Safety Analyses: The Cinderella of Biostatistics?

Impulse presentation
EFSPI 11th Statistical Leaders Meeting, 2020-07-23

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This session is a reflection and advertisement on the safety statistics in our day-to-day work.
What comes into your mind if you think about Statistics in Pharma

1. Efficacy?

2. Safety?

it's all about benefit / risk!
How present is Safety in our thinking?

**ICH E9 (R1)**

Let's take the new ICH E9 (R1) Addendum on Estimands and Sensitivity analysis in clinical trials as an example

Is this an Efficacy or an Safety Guideline, or both?

- Hits when searching for **effect, efficacy, safety, and risk**

  - 3 * safety/risk
  - 4 * efficacy
  - 46 * treatment effect

=> Efficacy only?

What came into your mind?

I must admit, my first association was efficacy, but treatment effect is both, isn’t it?

By the way the first sentence reads: "To properly inform decision making by ... clear descriptions of the **benefits and risks of a treatment** (medicine) for a given medical condition should be made available"
How present is Safety in our thinking
EMA Benefit-Risk project

Who knows about the EMA Benefit-Risk project?

Benefit-risk methodology

The European Medicines Agency's opinions are based on balancing the desired effects or 'benefits' of a medicine against its undesired effects or 'risks'. The Agency can recommend the authorisation of a medicine whose benefits are judged to be greater than its risks. In contrast, a medicine whose risks outweigh its benefits cannot be recommended for marketing.

Weighing up the benefits and risks of a medicine is a complex process, since it involves a large amount of data. In addition, there is always some uncertainty around the actual risks of a medicine, because they can only be determined by looking at the information available at a given point in time.

The project consisted of five 'work packages':

<table>
<thead>
<tr>
<th>Work package</th>
<th>Status</th>
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<tr>
<td>1. Describing the benefit-risk assessment models already being used in the European Union's regulatory network</td>
<td>Completed March 2010</td>
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<td>2. Assessing the suitability of the current tools and processes used in benefit-risk assessments</td>
<td>Completed August 2010</td>
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<td>3. Field-testing the most appropriate models in five European medicine regulatory agencies</td>
<td>Completed June 2011</td>
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<tr>
<td>4. Refining the most suitable models for use in medicines regulation to create a new benefit-risk tool</td>
<td>Completed February 2012</td>
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<td>5. Training European assessors to use the final tool</td>
<td>Started March 2012</td>
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Focus we give Safety

Example Visualisation - ASCO

- 42,500 attendees in 2019 to the Annual Meeting
- I would guess 99.9% of all presentations display efficacy using graphics for visualisation & 83.4% of all presentations display safety as tables only (and sometimes related AEs only)
Focus we give Safety Recognition

- During a submission - who is the star
  - the efficacy stats?
  - the safety stats?

- Moving to safety statistics – how might this be perceived
  - climbing up the job ladder?
  - put on the sideline?

- Do we recognise that for safety statistics a special skill set is needed?

- When do we start to think about safety in drug development
  - when writing the ISS SAP?
  - just after first patient in, e.g. we support the risk management plan early?

- What do we do when a new safety finding is recognised
  - throw the messenger into the dungeon?
  - congratulate the messenger that we have identify the risk early?
For reflection

- What is the value of safety analysis in your company?
- What is the value you give safety when communicating with your team?
- What is the resourcing provided on safety (stats & programming)?
- What is your view on the need of a special skill set?
- What is the complexity of safety analyses (prg & stats) compared to efficacy analyses?
- What is the data source your team is using for safety assessment?