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Medicines for Paediatric NASH – overview of current paediatric investigation plans

Presented by Chrissi Pallidis on 3 December 2018
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Paediatric NASH

- Incidence rising
- No licensed pharmacotherapy
- Need for effective and safe treatments
- Many new medicines in the pipeline

- How can we optimise development in children?

Paediatric NASH - differences

Histopathological differences:

-Type 1 (adult pattern) – steatosis with ballooning degeneration and lobular inflammation, with or without perisinusoidal fibrosis and without portal inflammation 17%

-Type 2 – macrovesicular hepatocellular steatosis with portal inflammation, with or without portal fibrosis in the absence of ballooning degeneration and perisunusoidal fibrosis 51%

Schwimmer et al

Agreed Paediatric Investigation Plans

- Elafibranor
- Simtuzumab
- Obeticholic acid
- GS-0976
- Selonsertib
- Cenicriviroc

3 additional procedures under discussion

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Waivers:

Mostly below 2 years, some below 8 years

Quality:

Development of age appropriate formulations

Non-clinical:

Juvenile toxicity studies in some cases

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Clinical

- Double-blind, placebo-controlled
- PK (either separately or as part of main study) in addition to safety and efficacy
- Primary endpoint: Proportion of subjects with fibrosis improvement (≥1-stage improvement in NASH CRN) with no worsening of NASH (defined as ≥1-point increase in hepatocellular ballooning or lobular inflammation)
- Secondary endpoints: liver biomarkers, incidence of liver-related clinical outcomes, assessment of liver fat by MRI, MR Spectroscopy, ultrasound
- Study duration: 12 months but also 88 weeks, 96 weeks

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Separate studies for 2 to <8 year olds in most PIPs

Deferred and to be conducted after studies in older children

Issues for discussion

- Age of patients in clinical studies?
- Endpoints – possibility of non-invasive methods of assessment?
- Optimal duration of studies?
- Extrapolation from adults?

Thank you for your attention

Further information

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