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AICE Associazione Italiana dei Centri Emofilia

HDTM Hrvatsko Društvo za Transfuzijsku Medicinu

SETS Sociedad Española de Transfusión Sanguínea y Terapia Celular

SISET Società Italiana per lo Studio dell'Emostasi e della Trombosi

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ABSTRACT BOOK

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OC099 - An Italian Survey on the real-world use of rFXIII (catridecacog) in patients with factor XIII deficiency

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Background. FXIII deficiency is an rare coagulation disease characterized by severe bleeding present at birth, particularly life-threatening intracranial haemorrhages (ICHs). These subjects should therefore be treated in prophylaxis with FXIII concentrates from childhood to prevent bleeding. However, in the literature the data relating to the use of FXIII in real life are insufficient.
The objective of this survey was to evaluate the characteristics of patients with FXIIII deficiency treated with rFXIII, the real dosage and frequency of the catridecacog administration used and the bleeding observed during the treatment.
Methods. All case of patients with FXIII deficiency treated with catridecacog at nine Italian Haemophilia Centres were collected in this Survey. Clinical features of patients, management and outcomes were subsequently statistically evaluated.
Results. Overall 17 patients with FXIII deficiency were collected, 75.0% presenting severe disorder. 8/15 were females. Mean age at diagnosis was 11 years (range birth-32 years). Two-thirds were a family disorder with a known genetic defect. In the 13/17 of cases the diagnosis was performed after major bleeding, only one of them was an ICH. These acute events were treated respectively with plasma (eight cases), pdFXIII (five cases), embolization (one case), rFXIII (one case), not reported (two cases). 76.5% of patients were subsequently put on prophylaxis with catridecacog at mean dosage of 33.1 IU/kg (range 25.0-80.0 IU/kg), on average every 4.0 weeks (range 3.0-8.0 weeks). Only two of them had muscular haematomas during a mean follow-up of 31 months, quickly resolved. Pharmacokinetics assessment was performed in the 88.2% of cases before starting prophylaxis. The other four patients, ¾ with severe FXIII, remained on-demand treatment. One of them experienced a subsequent severe ICH.
Conclusions. This is a first survey on real-world use of catridecacog performed in an Italian population of patients with FXIII deficiency. The efficacy and safety of rFXIII, used in most cases at the recommended dosage and frequency, was proven in all treated patients. The role of prophylaxis to prevent haemorrhagic recurrences in patient presenting severe disorder was also highlighted.

OC100 - Rational engineering of a novel factor IX albumin fusion protein results in enhanced coagulant activity and pharmacokinetic profile

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Background. Several approaches have been developed to prolong half-life of infused recombinant factor IX (FIX), such as genetic fusion with wild-type human albumin (HSA). However, to further widen the therapeutic window, rational engineering for improved binding to the neonatal Fc receptor (FcRn), which regulates HSA half-life, combined with the use of natural gain-of-function FIX variants, may result in products with more favourable features. The aim of this work was to develop a novel fusion protein with improved features conferred by the gain-of-function FIX-Padua variant and by an engineered HSA variant (QMP) with enhanced FcRn binding, and thus endowed with extended half-life.
Methods. The FIX-Padua variant was fused to engineered albumin through an optimized cleavable linker. Wild-type (FIX-HSA) and improved (Padua-QMP) purified proteins were characterized for activity (chromogenic and aPTT-based assays), FcRn binding properties (SPR and ELISA-based assays) and *in vivo* plasma persistence in humanized transgenic mouse models.
Results. The hyperactive features of the FIX-Padua variant were completely preserved upon HSA fusion, with an 8-to-15-fold improved activity. The presence of the HSA QMP variant greatly enhanced FcRn binding of

the engineered Padua-QMP fusion protein (K_d = 0.4 nM) in comparison with the wild-type (K_d = 200 nM). Notably, this translated into a more than 2-fold extended half-life of the Padua-QMP chimaera in human FcRn transgenic mice (2.5 days) compared to wild-type FIX-HSA (1.1 days) and to the commercially-available albutrepenonacog alfa (1.0 days) fusion proteins.

Conclusions. The combined improvements conferred by the FIX-Padua and QMP variants resulted in a novel engineered fusion protein with hyperactive features, enhanced FcRn binding and extended half-life in pre-clinical relevant human FcRn transgenic mouse models. This would translate into a widened therapeutic window and thus an amelioration of patients' quality of life.

OC101 - Long term complications after splenectomy in chronic pITP patients: a case control study

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Background. Splenectomy has always been considered a very efficacious surgical second line therapy for chronic primary Immune Thrombocytopenia (pITP), although some concerns have always arisen on short- and long-term complications of such procedure (bleedings, infections, thromboses). In the last decades in light of the introduction of new and very efficacious drugs for treatment of chronic pITP [rituximab, TPO-receptor agonists (TPO-RA)] clinicians have delayed or decreased the use of splenectomy. Aim of our study is to evaluate the long-term complications of this surgical procedure in a large pITP cohort to investigate their impact on patients clinical follow-up and therefore on the choice of splenectomy in this era.

Methods. All patients were followed in our Center between 1955 and 2018. All data were collected in a Microsoft Excel File and then processed with SPSS software.

Results. We enrolled 164 splenectomized patients and 1503 controls. Among controls, 896 underwent at least 1 therapy line, while 607 were only observed. After splenectomy, 68.3% of patients obtained a complete remission and 22% a partial remission; 37.8% of cases relapsed. Patients with PR had a statistically greater risk of relapse than patients in CR (p=0.004). Among splenectomized, 70.7% underwent vaccination against Streptococcus Pneumoniae, Haemophilus Influentiae, Neisseria Meningitidis, at least once; 87.2% of patients received antibiotic prophylaxis for at least 1 year after splenectomy. Infections prevalence was significantly higher in splenectomized patients compared with treated and observed subgroups (30.5% vs 13.8% or vs 6.1%; p<0.001). Comparing the prevalence of infectious events that needed hospitalization between splenectomized patients (28%), never treated patients (13.5%) and treated ones (28%) we did not observe a statistically significant difference (p=0.18). Prevalence of thromboses was significantly higher in splenectomized and treated patients compared to never treated ones (5.5% vs 4% vs 1.3%; p=0.03).

There were no statistically significant differences as regard cardiovascular and cerebrovascular events between splenectomized vs controls (p=0.23 and p=0.3 respectively). Rate of neoplasms was significantly higher in splenectomized patients compared to treated and never treated patients (7.32% vs 4.68% vs 2.1%; p=0.004).

Conclusions. Splenectomy presents an intrinsic higher risk of infections. The rate of thromboses and neoplasms is not different comparing splenectomized patients with treated ones, suggesting a possible role for medical therapies in such complications. We think splenectomy still has a role in the clinical course of chronic ITP, but it is necessary a very good infections prophylaxis and monitoring.

OC102 - Italian Registry on active adult ITP: structure and excerpta from initial data collected in 17 centers

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Background. Registry studies are increasingly used to obtain real-world clinical and patient-reported data. We present here on behalf of the 17 participating centers (complete list of authors and centers available from rodeghiero@hemato.ven.it) the first Italian ITP registry aimed at producing a dynamic picture of adult ITP natural history as modified by the various management