



## SESSION 3

### COMBINATION THERAPY

#### Advanced Therapies in IBD: Mix and match?

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In 2021, we can offer our patients with inflammatory bowel disease (IBD) hope. This is because we have several therapeutics with different modes of action already available, but also newer compounds that have either completed, or are in late-stage clinical development, that will likely enter the clinic over the next 3 years. Current available biologics and small molecules target key mediators of inflammation, including tumor necrosis factor, interleukins 12 and 23, integrins and Janus Kinases. Within the next 2–3 years we are likely to see at least three monoclonal antibodies to the p19 subunit of IL-23, two oral preferential JAK1 inhibitors and two oral sphingosine-1-phosphate receptor modulators. Newer biologics have several advantages including targeted inhibition of cytokines, safety and low immunogenicity; small molecules avoid immunogenicity, have a short half-life, and are convenient due to oral administration. That said, we do not see transformational efficacy thus far with any new agent. Use of combination therapy with an anti-TNF and immunomodulator is already well established as more effective than monotherapy, without increased risk of infection<sup>1</sup>. In order to raise the therapeutic ceiling for efficacy, the concept of combination biologics targeting different pathways is attractive for medically refractory disease. However, at this stage, evidence for efficacy and safety in IBD is limited to small case series<sup>2</sup> and also in patients where there is necessity to treat a concomitant immune disease<sup>3</sup>. In medical refractory cases where surgery is not an option, we should: (a) review medical records in detail to understand whether reported prior biological failures were indeed true failures; (b) try combination with different immunomodulators; (c) engage with the nearest clinical trial center to assess eligibility for a trial. Failing these options, combination biologics could be carefully considered with clear counselling of patients regarding their off-label use and unknown safety concerns. Thankfully, controlled clinical trials are now underway to explore the efficacy and safety of combination biologics in IBD<sup>4</sup>. In addition, bispecific antibodies are under development.

#### References

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2. Yang E, Panaccione N, Whitmire N, et al. Efficacy and safety of simultaneous treatment with two biologic medications in refractory Crohn's disease. *Aliment Pharmacol Ther*. 2020;51(11):1031–38.
3. Hirten RP, Iacucci M, Shah S, et al. Combining Biologics in Inflammatory Bowel Disease and Other Immune Mediated Inflammatory Disorders. *Clin Gastroenterol Hepatol*. 2018;16(9):1374–84.
4. <https://clinicaltrials.gov/ct2/show/NCT03662542>