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CONCLUSIONS

Participants:

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1. Ulcerative colitis (UC) and Crohn's disease (CD) are separate conditions with distinct clinical symptoms, treatment algorithms and probably genetic background and underlying pathology. As the consequence separate clinical trials are needed for each of these conditions.

2. Patients with indeterminate colitis (IC) should not be included into clinical trials for UC or CD.

3. The concept of overarching condition for PIP (inflammatory bowel disease, IBD) including UC, CD and IC needs to be further discussed. The advantages of such concept (simultaneous development of treatment for all IBD patients, common nonclinical and PK studies) were recognised.

4. Development of biologics for treatment of IBD in children should not mirror adult development. Clinical trials in children need to be designed specifically for paediatric population.

5. Randomised active comparator controlled studies are scientifically most preferable but hardly feasible. If selected, current standard of care for UC and CD should be used as active comparator. This needs to be updated for each disease before clinical trial.

6. Currently biologics can be recommended as the second line treatment only. Studies indentifying the population of patients that might benefit from biologics used as first treatment need to be performed. Markers allowing prediction of treatment response have to be actively looked for in clinical trials.

7. Mucosal healing is considered most appropriate primary end point for evaluation of efficacy in both UC and CD. Clinical scores (PCDAI and PUCAI) need to be evaluated simultaneously as secondary end points. Feasibility difficulties with need for repeated endoscopy need to be

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addressed (expected drop-outs in the calculation of size of study population, careful explanation given to patients and parents, limiting number of endoscopies to two or three…).

8. Extrapolation of efficacy and safety from adult studies is limited. It may be clear in extreme situations (lack of efficacy, poor safety profile, or very good efficacy and excellent safety in adults). However in most cases separate studies in children are needed. When efficacy studies are not feasible in children, the analysis of extrapolation of efficacy from adults must be performed to support paediatric development.

9. Long-term safety has to be studied always in children treated with immunomodulating substances, especially biologics. Whenever feasible patient registries should be used. Long-term follow-up should focus on occurrence of infections, autoimmune diseases and malignancies.

10. Positive experience of Paediatric Rheumatology International Trials Organisation (PRINTO) might serve as an inspiration for paediatric gastroenterology in development of international outcome measures, the design and management of clinical trials and patient registry and building of an international community for research in rare diseases.

11. PRINTO in collaboration with the Pediatric Rheumatology European Society (PRES) is currently implementing a worldwide pharmacovigilance project funded by the FP7 (Pharmachild) for children with juvenile idiopathic arthritis (JIA) treated with biologics ± methotrexate. PRINTO is willing to share the safety component of its technological web based platform with the gastroenterologists.