Haemostasis Registry

A Register to record all off-label use of recombinant activated Factor VII in Australia and New Zealand
Recombinant Activated Factor VII

- rFVIIa, NovoSeven®, eptacog alfa
- FVIIa is a naturally occurring initiator of haemostasis
- approved by TGA for the treatment of spontaneous & surgical bleeding in patients with
  - haemophilia A or B and with antibodies to factor VIII or factor IX
  - Factor VII Deficiency,
  - Glanzmann Thrombasthenia
- Licensed in Australia since 1998
rFVIIa outside Haemophilia

Treatment of traumatic bleeding with recombinant factor VIIa

Gili Kenet, Raphael Walden, Arieh Eldad, Uri Martinowitz

Surgical intervention failed to stop life-threatening bleeding caused by injury complicated by severe coagulopathy. Administration of recombinant factor VIIa immediately corrected the coagulopathy and bleeding stopped.

Lancet 1999;354:1879
‘Investigational Use’ of rFVIIa

- Life-threatening bleeding in patients with coagulation disturbances but without coagulation inhibitors
- Mortality rates of up to 40-60%
- Coagulation disturbances in these patients are multifactorial
- An increased risk of thrombosis is the major potential concern
Registry pre-history

• International voluntary register for off-label use set up by Novo Nordisk
• Highly biased case selection
• High level of suspicion from some clinicians
• No denominator
• Results basically unpublishable
Haemostasis Registry

- 2004 NovoNordisk Australia approaches Monash University DEPM to run Registry
- Funded through unrestricted Educational Grant
- Pilot program begins in Feb 2005 at Alfred Hospital
- Full project launched in May 2005
Aims

**investigate** the safety, efficacy and dosing of rFVIIa in investigational use

**monitor** the extent, indications for, dosages and appropriateness of use

**generate** information to assess cost-effectiveness and to support clinical use

**publish** based on analyses of local experience

**provide** data for physicians, hospitals and Regulatory Authorities
Governance

Steering Committee – meets twice annually

- 2 haematology experts
- 2 company representatives
- 2 registry experts (DEPM)
- Project Manager
- Database Manager
Staff

• Chief Investigator
• Project Manager - Full time
• Administrative Assistant
  – 1 x 0.6
  – 1 x 0.3
• Database Management
• Statistical Advice
How does the Registry work?

Hospital Contacts Registry to indicate interest
⇓
Complete Registry Set-Up Questionnaire
⇓
Ethics Approval
⇓
Begin Data Collection

Approval to collect de-identified data without patient consent
How does the Registry work?

Patient Treated with rFVIIa at hospital

Collect Data

Patients identified through pharmacy or blood bank records

Submit Data

Data entry via web based system
ASP.NET 2.0 + SQL Server

Data Verification

Reimbursement
Web Data Entry

MONASH University
Medicine, Nursing and Health Sciences

HAEMOSTASIS REGISTRY

New Case  Patient  Case Description  rFVIIa Administration  Laboratory Test Result  Replacement Therapy  Other Therapies  Adverse Events  Outcome  Supplementary  Reports & Documents  Logout

Select Patient  ALF - 0001

Changing Login Details
Change Password
Change Email Address
Change Security Question

Haemostasis Registry WEB DATA ENTRY HOME PAGE

This site is intended for data entry by Data collectors in participating Australian and New Zealand Hospitals.

For more information on the Haemostasis Registry Click on our logo ->

Contact Us:
Web Access  Data Manager  Information Systems Manager
M Prukawongsin  03 9903 0167

Project Information  Project Manager
Andrew Hannaford  03 9903 0001

The Haemostasis Registry is based:
Dept of Epidemiology & Preventive Medicine
Central & Eastern Clinical School
Faculty of Medicine,
Nursing & Health Sciences
Monash University

Postal address:
DEPM, Monash University
Alfred Hospital
Melbourne VIC 3004

Delivery address; 3rd floor
Burnet Building (side entrance)
99 Commercial Rd Malb 3004

Logout
### Supplementary Data

- Obstetric
- Cardiac Surgery
- Trauma
- Intracranial Haemorrhage
Data Verification

• Validation on Entry
  – Required Fields
  – Value Ranges
  – Enabling/disabling of dependent fields
  – Warning Messages for Unknown or extreme values
• Validation on Saving
  – Messages for Required Fields and Value Ranges
  – Date Ranges
  – Consistency Checks
• Final Manual Verification
Haemostasis Registry

- Originally envisaged to include 5-6 hospitals
- Participating Hospitals >70
- Includes all States and Territories of Australia and New Zealand
- Public, private, large and small hospitals
- Hospitals commit to provide all cases of rFVIIa use for critical bleeding in their hospital
Participating Hospitals
Audit – Part I

- Reconcile amount purchased with cases reported
- Ensures compliance with “all cases” policy

<table>
<thead>
<tr>
<th>Hospital Name</th>
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<tbody>
<tr>
<td>Date</td>
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<table>
<thead>
<tr>
<th>purchased directly from Novo Nordisk*</th>
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<tbody>
<tr>
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<tr>
<td>received from other hospitals</td>
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<tr>
<td>TOTAL RECEIVED</td>
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<table>
<thead>
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<th>cases reported to date</th>
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<tbody>
<tr>
<td>cases yet to be reported</td>
<td>mg</td>
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<tr>
<td>sent to other hospitals</td>
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</tr>
<tr>
<td>other</td>
<td>mg</td>
</tr>
<tr>
<td>stock on hand</td>
<td>mg</td>
</tr>
<tr>
<td>TOTAL USED</td>
<td>mg</td>
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</tbody>
</table>

I certify that the above information is correct to the best of my knowledge

___________________________ (sign)  Date__/__/__
Audit – Part IIa

Prince of Wales Hospital, Sydney

- Data collected by 2 (sometimes 3) people independently
- Matched and compared
- Numerical fields – high reproducability
- Text fields – essence similar but depend somewhat on understanding
Audit – Part IIb

- Randomly Selected
- Hospitals with >20 cases, 5% of cases
- Hospitals with <20 cases grouped and 5% of total randomly selected
- Data re-collected by Registry Staff directly from case notes
Collaboration with ASCTS

Cardiac Surgery
HR only collects ‘cases’, not controls
Looking at ASCTS to provide comparison
1. Baseline data
2. Matched Case/Control series
## 1. Baseline data

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<tr>
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<th>ASCTS</th>
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<tr>
<td>Stroke</td>
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<td>2.48</td>
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<td></td>
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<td>PE</td>
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<tr>
<td>MI</td>
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<td>0.73</td>
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<tr>
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<td>1.10</td>
<td>N.S.</td>
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</tbody>
</table>
2. Matched Case/Control Series

525 HR Cases ~ 14,000 ASCTS cases

Matching for procedure type, gender, urgency and ± 5 years of age

HR cases match with 0 and 2698 ASCTS cases
Communication with Stakeholders

Newsletters and emails
Communication

Hospital Data Report

Twice annually
+ Annual progress report
Conferences

Initial emphasis on recruitment and meeting people

Now based on communication of results
Recombinant Activated Factor VII in cardiac surgery: experience from the Australian and New Zealand Haemostasis Register
Strengths and Limitations

- Largest numbers of cases in all therapeutic areas in the world
- Collecting data on entire population
- High level of interest from local investigators
- Lack of Controls
- Missing data – especially lab results
- Some sub-groups have small numbers
Future Directions

• Obstetric publication
• Liver subcommittee
• More matching with other databases, eg trauma?
• More hospitals, more data