.75	5.13	17.48	-17.27	27.53	0.7692	
Month 66	Tacrolimus	7	11	38.89	11.49	24.16	53.61						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-38.89	11.49	-53.61	-24.16	0.0007	
	Tofacitinib 30-15-10 mg BID	5	8	38.46	13.49	21.17	55.75	-0.43	17.72	-23.14	22.29	0.9808	

Table 40. Percent of Subjects with Treatment Failure estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

		Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
Visit	Treatment	Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 72	Tacrolimus	9	5	50.00	11.79	34.90	65.10						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-42.86	13.65	-60.35	-25.37	0.0017	
	Tofacitinib 30-15-10 mg BID	7	6	53.85	13.83	36.13	71.57	3.85	18.17	-19.44	27.13	0.8323	
Month 78	Tacrolimus	9	0										
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	7	6	53.85	13.83	36.13	71.57						
Month 84	Tacrolimus	9	0										
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	7	6	53.85	13.83	36.13	71.57						
Month 90	Tacrolimus	9	0										
	Tofacitinib 15-10-5 mg BID	2	12	14.29	9.35	2.30	26.27						
	Tofacitinib 30-15-10 mg BID	7	6	53.85	13.83	36.13	71.57						
Month 96	Tacrolimus	9	0										
	Tofacitinib 15-10-5 mg BID	2	12	14.29	9.35	2.30	26.27						0.0072
	Tofacitinib 30-15-10 mg BID	8	6	53.85	13.83	36.13	71.57						0.8090

*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
If event did not occur, it was censored to last visit day or Day 2980, whichever was first. If event occurred after Day 2980, it was censored to Day 2980.
Treatment failure was the first occurrence of BPAR, graft loss, subject death, or premature discontinuation of trial medication for any reason.
Four deaths were recorded in the clinical database. One subject died approximately 9 months after last dose and 1 died during active treatment period. These 2 subjects, both of whom received tofacitinib, were included in the Kaplan-Meier analysis as events for death. One subject (who also received tofacitinib) died beyond the 12-month follow-up period after the last dose of tofacitinib and the discontinuation of the subject on Day 1044 was included as treatment failure. One subject was enrolled in the subject-specific protocol Amendment #1 and subsequently died; they were excluded from the current analyses. One additional subject who received tacrolimus died after discontinuation from study and the death was recorded only in the safety database (ARGUS). The subject was censored at the last visit in the KM analysis.
Abbreviations: BID = twice daily dosing; BPAR = biopsy proven acute rejection; CI = confidence interval; Cum.=cumulative; Diff. = difference; N = number of subjects; No. = number; SE = standard error.

Time to first BPCAN and time to first antibody-mediated rejection: Percentages of subjects with first BPCAN (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Full Analysis Set in Table 41.

The incidences of subjects with first BPCAN were low. From Day 1 through Month 66 there were no cumulative events in either the tofacitinib 15-10-5 mg BID group or the tacrolimus group and only 2 cumulative events of chronic allograft nephropathy in the tofacitinib 30-15-10 mg BID group. First BPCAN (treatment-emergent) was reported in only 1 subject in the tofacitinib 30-15-10 mg BID group in Study A3921021 Conclusive comparisons between treatment groups are not possible due to small numbers of subjects and events.

Table 41. Percent of Subjects with First BPCAN estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Day 1	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	0.00	0.00	0.00	0.00		
Month 1	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	0.00	0.00	0.00	0.00		
Month 3	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	
Month 6	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	
Month 9	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	
Month 12	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	
Month 15	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	
Month 18	Tacrolimus	0	17	0.00	0.00	0.00	9.03						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	12	7.69	7.39	0.00	17.16	7.69	7.39	-1.78	17.16	0.2980	

Table 41. Percent of Subjects with First BPCAN estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 24	Tacrolimus	0	17	0.00	0.00	0.00	9.03						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	15.38	10.01	2.56	28.21	0.1242	
Month 30	Tacrolimus	0	15	0.00	0.00	0.00	10.17						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	2	10	15.38	10.01	2.56	28.21	15.38	10.01	2.56	28.21	0.1242	
Month 36	Tacrolimus	0	15	0.00	0.00	0.00	10.17						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	2	10	15.38	10.01	2.56	28.21	15.38	10.01	2.56	28.21	0.1242	
Month 42	Tacrolimus	0	15	0.00	0.00	0.00	10.17						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	15.38	10.01	2.56	28.21	0.1242	
Month 48	Tacrolimus	0	14	0.00	0.00	0.00	10.86						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	15.38	10.01	2.56	28.21	0.1242	
Month 54	Tacrolimus	0	14	0.00	0.00	0.00	10.86						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	15.38	10.01	2.56	28.21	0.1242	
Month 60	Tacrolimus	0	13	0.00	0.00	0.00	11.64						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	15.38	10.01	2.56	28.21	0.1242	
Month 66	Tacrolimus	0	13	0.00	0.00	0.00	11.64						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	2	8	15.38	10.01	2.56	28.21	15.38	10.01	2.56	28.21	0.1242	

Table 41. Percent of Subjects with First BPCAN estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

		Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
Visit	Treatment	Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 72	Tacrolimus	0	6	0.00	0.00	0.00	23.53						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	2	7	15.38	10.01	2.56	28.21	15.38	10.01	2.56	28.21	0.1242	
Month 78	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86						
	Tofacitinib 30-15-10 mg BID	2	6	15.38	10.01	2.56	28.21						
Month 84	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	0	13	0.00	0.00	0.00	11.64						
	Tofacitinib 30-15-10 mg BID	2	6	15.38	10.01	2.56	28.21						
Month 90	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	0	13	0.00	0.00	0.00	11.64						
	Tofacitinib 30-15-10 mg BID	2	6	15.38	10.01	2.56	28.21						
Month 96	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	0	12	0.00	0.00	0.00	12.55						
	Tofacitinib 30-15-10 mg BID	2	6	15.38	10.01	2.56	28.21						0.0942

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis.
*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
Includes BPCAN diagnosed on biopsies done for-cause and read by the central pathologist.
If event did not occur, it was censored to last visit day or Day 2980, whichever was first. If event occurred after Day 2980, it was censored to Day 2980.
Abbreviations: BID = twice daily dosing; BPCAN = biopsy proven chronic allograft nephropathy; CI = confidence interval; Cum.= cumulative; Diff. = difference; N = number of subjects; No. = number; SE = standard error.

Time to rejection: Percentages of subjects with rejection (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Full Analysis Set in Table 42.

The cumulative number of events was low in each of the 3 treatment groups. No statistically significant differences were found between tofacitinib 15-10-5 mg BID or tofacitinib 30-15-10 mg BID and tacrolimus at each scheduled visit ($p>0.05$).

Table 42. Percent of Subjects with Rejection estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Day 1	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	0.00	0.00	0.00	0.00		
Month 1	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	-5.56	5.40	-12.47	1.36	0.3035	
Month 3	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	9.83	11.37	-4.74	24.40	0.3873	
Month 6	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	1.59	8.75	-9.62	12.80	0.8560	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	9.83	11.37	-4.74	24.40	0.3873	
Month 9	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 12	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 15	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 18	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	

Table 42. Percent of Subjects with Rejection estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 24	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 30	Tacrolimus	2	14	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	10	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 36	Tacrolimus	2	14	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	10	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 42	Tacrolimus	2	14	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 48	Tacrolimus	2	13	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 54	Tacrolimus	2	13	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 60	Tacrolimus	2	12	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 66	Tacrolimus	2	12	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	2	8	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	

Table 42. Percent of Subjects with Rejection estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

		Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
Visit	Treatment	Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 72	Tacrolimus	2	5	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96	-3.97	10.11	-16.93	8.99	0.6947	
	Tofacitinib 30-15-10 mg BID	3	6	27.47	14.10	9.40	45.54	16.36	15.93	-4.05	36.77	0.3043	
Month 78	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	3	6	27.47	14.10	9.40	45.54						
Month 84	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	12	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	3	6	27.47	14.10	9.40	45.54						
Month 90	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	12	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	3	6	27.47	14.10	9.40	45.54						
Month 96	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	11	7.14	6.88	0.00	15.96						0.7350
	Tofacitinib 30-15-10 mg BID	3	6	27.47	14.10	9.40	45.54						0.4466

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis.
*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
Rejection was first occurrence of biopsy proven acute rejection, antibody-mediated rejection, or suspicion for acute rejection. This included biopsies read by the central pathologist.
If event did not occur, it was censored to last visit day or Day 2980, whichever was first. If event occurred after Day 2980, it was censored to Day 2980.
Abbreviations: BID = twice daily dosing; CI = confidence interval; Cum.= cumulative; Diff. = difference; N = number of subjects; No. = number; SE = standard error.

Ordered categorical severity of first BPAR and first BPCAN: according to the Banff Classification: Banff Category 4 is classified as acute or active cellular rejection; Banff Category 2 is classified as antibody-mediated rejection.

Cumulative percentages of subjects with first BPAR and BPCAN are presented in for the Full Analysis Set in Table 43.

No subjects had any BPAR (acute/active cellular rejection, Banff category 4) or antibody mediated rejection (Banff category 2) in Study A3921021. One subject in the tofacitinib 30-15-10 mg BID group had a first BPCAN in Study A3921021; the BPCAN was categorized as moderate (Grade II). No subject in either the tofacitinib 15-10-5 mg BID group or the tacrolimus group had a first BPCAN in Study A3921021.

Table 43. Cumulative Percentages of Subjects with Ordered Categorical First BPAR (Banff Category 4), BPAR (Banff Category 2) and BPCAN (Full Analysis Set)

Visit	Treatment	N	Banff Category 4 n(%)	Banff Category 2 n(%)	BPCAN n(%)
Month 12	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)
Month 18	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)
Month 24	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)
Month 36	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)
Month 48	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)
Month 60	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)
Month 72	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)
Month 84	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)
Month 96	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)
Follow-up	Tacrolimus	18	0	0	0
	Tofacitinib 15-10-5 mg BID	14	0	0	0
	Tofacitinib 30-15-10 mg BID	13	0	0	1 (7.7)

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis.
Table only includes data from extension study A3921021.
Percentages were based on N.
Abbreviations: BID = twice daily dosing; BPAR = biopsy proven acute rejection; BPCAN = biopsy proven chronic allograft nephropathy; N = number of subjects in Full Analysis Set; n = cumulative number of subjects at each visit in each category.

Time to efficacy failure : Percentages of subjects with efficacy failure (defined as first BPAR, death, or graft loss; estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Full Analysis Set in Table 44.
Comparisons in proportions of subjects with efficacy failure at scheduled visits showed no statistically significant differences between each of the tofacitinib dose regimens and tacrolimus.

Comparing the Kaplan-Meier curves through Month 96 between tofacitinib 15-10-5 mg BID or tofacitinib 30-15-10 mg BID dose regimens and tacrolimus (based on Log-Rank test) showed no statistically significant difference (p=0.2058 and p=0.3925, respectively).

Table 44. Percent of Subjects with Efficacy Failure estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Day 1	Tacrolimus	0	18	0.00	0.00	0.00	8.55						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	0.00	0.00	0.00	0.00		
Month 1	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	0	13	0.00	0.00	0.00	11.64	-5.56	5.40	-12.47	1.36	0.3035	
Month 3	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	9.83	11.37	-4.74	24.40	0.3873	
Month 6	Tacrolimus	1	17	5.56	5.40	0.00	12.47						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-5.56	5.40	-12.47	1.36	0.3035	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	9.83	11.37	-4.74	24.40	0.3873	
Month 9	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 12	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 15	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 18	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	

Table 44. Percent of Subjects with Efficacy Failure estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 24	Tacrolimus	2	16	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	11	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 30	Tacrolimus	2	14	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	10	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 36	Tacrolimus	2	14	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	10	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 42	Tacrolimus	2	14	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 48	Tacrolimus	2	13	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 54	Tacrolimus	2	13	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 60	Tacrolimus	2	12	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	9	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	
Month 66	Tacrolimus	2	12	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	2	8	15.38	10.01	2.56	28.21	4.27	12.45	-11.68	20.23	0.7314	

Table 44. Percent of Subjects with Efficacy Failure estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 72	Tacrolimus	2	5	11.11	7.41	1.62	20.60						
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86	-11.11	7.41	-20.60	-1.62	0.1336	
	Tofacitinib 30-15-10 mg BID	3	7	25.96	13.21	9.03	42.89	14.85	15.15	-4.56	34.26	0.3269	
Month 78	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	0	14	0.00	0.00	0.00	10.86						
	Tofacitinib 30-15-10 mg BID	3	6	25.96	13.21	9.03	42.89						
Month 84	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	3	6	25.96	13.21	9.03	42.89						
Month 90	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96						
	Tofacitinib 30-15-10 mg BID	3	6	25.96	13.21	9.03	42.89						
Month 96	Tacrolimus	2	0										
	Tofacitinib 15-10-5 mg BID	1	13	7.14	6.88	0.00	15.96						0.2058
	Tofacitinib 30-15-10 mg BID	3	6	25.96	13.21	9.03	42.89						0.3925

*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
Efficacy failure is the first occurrence of biopsy proven acute rejection, graft loss or subject death.
Four deaths were recorded in the clinical database. One subject died approximately 9 months after last dose and 1 died during active treatment period; both received tofacitinib and both are included in the Kaplan-Meier analysis as events for death. One subject who received tofacitinib died beyond the 12-month follow-up period after the last dose of tofacitinib and was censored to Day 1104 (Last Visit day) in the analyses. One subject receiving tofacitinib, who was enrolled in the subject-specific protocol Amendment #1 and subsequently died, was excluded from the current analyses. One additional subject who received tacrolimus died after discontinuation from study and the death was recorded only in the safety database (ARGUS). The subject was censored at the last visit in the Kaplan-Meier analysis.
If event did not occur, it was censored to last visit day or Day 2980, whichever was first. If event occurred after Day 2980, it was censored to Day 2980.
Abbreviations: BID = twice daily dosing; CI = confidence interval; Cum.= cumulative; Diff. = difference; N = number of subjects; No. = number; SE = standard error.

Time to graft loss (defined as graft nephrectomy, retransplantation, return to dialysis for ≥6 consecutive weeks, or subject death): Percentages of subjects with graft survival (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Full Analysis Set in Table 45.

Up to Month 66, there was no incidence of graft loss in the tofacitinib treatment groups. At Month 72, 1 subject in the tofacitinib 30-15-10 mg BID group had an event of graft loss and at Month 84, 1 subject in the tofacitinib 15-10-5 mg BID group had an event of graft loss. Both events of graft loss were due to death. There were no events of graft loss in the tacrolimus group at any visit.

Table 45. Percent of Subjects with Graft Survival estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

Visit	Treatment	Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
		Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 66	Tacrolimus	0	13	100.00	0.00	88.36	100.00						
	Tofacitinib 15-10-5 mg BID	0	14	100.00	0.00	89.14	100.00	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	10	100.00	0.00	85.13	100.00	0.00	0.00	0.00	0.00		
Month 72	Tacrolimus	0	6	100.00	0.00	76.47	100.00						
	Tofacitinib 15-10-5 mg BID	0	14	100.00	0.00	89.14	100.00	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	9	90.00	9.49	77.84	100.00	-10.00	9.49	-22.16	2.16	0.2918	
Month 78	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	0	14	100.00	0.00	89.14	100.00						
	Tofacitinib 30-15-10 mg BID	1	8	90.00	9.49	77.84	100.00						
Month 84	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	1	13	92.86	6.88	84.04	100.00						
	Tofacitinib 30-15-10 mg BID	1	8	90.00	9.49	77.84	100.00						
Month 90	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	1	13	92.86	6.88	84.04	100.00						
	Tofacitinib 30-15-10 mg BID	1	8	90.00	9.49	77.84	100.00						
Month 96	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	1	12	92.86	6.88	84.04	100.00						
	Tofacitinib 30-15-10 mg BID	1	7	90.00	9.49	77.84	100.00						0.2542

*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.
**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.
Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.
Graft loss was defined as graft nephrectomy, retransplantation, return to dialysis for ≥6 consecutive weeks, or patient death.
If event did not occur, it was censored to last visit day or Day 2980, whichever was first. If event occurred after Day 2980, it was censored to Day 2980.
Abbreviations: BID = twice daily dosing; CI = confidence interval; Cum.= cumulative; Diff. = difference; N = number of subjects; No. = number; SE = standard error.

Time to subject death: Percentages of subjects surviving (estimated using Kaplan-Meier survival curves) and treatment comparisons are presented by visit for the Full Analysis Set in Table 46.

There were 2 deaths reported within the reporting period as specified by the study protocol. There was 1 event of death in the tofacitinib 15-10-5 mg BID at Month 84 and 1 event of death in the tofacitinib 30-15-10 mg BID group at Month 72.

Table 46. Percent of Subjects with Subject Survival estimated using Kaplan-Meier Survival Curves and Treatment Comparisons (Full Analysis Set)

		Estimated Rate (%)						Estimated Rate difference (Active-Tacrolimus) (%)					
						80% CI				80% CI			
Visit	Treatment	Cum. No. of events	N at risk	Rate	SE	Lower	Upper	Rate Diff.	SE	Lower	Upper	P-value*	P-value**
Month 66	Tacrolimus	0	13	100.00	0.00	88.36	100.00						
	Tofacitinib 15-10-5 mg BID	0	14	100.00	0.00	89.14	100.00	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	0	10	100.00	0.00	85.13	100.00	0.00	0.00	0.00	0.00		
Month 72	Tacrolimus	0	6	100.00	0.00	76.47	100.00						
	Tofacitinib 15-10-5 mg BID	0	14	100.00	0.00	89.14	100.00	0.00	0.00	0.00	0.00		
	Tofacitinib 30-15-10 mg BID	1	9	90.00	9.49	77.84	100.00	-10.00	9.49	-22.16	2.16	0.2918	
Month 78	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	0	14	100.00	0.00	89.14	100.00						
	Tofacitinib 30-15-10 mg BID	1	8	90.00	9.49	77.84	100.00						
Month 84	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	1	13	92.86	6.88	84.04	100.00						
	Tofacitinib 30-15-10 mg BID	1	8	90.00	9.49	77.84	100.00						
Month 90	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	1	13	92.86	6.88	84.04	100.00						
	Tofacitinib 30-15-10 mg BID	1	8	90.00	9.49	77.84	100.00						
Month 96	Tacrolimus	0	0										
	Tofacitinib 15-10-5 mg BID	1	12	92.86	6.88	84.04	100.00						
	Tofacitinib 30-15-10 mg BID	1	7	90.00	9.49	77.84	100.00						0.2542

*P-value for comparing rate differences between tofacitinib and tacrolimus using Wald test.

**P-value for comparing survival curves between tofacitinib and tacrolimus based on log-rank test.

Includes data from both A3921009 and A3921021, and only from subjects enrolled in A3921021.

Four deaths were recorded in the clinical database. One subject died approximately 9 months after last dose and 1 died during active treatment period; both received tofacitinib and both are included in the Kaplan-Meier analysis as events for death. One subject who received tofacitinib died beyond the 12-month follow-up period after the last dose of tofacitinib and was censored to Day 1104 (Last Visit day) in the analyses. One subject receiving tofacitinib, who was enrolled in the subject-specific protocol Amendment #1 and subsequently died, was excluded from the current analyses. One additional subject who received tacrolimus died after discontinuation from study and the death was recorded only in the safety database (ARGUS). The subject was censored at the last visit in the Kaplan-Meier analysis.

If event did not occur, it was censored to last visit day or Day 2980, whichever was first. If event occurred after Day 2980, it was censored to Day 2980.

Abbreviations: BID = twice daily dosing; BPCAN = biopsy proven chronic allograft nephropathy; CI = confidence interval; Cum.= cumulative; Diff. = difference; N = number of subjects; No. = number; SE = standard error.

Pharmacodynamic Results:

Flow cytometry of Lymphocyte Subsets: absolute cell counts for CD4+ (helper T-lymphocytes), CD8+ (cytotoxic T-lymphocytes), CD3-CD56+ (natural killer cells) and CD19+ (B-lymphocytes): Descriptive statistics for $CD8^+$, $CD19^+$, $CD4^+$ and $CD56^+$ fluorescence activated cell sorting counts at each time point and by treatment group are presented for the Safety Analysis Set in Table 47.

The mean CD8+, CD19+ and CD56+ counts were higher in the tacrolimus group compared with both tofacitinib groups, at the Month 12 and Month 24 visits. The mean CD4+ count was generally similar across the treatment groups at the Month 12 visit and was higher in the tacrolimus group compared with both tofacitinib groups, at the Month 24 visit.

Table 47. Summary of Fluorescence Activated Cell Sorting of Lymphocyte Subsets – Safety Analysis Set

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Absolute CD8+ FACS Counts (per μL)										
Month 12	Tacrolimus	15	284.67	218.43	76.73	76.0	154.0	182.0	374.0	782.0
	Tofacitinib 15-10-5 mg BID	14	207.43	97.19	46.86	98.0	112.0	196.0	285.0	363.0
	Tofacitinib 30-15-10 mg BID	12	232.33	110.61	47.61	54.0	147.5	232.0	301.0	429.0
Month 24	Tacrolimus	15	318.20	183.85	57.78	108.0	200.0	228.0	408.0	676.0
	Tofacitinib 15-10-5 mg BID	14	224.36	194.45	86.67	42.0	102.0	146.0	252.0	630.0
	Tofacitinib 30-15-10 mg BID	12	238.08	172.46	72.43	25.0	116.0	212.0	285.0	594.0
Absolute CD19+ FACS Counts (per μL)										
Month 12	Tacrolimus	15	197.53	209.42	106.02	0	68.0	143.0	204.0	760.0
	Tofacitinib 15-10-5 mg BID	14	169.64	97.97	57.75	21.0	77.0	170.0	225.0	384.0
	Tofacitinib 30-15-10 mg BID	12	127.42	67.08	52.65	40.0	83.0	109.5	182.5	238.0
Month 24	Tacrolimus	15	144.47	116.77	80.83	18.0	75.0	117.0	153.0	468.0
	Tofacitinib 15-10-5 mg BID	14	125.86	79.56	63.21	39.0	72.0	108.5	160.0	322.0
	Tofacitinib 30-15-10 mg BID	12	85.08	51.02	59.96	36.0	51.5	60.0	112.5	192.0
Absolute CD4+ FACS Counts (per μL)										
Month 12	Tacrolimus	15	612.80	339.75	55.44	88.0	408.0	473.0	915.0	1224.0
	Tofacitinib 15-10-5 mg BID	14	634.86	280.75	44.22	220.0	350.0	637.0	915.0	1020.0
	Tofacitinib 30-15-10 mg BID	12	565.00	222.61	39.40	336.0	392.5	497.0	656.5	1040.0
Month 24	Tacrolimus	15	599.13	216.61	36.15	258.0	444.0	590.0	752.0	1020.0
	Tofacitinib 15-10-5 mg BID	14	462.00	295.73	64.01	90.0	306.0	391.5	520.0	1200.0
	Tofacitinib 30-15-10 mg BID	12	457.83	202.29	44.18	195.0	310.0	438.0	563.5	944.0
Absolute CD56+ FACS Counts (per μL)[a]										
Month 12	Tacrolimus	15	152.67	198.33	129.91	18.0	44.0	99.0	140.0	750.0
	Tofacitinib 15-10-5 mg BID	14	50.14	43.96	87.67	7.0	16.0	43.0	77.0	176.0
	Tofacitinib 30-15-10 mg BID	12	35.58	30.60	85.98	0.0	13.0	26.0	46.5	96.0
Month 24	Tacrolimus	15	135.27	145.25	107.38	12.0	40.0	72.0	162.0	512.0
	Tofacitinib 15-10-5 mg BID	14	77.86	107.37	137.91	7.0	30.0	45.5	90.0	437.0
	Tofacitinib 30-15-10 mg BID	12	59.17	69.31	117.15	12.0	16.0	26.0	68.0	228.0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis; table only includes data from extension study A3921021.

Abbreviations: BID = twice daily; CV = coefficient of variation; FACS = fluorescence activated cell sorting; Min = minimum; Max = maximum; N = number of subjects in full analysis set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation

a CD56+ cell counts were reported as a measure of CD3-CD56+ cell counts as stipulated in the protocol.

HbA1c: Descriptive statistics for HbA1c are presented by visit for the Safety Analysis Set in Table 48.

At scheduled treatment visits, median HbA1c appeared numerically similar across the treatments (Table 14.4.8.8). Through Month 72, median HbA1c ranged from 5.4% (Month 36 and Month 42, tacrolimus) to 6.4% (Month 24 and Month 60 tofacitinib 15-10-5 mg BID) across the 3 groups.

Table 48. Descriptive Statistics of HbA1c (%) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 12	Tacrolimus	16	5.65	0.69	12.21	4.8	5.4	5.5	5.8	7.5
	Tofacitinib 15-10-5 mg BID	14	6.84	2.04	29.79	4.0	5.5	5.6	8.4	10.7
	Tofacitinib 30-15-10 mg BID	12	6.02	0.82	13.61	5.2	5.5	5.8	6.4	7.8
Month 24	Tacrolimus	16	5.63	0.68	12.13	4.1	5.3	5.6	6.0	7.0
	Tofacitinib 15-10-5 mg BID	14	7.12	2.20	30.91	5.3	5.5	6.4	8.1	13.0
	Tofacitinib 30-15-10 mg BID	12	6.28	1.24	19.77	5.1	5.3	5.9	7.3	9.1
Month 36	Tacrolimus	15	5.75	1.21	20.97	4.8	5.1	5.4	5.9	9.5
	Tofacitinib 15-10-5 mg BID	14	7.19	2.44	33.94	5.0	5.6	5.8	8.6	13.4
	Tofacitinib 30-15-10 mg BID	8	6.56	1.35	20.62	5.2	5.6	6.1	7.3	9.3
Month 42	Tacrolimus	15	5.81	1.08	18.62	4.9	5.2	5.4	6.1	9.1
	Tofacitinib 15-10-5 mg BID	14	7.40	2.56	34.54	5.1	5.5	6.0	9.3	12.6
	Tofacitinib 30-15-10 mg BID	9	6.68	1.64	24.49	5.1	5.3	6.2	8.1	9.8
Month 48	Tacrolimus	15	6.03	1.23	20.38	5.0	5.4	5.7	6.1	9.8
	Tofacitinib 15-10-5 mg BID	14	7.25	2.37	32.68	5.1	5.6	6.1	8.1	13.2
	Tofacitinib 30-15-10 mg BID	10	6.25	0.82	13.07	5.4	5.4	6.3	6.7	7.6
Month 54	Tacrolimus	14	6.39	1.86	29.05	5.0	5.4	5.7	6.2	11.7
	Tofacitinib 15-10-5 mg BID	14	7.25	1.94	26.76	5.4	5.6	6.3	9.4	10.2
	Tofacitinib 30-15-10 mg BID	10	6.43	1.28	19.98	5.2	5.3	6.1	7.2	8.9
Month 60	Tacrolimus	12	6.18	1.11	17.94	5.0	5.5	5.8	6.6	9.0
	Tofacitinib 15-10-5 mg BID	12	7.03	1.75	24.86	5.1	5.7	6.4	8.8	9.8
	Tofacitinib 30-15-10 mg BID	10	6.48	1.47	22.68	5.3	5.5	6.0	6.6	9.7
Month 66	Tacrolimus	12	6.13	1.29	21.12	4.8	5.4	5.7	6.4	9.6
	Tofacitinib 15-10-5 mg BID	14	6.99	1.82	26.06	5.1	5.5	6.3	7.9	10.5
	Tofacitinib 30-15-10 mg BID	10	6.52	1.59	24.41	5.0	5.5	5.9	6.7	9.9
Month 72	Tacrolimus	9	6.31	1.72	27.29	4.7	5.1	5.8	6.8	10.1
	Tofacitinib 15-10-5 mg BID	12	6.93	1.88	27.14	5.2	5.4	6.2	8.7	10.2
	Tofacitinib 30-15-10 mg BID	8	6.29	1.38	21.90	5.1	5.5	6.0	6.4	9.5
Month 78	Tofacitinib 15-10-5 mg BID	12	7.27	2.52	34.61	5.2	5.3	6.4	8.3	12.5
	Tofacitinib 30-15-10 mg BID	8	6.43	1.98	30.80	5.0	5.4	5.7	6.6	11.1

Table 48. Descriptive Statistics of HbA1c (%) by Visit (Safety Analysis Set)

Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 84	Tofacitinib 15-10-5 mg BID	12	6.66	1.85	27.81	5.0	5.5	5.7	7.9	10.8
	Tofacitinib 30-15-10 mg BID	8	5.99	1.00	16.71	5.1	5.4	5.7	6.3	8.2
Month 90	Tofacitinib 15-10-5 mg BID	12	6.38	1.80	28.24	4.8	5.2	5.4	7.0	10.6
	Tofacitinib 30-15-10 mg BID	7	6.54	2.08	31.73	5.3	5.5	5.9	6.2	11.2
Month 96	Tofacitinib 15-10-5 mg BID	11	6.32	1.42	22.47	5.1	5.2	5.5	7.4	9.4
	Tofacitinib 30-15-10 mg BID	6	6.77	2.44	36.06	5.2	5.3	5.9	6.8	11.6
Follow-up	Tacrolimus	3	6.5	2.00	30.73	5.20	5.2	5.5	8.8	8.8
	Tofacitinib 15-10-5 mg BID	13	6.65	1.76	26.44	5.00	5.4	6.2	7.0	10.7
	Tofacitinib 30-15-10 mg BID	6	7.22	2.71	37.52	5.10	5.4	6.2	8.1	12.3

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; CV = coefficient of variation; HbA1c = glycosylated hemoglobin; Max = maximum; Min = minimum; N = number of subjects in Safety Analysis Set per visit with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

β-cell function and insulin resistance using the HOMA: Descriptive statistics for HOMA-%B, HOMA-IR, ratio of serum proinsulin to insulin, and AUCs of serum glucose and serum insulin measured during an oral glucose tolerance test (OGTT) are presented by visit for the Safety Analysis Set in Table 49.

At Month 12, median HOMA-%B was lower in the tofacitinib 15-10-5 mg BID group (101.7 [interquartile range: 76.1, 220.6]) compared with the 30-15-10 mg BID group (147.2 [interquartile range: 133.8, 271.1]) but was similar to the tacrolimus group (119.3 [interquartile range: 100.1, 224.4]). At Month 24, median HOMA-%B was higher in the 30-15-10 mg BID group (152.8 [interquartile range: 115.0, 180.5]) compared with the tofacitinib 15-10-5 mg BID group (118.3 [interquartile range: 72.3, 144.5]) or tacrolimus group (87.2 [interquartile range: 60.4, 192.6]).

At Month 12, median HOMA-IR appeared numerically similar across the 3 treatments (2.1 [interquartile range: 1.6, 3.3] in the tacrolimus group, 1.3 [interquartile range: 1.0, 3.6] in the tofacitinib 15-10-5 mg BID group and 2.4 [interquartile range: 2.2, 3.1] in the tofacitinib 30-15-10 mg BID group). Median HOMA-IR also appeared numerically similar across the 3 treatments at Month 24: 2.1 (interquartile range: 0.9, 3.1) in the tacrolimus group, 1.7 (interquartile range: 1.1, 2.2) in the tofacitinib 15-10-5 mg BID group and 2.4 (interquartile range: 1.8, 3.3) in the tofacitinib 30-15-10 mg BID group.

For the ratio of serum proinsulin:insulin, the data from so few subjects (2-5 subjects per group) precludes conclusive comparisons between treatment groups.

At Month 12, the median AUC of serum glucose was 250.4 mg.h/dL (interquartile range: 204.0, 272.8) in the tacrolimus group, 243.4 mg.h/dL (interquartile range: 215.5, 261.8) in the tofacitinib 15-10-5 mg BID group, and 279.0 mg.h/dL (interquartile range: 243.5, 304.5) in the tofacitinib 30-15-10 mg BID group. At Month 24, the median AUC was 237.3 mg.h/dL (interquartile range: 179.1, 281.0) in the tacrolimus group, 234.8 mg.h/dL (interquartile range: 179.9, 265.5) in the tofacitinib 15-10-5 mg BID group, and 317.8 mg.h/dL (interquartile range: 207.3, 332.5) in the tofacitinib 30-15-10 mg BID group.

At Month 12, the median AUC of serum insulin measured during OGTT was higher in the tofacitinib 30-15-10 mg BID group (150.6 μU∗h/mL [interquartile range: 83.5, 193.5] compared with the tofacitinib 15-10-5 mg BID group (95.8 μU*h/mL [interquartile range: 51.3, 130.0]) or tacrolimus group (83.4 μU*h/mL [interquartile range: 49.5, 122.0]). At Month 24, the median AUC of serum insulin measured during OGTT was higher in the tofacitinib groups (155.6 μU*h/mL [interquartile range: 69.5, 163.8] 15-10-5 mg BID; 92.8 μU*h/mL [interquartile range: 77.5, 316.8] 30-15-10 mg BID) compared with tacrolimus (64.6 μU*h/mL [interquartile range: 50.9, 115.4]).

Table 49. Descriptive Statistics of HOMA-%B, HOMA-IR, Ratio of Fasting Serum Proinsulin (pmol/L): Insulin (pmol/L), AUC of Serum Glucose (mg/h/dL) Measured During OGTT, and AUC of Serum Insulin (µU*h/mL) Measured During OGTT by Visit (Safety Analysis Set)

Parameter Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
HOMA-%B										
Month 12	Tacrolimus	8	204.67	195.58	95.56	82.1	100.1	119.3	224.4	667.7
	Tofacitinib 15-10-5 mg BID	6	142.23	95.06	66.84	56.7	76.1	101.7	220.6	296.5
	Tofacitinib 30-15-10 mg BID	5	194.65	131.16	67.38	42.5	133.8	147.2	271.1	378.7
Month 24	Tacrolimus	9	224.75	333.49	148.39	40.2	60.4	87.2	192.6	1085.4
	Tofacitinib 15-10-5 mg BID	6	138.10	89.84	65.06	65.7	72.3	118.3	144.5	309.5
	Tofacitinib 30-15-10 mg BID	5	165.38	68.73	41.56	103.2	115.0	152.8	180.5	275.4
HOMA-IR										
Month 12	Tacrolimus	8	2.55	1.49	58.42	1.0	1.6	2.1	3.3	5.5
	Tofacitinib 15-10-5 mg BID	6	2.24	1.85	82.79	0.8	1.0	1.3	3.6	5.4
	Tofacitinib 30-15-10 mg BID	5	2.54	1.51	59.35	0.4	2.2	2.4	3.1	4.6
Month 24	Tacrolimus	9	2.67	2.76	103.44	0.4	0.9	2.1	3.1	9.4
	Tofacitinib 15-10-5 mg BID	6	9.01	18.37	203.98	0.8	1.1	1.7	2.2	46.5
	Tofacitinib 30-15-10 mg BID	5	2.68	1.19	44.46	1.5	1.8	2.4	3.3	4.4
Ratio of fasting proinsulin:insulin										
Month 12	Tacrolimus	5	0.15	0.07	47.75	0.0	0.1	0.2	0.2	0.2
	Tofacitinib 15-10-5 mg BID	3	0.32	0.04	12.16	0.3	0.3	0.3	0.4	0.4
	Tofacitinib 30-15-10 mg BID	3	0.40	0.31	77.24	0.1	0.1	0.4	0.7	0.7
Month 24	Tacrolimus	3	0.64	0.42	65.03	0.2	0.2	0.8	1.0	1.0
	Tofacitinib 15-10-5 mg BID	4	0.30	0.20	65.24	0.1	0.2	0.3	0.4	0.6
	Tofacitinib 30-15-10 mg BID	2	0.22	0.04	18.40	0.2	0.2	0.2	0.2	0.2
AUC serum glucose										
Month 12	Tacrolimus	10	234.78	58.78	25.04	107.5	204.0	250.4	272.8	304.0
	Tofacitinib 15-10-5 mg BID	6	254.25	72.34	28.45	174.5	215.5	243.4	261.8	387.0
	Tofacitinib 30-15-10 mg BID	6	281.54	52.39	18.61	219.3	243.5	279.0	304.5	364.0
Month 24	Tacrolimus	12	230.10	56.41	24.52	149.3	179.1	237.3	281.0	299.3
	Tofacitinib 15-10-5 mg BID	8	236.94	92.98	39.24	110.5	179.9	234.8	265.5	424.8
	Tofacitinib 30-15-10 mg BID	5	281.90	100.76	35.74	151.3	207.3	317.8	332.5	400.8

Table 49. Descriptive Statistics of HOMA-%B, HOMA-IR, Ratio of Fasting Serum Proinsulin (pmol/L): Insulin (pmol/L), AUC of Serum Glucose (mg/h/dL) Measured During OGTT, and AUC of Serum Insulin (µU*h/mL) Measured During OGTT by Visit (Safety Analysis Set)

Parameter Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
AUC serum insulin										
Month 12	Tacrolimus	10	85.05	37.57	44.18	37.3	49.5	83.4	122.0	138.5
	Tofacitinib 15-10-5 mg BID	6	99.96	54.22	54.24	43.3	51.3	95.8	130.0	183.8
	Tofacitinib 30-15-10 mg BID	6	153.46	92.11	60.03	38.7	83.5	150.6	193.5	303.8
Month 24	Tacrolimus	8	79.84	42.65	53.42	29.0	50.9	64.6	115.4	148.0
	Tofacitinib 15-10-5 mg BID	6	130.63	48.07	36.80	68.8	69.5	155.6	163.8	170.5
	Tofacitinib 30-15-10 mg BID	5	181.70	155.32	85.48	40.8	77.5	92.8	316.8	380.8

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.

The OGTT was only performed in subjects who were non diabetic prior to kidney transplantation and who did not require treatment with oral hypoglycemic agents, anti-diabetic agents, and/or insulin.

Abbreviations: AUC = area under the serum concentration-time curve; BID = twice daily; CV = coefficient of variation; HOMA-%B = homeostatic model assessment-β cell function; HOMA-IR = homeostatic model assessment – insulin resistance; Max = maximum; Min = minimum; N = number of subjects in Safety Analysis Set per visit with non-missing value; OGTT = oral glucose tolerance test; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Pharmacokinetic results:

Trough levels of tacrolimus: Descriptive statistics for trough concentrations of tacrolimus are presented in Table 50.

At Month 60 the mean tacrolimus concentration was 6.58 ng/mL (SD 3.78, 12 subjects).

Table 50. Descriptive Statistics of Trough levels of Tacrolimus (ng/mL) by Visit (Safety Analysis Set)

Visit	N	Mean	SD	CV(%)	Min	Q1	Median	Q3	Max
Month 9	16	7.00	1.55	22.13	4.0	6.0	7.0	8.0	10.0
Month 12	10	9.50	5.08	53.50	3.0	6.0	9.0	11.0	21.0
Month 18	17	8.00	2.81	35.08	4.0	6.0	8.0	9.0	16.0
Month 24	9	8.78	3.93	44.77	3.0	6.0	8.0	11.0	14.0
Month 30	12	6.17	2.55	41.40	3.0	4.5	6.0	8.0	12.0
Month 36	15	6.87	2.26	32.96	4.0	5.0	6.0	8.0	12.0
Month 42	13	7.08	1.85	26.09	3.0	6.0	7.0	8.0	10.0
Month 48	15	8.07	2.96	36.74	2.0	6.0	8.0	11.0	12.0
Month 54	1	10.00			10.0	10.0	10.0	10.0	10.0
Month 60	12	6.58	3.78	57.37	3.0	4.0	4.5	9.0	14.0
Month 72	8	7.13	1.64	23.05	4.0	6.5	7.0	8.5	9.0
Follow-up	1	8.00			8.0	8.0	8.0	8.0	8.0

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: CV = coefficient of variation; Max = maximum; Min = minimum; N = number of subjects in the Safety Analysis Set with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Trough levels of tofacitinib: Descriptive statistics for trough levels of tofacitinib are presented in Table 51.

Mean (SD) predose concentrations of tofacitinib at Month 60 were 10.69 (9.62) ng/mL for the 15-10-5 mg BID group and 15.03 (10.78) ng/mL for the 30-15-10 mg BID group which were approximately 30% and 50% lower, respectively, than their corresponding Month 12 or Month 24 values.

In the tofacitinib groups in addition to the predose sample, 2 samples were collected at approximately 30 (±10) minutes and 60 (±10) minutes postdose at the study visit prior to reducing the subject's tofacitinib dose and at the next study visit after the tofacitinib dose reduction. The number of subjects at each visit with values available postdose was low in both tofacitinib groups.

Table 51. Descriptive Statistics of Trough Levels of Tofacitinib (ng/mL) by Visit (Safety Analysis Set)

Visit	Time point	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 9	Predose	Tofacitinib 15-10-5 mg BID	13	40.97	46.65	113.85	1.0	13.3	19.1	33.4	139.0
		Tofacitinib 30-15-10 mg BID	11	12.38	7.60	61.39	1.9	5.7	10.7	18.8	25.9
	0.5 hours	Tofacitinib 30-15-10 mg BID	1	24.00			24.0	24.0	24.0	24.0	24.0
Month 12	Predose	Tofacitinib 15-10-5 mg BID	13	14.75	10.44	70.75	1.0	6.3	12.7	20.5	35.3
		Tofacitinib 30-15-10 mg BID	12	32.86	46.50	141.52	1.0	7.5	17.2	24.8	157.0
	1 hour	Tofacitinib 30-15-10 mg BID	1	51.50			51.5	51.5	51.5	51.5	51.5
Month 18	Predose	Tofacitinib 15-10-5 mg BID	12	13.77	10.60	76.97	1.0	5.8	8.7	21.1	36.0
		Tofacitinib 30-15-10 mg BID	10	7.84	7.37	94.07	1.0	2.7	6.8	8.9	24.9
	0.5 hours	Tofacitinib 30-15-10 mg BID	1	86.30			86.3	86.3	86.3	86.3	86.3
	1 hour	Tofacitinib 30-15-10 mg BID	1	80.70			80.7	80.7	80.7	80.7	80.7
Month 24	Predose	Tofacitinib 15-10-5 mg BID	14	15.43	11.14	72.21	4.1	7.5	10.0	26.1	37.1
		Tofacitinib 30-15-10 mg BID	12	28.15	45.77	162.62	3.8	6.6	16.7	25.8	170.0
	0.5 hours	Tofacitinib 15-10-5 mg BID	5	28.02	4.44	15.84	23.9	24.3	27.7	29.4	34.8
		Tofacitinib 30-15-10 mg BID	2	96.30	32.10	33.34	73.6	73.6	96.3	119.0	119.0
	1 hour	Tofacitinib 15-10-5 mg BID	6	40.88	9.28	22.70	28.0	34.5	41.0	46.6	54.3
		Tofacitinib 30-15-10 mg BID	3	72.33	35.80	49.50	31.2	31.2	89.3	96.5	96.5
Month 30	Predose	Tofacitinib 15-10-5 mg BID	14	6.53	5.37	82.14	1.0	1.8	5.4	12.5	15.1
		Tofacitinib 30-15-10 mg BID	9	16.18	19.46	120.27	3.8	6.5	9.8	15.0	66.3
	0.5 hours	Tofacitinib 15-10-5 mg BID	5	51.44	26.39	51.31	19.6	27.7	59.9	71.3	78.7
		Tofacitinib 30-15-10 mg BID	2	54.95	16.05	29.21	43.6	43.6	55.0	66.3	66.3
	1 hour	Tofacitinib 15-10-5 mg BID	5	57.78	10.90	18.87	45.9	48.2	58.9	63.8	72.1
		Tofacitinib 30-15-10 mg BID	2	98.45	30.48	30.96	76.9	76.9	98.5	120.0	120.0
Month 36	Predose	Tofacitinib 15-10-5 mg BID	14	6.73	4.49	66.64	1.3	2.8	6.2	11.1	16.0
		Tofacitinib 30-15-10 mg BID	8	13.28	9.88	74.41	4.3	7.3	9.4	19.5	29.6

Table 51. Descriptive Statistics of Trough Levels of Tofacitinib (ng/mL) by Visit (Safety Analysis Set)

Visit	Time point	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 42	Predose	Tofacitinib 15-10-5 mg BID	14	19.70	29.98	152.22	1.1	7.3	9.9	16.9	117.0
		Tofacitinib 30-15-10 mg BID	18	22.01	13.71	62.27	6.9	12.6	16.3	32.4	46.7
Month 48	Predose	Tofacitinib 15-10-5 mg BID	12	9.71	6.51	67.06	1.9	4.6	8.5	14.2	21.0
		Tofacitinib 30-15-10 mg BID	9	15.54	7.33	47.15	6.2	12.0	13.6	16.6	28.6
	0.5 hours	Tofacitinib 15-10-5 mg BID	1	1.00			1.0	1.0	1.0	1.0	1.0
		Tofacitinib 30-15-10 mg BID	1	55.70			55.7	55.7	55.7	55.7	55.7
	1 hour	Tofacitinib 15-10-5 mg BID	1	56.60			56.6	56.6	56.6	56.6	56.6
Month 54	Predose	Tofacitinib 15-10-5 mg BID	14	15.99	14.97	93.58	1.9	12.0	12.0	24.1	57.2
		Tofacitinib 30-15-10 mg BID	10	24.74	41.68	168.47	3.3	10.4	10.4	20.9	142.0
Month 60	Predose	Tofacitinib 15-10-5 mg BID	11	10.69	9.62	89.96	2.3	8.2	8.2	18.4	34.1
		Tofacitinib 30-15-10 mg BID	10	15.03	10.78	71.69	1.0	11.4	11.4	19.8	33.6
	0.5 hours	Tofacitinib 15-10-5 mg BID	1	41.10			41.1	41.1	41.1	41.1	41.1
Month 66	Predose	Tofacitinib 15-10-5 mg BID	11	14.64	15.04	102.76	2.1	9.0	9.0	17.7	48.3
		Tofacitinib 30-15-10 mg BID	10	22.78	18.11	79.49	5.3	17.9	17.9	37.8	60.1
	0.5 hours	Tofacitinib 15-10-5 mg BID	1	27.70			27.7	27.7	27.7	27.7	27.7
		Tofacitinib 30-15-10 mg BID	2	29.75	18.17	61.08	16.9	29.8	29.8	42.6	42.6
	1 hour	Tofacitinib 15-10-5 mg BID	1	18.90			18.9	18.9	18.9	18.9	18.9
		Tofacitinib 30-15-10 mg BID	1	29.10			29.1	29.1	29.1	29.1	29.1
Month 72	Predose	Tofacitinib 15-10-5 mg BID	9	10.07	14.63	145.30	2.3	4.7	4.7	9.1	47.2
		Tofacitinib 30-15-10 mg BID	7	20.43	20.53	100.47	7.0	11.8	11.8	24.7	64.5
Month 78	Predose	Tofacitinib 15-10-5 mg BID	10	4.13	3.00	72.76	1.4	3.6	3.6	5.2	10.3
		Tofacitinib 30-15-10 mg BID	8	18.94	18.48	97.58	4.4	6.5	10.0	29.0	56.3
Month 84	Predose	Tofacitinib 15-10-5 mg BID	11	21.46	37.92	176.72	1.5	3.8	5.0	17.0	126.0
		Tofacitinib 30-15-10 mg BID	5	11.93	6.59	55.24	4.5	9.5	11.0	12.2	22.5

Table 51. Descriptive Statistics of Trough Levels of Tofacitinib (ng/mL) by Visit (Safety Analysis Set)

Visit	Time point	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Month 90	Predose	Tofacitinib 15-10-5 mg BID	10	6.91	7.88	113.96	1.0	2.5	5.2	7.7	27.9
		Tofacitinib 30-15-10 mg BID	5	13.8	9.78	73.66	1.0	9.0	12.7	16.1	27.6
	0.5 hours	Tofacitinib 15-10-5 mg BID	1	17.70			17.7	17.7	17.7	17.7	17.7
Month 96	Predose	Tofacitinib 15-10-5 mg BID	10	21.07	39.16	185.85	1.3	3.2	4.5	18.5	130.0
		Tofacitinib 30-15-10 mg BID	6	31.97	24.39	76.29	5.0	11.5	26.9	53.6	67.9
Follow-up	Predose	Tofacitinib 15-10-5 mg BID	1	16.00			16.0	16.0	16.0	16.0	16.0
		Tofacitinib 30-15-10 mg BID	1	1.00			1.0	1.0	1.0	1.0	1.0
	0.5 hours	Tofacitinib 15-10-5 mg BID	2	2.57	2.23	86.54	1.0	1.0	2.6	4.2	4.2
		Tofacitinib 30-15-10 mg BID	4	5.39	5.28	98.02	1.0	1.0	4.5	9.8	11.6

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: CV = coefficient of variation; Max = maximum; Min = minimum; N = number of subjects in the Safety Analysis Set with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

Outcomes research results:

SF-36 V2 Standard: Descriptive statistics and change from baseline in SF-36 V2 component scores and in SF-36 V2 subscale scores are presented by visit for the Safety Population in Table 52 and Table 53, respectively.

The limitation of sample size precludes conclusive comparisons between treatment groups. However the changes from baseline in SF-36 V2 subscale scores were numerically similar across the treatment groups for each parameter examined at Month 12, Month 18 and Month 24. No notable trends were observed between the 3 treatment groups.

Table 52. Descriptive Statistics SF-36 V2 Component Scores and Change from Baseline by Visit and Scale (Safety Analysis Set)

			Score			Change from Baseline		
Parameter	**Visit**	**Treatment**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
SF-36 v2 Physical Component Summary	Month 12	Tacrolimus	12	54.33	7.83	12	9.61	6.21
		Tofacitinib 15-10-5 mg BID	13	51.71	10.22	11	6.23	8.75
		Tofacitinib 30-15-19 mg BID	9	46.05	8.70	9	3.20	10.71
	Month 18	Tacrolimus	15	53.76	8.18	13	10.82	6.29
		Tofacitinib 15-10-5 mg BID	12	50.67	10.48	9	5.65	7.84
		Tofacitinib 30-15-19 mg BID	10	46.89	9.61	8	2.76	10.26
	Month 24	Tacrolimus	16	50.82	9.33	13	9.67	5.55
		Tofacitinib 15-10-5 mg BID	13	52.17	8.06	10	7.09	7.25
		Tofacitinib 30-15-19 mg BID	12	48.85	7.40	10	4.36	8.60
SF-36v2 Mental Component Summary	Month 12	Tacrolimus	12	53.39	7.93	12	6.86	7.36
		Tofacitinib 15-10-5 mg BID	13	50.83	11.12	11	5.03	13.29
		Tofacitinib 30-15-19 mg BID	9	54.08	10.32	9	13.70	12.32
	Month 18	Tacrolimus	15	49.70	10.59	13	1.91	14.71
		Tofacitinib 15-10-5 mg BID	122	53.92	10.61	9	9.54	9.53
		Tofacitinib 30-15-19 mg BID	10	51.44	12.21	8	8.57	13.96
	Month 24	Tacrolimus	16	50.70	9.40	13	2.99	11.63
		Tofacitinib 15-10-5 mg BID	12	55.61	6.00	10	10.05	12.55
		Tofacitinib 30-15-19 mg BID	12	52.14	8.89	10	9.59	15.22

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; N = number of subjects in Safety Population per visit with non-missing value; SD = standard deviation; SF-36 = Short Form (36) health survey.

Table 53. Descriptive Statistics for SF-36 V2 Subscale Scores and Change from Baseline by Visit and Scale (Safety Analysis Set)

			Score			Change from Baseline		
Parameter	**Visit**	**Treatment**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
SF-36v2 Physical Function Domain (norm-based)	Month 12	Tacrolimus	13	53.49	8.32	13	8.82	10.58
		Tofacitinib 15-10-5 mg BID	13	47.82	14.75	12	0.51	12.47
		Tofacitinib 30-15-19 mg BID	9	47.56	10.97	9	5.23	14.94
	Month 18	Tacrolimus	15	53.16	7.68	13	9.90	10.46
		Tofacitinib 15-10-5 mg BID	12	50.29	11.22	10	4.50	9.92
		Tofacitinib 30-15-19 mg BID	10	44.42	11.12	8	2.56	15.58
	Month 24	Tacrolimus	16	50.84	9.44	13	8.48	10.27
		Tofacitinib 15-10-5 mg BID	13	52.70	8.47	11	3.91	7.12
		Tofacitinib 30-15-19 mg BID	12	47.39	9.28	10	4.30	9.86
SF-36v2 Role - Physical Domain (norm-based)	Month 12	Tacrolimus	13	49.65	11.30	13	13.77	8.16
		Tofacitinib 15-10-5 mg BID	13	51.85	10.67	12	12.92	14.51
		Tofacitinib 30-15-19 mg BID	9	42.57	13.20	9	11.67	14.14
	Month 18	Tacrolimus	15	52.01	8.19	13	15.60	6.36
		Tofacitinib 15-10-5 mg BID	12	50.26	8.89	10	9.54	9.68
		Tofacitinib 30-15-19 mg BID	10	46.12	11.37	8	12.53	9.44
	Month 24	Tacrolimus	16	48.12	14.6	13	12.30	8.76
		Tofacitinib 15-10-5 mg BID	13	53.69	6.69	11	13.23	13.13
		Tofacitinib 30-15-19 mg BID	12	51.45	6.42	10	17.18	13.81
SF-36v2 Bodily Pain Domain (norm-based)	Month 12	Tacrolimus	13	53.19	13.05	13	1.47	15.91
		Tofacitinib 15-10-5 mg BID	13	54.25	7.34	12	6.87	10.52
		Tofacitinib 30-15-19 mg BID	9	50.7	11.18	9	-0.83	14.54
	Month 18	Tacrolimus	15	53.53	9.59	13	0.83	11.32
		Tofacitinib 15-10-5 mg BID	12	54.32	11.78	10	8.08	12.98
		Tofacitinib 30-15-19 mg BID	10	52.64	10.01	8	-0.31	14.06
	Month 24	Tacrolimus	16	53.02	9.2	13	2.56	10.01
		Tofacitinib 15-10-5 mg BID	13	50.57	12.55	11	5.57	12.58
		Tofacitinib 30-15-19 mg BID	12	51.51	8.78	10	-1.25	12.99

Table 53. Descriptive Statistics for SF-36 V2 Subscale Scores and Change from Baseline by Visit and Scale (Safety Analysis Set)

			Score			Change from Baseline		
Parameter	**Visit**	**Treatment**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
SF-36v2 General Health Domain (norm-based)	Month 12	Tacrolimus	12	57.18	6.12	12	11.73	5.80
		Tofacitinib 15-10-5 mg BID	13	52.96	8.50	11	6.75	12.04
		Tofacitinib 30-15-19 mg BID	9	47.86	8.52	9	3.60	7.67
	Month 18	Tacrolimus	15	52.54	10.64	13	8.89	9.64
		Tofacitinib 15-10-5 mg BID	12	50.10	8.89	9	6.94	8.80
		Tofacitinib 30-15-19 mg BID	10	46.67	10.08	8	-1.29	11.83
	Month 24	Tacrolimus	16	49.54	10.37	13	8.06	8.96
		Tofacitinib 15-10-5 mg BID	13	54.33	8.23	10	9.11	7.86
		Tofacitinib 30-15-19 mg BID	12	48.14	6.20	10	1.83	8.55
SF-36v2 Vitality Domain (norm-based)	Month 12	Tacrolimus	13	59.78	5.67	13	11.05	9.58
		Tofacitinib 15-10-5 mg BID	13	55.64	13.28	12	9.23	15.29
		Tofacitinib 30-15-19 mg BID	9	58.61	11.86	9	16.30	8.87
	Month 18	Tacrolimus	15	53.55	10.11	13	7.14	13.36
		Tofacitinib 15-10-5 mg BID	12	57.44	11.69	10	11.67	13.49
		Tofacitinib 30-15-19 mg BID	10	53.75	10.58	8	10.85	6.96
	Month 24	Tacrolimus	16	54.14	10.88	13	8.90	10.52
		Tofacitinib 15-10-5 mg BID	13	59.55	7.19	11	15.51	11.96
		Tofacitinib 30-15-19 mg BID	12	50.96	9.75	10	7.18	14.06
SF-36v2 Social Function Domain (norm-based)	Month 12	Tacrolimus	13	48.96	8.37	13	4.14	10.79
		Tofacitinib 15-10-5 mg BID	13	46.48	13.14	12	7.62	14.76
		Tofacitinib 30-15-19 mg BID	9	50.43	9.10	9	11.95	12.55
	Month 18	Tacrolimus	15	49.59	9.85	13	4.55	14.54
		Tofacitinib 15-10-5 mg BID	12	50.58	10.11	10	11.83	11.84
		Tofacitinib 30-15-19 mg BID	10	50.49	12.53	8	8.74	13.77
	Month 24	Tacrolimus	16	51.36	7.72	13	7.03	12.68
		Tofacitinib 15-10-5 mg BID	13	52.27	7.00	11	11.73	11.49
		Tofacitinib 30-15-19 mg BID	12	51.03	9.17	10	9.68	15.38

Table 53. Descriptive Statistics for SF-36 V2 Subscale Scores and Change from Baseline by Visit and Scale (Safety Analysis Set)

			Score			Change from Baseline		
Parameter	**Visit**	**Treatment**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
SF-36v2 Role - Emotional Domain (norm-based)	Month 12	Tacrolimus	13	49.27	13.51	13	10.19	13.06
		Tofacitinib 15-10-5 mg BID	13	49.56	10.54	12	7.26	19.87
		Tofacitinib 30-15-19 mg BID	9	48.53	10.61	9	15.14	17.45
	Month 18	Tacrolimus	15	51.64	8.87	13	9.32	13.35
		Tofacitinib 15-10-5 mg BID	12	50.63	10.12	10	11.74	17.25
		Tofacitinib 30-15-19 mg BID	10	48.49	12.42	8	13.25	16.56
	Month 24	Tacrolimus	16	47.63	14.49	13	4.66	17.15
		Tofacitinib 15-10-5 mg BID	13	52.18	7.16	11	6.54	15.25
		Tofacitinib 30-15-19 mg BID	12	52.52	4.52	10	16.66	18.82
SF-36v2 Mental Health Domain (norm-based)	Month 12	Tacrolimus	13	54.05	8.04	13	2.98	6.64
		Tofacitinib 15-10-5 mg BID	13	51.71	9.67	12	4.62	8.71
		Tofacitinib 30-15-19 mg BID	9	52.35	9.08	9	5.54	13.64
	Month 18	Tacrolimus	15	49.21	11.37	13	-1.28	13.51
		Tofacitinib 15-10-5 mg BID	12	54.66	9.87	10	8.03	5.76
		Tofacitinib 30-15-19 mg BID	10	49.02	11.37	8	0.00	14.36
	Month 24	Tacrolimus	16	51.31	8.58	13	1.70	9.36
		Tofacitinib 15-10-5 mg BID	13	56.19	6.45	11	10.58	10.20
		Tofacitinib 30-15-19 mg BID	12	50.50	9.84	10	2.22	12.72
SF-36v2 TR Scale Score	Month 12	Tacrolimus	13	1.23	0.83	13	-1.31	1.55
		Tofacitinib 15-10-5 mg BID	13	1.23	0.83	12	-1.83	1.40
		Tofacitinib 30-15-19 mg BID	9	1.33	1.00	9	-1.78	2.11
	Month 18	Tacrolimus	15	1.53	0.74	13	-1.15	1.28
		Tofacitinib 15-10-5 mg BID	12	1.67	0.78	10	-1.10	1.37
		Tofacitinib 30-15-19 mg BID	10	1.70	1.06	8	-1.13	1.81
	Month 24	Tacrolimus	16	2.00	0.97	13	-0.92	1.19
		Tofacitinib 15-10-5 mg BID	13	1.62	0.77	11	-1.45	1.21
		Tofacitinib 30-15-19 mg BID	12	2.33	0.98	10	-0.70	1.25

Table 53. Descriptive Statistics for SF-36 V2 Subscale Scores and Change from Baseline by Visit and Scale (Safety Analysis Set)

			Score			Change from Baseline		
Parameter	**Visit**	**Treatment**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; N = number of subjects in Safety Population per visit with non-missing value; SD = standard deviation; SF-36 = Short Form (36) health survey.

ESRD-SCL: Descriptive statistics and change from baseline in ESRD-SCL modules are presented by visit for the Safety Population in Table 54.

The limitation of sample size precludes conclusive comparisons between treatment groups. However, the changes from baseline were generally similar across the treatment groups for each parameter examined at Month 12, Month 18 and Month 24. No notable trends were observed between the 3 treatment groups.

Table 54. Descriptive Statistics for ESRD-SCL-Transplantation Modules and Change from Baseline by Visit and Scale (Safety Analysis Set)

			Score			Change from Baseline		
Parameter	**Visit**	**Treatment**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Limited physical capacity	Month 12	Tacrolimus	13	0.22	0.25	13	-0.34	0.45
		Tofacitinib 15-10-5 mg BID	12	0.37	0.40	10	-0.34	0.25
		Tofacitinib 30-15-19 mg BID	8	0.29	0.40	8	-0.53	0.38
	Month 18	Tacrolimus	15	0.53	0.69	13	-0.20	0.54
		Tofacitinib 15-10-5 mg BID	12	0.41	0.38	9	-0.36	0.32
		Tofacitinib 30-15-19 mg BID	10	0.46	0.55	8	-0.30	0.63
	Month 24	Tacrolimus	16	0.60	0.69	13	-0.16	0.63
		Tofacitinib 15-10-5 mg BID	13	0.44	0.46	10	-0.23	0.28
		Tofacitinib 30-15-19 mg BID	11	0.55	0.46	9	-0.32	0.39
Limited cognitive capacity	Month 12	Tacrolimus	13	0.41	0.40	13	-0.37	0.59
		Tofacitinib 15-10-5 mg BID	12	0.45	0.45	10	-0.37	0.24
		Tofacitinib 30-15-19 mg BID	8	0.30	0.36	8	-0.36	0.65
	Month 18	Tacrolimus	15	0.63	0.89	13	-0.22	0.80
		Tofacitinib 15-10-5 mg BID	12	0.42	0.42	9	-0.39	0.45
		Tofacitinib 30-15-19 mg BID	10	0.29	0.43	8	-0.39	0.54
	Month 24	Tacrolimus	16	0.65	0.85	13	-0.25	0.89
		Tofacitinib 15-10-5 mg BID	13	0.57	0.67	10	-0.21	0.56
		Tofacitinib 30-15-19 mg BID	11	0.48	0.54	9	-0.26	0.72
Cardiac and renal dysfunction	Month 12	Tacrolimus	13	0.18	0.26	13	-0.48	0.68
		Tofacitinib 15-10-5 mg BID	13	0.27	0.31	9	-0.51	0.43
		Tofacitinib 30-15-19 mg BID	8	0.18	0.18	8	-0.52	0.49
	Month 18	Tacrolimus	14	0.25	0.38	12	-0.49	0.78
		Tofacitinib 15-10-5 mg BID	12	0.30	0.31	8	-0.50	0.41
		Tofacitinib 30-15-19 mg BID	9	0.22	0.20	7	-0.45	0.60
	Month 24	Tacrolimus	15	0.33	0.51	13	-0.46	0.61
		Tofacitinib 15-10-5 mg BID	13	0.31	0.35	9	-0.41	0.39
		Tofacitinib 30-15-19 mg BID	11	0.34	0.24	9	-0.33	0.44

Table 54. Descriptive Statistics for ESRD-SCL-Transplantation Modules and Change from Baseline by Visit and Scale (Safety Analysis Set)

			Score			Change from Baseline		
Parameter	**Visit**	**Treatment**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Side effects of corticosteroids	Month 12	Tacrolimus	13	0.29	0.35	13	-0.25	0.55
		Tofacitinib 15-10-5 mg BID	13	0.57	0.80	9	-0.02	0.66
		Tofacitinib 30-15-19 mg BID	8	0.70	0.83	8	0.18	0.61
	Month 18	Tacrolimus	14	0.39	0.65	12	-0.40	0.72
		Tofacitinib 15-10-5 mg BID	12	0.45	0.66	8	-0.23	0.43
		Tofacitinib 30-15-19 mg BID	10	0.58	0.61	8	0.03	0.52
	Month 24	Tacrolimus	15	0.53	0.64	13	-0.25	0.68
		Tofacitinib 15-10-5 mg BID	13	0.26	0.35	9	-0.31	0.55
		Tofacitinib 30-15-19 mg BID	11	0.69	0.66	9	0.13	0.53
Increased growth of gum and hair	Month 12	Tacrolimus	13	0.17	0.24	13	0.06	0.28
		Tofacitinib 15-10-5 mg BID	13	0.15	0.25	10	-0.06	0.40
		Tofacitinib 30-15-19 mg BID	8	0.08	0.15	8	-0.08	0.24
	Month 18	Tacrolimus	15	0.17	0.28	13	0.04	0.27
		Tofacitinib 15-10-5 mg BID	12	0.23	0.31	9	-0.04	0.46
		Tofacitinib 30-15-19 mg BID	10	0.14	0.16	8	-0.03	0.23
	Month 24	Tacrolimus	16	0.41	0.49	13	0.29	0.59
		Tofacitinib 15-10-5 mg BID	13	0.28	0.48	10	0.10	0.63
		Tofacitinib 30-15-19 mg BID	11	0.11	0.21	9	-0.07	0.17
Transplantation-associated psychological distress	Month 12	Tacrolimus	13	0.40	0.42	13	-0.49	0.56
		Tofacitinib 15-10-5 mg BID	12	0.50	0.41	10	-0.57	0.58
		Tofacitinib 30-15-19 mg BID	8	0.48	0.33	8	-0.61	0.42
	Month 18	Tacrolimus	15	0.70	0.81	13	-0.28	0.46
		Tofacitinib 15-10-5 mg BID	12	0.42	0.37	9	-0.57	0.55
		Tofacitinib 30-15-19 mg BID	10	0.47	0.19	8	-0.48	0.58
	Month 24	Tacrolimus	16	0.77	0.72	13	-0.30	0.51
		Tofacitinib 15-10-5 mg BID	13	0.45	0.40	10	-0.62	0.67
		Tofacitinib 30-15-19 mg BID	11	0.57	0.74	9	-0.61	0.70

Table 54. Descriptive Statistics for ESRD-SCL-Transplantation Modules and Change from Baseline by Visit and Scale (Safety Analysis Set)

			Score			Change from Baseline		
Parameter	**Visit**	**Treatment**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Global score	Month 12	Tacrolimus	13	0.28	0.26	13	-0.34	0.37
		Tofacitinib 15-10-5 mg BID	12	0.39	0.36	10	-0.36	0.24
		Tofacitinib 30-15-19 mg BID	8	0.33	0.25	8	-0.37	0.29
	Month 18	Tacrolimus	15	0.50	0.65	13	-0.21	0.57
		Tofacitinib 15-10-5 mg BID	12	0.38	0.34	9	-0.40	0.31
		Tofacitinib 30-15-19 mg BID	10	0.36	0.25	8	-0.31	0.36
	Month 24	Tacrolimus	16	0.57	0.59	13	-0.21	0.52
		Tofacitinib 15-10-5 mg BID	13	0.40	0.40	10	-0.30	0.31
		Tofacitinib 30-15-19 mg BID	11	0.47	0.41	9	-0.28	0.35

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: BID = twice daily; ESRD-SCL = End-Stage Renal Disease Symptom Checklist-Transplantation Modules; N = number of subjects in Safety Population per visit with non-missing value; SD = standard deviation.

HCRUQ: Descriptive statistics for the HCRUQ are presented by visit for the Safety Population in Table 55.

The limitation of sample size precludes conclusive comparisons between treatment groups particularly for number of other test or procedures, total number of previous hospitalizations, and number of emergency room visits (1-4 subjects per group). The mean number of doctor or healthcare professional visits was similar across the 3 groups at Month 12, Month 18 and Month 24. The mean number of visits ranged from 2.5 (SD 2.0) visits (tofacitinib 15-10-5 mg BID, Month 24 visit, 11 subjects) to 7.2 (SD 9.0) visits (tacrolimus, Month 18, 10 subjects) across treatment groups and visits.

Table 55. Descriptive Statistics of HCRUQ by Visit (Safety Analysis Set)

Parameter	Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Number of doctor/HCP visits	Month 12	Tacrolimus	9	3.1	3.1	98.3	1	2.0	2.0	3.0	11
		Tofacitinib 15-10-5 mg BID	10	2.7	2.5	90.8	1	1.0	1.5	3.0	8
		Tofacitinib 30-15-10 mg BID	4	6.3	3.9	61.8	1	3.5	7.0	9.0	10
	Month 18	Tacrolimus	10	7.2	9.0	125.2	1	2.0	3.5	7.0	29
		Tofacitinib 15-10-5 mg BID	9	6.4	7.5	116.1	1	2.0	3.0	9.0	24
		Tofacitinib 30-15-10 mg BID	6	5.8	2.7	46.5	2	3.0	7.0	8.0	8
	Month 24	Tacrolimus	12	5.1	4.2	83.2	1	1.5	4.5	6.5	15
		Tofacitinib 15-10-5 mg BID	11	2.5	2.0	77.3	1	1.0	2.0	4.0	6
		Tofacitinib 30-15-10 mg BID	9	5.0	6.3	125.7	1	1.0	4.0	5.0	21
Number of other tests/procedures	Month 12	Tacrolimus	1	1.0			1	1.0	1.0	1.0	1
		Tofacitinib 15-10-5 mg BID	4	2.0	1.4	70.7	1	1.0	1.5	3.0	4
		Tofacitinib 30-15-10 mg BID	4	2.3	1.9	84.1	1	1.0	1.5	3.5	5
	Month 18	Tacrolimus	4	2.5	1.7	69.3	1	1.5	2.0	3.5	5
		Tofacitinib 15-10-5 mg BID	3	2.0	1.7	86.6	1	1.0	1.0	4.0	4
	Month 24	Tacrolimus	4	3.8	2.8	73.4	1	1.5	3.5	6.0	7
		Tofacitinib 15-10-5 mg BID	3	1.3	0.6	43.3	1	1.0	1.0	2.0	2
		Tofacitinib 30-15-10 mg BID	4	2.8	2.2	80.6	1	1.5	2.0	4.0	6
Total number of previous hospitalizations	Month 12	Tacrolimus	1	2.0			2	2.0	2.0	2.0	2
		Tofacitinib 15-10-5 mg BID	1	1.0			1	1.0	1.0	1.0	1
		Tofacitinib 30-15-10 mg BID	2	1.0	0.0	0.0	1	1.0	1.0	1.0	1
	Month 18	Tacrolimus	3	1.3	0.6	43.3	1	1.0	1.0	2.0	2
		Tofacitinib 15-10-5 mg BID	1	1.0			1	1.0	1.0	1.0	1
		Tofacitinib 30-15-10 mg BID	1	2.0			2	2.0	2.0	2.0	2
	Month 24	Tacrolimus	3	1.0	0.0	0.0	1	1.0	1.0	1.0	1
		Tofacitinib 15-10-5 mg BID	3	1.0	0.0	0.0	1	1.0	1.0	1.0	1
		Tofacitinib 30-15-10 mg BID	1	1.0			1	1.0	1.0	1.0	1

Table 55. Descriptive Statistics of HCRUQ by Visit (Safety Analysis Set)

Parameter	Visit	Treatment	N	Mean	SD	CV (%)	Min	Q1	Median	Q3	Max
Number of emergency room visits	Month 12	Tacrolimus	1	1.0			1	1.0	1.0	1.0	1
		Tofacitinib 15-10-5 mg BID	1	1.0			1	1.0	1.0	1.0	1
		Tofacitinib 30-15-10 mg BID	2	1.0	0.0	0.0	1	1.0	1.0	1.0	1
	Month 18	Tacrolimus	3	1.3	0.6	43.3	1	1.0	1.0	2.0	2
		Tofacitinib 15-10-5 mg BID	3	1.0	0.0	0.0	1	1.0	1.0	1.0	1
		Tofacitinib 30-15-10 mg BID	1	2.0			2	2.0	2.0	2.0	2
	Month 24	Tacrolimus	4	1.0	0.0	0.0	1	1.0	1.0	1.0	1
		Tofacitinib 15-10-5 mg BID	2	1.0	0.0	0.0	1	1.0	1.0	1.0	1
		Tofacitinib 30-15-10 mg BID	2	1.0	0.0	0.0	1	1.0	1.0	1.0	1

Per site-specific Protocol Amendment 1, the data collected for 1 subject was excluded from this analysis. Table only includes data from extension study A3921021.
Abbreviations: CV = coefficient of variation; HCP = healthcare professional; HCRUQ = Healthcare Resource Utilization Questionnaire by Visit and Question; Max = maximum; Min = minimum; N = number of subjects in the Safety Analysis Set with non-missing value; Q1 = first quartile; Q3 = third quartile; SD = standard deviation.

CONCLUSION(S):

- The small number of subjects assigned to study treatment (tacrolimus, 18 subjects; tofacitinib 15-10-5 mg BID, 14 subjects; tofacitinib 30-15-10 mg BID, 13 subjects) precluded conclusive comparisons between treatment groups.

- There was no evidence that the rates of BPAR or treatment failure were higher in the tofacitinib groups compared with the tacrolimus group.

- A total of 2 deaths were reported in the tofacitinib groups within the reporting period of the study. One additional death occurred in the tacrolimus group approximately 5 months after the subject had received their last dose of tacrolimus. SAEs were reported for 25 subjects (7 subjects in the tacrolimus group, 10 subjects in the tofacitinib 15-10-5 mg BID group and 8 subjects in the tofacitinib 30-15-10 mg BID group).

- The cumulative rate of serious infection was higher in the tofacitinib treatment groups compared with tacrolimus through the entire treatment duration of Study A3921021 (at Month 60, cumulative rate [Kaplan-Meier estimate] was 11.5% [2 events] for tacrolimus, 42.9% [6 events] for tofacitinib 15-10-5 mg BID, and 30.8% [4 events] for tofacitinib 30-15-10 mg BID).

- There was a higher rate of herpes zoster infection in the tofacitinib 15-10-5 mg BID (3 [21.4%] subjects) group than in the tacrolimus (1 [5.6%] subject) or tofacitinib 30-15-10 mg BID (1 [7.7%] subject) groups.