Long-term Safety of Apremilast From a Pooled Analysis of 15 Randomized, Placebo-controlled Studies of Psoriasis, Psoriatic Arthritis, and Oral Ulcers Associated With Behçet's Syndrome

Philip J. Mease, MD[1]; Gülen Hatemi, MD[2]; Maria Paris, MD[3]; Sue Cheng, MD[3]; Peter Maes, BA[3]; Wendy Zhang, MD[3]; Rebecca Shi, MS[3]; Andrea Flower, MS[3]; Linda Stein Gold, MD[4]

[1]Swedish Medical Center/Providence St. Joseph Health and University of Washington School of Medicine, Seattle, WA, USA; [2]Istanbul University – Cerrahpaşa, School of Medicine, Istanbul, Turkey; [3]Amgen Inc., Thousand Oaks, CA, USA; [4]Henry Ford Health System, West Bloomfield, MI, USA

Introduction and Objectives

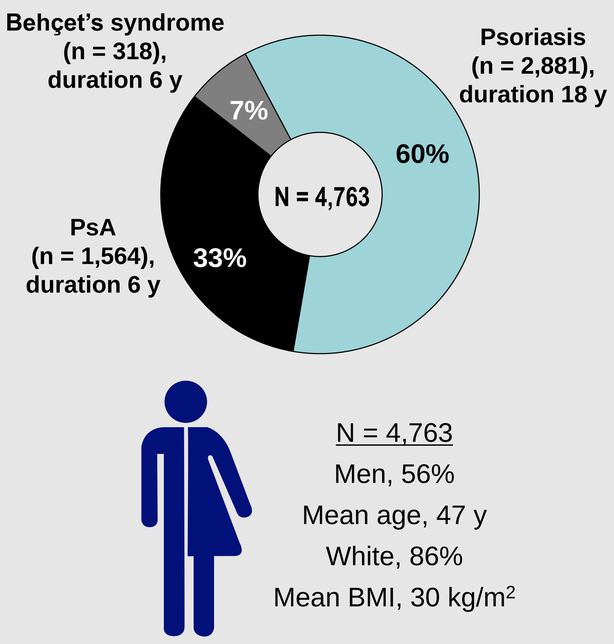
- Apremilast is an oral phosphodiesterase 4 inhibitor that, as of March 20, 2022, has been used by 706,585 patients (557,379 patient-years [PY] of exposure) worldwide
- The approved indications of apremilast are plaque psoriasis, psoriatic arthritis (PsA), and oral ulcers associated with Behçet's syndrome[1-3]
- This long-term pooled safety analysis assessed adverse events (AEs) of special interest, including thrombotic events, malignancies, major adverse cardiac events (MACE), serious infections, and depression

Methods

- **Design:** Data from up to 5 years of exposure to apremilast 30 mg twice daily (BID) (APR) were pooled from 15 randomized, placebo (PBO)-controlled studies across indications and divided into PBO-controlled and all-APR-exposure groups
  - Psoriasis (eight studies)
  - PsA (five studies)
  - Behçet's syndrome (two studies)
- **Patients:** Adults who met respective study eligibility criteria and received ≥1 dose of PBO or APR (PBO-controlled group) or ≥1 dose of APR (all-APR-exposure group) were assessed for safety

Patient Population

- During the PBO-controlled periods, 2,676 patients were randomized to APR and 2,087 were randomized to PBO
- Of the 4,763 patients included in the analysis, 4,183 patients were exposed to APR (6,788.0 PY)



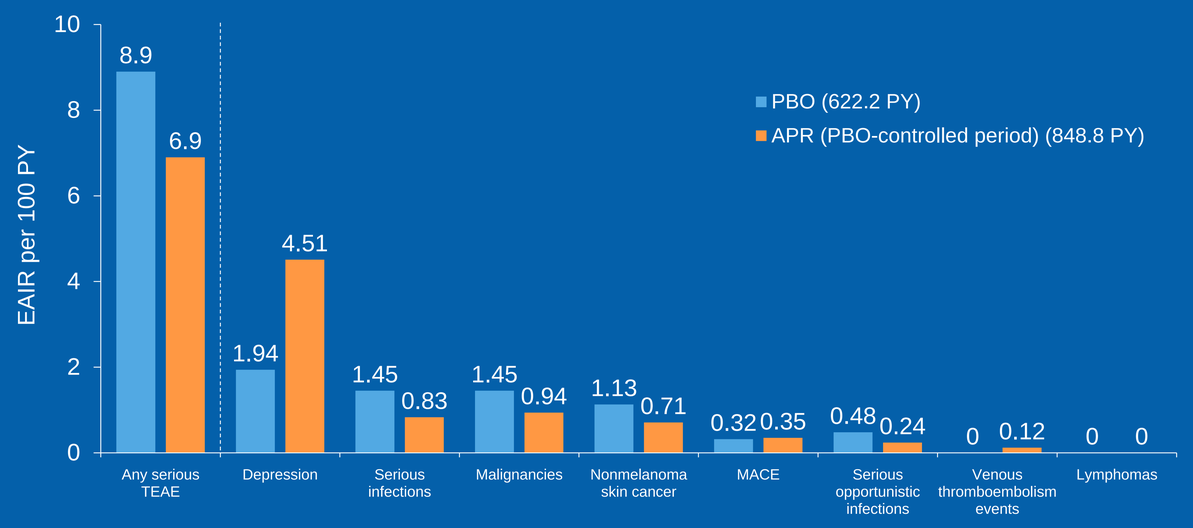
N = 4,763
Men, 56%
Mean age, 47 y
White, 86%
Mean BMI, 30 kg/m^2

BMI, body mass index; PsA, psoriatic arthritis.

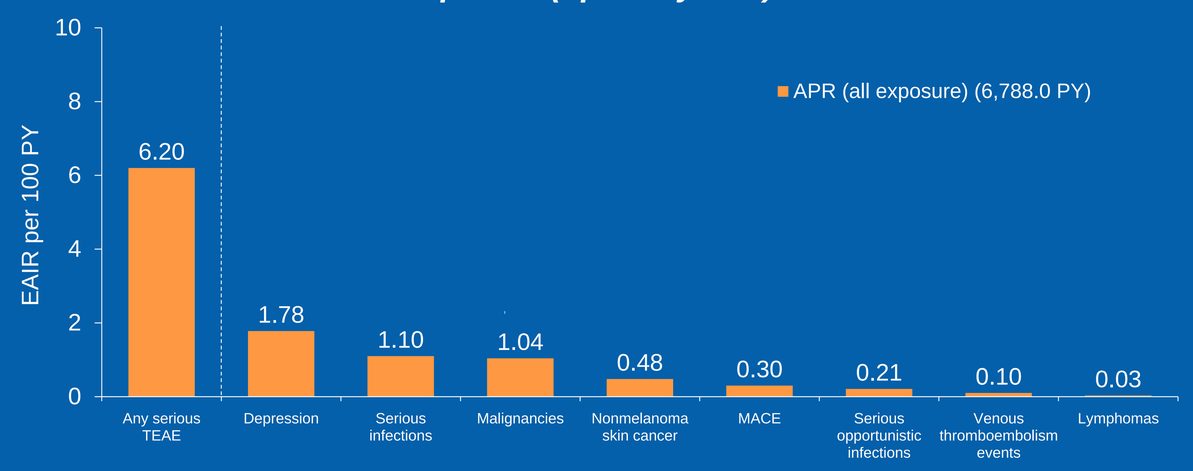
Key Takeaways

- **In the largest safety analysis of APR to date, the incidence rates of AEs of special interest and serious treatment-emergent AEs (TEAEs) were low despite the long-term APR exposure**
- **Results further establish APR as a safe oral option with a favorable benefit-risk profile for long-term treatment for psoriasis, psoriatic arthritis, and oral ulcers associated with Behçet's syndrome**

EAIRs per 100 PY for serious infections, malignancies, nonmelanoma skin cancer, and serious opportunistic infections were lower with APR versus PBO during the PBO-controlled period (up to 28 weeks)



EAIRs of AEs of special interest, including MACE, lymphomas, and venous thromboembolism events, remained low during the all-APR-exposure period (up to 5 years)



Includes patients who received at least one dose of the study drug. Patients started treatment with apremilast at week 0, week 12, week 16, or week 24 depending on early escape and re-randomization in the respective studies. For patients who discontinued before end of the PBO-controlled period, data up to 28 days after last dose date are included. All-APR-exposure includes PBO-controlled period and APR exposure period data up to 28 days after the last dose date, regardless of when patients started APR. Venous thromboembolism events are defined as deep vein thrombosis and pulmonary embolism. Throughout all-APR-exposure, EAIR/100 PY was 0.07 for deep vein thrombosis and 0.03 for pulmonary embolism.

AE, adverse event; APR, apremilast 30 mg BID; BID, twice daily; EAIR, exposure-adjusted incidence rate; MACE, major adverse cardiac events; PBO, placebo; PY, patient-years; TEAE, treatment-emergent adverse event.

Disclosures and Funding Statement

PJM: AbbVie, Amgen Inc., Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Sun, and UCB – grant/research support and consultant; Boehringer Ingelheim, GlaxoSmithKline – consultant; AbbVie, Amgen Inc., Eli Lilly, Janssen, Novartis, Pfizer, and UCB – speakers bureau. **GH:** AbbVie, Amgen Inc., and Celgene Corporation – grant/research support; AbbVie, Boehringer Ingelheim, Novartis, and UCB Pharma – speaker. **MP, SC, PM, WZ, RS, and AF:** Amgen Inc. – employees and stockholders. **LSG:** AbbVie, Amgen, Arcutis, Celgene Corporation, Dermavant, Dermira, Eli Lilly, Galderma, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, UCB, and Valeant – honoraria, grants, and/or research funding as a speaker, investigator, and advisory board member.

Funding: This study was funded by Amgen Inc. Writing support was funded by Amgen Inc. and provided by Christina Mulvihill, PharmD, of Peloton Advantage, LLC, an OPEN Health company, and Dawn Nicewarner, PhD, CMPP, employee of and stockholder in Amgen Inc.

References 1. Otezla [package insert]. Thousand Oaks, CA: Amgen Inc.; 2021. **2**. European Medicines Agency. Otezla Summary of Opinion (post authorisation) Amsterdam, The Netherlands: European Medicines Agency; 2020. **3**. Otezla EPAR summary for the public: European Medicines Agency; 2015.

For further information on the most common TEAEs, deaths during studies, and the studies included in the analysis, scan the QR code or follow the URL:

https://contents-amgen.com/prd/user-screen.html?content_id=325

Pooled Population Exposure

- Overall APR exposure: 6,788.0 PY
- Median APR exposure: 51 weeks (range: 0.1–316.1)

TEAEs in the PBO-Controlled Period

- Most TEAEs were mild or moderate, and rates of TEAEs leading to drug withdrawal were low during the PBO-controlled period

Overview of TEAEs During the PBO-Controlled Period

	PBO (n = 2,084, PY = 622.2)		APR (n = 2,673, PY = 848.8)	
	n (%)	EAIR/100 PY	n (%)	EAIR/100 PY
Any TEAE	1,113 (53)	279.1	1,780 (67)	433.5
Any severe TEAE	66 (3)	10.7	97 (4)	11.6
TEAEs leading to drug withdrawal	91 (4)	14.7	154 (6)	18.3
TEAEs leading to death	2 (0.1)	0.3	1 (<0.1)	0.1

APR, apremilast 30 mg BID; BID, twice daily; EAIR, exposure-adjusted incidence rate; PBO, placebo; PY, patient-years; TEAE, treatment-emergent adverse event.

- Gastrointestinal TEAEs were largely mild or moderate, usually began within the first 1 to 2 weeks of APR treatment, and typically resolved within 30 days

TEAEs in the APR-Exposure Period

- Most TEAEs were mild or moderate, and rates of TEAEs leading to drug withdrawal were low during the APR-exposure period

Overview of TEAEs During the APR-Exposure Period

	All APR Exposure (n = 4,183, PY = 6,788.0)	
	n (%)	EAIR/ 100 PY
Any TEAE	3,265 (78)	179.5
Any severe TEAE	353 (8)	5.5
TEAEs leading to drug withdrawal	387 (9)	5.7
TEAEs leading to death	9 (0.2)	0.1

APR, apremilast 30 mg BID; BID, twice daily; EAIR, exposure-adjusted incidence rate; PY, patient- years; TEAE, treatment-emergent adverse event.

- Common TEAEs were consistent with those previously reported in the individual clinical trials

Presented at: 2023 Fall Clinical Dermatology Conference (FC23); October 19–22, 2023; Las Vegas, NV, USA