KalVista Pharmaceuticals

KVD900 is an on-demand therapy for HAE taken at the first signs of an attack.

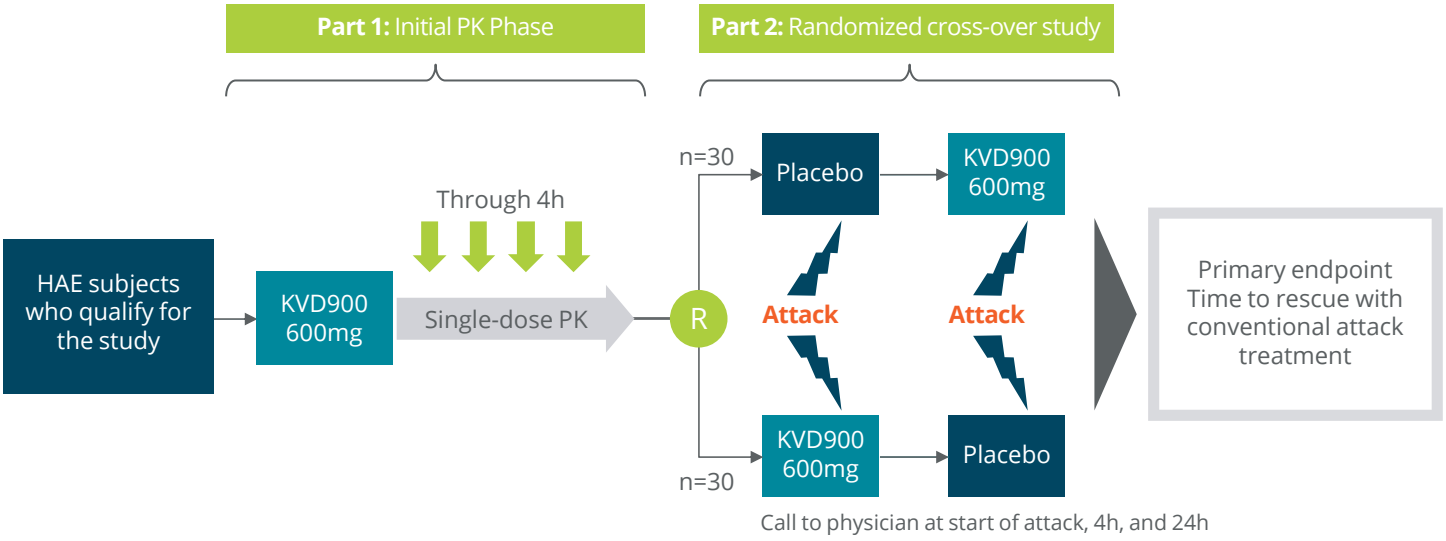
KVD900 is a small-molecule plasma kallikrein inhibitor that prevents bradykinin activation to halt attack progression and limit tissue swelling. It is an oral agent being developed as an on-demand treatment for HAE attacks.[1-3]

KVD900 allows patients to act as soon as possible to rapidly halt progression and reduce severity of attacks with sustained control over 24 hours.[4]

STUDY DESIGN AND PATIENT DEMOGRAPHICS

This randomized, double-blind, placebo-controlled, two-part crossover clinical trial assessed HAE patients from 25 clinical sites in the United States and Europe. Sixty-eight adult patients with type 1 and 2 HAE were assigned to receive either KVD900 or placebo. The primary endpoint was time to rescue with conventional attack treatment.[5]

KVD900 Phase 2 Clinical Trial Design[4]



Demographic Characteristics[4]

Age, years	Mean (SD) Range	38.3 (13.23) 19–68
Gender (m/f)	n (%)	31/37 (45.6/54.4)
BMI (kg/m2)	Mean (SD) Range	27.3 (5.47) 18.8–40.9
Type I / II	n (%)	68 (100%)

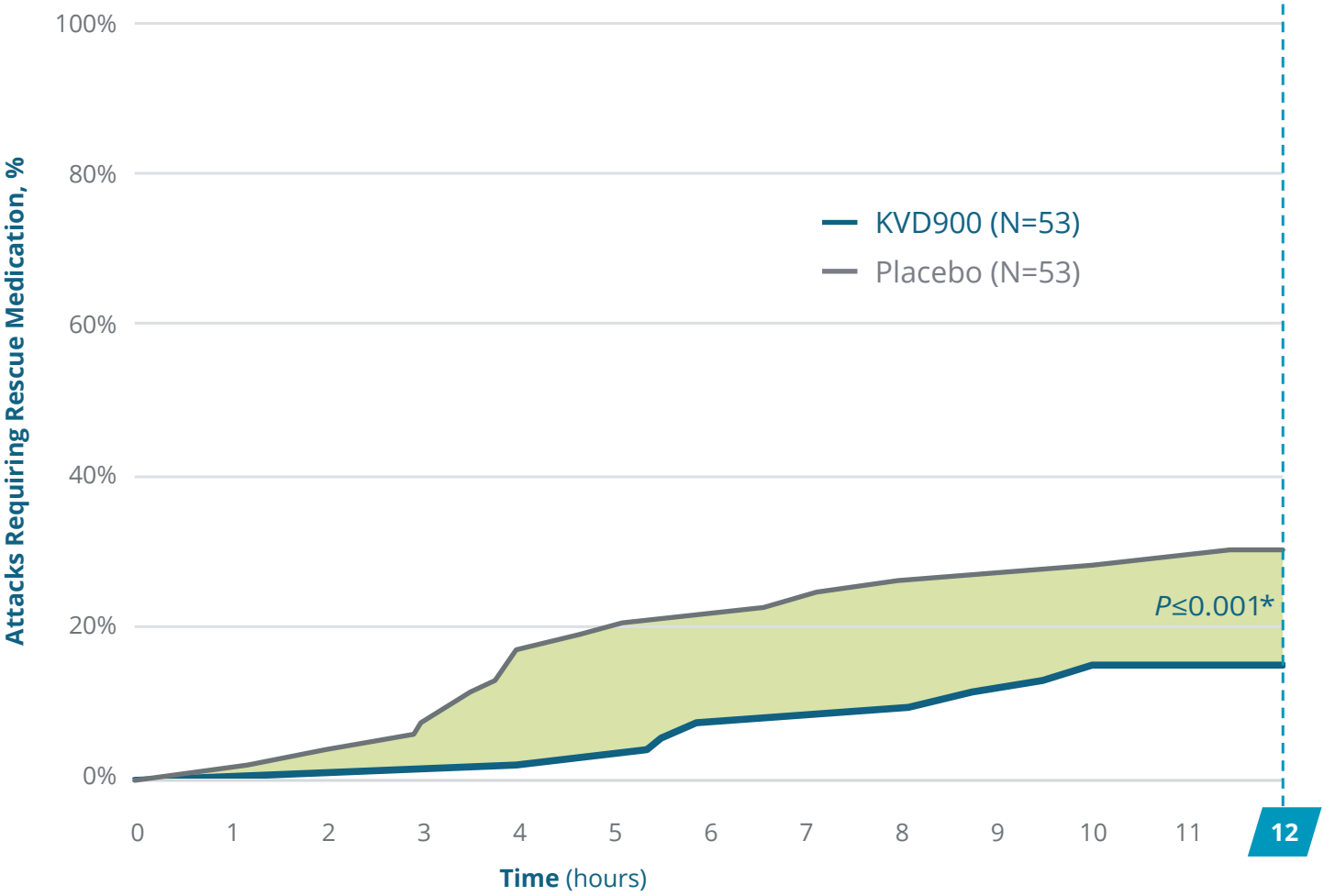
EFFICACY

Attacks treated with KVD900 significantly reduced the need for rescue therapy compared to placebo

Significant reduction observed in number of attacks requiring rescue therapy compared to placebo over 12 hours (P=0.001*), with 15% of attacks treated with KVD900 rescued compared to 30% with placebo (P=0.0595†)[4]

PRIMARY ENDPOINT

Proportion of Attacks Requiring Use of Rescue Medication‡[4]



*Gehan's Generalized Wilcoxon Test (time to event).
†Prescott's test (proportion of attacks within 12 or 24 hours).
‡Full analysis set. Censoring occurs where a subject did not improve or conventional attack treatment is used within 12h post-study drug dosing.

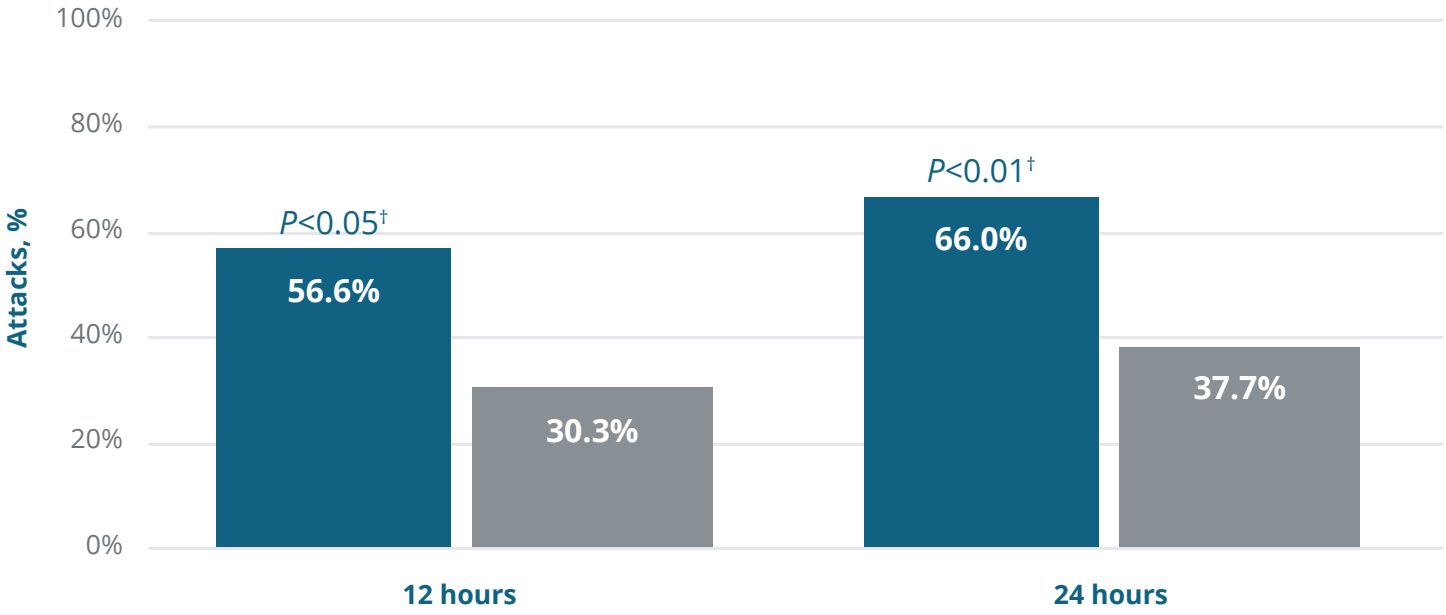
EFFICACY

KVD900 significantly reduced attack severity compared to placebo

Significant decreases in attack severity were observed over 24 hours (P=0.0008*), with 66% of attacks treated with KVD900 improving by ≥1 level on the PGI-S scale compared to 38% with placebo (P=0.0069†)[4]

SECONDARY ENDPOINT

Improvement From Baseline by One Level or More on the PGI-S Over 24 Hours[‡4]



*Gehan's Generalized Wilcoxon Test (time to event).

†Prescott's test (proportion of attacks within 12 or 24 hours).

‡Full analysis set. HAE attack severity assessed using the PGI-S scale. Censoring occurs where a subject did not improve in severity or conventional attack treatment is used within 24h post-study drug dosing.

SAFETY

KVD900 is generally safe and well-tolerated.

Only mild and transitory adverse events were observed in the phase 2 clinical study. Instances of adverse events were similar to placebo[4]

Adverse events reported in ≥1% of patients in the phase 2 study (N=68)[4]*

Open label (Part 1):
Flushing (2.9%), headache (2.9%), back pain (1.5%), dizziness (1.5%), nausea (1.5%), malaise (1.5%)

Randomized crossover portion (Part 2):

- KVD900: back pain, headache, and upper abdominal pain (one event each; 1.7%)
- Placebo: headache, anal incontinence (one event each; 1.8%)

*Within 48 hours of trial drug administration.

BMI, body mass index; HAE, hereditary angioedema; PGI-S, Patient Global Impression of Severity; PK, pharmacokinetics; SD, standard deviation.

1. KalVista Pharmaceuticals. KVD900 for HAE. 2021. Accessed January 21, 2021. https://www.kalvista.com/products-pipeline/kvd900-hae
2. Hampton SL, De Donatis GM, Murugesan N, et al. KVD900 as a single dose, rapid, oral plasma kallikrein inhibitor for the on-demand treatment of hereditary angioedema attacks: pharmacokinetic and pharmacodynamic results from a phase 1 single ascending dose study. Presented at the American Academy of Allergy Asthma and Immunology Annual Meeting. February 22-25, 2019; San Francisco, California, USA. Poster AB39.
3. Maetzel A, Smith MD, Morten RM. Rapid and nearly complete suppression of plasma kallikrein activity with the oral inhibitor KVD900: results of a phase 1 study evaluating KVD900's potential as a treatment for acute attacks of HAE. Presented at the European Academy of Allergy and Clinical Immunology Annual Meeting. June 1-5, 2019; Lisbon, Portugal. Poster PDS21.
4. Data on file. KalVista Pharmaceuticals, Inc.
5. A phase II, cross-over clinical trial evaluating the efficacy and safety of KVD900 in the on-demand treatment of angioedema attacks in adult subjects with hereditary angioedema type I or II. ClinicalTrials.gov identifier: NCT04208412.Updated January 6, 2021. Accessed April 27, 2021. https://clinicaltrials.gov/ct2/show/NCT04208412

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