Integrated Safety Analysis of Abrocitinib for the Treatment of Moderate-to-Severe Atopic Dermatitis From the Phase 2 and Phase 3 Clinical Trial Program

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Presented at the 2nd Annual San Diego Dermatology Symposium:
A Live Virtual Experience
June 11-13, 2021

Editorial/medical writing support under the guidance of the authors was provided by Irene Park, PhD, and Mariana Ovnic, PhD, at ApotheCom, San Francisco, CA, USA, and was funded by Pfizer Inc., New York, NY, USA, in accordance with Good Publication Practice (GPP3) guidelines (*Ann Intern Med*. 2015;163:461-464).
These studies were funded by Pfizer Inc.

Disclosures

ELS reports grants from Pfizer Inc., Eli Lilly, Kyowa Kirin, LEO Pharma, Merck, and Regeneron and personal fees from Pfizer Inc., Bausch Health (Valeant), Dermira, Eli Lilly, Galderma, LEO Pharma, Menlo Therapeutics, Novartis, Regeneron, and Sanofi-Genzyme.

JIS is an investigator for AbbVie, Celgene, Eli Lilly, GSK, Kiniksa, LEO Pharma, Menlo Therapeutics, Realm Therapeutics, Regeneron, Roche, and Sanofi; a consultant for Pfizer Inc., AbbVie, Anacor, AnaptysBio, Arena Pharmaceuticals, Asana Biosciences, Dermira, Dermavant, Eli Lilly, Galderma, GSK, Glenmark, Incyte, Kiniksa, LEO Pharma, MedImmune, Menlo Therapeutics, Novartis, Realm Therapeutics, Regeneron, and Sanofi; a speaker for Regeneron and Sanofi; and an advisory board member for Pfizer Inc., Dermira, LEO Pharma, and Menlo Therapeutics.

AN is an investigator for AbbVie, Eli Lilly, Incyte, LEO Pharma, Novartis, and Sanofi; a consultant for Pfizer Inc., AbbVie, Eli Lilly, Galderma, LEO Pharma, Novartis, and Sanofi; a speaker for AbbVie, Regeneron, and Sanofi; and an advisory board member for Pfizer Inc., AbbVie, LEO Pharma, and Sanofi.

KW reports research grants from Bristol Myers Squibb and consultant honoraria from Pfizer Inc., Eli Lilly, Bristol Myers Squibb, UCB, AbbVie, Gilead, Roche, Novartis, Regeneron, and Sanofi.

EG-Y is an advisory board member for Pfizer Inc., Celgene, Dermira, Galderma, Glenmark, MedImmune, Novartis, Regeneron, Sanofi, Stiefel/GlaxoSmithKline, Vitae, and Asana Biosciences (honoraria); a consultant for Pfizer Inc., AbbVie, Anacor, Celgene, Dermira Galderma, Glenmark, LEO Pharma, MedImmune, Novartis, Regeneron, Sanofi, Stiefel/GlaxoSmithKline, Vitae, Mitsubishi Tanabe, Eli Lilly, Asana Biosciences, Kiowa Kirin, and Almirall (honoraria); and an investigator for Celgene, LEO Pharma, MedImmune, Regeneron, and Eli Lilly (grants to institution).

KMH reports consultant honoraria from Pfizer Inc.

MZ, SAF, SJ, AJT, RR are employees and shareholders of Pfizer Inc.

Introduction, Objectives, and Study Design

Introduction

- Abrocitinib is an oral, once-daily JAK1 selective inhibitor under investigation for the treatment of moderate-to-severe AD
- Results of pivotal trials demonstrated the efficacy of abrocitinib 200 mg and 100 mg across a variety of clinical settings[1-3]

Objectives

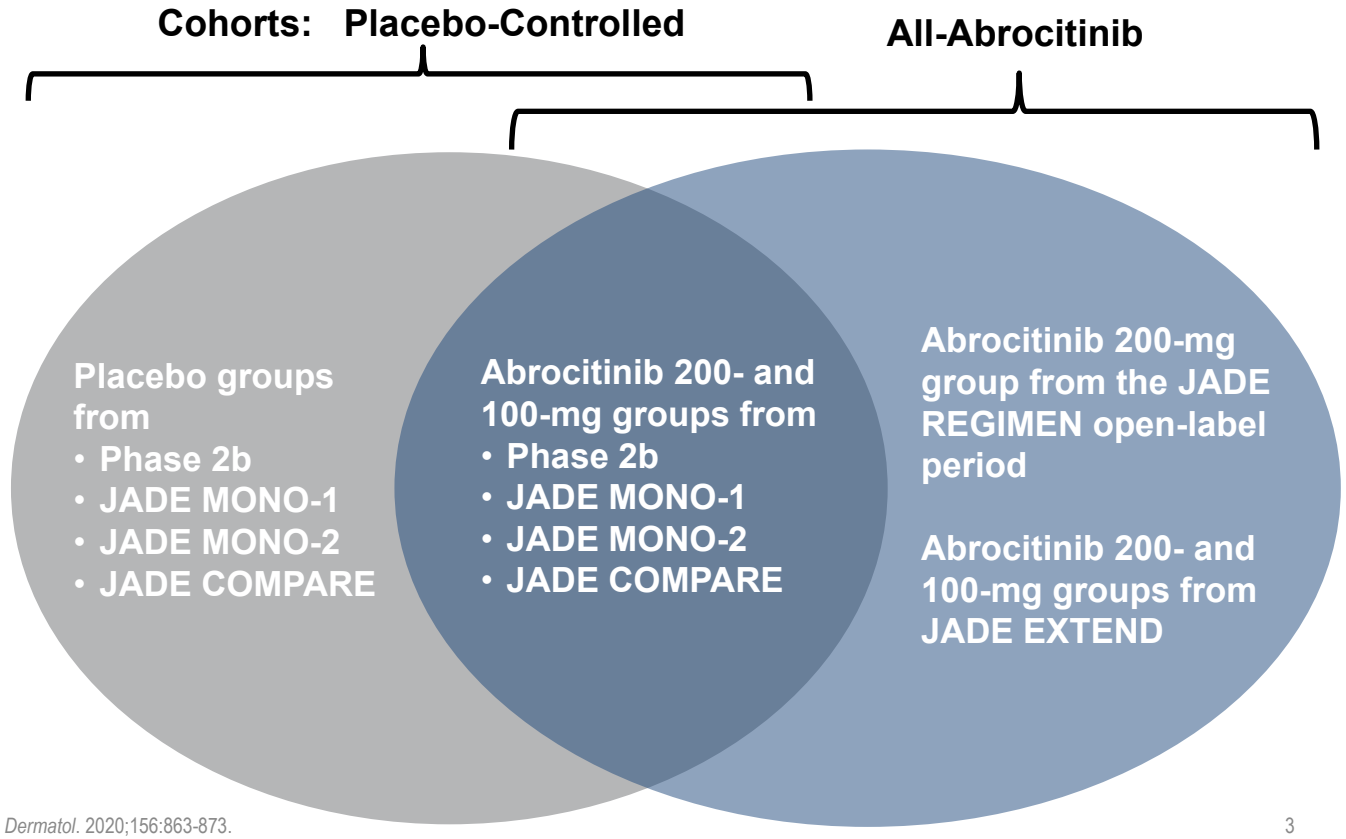
- To analyze the short- and long-term safety of abrocitinib in an integrated analysis of 1 phase 2 study, 4 phase 3 studies, and 1 long-term extension study
- To examine adverse events of interest and laboratory values

Study Design

- Safety data were pooled from 6 studies:
  1. Phase 2b (NCT02780167)
  2. JADE MONO-1 (NCT03349060)
  3. JADE MONO-2 (NCT03575871)
  4. JADE COMPARE (NCT03720470)
  5. JADE REGIMEN (NCT03627767)
  6. JADE EXTEND (NCT03422822)
- 2 cohorts were analyzed:
  1. Placebo-controlled: patients from 12- to 16-week studies
  2. All-abrocitinib: all patients who received ≥1 abrocitinib dose
- Data cutoff: April 22, 2020

Exposure

- Among 2856 patients in the all-abrocitinib cohort, 1248 had ≥24 weeks and 606 had ≥48 weeks of abrocitinib exposure



AD, atopic dermatitis; JAK1, Janus kinase 1.

1. Gooderham MJ et al. *JAMA Dermatol*. 2019;155:1371-1379. 2. Simpson EL et al. *Lancet*. 2020;396:255-266. 3. Silverberg JI et al. *JAMA Dermatol*. 2020;156:863-873.

Baseline Characteristics, Exposure, and Safety Summary

Demographics and Baseline Characteristics

		Placebo-Controlled Cohort n=1540	All-Abrocitinib Cohort n=2856
Age, median (IQR), y		33.0 (24.0-46.0)	31.0 (22.0-44.0)
Age group, n (%)	<18 years	124 (8.1)	364 (12.7)
	18-64 years	1322 (85.8)	2347 (82.2)
	≥64 years	94 (6.1)	145 (5.1)
Female, n (%)		710 (46.1)	1303 (45.6)
Race, n (%)	White	1058 (68.7)	2063 (72.2)
	Black or African American	104 (6.8)	170 (6.0)
	Asian	336 (21.8)	553 (19.4)
	Other	42 (2.7)	70 (2.5)
IGA, n (%)	Moderate (3)	63.1	61.4
	Severe (4)	36.9	38.6
EASI, median (IQR)		25.6 (19.6-37.5)	26.9 (20.2-37.6)
Prior topical agents only, n (%)		845 (54.9)	1382 (48.4)
Prior systemic therapy, n (%)		676 (43.9)	1454 (50.9)
Dupilumab		45 (2.9)	108 (3.8)

Safety Summary (placebo-controlled cohort)

	Placebo n (%) n=342	Abrocitinib 100 mg n (%) n=608	Abrocitinib 200 mg n (%) n=590
Patients evaluable for AEs	342	608	590
No. of AEs	360	816	921
Patients with AEs	188 (55.0)	371 (61.0)	403 (68.3)
Patients with SAEs	11 (3.2)	19 (3.1)	11 (1.9)
Patients with severe AEs	20 (5.8)	29 (4.8)	19 (3.2)
Deaths[a]	0	1 (0.2)	2 (0.3)
Dose-related TEAEs[b]			
Nausea	7 (2.0)	37 (6.1)	86 (14.6)
Headache	12 (3.5)	36 (5.9)	46 (7.8)
Acne	0	10 (1.6)	28 (4.7)
Herpes simplex	3 (0.9)	10 (1.6)	17 (2.9)

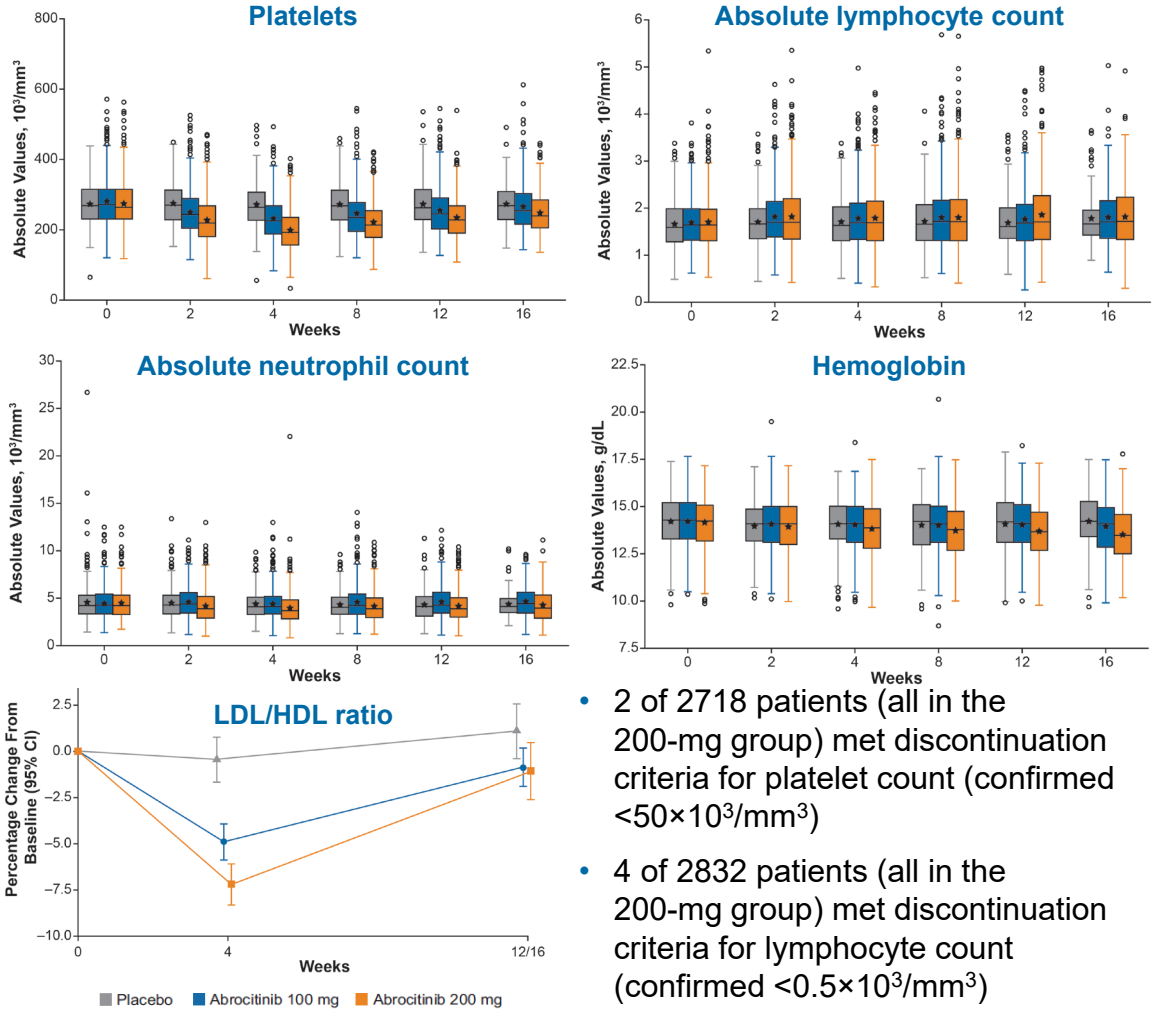
AE, adverse event; EASI, Eczema Area Severity Index; IGA, Investigator's Global Assessment; IQR, interquartile range; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

[a]A 69-year-old Black woman (200-mg group) tested positive for COVID-19 on day 84, was hospitalized, and died of COVID-19 on day 107; a 78-year-old White woman (200-mg group) received a diagnosis of gastric adenocarcinoma on study day 43 by computed tomography, which showed carcinomatosis with multifocal hepatic metastases, and she died of gastric adenocarcinoma ~7 months after study discontinuation; a 73-year-old White woman (100-mg group) with a history of aortic sclerosis and calcification and untreated hypertension died suddenly on day 107, which was 22 days after discontinuation of abrocitinib.

[b]These AEs infrequently led to discontinuation.

Laboratory Values, Incidence Rates, and Conclusions

Laboratory Values



- 2 of 2718 patients (all in the 200-mg group) met discontinuation criteria for platelet count (confirmed <50×10³/mm³)
- 4 of 2832 patients (all in the 200-mg group) met discontinuation criteria for lymphocyte count (confirmed <0.5×10³/mm³)

Incidence Rates (all-abrocitinib cohort)

	Abrocitinib 100 mg n/100 PY (95% CI) n=885	Abrocitinib 200 mg n/100 PY (95% CI) n=1971
Serious infections	2.65 (1.55-4.25)	2.33 (1.49-3.47)
Herpes zoster	2.04 (1.09-3.49)	4.34 (3.15-5.82)
Herpes simplex	8.73 (6.56-11.39)	11.83 (9.77-14.19)
Eczema herpeticum	2.34 (1.31-3.86)	0.78 (0.34-1.53)

- Incidence rates for all abrocitinib-treated patients, including both doses (n/100 PY [95% CI]), were

OI: 0.60 (0.29-1.10)
MACE: 0.18 (0.04-0.52)
VTE: 0.30 (0.10-0.70)
Malignancies[a]: 0.24 (0.07-0.61)
NMSC: 0.42 (0.17-0.86)
GI perforation: 0.18 (0.04-0.52)

Conclusions

- Results of this integrated safety analysis were consistent with results in individual trials; there were no unexpected safety findings
- Abrocitinib was well tolerated, with a safety profile appropriate for long-term treatment in this population

GI, gastrointestinal; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; OI, opportunistic infection; PY, patient-year; VTE, venous thromboembolism.
[a]Excluding NMSC.