JOHNSON & JOHNSON CONSUMER INC.

SUMMARY CLINICAL STUDY REPORT

PROTOCOL TITLE:	A Clinical Evaluation of the Safety and Efficacy of a Moisturizing Cream and Baby Wash in the Management of Mild to Moderate Atopic Dermatitis in Infants, Toddlers, and Children
PROTOCOL NUMBER:	CCSSKB003103 Amendment 3, Final Version 4.0, 19 July 2022 Amendment 2, Final Version 3.0, 27 January 2022 Amendment 1, Final Version 2.0, 11 March 2021 Final Version 1.0, 13 January 2021
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STUDY INITITION DATE (First Subject First Visit):	21 January 2021
STUDY COMPLETION DATE (Last Subject Completed):	22 February 2022
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STUDY INITITION DATE (First Subject First Visit):	26 September 2022
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The principles of the International Council for Harmonisation (ICH) Guidelines for Good Clinical Practice (GCP E6 (R2)) were applied to this study.

PURPOSE

Eczema is a chronically relapsing skin disease associated with erythema, scaly and oozing plaques, and severe pruritus.[1] Signs and symptoms of eczema are associated with a compromised immune system and also a defective skin barrier. Eczema subjects experience frequent cutaneous infections, and *Staphylococcus aureus* is commonly cultured from lesional and non-lesional eczematous skin.[2] Disease states, severity, and treatments are related to microbial dynamics in this common skin disorder.[2] Atopic dermatitis is the most common form of eczema. As a result, clinicians and academic researchers often use the terms "eczema" and "atopic dermatitis" interchangeably. For example, the ADSI score stands for "atopic dermatitis severity index" but is used to grade eczema lesions in clinical studies and will be utilized in this study to assess severity of lesions as compared to EASI which will be used to assess overall eczema severity.

This multi-center, open-label, 4-week clinical trial was conducted for Johnson & Johnson Consumer Inc. to evaluate the effectiveness (assessed by clinical evaluation of eczema/atopic dermatitis severity and parent-perceived benefits) and tolerability (assessed by clinical grading and parent-perception) of the investigational cream when used in conjunction with a baby wash in babies, toddlers, and children with mild to moderate atopic dermatitis.

The secondary objective is to compare the changes in the skin microbiome that occurred in lesional and adjacent non-lesional skin sites with the use of a moisturizing cream, and to assess whether these changes correlated with changes in clinical and parent-perceived benefits.

STUDY DESIGN SUMMARY

A total of 29 subjects completed study participation.

During the course of the study, parent subjects used the IP wash [redacted] when bathing the child subjects at least 3 times per week (but not more than once per day), and used the IP cream [redacted] on the child subjects (on the entire face and body) twice per day, as directed. Parent subjects performed the first application of the IP cream at the study site after completion of baseline evaluations.

Clinical evaluations were conducted at visit 1 (baseline/day 0 and post-application), visit 2 (day 1), visit 3 (day 3), visit 4 (day 7), and visit 5 (day 28). Study procedures were not performed while a child subject was crying or visibly distressed. If a child subject was crying or visibly distressed, re-acclimation was under the PI/ Sub-I's discretion for clinical and subjective assessments, and re-acclimation was required for at least 5 minutes prior to instrumental measurements and sampling collection.

Subject pairs participated in the following procedures at the indicated time points:

- Eczema Area Severity Index (EASI) Grading
  At baseline and days 1, 3, 7, and 28, the PI/Sub-I evaluated each child subject for the eczema area and severity index (EASI).

- Atopic Dermatitis Severity Index (ADSI) Grading
  At baseline and days 1, 3, 7, and 28, the PI/Sub-I evaluated each child subject's target lesion for the atopic dermatitis severity index (ADSI).

- Cutaneous Tolerance Grading
  At baseline, post-application, and days 1, 3, 7, and 28, child subjects were evaluated for objective and subjective irritation parameters on the face, arms, legs, and torso (chest and back) separately.
  - Objective irritation (clinician rated): The PI/Sub-I assessed each child subject for dryness, redness/erythema, rash/irritation, and tactile roughness.
  - Subjective irritation (parent rated): Parent subjects assessed the child subject for burning/stinging and itching.

Transepidermal water loss (TEWL), skin hydration, and skin pH measurements, and microbiome sample collection were performed on a target lesion site (the same target lesion selected for ADSI) and a non-lesion site (an area adjacent to the target lesion site).

- Transepidermal Water Loss (TEWL) Measurements
  At baseline and days 1, 3, 7, and 28, TEWL was measured from each child subject using DermaLab® TEWL instrument equipped with Cortex Technologies at The Education & Research Foundation, Inc., and using cyberDERM RG-1 Evaporimeter equipped with dual probes at Dermatology Consulting Services, PLLC.

- Skin Hydration Measurements
  At baseline and days 1, 3, 7, and 28, skin hydration was measured from each child subject using DermaLab® Hydration instrument.

- Skin pH Measurements
  At baseline and days 1, 3, 7, and 28, skin pH was measured from each child subject using DermaLab® Skin pH instrument.

- Microbiome Sample Collection
  At baseline and days 1, 3, 7, and 28, microbiome samples were collected from each child subject using a swabbing technique to collect the skin microflora. A total of 2 swabs were collected from each child subject at each time point.

- Infant Dermatitis Quality of Life Index (IDQoL)
  At baseline and days 1, 3, 7, and 28, parent subjects completed the infant dermatitis quality of life index (IDQoL), a validated questionnaire to assess the impact of AD on the quality of life in infants, toddlers, and children.

- Brief Infant Sleep Questionnaire – Revised (BISQ-R)
  At baseline and days 1, 3, 7, and 28, parent subjects completed the revised brief infant sleep questionnaire (BISQ-R), a validated self-reported scale intended for use by parents in evaluating their children's sleep.

- Caregiver Assessment of Itch
  At baseline and days 1, 3, 7, and 28, parent subjects assessed how much itching and scratching the child subject had been exhibiting over a specified time period.

- Parental Questionnaire
  At post-application and day 28, parent subjects completed a Sponsor-provided parental questionnaire regarding product performance.

Throughout the study, parent subjects recorded corticosteroid usage (if any) on their child subjects.

STATISTICAL ANALYSIS SUMMARY

Overall Conclusions

Overall results from this multi-center, open-label clinical trial indicate that, under the conditions of this test, the Sponsor's IPs [redacted] were effective in improving the severity of overall eczema and of a target lesion when used over the course of 4 weeks on babies, toddlers, and children with mild to moderate atopic dermatitis. The IPs were both considered well tolerated by the subjects as assessed by clinical grading and parent perception and did not adversely impact the skin pH. There were no statistically significant differences in TEWL, skin hydration, or skin pH between the lesional and non-lesional skin sites at any time point.

Results showed a statistically significant decrease (improvement) in EASI grading scores of the overall eczema severity and ADSI grading scores of the target lesion at days 1, 3, 7, and 28 when compared with baseline for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined).

Analysis of the instrumental measurements showed the following results when compared with baseline:

- For TEWL:
  - For the lesion site, there was a statistically significant decrease in values (improvement in skin barrier properties) at day 28 for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined).
  - For the non-lesion site, there was a statistically significant decrease in values (improvement in skin barrier properties) at days 3, 7, and 28 for all subjects combined; and at days 7 and 28 separately for each race (White or Caucasian; and Black or African American and multi-racial combined).
- For skin hydration:
  - For the lesion site, there was a statistically significant increase in values (improvement in skin moisturization) at days 1, 3, 7, and 28 for all subjects combined and separately for White or Caucasian subjects.
  - For the non-lesion site, there was a statistically significant increase in values (improvement in skin moisturization) at days 1, 3, 7, and 28 for all subjects combined; and at days 1, 7, and 28 separately for White or Caucasian subjects.
  - Separately for Black or African American and multi-racial subjects combined, there was no statistically significant change in skin hydration values of the lesion or non-lesion site at any evaluated post-baseline time point.

- For skin pH:
    - For the lesion site, there was a statistically significant decrease in values at days 3, 7, and 28 for all subjects combined; and at day 28 separately for Black or African American and multi-racial subjects combined.
    - For the non-lesion site, there was a statistically significant decrease in values at day 1 for all subjects combined and separately for Black or African American and multi-racial subjects combined.
    - Separately for White or Caucasian subjects, there was no statistically significant change in skin pH values of the lesion or non-lesion site at any evaluated post-baseline time point.

Comparisons between the lesion and non-lesion sites, based on the mean change from baseline, indicated no statistically significant differences in TEWL, skin hydration, or skin pH at any time point for all subjects combined or separately by race.

Analysis of the cutaneous tolerance grading on the global body showed the following results when compared with baseline:

- For objective irritation (clinician rated), there was a statistically significant decrease (improvement) in scores for:
    - Dryness and tactile roughness at post-application and days 1, 3, 7, and 28; and redness/erythema at days 1, 3, 7, and 28 for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined)
    - Rash/irritation at days 1, 3, 7, and 28 for all subjects combined and separately for White or Caucasian subjects; and at days 7 and 28 separately for Black or African American and multi-racial subjects combined.
- For subjective irritation (parent rated), there was a statistically significant decrease (improvement) in scores for itching at post-application and days 1, 3, 7, and 28 for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined). There was no statistically significant change in scores for burning/stinging at any evaluated post-baseline time point for all subjects combined or separately by race (White or Caucasian; or Black or African American and multi-racial combined).

Results showed a statistically significant decrease (improvement) in the child subject's itching and scratching (via the caregiver assessment of itch) and a statistically significant improvement in the child subject's quality of life (via IDQoL) at days 1, 3, 7, and 28 when compared with baseline for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined).

Analysis of selected questions from the BISQ-R showed a statistically significant increase in parent subjects' response values for the question "How long does it usually take your child to fall asleep?" at day 1 separately for White or Caucasian subjects; and a statistically significant decrease in parent subjects' response values for the question "How much total time does your child spend sleeping during the DAY (between when your child wakes for the day and goes to bed at night)?" at day 28 for all subjects combined, when compared with baseline.

RESULTS AND FINDINGS

Eczema Area Severity Index (EASI) Grading

Analysis of the EASI grading of the overall eczema severity showed a statistically significant decrease (improvement) in scores at each evaluated post-baseline time point (days 1, 3, 7, and 28) when compared with baseline for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined).

Atopic Dermatitis Severity Index (ADSI) Grading

Analysis of the ADSI grading of the target lesion showed a statistically significant decrease (improvement) in scores at each evaluated post-baseline time point (days 1, 3, 7, and 28) when compared with baseline for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined).

Microbiome Analysis

At the population-level, summary analysis such as richness and Shannon-diversity showed no significant differences in the microbiota of skin swabs were observed between the non-lesion and lesion sites at Baseline to Day 28. Bray-Curtis beta diversity analysis confirmed there were no significant shifts in the overall composition of the skin microbiota after investigational product use.

At individual bacteria-level, some species appeared to be affected based on diminishing or increasing frequency of presence after treatment also potentially reducing *Staphylococcus aureus* proportions in lesion sites, however secondary quantitative analysis using qPCR is underway to confirm these observations.

Cutaneous Tolerance Grading

Analysis of the cutaneous tolerance grading on the global body showed the following results when compared with baseline:

- For objective irritation (clinician rated), there was a statistically significant decrease (improvement) in scores for:
    - Dryness and tactile roughness at each post-baseline time point (post-application and days 1, 3, 7, and 28); and redness/erythema at days 1, 3, 7, and 28 for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined)
    - Rash/irritation at days 1, 3, 7, and 28 for all subjects combined and separately for White or Caucasian subjects; and at days 7 and 28 separately for Black or African American and multi-racial subjects combined.
- For subjective irritation (parent rated), there was a statistically significant decrease (improvement) in scores for itching at each post-baseline time point (post-application and days 1, 3, 7, and 28) for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined). There was no statistically significant change in scores for burning/stinging at any evaluated post-baseline time point (post-application or day 1,

3, 7, or 28) for all subjects combined or separately by race (White or Caucasian; or Black or African American and multi-racial combined).

Caregiver Assessment of Itch

Analysis of the caregiver assessment of itch showed a statistically significant decrease (improvement) in parent subject's response values regarding the child subject's itching and scratching (1 = none, 2 = a little, 3 = a lot, and 4 = all the time) at each evaluated post-baseline time point (days 1, 3, 7, and 28) when compared with baseline for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined).

Infant Dermatitis Quality of Life Index (IDQoL)

Analysis of the IDQoL group total score showed a statistically significant decrease (improvement) in parent subject's response values regarding the child subject's quality of life at each evaluated post-baseline time point (days 1, 3, 7, and 28) when compared with baseline for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined).

Brief Infant Sleep Questionnaire – Revised (BISQ-R)

Analysis of selected questions from the BISQ-R showed a statistically significant increase in parent subjects' response values for the question "How long does it usually take your child to fall asleep?" at day 1 separately for White or Caucasian subjects; and a statistically significant decrease in parent subjects' response values for the question "How much total time does your child spend sleeping during the DAY (between when your child wakes for the day and goes to bed at night)?" at day 28 for all subjects combined, when compared with baseline

There was no statistically significant change in parent subjects' response values for the following questions at any evaluated post-baseline time point (day 1, 3, 7, or 28) for all subjects combined or separately by race (White or Caucasian; or Black or African American and multi-racial combined).

- How many times does your child usually wake up during the night?
- How much total time during the NIGHT is your child usually awake (between when your child goes to bed and wakes for the day)?
- What is the longest stretch of time that your child is asleep during the NIGHT without waking up?
- How much total time does your child spend sleeping during the NIGHT (between when your child goes to bed and wakes for the day)?

Parent Perceived Product Efficacy (Parental Questionnaire)

Results of the self-assessment questionnaires showed that the following percentage of all subjects responded favorably (strongly agree or agree somewhat) to the listed number of questions at the indicated time point: more than 75% to 3 of 10 inquiries at post-application; and more than 80% to 32 of 33 inquiries at day 28.

Transepidermal Water Loss (TEWL) Measurements

Analysis of the TEWL measurements showed the following results when compared with baseline:

- For the lesion site, there was a statistically significant decrease in values (improvement in skin barrier properties) at day 28 for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined).
- For the non-lesion site, there was a statistically significant decrease in values (improvement in skin barrier properties) at days 3, 7, and 28 for all subjects combined; and at days 7 and 28 separately for each race (White or Caucasian; and Black or African American and multi-racial combined).

Comparisons between the lesion and non-lesion sites, based on the mean change from baseline for TEWL measurements, indicated no statistically significant differences at any time point (day 1, 3, 7, or 28) for all subjects combined or separately by race (White or Caucasian; or Black or African American and multi-racial combined).

Skin Hydration Measurements

Analysis of the skin hydration showed the following results when compared with baseline:

- For the lesion site, there was a statistically significant increase in values (improvement in skin moisturization) at each evaluated post-baseline time point (days 1, 3, 7, and 28) for all subjects combined and separately for White or Caucasian subjects.
- For the non-lesion site, there was a statistically significant increase in values (improvement in skin moisturization) at each evaluated post-baseline time point (days 1, 3, 7, and 28) for all subjects combined; and at days 1, 7, and 28 separately for White or Caucasian subjects.
- Separately for Black or African American and multi-racial subjects combined, there was no statistically significant change in skin hydration values of the lesion or non-lesion site at any evaluated post-baseline time point (day 1, 3, 7, or 28).

Comparisons between the lesion and non-lesion sites, based on the mean change from baseline for skin hydration measurements, indicated no statistically significant differences at any time point (day 1, 3, 7, or 28) for all subjects combined or separately by race (White or Caucasian; or Black or African American and multi-racial combined).

Skin pH Measurements

Analysis of the skin pH showed the following results when compared with baseline:

- For the lesion site, there was a statistically significant decrease in values at days 3, 7, and 28 for all subjects combined; and at day 28 separately for Black or African American and multi-racial subjects combined.
- For the non-lesion site, there was a statistically significant decrease in values at day 1 for all subjects combined and separately for Black or African American and multi-racial subjects combined.
- Separately for White or Caucasian subjects, there was no statistically significant change in skin pH values of the lesion or non-lesion site at any evaluated post-baseline time point (day 1, 3, 7, or 28).

Comparisons between the lesion and non-lesion sites, based on the mean change from baseline for skin pH measurements, indicated no statistically significant differences at any time point (day 1, 3, 7, or 28) for all subjects combined or separately by race (White or Caucasian; or Black or African American and multi-racial combined).

OVERALL CONCLUSIONS

Overall results from this multi-center, open-label clinical trial indicate that, under the conditions of this test, the Sponsor's IPs [redacted] were effective in improving the severity of overall eczema and of a target lesion when used over the course of 4 weeks on babies, toddlers, and children with mild to moderate atopic dermatitis. The IPs were both considered well tolerated by the subjects as assessed by clinical grading and parent perception and did not adversely impact the skin pH. There were no statistically significant differences in TEWL, skin hydration, or skin pH between the lesional and non-lesional skin sites at any time point.

Results showed a statistically significant decrease (improvement) in EASI grading scores of the overall eczema severity and ADSI grading scores of the target lesion at days 1, 3, 7, and 28 when compared with baseline for all subjects combined and separately for each race (White or Caucasian; and Black or African American and multi-racial combined).

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