# NEXT STEP IN IBD TREATMENT

At the IBD Nordic Conference, three Satellite symposiums were held. The first was sponsored by Pfizer, and had Prof Silvio Danese talking about the new JAK-inhibitor tofacitinib.

Chair Dr Michael Eberhardson introduced Prof Silvio Danese, who is the President of ECCO.

He started by describing the success and failure in IBD drug development.

– The failures have been many, Prof Danese remarked.

**Comparison with flight networks**

Prof Danese said that approximately 75 % of UC patients treated with TNF inhibitors do not achieve steroid-free remission within one year.

– Can we do a better job, he asked rhetorically.

Small molecules in development target intracellular pathways involved in cytokine signalling. Tofacitinib is the first one of these that is available. It is a JAK inhibitor.

– When I talk about JAK inhibitors, I usually make a comparison with flight networks, Prof Danese continued and presented a map over flight routes in Europe.

He explained that you only block one of these routes with other inhibitors.

– With JAK-inhibitors you block the *hub,* that control *many* flights, he underlined.

Prof Danes explained the mechanisms of JAK inhibition and the JAK/STAT pathway. JAK inhibition gives a reduced production of cytokines that modulate the immune response.

– Many IBD-relevant cytokines converge on, and initiate, intracellular signalling through JAK pathways. That's the concept of the hub – you block several cytokines.

**Similar effect in anti-TNF experienced patients**

Prof Danese then described the OCTAVE Induction 1 and Induction 2 studies, which constituted the tofacitinib phase III programme. The maintenance study was OCTAVE Sustain, and the long-term extension study is called OCTAVE Open.

– Significantly more patients achieved primary endpoint at week 8 over placebo in the Induction 1 and 2 studies.

Treatment effect for remission was similar in anti-TNF treated and anti-TNF naive patients. Tofacitinib also had a significant effect versus placebo on mucosal healing at week 8 in both these groups.

– In OCTAVE Sustain, the primary endpoint was remission at week 52. A significantly greater proportion of patients receiving tofacitinib met this, compared to placebo, Prof Danese continued.

**Potential for first line after 5-ASA and steroids**

The general safety was shown to be as we expect from anti-TNFs.

– There is a dose-dependent increased risk for herpes zoster with tofacitinib. But no patient had to discontinue the study due to adverse events, Prof Danese said.

He added that there is also a rise in lipids.

– The rate of HDL/LDL increases initially, but then remains stable over time.

At the end of his talk, Prof Danese asked how we choose which drug to prescribe.

– There is a lack of head-to-head trials, and there are today multiple options for patients.

Tofacitinib is a potential first line advanced therapy for UC – after 5-ASAs and steroids.

– It has a short serum half-life, is taken orally and immunogenicity is not expected from a small molecule. It is shown to be effective in patients previously treated with TNF-inhibitors, he summarised.

There is also experience of tofacitinib in RA, where the drug has generated a lot of safety data.

Prof Danese ended his lecture with a case from his clinic. It was a man who was one of the first to be included in the OCTAVE trials, and received induction with tofacitinib 10 mg.

– He was a candidate for colectomy – but clinical improvement was observed at day 5. He has continued remission since 2014 at tofacitinib 5 g – and he has had no steroid use since then. Probably you will experience this in your clinic too!

**Per Lundblad**