Individualised prophylaxis with Nuwiq® (Human-cl rhFVIII) in adult PTPs with severe haemophilia A

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Background
In haemophilia A patients receiving replacement therapy, trough FVIII plasma concentrations and the amount of time per week that the FVIII level is above a certain threshold are mainly determined by the half-life of the FVIII concentrate used and the dosing frequency.

To optimise prophylactic treatment, there is a call to individualise therapy, requiring knowledge of each patient’s pharmacokinetic (PK) response to the substituted FVIII. PK responses vary considerably between patients.

Nuwiq® (simoctocog alfa) is a 4th generation recombinant FVIII concentrate without chemical modification or fusion with any other protein. It is produced in a human cell line that adds only human-specific post-translational modifications.

The GENA-21 (NuPreva) study assessed PK-guided personalised prophylaxis with Nuwiq® in 66 previously treated adults (PTPs) with severe haemophilia A. The main results were:

- The median dosing interval was 3.5 days.
- 58% of patients received two or fewer infusions per week.
- 73% of patients did not bleed during the 6-month personalised prophylaxis period.
- 83% of patients did not have a spontaneous bleed during the 6 months.

This was achieved without increasing the FVIII dose for prophylaxis.

Inclusion and Exclusion Criteria

Inclusion Criteria
(a) Severe haemophilia A (FVIII:C <1%) according to medical history
(b) Male patients ≥18 years of age
(c) Previous treatment with a FVIII concentrate (irregular prophylaxis with good compliance or on-demand treatment)
(d) Good documentation regarding dosing and bleeding frequency in the 6 months preceding study start
(e) Immunocompetence (CD4+ count >200/μL)
(f) Freely given written informed consent

Exclusion Criteria
(a) Any coagulation disorder other than haemophilia A
(b) Present or past FVIII inhibitor activity (>0.6 BU) according to medical history
(c) Severe liver or kidney disease (ALT and AST levels >5 times upper limit of normal, creatinine >120 μmol/L)
(d) Treatment with any investigational medicinal product (IMP) except FVIII IMP within 14 days prior to the screening visit
(e) Dose recommendation was provided for 30 patients. The characteristics of these patients compared with those enrolled in GENA-21 are shown in Table 2.

No data are available as yet from the GENA-21b study on the efficacy and safety of Nuwiq®.

Patients’ Characteristics
As of end of January 2017, individualised PK-guided dose recommendations were provided for 30 patients.

The median dosing interval was 3.5 days (and beginning of Phase II).

Values are median (range) unless stated otherwise

Dose recommendation was provided based on:
- Dose should not be >80 IU/kg
- C0 <0.01 IU/mL
- Longest injection interval
- Investigator discretion

Conclusions
Both in patients treated previously on-demand and in those prophylactically, PK-guided prophylaxis with Nuwiq® resulted in an extension of the treatment intervals to two times per week or less in more than half of the patients. The weekly dose was reduced compared with that for routine prophylaxis.

References