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

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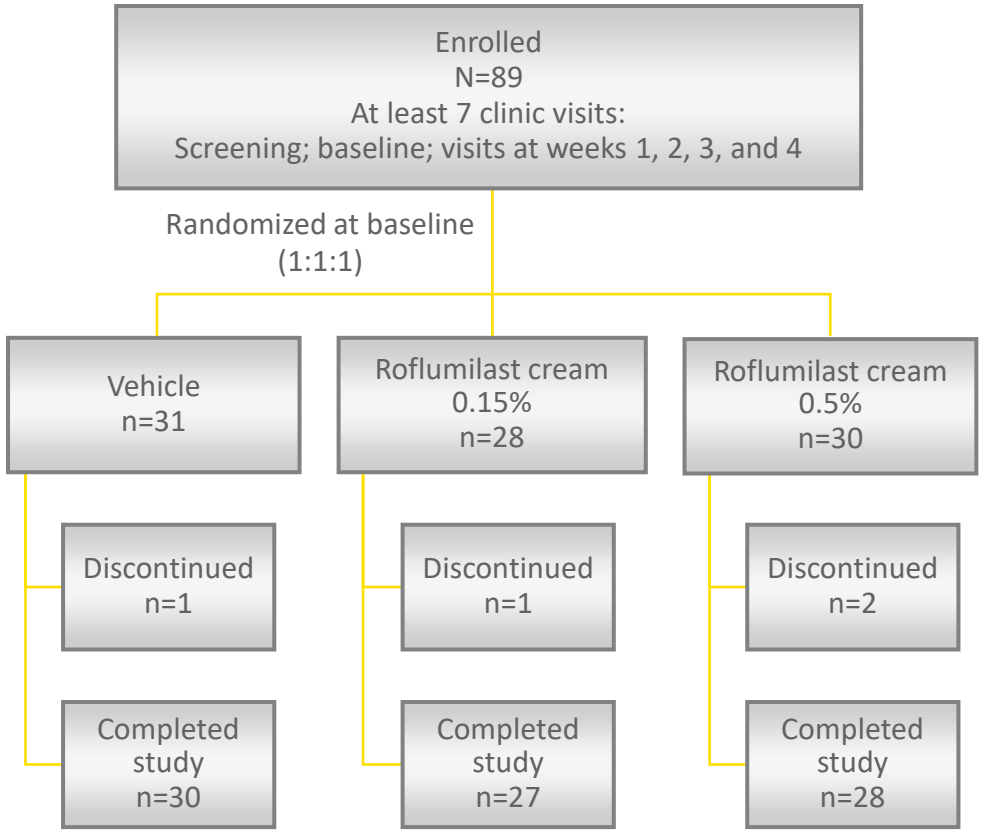
Safety and Efficacy of Topical Roflumilast Cream (ARQ-151) in Subjects With Mild or Moderate Plaque Psoriasis: Background and Methods

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

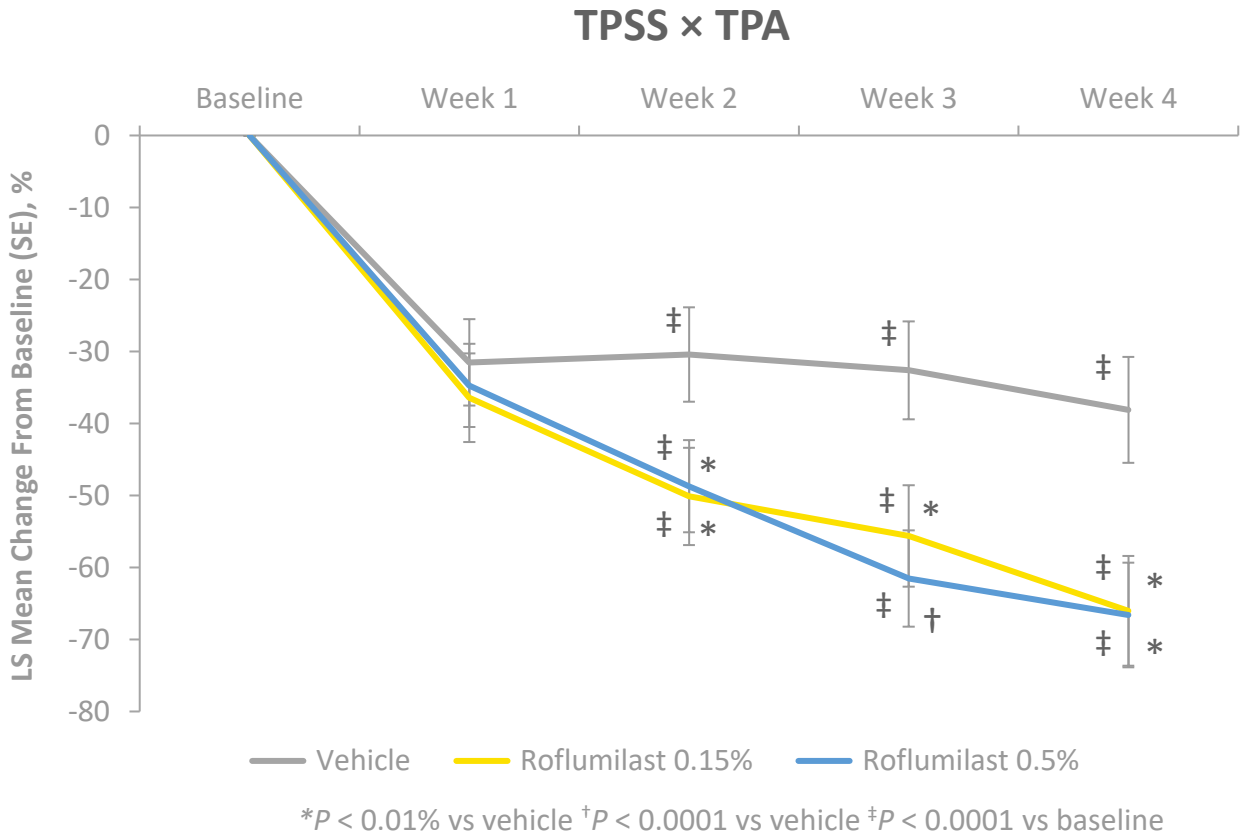
- Parallel-group, randomized, double-blind, vehicle-controlled study of adult subjects (≥18 years) with chronic plaque psoriasis (disease duration ≥6 months) covering 0.5%–5.0% of total BSA, excluding face, scalp, intertriginous areas, palms, and soles (ClinicalTrials.gov NCT03392168)
- Subjects received 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



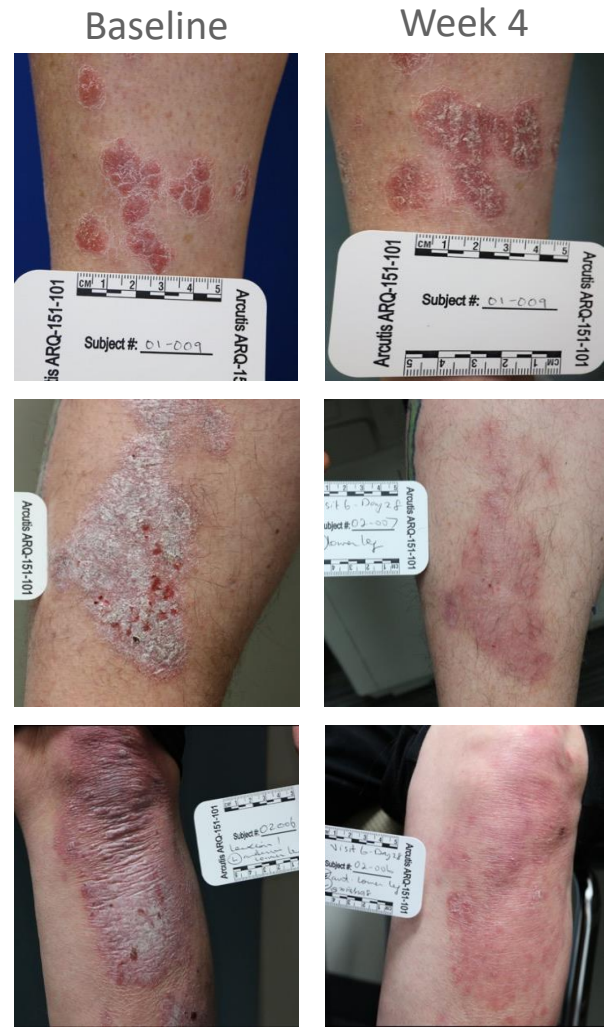
*TPSS: Target Plaque Severity Score was determined for each target plaque as the sum of erythema, thickness, and scaling, each rated on scale of 0 (none) to 4 (very severe). TPA: target plaque area (cm^2) was determined by multiplying the target plaque longest diameter by the widest perpendicular diameter.

[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.