Hereditary angioedema (HAE) is a rare and potentially life-threatening genetic disease involving abnormal functioning of the kallikrein-kinin system leading to increased vascular permeability and}

**Background**

- Results confirmed efficacy of sebetralstat 600 mg for symptom resolution and attack resolution in both abdominal and peripheral attack locations.
- Sebetralstat 600 mg achieved symptom relief in 50.0% of abdominal attacks and 50.0% of peripheral attacks within 12 hours (PGI-C) (%).
- More abdominal (61.1%) than peripheral (50.0%) attacks achieved resolution within 24 hours on PGI-S (VAS) (%).

**Methods**

- **Patient Selection:** Patients enrolled were aged ≥ 18 years with HAE type I or II who had ≥ 3 attacks in the past 93 days and were not on prophylactic therapy.
- **Study Design:** A phase 2, randomized, double-blind, placebo-controlled, 2-sequence, 2-period crossover trial was conducted to compare sebetralstat 600 mg with placebo in people with HAE.
- **Randomization:** Patients were randomized to treat 2 mild to moderate HAE attacks with sebetralstat 600 mg or placebo, followed by a washout period of 7 days before crossover to the alternate treatment.
- **Endpoints:** The primary endpoints were achievement of symptom relief and attack resolution as measured by Patient Global Impression of Change (PGI-C) and Patient Global Impression of Severity (PGI-S) scales, respectively.

**Results**

- **Symptom Relief:**
  - Of sebetralstat-treated attacks, 18 (31.0%) were categorized as abdominal and 40 (69.0%) as peripheral.
  - 12.5% of abdominal attacks and 22.5% of peripheral attacks achieved symptom relief as assessed on PGI-C within 12 hours.

- **Attack Resolution:**
  - Of abdominal attacks treated with sebetralstat, 83.3% achieved resolution within 24 hours compared to 66.7% of abdominal attacks treated with placebo.
  - Of peripheral attacks treated with sebetralstat, 80.0% achieved resolution within 24 hours compared to 50.0% of peripheral attacks treated with placebo.

- **Baseline Attack Severity:**
  - Baseline attack severity was evaluated by Patient Global Impression of Severity (PGI-S) scale (numeric values from 0 to 4 represented categorical PGI-S scores from “None” to “Very Severe”).
  - There was a tendency for abdominal attacks to be rated as more severe than peripheral attacks at baseline.

**Conclusions**

- **Efficacy of Oral Plasma Kallikrein Inhibitor Sebetralstat (KVD900) by Attack Location in a Phase 2 Clinical Trial**
- **Sebetralstat provides symptom relief and attack resolution for people living with HAE, regardless of attack location or severity.**
- **Oral on-demand treatment offers a new option for patients with HAE, improving patient experience and potentially reducing the burden of disease management.**

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**References**