Registries as a source of Real World Evidence (RWE)

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Disclaimer

The views expressed are those of the speaker and should not be taken to represent the views of IQVIA or its related companies.

The views expressed should not be taken to represent the views of my former employer: the European Medicines Agency.
• Definition of a registry
• Different types of registries
• What evidence are we trying to generate?
• Use of registries throughout the product life-span
• EMA’s registry initiatives
It’s not listed on their registry, but have you considered a sesame seed toaster?
Registry

An organised system that uses observational methods to collect uniform data on specified outcomes in a population defined by a particular disease, condition or exposure.

A patient registry is an organised system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes.

Annex 1 to GVP: Definitions  EMA/876333/2011 (rev.4)

AHRQ - Registries for evaluating Patient Outcomes: A user’s guide
Registries – the big, the small and the ugly
Classification of registries

• Product registries

• Disease registries

• Procedure or health services registries
  ≈ Event
Data types in a registry

Entry point

Disease
Drug
Device
Event

Identifier/contact
Demographics
Relevant Medical history

Patient data

Prescriptions
Confounders
Other

Outcomes
Registry as a core for scientific research

<table>
<thead>
<tr>
<th>Core clinical data from HCPs</th>
<th>Core PRO</th>
<th>Additional study or centre clinical data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centre 1</td>
<td></td>
<td>Yellow</td>
</tr>
<tr>
<td>Centre 2</td>
<td></td>
<td>Green</td>
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<tr>
<td>Centre 3</td>
<td></td>
<td>Red</td>
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<td>Centre 4</td>
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<td>Yellow</td>
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<td>Centre 5</td>
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<td>Centre 6</td>
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<td>Yellow</td>
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<tr>
<td>Centre 7</td>
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<td>Green</td>
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<tr>
<td>Centre n</td>
<td></td>
<td>Blue</td>
</tr>
</tbody>
</table>

- Yellow: Extra data collected by centres with patients enrolled in clinical trial 1
- Green: Extra data collected by centres with patients enrolled in clinical trial 2
- Red: Extra data collected by centres with patients enrolled in PASS
- Blue: Extra data collected by physician with own research programme
ALL ANIMALS ARE EQUAL
BUT SOME ANIMALS ARE MORE EQUAL THAN OTHERS

George Orwell
1945
Evidence
Why do we need evidence?
Who makes which decisions?

- Shall I authorise this drug? Which indication?
- Shall I prescribe this drug? Which patients? For how long?
- Shall I take this drug? What are the alternatives? What are the side effects?
- Does this drug offer good value for money? How does it compare with other treatments?
Different stakeholders need different evidence!
Use of registries
### Uses of registries for evidence generation: early

<table>
<thead>
<tr>
<th></th>
<th>Regulator</th>
<th>HTA body/ Payer</th>
<th>Provider</th>
<th>Patient</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease epidemiology</td>
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<td>X</td>
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<td>X</td>
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<tr>
<td>Patient journey</td>
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<td>Existing treatments</td>
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<tr>
<td>Unmet medical need</td>
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<td>Identify biomarkers</td>
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<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Burden of disease</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Resource use</td>
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<tr>
<td>Co-morbidities</td>
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</tbody>
</table>
Use of registry data to get information on disease epidemiology

• Who gets this disease?
  • Demographics
  • Are there variants of the disease – eg spinal muscular atrophy

• What are the risk factors/causes for this disease?
  • Different genetic mutations,
  • Hypertension, hyperlipidaemia etc for Myocardial Infarction

• What is the natural history of the disease?
  • Relapsing/remitting
  • Progressive
  • Moving between degrees of severity (eg critical limb ischaemia)
# Use of registry data as external comparator in initial EU MA

<table>
<thead>
<tr>
<th>Situation</th>
<th>Procedure</th>
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</thead>
<tbody>
<tr>
<td>Metastatic Merkel Cell Carcinoma (MCC)</td>
<td>Initial marketing authorisation for avelumab</td>
</tr>
</tbody>
</table>

## Issue

RCT not possible

## Data

88 patients from a Phase II single arm open label study of avelumab compared with retrospective data from 20 patients in a US Oncology network and 34 patients in a EU MCC Registry undergoing chemotherapy.

## Results

Overall estimated mean survival for 2nd line avelumab was 12.9 months. Overall median survival was 4.4 months US vs 5.3 months EU for 2nd+ line chemotherapy. BOR for 1st line avelumab was 71.4%. BOR for 1st line chemo was 31.3% US vs 29.4% EU.

## Outcome

“Taking into account the intrinsic limitation of single arm studies, the rarity of the disease and the challenges to compare the results with data from historical controls and in the literature, the currently available data are deemed to support the efficacy of avelumab in both pre-treated and chemotherapy-naïve patients.”
### Uses of registries for evidence generation: later

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</tr>
</thead>
<tbody>
<tr>
<td>Drug utilisation</td>
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<tr>
<td>Long term f/u outcomes</td>
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<td>Overall effectiveness</td>
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<tr>
<td>effectiveness/efficacy</td>
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<tr>
<td>Identification of adrs</td>
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<tr>
<td>Identification of risk factors for</td>
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<tr>
<td>adrs</td>
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</table>
# Studies required by EMA for gene therapy products

<table>
<thead>
<tr>
<th>Name</th>
<th>Date authorised</th>
<th>Indication</th>
<th>Vector</th>
<th>Studies</th>
<th>Final report date</th>
</tr>
</thead>
</table>
| Glybera               | 25/10/2012 (expired) | Adult patients with familial LPLD, confirmed by genetic testing, with detectable levels of LPL protein suffering from severe or multiple pancreatitis despite fat restriction | AAV1 + CMV promotor, woodchuck hepatitis post transcriptional regulatory element + AAV2 | 1. LPLD registry (cat 1) (+ untreated patients)  
2. Assessment of immune response at baseline, 6 months and 12 months in a clinical study (cat 3)  
3. Clinical study to provide chylomicron metabolism data in 12 new patients and healthy volunteers (cat 3)  
4. LTFU of study CT-AMT-011-01 | Dec 2017  
Not stated  
Rolled over into registry at end of trial. |
| Strimvelis            | 26/05/2016           | Rx of patients with ADA-SCID for whom no suitable HLA-matched stem cell donor is available. | Replication deficient gama-retroviral vector | 1. Registry (cat 1) of patients treated with Strimvelis  
2. LTFU of patients from study AD115611 (cat 3) (patients also being rolled over into registry)  
3. Effectiveness of educational material (cat 3)  
4. Methodology to investigate retroviral insertion site analysis (cat 3) | Q4 2037*  
Q1 2020  
Q1 2021  
Q4 2024 |
| Luxturna              | 22/11/2018           |  |  | 1. Non-interventional PASS in disease registry of patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic RPE65 mutations (cat 1)  
2. 15 year follow up of patients in the clinical programme (cat 1) | 30 June 2030  
31 Dec 2031 |

LPLD = lipoprotein lipase deficiency; ADA-SCID = adenosine deaminase deficiency severe combined immunodeficiency; LTFU = long term follow-up
European Medicines Agency Registry Initiatives
EMA initiative on patient registries

Launched September 2015

**Aim:** To provide an adequate source of post-authorisation data for regulatory decision making
- To make better use of existing registries
- Facilitate the establishment of high quality new registries if no suitable existing ones

**Actions:** Inventory of patient registries
- Cross Committee task force
- Patient Registries workshop
- Disease specific workshops
  - Haemophilia
  - Chimeric antigen receptor (CAR) T-cell therapy
  - Multiple sclerosis
  - Cystic fibrosis
EMA Inventory of Registries

http://www.encepp.eu/
Finding registries in the ENCePP Resources Database
Orphanet: Rare disease registries in Europe

- 7000+ rare diseases
- 747 rare disease registries in the EU +
- 686 rare diseases included

### Affiliation

- Public
- Private not for profit
- Private for profit
- Not defined

https://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf
Conclusions

• Registries are an organised system that use observational methods to collect uniform data on specified outcomes in a population defined by a particular disease, condition or exposure.

• The most common types are disease or product registries

• They can vary in size, complexity and geographical location

• They are designed for a specific research purpose

• To be useful, the data need to be of sufficient quality and to contain the data elements of interest.

• They have multiple uses both pre- and post-authorisation