CLINICAL STUDY REPORT SYNOPSIS

SYNOPSIS

Study Title: A Phase 1, Randomized, Double-Blind, Vehicle-Controlled, Parallel Cohort Study to Evaluate the Safety, Tolerability, Skin Irritation Potential and Pharmacokinetics of Multiple-Dose, Topical Administration of PF-07038124 to Japanese Healthy Participants

Study Number: C3941003

Regulatory Agency or Public Disclosure Identifier Number: NCT04863417

Study Phase: Phase 1

Name of Study Intervention: PF-07038124

Name of Sponsor/Company: Pfizer Inc.

CSR Version and Report Date: Final, 06 Mar 2022

Number of Study Centers and Investigators:

Twelve participants were enrolled in this study. This study was conducted by principal investigator at 1 center in Japan.

A list of study centers and investigators involved in this study is provided in Appendix 16.1.4.1.

Publications:

None

Study Period:

The study was initiated on 30 June 2021 and completed on 09 September 2021. This study was neither discontinued nor interrupted.

Rationale:

The purpose of this study was to evaluate the multiple-dose safety, tolerability, skin irritation potential, and pharmacokinetics (PK) of PF-07038124 in Japanese healthy participants. The data provided in this study support for clinical development in Japanese participants with atopic dermatitis and psoriasis.

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Objectives, Endpoints, and Statistical Methods:

Table S1. Study Objectives and Endpoints

Objectives	Endpoints
Primary: • To evaluate the safety, tolerability, and skin irritation potential of PF-07038124, following multiple doses applied topically, in Japanese healthy participants	• Incidence of TEAEs and SAEs, clinically significant changes in vital signs, ECG, and laboratory tests during the entire study • Incidence and severity of local skin irritation at time points (Days 1 to 11)
Secondary: • To characterize the PK of PF-07038124, following topical administration, in Japanese healthy participants	• PF-07038124 PK parameters following topical application on Days 1 and 10, as data permit: AUC_{tau}, and C_{max}, if applicable
CCI [redacted]	• CCI [redacted]

Abbreviations: AUC_{tau}=area under the plasma concentration-time profile from time 0 to time tau, the dosing interval, where tau = 24 hours; CCI [redacted] C_{max}=maximum plasma concentration; CCI [redacted] ECG= electrocardiogram; PK=pharmacokinetics; CCI [redacted] SAEs=serious adverse events; SoA=schedule of activities; CCI [redacted] TEAEs=treatment-emergent adverse events; CCI [redacted]

All safety analyses were performed on the safety analysis set. Participants were analyzed according to the product they actually received. Safety data were presented in tabular and/or graphical format and summarized descriptively, where appropriate. The primary endpoints were summarized descriptively through appropriate data tabulations, descriptive statistics, categorical summaries, and/or graphical presentations in order to evaluate the safety, tolerability, and skin irritation potential of PF-07038124.

All participants randomly assigned to study intervention who received a dose of PF-07038124 and in whom at least 1 plasma sample concentration value was reported. All participants randomly assigned to study intervention who received a dose of PF-07038124 and who had at least 1 of the PK parameters of interest calculated.

The plasma PK parameters were summarized descriptively by treatment group in accordance with Pfizer data standards, as data permit. CCI [redacted]

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Methodology:

This was a Phase 1, randomized, double-blind, vehicle-controlled, parallel cohort study to evaluate the safety, tolerability, skin irritation potential, and PK of PF-07038124 in Japanese healthy adult participants. This study consisted of 2 cohorts to evaluate 2 administration areas in parallel: PF-07038124 at 0.01% concentration and vehicle to 2000 cm^2 of skin (Cohort 1; approximately 10% body surface area [BSA]) or 4000 cm^2 of skin (Cohort 2; approximately 20% BSA).

Participants were randomized to receive PF-07038124 or vehicle in a ratio of 4:2 (4 PF-07038124: 2 vehicle) per cohort. Each participant received multiple doses of PF-07038124 or vehicle, starting on Day 1 topically applied for 10 consecutive days; applied once daily (QD) in the AM for Cohort 1 and Cohort 2.

The total participation time for each participant was approximately 66 days, including the screening period of up to 28 days, the double-blind treatment period of 10 days, and the follow-up period of 28 days from last dose of the study intervention.

Number of Participants (Planned and Analyzed):

Approximately 12 Japanese healthy adult participants were planned to participate in this study. Overall, 12 participants were enrolled and randomly assigned to the treatment and were included in the safety analysis set. The 8 participants of PF-07038124 treatment group were included in the PK analysis set.

Diagnosis and Main Criteria for Inclusion and Exclusion:

Enrolled in this study were male and female healthy participants who were 20 to 55 years of age, inclusive, with body mass index (BMI) of 17.5 to 25 kg/m^2 and a total body weight >50 kg (110 lb); participants had 4 biologically Japanese grandparents who were born in Japan; participants who were willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures.

Participants were excluded if they had any visible skin damage or skin condition (eg, sunburn, excessively deep tans, uneven skin tones, tattoos, scars, excessive hair, numerous freckles, or other disfigurations); had a history of or had active forms of dermatitides/eczematous conditions or other inflammatory skin diseases that would interfere with evaluation of the test site reaction; had undergone significant trauma or major surgery within 4 weeks of screening.

Study Interventions, Dose, Mode of Administration, and Batch Number(s):

The study intervention was applied in blinded fashion, at the clinical research unit. All applications of the study intervention were dispensed and applied by study site staff from Day 1 through Day 10. Every effort was made for the dose applications on Day 2 to Day 10 to be completed at 24 ± 2 hour intervals from the recorded time of completion of the Day 1 dose application, for each participant (Table S2).

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The application area included a treatment area of 2000 cm^2±200 cm^2 (approximately 10% BSA) for Cohort 1. For Cohort 2, the treatment area was 4000 cm^2±400 cm^2 (approximately 20% BSA). The application area included the back as well as other extremities, abdomen and/or chest, identified by the investigator.

Table S2. Study Interventions Administered

Investigational Product Description	Vendor Lot Number	Pfizer Lot Number	Strength/Potency	Dosage Form
PF-07038124 0.1 mg/g Topical Ointment in 60 g Tube	K200721A	20-003576	0.1 mg/g	Ointment
Placebo for PF-07038124 Topical Ointment in 60 g Tube	K200714A	20-003423	0 mg/g	Ointment

CCI

Duration of Study Intervention:

The study intervention was applied QD for 10 consecutive days from Day 1 AM through Day 10 AM.

Summary of Results:

Demographic and Other Baseline Characteristics:

All enrolled participants were male, Asian (Japanese), and between 33 to 53 years old. The total mean (standard deviation [SD]) age was 41.6 (7.46) years. Across all treatment groups, body weight ranged from 52.5 to 74.6 kg and BMI ranged from 17.6 to 24.4 kg/m^2.

Exposure:

All participants completed treatment for 10 days in Cohorts 1 and 2.

Safety Results:

In total, 1 all-causality mild treatment-emergent adverse event (TEAE) was reported and was not considered to be treatment-related by the investigator. One participant in PF-07038124 4000 cm^2 treatment group experienced a TEAE of alanine aminotransferase increased of mild severity (Table S3).

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Table S3. Treatment-Emergent Adverse Events (All Causalities) - Safety Analysis Set (Protocol C3941003)

Number (%) of Participants	PF-07038124 2000 cm^2 n (%)	Vehicle 2000 cm^2 n (%)	PF-07038124 4000 cm^2 n (%)	Vehicle 4000 cm^2 n (%)	Pooled Vehicle n (%)	Total n (%)
Participants evaluable for adverse events	4	2	4	2	4	12
Number of adverse events	0	0	1	0	0	1
Participants with adverse events	0	0	1 (25.0)	0	0	1 (8.3)
Participants with serious adverse events	0	0	0	0	0	0
Participants with severe adverse events	0	0	0	0	0	0
Participants discontinued from study due to adverse events[a]	0	0	0	0	0	0
Participants discontinued study drug due to AE and continue Study[b]	0	0	0	0	0	0
Participants with dose reduced or temporary discontinuation due to adverse events	0	0	0	0	0	0

Includes data up to 365 days after last dose of study drug.
Except for the Number of Adverse Events participants are counted only once per treatment in each row.
Serious Adverse Events - according to the investigator's assessment.
a. Participants who have an AE record that indicates that the AE caused the participant to be discontinued from the study.
b. Participants who have an AE record that indicates that Action Taken with Study Treatment was Drug Withdrawn but AE
did not Cause the Participant to be discontinued from Study.
MedDRA v24.0 coding dictionary applied.
PFIZER CONFIDENTIAL SDTM Creation: 12OCT2021 (13:45) Source Data: adae Table Generation: 15OCT2021 (18:14)
(Database snapshot date : 08OCT2021) Output File: ./csr6/C3941003/adae_s010
Table 14.3.1.2.1 PF-07038124 is for Pfizer internal use.

In general, all participants were rated with Score 0 using Draize scoring and did not have any visible skin reaction.

There were no deaths, serious adverse events (AEs), severe AEs, permanent discontinuations, temporary discontinuations or dose reductions due to AEs reported in this study. None of the laboratory abnormalities were reported as an AE or considered clinically significant. No change from baseline in electrocardiogram and vital signs were considered clinically significant and none were reported as an AE.

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Pharmacokinetic Results:

The PK of PF-07038124 were assessed on Day 1, Day 4, Day 7, and Day 10. All concentrations on Day 1, Day 4, and Day 7 were below the limit of quantification (BLQ) for both treatments. The majority of concentrations on Day 10 were BLQ: up to 24 hours postdose, >93% and 65% of plasma PK samples of PF-07038124 were BLQ of 10 pg/mL for PF-07038124 2000 cm^2 treatment and PF-07038124 4000 cm^2 treatment, respectively. Based on high percentage of BLQ values were observed, a limited number of participants had valid parameter values.

The geometric mean (minimum, maximum) in area under the plasma concentration-time profile from time 0 to time tau, the dosing interval, where tau = 24 hours (AUC_{tau}) on Day 10 for PF-07038124 4000 cm^2 treatment was 0.1650 pg•hr/mL (0.000, 287 pg•hr/mL). The geometric mean (minimum, maximum) in maximum plasma concentration (C_{max}) on Day 10 for PF-07038124 2000 cm^2 treatment and PF-07038124 4000 cm^2 treatment was 0.001965 pg/mL (0.000, 14.9 pg/mL) and 0.03911 pg/mL (0.000, 17.6 pg/mL), respectively. It's hard to assess the dose-proportionality because the valid parameter values were limited; however, number of concentrations that were above the upper limit of quantitation of PF-07038124 4000 cm^2 treatment was higher than that of PF-07038124 2000 cm^2 treatment. Inter-participant variability for PF-07038124 exposure based on geometric percent coefficient of variation were large because the majority of concentrations were BLQ.

Pharmacodynamic Results: (Not Applicable)

Other Results: (Not Applicable)

Conclusions:

Safety:

All PF-07038124 topical doses (0.01% QD in 2000 cm^2 of skin area and 0.01% QD in 4000 cm^2 of skin area) were generally safe and well-tolerated both locally and systemically in Japanese healthy participants evaluated in this study.

PK:

Following multiple topical administration of PF-07038124 in Japanese healthy participants, all concentrations were BLQ on Day 1, Day 4, and Day 7. The majority of concentrations were BLQ on Day 10: up to 24 hours postdose, >93% and 65% of plasma PK samples of PF-07038124 were BLQ of 10 pg/mL for PF-07038124 2000 cm^2 treatment and PF-07038124 4000 cm^2 treatment, respectively.