Key findings

Jivi offers

longer half-life and higher AUC

with reduced clearance vs. rFVIII-FS[1]

The improved PK parameters for Jivi vs. rFVIII-FS suggest that

FVIII levels are sustained above threshold

after multiple doses[1]

This could mean

extended intervals between prophylaxis infusions

with Jivi, while maintaining low bleeding rates[1]

AUC, area under the curve; AUC_{norm}, dose-normalized area under the curve; CI, confidence interval; LS, least-squares; PK, pharmacokinetic; rFVIII-FS, recombinant factor VIII (sucrose formulated); $t_{1/2}$: half-life.

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COMPREHENSIVE PK: A PUBLICATION SUMMARY

Jivi®, a PEGylated recombinant factor VIII, exhibits a prolonged half-life, and higher area under the curve in patients with severe hemophilia A: Comprehensive pharmacokinetic assessment from clinical studies

1. Shah A *et al*. Haemophilia 2018; 24(5): 733–740.

THE STUDY

Objective

To understand the PK profile of Jivi in adults, adolescents and children with severe hemophilia A[1]

Methods

Data was analyzed from three studies measuring blood FVIII levels following Jivi or rFVIII-FS infusion[1]

Results

Jivi had reduced clearance that resulted in a ~1.4-fold increase in half-life and AUC_{norm}[1]

Conclusion

Jivi shows an extended half-life and increased AUC vs. standard-acting FVIII product, rFVIII-FS. These PK characteristics will result in higher FVIII levels for longer duration[1]

Background

- Despite the benefits of prophylaxis with replacement FVIII products in patients with severe hemophilia A, regimens typically require frequent infusions[1]
- These can be cumbersome and lead to suboptimal treatment adherence[1]
- Longer-acting FVIII products vs. standard-acting products maintain FVIII levels above threshold for longer periods of time[1]
- This improvement in PK profile could mean extended intervals between infusions, which may result in better protection from bleeding compared to standard acting products[1]

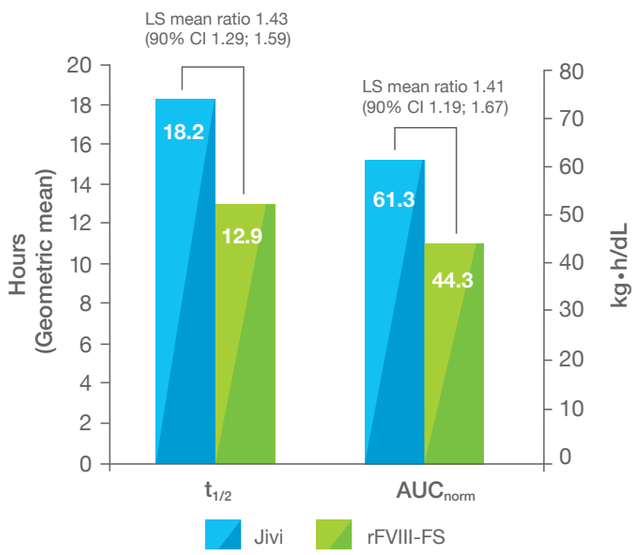
Study methods

- PK data from three key studies were analyzed:
  - A phase 1 trial in patients with severe hemophilia A, aged 18 to 65 years[1]
  - Two phase 2/3 trials in previously-treated patients with severe hemophilia A: PROTECT VIII (12 to 65 years) and PROTECT VIII Kids (<12 years)[1]
- Patients received Jivi or rFVIII-FS infusions, before blood samples were taken at pre-defined times[1]
- FVIII levels were monitored in the samples using chromogenic assays and one-stage assays[1]
- The analysis looked at PK parameters $t_{½}$, AUC and clearance which are considered the most important surrogate efficacy endpoints for new FVIII products[1]

Results

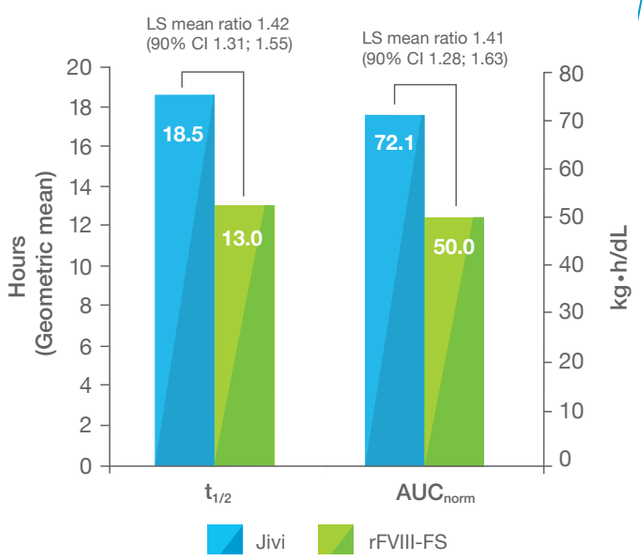
- Jivi PK parameters superior to rFVIII-FS [1]
  - The phase 1 trial showed that Jivi had reduced clearance vs. rFVIII-FS, resulting in:
    - Longer* $t_{1/2}$
    - Greater† AUC_{norm}

PK parameters: Cohort 1



Cohort 1: 25 IU/kg rFVIII-FS followed by 25 IU/kg Jivi twice weekly for 8 weeks

PK parameters: Cohort 2



Cohort 2: 50 IU/kg rFVIII-FS followed by 60 IU/kg Jivi every 7 days for 8 weeks

Geometric mean $t_{1/2}$ and AUC_{norm} in adult patients: improved with Jivi vs. rFVIII-FS

- Similar PK following single-dose and multiple-dose administration [1]
  - In PROTECT VIII, PK parameters were similar after the first and last dose of Jivi

- Similar PK in adults and adolescents [1]
  - As with other FVIII products, the PK profile of Jivi was age dependent; however, PK was comparable between adults and adolescents

* ~1.4-fold increase.

† Cohort 1, 61.3 vs. 44.3 kg • h/dL; cohort 2, 72.1 vs. 50.0 kg • h/dL following a single infusion.