



RESUM DEL CONGRES DE LA EAHAD2022 (1-4 febrer)

Principals idees a remarcar

1. El Congrés #EAHAD2022 ha deixat molta informació, aportat resultats d'estudis de recerca, explicat pràctiques mèdiques. Estem en un moment de gran progrés en el tractament de les coagulopaties congènites.

Clinical trials of gene therapy in haemophilia: Current status

17 New studies of gene therapy currently planned or recruiting patients¹

- 11 Haemophilia A
- 6 Haemophilia B

- A variety of viral vectors are under investigation^{2,3}
- Most studies are using AAV vectors, but other vectors are also being evaluated²
- Transgenes include FVIII B-domain deleted and FIX high-activity variants²

For more information on these studies, please visit: <https://clinicaltrials.gov>

Gene therapy for haemophilia is currently still in development and under investigation and is not currently available nor proven safe or effective.
AAV, adeno-associated virus; FVIII, factor VIII; FIX, factor IX.
1. ClinicalTrials.gov (search as per 5th January 2022): <https://clinicaltrials.gov> (Accessed January 2022). 2. Batty P, Ullrich P. Int J Lab Hematol 2021;43(Suppl 1):117-23. 3. Batty P, Ullrich P. Hemasphere 2021;5(3):e540.

PedNet cohort – no difference between pdFVIII and reFVIII

PedNet Hemophilia Registry

	Plasma products	Recombinant products
Patients (n=883)	225	658
Inhibitors - all n (%)	63 (28.0)	191 (29.0)
Inhibitors - high titre n (%)	49 (21.8)	138 (21.0)

Update 2021
N = 1076 PUPs
31.0% all inhibitors; 22.6% high titre inhibitors

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ARE EHL-FIX SIMILAR ?

A VISUAL SUMMARY OF CURRENT EVIDENCE

Cédric Hermans

	rFIX-Fc	rFIX-FP	N9-GP
PK studies	+++	+++	+++
Tissue distribution studies	+++	++	+
Prophylaxis 1x/7-14 days (> 14)	1x/7-14 days (> 14)	1x/7-14-21 days	1x/7days
Prophylaxis 1x / 21 days	Not validated	Approved	Not validated
On-demand treatment	+++	+++	+++
Peri-op management	+++	+++	+++
Real-World data	+++	+++	Ongoing
PUPs	1 INH/33 PUPs / EMA	No data	One study / no EMA
ITI efficacy	Reports	No reports	No reports
FIX Consumption	++	++	++
Compliance	++	++	++
Studies on assays	+++	+++	+++

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HMB-001 | Mechanism of Action of a Novel Bispecific Antibody

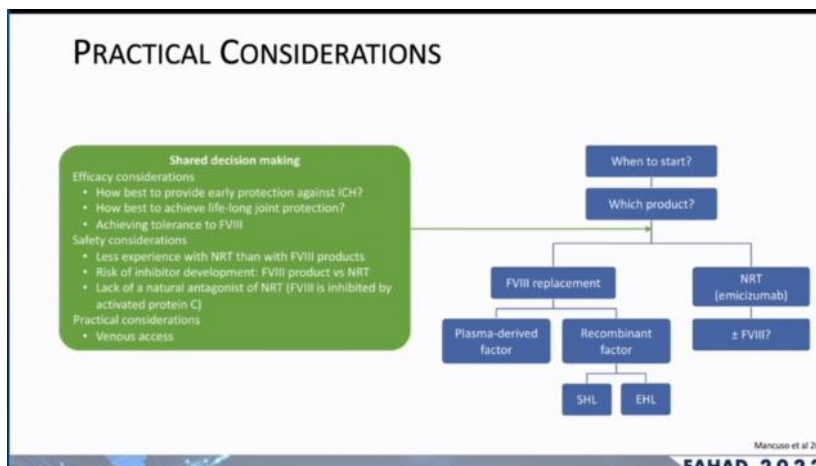
- HMB-001 binds endogenous FVIIa and TLT-1 receptor
 - Accumulate fully functional endogenous FVIIa in the circulation by the anti-FVIIa arm
 - Recruit endogenous FVIIa selectively on the activated platelet by the anti-TLT-1 arm
- HMB-001 is designed for prophylaxis across multiple bleeding disorders based on the clinically validated efficacy and safety of recombinant FVIIa

Multiple Indications:
Glanzmann Thrombasthenia
Factor VII Deficiency
Hemophilia B +/- Inhibitors
Bernard-Soulier
Von Willebrand Disease type 3

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2. L'atenció personalitzada és ja una realitat: factors de llarga durada, noves molècules, teràpia gènica, tractaments de l'inhibidor, ...



OPTIMAL START OF HAEMOPHILIA TREATMENT IN PUPS

- SOME EVIDENCE AND SOME PERSONAL IDEAS -

- ✓ Prophylaxis
 - Individual start and choice of regimen
 - Low dose, once weekly with escalation strategy avoiding bleeds
 - Multidisciplinary support
 - Shared and informed decision making
- ✓ Choice of concentrate
 - Shared and informed decision making
- ✓ Awareness that
 - ✓ Prophylaxis prevents bleeds and sequelae
 - Most risk factors for inhibitor development cannot be influenced in "real life"
 - Current available clinical data from cohorts on inhibitor development do not include modern (non) factor concentrates
 - Concepts and data needed – as fast as the development of novel therapeutics

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CON3 - SESSION 3 – NON-REPLACEMENT THERAPIES

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Thoughts

- Multiple treatment strategies under investigation
 - Not known which will be licensed
- Trade off between reduced injections, route and fewer (or no) peaks of thrombin
 - How to tailor to life style?
 - Achieving zero bleeds is elusive
- How will treatments be monitored?
 - Does thrombin generation with different treatments mean the same for *in vivo* haemostasis?
 - How to monitor and prescribe combinations of treatment?
- What are the risks of thrombosis and DIC?
 - Treatment of bleeds with FVIII/IX or bypassing agent when inhibitors suppressed or with bispecific antibody
 - Infectious or inflammatory states

Peter Collins

Conclusions

- Haemophilia treatment is likely to be very different in 10 years time
 - How will the best option for each person be established?
 - Haemophilia treatment may require very specialised knowledge of haemostasis
 - More need to centralise in specialist centres
- Beware of unintended consequences
 - Risk benefit ratio depends on significance of "unmet need"
- In non-inhibitor people with haemophilia
 - Current FVIII/IX replacement therapy is very safe and efficacious
 - Higher trough levels are achievable
- Long term outcomes of new treatments may not be known for 20 years



ACH Associació Catalana de l'Hemofília

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3. També s'ha parlat de fisioteràpia, seguiment pacients amb VHC o VIH, covid-19, ajuda humanitària, aspectes psicosocials i com treballar l'adversitat.

INTRODUCTION

- Current physical assessment of people with haemophilia (PWH) focuses on joint structure; less on an individual's ability to perform activities.
- Previous work - 11 activities from The International Classification of Function (ICF) that PWH had most difficulty performing.
- Top 3 activities problematic for PWH were walking long distances, hopping and running.

David Stephensen

„Long-HepC“?

> J Infect Dis. 2016 Dec 15;214(12):1965-1974. doi: 10.1093/infdis/jiw457. Epub 2016 Sep 18.

Direct-Acting Antiviral-Induced Hepatitis C Virus Clearance Does Not Completely Restore the Altered Cytokine and Chemokine Milieu in Patients With Chronic Hepatitis C

Julia Hengst¹, Christine Susanne Falk^{2,3,4}, Verena Schlaphoff¹, Katja Deterting¹, Michael Peter Manns^{1,3,4}, Markus Cornberg^{1,4}, Heiner Wedemeyer^{1,2,3}

- + MAIT Cells: Hengst et al., EJI 2016
- + NK Cells: Strunz et al., Nat Comm 2018
- + gd T cells: Ravens et al., Front Immunol 2018
- + HCV-specific T cells, Aregay et al., J Hepatol 2019
- + post-liver transplantation, Aregay et al., Liver Transplantation 2021
- + unconventional T cells after acute hepatitis C, Du et al., Eur J Immunol 2022

CON1 - SESSION 1 - MULTIDISCIPLINARY EDUCATIONAL SESSION – MTD TEAM'S RESPONSE IN TIMES OF DISASTER/CRISIS

Covid 19 Lessons Identified
Getting ready for the next serious crisis

Petr Pavel

Petr PAVEL, General (ret.) - 2 Feb 2022

SUMMARY ON THE WFH HUMANITARIAN AID PROGRAM

- Started in 1996.
- The largest worldwide humanitarian aid program that channels Clotting factor Concentrates (CFCs).
- Since 1996, donated more than 1,3 billion IU of CFCs.
- Donations reached 110 countries and benefited more than 22,000 patients.
- Witnessed rapid expansion for the last seven years with more donors signing multiyear donation agreements.
- Proved to be vital to countries hit by natural disasters.

Assad Haffar

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4. Els centres de tractament hauran de passar una nova acreditació per ser reconeguts a nivell europeu. Els pacients podrem donar la nostra opinió. EHC i EAHAD serà qui ho liderarà a partir del 2023. Cal veure com ens tindran en compte.

NEW ACCREDITATION OF EUROPEAN HAEMOPHILIA CENTRES

- created by collaboration between **EAHAD** and **EHC**
- driven by the new changing landscape of haemophilia treatment and emerging of new treatment possibilities

- | | |
|--|---|
| 1
New European guidelines for the certification of haemophilia centres | 2
On-site auditing process |
| <ul style="list-style-type: none">• new set of standards• specialized services required to monitor patients receiving new treatments• hub-and-spoke model for gene therapy | <ul style="list-style-type: none">• assesses and improves patient care• creating a culture of quality improvement• offers education to participants |

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AUDIT TEAMS

- multidisciplinary
- include patient representative
- every member will be responsible for her/his speciality
- harmonisation: the auditors will apply the same rule for each centre
- training for the auditors

Ana Boban

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CON6 - SESSION 6 – DELIVERY OF CARE

ON-SITE AUDIT PROCESS

DOCUMENTS REVIEW

- application forms send by the centres
- additional documents and certificates

VISIT TO THE CENTRE

- processes based on the pre-defined quality standards
- multidisciplinary team interviews
- review of facilities
- evaluating patients' satisfaction and involvement in their care

ISSUE OF CERTIFICATE

- producing the report and the feedback to the audited centre

Ana Boban

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CON6 - SESSION 6 – DELIVERY OF CARE

FUTURE IS NOW

- new treatment opportunities are emerging
- treatment outcomes are expected to significantly improve
- new treatment changes call for changes in haemophilia centres
- EAHAD/EHC new Audit and Certification process will help haemophilia centres to be prepared for the next generation of haemophilia treatments

Ana Boban

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5. Actualment hi ha moltes bases de dades i registres per monitoritzar diferents aspectes fins i tot els efectes adversos, com el EUHASS (Vigilància europea de seguretat de l'hemofília)

ON6 - SESSION 6 – DELIVERY OF CARE

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Michael Makris

Start – 1st October 2008

27 European Countries → 92 Haemophilia Centres

Adverse events

- Reported as they occur
- Confirm all events reported every 3 months

Annually

- Patients registered by diagnosis and severity
- Patients treated by product

All inherited bleeding disorders + acquired haemophilia/VWD
All products including platelets, FFP and DDAVP

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EUHASS 2022 Update
European Haemophilia Safety Surveillance (EUHASS)

Michael Makris
Infection, Immunity and Cardiovascular Disease,
University of Sheffield, United Kingdom

- EUHASS activity started 1st October 2008 → its mission is to capture adverse events
- Total patients** registered 2020 are **42,244** and **treated are 10,682**
- Events reported up to 12th January 2022 (TOTAL events: 3734):

- Malignancy:** 833
 - Hepatocellular carcinoma: 169
- Inhibitors** (first occurrence): 602
- Thrombosis:** 327
 - Myocardial infarction: 55
 - FEIBA and Novoseven, concentrates more associated
- Allergic or acute reaction:** 227
 - Anaphylaxis: 35 episodes
- Transfusion transmitted infections (2008 – 2020): 0**
- COVID-19** March-December 2020 (Pre-vaccination)
 - Total number of infected: 253
 - Died 9.5% (24)
 - Acquired Haemophilia/VWD 68.8% (11/16)
 - FXI Deficiency 20% (3/15)
 - Hemophilia A 4.7% (7/149)
 - Hemophilia B 5.7% (2/35)
 - VWD 0
 - Other bleeding disorders 8.3% (1/12)
- Cause of death 2008-2020**
 - Intracranial haemorrhage (ICH): 204/1703 (12%)

Flora Peyvandi

Barcelona, 7 de febrer de 2022