Achieving an Itch-Free State With Upadacitinib: A Post-Hoc Analysis of Data From the Phase 2b Randomized, Double-Blind, Placebo-Controlled Trial in Moderate-to-Severe Atopic Dermatitis

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Presented at the Revolutionizing Atopic Dermatitis (RAD) 2020 Virtual Congress, April 5, 2020, Chicago, Illinois

OBJECTIVES

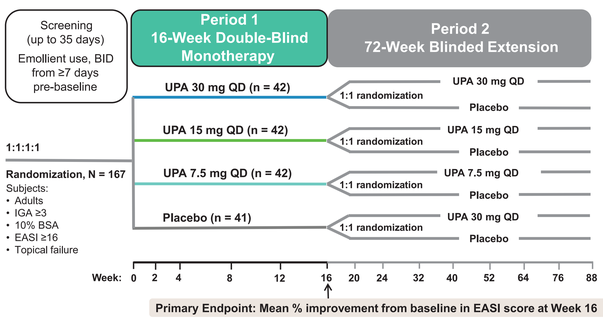
- To compare the proportions of upadacitinib-treated patients achieving an itch-free state vs placebo

BACKGROUND

- Atopic dermatitis (AD) is a chronic, inflammatory skin disease characterized by pruritus and eczematous lesions
- The selective Janus Kinase 1 inhibitor, upadacitinib (UPA), is being investigated for treatment of AD and other immune-mediated diseases[1]

METHODS

STUDY DESIGN



BID, twice daily; BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; QD, once daily; UPA, upadacitinib.

- Patient-reported itch was assessed daily using the Pruritus NRS (0 = no itch; 10 = worst imaginable itch)
  - An itch-free state was defined as a Pruritus NRS weekly rolling average of 0/1 after rounding to the nearest integer
  - Patient-weeks were tallied to characterize the time spent in an itch-free state
- Itch was also assessed by SCORAD Itch VAS and POEM Itch
- Treatment differences between UPA and placebo were assessed by the Cochran-Mantel-Haenszel test
- Missing data were addressed using non-responder imputation for categorical variables and last observation carried forward for continuous variables

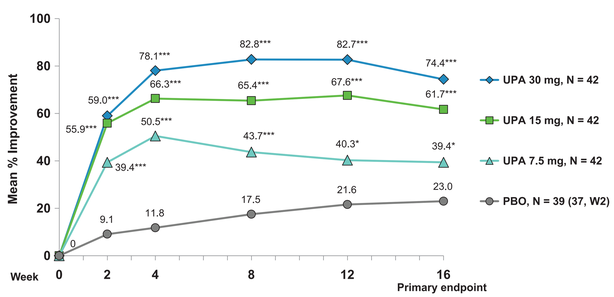
RESULTS

Table 1. Demographics and Baseline Characteristics

		Placebo, n = 41	UPA, QD 7.5 mg, n = 42	UPA, QD 15 mg, n = 42	UPA, QD 30 mg, n = 42
Female, n (%)		17 (42)	14 (33)	12 (29)	20 (48)
Age (years), mean [SD]		40 [18]	42 [15]	39 [15]	40 [15]
Race[a], n (%)	White	28 (68)	24 (57)	21 (50)	23 (55)
	Black, African American	6 (15)	7 (17)	10 (24)	6 (14)
	Asian	7 (17)	9 (21)	9 (21)	13 (31)
BMI, mean [SD]		26 [7]	28 [6]	27 [7]	27 [6]
Region, n (%)	US/PR/Canada	29 (71)	29 (69)	29 (69)	29 (69)
	EU/AUS/Japan	12 (29)	13 (31)	13 (31)	13 (31)
Years since AD symptom onset, mean [SD]		31 [19], n = 40	34 [18], n = 42	24 [15], n = 40	27 [16], n = 40
EASI, mean [SD]		32.6 [14.5]	31.4 [15.8]	31.4 [12.3]	28.2 [11.6]
BSA, mean [SD]		45.7 [22.8]	46.9 [24.9]	50.6 [21.5]	42.1 [20.4]
Pruritus NRS, mean [SD]		6.5 [1.9], n = 39	6.8 [1.8], n = 40	6.4 [1.7], n = 37	6.3 [2.1]

[a]American Indian or Alaska Native (1 UPA 15 mg); Native Hawaiian or other Pacific Islander (2 UPA 7.5 mg and 1 UPA 15 mg).
AD, atopic dermatitis; AUS, Australia; BMI, body mass index; BSA, body surface area; EASI, Eczema Area Severity Index; EU, European Union; NRS, numerical rating scale; PR, Puerto Rico; SD, standard deviation; US, United States.

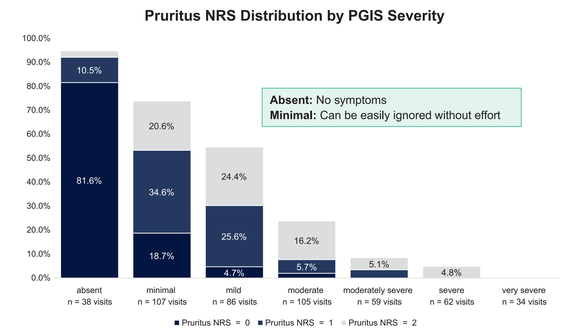
Figure 1. Mean % Improvement From Baseline in EASI Through Week 16



Statistical significance: ***P <.001, **P <.01, *P <.05, UPA vs placebo. Missing data handled by last observation carried forward.

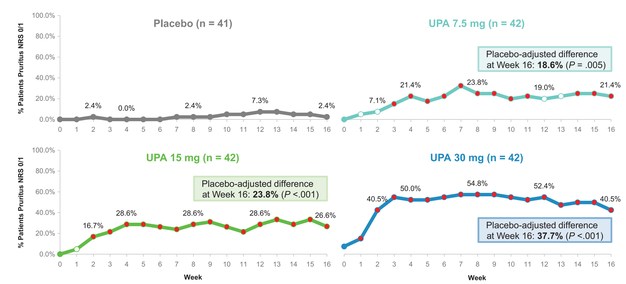
Figure 2. Identifying an Itch-Free State

- Patients assessed their overall symptom severity using a single-item Patient Global Impression of Severity (PGIS) scale
- Distribution patterns of Pruritus NRS by PGIS suggest that Pruritus NRS ≤1 is a reasonable threshold for identifying patients whose overall symptom severity is absent or minimal



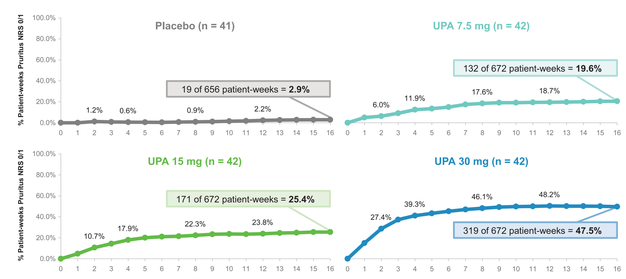
Distributions are based on visits during the first 16 weeks of the trial where both Pruritus NRS and PGIS data are available (observed cases). Pruritus NRS is based on a weekly rolling average and rounded to the nearest integer. NRS, numerical rating scale; PGIS, Patient Global Impression of Severity.

Figure 3. % Patients With Pruritus NRS 0/1



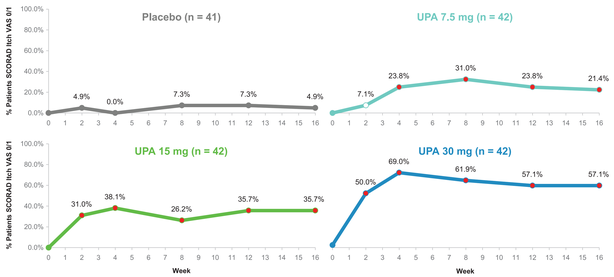
Red markers indicate P <.05 vs placebo; white markers indicate P ≥.05 vs placebo. Missing data handled by non-responder imputation. mg, milligrams; NRS, numerical rating scale; UPA, upadacitinib.

Figure 4. Cumulative % Patient-weeks With Pruritus NRS 0/1



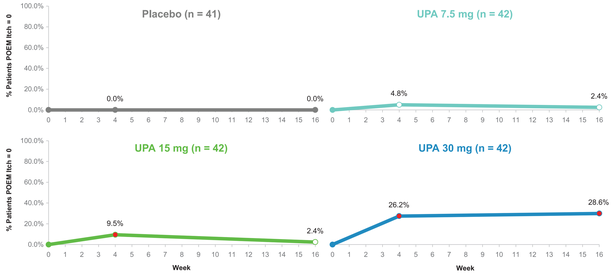
The % of patient-weeks with Pruritus NRS 0/1 is cumulative and considers data from Baseline to the time point denoted on the x-axis. Missing data handled by non-responder imputation. mg, milligrams; NRS, numerical rating scale; UPA, upadacitinib.

Figure 5. % Patients With SCORAD Itch VAS 0/1



Red markers indicate P <.05 vs placebo; white markers indicate P ≥.05 vs placebo. Missing data handled by non-responder imputation. mg, milligrams; SCORAD, Scoring Atopic Dermatitis; UPA, upadacitinib; VAS, visual analog scale.

Figure 6. % Patients With POEM Itch = 0 (zero days of itch in past week)



Red markers indicate P <.05 vs placebo; white markers indicate P ≥.05 vs placebo. Missing data handled by non-responder imputation. mg, milligrams; POEM, Patient Oriented Eczema Measure; UPA, upadacitinib.

CONCLUSIONS

- Upadacitinib treatment for 16 weeks resulted in significant improvements in pruritus vs placebo
- Upadacitinib-treated subjects achieved a higher proportion and duration of an itch-free state vs placebo
- The positive benefit/risk profile of upadacitinib supports proceeding to phase 3 trials in AD

TRANSPARENCY

ROLE OF AUTHOR AND SPONSOR

Design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the presentation. All authors contributed to the development of the publication and maintained control over the final content.

AUTHOR DISCLOSURES

Jonathan I Silverberg received honoraria as a consultant for AbbVie, Asana, Anaptysbio, Eli Lilly, Galderma, GlaxoSmithKline, Glenmark, Kiniksa, LEO, Menlo, Pfizer, Realm, Dermavant, and Regeneron-Sanofi; and received research grants as an investigator from GlaxoSmithKline. **Kristian Reich** received honoraria for advisory board service, speaker service and educational development, and grants for investigator service from AbbVie, Affibody, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO, Lilly, Medac, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Takeda, UCB Pharma, and Xenoport. **Brian Calimlim, Yihua Gu, Xiaofei Hu,** and **Henrique D Teixeira** are employees of AbbVie and may own AbbVie stock or stock options. **Emma Guttman-Yassky** received honoraria as a consultant for AbbVie, Allergan, Almirall, Anacor, AnaptysBio, Asana Biosciences, Celgene, Concert, Dermira, DBV Technologies, DS Biopharma, Galderma, Gilead, Glenmark, Immune, Kyowa Kirin, LEO Pharma, Mitsubishi Tanabe, Novartis, Pfizer, Puricore, Regeneron, Sanofi, Stiefel/GSK, Sun Pharma, Vitae, and Ziarco. Received research grants for investigator services from AbbVie, Asana, Celgene, Dermira, Galderma, Glenmark, Immune, Innovaderm, LEO Pharma, Lilly, Medimmune, Novartis, Regeneron, Pfizer, and Vitae.

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1. Pipeline – Our Science | AbbVie. https://www.abbvie.com/our-science/pipeline.html (accessed 17 May 2019).

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