SUPPLEMENTARY FILE 1 | PICO search questions per working group

**WG1. Risk stratification of patients**

1. In children with a new diagnosis of Crohn’s disease, which patient factors, disease factors, or initial treatment response factors predict a complicated disease course that warrants early use of biologicals or surgery?

**WG2. Treatment targets and monitoring response**

2. In patients with luminal CD, what is the best marker to determine adequate response to treatment?

**WG3. Induction therapy (EEN, steroids, anti-TNF)**

3. In patients with newly diagnosed luminal CD, which is the most optimal individualized induction treatment for remission (EEN/dietary therapy, mesalazine/sulfasalazine, steroids, anti-TNF)?

4. In patients with complicated disease behavior at diagnosis (eg internal fistulizing/fixed stricture/abscessing disease), which is the most optimal individualized induction treatment for remission (EEN/dietary therapy, steroids, anti-TNF, surgical intervention)?

**WG4. Anti-TNF (combo vs. monotherapy, dose-escalation)**

5. In paediatric or adult patients with Crohn’s disease, is anti-TNF (infliximab/adalimumab/golimumab/ certolizumab) effective and safe in inducing and maintaining clinical and/or endoscopic response and remission?

6. In paediatric or adult patients with Crohn’s disease, is anti-TNF (infliximab/adalimumab) monotherapy compared to combination therapy with an immunomodulator (thiopurine/methotrexate) effective and safe in inducing and maintaining clinical and/or endoscopic response and remission?

7. In paediatric or adult patients with Crohn’s disease being treated with anti-TNF (infliximab/adalimumab) is dosing guided by therapeutic drug monitoring compared to empiric dose adjustments advantageous in inducing and maintaining durable clinical and/or endoscopic response and remission?

8. In paediatric or adult patients with Crohn disease in endoscopic and/or clinical response or remission on anti-TNF (infliximab/adalimumab) as mono- or combination therapy with an immunomodulator (thiopurine or methotrexate), is endoscopic and/or clinical response or remission maintained after stopping versus continuing the immunomodulator and/or anti-TNF without any change?

**WG5. Immunomodulators (thiopurines, methotrexate, thalidomide)**

9. In paediatric or adult patients with Crohn’s disease, is immunomodulator (thiopurines, methotrexate, thalidomide) monotherapy effective and safe in inducing and maintaining clinical and/or endoscopic response and remission?

10. In paediatric or adult patients with Crohn’s disease, is methotrexate compared to thiopurine (azathioprine, mercaptopurine) more effective and/or more safe in maintaining clinical and/or endoscopic response and remission?

11. In paediatric or adult patients with Crohn’s disease being treated with thiopurine (azathioprine, mercaptopurine) is dosing guided by TPMT level or genotyping and/or therapeutic drug monitoring/metabolite level compared to empirical dose adjustments advantageous in maintaining clinical and/or endoscopic remission, and safety?

**WG6. New biologics (vedolizumab, ustekinumab)**

12. In paediatric or adult patients with Crohn’s disease, is vedolizumab (compared to placebo or any other medication) effective and safe in inducing and maintaining clinical and/or endoscopic response and remission?

13. In paediatric or adult patients with Crohn’s disease, is ustekinumab (compared to placebo or any other medication) effective and safe in inducing and maintaining clinical and/or endoscopic response and remission?
**WG7. Nutritional therapy as maintenance therapy (maintenance enteral nutrition, MEN)**

14. What is the treatment outcome of nutritional therapy for maintenance of remission in Crohn's disease?

**WG8. Microbial manipulation**

15. What is the clinical efficacy and safety of microbial manipulation (including fecal Tx, probiotics and antibiotics), when compared to no treatment, placebo, other pharmacological or non-pharmacological treatment in the induction and maintenance of remission of patients with Crohn’s disease?

**WG9. Perianal management**

16. In patients with perianal Crohn’s disease, what is the optimal medical and surgical management?

**WG10. Other surgical therapies (ileocaecal resection, stenosis dilatation)**

17. What is the efficacy and safety of ileocaecal resection when compared to pharmacological treatment in the maintenance of remission in patients with stricturing ileocaecal Crohn's disease.