ARQ-151, Roflumilast Cream, Improved Psoriasis in Phase 2a Study

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Disclosure: This work was supported by Arcutis Biotherapeutics, Inc.

KAP has been an advisor to and/or received speakers' honoraria and/or received grants from and/or participated in clinical trials of the following companies: AbbVie, Affibody AB, Akros, Amgen, Anaptys Bio, Arcutis, Astellas, Bausch Health, Baxalta, Biogen Idec, Boehringer-Ingelheim, Bristol-Myers Squibb, CanFite, Celgene, Centocor, Coherus, Dermira, Dow Pharmaceuticals, Eli Lilly and Company, Galderma, Genentech, GSK, Isotechnika, Janssen-Cilag, Johnson & Johnson, Kyowa Hakko Kirin, Leo Pharma, Merck Sharp & Dohme, Merck Serono, Mylan, Novartis, Pfizer, Regeneron Pharmaceutical, Sanofi-Aventis, Roche, Sun Pharma, Takeda, UCB Pharma, and Valeant. MG is an investigator for Arcutis Biotherapeutics Inc. MD, CM, DWO, DB, AT, and HW are employees of Arcutis Biotherapeutics, Inc.

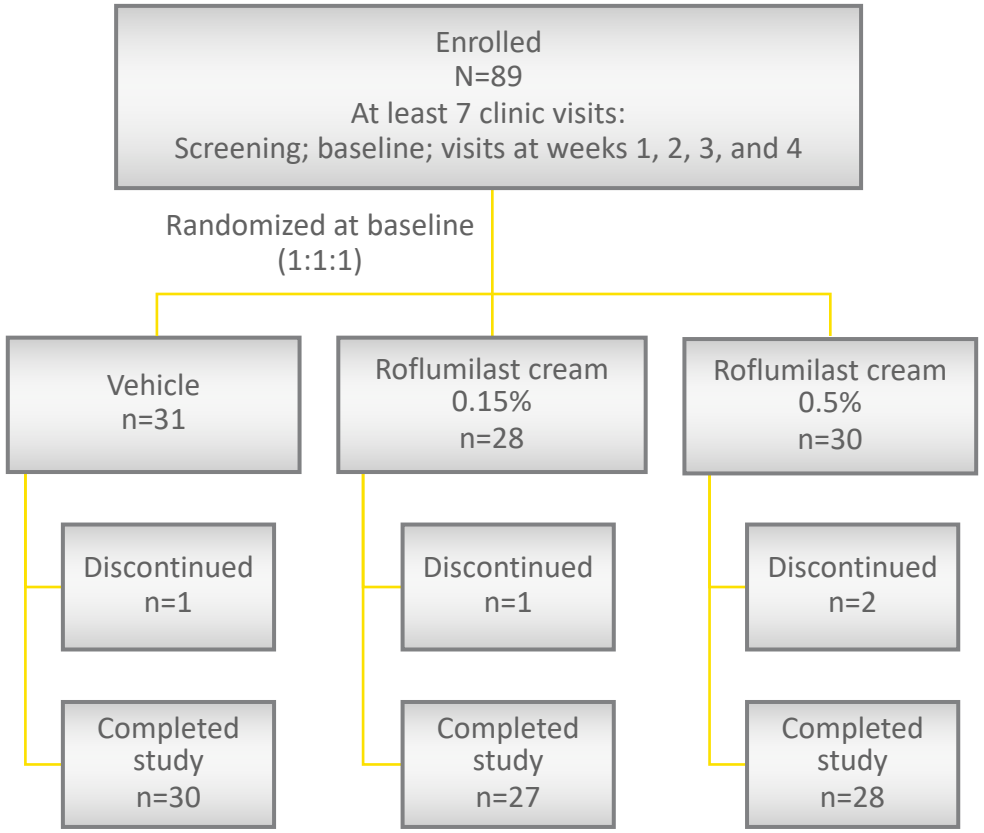
Safety and Efficacy of Topical Roflumilast Cream (ARQ-151) in Subjects With Mild or Moderate Plaque Psoriasis: Background and Methods

Background

- Options for topical treatment of chronic plaque psoriasis are limited to potent steroids or vitamin D, both of which have long-term tolerability issues
- Roflumilast cream (ARQ-151) is a potent, selective phosphodiesterase-4 (PDE-4) inhibitor under clinical investigation for treatment of mild or moderate plaque psoriasis
  - PDE-4 inhibition decreases production of TNFα, IFNϒ, IL-17, and IL-23[1,2]
  - Approximately 25- to 300-fold more potent than currently available PDE-4 inhibitors (depending on PDE-4 subtype), exhibiting half-maximal inhibitory concentration values of both roflumilast and roflumilast N-oxide for PDE-4 isoforms and subtypes at subnanomolar potency[3,4]
- Objective of this phase 1/2a study was to evaluate the safety and efficacy of 2 concentrations of roflumilast cream versus vehicle in subjects with chronic plaque psoriasis

Methods

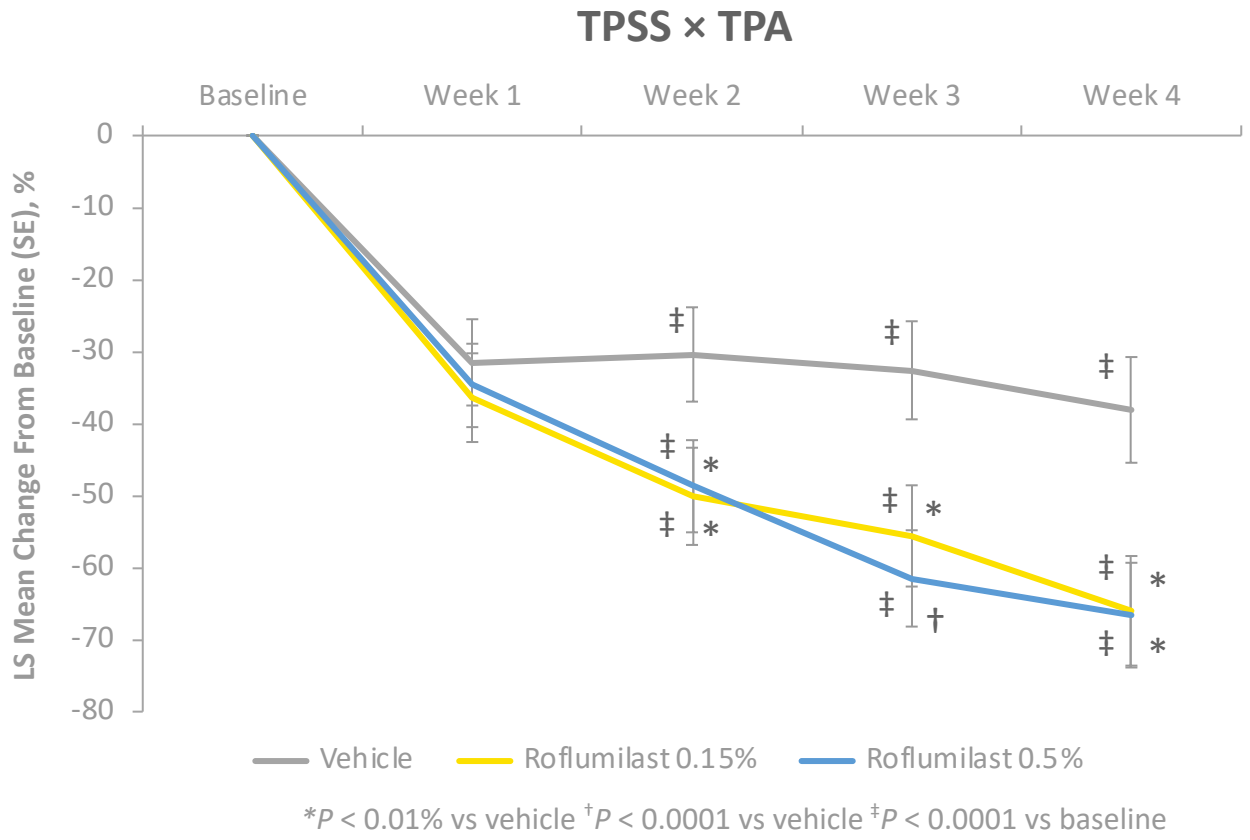
- Parallel-group, randomized, double-blind, vehicle-controlled study of adult subjects (≥18 years) with chronic plaque psoriasis (disease duration ≥6 months) covering 0.5%–5.0% of total BSA, excluding face, scalp, intertriginous areas, palms, and soles (ClinicalTrials.gov NCT03392168)
- Subjects received roflumilast cream 0.15% or 0.5% or vehicle applied once daily for 28 days
- Primary efficacy endpoint: % change from baseline at week 4 in TPSS × TPA* between each dose of roflumilast compared with vehicle



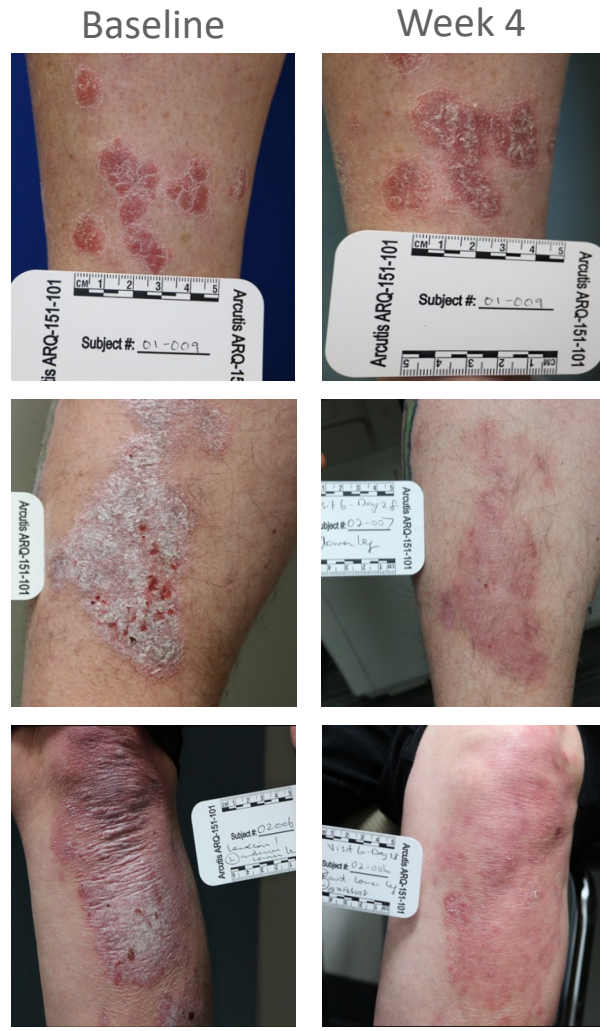
*TPSS: Target Plaque Severity Score was determined for each target plaque as the sum of erythema, thickness, and scaling, each rated on scale of 0 (none) to 4 (very severe). TPA: target plaque area (cm^2) was determined by multiplying the target plaque longest diameter by the widest perpendicular diameter.

[1]Li H, et al. *Front Pharmacol* 2018;9:1048. [2]Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413-422. [3]Hatzelmann A, et al. *Pulm Pharmacol Ther* 2010;23:235-256. [4]Kitzen J, et al. *Pharmaol Pharm* 2018;9:357-381.

Roflumilast Improved Severity of Plaque Psoriasis



Roflumilast cream 0.15% and 0.5% resulted in 66% and 67% improvement from baseline in TPSS × TPA at week 4 compared with 38% for vehicle



Data are presented for modified intent-to-treat population. Estimates for LS means and *P* values are from a mixed model for repeated measures.
LS: least squares; SE: standard error; TPA: target plaque area; TPSS: Target Plaque Severity Score.

All TEAEs Were Mild or Moderate

TEAE,* n (%)	Vehicle (n=31)	Roflumilast 0.15% (n=28)	Roflumilast 0.5% (n=30)
Subjects with ≥1 TEAE	11 (36)	7 (25)	12 (40)
Maximum severity of TEAE			
Mild	6 (19)	3 (11)	7 (23)
Moderate	5 (16)	4 (14)	5 (17)
Severe	0	0	0
Death related to AE	0	0	0
Subjects with a treatment-related TEAE	8 (26)	2 (7)	7 (23)
Subjects with a TEAE leading to discontinuation of study drug	0	0	0
Subjects with an SAE	0	0	0

TEAE, n (%)	Vehicle (n=31)	Roflumilast 0.15% (n=28)	Roflumilast 0.5% (n=30)
Application site conditions	8 (26)	2 (7)	7 (23)
Erythema	4 (13)	1 (4)	4 (13)
Pain	5 (16)	1 (4)	2 (7)
Edema	1 (3)	0	1 (3)
Papules	1 (3)	0	1 (3)
Pruritus	0	1 (4)	1 (3)
Nasopharyngitis	0	2 (7)	2 (7)
Gastroenteritis viral	1 (3)	1 (4)	0
Influenza	2 (7)	0	0
Upper respiratory tract infection	0	2 (7)	1 (3)
Muscle strain	2 (7)	1 (4)	1 (3)
Limb injury	1 (3)	1 (4)	0

*Occurring in more than 1 subject across the treatment groups.

Data are presented for safety population. AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Conclusions

- PDE-4 inhibition represents a validated mechanism of action for oral psoriasis therapy, but a new mechanism of action for topical psoriasis treatment
- Improvement in TPSS × TPA at week 4 was statistically significant for roflumilast 0.15% and 0.5% compared with vehicle
- Statistical separation from vehicle was reached for both roflumilast concentrations as early as week 2, and the difference between active treatment and vehicle continued to increase through week 4
- AEs (all mild/moderate) were uncommon and similar between active arms and vehicle, with application site reactions being the most common
- No severe or serious TEAEs were reported and no subjects discontinued treatment because of an AE

Roflumilast cream, an investigational once-daily topical PDE-4 inhibitor, was well-tolerated and led to substantial and early improvements in subjects with chronic plaque psoriasis in this phase 2a study

AE: adverse event; PDE-4: phosphodiesterase-4; TEAE: treatment-emergent adverse event; TPA: target plaque area; TPSS: Target Plaque Severity Score.