SYNOPSIS

Study Title: A Phase 2b, Multicenter, Randomized, Placebo- and Active-comparator-controlled, Double-blind Study to Evaluate the Safety and Efficacy of Bermekimab (JNJ-77474462) for the Treatment of Participants with Moderate to Severe Atopic Dermatitis

Study Number: 77474462ADM2001

Study Phase: Phase 2b

Name of Study Intervention: JNJ-77474462 (bermekimab)

Name of Sponsor/Company: Janssen Research & Development, LLC

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Status: Approved

Date: 18 October 2022

Prepared by: Janssen Research & Development, LLC

Study Name: GENESIS

Regulatory Agency Identifier Number:

IND	112459
NCT	NCT04791319

Number of Study Center(s) and Countries:

This study was conducted at 45 centers that enrolled participants in Canada, Germany, Japan, Poland, and the United States of America.

Publications (if any):

None

Study Period:

17 May 2021 to 31 March 2022

Rationale:

This was a Phase 2 randomized, placebo- and active-comparator-controlled, multicenter study to assess the safety, efficacy, PK, immunogenicity, and PD of bermekimab in adult participants with moderate to severe AD.

Bermekimab is a human monoclonal antibody, that binds the cytokine IL-1α with high affinity and is an effective blocker of IL-1α biological activity. IL-1α is a key mediator of sterile inflammatory responses and has been implicated in the pathology of advanced cancer, cardiovascular disease, and rheumatologic disease. Clinical evidence generated to date suggests that targeting IL-1α may be an effective treatment in undermining the inflammatory process that drives a wide array of diseases, including dermatologic conditions.

In previous dermatology studies, bermekimab demonstrated therapeutic activity profile.

Objectives and Endpoints

Objectives	Endpoints
Primary	
To evaluate the efficacy of bermekimab in participants with moderate to severe AD	Proportion of participants with EASI-75 (≥75% improvement from baseline) at Week 16
Secondary	
To characterize additional assessments of efficacy for bermekimab in participants with moderate to severe AD	• Proportion of participants with both vIGA-AD of 0 or 1 and a reduction from baseline of ≥2 points at Week 16 • Proportion of participants with improvement (reduction) of eczema-related itch NRS ≥4 from baseline to Week 16 among participants with a baseline itch value ≥4 • Proportion of participants with EASI-90 at Week 16
To evaluate the efficacy of bermekimab relative to dupilumab in participants with moderate to severe AD	• Proportion of participants with EASI-75 at Week 16 • Proportion of participants with EASI-90 at Week 16 • Proportion of participants with both vIGA-AD of 0 or 1 (on a 5-point scale) and a reduction from baseline of ≥2 points at Week 16 • Proportion of participants with improvement (reduction) of eczema-related itch NRS ≥4 from

Objectives	Endpoints
	baseline to Week 16 among participants with a baseline itch value ≥4
To assess the safety and tolerability of bermekimab in participants with moderate to severe AD	• Number/proportion of participants with TEAEs • Number/proportion of participants with treatment-emergent SAEs
To evaluate the PK and immunogenicity of bermekimab in adult participants with moderate to severe AD	• Bermekimab concentration over time • The incidence of antibodies to bermekimab
Exploratory	
To further characterize efficacy of bermekimab in participants with moderate to severe AD	• Improvement from baseline to Week 16 in SCORAD • Change from baseline to Week 16 in DLQI • Improvement from baseline to Week 16 in POEM • Improvement from baseline to Week 8 in eczema-related itch NRS • Improvement from baseline to Week 8 in eczema-related pain NRS • Improvement from baseline to Week 16 in eczema-related pain NRS • Improvement from baseline to Week 16 in itch as measured by the ADIS • Proportions of participants with a PGIS score of 1 (none) or 2 (mild) at Week 16 • Change from baseline to Week 16 in PROMIS-29 total score and sub-scores • Hand Dermatitis IGA at Week 16.
To assess the impact of treatment with bermekimab on selected biomarkers	Changes in cellular and molecular biomarkers in skin and blood from baseline

Methodology:

This was a randomized, double-blind, placebo- and active-comparator-controlled interventional study conducted at multiple sites that evaluated bermekimab in participants with AD. The study was designed to evaluate the efficacy, safety, PK, and immunogenicity of bermekimab in adult participants with moderate to severe AD. The planned total sample size was approximately 200 participants.

Individual study duration was planned to be approximately 40 weeks. Participants who met the eligibility criteria at screening were to be randomly randomized in a 1:1:2:2 ratio to one of 4 treatment groups:

Group 1: Placebo

Participants were to receive placebo weekly through Week 15. At Week 16, participants were to crossover to receive bermekimab 700 mg weekly through Week 31.

Group 2: Bermekimab 350 mg SC qw

Participants were to receive bermekimab 350 mg at Week 0 and every Week thereafter through Week 31.

Group 3: Bermekimab 700 mg SC qw

Participants were to receive bermekimab 700 mg at Week 0 and every Week thereafter through Week 15. At Week 16, participants who achieved an EASI-75 response were to be rerandomized in a 1:1 ratio either to continue to receive bermekimab 700 mg weekly, or to receive bermekimab 350 mg weekly, through Week 31. At Week 16, participants who did not achieve an EASI-75 response were to continue to receive bermekimab 700 mg weekly through Week 31.

Group 4: Comparator/Reference Arm (Dupilumab)

Participants were to receive a loading dose of dupilumab 600 mg at Week 0 followed by dupilumab 300 mg q2w beginning at Week 2 through Week 14. Participants who achieved an EASI-75 response at Week 16 were to continue on dupilumab 300 mg q2w from Week 16 through Week 30. At Week 16, participants who did not achieve an EASI-75 response (ie, dupilumab nonresponders) were to receive placebo weekly at Weeks 16 through 18 (ie, washout period), and bermekimab 700 mg weekly from Week 19 through Week 31.

There were 2 DBLs planned for this study. The study was prematurely terminated on 02 February 2022 following results from the futility analysis. Hence, only 1 DBL occurred (19 April 2022).

Number of Participants (planned and analyzed):

Planned: Approximately 200 participants were targeted for enrollment.

Analyzed: A total of 199 participants were randomized while 198 participants received at least 1 dose of the assigned study intervention: 33 participants in the placebo treatment group, 100 participants in the combined bermekimab group (33 participants: 350 mg; 67 participants: 700 mg), and 65 participants in the dupilumab treatment group. One participant was randomized to the dupilumab treatment group but was not treated.

Diagnosis and Main Criteria for Inclusion and Exclusion:

The target population consisted of adult men or women with moderate to severe AD. Participants had to have AD present for at least 1 year before the first administration of study intervention and must have demonstrated an inadequate response to treatment for AD with topical medications or for whom topical treatments are otherwise medically inadvisable, an EASI score ≥16, an IGA score ≥3, and an involved percent BSA ≥10% at both screening and at baseline. Participants were required to apply moisturizers at least once daily for at least 7 days before randomization and continue the treatment throughout the study.

Study Interventions, Dose, Mode of Administration, and Batch Numbers:

The study intervention presentation used in this study was a sterile liquid formulation of 350 mg (175 mg/mL) of bermekimab in a PFS with an injectable volume of 2.0 mL. Commercially available dupilumab was provided by the sponsor as a sterile liquid formulation of 300 mg (150 mg/mL) in a PFS with an injectable volume of 2.0 mL. Placebo was provided by the sponsor.

The manufacturing lot numbers for the study intervention(s) dispensed in the study are provided below:

Lot Numbers	Kit	DP Lot Number	Expiry Date
4382267	ACT	062620M1A	26-Dec-2021
4382268	ACT	051520M1	15-Nov-221
4382269	ACT	062420M1	24-Dec-2021
4382439	ACT	042320M1	23-Apr-2022
4382563	ACT	013020M1	30-Jan-2022
4382564	ACT	022120M1	21-Feb-2022
4382565	ACT	022620M1	26-Feb-2022
4382566	ACT	022620M1	26-Feb-2022
4382936	ACT	062620M1D	26-Jun-2022
4383027	ACT	042920M1	29-Apr-2022
4383115	ACT	062620M1C	26-Jun-2022
4384320	ACT	052120M1	21-Nov-2022
4384380	ACT	051820M1	18-Nov-2022
T312619	DUPI	0LU22A	30-Apr-2023
T313496	DUPI	0LU22A	30-Apr-2023
T320300	DUPI	0LU22A	30-Apr-2023
T310008	PBO	092920M1A	29-Sep-2022
T310068	PBO	011420M1	14-Jan-2022
T310976	PBO	091520M1D	23-Sep-2022
T313494	PBO	091520M1B	17-Sep-2022
T313495	PBO	091520M1A	15-Sep-2022
T310918	PBO	092920M1B	1-Oct-2022

Duration of Study Intervention:

A screening period occurred approximately 4 weeks before Week 0. All participants were to enter the safety follow-up after Week 31 through Week 36. The total duration of study was required to be approximately 40 weeks.

Statistical Methods:

This study was designed to enroll approximately 200 participants in order to have sufficient power to detect a difference between the bermekimab groups and the placebo group for the primary endpoint of the proportion of participants achieving EASI-75 at Week 16. The sample size was also chosen to have adequate confidence level for the difference between the bermekimab 700 mg group and the dupilumab group.

The EASI-75 response rate in the bermekimab 400 mg qw group was approximately 35% at Week 16 and 70% at Week 7 from the placebo-controlled study (77474462ADM2002) and the open-label study (2018-PT044), respectively. The EASI-75 response rates at Week 16 were 15% and 12% with placebo and 51% and 44% with dupilumab, respectively, in the two Phase 3 trials of dupilumab versus placebo in the treatment of adult participants with moderate to severe AD.

The EASI-75 response at Week 16 were assumed to be 15% for placebo, 45% to 50% for dupilumab, and 50% to 70% for the bermekimab 350 mg and 700 mg treatment groups, respectively. Based on these

assumptions, approximately 200 participants were planned to be randomized in a 1:1:2:2 ratio to the placebo (n=33), bermekimab 350 mg (n=33), bermekimab 700 mg (n=67), or dupilumab (n=67) treatment groups. These sample sizes provided the study with at least 88% power to detect a treatment difference between the bermekimab treatment groups and the placebo group in EASI-75 at Week 16 based on a 2-sample Z-test at a Type I error rate of 0.05 (2-sided). These sample sizes also provided at least 88% power to detect a treatment difference between the dupilumab and placebo treatment group in EASI-75 at Week 16 at a 2-sided significance level of 0.05.

SUMMARY OF RESULTS AND CONCLUSIONS:

Demographic and Baseline Characteristics:

A total of 268 participants with moderate to severe AD from 45 sites across Canada, Germany, Japan, Poland, and the United States of America were screened; of which, 57 (21.3%) participants were screen failures. Of these, 198 participants were randomized and received at least 1 dose of the assigned study intervention: 33 participants in the placebo treatment group, 100 participants in the combined bermekimab group (33 participants: 350 mg; 67 participants: 700 mg), and 65 participants in the dupilumab treatment group.

The participants had a mean (SD) age of 36.0 (13.65) years, a mean (SD) body weight of 77.9 (18.00) kg, and a mean (SD) BMI of 26.3 (5.18) kg/m^2. There were more male participants compared to female participants (111 [56.1%] versus 87 [43.9%]) and majority of the participants were White (142 [71.7%]).

The most common medical histories were allergic/immunologic in nature (106 [53.5%] participants): food allergy, allergy to animals, allergic rhinitis, and seasonal allergy. Asthma was also a common history reported in 51 (25.8%) participants.

Most participants in the study had previously used topical agents (197 [99.5%] participants). Systemic or intralesional corticosteroids were used by 82 (41.4%) participants.

Three major protocol deviations were reported during the study through Week 36: 1 (3.0%) participant from the bermekimab 350 mg treatment group and 2 (3.1%) participants from the dupilumab treatment group. Two participants had reportedly received protocol-defined prohibited concomitant medications: prednisone and measles vaccine. The participant who received the measles vaccine discontinued participation in the study. One participant from the dupilumab treatment group missed assessments at Weeks 5 and 8, and more than 4 ADIS responses were missing between visits.

Exposure:

The mean (SD) cumulative dose of bermekimab and dupilumab in participants through Week 31 were 5332.1 (3034.76) mg and 1771.4 (683.48) mg, respectively.

Efficacy Results:

The primary efficacy analysis set was planned to be based upon the FAS, defined as randomized participants (n=199) who received at least 1 dose of study intervention (n=198). Due to the early termination of this study, a large number of participants discontinued treatment prior to Week 16. The mFAS was defined as those FAS participants who could have reached a visit by the time of the decision was made to terminate the study on 02 February 2022. The main analyses for the primary and major secondary endpoints are based on the mFAS through Week 16 (excluded participants with projected Week 16 visit occurring after study termination date). The mFAS through Week 16 included a total of 130 participants: 21 participants in the

placebo treatment group, 24 participants in the bermekimab 350 mg treatment group, 42 participants in the bermekimab 700 mg treatment group, and 43 participants in the dupilumab group treatment group.

Primary Efficacy Endpoint:

The treatment difference observed in the bermekimab treatment groups (350 mg and 700 mg) versus the placebo group at Week 16 was similar ie, 7.1% (95% CI: -12.1%, 26.2%; p-value: 0.489) and 7.1% (95% CI: -9.4%, 23.7%; p-value: 0.448), respectively.

Both bermekimab treatment groups (350 mg and 700 mg) showed numerically higher but not statistically significant response than placebo. The treatment difference observed in the dupilumab treatment group versus the placebo group was similar ie, 42.0% (95% CI: 22.9%, 61.1%; p-value: 0.001) as previously reported.

Secondary Efficacy Endpoints:

EASI-90

The treatment difference observed in the bermekimab treatment groups (350 mg and 700 mg) versus the placebo group at Week 16 was low and similar ie, 2.9% (95% CI: -15.1%, 20.9%; p-value: 0.758) and 2.4% (95% CI: 13.2%, 18.0%; p-value: 0.780), respectively. The treatment difference for the dupilumab group versus the placebo group was similar to results previously reported ie, 25.4% (95% CI: 6.5%, 44.2%; p-value: 0.034).

vIGA AD of 0 or 1 and a Reduction from Baseline of ≥2 Points

The treatment difference observed in the bermekimab treatment groups (350 mg and 700 mg) versus the placebo group at Week 16 was low and similar ie, 2.9% (95% CI: -15.1%, 20.9%; p-value: 0.758) and 2.4% (95% CI: 13.2%, 18.0%; p-value: 0.780), respectively. The treatment difference for the dupilumab group versus the placebo group was similar to results previously reported ie, 18.0% (95% CI: -0.1%, 36.1%; p-value: 0.103).

Proportion of Participants with Improvement (Reduction) of Eczema-Related Itch NRS ≥4

The treatment difference observed in the bermekimab treatment groups (350 mg and 700 mg) versus the placebo group at Week 16 was 9.3% (95% CI: -13.3%, 31.8%; p-value: 0.434) and -4.6% (95% CI: -21.0%, 11.7%; p-value: 0.559), respectively.

Through Week 16, no clear difference from the placebo group in response rates was observed in eczema-related itch NRS based on percentage improvement.

The response rate in dupilumab group was numerically higher (21.8% [95% CI: 1.1%, 42.5%; p-value: 0.083]) than the placebo group but not statistically significant. A small number of participants who had NRS ≥4 at the baseline may have impacted this analysis.

Proportion of Participants Achieving EASI-75 and EASI-90 Through Week 16

The dupilumab treatment group showed clear separation from placebo starting from Week 2 in EASI-75 but the bermekimab treatment groups (350 mg and 700 mg) did not show clear separation from placebo over time.

In the dupilumab treatment group, 20.0% (9 of 45) of the participants began to show response at Week 4 in the 4-point improvement in itch. At Week 16, 41.9% (13 of 31) participants responded.

Proportion of Participants Achieving EASI-75 and EASI-90 from Week 16 Through Week 36

At Week 16, participants in the placebo group crossed over to receive bermekimab 700 mg weekly.

At Week 16, participants who achieved an EASI-75 response in bermekimab 700 mg group were rerandomized in a 1:1 ratio either to continue to receive bermekimab 700 mg weekly, or to receive bermekimab 350 mg weekly. Participants who did not achieve an EASI-75 response continued to receive bermekimab 700 mg weekly.

Participants who switched from the placebo treatment group to the bermekimab 700 mg treatment group showed some improvement based on EASI-75. The number of EASI-75 responders in the bermekimab treatment group were low and maintained over time. Participants in the dupilumab treatment group did not show clear efficacy especially on percentage change in EASI.

The number of participants who reached Week 36 was small and the number of participants in each group was small, therefore the results were difficult to interpret.

Safety Results:

Summaries of AEs and other safety data are based on 198 participants who received at least 1 dose of double-blind study intervention.

Adverse Events

Through Week 16

- Eighteen (54.5%) participants from the placebo treatment group, 66 (66.0%) participants from the combined bermekimab treatment groups, and 33 (50.8%) participants from the dupilumab treatment group reported ≥1 AEs through Week 16.
- The highest number of TEAEs were reported in the SOC of Infections and infestations followed by Skin and subcutaneous tissue disorders. The most commonly reported TEAEs were dermatitis atopic, injection site erythema, and nasopharyngitis.
- Two (6.1%) participants from the placebo treatment group, 6 (6.0%) participants from the combined bermekimab treatment group, and 2 (3.1%) participants from the dupilumab treatment group reported AEs that were assessed as severe through Week 16. The majority of these AEs were AD followed by single reports of eczema herpeticum, viral infection, AST increase, and toothache.
- Five (15.2%) participants from the placebo treatment group, 24 (24.0%) participants from the combined bermekimab treatment group, and 11 (16.9%) participants from the dupilumab treatment group reported AEs that were assessed as related to the study intervention.

Through Week 36

- 18 (54.5%) participants from the placebo treatment group, 84 (64.6%) participants from the combined bermekimab treatment groups, and 40 (61.5%) participants from the dupilumab treatment group reported ≥1 AE.
- The highest number of AEs were reported in the SOC of Infections and infestations followed by Skin and subcutaneous tissue disorders. The most commonly reported AEs were COVID-19 infection (25 events) and nasopharyngitis (27 events).
- AEs of severe intensity were reported in 2 (6.1%) participants from the placebo group, 7 (5.4%) participants from the bermekimab combined treatment group, and 3 (4.6%) participants from the dupilumab treatment group.

- The most frequently reported severe AE was AD (9 participants); all other severe AEs were reported once in the bermekimab and dupilumab treatment groups.
- AEs that were assessed as related to the study intervention were reported in 5 (15.2%) participants from the placebo group, 28 (21.5%) participants from the bermekimab combined treatment group, and 12 (18.5%) participants from the dupilumab treatment group.
- Injection site erythema and upper respiratory tract infection (14 events each) and AD (12 events) were the most commonly reported AEs that were assessed as related to their respective study interventions.

Deaths: There we no deaths reported during the study.

SAEs:

Through Week 16

Three (3.0%) participants from the combined bermekimab treatment group reported SAEs during the study; 2 cases of worsening AD, 1 case of severe AST increased, and 1 case of auricular haematoma most likely due to traumatic origin (exercise); none of these SAEs were assessed by the investigator as related to the study intervention. No SAEs were reported in the placebo and dupilumab treatment groups.

Through Week 36

No new SAEs were reported after Week 16. At the time of this report, all reported SAEs had resolved.

Discontinuations due to AEs:

Through Week 16

One (3.0%) participant from the placebo treatment group and 4 (6.0%) participants from the bermekimab 700 mg treatment group discontinued study intervention due to AEs. The primary reason for discontinuation was AD. One (1.5%) participant from the bermekimab 700 mg treatment group discontinued study intervention due to moderate folliculitis. No discontinuations were reported in dupilumab treatment group.

Through Week 36

One (3.0%) participant from the placebo treatment group, 1 (1.5%) participant from the dupilumab treatment group, and 5 (7.5%) participants from the bermekimab 700 mg treatment group discontinued study intervention due to AEs. The primary reason for discontinuation was AD. One (1.5%) participant from the bermekimab 700 mg treatment group discontinued study intervention due to moderate folliculitis while the 1 (1.5%) participant from the dupilumab treatment group discontinued due to COVID-19 infection.

Other Adverse Events:

- Infections:
  - Through Week 16: the frequency of infections was numerically higher in the combined bermekimab treatment group (36 [36.0%] participants) compared to placebo (7 [21.2%] participants) and dupilumab (17 [26.2%] participants) treatments groups. The most commonly reported AEs were upper respiratory infection and nasopharyngitis. Of these, 10 (10.0%) participants from the combined bermekimab treatment group and 4 (6.2%) participants from the dupilumab treatment group required oral or parenteral antimicrobial treatment. No serious infection was reported.

  - Through Week 36: the frequency of infections was numerically higher in the combined bermekimab treatment group (54 [41.5%] participants) compared to placebo (7 [21.2%] participants) and dupilumab (22 [33.8%] participants) treatments groups. The most commonly reported AEs were COVID-19 infection and upper respiratory infection. Of these, 16 (12.3%) participants from the combined bermekimab treatment group and 5 (7.7%) participants from the dupilumab treatment group required oral or parenteral antimicrobial treatment due to the infections. No serious infection was reported.

- ISRs: Overall, 4 (3.1%) participants from the placebo treatment group, 10 (10.0%) participants from the combined bermekimab treatment group and 2 (3.1%) participants from the dupilumab treatment group reported ISRs. These events were all mild in intensity. The most common ISRs were erythema, swelling, and pruritis.
- Anaphylactic or Serum Sickness Reactions: No anaphylactic or serum sickness reactions were reported during the study.
- COVID-19 Associated AEs: 4 (12.1%) participants from the placebo treatment group, 19 (14.6%) participants from the combined bermekimab treatment group, and 5 (7.7%) participants from the dupilumab treatment group reported COVID-19 associated AEs. Of these, 2 (1.5%) participants from the combined bermekimab treatment group were asymptomatic while 1 (1.5%) participant from the dupilumab treatment group had suspected COVID-19 infection. The majority of the events were assessed as mild or moderate in severity and not related to the study intervention.

Clinical Laboratory Evaluations:

- Hematology: There were no clinically significant findings.
  - Through Week 16: two instances of CTCAE Grade 2 neutropenia in the bermekimab 700 mg group were reported.
  - Through Week 36: Apart from the 2 participants with neutropenia reported through the Week 16 timepoint, an additional case of Grade 2 neutropenia was observed in a participant who subsequently had switched from the placebo treatment group to the bermekimab 700 mg treatment group. The participant had Grade 1 neutropenia (1.79×10^9/L) on Study Day 85 followed by Grade 2 neutropenia (1.39×10^9/L) on Study Day 203. No infection associated with any of these instances of neutropenia were reported. The participant had recovered whilst continuing to receive the study intervention.
- Clinical Chemistry: There were no clinically significant findings.

Other Safety Evaluations

There were no clinically meaningful findings in the vital sign measurements and ECG data in this study. The assessments and observations were comparable across intervention groups.

Pharmacokinetic Results:

Concentrations over time:

- For the bermekimab 350 mg qw group, the trough serum bermekimab concentration reached steady-state by approximately Week 12. The mean and median steady-state trough serum bermekimab concentrations for this group were 46.90 and 49.67 µg/mL, respectively, at Week 12 and were maintained through Week 32 (mean: 48.68 µg/mL; median: 47.28 µg/mL).

- For the bermekimab 700 mg, steady-state trough serum bermekimab were achieved by Week 4. The mean and median trough serum bermekimab concentrations for this group at Week 4 were 83.07 and 91.37 μg/mL, respectively.
- For the placebo to bermekimab 700 mg qw crossover group, the mean and median steady-state trough serum bermekimab concentrations at Week 20 were 86.49 and 96.93 μg/mL, respectively, and were maintained through Week 28 (mean: 99.41 μg/mL; median: 122.01 μg/mL).

The serum bermekimab concentrations were above quantifiable levels in almost all samples in participants who received bermekimab injections.

In the 700 mg qw group, participants with a higher body weight (>80 kg) were associated with lower mean and median serum bermekimab concentrations. There was no apparent trend for the bermekimab 350 mg qw group.

In the 700 mg qw group, participants with baseline EASI ≥28 were associated with lower mean and median serum bermekimab concentrations. Baseline EASI score did not appear to have an effect on serum bermekimab concentrations in bermekimab 350 mg qw group. The number of participants with baseline EASI ≥28 was very small (n=1 to 6) in placebo to bermekimab 700 mg qw crossover group.

Immunogenicity Results:

Antibodies to Bermekimab

The overall incidence of antibodies to bermekimab was 6.2% (6/97) through Week 16 and 12.1% (14/116) through Week 36. Among the 14 participants who were positive for antibodies to bermekimab through Week 36, 1 (5.3%), 9 (27.3%) and 4 (6.3%) participants were in the placebo to bermekimab 700 mg qw crossover group, bermekimab 350 mg qw group and bermekimab 700 mg qw treatment group, respectively.

The highest titer of antibodies to bermekimab observed was 1:2880. Most of the participants (10 out of 14 participants) who were positive for antibodies to bermekimab had low titers (<1:100).

Antibodies to Bermekimab and Serum Bermekimab Concentrations

In the bermekimab 700 mg qw treatment group, participants with lower mean and median serum bermekimab concentrations were positive for antibodies to bermekimab. However, the number of participants who were positive for antibodies to bermekimab was very small (n=1 to 4 at different visits).

No apparent difference in mean serum bermekimab concentrations was observed between participants who were positive and negative for antibodies to bermekimab in the 700 mg qw group through Week 36.

Only 1 participant in the placebo to bermekimab 700 mg qw crossover group was positive for antibodies to bermekimab. Hence effect on serum bermekimab concentrations cannot be evaluated.

Conclusions:

- Based on the results of EASI, IGA, and itch NRS, the lack of supportive positive data on efficacy, particularly from the higher dose (700 mg) group, suggests that there may not have been substantial additional benefit for participants with AD from a higher dose of bermekimab. Hence, following the interim analysis, this study was terminated.

- Based on the available safety data, bermekimab 700 mg and 350 mg qw were well tolerated in participants with AD and no new safety concerns were observed with the study participants.
- An imbalance in ISRs was noted between bermekimab and placebo. All ISRs were mild in intensity and there were no serious cases or discontinuations due to ISR.

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