ePDS: 1013

A single on-demand treatment with orally administered KVD900 significantly slows progression and accelerates resolution of attacks in patients with hereditary angioedema (HAE): Results of a phase 2, placebo-controlled, double-blind cross-over trial

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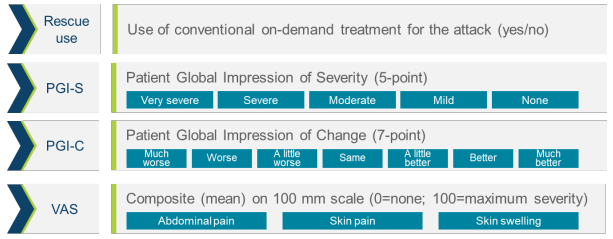
Background

- On-demand treatment of HAE attacks is recommended to prevent attack progression and the development of potentially life-threatening angioedema episodes
- In a previous study[1], the oral, small-molecule plasma kallikrein inhibitor KVD900 was shown to suppress plasma kallikrein activity by >90% within the first 30 minutes of administration to healthy volunteers

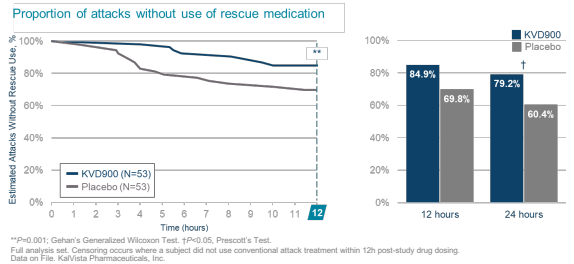
1: Maetzel A et al. Eur J Allergy & Clin Immunol. Conference: European Academy of Allergy and Clinical Immunology Congress. Lisbon Portugal. 74 (Supplement 106) (pp 271-272), 2019.

Measures



Standard, well-accepted outcome measures

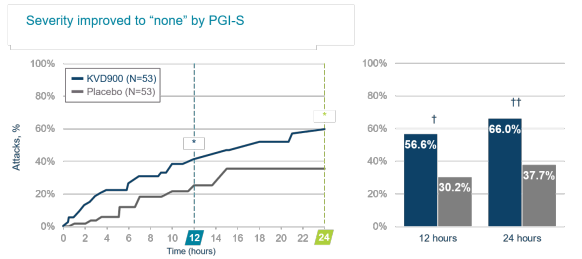
Use of conventional attack treatment



**P=0.001; Gehan's Generalized Wilcoxon Test. †P<0.05, Prescott's Test.
Full analysis set. Censoring occurs where a subject did not use conventional attack treatment within 12h post-study drug dosing.
Data on File. KalVista Pharmaceuticals, Inc.

Primary endpoint: KVD900 significantly slowed attack progression to use of rescue medication

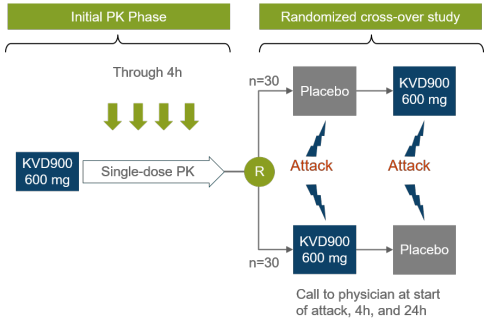
Attack resolution



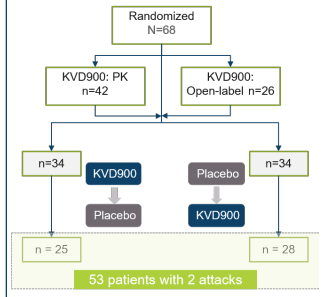
*P<0.01, Gehan's Generalized Wilcoxon Test. †P<0.05; ††P<0.01, Prescott's Test. HAE, hereditary angioedema; PGI-S, Patient Global Impression of Severity scale. Full analysis set. HAE attack severity assessed using the PGI-S scale. Censoring occurs where a subject did not achieve complete HAE attack resolution or conventional attack treatment is used within 24h post-study drug dosing.

KVD900 significantly accelerated time to complete attack resolution

Study design



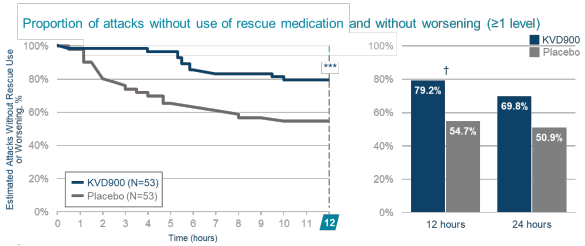
Study flow and demographics



Demographic Characteristics (N=68)

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)

Use of rescue or PGI-S worsening



***P≤0.0001, Gehan's Generalized Wilcoxon Test. †P<0.05, Prescott's Test.
Full analysis set. Attack progression defined as attack worsening by ≥1 level (rated as "none", "mild", "moderate", "severe", or "very severe") by PGI-S. Censoring occurs where a subject did not improve or conventional attack treatment is used within 12h post-study drug dosing.

KVD900 significantly slowed attack progression to use of rescue medication or PGI-S worsening

Safety

Treatment-related adverse events*

	Part 1 KVD900 N=68	Part 2 KVD900 N=58	Part 2 Placebo N=55
Total (events/patients)	**8 / 5 (7.4%)**	**3 / 3 (5.2%)**	**2 / 2 (3.6%)**
Gastrointestinal Disorders	1 (1.5%)	1 (1.7%)	1 (1.8%)
Abdominal Pain Upper	-	1	-
Anal Incontinence	-	-	1
Nausea	1	-	-
General Disorders	1 (1.5%)	-	-
Malaise	1	-	-
Musculoskeletal Disorders	1 (1.5%)	1 (1.7%)	-
Back Pain	1	1	-
Nervous System Disorders	3 (4.4%)	1 (1.7%)	1 (1.8%)
Dizziness	1	-	-
Headache	2	1	1
Vascular Disorders	2 (2.9%)	-	-
Flushing	2	-	-

*Within 48 hours of trial drug administration

Almost all events were single, mild or moderate cases; no serious or severe events were observed

Inclusion/exclusion criteria

Inclusion criteria

- Confirmed type I or II HAE
- >3 documented HAE attacks in past 93 days
- Access to conventional attack treatment

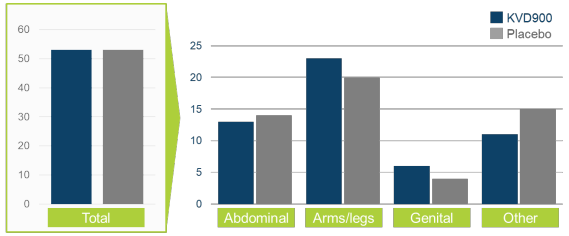
Exclusion criteria

Treatment with:

- HAE prophylaxis
- ACE inhibitors
- Estrogen-containing medications
- Androgens or fibrinolytics
- Strong CYP3A4 or CYP2C9 inhibitors and inducers

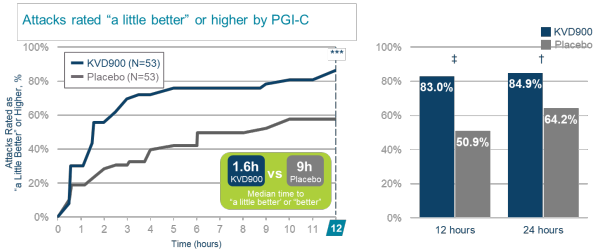
Clinically relevant patient population

Attack location



Representative distribution of attacks by location

PGI-C



***P≤0.0001, Gehan's Generalized Wilcoxon Test. †P<0.05; ‡ P<0.005, Prescott's Test. HAE, hereditary angioedema; PGI-C, Patient Global Impression of Change. Full analysis set. Change in HAE attack severity assessed using the 7-point transition question PGI-C. Censoring occurs where an attack rating of 'a little better' or higher for two consecutive time points does not occur, or conventional attack treatment is used within 24h post-study drug dosing.
Data on File. KalVista Pharmaceuticals, Inc.

KVD900 significantly accelerated time to improvement

Conclusions

- **Early use of KVD900 halts attack progression**
  - Use of KVD900 at attack onset significantly increases time without needing rescue
- **KVD900 is efficacious within the first hours of the attack**
  - Use of KVD900 significantly shortens the time to improvement of attack symptoms
- **KVD900 accelerates attack resolution**
  - Use of KVD900 significantly shortens the time to attack resolution
- **KVD900 is generally safe and well tolerated**

Conflicts: # Paid Scientific Advisors, * Employees of and § Consultants to KalVista Pharmaceuticals