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| **Sponsor:** sanofi<br>**Drug substance(s):** SAR231893 - dupilumab | **Study Identifiers:** WHO: U1111-1280-5194<br>**Study code:** LPS17713 |

**Title of the study:**

A Phase 4, multicenter study to evaluate pharmacokinetics, safety and effectiveness of dupilumab in Chinese participants aged ≥6 years to <18 years with moderate-to-severe atopic dermatitis

**Study center(s):**

This study was conducted at 3 centers that enroll participants in China.

**Study period:**

Study initiation date: 23 August 2023 (first participant first visit)

Study completion date: 10 July 2025 (last participant last visit)

Study Status: Completed

**Phase of development:** 4

**Objectives:**

**Primary:**

To evaluate PK of dupilumab in Chinese pediatric population aged ≥6 years to <18 years with AD

**Secondary:**

- To evaluate safety of dupilumab in Chinese pediatric population aged ≥6 years to <18 years with AD
- To evaluate effectiveness of dupilumab in Chinese pediatric population aged ≥6 years to <18 years with AD

**Methodology:**

This was a 16-week, multicenter study to evaluate PK, safety and effectiveness of dupilumab in Chinese participants aged ≥6 years to <18 years of age with moderate-to-severe AD who received dupilumab according to China-approved prescribing information. Only patients who participated in study OBS17243 and received dupilumab according to China prescribing information were enrolled in this study. There were no other study related requirements regarding prior or concomitant treatments for AD or comorbid conditions in the present Study LPS17713 and Study OBS17243.

Study details included:

- The study duration was 16 weeks.
- The number of visits was 3.

**Number of study participants:**

It was anticipated that approximately 30 adolescents aged ≥12 years to <18 years and 30 children aged ≥6 years to <12 years needed to be enrolled to achieve approximately 20 adolescents aged ≥12 years to <18 years and 20 children aged ≥6 years to <12 years with evaluable PK at least at Week 12.

Twenty-three adolescent participants aged ≥12 years to <18 years and 30 children aged ≥6 years to <12 years were enrolled. The intent-to-treat (ITT) population and the safety population were comprised of all 53 participants. The PK population were comprised of 45 participants.

**Diagnosis and criteria for inclusion:**

Inclusion criteria

・Enrolled in Study OBS17243.

・Signed informed consent by the parent/legally authorized representative and assent by the participants appropriate to the participants' age. Assent is collected from participants as per China law and regulation.

**Study products**

Not applicable. Participants who were enrolled in the present Study LPS17713 were treated with dupilumab independently of the study under the only responsibility of the Investigator (refer to Study OBS17243).

**Duration of study intervention:**

Not applicable. The prescription of therapies including dupilumab was only under the responsibility of the Investigator. Even if treatment with dupilumab was discontinued permanently or temporarily, participants were encouraged to stay in the present Study LPS17713 for data collection purpose. PK samples were collected at Visit 2 (Week 12) and Visit 3 (Week 16) only in participants without any missed dose until Week 12 according to China prescribing information.

**Criteria for evaluation:**

Primary

Trough concentration of dupilumab in serum over time

Secondary

• Incidence of AEs during 16 weeks* including all AEs, SAEs, AEs leading to study treatment discontinuation, and AEs leading to death

• Proportion of participants with a vIGA score of 0 to 1 (on a 5-point scale) at Week 16

• Proportion of participants with EASI-75 (≥75% improvement from baseline) at Week 16

• Percent change from baseline to Week 16 in Pruritus NRS for participants aged ≥6 years to <18 years

**Statistical considerations:**

Primary endpoint

The primary endpoint was trough concentration of dupilumab in serum over time (at Week 12 and Week 16). The primary endpoint was summarized by descriptive statistics (such as mean, geometric mean, median, standard deviation [SD], standard error of mean [SEM], coefficient of variation [CV], minimum, and maximum values) in the PK population.

Secondary endpoints

For safety endpoints, descriptive analyses were conducted in the safety population. Adverse event (AE) incidence tables were provided for all types of AEs: AEs, SAEs, AEs leading study treatment discontinuation, and AEs leading to death during 16 weeks. For efficacy endpoints, descriptive analyses were conducted in the ITT population. Categorical data were summarized using counts and percentages. Continuous data were summarized using the number of participants (n), minimum (min), maximum (max), mean, median, SD, upper quartile (Q3), and lower quartile (Q1). The two-sided 95% CIs was presented if applicable.

**Summary Results:**

**Demographic and other baseline characteristics:**

A total of 53 participants were screened and successfully enrolled, including 30 participants aged ⩾6 to <12 years and 23 participants aged ⩾12 to <18 years. Overall, 27 (50.9%) participants were male, and 26 (49.1%) participants were female. The mean (SD) onset age of AD was 6.1 (4.80) years old, with a median duration of 42.0 months (range: 0.0, 190.0 months). Eczema skin lesions (n=52, 98.1%) was the most common clinical symptom, followed by itching (n=51, 96.2%), dry skin (n=50, 94.3%), redness and swelling (n=42, 79.2%).

The physician-assessed clinical signs of AD, including IGA and EASI scores, were comparable between participants aged ⩾6 to <12 years and those ⩾12 to <18 years, indicating moderate-to-severe disease at baseline. The mean (SD) pruritus NRS score was 7.6 (1.38), 7.9 (1.41), and 7.2 (1.28) for all participants, participants aged ⩾6 to <12 years, and participants aged ⩾12 to <18 years, respectively.

Forty-seven (88.7%) participants had at least one medical history of atopic disease other than AD, including 26 (86.7%) aged ⩾6 to <12 years and 21 (91.3%) aged ⩾12 to <18 years. Eleven (20.8%) participants had at least one other comorbidities of AD, including 3 (10.0%) aged ⩾6 to <12 years, and 8 (34.8%) aged ⩾12 to <18 years. In the cohort aged ⩾6 to <12 years, 26.7% and 76.7% of participants had at least one prior and concomitant medication for AD, respectively, and 69.6% and 87.0% in the cohort aged ⩾12 to <18 years, respectively.

**Exposure:**

Dupilumab was administered on a weight-based regimen according to the label. The dosage regimens of initial loading dose 600 mg+300 mg Q4W (n=21, 39.6%), initial loading dose 400 mg+200 mg Q2W (n=24, 45.3%), and initial loading dose 600 mg+300 mg Q2W (n=8, 15.1%) were applied to pediatric patients 6 to 17 years of age who weighed 15 to less than 30 kg, 30 to less than 60 kg, and 60 kg or more, respectively. The mean (SD) exposure duration, i.e., from the first dupilumab injection to 14 days after the last dupilumab injection for Q2W dose frequency and to 28 days after the last dupilumab injection for Q4W dose frequency, was 104.7 (27.90) days (range: 14, 144 days).

**Efficacy results:**

At Week 16, the proportion with vIGA-AD score of 0 or 1 was 25.0% (12/48) with 6 responders each originating from the cohort aged ⩾6 to <12 years (23.1%; 6/30) and ⩾12 to <18 years (27.3%; 6/23).

Proportion of participants with EASI-75 at Week 16 was 70.8% (34/48) for all participants, 73.1% (19/26) for participants in the cohort aged ⩾12 to <18 years and 68.2% (15/22) for participants aged ⩾6 to <12 years, respectively.

The mean (SD) percent change in pruritus NRS from baseline to Week 16 was -56.0% (39.49%) for all participants, -69.8% (24.50%) for participants aged ⩾6 to <12 years, and - 38.0% (48.15%) for participants aged ⩾12 to <18 years, respectively.

**Safety results:**

A total of 16 (30.2%) participants reported 32 AEs, including 25 AEs in 11 (36.7%) participants aged ⩾6 to <12 years and 7 AEs in 5 (21.7%) participants aged ⩾12 to <18 years. The most common AE was infections and infestations (n=10, 18.9%) at SOC level and upper respiratory tract infection (n=6, 11.3%) at PT level. Among the reported AEs, 2 events (both of pyrexia) that occurred in 1 (1.9%) participant were considered related to dupilumab and of moderate intensity. Almost all AEs occurred were of mild to moderate intensity for all participants except for 1 participant in the cohort aged ⩾6 to <12 years experienced severe AE. One (1.9%) participant in the cohort aged ⩾6 to <12 years reported 1 SAE of tonsillitis bacterial. No SAE was considered as related to dupilumab. Four (7.5%) participants reported 4 overdose events, all of which were asymptomatic and occurred in the cohort aged ⩾6 to <12 years. No AEs led to study treatment discontinuation or death.

**Pharmacokinetic results:**

The observed mean (SD) trough concentration of dupilumab was 115.4 (56.5) mg/L at Week 12 (n=18) and 94.1 (41.7) mg/L at Week 16 (n=18) for participants on the initial loading dose 600 mg + 300 mg Q4W (aged ⩾6 to <12 years); 72.3 (37.4) mg/L at Week 12 (n=21) and 73.1 (33.7) mg/L at Week 16 (n=19) for participants on the initial loading dose 400 mg + 200 mg Q2W regimen (aged ⩾6 to <18 years); 60.5 (23.1) mg/L at Week 12 (n=6) and 61.3 (13.3) mg/L at Week 16 (n=5) for participants on the initial loading dose 600 mg + 300 mg Q2W regimen (aged ⩾12 to <18 years), respectively. In general, the trough concentrations overlapped across age groups.

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