INTEGUMENT-INFANT: A Phase 2, 4-Week, Open-Label Safety Study of Roflumilast Cream 0.05% in Infants Aged 3 Months to Less Than 2 Years With Atopic Dermatitis

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DISCLOSURES

This study was funded by Arcutis Biotherapeutics, Inc. AAH, LFE, MEG, AP, JCB, TF, SEK, VHP, RS, LS, and LWL are investigators, speakers, and/or consultants for and received grants/research funding and/or honoraria from Arcutis Biotherapeutics, Inc. DH, JN, SK, and PB are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided upon request.

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INTRODUCTION

- AD is a chronic inflammatory skin disease that is most commonly diagnosed before 5 years of age, with the greatest incidence occurring in infants aged 3–6 months[1,2]
- Typical treatments for infants with AD include over-the-counter moisturizers and prescription topical therapies, including corticosteroids (TCSs), calcineurin inhibitors (TCIs), and a phosphodiesterase-4 (PDE4) inhibitor (crisaborole)[3-6]
  - Each of these treatments may have limited efficacy, associations with AEs, lack of approval for long-term use, and/or poor tolerance in infants
- Roflumilast is a selective and highly potent PDE4 inhibitor formulated as a water-based cream or foam that does not contain ethanol, propylene glycol, formaldehyde, or fragrances that can irritate the skin[7-9]
- Once-daily roflumilast cream 0.15% is approved for the treatment of mild-to-moderate AD in adult and pediatric patients aged ≥6 years[8]
- Efficacy and safety of roflumilast cream 0.05% in children aged 2–5 years with mild-to-moderate AD was demonstrated in the 4-week, randomized, vehicle-controlled, phase 3 INTEGUMENT-PED trial (NCT04845620)[9]

Objective

The primary objective of the INTEGUMENT-INFANT study is to assess the safety and tolerability of roflumilast cream 0.05% QD in patients aged ≥3 months to <2 years with AD

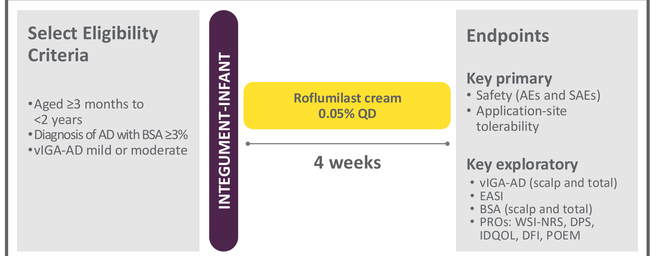
- Efficacy will also be assessed via exploratory endpoints

METHODS

Study Design

- INTEGUMENT-INFANT (NCT06998056) is a phase 2, open-label, single-arm, 4-week study

INTEGUMENT-INFANT Study Design



Patient Population

- The patient population will consist of ≈100 infants and toddlers with AD and a vIGA-AD of mild or moderate at study entry

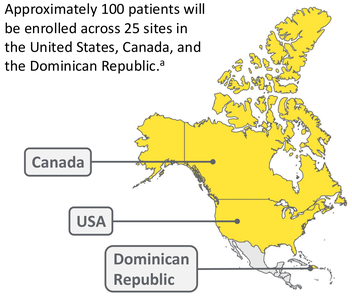
Select Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
✓ Males and females, aged ≥3 months to <2 years at baseline	✗ Unstable AD or consistent requirement for high-potency TCSs
✓ Diagnosed with mild-to-moderate AD[a] for ≥1 month prior to or at the screening visit	✗ Known genetic dermatological conditions that overlap with AD
✓ vIGA-AD of mild or moderate at baseline	✗ Skin conditions other than AD that interfere with evaluations
✓ Has AD involvement of ≥3% BSA (including the scalp and non-scalp areas) at baseline. Scalp involvement is allowed but not required	✗ Cannot discontinue excluded treatments[b] prior to baseline and during the study
✓ In good health as judged by the investigator, based on medical history, vital signs, and physical examination	✗ Breastfeeding mothers requiring high dose systemic corticosteroids or immunotherapy
✓ Parent(s)/legal guardian(s) are considered reliable and capable of adhering to the protocol and visit schedule, according to the judgment of the investigator	✗ Significant active systemic or localized infection
✓ Informed consent of a parent(s) or legal guardian(s), as required by local laws	✗ Serious medical condition, clinically significant vital signs, or physical examination abnormality
	✗ Currently undergoing allergy testing or food challenges
	✗ History of major surgery within 4 weeks prior to baseline or planned during study participation

[a]Based on Hanifin-Rajka criteria.[10] [b]Excluded treatments are biologics, systemic treatments that could affect AD, light therapy, sedating and nonsedating antihistamines (nonsedating antihistamines started prior to baseline and used in a stable regimen are allowed), TCSs (eye/ear drop, inhaled, and nasal preparations are allowed), TCIs, crisaborole, all other investigational drugs, systemic antibiotics (except for short courses ≤14 days), strong cytochrome P-450 CYP3A4 inhibitors, topical antibacterial medications, products including soaps, dilute bleach baths, and sodium hypochlorite-based products.

Study Sites

Approximately 100 patients will be enrolled across 25 sites in the United States, Canada, and the Dominican Republic.[a]



[a]The number of countries and/or sites may be adjusted if necessary.

Study Endpoints

- Primary endpoints include the safety and application-site tolerability of roflumilast cream 0.05%
  - Patients aged <6 years (including infants and toddlers) have higher BSA to body mass ratios and often have greater BSA involvement than patients aged ≥6 years (for whom cream 0.15% is approved); therefore, roflumilast cream 0.05% was evaluated in the INTEGUMENT-PED trial and this study. This is expected to result in consistent pharmacokinetic, efficacy, and safety profiles in patients aged ≥3 months to <2 years and those aged 2–5 years or ≥6 years
- Efficacy will be assessed through exploratory endpoints, including investigator-assessed and patient-reported outcomes

Primary endpoints (safety)

Safety and tolerability

- AEs
- SAEs
- Application-site tolerability
- Clinically significant changes in vital signs, as determined by the investigator

Exploratory endpoints (efficacy)

Disease severity

- vIGA-AD (scalp and total)
- EASI
- BSA (scalp and total)

Itch, QoL, and patient experience

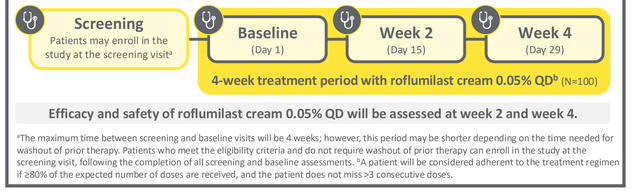
- WSI-NRS
- DPS
- IDQOL
- DFI
- POEM
- Study participant survey[a]

[a]The study participant survey will be completed by the parent(s)/caregiver(s) to evaluate the effects of roflumilast cream 0.05% QD.

Patient Participation

- Patient participation involves up to 4 clinic visits, including screening, baseline, week 2 and week 4; patients who meet the eligibility criteria and do not require washout of prior therapy can enroll at the screening visit. The interval between the screening and baseline visits can be up to 4 weeks; therefore, the anticipated maximum duration of patient participation is 8 weeks
- Parent(s)/caregiver(s) will apply roflumilast cream 0.05% to treatment areas identified at baseline (including on the scalp) for the duration of the study, regardless of whether those areas are clear prior to week 4, as well as to new lesions that develop during the study

Patient Participation



Efficacy and safety of roflumilast cream 0.05% QD will be assessed at week 2 and week 4.

[a]The maximum time between screening and baseline visits will be 4 weeks; however, this period may be shorter depending on the time needed for washout of prior therapy. Patients who meet the eligibility criteria and do not require washout of prior therapy can enroll in the study at the screening visit, following the completion of all screening and baseline assessments. [b]A patient will be considered adherent to the treatment regimen if ≥80% of the expected number of doses are received, and the patient does not miss >3 consecutive doses.

Statistical Analysis

- The safety population will include all patients who are enrolled and receive ≥1 dose of roflumilast cream 0.05%. This population will be used for all analyses. All safety and efficacy data will be summarized using descriptive statistics

CONCLUSIONS

- When complete, the INTEGUMENT-INFANT study will provide much needed safety, tolerability, and efficacy data for the potential use of roflumilast cream 0.05% QD in patients aged ≥3 months to <2 years with mild-to-moderate AD
- INTEGUMENT-INFANT will be the first study to examine treatment of the scalp with roflumilast cream in patients with AD
- For more information, please contact Arcutis at medinfo@arcutis.com

ABBREVIATIONS

AD, atopic dermatitis; AE, adverse event; BSA, body surface area affected; DFI, Dermatitis Family Impact Questionnaire; DPS, Dynamic Pruritus Score; EASI, Eczema Area and Severity Index; IDQOL, Infants' Dermatitis Quality Of Life Index; PDE4, phosphodiesterase 4; POEM, Patient-Oriented Eczema Measure; PRO, patient-reported outcome; QD, once daily; QoL, quality of life; SAE, serious adverse event; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid; vIGA-AD, Validated Investigator Global Assessment for AD; WSI-NRS, Worst Scratch/Itch-Numeric Rating Scale.

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