

EUHASS

(European Haemophilia Safety Surveillance)

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Disclosure

- Consultancy: CSL Behring, NovoNordisk
- Travel and honoraria to give lectures: Baxter, Bayer, Biogen, Biotest, Octapharma, Pfizer
- EUHASS financial support from Industry:
Baxter, Bayer, Biotest, CSL Behring, Grifols, Kedrion,
Novo Nordisk, Octapharma, Pfizer, SOBI/Biogen
Partial support: BPL, LFB

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Background: AEs in Haemophilia

- Patients with haemophilia have suffered more from AEs than any other group
- Haemophilia treaters deal with the effects of AEs daily
- Reporting systems have been available for years but are poorly used
- It is not all about inhibitors in PUPs
- It is not all about FVIII replacement therapy

Some Current AE Issues

- Inhibitor in haemophilia A PUPs
 - 2nd vs 3rd generation: PedNet, UKHCDO, FranceCoag vs EUHASS
 - PD vs Recombinant: FranceCoag vs PedNet, EUHASS
- Inhibitors in PTPs
 - Full length vs B-domain deleted
- FXI concentrate thrombogenicity
- Do fibrinogen concentrates cause thrombosis?
- Perioperative FVII concentrate related thrombotic risk
- Product thrombogenicity in 2A von Willebrand disease
- Variant CJD risk with UK cryoprecipitate since fibrinogen concentrate is not licensed for acquired disorders in the UK

EUHASS

(European Haemophilia Safety Surveillance)

- Adverse event surveillance scheme
- European
 - Identical system in Canada (CHES)
- Sentinel centres
- Prospective
- Electronic
- English language
- Started 1st Oct 2008



EUHASS practicalities

- Project lead: M Makris, Project manager: E Gilman
- Data ownership: EAHAD (Professionals organisation) and EHC (Patients organisation)
- IT management: MDSAS Ltd based in Manchester and also supporting UKHCDO and CHESS
- Funding
 - 2008-2011: European Commission (60%) + Industry (40%)
 - 2011-2012: EAHAD
 - 2012-2015: European Commission (60%) + Industry (40%)
 - 2015+ Industry

EUHASS Participating Centres



EUHASS: data on adverse events

Please Select Event Type..



Allergic or Other
Acute Event



Transfusion Transmitted
Infection Event



Inhibitor Event



Thrombosis Event



Malignancy Event



Death Event



Poor Efficacy
Event



Other Possible Adverse
or Unusual Event



EUHASS DATA ENTRY SITE

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My Guide
Please complete the form completely and accurately.
* - Required field
? - Help text
P - Print Page

Inhibitor Event

Please only report inhibitors to EUHASS once you have two positive test results
For help completing this form click [here](#)

Patient Information

* Patient Soundex ? Click image to generate Soundex code

* Patient Age ? Years Months

* Event Date ? Month 2015

* Patient Gender ? ☐ Male ☐ Female

* Patient Diagnosis ? Please Select..

* Patient Factor Level ? Units ? Please Select..

(if <1% please enter as 0)

Event Information

* Is this the first ever inhibitor? ? ☐ Yes ☐ No, reappearance of a previous inhibitor

* Infusion Information: Enter products used in the 3 months prior to the inhibitor detection, starting with the most recent product used before the inhibitor occurred. ?

Product Not in List?

*Product - start with the most recently used product Batch Number:

Please Select..

[Add another batch or product \(+\)](#)

* Please confirm the Last Product Used before inhibitor detection ? Please Select..

* Additional Blood Products ? ☐ Yes ☐ No

* Total Lifetime Exposure Days to any FVIII/IX concentrate ?

* Date of last negative inhibitor test ? OR ☐ No previous inhibitor tests performed

* 1st Positive Level / Date ? /

* 2nd Positive Level / Date ? /

* Assay Used ? Please Select..

* Positive Test Cut-Off ?

Comment ?

[Submit](#)

EUHASS data entry form for inhibitor reporting.

Specific help information for each data point. This is text +/- video guidance

Patients for Surveillance

- Haemophilia A and B – all severities
- All VWD 2, 3 and severe type 1 (<15% VIII:RCo)
- Other coagulation factor deficiencies
- Since 2012:
 - acquired disorders haemophilia and VWD
 - Severe inherited platelet disorders

Data submitted

- Event specific
 - Generic and event specific questions
 - Events reported live when they occur, or
 - 3 monthly
- Cumulative data on surveyed population
 - Annually
 - By diagnosis
 - By clotting factor concentrate

EUHASS: No. of patients at risk



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Please Select Summary..



Total Patients Registered



Patients Treated by
Product

Developed by MDSAS 2008

EUHASS Data: First 5 Years

1 Oct 2008 – 31 Dec 2013

- 78 haemophilia centres
- 26 European countries
- 35,567 patients

EUHASS Patients Under Surveillance

Jan 2013- Dec 2013

	Total	Severe	Concentrate treated during the year
Haemophilia A	15,926	6,750	8,049
Haemophilia B	3,365	1,169	1,525
Other bleeding disorders	16,276	1,989	2,022
Total	35,567	9,908	11,596

Adverse Events Reported

	Year 1-5
Centres reporting	78
Allergic/Acute reactions	113
Transfusion-transmitted infections	0
Inhibitors – first occurrence	259
Inhibitors – recurrence	31
Thrombosis within 30 days of concentrate	73
Thrombosis with no concentrate in 30 days	51
Malignancies	262
Deaths (from any cause)	434
TOTAL	1223

Data checks

- Automatic logic tests at the time of data submission
- Project lead informed live at time of event reporting. Follow-up questions and comments added to events
- Lists of events and at risk patient data sent back to centres to confirm accuracy. Only confirmed results used

Publications

- Background
 - Makris et al. Thrombosis Research 2011; 127 (suppl 2):S22-S25
- Method for PUP inhibitor Analysis
 - Fischer et al. Haemophilia 2012; 18:e241
- Inhibitors in severe PUPs and PTPs
 - Fischer et al. Thrombosis and Haemostasis 2015; 113:968-975
- Inhibitors in moderates and milds
 - Fischer et al. Thrombosis and Haemostasis (in press)
- Overlap between registries
 - Fischer et al. Haemophilia (in press)

Reports

- 3monthly
 - Mainly with lists of events
 - Jan-Mar 2015: Released May 2015
- Annual report
 - With some analysis on rates
- Product specific reports
 - 63 reports issued

EUHASS strengths

- Large
- Prospective
- Simple
- Live reporting at time of event possible
- All bleeding disorders
- All adverse events
- All products
- All European countries

EUHASS weaknesses

- PUP inhibitor rates depend on constant usage
- Limited data collected
- No central testing of inhibitors
- No audit of data by visiting centres
- Anonymous
- Variability in reporting on time
- Not GCP level reporting
- No long term funding
- No efficacy data

Clinical trial product reporting

- Centres participating in clinical trials sign confidentiality agreements that essentially prevent them from reporting adverse events to registries by product name
- EUHASS has a single product category called “Unlicensed Clinical Product”.
- EUHASS does not know the name but collects the event
- Proposal: Allow centres to report adverse events with trial products by name but ask registries not to make this public until a product is licensed

Registry overlap

- So far not a big problem
- We know the centres participating in the different registries and the time the centres participated in the different registries
- Duplicate reporting in EUHASS prevented by soundex coding

From 2014 onwards

- UKHCDO is the UK National registry. Has an adverse event reporting system which is initially identical to EUHASS.
- Any reported event from participating centres gets anonymised and passed electronically to EUHASS
- For any inhibitors the UKHCDO asks for much more detailed information which is not passed onto EUHASS