The importance of D-E-R characterisation in dose selection, labelling and B/R

Children

EMA EFPIA workshop on the importance of dose finding and dose selection for the successful development, licensing and lifecycle management of medicinal products

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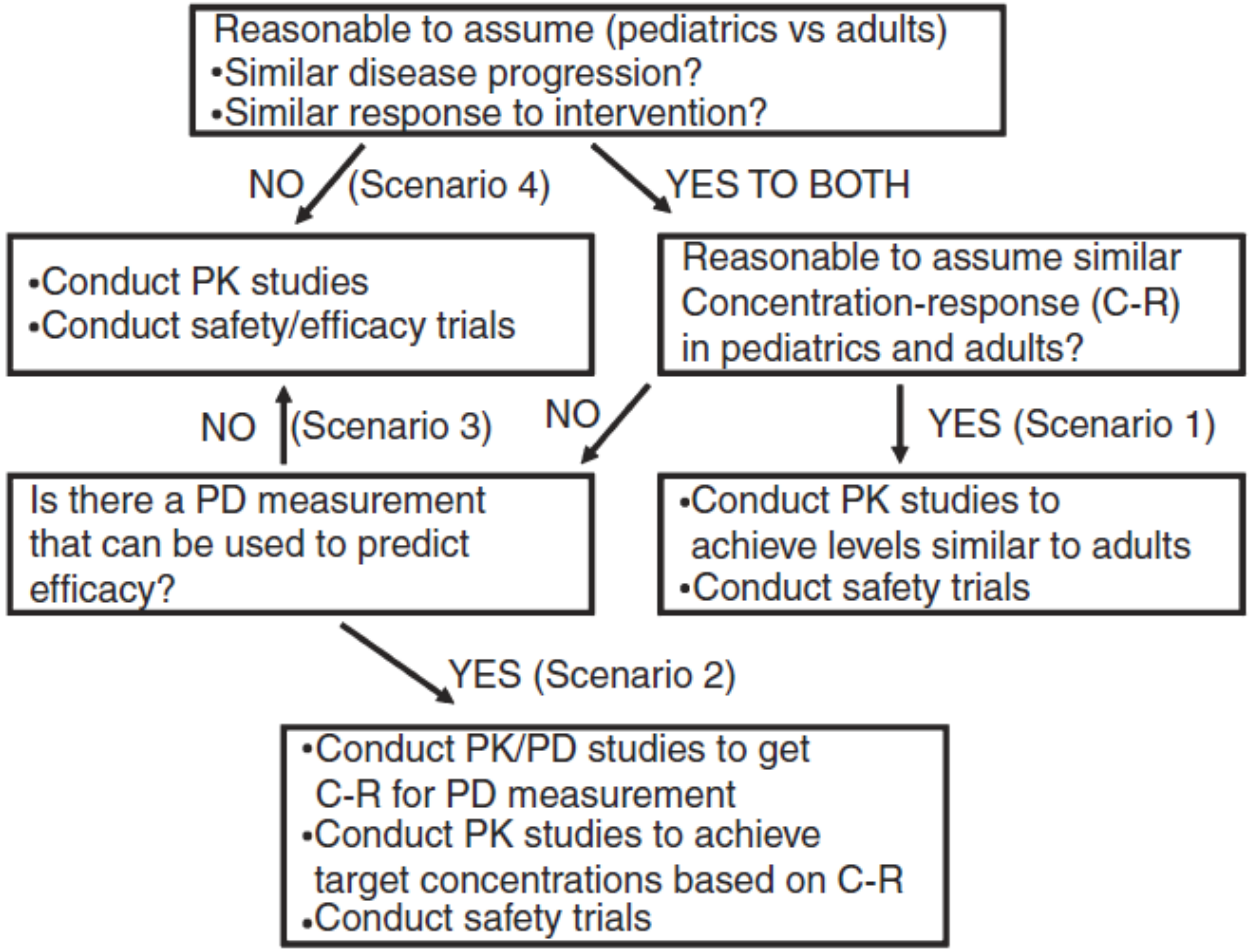
Pediatric study decision tree



Manolis et al. 2011

Pre-requisite

- Knowledge of the D-E-R in adults
  - Might not be well understood at the time of the PIP development
  - Case of pediatric specific drugs

Maximising the D-E-R knowledge

- Use of all available knowledge
  - What should be included for extrapolation
- Same class of drug
  - Possibility to share models and go for simpler study
- Use of pre-clinical models
  - How much weighting ?
- Flat D-E-R

Facing the reality of enrollement difficulty (1/2)

- Standard study design for all countries
- How regulators can support industry in recruitment difficulty
- Guidance on the number of subject
  - is Wang et al. paper enough ?
  - how much safety is needed ?
- Integrated Ph I-II-III study (study combining PK and safety)

Facing the reality of enrollement difficulty (2/2)

- Acceptance of innovative design based on M&S, adaptive design using:
  - Efficacy
  - Safety
  - Pharmacokinetics
- Is a full D-E-R characterisation needed ?
- Group specifities
  - Are adolescents part of pediatric population
- Conduct an open-label safety study in a pediatric population*
  - DB is cleanest to show efficacy and safety
  - Not many subjects to enroll
  - How ethical is to expose limited population to placebo
  - Increases safety database
  - Virtual comparison (simulations) of drug and placebo (disease progression model) as in DB study

Berde CB et al. 2012

Open questions

- How can we ensure that we don’t miss the opportunity to make the adult development data also useful for paediatric development ?
- How to ensure a state of the art paediatric development ?
  - In phase with recruitment reality
- How do we best support the generation of system data ?