Dear ECCO Members,
Dear IBD National Study Group Representatives,
Dear Colleagues,

Treatment failure remains a significant obstacle in the management of patients with ulcerative colitis despite the continuous expansion of the therapeutic armamentarium. Literature supports within treatment class switch for patients who lost response to an anti-TNF. However, this is generally not recommended for patients with a primary non-response to a drug of the same class. **With the newer molecules such as JAK-inhibitors (tofacitinib, filgotinib, upadacitinib) even less is known about the effectiveness and safety of within class switch**. Data from studies on rheumatoid arthritis, another immune mediated inflammatory disease in which JAK-inhibitors are indicated, support a within class treatment switch, but little evidence exists to guide this same decision in patients with ulcerative colitis. Multiple treatment options are already available for patients with ulcerative colitis, and many more will be released in the near future. In this scenario, multi-refractory patients might be offered a second JAK-inhibitor treatment after having already been exposed to a drug of the same class before needing surgery, if this will be supported by real world data.

Our aim is to assess the effectiveness and safety of within treatment class switch for JAK-inhibitors in patients with ulcerative colitis having already been treated with a JAK-inhibitor. With this email, three European Referral Centres for IBD (Florence, Ljubljana, and Ghent) would like to ask different European IBD Centres to collaborate on this topic in a **retrospective, multi-centre observational cohort study.** The primary outcome will be to assess steroid-free clinical remission after 12 weeks of treatment with a second JAK-inhibitor after being already exposed to another JAK-inhibitor. If an adequate group of patients will be included, comparative analyses based on different sequences and/or reason for stopping the first JAK-inhibitor might be performed.

Each participating centre will be requested to retrospectively collect data on patients that underwent at least an induction cycle with a second JAK-inhibitor after being already exposed to another drug of the same class. The final version of the study protocol (see attached) has been reviewed extensively by the Clinical Committee (ClinCom) of ECCO.

Who can collaborate?

- IBD Centres with the possibility to retrieve data on patients with UC and their treatment history.
- IBD Centres who are willing to fill out an electronic clinical research form (eCRF) through the REDCap® software for all included patients.
- IBD Centres who are willing to verify themselves if approval by their local ethical committee and informed consent of the patient is mandatory in their jurisdiction for a retrospective non-interventional study. If so, the IBD Centre will be responsible for the submission to the local ethical committee as well as collection of the informed consent.

If you are interested in collaboration to this study, please contact tommaso.innocenti@unifi.it, gabriele.dragoni@unifi.it, jurij.hanzel@gmail.com or triana.lobatonortega@uzgent.be by **September 20th 2024**, stating also if you need ethical approval and informed consent for each patient, and when you will expect this. Please also forward this email to other IBD Centres in your country.

We will aim for the submission of an abstract for ECCO 2025 and a full manuscript shortly thereafter. The author list will take into account the number of patients included in the study and the authorship policy of

the target Journal. Depending on the Journal authorship policy, an investigator per participating Centre will be included as a co-Author, and a second name from each Centre can be tagged in the Study Group.

We truly hope that this retrospective study will become a success and might lead to an intense collaboration.

Sincerely,

Dr. Tommaso Innocenti
Dr. Gabriele Dragoni
Dr. Jurij Hanžel
Dr. Triana Lobaton