

## Supplementary File 1: Intestinal ultrasonography studies

### Validation of IBUS-SAS

**Aims:** To validate the Intestinal Bowel Ultrasound Group Segmental Activity Score (IBUS-SAS) against objective measures of inflammatory activity in Crohn's Disease (CD).

**Methods:** Intestinal ultrasonography (IUS) will be performed on all patients from the cohort. Acquisition and documentation of all scans will include a minimum of three cine loops (one cross-sectional, one longitudinal, and one with colour Doppler imaging) for all pathological segments<sup>1,2</sup>. In non-pathological segments, one still image will be recorded. The sonographer will assess IBUS-SAS from the worst segment and will assess all segments for the presence of transmural remission (defined as BWT of 3 mm or less without colour Doppler signal)<sup>3</sup>. The baseline and one-year follow-up scans of CD patients recruited within the first year of study will be centrally read (blinded to other measures of inflammation) by two experts in IUS and used for subsequent analyses.

**Statistics:** IBUS-SAS scores will be correlated to SES-CD<sup>4</sup> and MARIAs<sup>5</sup> for each patient and segment using Spearman's coefficient test. The accuracy of IBUS-SAS for predicting active disease (including subclassifications, as described in Table 4) will be evaluated by the receiver operator characteristic area under the curve. Kappa statistics will be used to assess agreement between SES-CD, MARIAs, and faecal calprotectin (FC) for binary classification of active and severe disease.

**Responsiveness:** Changes in IBUS-SAS scores will be examined on a segmental basis and compared to changes in SES-CD and MARIAs. IBUS-SAS from ulcerated segments at baseline will be compared with one-year follow-up IBUS-SAS for those in endoscopic remission and those not in endoscopic remission.

### The predictive value of IUS

**Aims:**

To determine which IUS parameters at diagnosis and at three months, as well as the absolute and relative changes between the two timepoints, most accurately predict objective signs of response/remission one year after diagnosis.

**Methods:**

Patients in the cohort are scanned with IUS at diagnosis and after three months of follow-up. The sonographer will assess the IBUS-SAS score on the most affected segment and will assess all segments for the presence of transmural remission (defined as BWT of 3 mm or less without colour Doppler signal<sup>3</sup>). As specified in the study protocol, all patients are expected to undergo ileo-colonoscopy 12 months after diagnosis with endoscopic assessment using the Simple Endoscopic Score in CD (SES-CD)<sup>4</sup> for patients with CD and the Mayo Endoscopic Score<sup>6</sup> for patients with ulcerative colitis (UC) or unclassified inflammatory bowel disease (IBD-U).

**Statistics**

The distinct parameters within the IBUS-SAS score measured at diagnosis and after three months of follow-up, as well as any absolute and relative changes between the two timepoints, will be correlated to the primary and secondary outcomes defined below. Prospective IUS response is defined as a reduction of bowel wall thickness (continuous measurements) of more than 25%, or more than 2.0 mm, or of more than 1 mm in combination with one colour Doppler signal reduction.

**Primary outcome:**

Endoscopic response/remission in CD and UC/IBD-U at 12 months.

For patients with CD, endoscopic remission is defined as a SES-CD score less than 2 and endoscopic response as a reduction in SES-CD of more than 50% for CD. For patients with UC/IBD-U, endoscopic remission is defined as a Mayo Endoscopic Score of 0 and endoscopic response is defined as a 50% reduction.

Secondary outcomes within one year of follow-up:

Abdominal surgery for IBD, including resection, balloon dilatation, strictureplasty, stoma surgery and perianal surgery

Hospital admission for IBD

Treatment intensification, including initiation, change or dose escalation of biological treatment for IBD

Biochemical remission, defined as a FC less than 250 µg/g or C-reactive protein less than 5 mg/L

Clinical remission, defined as HBI of 4 or less in CD and a SCCAI score of 2 or less in UC

## References

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3. Wilkens R, Novak KL, Maaser C, Panaccione R, Kucharzik T. Relevance of monitoring transmural disease activity in patients with Crohn's disease: current status and future perspectives. *Therap Adv Gastroenterol*. 2021;14:175628482110066. doi:10.1177/17562848211006672
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