Medicines for Paediatric liver disease – overview of current paediatric investigation plans
Paediatric investigation plans (PIPs)

- Mandated by the EU paediatric regulation
- Early in development
- Must include studies considered necessary for authorisation in children (quality, non-clinical, clinical)
- **Paediatric Committee** (PDCO) decides on need and significant therapeutic benefit
- Regular Paediatric Cluster meetings to discuss development plans with international regulatory bodies incl. FDA.
How does the Paediatric Committee (PDCO) decide on a PIP?

- PDCO composed of clinicians, regulators (paediatricians and assessors experienced with paed medicines), representatives of patient organisations and healthcare professionals
- Submission of proposal by applicant at early stage of drug development
- Guidelines (clinical, regulatory)
- Previous decisions
- Interaction with stakeholders (patients, academia, other regulators)
- Unmet need/significant therapeutic benefit
- PDCO/EMA adopts an opinion and final decision outlining the paediatric development and defining key elements of the studies included.
Paediatric liver diseases

Cholestatic disease PIPs agreed:

- **PFIC** (2)
- **Biliary atresia** (2)
- **Alagille syndrome** (1)
- **PSC** (3)

Waivers in

- **PBC** (5)

*In comparison: 14 PIPs in Non-alcoholic steatohepatitis and many in the pipeline*
PDCO current approach

Waivers:
Usually development from birth (e.g. Alagille, BA, PFIC)

Quality:
Development of age appropriate formulations

Non-clinical:
Juvenile toxicity studies in some cases
PDCO current approach

Clinical

• Placebo controlled
• PK (either separately or as part of main study) in addition to safety and efficacy
• Primary endpoint:
  • Can be change in serum bile acids or events such as alive with native liver
  • Sentinel events (ascites, bleeding oesophageal varices etc.)
• Study duration: from 12 months to 96 weeks
PDCO current approach

Difficulties encountered:

- Absence of validated, surrogate endpoints; events such as liver transplantation may need long studies
- Correlation of endpoints such as reduction in bile acids to meaningful events for patients
- Rare diseases
- Competing programmes
- Differences in clinical management across regions
Thank you for your attention

Further information

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