Improvement in health status and quality of life in patients with haemophilia B treated with nonacog beta pegol, an extended half-life glycopegylated recombinant FIX product

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Objective

- To assess the health-related quality of life (HRQoL) of individuals with haemophilia B treated with nonacog beta pegol (N9-GP), in a phase III pivotal trial and its open-label extension trial.

Conclusions

- Adult patients with haemophilia B receiving prophylaxis with 40 IU/kg N9-GP weekly reported an improvement in health status as assessed by EQ-5D VAS and significant improvements in haemophilia-specific HRQoL as assessed by HAEM-A-QOL. The improvements were maintained through the extension trial indicating the ongoing benefit from extended prophylaxis.
- Patients who switched from 10 to 40 IU/kg N9-GP reported an improvement in the 'HAEM-A-QOL Total' score, confirming the quality of life benefits of weekly prophylaxis with 40 IU/kg N9-GP.

Introduction

- Current standard of care includes regular prophylaxis (PPX), characterised by self-infusion of either recombinant or plasma-derived factor IX (FIX) product on 2-3 occasions a week.
- Extended half-life FIX products, that enable once weekly infusions while maintaining higher levels of FIX than what is currently obtainable, might result in further improvements in HRQoL.

Methods

Study design

- Patients with haemophilia B aged 13-70 years included in a single-blind, randomised, multinational phase III pivotal trial (paradigm™2) and its open-label extension (paradigm™4).[1,2]
- Patients treated on-demand (OD) for 28 weeks, or randomised to once weekly PPX with 10 or 40 IU/kg N9-GP for 52 weeks. In the extension trial, patients could continue on the same treatment or switch to the alternate dosing regimen at any time.
- HRQoL was assessed using HAEMO-QOL-III/HAEM-A-QOL age and haemophilia-specific questionnaires and EQ-5D-3L at baseline (BL) paradigm™2; end-of-trial (ET) paradigm™2 (coinciding with entry into paradigm™4); and end-of-trial paradigm™4.

HRQoL instruments

- HAEMO-QOL/HAEM-A-QOL questionnaires[3,4]
  - HAEM-A-QOL: completed by adults aged 17-70 years; 46 items measuring 10 HRQoL domains
  - HAEMO-QOL-III: completed by adolescents aged 13-16 years; 77 items measuring 12 HRQoL domains
  - Domain scores and Total score range from 0 to 100, (lower score = better haemophilia-related quality of life)
- EQ-5D-3L[5]
  - 5 dimensions assessing health status with 3 response levels per dimension: no, some or extreme problems.
  - Visual Analogue Scale (VAS), rating patients' global health status ranges from 0 (worst imaginable health state) to 100 (best imaginable health state).

Statistical analysis

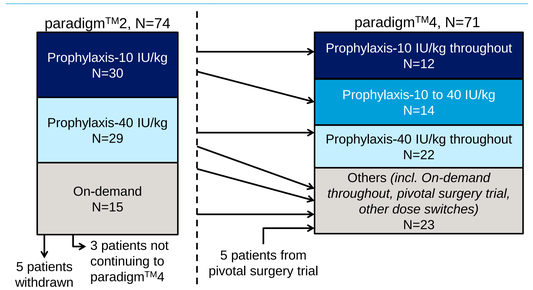
- Changes in HRQoL scores were compared to 0 (no change) using a signed rank test.
- No adjustment for multiple testing was performed.

Results

Patients' characteristics

- 74 patients were included in paradigm™2: 59 adults aged ≥ 17 years and 15 adolescents aged 13-16 years.
- Patients' disposition is presented in Figure 1.

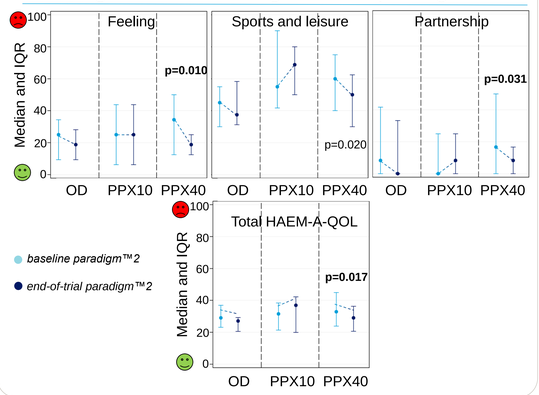
Figure 1 Patients' disposition.



HAEMO-QOL III/HAEM-A-QOL - paradigm™2

- No statistically significant difference in HAEMO-QOL III scores for adolescents in any arm from BL to ET.
- Significant improvements in the 'HAEM-A-QOL Total' score and 3 domains for adults receiving PPX 40 IU/kg; no improvements in those with PPX 10 IU/kg or OD (Figure 2).

Figure 2 Improved HAEM-A-QOL scores for adults receiving PPX with 40 IU/kg N9-GP in paradigm™2.



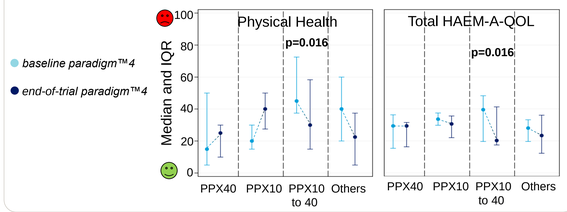
EQ-5D - paradigm™2

- Statistically significant improvement in mean VAS score (8.2±17.2; p=0.030) was observed in the PPX 40 IU/kg arm, while change was not significant in the other arms.
- At ET paradigm™2, fewer patients reported problems in the EQ-5D 'Mobility' and 'Pain/Discomfort' dimensions, in particular those receiving PPX 40 IU/kg:
  - 51.7% reported some or extreme problems with 'Mobility' at BL vs. 20.7% at ET in the PPX 40 IU/kg.
  - 44.8% reported some or extreme problems with 'Pain/Discomfort' at BL vs. 27.6% at ET in the PPX 40 IU/kg.

HRQoL in the open-label extension - paradigm™4

- Adult patients who switched from PPX 10 to 40 IU/kg reported trends toward improvements for all HAEM-A-QOL scores, including a statistically significant improvement in the 'HAEM-A-QOL Total' score (-12.5±8.7, p=0.016) and 'Physical health' domain (-23.1±14.4, p=0.016) (Figure 3).
- No statistically significant changes observed in patients continuing on the same dose or with other switches.
- EQ-5D scores were stable during the extension trial.

Figure 3 Improved HAEM-A-QOL scores for adults receiving PPX with 40 IU/kg N9-GP in paradigm™4).



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Conflict of interest disclosure

PC has served on advisory boards for Baxter Healthcare, Biogen Idec, CSL Behring, Novo Nordisk, Pfizer, Sobi; has received research funding from CSL Behring, Novo Nordisk, Pfizer. SK has been study local principal investigator for several Novo Nordisk and Biogen clinical trials; has served on advisory boards for Biogen Idec. DLY has been local principal investigator for several Novo Nordisk clinical trials; has served on advisory boards for Octapharma and CSL Behring. CSH is an employee of Novo Nordisk A/S. JM, an employee of Mapi, was a paid consultant to Novo Nordisk A/S.

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