EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update from EMA Workshop on extrapolation of efficacy in children

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Presented by Andrew Thomson on 3 June 2016
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Background

Draft Reflection Paper published 1st April

Workshop took place 17th – 18th May

Aim is to upgrade from draft status the Reflection Paper taking on board comments from stakeholders

Will open for consultation once the draft is finalised

Workshop aimed to:

- Explain the RP to those attending
- See if the concept ‘made sense’ to developers, by using case studies

Setting the scene

Opening remarks and the setting of the scene

Presentations from modellers, statisticians, clinicians, on their general views on the Reflection Paper, both regulators and industry

Early degree of harmony across disciplines with the need for this paper, that the scope was sufficient (for now), and that it could, in general, be workable

Presentations on summarising data and how to go about this, and interpret the summaries

Update from 3 FP7 funded projects and the types of questions that are being answered that may be useful for extrapolation

Case Studies (1)

Everolimus

Ongoing study with real difficulty in recruiting patients

Fundamental problem in comparing Adult & Paediatric data for liver transplantation - everolimus treatment is initiated 1.5 – 6 months after transplantation in children, whereas it is initiated 1 month after in adults. Risk of transplant rejection is lower in general. Model used to make comparisons as similar as possible

Also looked at kidney transplantation, where a network-meta analysis was performed to try and understand how the treatment fitted in with the totality of knowledge in the literature

Case Studies (2)

Macitentan (PAH) – How to leverage knowledge from registry data by building a Bayesian model that was acceptable to all health authorities

Ultimately decided on a more traditional approach but presentation highlighted the steps went through to look at the different design options and come up with the

Golimumab (in UC) – How to go about building a structure to understand the dose required in different age ranges, and to leverage adult data as well as paediatric data in other conditions

Cimzia (in JIA) – how to design a programme that did not require efficacy, nor a PK study, but a PD study with some PK measurements at an interim analysis to confirm dosing

Case Studies (3)

- Leviracetam (Briviact) Lots of data, knowledge of other compounds, MoA, etc. Final package included:
- PK modelling but no dose-finding study in children, no intravenous PK study in children
- Paediatric dose adaptations to support application for new indications
- 1 PK and safety study in children 1 month – 16 years, with no placebo group
- Long-term safety follow-up
- PK/PD modelling allowed extrapolation of efficacy from adults: no pivotal efficacy study

Questions still unanswered – further work to do

- In what situations can we say we do not need any more efficacy data, and can rely on paediatric PK, adult efficacy, and modelling alone?
- When a reduced efficacy data package is agreed upon, how do we decide how much efficacy data is enough?
- How can we construct a Bayesian prior distribution for (age-specific) paediatric efficacy from adult efficacy, paediatric PK and modelling
- How can we use and interpret this information?

Next Steps

- Reflect on the outputs and decide on the updates to the draft RP:
  - Multidisciplinary across modellers, statisticians and clinicians (at various committees)
- Finalise and publish for consultation envisaged Q3 2016
- Formal consultation period open as per usual – length TBC
- Collect case studies using the framework to build body of evidence as to how it is working in practice
- Update RP into full ,final version, based on comments received during consultation and experience gained as well.

Thank you for your attention

Further information

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