PDS21

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

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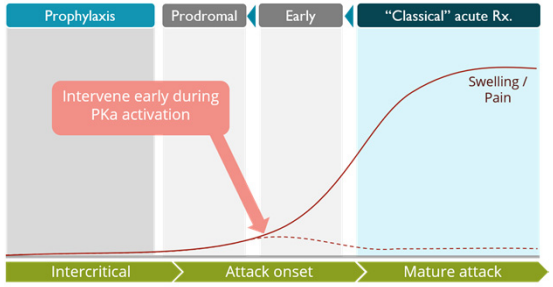
Background

- HAE attacks are unpredictable in frequency and severity
- Immediate access to on-demand treatment for HAE attacks is mandatory
- Early initiation of on-demand treatment significantly shortens attack duration
- A rapid oral, on-demand treatment may stop attacks early at onset, addressing a significant worldwide need of HAE patients



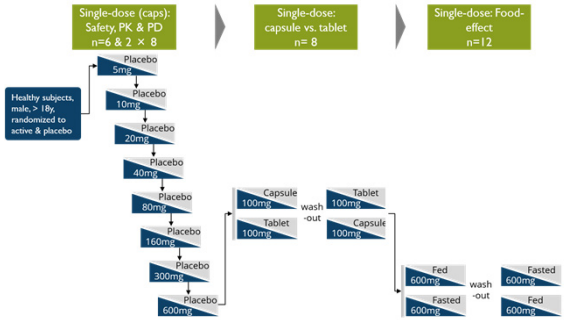
Early inhibition of plasma kallikrein activation may pre-empt swelling and pain

Objectives

Single doses of KVD900 (powder in capsule & tablet) in healthy male volunteers:

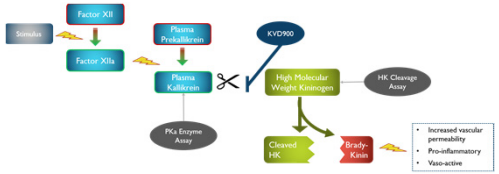
- ..safety and tolerability
- ..pharmacokinetics (PK)
- ..pharmacodynamics (PD)
- ..exposure fasted vs. fed

Methods



Methods - Analytics

- Tandem MS-MS for KVD900 concentrations
- Dextran sulfate (DXS) stimulation (whole plasma):
  - fluorogenic enzyme assay (whole plasma)
  - capillary-based high molecular weight kininogen (HK) cleavage immunoassay (whole plasma)

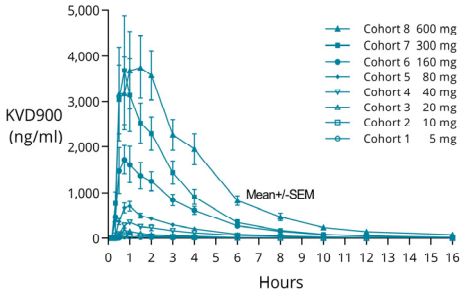


Results - Safety

- No SAEs reported
- 25/26 AEs were mild
  - One moderate (headache at 10mg)
  - No GI AEs considered related to KVD900
- No subjects withdrawn
- No clinically significant changes in vital signs, ECG, safety labs

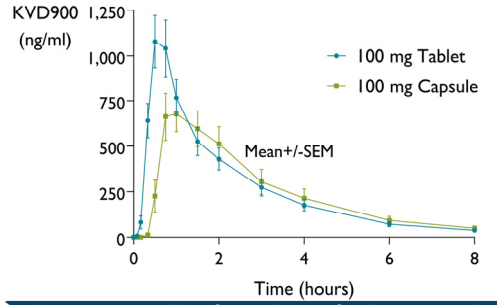
Administration of single doses of KVD900 up to 600 mg is generally safe & well tolerated

PK: capsules



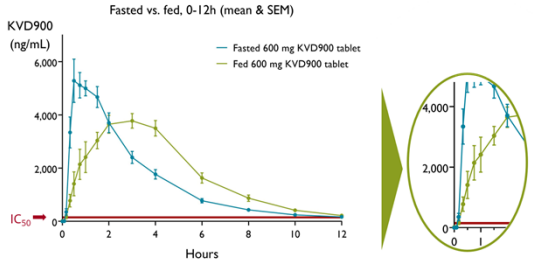
KVD900 rapidly achieves maximal plasma exposure

PK: caps. vs. tablets



The KVD900 tablet formulation further exceeds the fast absorption seen with the capsule

PK: Food effect



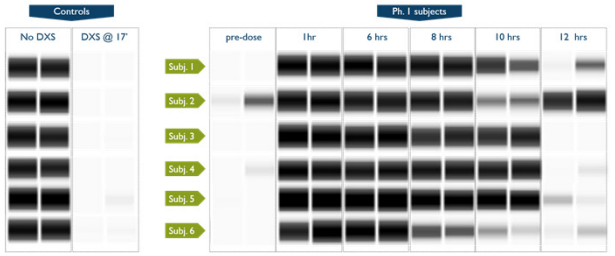
KVD900 concentrations rapidly exceed multiples of IC50 within 20 minutes irrespective of food intake

Pharmacodynamics

PKa Enz. Assay | HK Cleavage Assay

KVD900 maintains near complete suppression of PKa enzyme activity

PD: HK cleavage



HK cleavage protection is upheld for up to 12 hrs

Conclusions

- Single oral administration of up to 600 mg KVD900 is generally safe and well tolerated
- KVD900 achieves rapid suppression of plasma kallikrein activity
- KVD900 achieves sustained protection of HK
- KVD900 concentrations rapidly exceed multiples of IC50 within 20 minutes irrespective of food intake
- Phase 2 study currently ongoing to evaluate KVD900 for on-demand suppression of attacks

Conflicts: All authors are or were employees of KalVista Pharmaceuticals during the execution of this work