Reduction in Pruritus Across Indications in Phase 3 Trials of Topical Roflumilast

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INTRODUCTION

- Pruritus is one of the most burdensome symptoms in patients with psoriasis, seborrheic dermatitis (SD), and atopic dermatitis (AD), affecting sleep and quality of life[1]
  - Patient perception of pruritis varies greatly among various skin diseases[2-4]
- Phosphodiesterase 4 (PDE4) inhibitors may reduce pruritus by inhibiting production of inflammatory itch mediators[5]
  - PDE4 inhibitors also act through mechanistic pathways independent of the anti-inflammatory action of PDE4 in mouse models of dermatoses[6-9]
- In this poster, we evaluate the reduction in pruritus in six Phase 3 clinical trials of topical roflumilast in patients aged ≥9 years with SD or ≥12 years with psoriasis and AD

Table 1. Study Designs

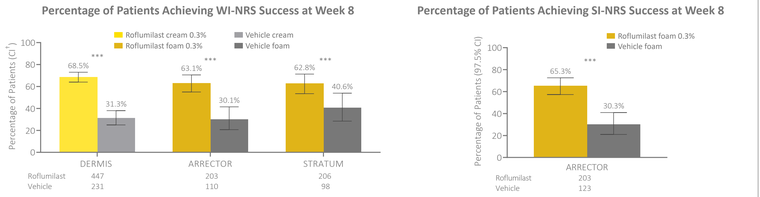
Trial	Treatment Groups	Inclusion Criteria	WI-NRS and SI-NRS Scores, Mean (SD)	Itch Assessments
DERMIS-1/-2[10] (Psoriasis; NCT04211363 and NCT04211389)	Roflumilast cream 0.3% (N=576) Vehicle (N=305)	≥2 years of age BSA: 2–20% IGA: ≥2 (Mild) PASI: ≥2	Roflumilast: 5.7 (2.7) Vehicle: 5.9 (2.8)	Baseline, Weeks 2, 6, 4, 8
ARRECTOR (Scalp and Body Psoriasis; NCT05028582)	Roflumilast foam 0.3% (N=281) Vehicle (N=151)	≥12 years of age BSA: ≤25% (≤20% non-scalp, ≥10% scalp) S-IGA: ≥3 (Moderate) B-IGA: ≥2 (Mild) PSSI: ≥6 PASI: ≥2	WI-NRS Roflumilast: 5.6 (2.8) Vehicle: 5.5 (2.8) SI-NRS Roflumilast: 5.9 (2.8) Vehicle: 6.1 (2.5)	Baseline, Days 2–56
STRATUM (Seborrheic Dermatitis; NCT04973228)	Roflumilast foam 0.3% (N=304) Vehicle (N=153)	≥9 years of age BSA: ≤20% IGA: ≥3 (Moderate)	Roflumilast: 5.1 (2.3) Vehicle: 4.7 (2.3)	Baseline, Days 2–56
INTEGUMENT-1/-2 (Atopic Dermatitis; NCT04773587 and NCT04773600)	Roflumilast cream 0.15% (N=884) Vehicle (N=453)	≥6 years of age BSA: ≥3% vIGA-AD: 2 (Mild) to 3 (Moderate) EASI: ≥5	Roflumilast: 6.1 (2.1) Vehicle: 5.9 (2.2)	Baseline, Days 2–29

B-IGA: Body-Investigator Global Assessment; BSA: body surface area; EASI: Eczema Area and Severity Index; IGA: Investigator Global Assessment; PASI: Psoriasis Area and Severity Index; PSSI: Psoriasis Scalp Severity Index; S-IGA: Scalp-Investigator Global Assessment; SD: standard deviation; SI-NRS: Scalp Itch-Numeric Rating Scale; vIGA-AD, Validated Global Assessment for Atopic Dermatitis; WI-NRS: Worst Itch-Numeric Rating Scale.

RESULTS

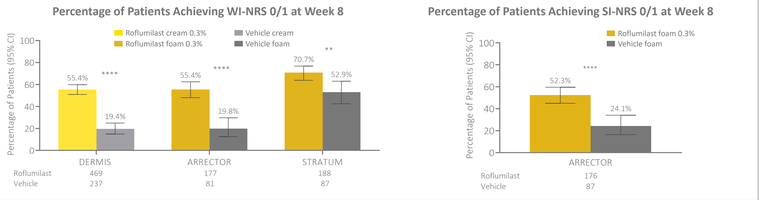
- Efficacy, safety, and tolerability for all six Phase 3 studies were previously reported
- More roflumilast- than vehicle-treated patients achieved improvement in pruritus as measured by Worst Itch-Numeric Rating Scale (WI-NRS) Success and Scalp Itch-Numeric Rating Scale (SI-NRS) Success (≥4-point improvement in patients with baseline score ≥4) at the final assessment in each trial (Figures 1–3)
- Similarly, differences favoring roflumilast were also observed for achievement of WI-NRS scores of 0 or 1 (in patients with baseline score ≥2) at the final assessment for all trials (Figures 2 and 3)
- Pruritus scores improved as early as 24 hours in patients with psoriasis (ARRECTOR) and AD (INTEGUMENT) and by 48 hours in patients with SD (STRATUM; Figures 4–6), as compared with vehicle

Figure 1. Percentage of Patients Achieving WI-NRS (A) and SI-NRS (B) Success at Week 8



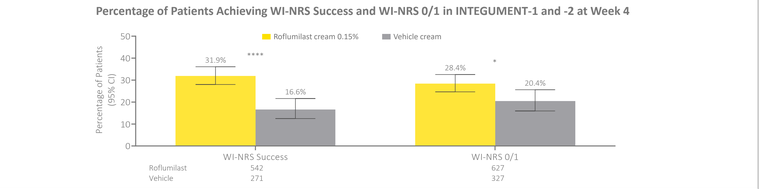
***P≤0.0001. †CIs are 95% for DERMIS, 97.5% for ARRECTOR, and 99% for STRATUM.
WI-NRS Success: achievement of ≥4-point improvement from baseline in patients aged ≥12 years with baseline WI-NRS ≥4. Analyses of weekly average with multiple imputation to handle missing data. SI-NRS Success: achievement of ≥4-point improvement from baseline in patients aged ≥12 years with baseline SI-NRS ≥4.
CI: confidence interval; SI-NRS: Scalp Itch-Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

Figure 2. Percentage of Patients Achieving WI-NRS (A) and SI-NRS 0/1 (B) at Week 8



**P<0.01, ****P<0.0001.
WI-NRS 0/1 and SI-NRS 0/1 were assessed in patients with baseline WI-NRS and SI-NRS ≥2. Analyses of weekly average with multiple imputation to handle missing data.
CI: confidence interval; SI-NRS: Scalp Itch-Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

Figure 3. Percentage of Patients Achieving WI-NRS Success and WI-NRS 0/1 in INTEGUMENT-1 and -2 at Week 4

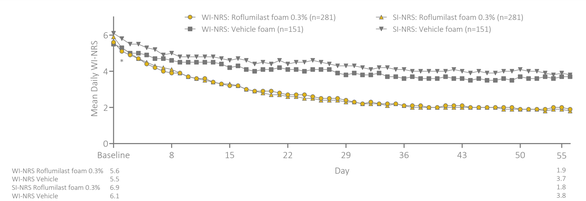


*P=0.0087; ****P<0.0001.
WI-NRS Success: achievement of ≥4-point improvement from baseline in patients aged ≥12 years with baseline WI-NRS ≥4. WI-NRS 0/1 was assessed in patients with baseline WI-NRS ≥2. Analysis of observed daily assessments.
CI: confidence interval; WI-NRS: Worst Itch-Numeric Rating Scale.

CONCLUSIONS

- Once-daily topical roflumilast provided consistent and rapid improvements in itch across psoriasis, SD, and AD, with improvement as early as 24–48 hours, as compared with vehicle-treated patients
  - Across indications, a significant proportion of patients achieved an itch-free state (WI-NRS and SI-NRS 0/1)
- These results highlight the potential for roflumilast to reduce this burdensome symptom substantially across inflammatory dermatoses

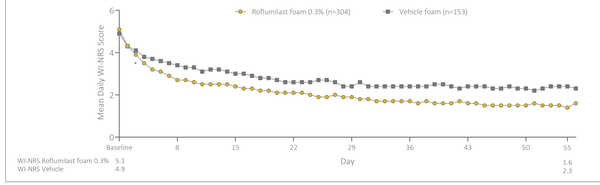
Figure 4. Daily Itch Improvement of Scalp and Body Psoriasis From the ARRECTOR Trial



LS mean change in daily itch NRS score from baseline was significant on Day 1 (approximately 24 hours after first application) for roflumilast foam 0.3% versus vehicle (both WI-NRS and SI-NRS; P<0.05)

*P<0.05 for difference from vehicle at 24 hours post application and for all timepoints assessed after.
LS: least squares; NRS: Numeric Rating Scale; SI-NRS: Scalp Itch-Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

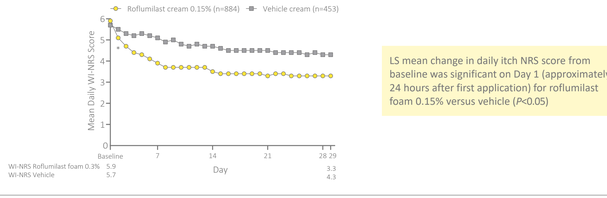
Figure 5. Daily Itch Improvement in Seborrheic Dermatitis From the STRATUM Trial



LS mean change in daily itch NRS score from baseline was significant on Day 2 (approximately 48 hours after first application) for roflumilast foam 0.3% versus vehicle (P<0.05)

*P<0.05 for difference from vehicle at 48 hours post application and for all timepoints assessed after.
LS: least squares; NRS: Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

Figure 6. Daily Itch Improvement in Atopic Dermatitis From the Pooled INTEGUMENT Trials



LS mean change in daily itch NRS score from baseline was significant on Day 1 (approximately 24 hours after first application) for roflumilast foam 0.15% versus vehicle (P<0.05)

*P<0.05 for difference from vehicle at 24 hours post application and for all timepoints assessed after.
Assessed in all patients, not just those aged ≥12 years.
LS: least squares; NRS: Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

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DISCLOSURES

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