Background
- Hypoallergenic (HAC) is a genetic disorder that manifests as unpredictable attacks of tissue swelling caused by uncontrolled activation of the kallikrein-kinin system.
- Globally, the prevalence of HAC type 1 is 1:2,000 to 1:10,000.
- Most participants in a recent sebetralstat phase 2 trial were White (Caucasian).

Analysis Populations
- The mean (SD) age of participants was 36.0 (26.7) years; 47 participants (46%) were male, and 57 participants (54%) were female.
- Baseline characteristics were balanced across the 3 populations in each cohort.

Methods
- The phase 1 trial was designed to evaluate whether the pharmacokinetics (PK), pharmacodynamics (PD), and safety profiles of sebetralstat were similar in healthy Japanese, Chinese, and White (Caucasian) adults.

Objective
- The phase 1 trial was designed to determine whether the PK, PD, and safety profiles of sebetralstat were similar in healthy, Japanese adults, healthy Chinese adults, and healthy, White (Caucasian) adults as defined according to the study definitions of Japanese, Chinese, and White.

Study Design
- This was an open-label, randomized, double-blind, placebo-controlled, phase 1 trial, healthy Japanese, Chinese, and White (Caucasian) adults were enrolled.

Key Eligibility Criteria
- Participants had to be healthy, male or female, nonsmokers aged 18-55 years with a body mass index between 18.5 and 30 kg/m².
- No history of alcohol or drug use in the past 30 days, and no use of medications for the treatment of HAE for at least 30 days before the study.

Endpoints
- Pharmacokinetic concentrations of sebetralstat were determined using a validated liquid chromatography with tandem mass-spectrometry method.
- Concentration-time curves were assessed for the following parameters:
  - Area under the concentration-time curve from time 0 to the last observed concentration (AUC0-t), extrapolated to infinity (AUC0-∞).
  - Maximum observed plasma concentration (Cmax).
  - Time to maximum observed plasma concentration (Tmax).
- Pharmacodynamic activity was assessed by measuring decrease in plasma kallikrein activity using a luminescent-based assay in plasma samples collected 30 minutes to 4 hours after administration.

Results
- PK, PD, and safety profiles were comparable in healthy Japanese, Chinese, and White adults after administration of a single dose of sebetralstat 600 mg, 400 mg, or 1200 mg.

Pharmacokinetics
- Pharmacokinetic parameters were similar across healthy Japanese, Chinese, and White adults after administration of a single dose of sebetralstat 1200 mg, 600 mg, or 400 mg.

Pharmacodynamics
- PK, PD, and safety profiles were consistent across healthy Japanese, Chinese, and White adults after administration of a single dose of sebetralstat 600 mg, 400 mg, or 1200 mg.

Safety
- Sebetralstat was well-tolerated in Japanese, Chinese, and White adults (Table 3).

Conclusions
- Sebetralstat PK, PD, and safety profiles were comparable in healthy Japanese, Chinese, and White adults.

References

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Table 1. Baseline Characteristics

Table 2. Summary of Plasma PK Parameters of Sebetralstat After a Single Oral Dose

Table 3. Safety