CLINICAL STUDY REPORT SYNOPSIS

Sponsor: Pfizer, Inc.

Investigational Product: Abrocitinib (PF-04965842)

Clinical Study Report Synopsis: Protocol B7451029

Protocol Title: A Phase 3 Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, Parallel Group, Multi-Center Study Investigating the Efficacy and Safety of PF-04965842 and Dupilumab in Comparison With Placebo in Adult Subjects on Background Topical Therapy, With Moderate to Severe Atopic Dermatitis

Investigators: Refer to Appendix 16.1.4.1 for a list of investigators involved in this study.

Study Center(s): 194 sites in 18 countries, United States (n=46), Poland (n=36), Republic of Korea (n=7), Japan (n=12), Australia (n=10), Bulgaria (n=5), Canada (n=11), Germany (n=13), United Kingdom (n=11), Latvia (n=5), Hungary (n=5), Czech Republic (n=7), Chile (n=4), Spain (n=5), Italy (n=2), Mexico (n=4), Slovakia (n=5), and Taiwan (n=6). Refer to Appendix 16.1.4.1 for a list of sites involved in this study.

Publications Based on the Study: None

Study Initiation Date: First Subject First Visit: 29 OCT 2018

Study Completion Date: Last Subject Last Visit: 06 MAR 2020;

Primary Completion Date: 27 DEC 2019

Report Date: 28 May 2020

Previous Report Date(s): Not applicable

Phase of Development: Phase 3

Primary and Secondary Study Objectives and Endpoints:

Table S1. Study Objectives and Endpoints

Type	Objective	Endpoint
Primary		
Efficacy	• To compare the efficacy of 100 mg and 200 mg once daily (QD) of PF-04965842 versus placebo in adult subjects on background topical therapy with moderate to severe atopic dermatitis (AD).	• Response based on achieving the Investigator's Global Assessment (IGA) of clear (0) or almost clear (1) (on a 5-point scale) and a reduction from baseline (pre-dose Day 1) of ≥2 points at Week 12.
		• Response based on achieving the Eczema Area and Severity Index (EASI)-75 (≥75% improvement from baseline) at Week 12.

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Secondary		
Efficacy	• To compare the efficacy of PF-04965842 versus dupilumab in terms of attaining a clinically significant improvement in the severity of pruritus for adult subjects on background topical therapy with moderate to severe AD.	**Key Secondary Endpoint** • Response based on achieving at least 4 points improvement in the severity of Pruritus Numerical Rating Scale (NRS) from baseline at Week 2.
	• To estimate the difference in efficacy measures between two doses of PF-04965842 and dupilumab for adult subjects on background topical therapy with moderate to severe AD.	**Key Secondary Endpoints** • Response based on achieving the IGA of clear (0) or almost clear (1) (on a 5-point scale) and a reduction from baseline of ≥2 points at Week 16. • Response based on achieving EASI-75 (≥75% improvement from baseline) at Week 16.
Efficacy	• To estimate the effect of PF-04965842 on additional efficacy endpoints and patient-reported outcomes over time in adult subjects on background topical therapy with moderate to severe AD.	**Secondary Efficacy Endpoints** • Response based on achieving the IGA of clear (0) or almost clear (1) (on a 5-point scale) and ≥2-point reduction from baseline at all scheduled time points except Week 12 and Week 16. • Response based on achieving a ≥75% improvement in the EASI total score (EASI-75) at all scheduled time points except Week 12 and Week 16. • Response based on achieving a ≥50%, ≥90%, and 100% improvement in the EASI total score (EASI-50, EASI-90, and EASI-100) at all scheduled time points. • Response based on achieving at least 4 points improvement in the severity of Pruritus NRS from baseline at all scheduled time points except Week 2. • Time from baseline to achieve at least 4 points improvement in the severity of Pruritus NRS scale. • Change from baseline in the percentage Body Surface Area (BSA) affected at all scheduled time points. • Change from baseline of Patient Global Assessment (PtGA) at all scheduled time points. • Change from baseline in Dermatology Life Quality Index (DLQI) at all scheduled time points. • Change from baseline in EuroQol Quality of Life 5-Dimension 5-Level Scale (EQ-5D-5L) at all scheduled time points. • Change from baseline in Hospital Anxiety and Depression Scale (HADS) at all scheduled time points.

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		• Change from baseline in Patient Oriented Eczema Measure (POEM) at all scheduled time points. • Change from baseline in Pruritus and Symptoms Assessment for Atopic Dermatitis (PSAAD) total score at all scheduled time points. • Response based on a ≥50% and ≥75% improvement in Scoring Atopic Dermatitis (SCORAD50, SCORAD75) from baseline at all scheduled time points. • Change from baseline at all scheduled time points in SCORAD subjective assessments of itch and sleep loss. • Steroid free days at Week 16.
Safety	• To compare the safety and tolerability of 100 mg and 200 mg QD of PF-04965842 and dupilumab versus placebo in adult subjects on background topical therapy with moderate to severe AD. • To estimate the safety and tolerability of the two doses of PF-04965842 versus dupilumab, for adult subjects on background topical therapy with moderate to severe AD.	• Incidence of treatment-emergent adverse event (AE)s. • Incidence of serious adverse event (SAE)s and AEs leading to discontinuation. • Incidence of clinical abnormalities and change from baseline in clinical laboratory values, electrocardiogram (ECG) measurements, and vital signs.

METHODS

Study Design: This was a randomized, double-blind, double-dummy, placebo-controlled, parallel-group, multi-center study to assess the efficacy and safety of abrocitinib 100 mg or 200 mg QD and dupilumab (as per label) compared with placebo in adult subjects on background topical therapy, with moderate to severe AD. The treatment duration was 20 weeks. A total of 838 subjects were randomized from 194 sites globally. There was a primary efficacy assessment at Week 12, and key secondary efficacy assessments at Week 2 and Week 16. Efficacy and safety endpoints were assessed throughout the entire study.

Diagnosis and Main Criteria for Inclusion: Subjects aged 18 years or older at the time of informed consent and met following AD criteria were enrolled:

- Clinical diagnosis of chronic AD for at least 1 year prior to Day 1 and had confirmed AD (Hanifin and Rajka criteria) at the screening and baseline visits.

- Documented recent history (within 6 months before the screening visit) of inadequate response to treatment with medicated topical therapy for AD for at least 4 weeks, or who had required systemic therapies for control of their disease. Medicated topical therapy

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was defined as a topical product containing an active pharmaceutical ingredient indicated for the treatment of AD, irrespective of whether it is an over the counter or prescribed product.

- Moderate to severe AD (affected BSA ≥10%, IGA ≥3, EASI ≥16, and Pruritus NRS severity score ≥4 on the day of the baseline visit).

- During the 7 days prior to Day 1, the subject must have used only non-medicated topical therapy without other active ingredients indicated to treat AD, or other additives which could affect AD at least twice daily, with response to treatment remaining inadequate at baseline.

Study Treatment: Blinded abrocitinib, 100 mg tablets, and its matched placebo tablets were provided in separate bottles. Subjects were dispensed two bottles of tablets, depending on the study group, and were given clear dosing instructions to take one tablet from each bottle, once daily (Table S2).

Blinded dupilumab, 300 mg/2 mL, and its matching placebo were provided as prefilled syringes for subcutaneous injection. Two subcutaneous injections (loading dose of 600 mg or placebo) were administered at baseline and one subcutaneous injection was administered every 2 weeks (Q2W) as per the protocol Schedule of Activities.

Table S2. Investigational Product Description

Investigational Product Description	Vendor Lot Number	Pfizer Lot Number	Strength/ Potency	Dosage Form
Placebo for Dupilumab 300 mg/2.0 ml Pre-Filled 2.25 ml Syringe Barrel	3-FIN-3168	18-002278	0 mg/ml	Prefill syringe
Placebo for PF-04965842 Round White Film Coated Tablet (9 mm)	GR-SDM	18-002727	0 mg	Tablet
PF-04965842 100 mg Round White Film Coated Tablet (DC)	GR-SDM	18-002731	100 mg	Tablet
PF-04965842 100 mg Round White Film Coated Tablet (DC)	GR-SDM	18-001886	100 mg	Tablet
Placebo for PF-04965842 Round White Film Coated Tablet (9 mm)	GR-SDM	17-003139	0 mg	Tablet
Dupilumab 300 mg/2 ml single-dose prefilled syringe with needle shield	8L067A	18-003068	300 mg	Commercial product
Dupilumab 300 mg/2 ml single-dose prefilled syringe with needle shield	8L310A	18-003459	300 mg	Commercial product
PF-04965842 100 mg Round White Film Coated Tablet (DC)	GR-SDM	18-001885	100 mg	Tablet
Dupilumab 300 mg/2 ml single-dose prefilled syringe with needle shield	8L244A	18-002973	300 mg	Commercial product
Dupilumab 300 mg/2 ml single-dose prefilled syringe with needle shield	7L616A	18-001641	300 mg	Commercial product

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Table S2. Investigational Product Description

Investigational Product Description	Vendor Lot Number	Pfizer Lot Number	Strength/ Potency	Dosage Form
Dupilumab 300 mg/2 ml single-dose prefilled syringe with needle shield	8L926A	19-001382	300 mg	Commercial product
Placebo for Dupilumab 300 mg/2.0 ml Pre-Filled 2.25 ml Syringe Barrel	3-FIN-3414	19-001544	0 mg/ml	Prefill syringe

Efficacy Evaluations:

Co-primary endpoints:

- Response based on the IGA score of clear (0) or almost clear (1); and a reduction from baseline of ≥2 points at Week 12;
- Response based on the EASI ≥75% improvement from baseline (EASI-75) at Week 12.

Key secondary efficacy endpoints:

- Response based on ≥4 points improvement from baseline in the peak pruritis NRS (PP-NRS4) for severity at Week 2;
- Response based on achieving the IGA of clear (0) or almost clear (1) (on a 5-point scale) and a reduction from baseline of ≥2 points at Week 16;
- Response based on achieving EASI-75 (≥75% improvement from baseline) at Week 16.

Secondary efficacy endpoints:

- Response based on achieving the IGA of clear (0) or almost clear (1) (on a 5-point scale) and ≥2 point reduction from baseline at all scheduled time points except Week 12 and Week 16;
- Response based on achieving a ≥75% improvement in the EASI total score (EASI-75) at all scheduled time points except Week 12 and Week 16;
- Response based on achieving a ≥50%, ≥90% and 100% improvement in the EASI total score (EASI-50, EASI-90 and EASI-100) at all scheduled time points;
- Percent change from baseline in total EASI score (included in the SAP, not in the protocol);
- Response based on achieving NRS4 at all scheduled time points except Week 2;

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- Time from baseline to achieve NRS4;
- Percent change from baseline in severity of PP-NRS each day from Days 2-15, Weeks 4, 8, 12, and 16 (included in the statistical analysis plan [SAP], not in the protocol);
- Change from baseline and percent change from baseline in the percentage body surface area (%BSA) affected at all scheduled time points;
- Steroid-free days by Week 16;
- Response based on a ≥50% and ≥75% improvement in SCORAD (SCORAD50, SCORAD75) from baseline at all scheduled time points;
- Percent change from baseline and change from baseline at all scheduled time points in the SCORAD total score;
- Percent change from baseline and change from baseline at all scheduled time points in SCORAD subjective assessments of sleep loss.

Patient Reported Outcomes (PRO) secondary endpoints:

- Change from baseline of PtGA at all scheduled time points;
- Change from baseline in DLQI at all scheduled time points;
- Change from baseline in EQ-5D-5L at all scheduled time points;
- Change from baseline in each component (anxiety and depression) of the HADS at all scheduled time points;
- Change from baseline in POEM at all scheduled time points;
- Change from baseline in PSAAD total score at all scheduled time points.

Pharmacokinetic, Pharmacodynamic, and Pharmacogenomic Evaluations: These evaluations were not conducted in this study.

Safety Evaluations: Safety was assessed by the spontaneous reporting of AEs, physical examinations, vital signs, and clinical laboratory results in all subjects who received at least 1 dose of the investigational product. The safety endpoints included incidence of treatment-emergent AEs (TEAEs), incidence of SAEs and AEs leading to discontinuation, and incidence of clinical abnormalities and change from baseline in selected clinical laboratory values, ECG measurements, and vital signs.

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Statistical Methods: Abrocitinib 200 mg QD was declared superior to placebo if the null hypothesis of no difference between abrocitinib 200 mg QD versus placebo for both co-primary endpoints was rejected at the 5% significance level. Similarly, abrocitinib 100 mg QD was declared superior to placebo if the null hypothesis of no difference between abrocitinib 100 mg QD versus placebo for both co-primary endpoints was rejected at the significance level specified below.

A sequential Bonferroni-based iterative multiple testing procedure to strongly control the familywise Type 1 error at 5% was used for assessing each of the two abrocitinib doses (200 mg QD and 100 mg QD) versus placebo on the primary and key secondary endpoints. The procedure belongs to a class of consonant multiple test procedures which are a subclass of the closed test procedures.

The procedure first assessed the co-primary endpoints (IGA and EASI-75 at Week 12 for 200 mg QD versus placebo) at the 5% level. If this hypothesis was not rejected, then statistical significance was not claimed for any subsequent hypotheses. If this hypothesis was rejected, assessing for statistical significance continued for the co-primary endpoints (IGA and EASI-75 at Week 12) for the 100 mg QD versus placebo comparison. If this hypothesis was not rejected, then no statistical significance was claimed for any subsequent hypotheses. If this hypothesis was rejected, then assessments continued as follows:

1. A series of hypotheses related to the severity of pruritus (NRS4) at Week 2 were assessed at the 2.5% level in the following order (Sequence A): 200 mg abrocitinib versus placebo, 100 mg abrocitinib versus placebo, 200 mg abrocitinib versus dupilumab, 100 mg abrocitinib versus dupilumab.

2. If all hypotheses in Sequence A were rejected, then the unused alpha level of 2.5% was passed on to the assessing for the Week 16 endpoints at a 5% significance level in the following order (Sequence B): IGA, 200 mg abrocitinib versus placebo; EASI-75, 200 mg abrocitinib versus placebo, IGA, 100 mg abrocitinib versus placebo; EASI-75, 100 mg abrocitinib versus placebo. The statistical significance for each hypothesis in Sequence B could not be claimed unless the prior hypothesis in the sequence was statistically significant. In Sequence B, if one hypothesis was not rejected at alpha level of 5% then no statistical significance was claimed for any subsequent hypotheses in the sequence.

3. In Sequence A, if one hypothesis was not rejected at alpha level of 2.5% then no statistical significance was claimed for any subsequent hypotheses in the sequence. In this case, the assessing for statistical significance in Sequence B was at the 2.5% level. If all hypotheses in Sequence B were rejected, then the unused alpha level of 2.5% was passed back for assessing the hypotheses in Sequence A at the 5% level. In Sequence B, if one hypothesis was not rejected at alpha level of 2.5 % then no statistical significance was claimed for any subsequent hypotheses in the sequence.

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After statistical significance was demonstrated at Week 2, in order to be more rigorous about the onset of relief of severity of pruritus, a step-down approach with the NRS4 endpoint from Week 2 to earlier time points was utilized as an additional family of hypothesis tests.

In general, for descriptive analyses, number and percent were presented for binary variables. Number, mean, standard deviation, median, first and third quartiles were presented for continuous variables.

Estimates of the pairwise differences along with the two-sided 95% confidence interval (CI) were provided among the treatment groups, abrocitinib 200 mg QD, abrocitinib 100 mg QD, dupilumab, and placebo.

RESULTS

Subject Disposition and Demography: A total of 1234 subjects were screened, and 838 subjects were randomized. Similar proportions of subjects across the treatment groups were ongoing in the study after completing 16 weeks. Subject discontinuations were low; the most common reasons for discontinuations were withdrawal by subjects (various reasons including personal reasons and lack of efficacy) and AEs (Table S3).

Table S3. Disposition Events Summary

Number (%) of Subjects	Placebo (N=131) n (%)	PF-04965842 100mg QD (N=238) n (%)	PF-04965842 200mg QD (N=226) n (%)	Dupilumab 300mg Q2W (N=242) n (%)
Discontinued	14 (10.7)	21 (8.8)	18 (8.0)	19 (7.9)
Adverse Event	5 (3.8)	5 (2.1)	8 (3.5)	6 (2.5)
Lack of Efficacy	0	1 (0.4)	0	1 (0.4)
Lost to Follow-Up	1 (0.8)	2 (0.8)	1 (0.4)	2 (0.8)
Pregnancy	0	0	1 (0.4)	1 (0.4)
Protocol Deviation	2 (1.5)	2 (0.8)	2 (0.9)	1 (0.4)
Withdrawal By Subject	5 (3.8)	9 (3.8)	3 (1.3)	6 (2.5)
Medication Error Without Associated Adverse Event	0	1 (0.4)	1 (0.4)	0
Other	1 (0.8)	1 (0.4)	2 (0.9)	2 (0.8)
Ongoing	117 (89.3)	217 (91.2)	208 (92.0)	223 (92.1)

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Table S3. Disposition Events Summary

	Placebo (N=131)	PF-04965842 100mg QD (N=238)	PF-04965842 200mg QD (N=226)	Dupilumab 300mg Q2W (N=242)
Number (%) of Subjects	**n (%)**	**n (%)**	**n (%)**	**n (%)**

Disposition status was ongoing for subjects who did not discontinue from the study before Week 16.
Three subjects (13089008, 13469002, 12479010) had an AE that started before Week 16 and discontinued due to that AE after Week 16. Those subjects were considered as ongoing in this table.
PFIZER CONFIDENTIAL SDTM Creation: 01FEB2020 (21:17) Source Data: adds Output File: ./nda1_cdisc/B7451029_CSR/adds_s001 Date of Generation: 07FEB2020 (07:56)
Table 14.1.1.2 is for Pfizer internal use.

Baseline demographic characteristics were balanced across treatment groups; the median age was 34 years. Majority of the subjects were White (72.4%) and non-Hispanic or Latino (83.8%); 21.3% were of Asian descent and 4.2% were Black or African Americans. Randomized subjects were representative of the moderate (64.6%) or severe (35.4%) AD population at baseline per the IGA score; also, the median EASI was 27.2 and median BSA involvement was 45.6%. The baseline PRO values were representative of a high burden of disease and impact on quality of life (QoL). DLQI scores showed that subjects reported their disease had a "very large effect" on their QoL (median: 15.0). POEM scores indicated subjects reported their symptoms were "severe" (median: 22.0). Proportions of subjects who had received prior systemic or topical treatment for AD were similar across treatment groups.

Efficacy Results:

Co-primary Endpoints: The study met both co-primary endpoints of IGA and EASI-75 responses at Week 12, demonstrating that both abrocitinib 200 mg and 100 mg treatment groups were superior to the placebo group. Also, responses with abrocitinib 200 mg dose were higher than responses with abrocitinib 100 mg dose (Table S4, Table S5).

Additional supportive analyses for both co-primary endpoints were performed using the Per Protocol Analysis Set (PPAS) population and using the Full Analysis Set (FAS) population with a tipping point (TP) analysis where all missing responses were multiply imputed. For both co-primary endpoints, the results of the PPAS and TP analyses were consistent with the FAS primary analysis and conclusions remain unchanged.

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Table S4. Proportion of Subjects Achieving IGA Response of 'Clear' or 'Almost Clear' and >=2 Points Improvement from Baseline at Week 12 - CMH (FAS, NRI)

	Placebo	PF-04965842 100mg QD	PF-04965842 200mg QD	Dupilumab 300mg Q2W
N	129	235	219	241
n (%)	18 (14.0)	86 (36.6)	106 (48.4)	88 (36.5)
95% CI	(8.0, 19.9)	(30.4, 42.8)	(41.8, 55.0)	(30.4, 42.6)
Active - Placebo [1]				
Estimate (%)		23.1	34.8	22.5
95% CI		(14.7, 31.4)	(26.1, 43.5)	(14.2, 30.9)
Two-sided P-value [2]		<.0001	<.0001	
PF-04965842 - Dupilumab [1]				
Estimate (%)		0.5	12.4	
95% CI		(-8.0, 9.1)	(3.5, 21.3)	
200 mg QD - 100 mg QD [1]				
Estimate (%)			12.1	
95% CI			(3.2, 21.1)	

Full Analysis Set (FAS) was defined as all randomized subjects who received at least one dose of study medication.
Baseline was defined as the last measurement prior to first dosing (Day 1).
If a subject withdrew from the study, then this subject was counted as non-responder after withdrawal.
CI = confidence interval; CMH = Cochran-Mantel-Haenszel; IGA = investigator's global assessment; N = number of subjects in the analysis set with NRI at the specified visit; n (%) = number of subjects with response(percentage based on N); NRI = non-responder imputation.
[1] The estimate and confidence interval (CI) for difference were calculated based on the weighted average of difference by disease severity group using the normal approximation of binomial proportions. CI for the response rate was based on normal approximation (or the Clopper-Pearson exact method when there were 0 or 100% responders).
[2] P-value was calculated using the Cochran-Mantel-Haenszel (CMH) method adjusted by baseline disease severity.
PFIZER CONFIDENTIAL SDTM Creation: 01FEB2020 (21:42) Source Data: adad Output File: ./nda1_cdisc/B7451029_CSR/adad_s102_1 Date of Generation: 06FEB2020 (05:07)
Table 14.2.1.1.1.1 is for Pfizer internal use.

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Table S5. Proportion of Subjects Achieving EASI Response >= 75% Improvement from Baseline at Week 12 - CMH (FAS, NRI)

	Placebo	PF-04965842 100mg QD	PF-04965842 200mg QD	Dupilumab 300mg Q2W
N	129	235	219	241
n (%)	35 (27.1)	138 (58.7)	154 (70.3)	140 (58.1)
95% CI	(19.5, 34.8)	(52.4, 65.0)	(64.3, 76.4)	(51.9, 64.3)
Active - Placebo [1]				
Estimate (%)		31.9	43.2	30.9
95% CI		(22.2, 41.6)	(33.7, 52.7)	(21.2, 40.6)
Two-sided P-value [2]		<.0001	<.0001	
PF-04965842 - Dupilumab [1]				
Estimate (%)		0.8	12.0	
95% CI		(-8.1, 9.6)	(3.3, 20.7)	
200 mg QD - 100 mg QD [1]				
Estimate (%)			11.5	
95% CI			(2.8, 20.2)	

Full Analysis Set (FAS) was defined as all randomized subjects who received at least one dose of study medication.
Baseline was defined as the last measurement prior to first dosing (Day 1).
If a subject withdrew from the study, then this subject was counted as non-responder after withdrawal.
CI = confidence interval; CMH = Cochran-Mantel-Haenszel; EASI = eczema area and severity index; N = number of subjects in the analysis set with NRI at the specified visit; n (%) = number of subjects with response (percentage based on N); NRI = non-responder imputation.
[1] The estimate and confidence interval (CI) for difference were calculated based on the weighted average of difference by disease severity group using the normal approximation of binomial proportions. CI for the response rate was based on normal approximation (or the Clopper-Pearson exact method when there were 0 or 100% responders).
[2] P-value was calculated using the Cochran-Mantel-Haenszel (CMH) method adjusted by baseline disease severity.
PFIZER CONFIDENTIAL SDTM Creation: 01FEB2020 (21:43) Source Data: adea Output File: ./nda1_cdisc/B7451029_CSR/adea_s104 Date of Generation: 06FEB2020 (02:53)
Table 14.2.1.1.3.1 is for Pfizer internal use.

Key Secondary Endpoints:

- Both abrocitinib groups had statistically significant improvement compared with placebo in all 3 key secondary endpoints ($p \leq 0.0002$): proportion of subjects with PP-NRS4 at Week 2, IGA response at Week 16, and EASI-75 at Week 16 (Table S6, Table S7, Table S8).

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- At Week 2, abrocitinib 200 mg group compared with the dupilumab group, had statistically significantly higher proportion of subjects with PP-NRS4, indicating earlier onset of action (p<0.0001; Table S6).
- At Week 16, abrocitinib 200 mg group compared with the dupilumab group, showed higher proportion of IGA responders, based on 95% CI of the treatment difference between the groups (Table S7).
- At Week 16, proportion of EASI-75 responders was numerically greater in abrocitinib 200 mg group than in dupilumab group and was numerically lesser in abrocitinib 100 mg group than in dupilumab group; 95% CI for the differences did not support true difference in treatment responses (Table S8).

Table S6. Proportion of Subjects Achieving Pruritus NRS Severity Response >=4 Points Improvement from Baseline at Week 2 - CMH (FAS with Baseline >=4, NRI)

	Placebo	PF-04965842 100mg QD	PF-04965842 200mg QD	Dupilumab 300mg Q2W
N	130	236	226	239
n (%)	18 (13.8)	75 (31.8)	111 (49.1)	63 (26.4)
95% CI	(7.9, 19.8)	(25.8, 37.7)	(42.6, 55.6)	(20.8, 31.9)
Active - Placebo [1]				
Estimate (%)		17.9	34.9	12.5
95% CI		(9.5, 26.3)	(26.0, 43.7)	(4.4, 20.7)
Two-sided P-value [2]		0.0002	<.0001	
PF-04965842 - Dupilumab [1]				
Estimate (%)		5.2	22.1	
95% CI		(-2.9, 13.4)	(13.5, 30.7)	
Two-sided P-value [2]		0.2084	<.0001	
200 mg QD - 100 mg QD [1]				
Estimate (%)			17.2	
95% CI			(8.4, 26.0)	

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Table S6. Proportion of Subjects Achieving Pruritus NRS Severity Response >=4 Points Improvement from Baseline at Week 2 - CMH (FAS with Baseline >=4, NRI)

	Placebo	PF-04965842 100mg QD	PF-04965842 200mg QD	Dupilumab 300mg Q2W

Full Analysis Set (FAS) was defined as all randomized subjects who received at least one dose of study medication.
Baseline was defined as the last measurement prior to first dosing (Day 1).
If a subject withdrew from the study, then this subject was counted as non-responder after withdrawal.
CI = confidence interval; CMH = Cochran-Mantel-Haenszel; N = number of subjects in the analysis set with NRI at the specified visit; n (%) = number of subjects with response(percentage based on N); NRI = non-responder imputation; NRS = numeric rating scale.
[1] The estimate and confidence interval (CI) for difference were calculated based on the weighted average of difference by disease severity group using the normal approximation of binomial proportions. CI for the response rate was based on normal approximation (or the Clopper-Pearson exact method when there were 0 or 100% responders).
[2] P-value was calculated using the Cochran-Mantel-Haenszel (CMH) method adjusted by baseline disease severity.
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Table 14.2.3.2.1 is for Pfizer internal use.

Table S7. Proportion of Subjects Achieving IGA Response of 'Clear' or 'Almost Clear' and >=2 Points Improvement from Baseline at Week 16 - CMH (FAS, NRI)

	Placebo	PF-04965842 100mg QD	PF-04965842 200mg QD	Dupilumab 300mg Q2W
N	124	230	221	232
n (%)	16 (12.9)	80 (34.8)	105 (47.5)	90 (38.8)
95% CI	(7.0, 18.8)	(28.6, 40.9)	(40.9, 54.1)	(32.5, 45.1)
Active - Placebo [1]				
Estimate (%)		22.1	35.0	25.6
95% CI		(13.7, 30.5)	(26.3, 43.7)	(17.1, 34.1)
Two-sided P-value [2]		<.0001	<.0001	
PF-04965842 - Dupilumab [1]				
Estimate (%)		-3.5	9.4	
95% CI		(-12.2, 5.2)	(0.4, 18.5)	
200 mg QD - 100 mg QD [1]				
Estimate (%)			13.1	

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Table S7. Proportion of Subjects Achieving IGA Response of 'Clear' or 'Almost Clear' and >=2 Points Improvement from Baseline at Week 16 - CMH (FAS, NRI)

	Placebo	PF-04965842 100mg QD	PF-04965842 200mg QD	Dupilumab 300mg Q2W
95% CI			(4.2, 22.1)	

Full Analysis Set (FAS) was defined as all randomized subjects who received at least one dose of study medication.
Baseline was defined as the last measurement prior to first dosing (Day 1).
If a subject withdrew from the study, then this subject was counted as non-responder after withdrawal.
CI = confidence interval; CMH = Cochran-Mantel-Haenszel; IGA = investigator's global assessment; N = number of subjects in the analysis set with NRI at the specified visit; n (%) = number of subjects with response(percentage based on N); NRI = non-responder imputation.
[1] The estimate and confidence interval (CI) for difference were calculated based on the weighted average of difference by disease severity group using the normal approximation of binomial proportions. CI for the response rate was based on normal approximation (or the Clopper-Pearson exact method when there were 0 or 100% responders).
[2] P-value was calculated using the Cochran-Mantel-Haenszel (CMH) method adjusted by baseline disease severity.
PFIZER CONFIDENTIAL SDTM Creation: 01FEB2020 (21:42) Source Data: adad Output File: ./nda1_cdisc/B7451029_CSR/adad_s102_3 Date of Generation: 06FEB2020 (05:05)
Table 14.2.1.2.1 is for Pfizer internal use.

Table S8. Proportion of Subjects Achieving EASI Response >= 75% Improvement from Baseline at Week 16 - CMH (FAS, NRI)

	Placebo	PF-04965842 100mg QD	PF-04965842 200mg QD	Dupilumab 300mg Q2W
N	124	229	221	232
n (%)	38 (30.6)	138 (60.3)	157 (71.0)	152 (65.5)
95% CI	(22.5, 38.8)	(53.9, 66.6)	(65.1, 77.0)	(59.4, 71.6)
Active - Placebo [1]				
Estimate (%)		29.7	40.4	34.7
95% CI		(19.5, 39.9)	(30.4, 50.4)	(24.6, 44.8)
Two-sided P-value [2]		<.0001	<.0001	
PF-04965842 - Dupilumab [1]				
Estimate (%)		-5.1	5.5	
95% CI		(-13.9, 3.7)	(-3.1, 14.1)	

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Table S8. Proportion of Subjects Achieving EASI Response >= 75% Improvement from Baseline at Week 16 - CMH (FAS, NRI)

	Placebo	PF-04965842 100mg QD	PF-04965842 200mg QD	Dupilumab 300mg Q2W
200 mg QD - 100 mg QD [1]				
Estimate (%)			10.7	
95% CI			(2.0, 19.4)	

Full Analysis Set (FAS) was defined as all randomized subjects who received at least one dose of study medication.
Baseline was defined as the last measurement prior to first dosing (Day 1).
If a subject withdrew from the study, then this subject was counted as non-responder after withdrawal.
CI = confidence interval; CMH = Cochran-Mantel-Haenszel; EASI = eczema area and severity index; N = number of subjects in the analysis set with NRI at the specified visit; n (%) = number of subjects with response (percentage based on N); NRI = non-responder imputation.
[1] The estimate and confidence interval (CI) for difference were calculated based on the weighted average of difference by disease severity group using the normal approximation of binomial proportions. CI for the response rate was based on normal approximation (or the Clopper-Pearson exact method when there were 0 or 100% responders).
[2] P-value was calculated using the Cochran-Mantel-Haenszel (CMH) method adjusted by baseline disease severity.
PFIZER CONFIDENTIAL SDTM Creation: 01FEB2020 (21:43) Source Data: adea Output File: ./nda1 cdisc/B7451029 CSR/adea s104 1 Date of Generation: 06FEB2020 (02:55)
Table 14.2.2.1.1 is for Pfizer internal use.

Secondary Efficacy Endpoints: Additional secondary efficacy endpoints (IGA, EASI, PP-NRS, BSA, steroid-free days, and SCORAD) demonstrated improved efficacy in both abrocitinib groups compared with the placebo group. The treatment effect of the abrocitinib 200 mg group was consistently higher than the abrocitinib 100 mg group. Abrocitinib consistently had earlier onset of action than dupilumab and over time abrocitinib 200 mg tended to be more effective than dupilumab.

- **IGA**: At Weeks 2, 4, and 8 (also, at Week 12 [co-primary] and Week 16 [key secondary]), both abrocitinib treatment groups showed statistically higher proportions of subjects with IGA responses compared with the placebo group ($p \leq 0.0093$). Both abrocitinib groups had greater proportions of IGA responders than the dupilumab group at Week 2, and the 200 mg group had more responders than dupilumab group at Weeks 4, 8, 12, and 16; these were true treatment differences per 95% CIs.

- **EASI-75**: At Weeks 2, 4, and 8, (also, at Week 12 [co-primary] and Week 16 [key secondary]) both abrocitinib treatment groups, compared with placebo group, showed statistically significantly greater proportions of subjects with EASI-75 responses ($p \leq 0.0006$). Both abrocitinib treatment groups had greater proportions of EASI-75 responders than the dupilumab group at Week 2, and the 200 mg group had more responders than dupilumab group at Weeks 4, 8, and 12; these were true treatment differences per 95% CIs.

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- **EASI-50, EASI-90, EASI-100**: Both abrocitinib treatment groups had statistically significantly greater proportions of EASI-50 ($p<0.0001$) and EASI-90 ($p\leq0.0186$) responders compared with the placebo group at all time points. Statistically significantly greater EASI-100 response was observed in abrocitinib 200 mg and 100 mg groups compared with the placebo group as early as Week 2 ($p=0.0142$) and Week 8 ($p=0.0041$), respectively; the statistically significant differences were maintained at each timepoint up to Week 16 ($p\leq0.0095$). Abrocitinib 200 mg group had greater proportion of EASI-100 responders than the dupilumab group at Weeks 2, 4, 8, 12, and 16; based on 95% CIs.

- **Total EASI, change from baseline**: The least squares mean (LSM) of percent change from baseline in the total EASI score demonstrated statistically significant improvement in both abrocitinib treatment groups compared with the placebo group at all scheduled time points ($p<0.0001$). Both abrocitinib treatment groups had greater improvement than the dupilumab group at Week 2, and the 200 mg group maintained the improvement over dupilumab at Weeks 4, 8, and 12; these were true treatment differences per 95% CIs.

- **PP-NRS4**: As early as Day 4 and Day 9, abrocitinib 200 mg ($p=0.0023$) and 100 mg ($p=0.0202$) groups, respectively, had statistically significantly higher proportions of PP-NRS4 responders compared with the placebo group; the statistical significance was maintained at all timepoints up to Week 16 ($p\leq0.0106$). As compared with the dupilumab group, abrocitinib 200 mg group had statistically significantly greater proportions of PP-NRS4 responders as early as Day 4 ($p<0.0001$) and at all timepoints up to Day 15 ($p\leq0.0049$); also, at all subsequent timepoints up to Week 8 (based on 95% CI).

- **Time to PP-NRS4**: The Kaplan-Meier analysis to estimate the time to first PP-NRS4 showed the time to response was statistically significantly faster in both abrocitinib groups compared with the placebo group with 50% achieving a PP-NRS4 response in 200 mg and 100 mg groups by 13 and 29 days, respectively. Also, the response was faster in abrocitinib 200 mg group than in the dupilumab group; median time to achieve first PP-NRS4 response in abrocitinib 200 mg group and dupilumab group was 13 days and 31 days, respectively; the 95% CIs supported a true difference in treatment response.

- **PP-NRS, change from baseline**: As early as Day 2, the LSM of percent change from baseline in PP-NRS was improved in both abrocitinib groups compared with the placebo group ($p\leq0.0331$), demonstrating a rapid onset of the treatment effect, which was maintained at all timepoints ($p\leq0.0200$). At Day 2, both abrocitinib treatment groups had greater improvement in LSM of percent change from baseline in PP-NRS than the dupilumab group, which was maintained in the 200 mg group at all timepoints up to Week 12; based on 95% CIs.

- **SCORAD50 and SCORAD75**: Both abrocitinib treatment groups demonstrated statistically significantly higher proportions of subjects with SCORAD50 and SCORAD75 responses compared with the placebo group as early as Week 2 ($p\leq0.034$);

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maintained at all timepoints up to Week 16 ($p \leq 0.0026$). Proportion of SCORAD50 responders was higher in abrocitinib 200 mg group than in dupilumab group at Weeks 2, 4, and 8; proportion of SCORAD75 responders was higher in abrocitinib 200 mg group than in dupilumab group at Weeks 2, 4, 8, 12, and 16 (supported by 95% CIs).

- **SCORAD total score, change from baseline**: Based on the mixed effect repeated measures (MMRM) analysis, both abrocitinib treatment groups demonstrated statistically significantly greater decreases compared with the placebo group in absolute and percent change from baseline of SCORAD total score, beginning at Week 2 that were maintained up to Week 16 ($p<0.0001$). The decreases in abrocitinib 200 mg group were greater than those in dupilumab group, at Weeks 2, 4, 8, and 12, based on 95% CIs.

- **SCORAD visual analog scale (VAS), change from baseline:** Both abrocitinib treatment groups demonstrated statistically significant decreases (improvement) compared with the placebo group in LSM of change from baseline in SCORAD VAS of sleep loss at Weeks 2, 4, 8, 12, and 16 ($p \leq 0.0002$ for absolute change and $p \leq 0.0008$ for percent change). Abrocitinib 200 mg group showed greater decrease than dupilumab group in LSM of absolute change from baseline in SCORAD VAS of sleep loss at Weeks 2, 4, 8, and 16; based on 95% CIs.

- **Percent BSA, change from baseline**: Based on the MMRM analysis, both abrocitinib groups demonstrated statistically significant decreases from baseline in %BSA (absolute change and percent change) compared with the placebo group as early as Week 2, maintained at Weeks 4, 8, 12, and 16 ($p<0.0001$). At Week 2, abrocitinib 200 mg group showed greater decreases from baseline in %BSA (absolute and percent change) than in the dupilumab group; the decreases in absolute change were maintained at Weeks 4, 8, 12, and 16 and decreases in percent change were maintained at Week 4 and Week 8; supported by 95% CIs .

- **Steroid-free days**: LSM of number of days up to Week 16 when corticosteroid was not used was statistically significantly higher in the abrocitinib 200 mg group compared with the placebo group ($p=0.0082$).

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PtGA: The LSM of change from baseline in PtGA scores was statistically significantly improved (lower) in both abrocitinib treatment groups compared with the placebo group beginning at Week 2 that were maintained up to Week 16 ($p \leq 0.0002$). Abrocitinib 200 mg group showed more improved LSM of change from baseline in PtGA scores than the dupilumab group at Weeks 2, 4, 8, and 12; based on 95% CIs.

DLQI: The LSM of change from baseline in DLQI scores was statistically significantly improved (lower than baseline) in both abrocitinib treatment groups compared with the placebo group at Weeks 2, 12, and 16 ($p \leq 0.0003$). Abrocitinib 200 mg group showed more improved LSM of change from baseline in DLQI scores than the dupilumab group at

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Weeks 2, 12, and 16; based on 95% CIs. Also, there were statistically significantly greater proportion of DLQI responders (≥4 points improvement from baseline) in both abrocitinib groups than in placebo group.

EQ-5D-5L: The LSM of change from baseline was statistically improved (higher) for both abrocitinib treatment groups compared with the placebo group at Week 12 ($p<0.0001$) and Week 16 ($p\leq0.0342$). The LSM of change from baseline was more improved in abrocitinib 200 mg group than in dupilumab group at Week 12; based on 95% CIs. The analyses for data on EQ VAS scores showed improvement in abrocitinib 200 mg group compared with the placebo group at Week 12 ($p<0.0001$) and Week 16 ($p<0.0001$).

HADS: The LSMs of change from baseline in HADS anxiety and depression subscales were statistically significantly improved (lower) for both abrocitinib treatment groups compared with the placebo group at Week 12 and Week 16 ($p\leq0.0222$).

POEM: The LSM of change from baseline in POEM scores was statistically significantly improved (lower) for both abrocitinib treatment groups compared with the placebo group at Week 12 and Week 16 ($p<0.0001$). The LSM of change from baseline in POEM scores was more improved in abrocitinib 200 mg group than in dupilumab group at Week 12 and Week 16; based on 95% CIs.

PSAAD: As early as Week 1, both abrocitinib treatment groups showed statistically significant improvement (lower than baseline) compared with placebo group in LSM of change from baseline in PSAAD scores; the improvement was maintained at each weekly timepoint up to Week 16 ($p\leq0.0001$). The LSM of change from baseline in PSAAD scores was more improved in abrocitinib 200 mg group than in dupilumab group starting at Week 1 and at each weekly timepoint up to Week 10; based on 95% CIs

Safety Results:

- The proportion of subjects with all-causality TEAEs was higher for the abrocitinib 200 mg group compared to the abrocitinib 100 mg, dupilumab and placebo groups (Table S9).
    - The majority of all-causality TEAEs were mild or moderate.
    - The incidence of subjects reporting severe all-causality TEAEs was low and similar between all treatment groups.
    - The highest incidence of treatment-related TEAEs occurred in the abrocitinib 200 mg group (approximately 30%), with similar incidence in the abrocitinib 100 mg, dupilumab and placebo groups (approximately 20%).
- Serious TEAEs were reported in similar proportion of subjects across the treatment groups. No deaths were reported in the study (Table S9).

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- Discontinuations from the study due to TEAEs were low and similar across the treatment groups (Table S9).

Table S9. Treatment-Emergent Adverse Events (All Causalities) - Safety Analysis Set

Number (%) of Subjects	Placebo n (%)	PF-04965842 100mg QD n (%)	PF-04965842 200mg QD n (%)	Dupilumab 300mg Q2W n (%)
Subjects evaluable for adverse events	131	238	226	242
Number of adverse events	150	269	308	223
Subjects with adverse events	70 (53.4)	121 (50.8)	140 (61.9)	121 (50.0)
Subjects with serious adverse events	5 (3.8)	6 (2.5)	2 (0.9)	2 (0.8)
Subjects with severe adverse events	3 (2.3)	5 (2.1)	4 (1.8)	2 (0.8)
Subjects discontinued from study due to adverse events [1]	5 (3.8)	6 (2.5)	10 (4.4)	8 (3.3)
Subjects discontinued study drug due to AE and continued Study [2]	2 (1.5)	2 (0.8)	1 (0.4)	0
Subjects with temporary discontinuation due to adverse events	9 (6.9)	15 (6.3)	12 (5.3)	9 (3.7)

Included data up to 28 days after last dose of study.
Except for the number of adverse events subjects were counted only once per treatment in each row.
Serious Adverse Events - according to the investigator's assessment
[1] Subjects who had an AE record that indicated that the AE caused the subject to be discontinued from the study. Three subjects (13089008, 13469002, 12479010) had an AE that started before Week 16 and discontinued due to that AE after Week 16. Those AEs were also included in this table.
[2] Subjects who had an AE record that indicated that action taken with study treatment was drug withdrawn but AE did not cause the subject to be discontinued from study
MedDRA v22.1 coding dictionary applied.
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Table 14.3.1.2.1 is for Pfizer internal use.

Conclusion(s):

EFFICACY

Co-Primary Endpoints:

- The study met both co-primary endpoints of IGA and EASI-75 responses at Week 12, demonstrating that both abrocitinib 200 mg and 100 mg treatment groups were superior to the placebo group.

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- IGA responses and EASI-75 responses in the abrocitinib 200 mg group were higher than the abrocitinib 100 mg group.
- Sensitivity analyses of IGA and EASI-75 responses were consistent with the primary analyses.
- The treatment effects for both IGA response and EASI-75 response were similar across subgroups.

Key Secondary Endpoints:

- Both abrocitinib groups had statistically significant improvement compared with placebo in all 3 key secondary endpoints ($p \leq 0.0002$): proportion of subjects with PP-NRS4 at Week 2, IGA response at Week 16, and EASI-75 at Week 16.
- At Week 2, abrocitinib 200 mg group compared with the dupilumab group, had statistically significantly higher proportion of subjects with PP-NRS4, indicating earlier onset of action ($p<0.0001$).
- At Week 16, abrocitinib 200 mg group compared with the dupilumab group, showed higher proportion of IGA responders, based on 95% CI of the treatment difference between the groups.
- At Week 16, proportion of EASI-75 responders was numerically greater in abrocitinib 200 mg group than in dupilumab group and was numerically lesser in abrocitinib 100 mg group than in dupilumab group; 95% CI for the differences did not support true difference in treatment responses.

Other Secondary Endpoints:

Additional secondary efficacy endpoints (IGA, EASI, PP-NRS, BSA, SCORAD, and steroid-free days) demonstrated improved efficacy in both abrocitinib groups compared with the placebo group. The treatment effect of the abrocitinib 200 mg group was consistently higher than the abrocitinib 100 mg group.

Also, abrocitinib consistently had earlier onset of action than dupilumab. Over time abrocitinib 200 mg tended to be more effective than dupilumab, while abrocitinib 100 mg tended to be comparable to dupilumab.

IGA Responses (Clear (0) or Almost Clear (1) and ≥2 Point Reduction from Baseline)

- Both abrocitinib treatment groups had statistically significantly greater proportion of IGA responders compared with placebo at all time points.

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- Both abrocitinib groups had greater proportions of IGA responders than the dupilumab group at Week 2, and the 200 mg group had more responders than dupilumab group at Weeks 4, 8, 12, and 16; these were true treatment differences per 95% CIs.

EASI

- Both abrocitinib treatment groups had statistically significantly greater proportions of EASI-50, EASI-75 and EASI-90 responders compared with the placebo group at all time points. Statistically significantly greater EASI-100 response was observed in abrocitinib 200 mg and 100 mg groups compared with the placebo group as early as Week 2 and Week 8, respectively; the statistically significant differences were maintained at each time point up to Week 16.

- Both abrocitinib treatment groups compared with the placebo group demonstrated statistically significant improvement from baseline in the total EASI score at each timepoint up to Week 16.

- Both abrocitinib group had earlier onset of action than dupilumab group based on observations in change from baseline in the total EASI score and responders for EASI-50, EASI-75, EASI 90, and EASI 100; the greater than dupilumab responses were maintained for longer duration in the abrocitinib 200 mg group.

PP-NRS for Severity

- As early as Day 2, the LSM of percent change from baseline in PP-NRS was lower in both abrocitinib groups compared with the placebo group, demonstrating a rapid onset of the treatment effect, which was maintained at each timepoint up to Week 16.

- The median time to achieve first PP-NRS4 was faster in both abrocitinib treatment groups compared with the placebo group.

- Both abrocitinib groups had earlier onset of action than the dupilumab group; median time to PP-NRS4 was 31 days in the dupilumab group. The greater difference in PP-NRS effect was maintained longer in abrocitinib 200 mg group.

SCORAD

- Both abrocitinib treatment groups compared with the placebo demonstrated statistically significantly greater decreases in SCORAD total score and SCOARD VAS for sleep loss as early as Week 2 and maintained at each timepoint up to Week 16.

- Both abrocitinib treatment groups demonstrated statistically significantly greater SCORAD75 and SCORAD50 responses compared with the placebo group beginning at Week 2 and maintained at each timepoint up to Week 16.

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- At Week 2, both abrocitinib groups demonstrated greater decrease than dupilumab group in SCORAD total score, greater proportions of SCORAD50 and SCORAD75 responders, and greater decrease from baseline in SCORAD VAS for sleep loss; the effects were maintained longer in abrocitinib 200 mg group.

BSA

- Both abrocitinib treatment groups compared with placebo demonstrated statistically significant decreases in %BSA as early as Week 2 and maintained at each timepoint up to Week 16.

- At Week 2, abrocitinib 200 mg group demonstrated greater decreases in %BSA than in the dupilumab group.

Steroid-free days:

- Number of days up to Week 16 when corticosteroid was not used was statistically significantly lower in the abrocitinib 200 mg group compared with the placebo group.

Patient-Reported Outcomes (PROs):

Favorable and improved differences across all PRO measures were observed for both abrocitinib treatment groups compared with the placebo group. Treatment differences emerged as early as Week 2 and were maintained at subsequent time points up to Week 16. Abrocitinib 200 mg group tended to demonstrate more treatment effect than the abrocitinib 100 mg group. Abrocitinib groups generally had earlier onset than dupilumab group.

- **PtGA**: Scores were statistically significantly improved in both abrocitinib groups compared with the placebo group from Week 2 to Week 16; and the abrocitinib 200 mg group showed more improvement than the dupilumab group from Week 2 to Week 12.

- **DLQI**: Scores were statistically significantly improved in both abrocitinib groups compared with the placebo group at Weeks 2, 12, and 16; the 200 mg group showed more improvement than the dupilumab group at Weeks 2, 12, and 16. Also, there were statistically significantly greater proportions of responders (≥4 points improvement from baseline) in both abrocitinib groups than in placebo group.

- **EQ-5D-5L**: Index value was statistically significantly improved for both abrocitinib groups compared with the placebo group at Weeks 12 and 16, and more improved in 200 mg group than dupilumab group at Week 12. The VAS score was improved for abrocitinib 200 mg group compared with the placebo group at Weeks 12 and 16.

- **HADS**: Both abrocitinib groups compared with the placebo group had statistically significant improvement in symptoms associated with depression and anxiety at Weeks 12 and 16.

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- **POEM**: Scores were statistically significantly improved in both abrocitinib groups compared with the placebo group at Weeks 12, and 16; and the 200 mg group showed more improvement than the dupilumab group at both timepoints.

- **PSAAD**: As early as Week 1, the scores were statistically significantly improved in both abrocitinib groups compared with the placebo group, and improvement was maintained at each weekly timepoint up to Week 16; the 200 mg group showed more improvement than the dupilumab group at Week 1 and maintained it at each weekly timepoint up to Week 10.

SAFETY

- Abrocitinib was well tolerated. The observed safety events were consistent with those seen in other abrocitinib studies.

- A higher proportion of subjects with all-causality TEAEs occurred in the abrocitinib 200 mg group compared with the abrocitinib 100 mg, dupilumab and placebo groups.

  - All-causality TEAEs that appeared more commonly in the abrocitinib groups relative to the dupilumab or placebo groups included nausea, headache, nasopharyngitis, upper respiratory tract infection, herpes simplex, blood creatine phosphokinase increased and acne. A higher incidence of conjunctivitis was observed in the dupilumab group compared to either abrocitinib group or placebo.

  - The incidence of TEAEs related to atopic dermatitis was more frequent in the placebo group compared with either abrocitinib group and the dupilumab group.

  - The majority of all-causality TEAEs were mild or moderate in severity.

  - The incidence of severe all-causality TEAEs was low and similar between all treatment groups.

- No deaths were reported in the study.

- The incidence of SAEs was low and similar across the treatment groups.

- Discontinuations from the study due to TEAEs were low and similar across the treatment groups.

- The incidence of herpes zoster was low, one subject (1/238 [0.4%]) in the abrocitinib 100 mg QD group had a severe TEAE, and no subjects in the abrocitinib 200 mg group, dupilumab group or placebo group had a severe TEAE.

- Platelet counts decreased in a dose-dependent manner in both abrocitinib groups with a nadir at Week 4 and returned toward baseline through Week 16 despite continued

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abrocitinib administration in the majority of subjects. No changes from baseline were observed for the dupilumab group. No subjects met pre-specified monitoring criteria, and no subject met pre-specified discontinuation criteria. Median lymphocyte counts, neutrophil counts, and hemoglobin values showed no clinically meaningful median changes.

- There were increases in both abrocitinib groups for total cholesterol, low density lipoprotein (LDL)-cholesterol, and high density lipoprotein (HDL)-cholesterol, where dose-dependent changes were observed for total cholesterol, HDL-cholesterol and triglycerides. There were no changes over time in LDL/HDL ratio. No meaningful changes were observed in the dupilumab group.

- Dose-dependent increases in creatine kinase were observed in the abrocitinib groups compared with the placebo group but were not clinically meaningful. No median changes from baseline creatine kinase values were observed for the dupilumab group. There were no TEAEs of rhabdomyolysis.

- Two (2) adjudicated malignancy events (abrocitinib 200 mg group and dupilumab group) occurred in the study. One subject had actinic keratosis (abrocitinib 200 mg group) per histopathology review. None of the subjects had any findings from cardiovascular review or opportunistic infections review.

- There was no pattern of concern in ECG, and vital signs and no unexpected laboratory abnormalities were observed.