EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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

Presented by Chrissi Pallidis on 19 March 2021
European Medicines Agency – Paediatric Medicines Office

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

chrissi.pallidis@ema.europa.eu

European Medicines Agency
Domenico Scarlattilaan 6 | 1083 HS Amsterdam | The Netherlands
Send a question via our website www.ema.europa.eu/contact

Follow us on **@EMA_News**