Rare diseases and orphan drugs: The HTA perspective

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Disclaimer

The views presented here are my own and should not be considered the views of NoMA, EMA or all HTAs in general.
What makes XXXX so special?

• XXXX can be:
  • Small populations
  • ATMPs
  • Orphan drugs (COMP)
  • Personalized medicine
  • Histology independent (agnostic)
What makes small populations so special?

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- The robustness of evidence required by regulators / health technology assessing agencies

- Unless a deviation is agreed on beforehand by all stakeholders, the gold standard for drug approval is still the randomized clinical trial (RCT)
The gold standard, the RCT

Might not be considered feasible due to

• Size of the population
• Inability to measure a ‘relevant’ outcome
• Ethical concerns
• Time required to run such trials
• Ability to fill evidence gaps
Notat 13.12.2017

Ordning for hurtig metodevurdering av legemidler for særskilt små pasientgrupper med svært alvorlig tilstand

Gyldig fra 01.01.2018
How Norway plans to handle small populations

• Rare is not a criterion in itself, it is the context that is relevant

• The requirements regarding the quality of effect documentation can be lowered

• The willingness to pay might be higher than usual
  • Global prevalence of 1/100 000 + less than 50 patients in Norway
  • Absolute shortfall of ~30 QALYs
  • Expected gain of at least 2 QALYs
Why is what is good enough for approval not good enough for reimbursement?
Healthcare Technology Assessment (HTA)

- is the **systematic evaluation** of the **properties, effects, and/or impacts** of health technology.

**Purpose** - to address the **direct, indirect, intended, and unintended benefits and consequences of the adoption of healthcare technology**.

-Hailey, Babidge, Cameron, & Davignon 2010
Benefit/Risk versus Cost-effectiveness

• RCT

Efficacy
Does it work in experimental setting
Population selected
Placebo or a selected comparator

• Real world

Effectiveness
How does it work in medical practice
Patients as they come
Many alternative treatments
Models to ‘predict’ the future

• All models are wrong; some models are useful
  George E. P. Box; Norman R. Draper (1987)
Models to ‘predict’ the future

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• Health economic models predict the future based on available data from different sources
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HTA: the basics

• The aim is to maximize the health of the total population within the given budget
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Choice

A  Costs  Outcomes  (benefits/consequences)

B  Costs  Outcomes  (benefits/consequences)

Economic evaluation

‘the comparative analysis of alternative courses of action in terms of both their costs and consequences’

(Drummond McGuire, 2001)

ICER =  Incremental costs (A-B)  Incremental benefit (A-B)
Data, we need data..........................
Data, we need data..................

• Nope not this guy but
Data, we need data

- Nope not this guy but
- Robust comparative (randomized) data
- Cost utility analysis require even better data
  - To run a lifetime horizon model extrapolations is almost always required
  - Transition probabilities between health states must be informed by enough data
Data, we need data

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• Robust comparative (randomized) data
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  • And we need utility, safety and QoL data
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  • And we need utility, safety and QoL data

• We need to talk!
Advanced Therapy Medicinal Products for Rare Diseases: State of Play of Incentives Supporting Development in Europe

Andreas M. Farkas¹, Segundo Mariz¹, Violeta Stoyanova-Beninska²,³, Patrick Celis¹, Spiros Vamvakas¹, Kristina Larsson¹ and Bruno Sepodes³,⁴★

Who develops ATMPs
Do they talk to EMA / HTAs?

- Yes: 29.8%
- No: 70.2%
Marketing authorisation of orphan medicines in Europe from 2000 to 2013

Matthias P. Hofer¹, Hanna Hedman¹, Maria Mavris¹, Franz Koenig², Thorsten Vetter¹, Martin Posch², Spiros Vamvakas¹, Jan Regnstrom¹ and Stiina Aarum¹

¹ European Medicines Agency, 30 Churchill Place, Canary Wharf, London E14 5 EU, UK
² Center for Medical Statistics, Informatics, and Intelligent Systems, Section for Medical Statistics, Medical University Vienna, Spitalgasse 23, 1090 Vienna, Austria
FIGURE 2
The uptake of scientific advice (in percentage) over time for orphan marketing authorisation applications (blue) versus non-orphan marketing authorisation applications (red).

<table>
<thead>
<tr>
<th>Year</th>
<th>SA Submission</th>
<th>SA Assessment</th>
<th>MAA Assessment</th>
<th>MAA Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006–2009</td>
<td>62/149</td>
<td>74</td>
<td>4</td>
<td>Positive</td>
</tr>
<tr>
<td>2010–2013</td>
<td>74/168</td>
<td>37/44</td>
<td>9</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>37/64</td>
<td>95</td>
<td>13</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Total N=51

Acceptable N=18 (35%)
Compliant N=17 (94%)
Not acceptable N=33 (65%)
Compliant N=17 (52%)
Non compliant N=16 (48%)
Positive N=13 (76%)
Negative N=4 (24%)
Positive N=13 (76%)
Negative N=4 (24%)
Positive N=3 (19%)
Negative N=13 (81%)
Development of archetypes for non-ranking classification and comparison of European National Health Technology Assessment systems

Nicola Allen, Franz Pichler, Tina Wang, Sundip Patel, Sam Salek

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b Centre for Innovation in Regulatory Science (formerly EMR International Institute for Regulatory Science), Hatton Garden, London EC1N 8JS, UK
c FRS LSE and Company, Elwood Manor, Winkfield, Slough, SL2 6YH, UK
3 Collaboration between regulators, HTAs and payers

The regulation and assessment of medicines can no longer be carried out in isolation. Strong collaboration between regulators, HTA bodies and payers can boost medicine development and facilitate an early and affordable access for patients to innovative treatments. Chantal Bélongey, Ad Schuurman and Michael Berntgen discuss the challenges and benefits of fostering mutual understanding among decision-makers.
Scientific advice and protocol assistance requests received - subset special programmes

- **Requests for parallel SA and protocol assistance with international regulators**
- **Requests for joint SA and protocol assistance with HTA**
- **Scientific advice for PRIME products**
- **Requests for qualification of novel methodologies**