A Cost-effectiveness Analysis of PK-driven Prophylaxis Using myPKFit vs. Standard Prophylaxis in Haemophilia A

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INTRODUCTION

• The mainstay of hemophilia A therapy is represented by prophylaxis of bleeding and prevention of arthropathy. Prophylactic FVIII regimens have been shown to be effective in reducing bleeding frequency in patients with severe haemophilia A. Results from Swedish studies, as well as those of numerous other studies, have proven the efficacy of a standard regimen of regular infusions with 0.40–0.63 IU rFVIII concentrate every other day or at least 3 times a week in reducing bleeding episodes, decreasing hospitalization, and improving long-term joint function.1 2

• Maintaining FVIII levels above 1% and so converting severe hemophilia (with FVIII < 1%) into a more moderate form of the disease was the rationale of these regimens. This target was chosen in order to conveniently optimize budget constraints, frequency of dosing and access to rFVIII.3

• Despite the effectiveness, probably due to less than expected or insufficient FVIII levels occurring between infusions, a relatively significant number of patients still bled, as already suggested by early studies comparing weekly dosing frequencies.4 5

• Because of the high costs associated with factor concentrates, a generalized increase of dosages would not be sustainable in the great majority of countries. An alternative approach might be to identify individualized optimal treatment regimens, and one of these methodologies is the pharmacokinetic (PK).

STUDY OBJECTIVES

• The aim of this study is to assess the cost-effectiveness profile of rFVIII PK-driven prophylaxis as compared with standard regimens in a virtual population of severe haemophilia A subjects.

METHODS

• In order to perform an individual simulation over a hypothetical population of severe haemophilia A patients, a microsimulation model was developed and the analysis was performed over a 1-year time horizon in the Italian cost setting.

• Patients of the simulated cohort were assumed to be treated with rFVIII PK-driven prophylaxis or with standard FVIII regimen, and an estimate of the consumption, costs, annual joint bleeding rate (AJBR) and the incremental cost-effectiveness ratio (ICER) expressed as € per joint bleed avoided was calculated out.

• The rFVIII PK-driven prophylaxis was based on the population PK model, developed by Björkman et al.,6 which is a two-compartment model with the primary PK parameters being clearance (CL), volumes of distribution of the central and peripheral compartment (V1, V2), and inter-compartmental clearance (Q).

• An exponential model is applied for individual clearance (CL) and plasma volume (V1) to account for inter-individual and inter-occasion variance.7 To obtain the FVIII concentration in time for each simulated patient, the Björkman equation was implemented in the microsimulation model.

• A simulated population of 10,000 patients, derived from a previous model that modeled use of the same PK model in a simulated population of 1,000 severe haemophilia A subjects,9 where each patient from this cohort was replicated 10 times with different CL and V1 randomly extracted from the covariance matrix reported by Björkman et al.6 A population of 10,000 severe haemophilia A patients characterized by age, body weight, CL and V1 with a mean age of 27.8 years and a mean BW of 73.8 Kg.

• The ABJR was used as efficacy parameter to compare the two prophylaxes. The ABJR for each simulated patient in the two arms was estimated based on the relationship between PKFVIII concentration and bleeding rate reported by Den Uyl et al.7 8

• For each simulated patient the number of ABJR is calculated by weighting the percent of time spent in each concentration interval for the bleeding rate associated.

RESULTS

• The simulation showed that 10.6% of simulated patients treated with the standard prophylaxis [30 IU/kg every 48 hours] had a minimum concentration of FVIII below 1 IU/L and 27.8% above 5 IU/L (Figure 2).

• Overall, during this simulation, with the PK-driven prophylaxis the mean ABJR decreased from 1.912 to 0.840. The mean FVIII dose for PK-driven prophylaxis was 29.64 IU/kg, with a mean reduction of 0.39 IU/kg with respect to standard prophylaxis.

• $308,022 was the average annual cost of FVIII to cover the prophylaxis and the management of bleedings with PK-driven prophylaxis and $505,699 with standard prophylaxis, with a total saving of $16,797 per patient-year.

• PK-driven prophylaxis, from the cost-effectiveness point of view, resulted dominant over standard prophylaxis (Table 1), as it was less costly and more effective (reduction of ABJR).

• 27.8% of the simulated population had a FVIII level < 5 IU/L and an ABJR of 0.260 with the standard prophylaxis: 14.6% of them had a FVIII minimum level above 10 IU/L. With the PK driven prophylaxis the FVIII dose was adjusted to have the minimum concentration of FVIII equal to 5 IU/L. An average dose reduction of 0.66 IU/kg and an increased ABJR of 0.14 were observed. On the other side the dose was increased to simulated patients with a faster pharmacokinetics who had a minimum FVIII concentration < 1.0 IU/L (10.6%) in order to reach the goal of minimum 1.0 IU/L. The dose was increased on the average to 49.23 IU/kg in these patients with the consequent reduction of 1.032 in the ABJR (Table 2).

Figure 1: Concept of the Microsimulation Model

Table 1: Concept of the Microsimulation Model

Table 2: Outcomes of the Simulation in the Group of Patients that with Standard Prophylaxis had a Minimum FVIII Concentration Below 1 IU/L (10.6%) and in the Group that had a Minimum FVIII Concentration Above 5 IU/L (27.8%).

DISCUSSION & CONCLUSION

• Accounting for patients' individual PK characteristics, PK-driven prophylaxis appears to be a promising strategy for optimization of available resources and improvement in quality of life in the severe haemophilia population. myPKFit showed to be able to support the assessment of individual PK in subject with severe haemophilia A in real clinical practice.

REFERENCES