Experience from the DEEP trial

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I THOUGHT YOU BROUGHT THE PROVISIONS!!

LEAVE LEAVE LEAVE LEAVE
Deferiprone (DFP)

• Oral iron chelator drug
• Requires three or four times daily dosing for adequate 24 hr. drug levels
• Wide experience of DFP in patients with iron overload (specifically thalassaemia)
• Limited data are available for younger children
• DFP still approved only for second line treatment.
Context

• Additional data on DFP included by the Paediatric Committee at the EMA in the 2009 PDCO Priority List

• An independent research Consortium (DEEP-Deferiprone Evaluation in Paediatrics) funded under the FP7 Framework Research program “HEALTH-2010.4.2-1: Off-patent medicines for children”.
Main objective

• To undertake a multicentre, randomised, open label, non-inferiority active-controlled trial to evaluate the efficacy and safety of deferiprone compared to deferasirox in paediatric patients aged from 1 month to less than 18 years affected by transfusion dependent haemoglobinopathies.” (EudraCT:2012-000353-31)
Components

- Pharmacokinetic study in children (DEEP 1)
- RCT comparing deferiprone with the other licensed oral chelator, deferasirox (DEEP-2)
- 3 yr. retrospective and prospective Phase 4 safety study of deferiprone in children (DEEP 3)
Novel aspects

- Pharmacokinetic study in children age <6 yrs. before inclusion in DEEP 2
- Evaluation of chelator safety and efficacy in very young children (<2 yrs. old)
- Use of oral chelators as first line therapy in chelation-naïve patients
- Using composite primary end point of iron overload (serum ferritin and myocardial iron T2*)
- Health care utilization and QOL assessment incorporated to enable HTA assessment
Challenges-EU and non-EU countries

• Varying national and local requirements and delays in obtaining trial authorizations
• Timeliness of recruitment
• Centralization of sample analysis
• Trial monitoring in very different health care settings across EU and Mediterranean
Achievements

• Development of a consortium of specialist centres treating transfusion-dependent anaemia

• Collaboration with pharmaceutical company (Apopharma) in developing a new liquid formulation for paediatric use

• Collaboration with Resonance Health in use of standardised and centralised MRI protocols for measuring iron overload (Liver and myocardial iron)
Outcomes so far

- PK study (DEEP-1) shows comparable pharmacokinetics in children age <6 and older subjects, justifying standard mg/kg dosing across all age ranges
- Recruitment target met - 21 centres, 393 patients randomized
- At the end of October 2016, 113 patients have successfully completed the study as per protocol and further 221 patients are in treatment with one of the two IMPs.
Experience in the UK: Set-up

- REC and NHS R and D authorizations
- Redrafting of patient information sheets, consent and assent forms
- Local institutional contract with sponsor
- DEEP adopted onto NHS CRN portfolio
- Approximately 15 centres approached, 4 agreed to participate
Conducting the DEEP-2 trial

- Recruitment at our centre was quite easy and we met recruitment target by Aug 2016
- Two of four centres did not recruit
- With adoption on the NIHR Clinical trials portfolio we were able to utilize paediatric clinical trials infrastructure (nurses, administration, radiology support)
Problems

- Very time consuming for PI
- Staffing – three dedicated nurses at our site alone
- Funding- contract does not cover actual costs of activity
- Trial protocol too detailed, resulting in multiple protocol violations not relevant to end points
- Trial monitoring- rather unpredictable and erratic
Overall reflections

• Oral medication three times daily was challenging for school-age children
• Participation in a clinical trial helps with long-term management of adherence to medication
• Useful experience for design of future trials in this patient group, and collaboration with international centres
Thank you

CVBF
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European Network of Excellence for Paediatric Clinical Research