**Efficacy of the Oral Plasma Kallikrein Inhibitor Sebetralstat (KVD900) by Attack Location in a Phase 2 Clinical Trial in Patients With Hereditary Angioedema**

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**Background**

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 compromised by spontaneous, vascular, and/or other attacks partially leading to swelling and/or edema.

**Methods**

Sebetralstat (KVD900) is a novel investigational oral plasma kallikrein inhibitor for on-demand treatment of HAE attacks. In a phase 2, randomized, placebo-controlled, crossover trial, patients were treated with a single oral dose of 600 mg of sebetralstat on 2 mild to moderate HAE attacks, 1 of which was an abdominal attack and 1 of which was a peripheral attack. Improvement on Patient Global Impression of Severity (PGI-S) scale was defined as improvement from baseline by 1 or more levels within 12 hours.

**Results**

Sebetralstat treatment resulted in rapid symptom relief for both abdominal and peripheral attacks. Abdominal attacks tended to resolve more quickly than peripheral attacks as evaluated on the Symptom Relief subscale (PGI-C) within 12 hours by abdominal location (Figures 5 and 6). Improvement on PGI-S scale was defined as improvement from baseline by 1 or more levels within 12 hours. Of sebetralstat-treated attacks, 18 (31.0%) were categorized as abdominal and 40 (69.0%) as peripheral. Baseline attack severity was evaluated by PGI-S scale (numeric values from 0 to 4 were used to align with categorical PGI-S scores from 0=very slight to 4=severe). All results were analyzed using descriptive statistics; symptom evaluation scales are shown in Figure 2. At baseline, abdominal attacks tended to be rated as more severe than peripheral attacks at baseline (Table 1). Of abdominal attacks, 2 (11.1%) attacks included both abdominal and peripheral symptoms (abdomen and genitals; abdomen and arm). There was a tendency for abdominal attacks to be rated as more severe than peripheral attacks at baseline (Table 1). Abdominal pain: 41.2 (abdominal), 2.2 (peripheral). Skin swelling: 23.2 (abdominal), 34.9 (peripheral).

**Conclusions**

Sebetralstat treatment resulted in rapid symptom relief for both abdominal and peripheral attacks, with approximately 80% achieving symptom relief within 12 hours regardless of attack location as evaluated by a score of “A Little Better” or higher for 2 consecutive timepoints on the PGI-C scale.

Abdominal attacks tended to resolve more quickly than peripheral attacks as observed in this study consistent with previously reported findings for other acute therapies. The results of this phase 2a clinical trial demonstrate that sebetralstat provides symptom relief and attack resolution for people living with HAE, regardless of abdominal or peripheral attack location.