Dear ECCO National Representatives,

Dear IBD National Study Group Representatives,

Dear Colleagues,

Evidence on the efficacy of **ustekinumab as a second-line treatment after vedolizumab failure in anti-TNFα naive patients** has not been studied. Ustekinumab appears to be inferior in biologic-experienced patients. However, based on the results of less than a dozen patients experienced to vedolizumab only from clinical trials, this seems to be particularly true for anti-TNFα experienced patients only. The relevance of this knowledge concerns the fact that vedolizumab and ustekinumab are considered the top-tier safest biologic medications for inflammatory bowel disease (IBD). Both these drugs are important therapeutic options in a particular pool of patients not suitable to anti-TNFα drugs, namely those with present or previous malignancies and elderly. Once vedolizumab failure is established, most patients will be offered ustekinumab therapy, and **robust evidence on efficacy and safety of this second-line treatment regimen in this setting is lacking**. As stressed, this is a **research gap** that may be attainable with a European scale effort to gather these patients for outcome evaluation.

With this email, the Gastroenterology Department of the Centro Hospitalar Universitário do Algarve (Portimão, Portugal) would like to invite all interested European IBD centres to collaborate on this topic in a retrospective multicentre observational cohort study. The aim of this study is to **assess clinical remission under ustekinumab as second-line treatment after vedolizumab failure in anti-TNFα naïve patients**.

Each participating centre will be requested to retrospectively collect data on **adult** patients with a diagnosis of ulcerative colitis or Crohn's disease, that are/were on **ustekinumab as second biologic with the first being either anti-TNFα or vedolizumab only**.

This initiative has been thoroughly discussed by the Clinical Committee (ClinCom) of ECCO, at the 7th National Study Group Meeting. The proposal received positive feedback and the final version of the study protocol has been approved in December 2022. The study has received approval by the local Ethical Committee of the Coordinating Centre (CHUA – Centro Hospitalar Universitário do Algarve).

Who can collaborate?

Every IBD centre with a retrospective database or list of adult IBD patients, with easily retrievable data and a low risk of missed cases, who are willing to provide information about their patients.

In case you and your centre are interested in participating in this study, please contact usafestudy@gmail.com by **31st of May 2023**.

Within a few days, you will receive an email with the following documents:

- U-SAFE protocol.
- Excel database with centre and patient codes assigned.
- U-SAFE Form (guidance document on how and what to include in the Excel database).

If ethical approval and/or informed consent for each patient are required, please inform us in due time, so we may provide the documents needed. Data collection will last about **three months** after local Ethic Committee approval. Considering a period of **four months** for analysis of data, the total duration of study will be of **twelve months**.

We will aim for the submission to the **ECCO'24 Congress** and a **full manuscript** afterwards. The publication list will consider the number of patients included in the study, as specified in the study protocol. Of note, IBD centres that collaborate with this multicentre cohort study are not allowed to publish their own data independently, without contacting the study PI first.

We truly hope that this collaborative retrospective study will allow us to cover this important research gap in the field of IBD.

Looking forward to your collaboration,

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