27874 Correlation of itch response to roflumilast cream with disease severity and patient-reported outcomes in patients with chronic plaque psoriasis

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Trifarotene transcriptomics analysis and acne-related gene expression
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Trifarotene cream, 0.005% is an FDA approved topical retinoid indicated for treatment of facial and truncal acne and has received positive outcome through the European Decentralized Procedure. Trifarotene is the first novel topical retinoid molecule approved for acne treatment in 20 years, and the only approved retinoid that specifically acts through retinoic acid receptor gamma. This study investigated new potential pathways through which trifarotene exerts its efficacy in acne by analyzing the changes in gene expression in the skin of acne patients. Subjects with moderate inflammatory acne of the back were treated with trifarotene 0.005% or vehicle cream on dedicated back areas for 27 days, and 4 biopsies were collected on each subject (non-involved skin, acne papule, trifarotene, and vehicle-treated site).

Large-scale gene expression profiling of the biopsies was performed using Affymetrix technology, and treatment specific gene expression profiles were generated using statistical modeling. This analysis highlighted a specific gene expression profile, comprising of 67 genes uniquely driven by Trifarotene treatment generated using statistical modeling. This analysis showed that Trifarotene reorganizes the epidermal differentiation and proliferation processes of the papule. Altogether, these results show that Trifarotene has a unique action in acne treatment by acting on epidermal differentiation and proliferation (Aubert et al., 2018) as well as on innate and adaptive immune cells in acne pathogenesis.

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Correlation of itch response to roflumilast cream with disease severity and patient-reported outcomes in patients with chronic plaque psoriasis
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Roflumilast cream is a nonsteroidal, selective phosphodiesterase-4 inhibitor in development for plaque psoriasis (PsO). A Phase 2b, double-blinded trial randomized adults with PsO (2-20% body surface area) to once daily roflumilast 0.3%, roflumilast 0.15%, or vehicle for 12 weeks (NCT04682588). Throughout the trial, itch and its impact were evaluated via patient-reported outcomes (PROs): Worst Itch Numeric Rating Scale (WI-NRS), Itch related Sleep Loss (IRSL), and Dermatology Life Quality Index (DLQI). This posthoc analysis reports correlation of WI-NRS with other PROs and with disease severity. Overall, 551 patients were randomized (109 to roflumilast 0.3%, 113 to 0.15%, and 109 to vehicle). At baseline, the mean WI-NRS score was 5.87. Throughout the trial, both roflumilast doses showed similar improvements in WI-NRS starting at Week 2 and were significantly superior to vehicle (P < .002). At baseline, Pearson correlation coefficients (PCCs) for WI-NRS and Psoriasis Area and Severity Index (PASI) were 0.189, 0.282, 0.205 for roflumilast 0.3%, roflumilast 0.15%, and vehicle, respectively (P ≤ .033 for all correlations); for WI-NRS and BLSL 0.548, 0.646, 0.652 (P < .001); for WI-NRS and DLQI 0.445, 0.417, 0.422 (P < .001); for PASI and BLSL 0.369, 0.365 (P < .001); for WI-NRS and DLQI 0.607, 0.823, 0.529. Treatment with roflumilast resulted in rapid and robust improvement in the severity of itch associated with PsO. Itch response to roflumilast was independent of disease severity and positively correlated with patient-reported sleep loss and quality of life improvement.

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The PASI-HD improved precision in measuring disease severity in subjects with mild to moderate plaque psoriasis treated with roflumilast cream, a phosphodiesterase-4 inhibitor
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This study evaluated the PASI-HD, a high resolution version of the PASI designed to obtain higher discrimination in low body surface area (BSA) cases. We performed a post hoc analysis looking at PASI-HD improvement between baseline and the week 12 endpoint for the roflumilast 0.3% and placebo treatment groups. The PASI-HD was calculated for each subject (non-involved skin, acne papule, roflumilast, and vehicle-treated site). All statistical analyses were performed using R.

Results: A total of 83 (n=40) patients were randomized to the roflumilast 0.3% and placebo groups. At baseline, patients in the roflumilast group had a mean PASI of 4.73 and a mean PASI-HD of 6.96, while patients in the placebo group had a mean PASI of 3.95 and a mean PASI-HD of 4.69. Significant improvement was seen in both treatment groups with roflumilast 0.3% showing a mean 3.8 reduction in PASI-HD at week 12 compared to placebo. The statistical comparison between treatment groups showed a significant difference in PASI-HD at week 12 (p = .04).

Conclusion: The PASI-HD was able to show robust improvement in the severity of itch associated with PsO. Itch response to roflumilast was independent of disease severity and positively correlated with patient-reported sleep loss and quality of life improvement.

Commercial Disclosure: Financial support for this study was provided by Galderma. Krishnaswamy JK, York JP, Chordua R are employees of Galderma. S Blanchet-Réthoré, Dreno B are investigators and consultants for Galderma.

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Differences in pediatric vs adult clinical trial designs for atopic dermatitis
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Despite an increasing burden of atopic dermatitis (AD) in all ages, the distribution of participant age and trial characteristics remains unelucidated. The aim of this study was to compare trial characteristics between pediatric and adult AD trials. We collected data from ClinicalTrials.gov on AD therapeutic trials completed between 2003-2019 and further stratified trials by pediatric (mean or median age <18 years of the experimental group participants) or adults. Trials without results on outcome scores were excluded. Outcome scores were categorized as: score (S), Area Under the Curve (AUC), Area Under the Receiver Operating Characteristic Curve, and Continuous Variable (CV). We compared the characteristics of each clinical manifestations (erythema, induration, desquamation) regardless of severity. The higher level of discrimination with PASI-HD allows for more accurate evaluation of treatment efficacy in patients with smaller areas of involvement, while preserving anatomy and severity measures.

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