guardian™5: a prospective non-interventional study of the treatment of severe and moderately severe haemophilia A with turoctocog alfa

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Objective

- To further investigate, in a real-world setting, the safety and effectiveness of turoctocog alfa in the treatment of patients with severe to moderately severe haemophilia A (FVIII ≤2%).

Outcomes

- The results of this study will provide information on the real-world, long-term safety and effectiveness of turoctocog alfa in routine clinical practice.
- The guardian™5 study began in June 2014 and is enrolling participants from a range of countries in Europe and North America.

Introduction

- Turoctocog alfa is a B-domain-truncated recombinant coagulation factor VIII (rFVIII) product developed by Novo Nordisk for the prevention and treatment of bleeding in patients with haemophilia A.
- guardian™ is an ongoing, multinational clinical activity programme consisting of several trials and studies designed to investigate the pharmacokinetics, safety and effectiveness of turoctocog alfa in the treatment of haemophilia A.
  - guardian™1 and guardian™3 assessed the safety and efficacy of turoctocog alfa in previously treated adults (≥12 years) and children (<12 years), respectively.
  - guardian™2 is an extension trial of guardian™1 and guardian™3.
  - guardian™4 is investigating turoctocog alfa treatment in previously untreated patients (PUP).
- The EMA guideline stipulates post-marketing studies should be undertaken for rFVIII products to ensure consistency between outcomes in pre-authorisation clinical trial data and routine clinical use.[1]
- guardian™5 (NCT02035384) is a non-interventional, prospective, post-authorisation safety study (PASS) that has been developed to meet this EMA guideline.[1]

- guardian™5 further investigates, in a real-world setting, the safety and effectiveness of turoctocog alfa in the treatment of patients with severe to moderately severe haemophilia A (FVIII ≤2%).

Methods

- Patient enrolment for guardian™5 began in June 2014 and is ongoing (study design is shown in Figure 1).
- The study aims to screen 80 patients in order to enrol approximately 70 patients from Europe and North America.
- Currently, centres from 13 countries are participating: Austria, France, Germany, Greece, Hungary, Italy, the Netherlands, Slovakia, Slovenia, Spain, Sweden, Switzerland and the US.
  - Additional countries within Europe and North America are invited to enrol participants as the study progresses.
- Patients receive turoctocog alfa either as an on-demand therapy or as prophylaxis for the duration of the study; directions for use are at the discretion of the treating physician in accordance with the local label.
- Patients are evaluated until ≥50 patients have reached ≥100 exposure days (EDs), which is expected to take approximately 4 years from first patient first visit.

Inclusion criteria

- Male, previously treated patients (PTP; >150 EDs) with congenital severe or moderately severe haemophilia A (FVIII ≤2%).
- Patients with a history of inhibitors may be enrolled if they have undergone successful immune tolerance induction (ITI).

Exclusion criteria

- Treatment with any investigational drug 30 days prior to enrolment into the study.
- Any contraindications for use as per turoctocog alfa prescribing information or summary of product characteristics.
- Previous participation in the guardian™ clinical trial programme.

Outcomes

- guardian™5 will provide information on the long-term safety and effectiveness of turoctocog alfa when used in routine clinical practice.
- The primary outcome of guardian™5 is the incidence of inhibitors (≥0.6 Bethesda units/ml).
- The secondary outcomes include:
  - Adverse reactions and serious adverse reactions.
  - Haemostatic effect in the treatment of bleeds, assessed by the patient or physician using a four-point scale (‘excellent’, ‘good’, ‘moderate’ or ‘none’).
  - Haemostatic effect during surgical procedures assessed using a four-point scale (‘excellent’, ‘good’, ‘moderate’ or ‘none’).
  - Annualised bleeding rate for prevention and on-demand treatment.
- Enrolment is ongoing with data completion for the primary outcome expected in 2018.

Reference

1. European Medicines Agency 2011. EMA/CHMP/BPWP/144533/2009.

Conflict of interest disclosure

IM, LK, SK, HG and IK are employees of Novo Nordisk.

This study was sponsored by Novo Nordisk and is registered with ClinicalTrials.gov (NCT02035384).
The authors acknowledge the medical writing assistance of AXON.
Presented at the World Federation of Hemophilia (WFH) World Congress, July 24–28, 2016, Orlando, FL, USA.

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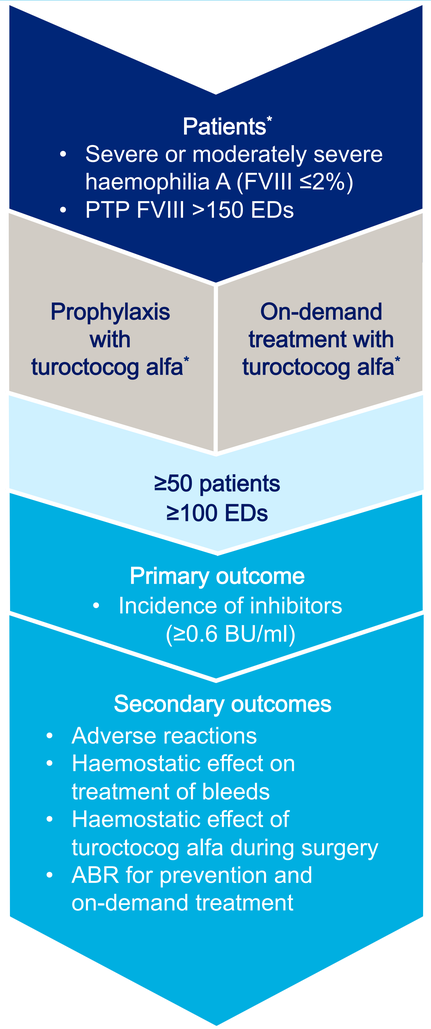
Figure 1 guardian™5 study design



Key patient inclusion criteria are shown in dark blue; turoctocog alfa treatment options are shown in grey; study exposure is shown in light blue; outcomes are shown in bright blue.
*Patients are treated with commercially available turoctocog alfa, according to the label, as prescribed by the treating physician in daily clinical practice. ABR, annualised bleeding rate; BU, Bethesda units; EDs, exposure days; PTP, previously treated patients.

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Poster Presented at:
Clotting Factor Concentrates
Stephanie Gibbons
DOI: 10.3252/pso.au.WFH2016.2016
22--PO-M
WFH2016