P051 | Benefits of switch to FVIII-FC: Experience of prophylaxis in eight patients

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Introduction: Recombinant Factor VIII-Fc (rFVIII-Fc; Efmoroctocog alpha), a fusion protein with the Fc portion of IgG1, is the first extended half-life (EHL) product available in Italy. We here report data so far collected about prophylaxis with FVIII-Fc in patients with hemophilia A followed at Hemophilia Centre of Parma.

Methods: According to expert recommendations, patients candidate to switch from prophylaxis with standard half-life FVIII concentrate to rFVIII-Fc underwent a pharmacokinetic (PK) study. At baseline FVIII:C and FVIII inhibitor were assessed after a wash out of at least 72-96 hours. Blood samples for FVIII:C were collected at 0.25, 0.5, 1, 3, 6, 24, 48, 72 and 96 hours after the infusion of 40-50 IU/kg rFVIII-Fc. After the definition of prophylaxis regimen and start of rFVIII-Fc therapy patients underwent clinical and laboratory follow-up monthly for the first three months (bleeding and infusion report; FVIII:C and inhibitor assessment, satisfaction to treatment), then every 3 months.

Results: Eight patients (6 severe and 2 moderate hemophilia A; age, mean±1SD, 29.8 ± 12.78) were switched to rFVIII-Fc. The mean follow up after switch was 4.8 ± 3.7 months. At PK analysis, mean in vivo recovery and half-life were 2.42 ± 0.23 and 19.24 ± 3.81 hours, respectively. All patients were prescribed a twice weekly prophylaxis regimen, except the youngest one over the first month (every 3 days). Mean prophylactic FVIII dose was 47 ± 2.36 IU/Kg. Due to good clinical outcomes and satisfactory trough levels (>3 IU/dL, 96 h) the intervals between infusions were prolonged every 4 days within 1-4 months in 5 patients. All patients reported high satisfaction to treatment due to less frequent venipunctures and higher sense of protection without any change in their lifestyle and physical activities. The concentrate was well tolerated, no adverse events or inhibitor development being detected. On the whole, as compared to the year before switch, prophylaxis with rFVIII-Fc allowed a mean reduction of 40% of the infusion number and of 13% of FVIII consumption, estimated according to the last prescribed regimen.

Discussion/Conclusion: Our experience show that switching to prophylaxis with a EHL FVIII concentrate (rFVIII-Fc) is safe and allows to maintain good clinical outcomes, significantly reducing the infusion numbers and factor consumption and improving patients' sense of protection.

Disclosure of Interest: None declared.

P052 | Assessment of clotting activity of recombinant fix FC fusion protein in European hemophilia treatment centers

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Introduction: As extended-half-life therapies become available, such as recombinant FIX Fc fusion protein (rFIXFc), it is important to ensure the reliability of their therapeutic monitoring. The objective of this field study was to assess agreement between European hemostasis laboratories in measuring FIX activity in plasma samples containing various levels of rFIXFc.

Methods: Human FIX immunodepleted plasma was spiked with rFIXFc (Alprolix®) at three nominal levels (based on the manufacturer's labeled potency). Samples were shipped frozen to laboratories across Europe and tested for FIX activity by the labs' own aPTT based one-stage clotting assay and plasma standard. The required information was recorded independently by each laboratory and used for central data analysis.

Results: 79 sets of results were received from 59 participating hemostasis laboratories in 12 European countries during Sept 2016-Oct 2017. Overall, 9 commercial aPTT reagents were used on 5 types of analyzers, yielding a total of 16 aPTT+analyzer combinations. Reported FIX clotting activity of the 0.80, 0.20 and 0.05 IU/mL plasma samples, ranged from 0.46 to 1.36 IU/mL (mean = 0.75; CV = 24.0 %), 0.12 to 0.42 IU/mL (mean = 0.21; CV = 27.5 %) and 0.03 to 0.14 IU/mL (mean = 0.06; CV = 32.6 %), respectively. A one-way ANOVA between 9 aPTT+analyzer combinations indicated a statistical significant difference between FIX clotting activity recovered from each level of rFIXFc samples ($P < .0001$). For CK-Prest™+Stago analyzer combinations (n = 23) the mean of observed recoveries at the 0.80, 0.20 and 0.05 IU/mL plasma samples were 0.58 (12.0% CV), 0.16 (12.5% CV), 0.05 IU/mL (18.5% CV), respectively. A relative deviation in FIX activity was also noted comparing different analyzers with the same silica aPTT reagents.

Discussion/Conclusion: This field study revealed a dose-dependent variability in overall FIX measurement and between each combination of aPTT+analyzer throughout Europe. Most laboratories measured FIX clotting activity of rFIXFc plasma samples within 30% of target levels using routine assay methods and plasma standards. Results are consistent with previously published data on laboratory rFIXFc activity assay performance across other regions. Interestingly, better FIX accuracy with the CK-Prest+Stago assay system was reached than previously described.

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