From left, Jonas Halfvarson, Ernest Choy and Geert D'Haens.

JAK INHIBITION IN UC – PRACTICAL GUIDANCE FOR THE CLINIC

Tofacitinib is the first in the class of JAK inhibitor therapies and represents a new addition to the UC treatment armamentarium. In a satellite symposium sponsored by Pfizer this was discussed.

Chair Prof Geert D'Haens, The Netherlands, pointed out that tofacitinib was first approved for patients with rheumatoid arthritis (RA), so he introduced rheumatologist Prof Ernest Choy, UK, who talked about their experience with the drug.

Provisional statement from EMA

Prof Choy explained that infliximab, adalimumab, golimumab, tofactinib, corticosteroids and ustekinumab are used in *both* RA and UC. But tofacitinib has a more rapid onset of action, compared to the monoclonal antibodies.

– The therarapeutic indication for tofacitinib in adult patients with moderately to severe UC is for patients who have had an inadequate response, lost response – or were intolerant to either conventional therapy or a biologic agent.

JAK inhibition selectively is relative and not absolute.

– The clinical relevance of selectivity can only be determined through assessing clinical and biological effects in patients. JAK1 is an effective target in RA, although risk for herpes zoster reactivation is a class effect, Prof Choy underlined.

An increased risk of pulmonary embolism has been reported for tofacitinib 10 mg twice daily in patients with RA who are aged 50 years or more, and have one or more risk factors for pulmonary disease. This has caused EMA to issue a provisional statement that tofacitinib is contraindicated in these patients.

– The current recommendation relates to provisional measures based on the preliminary data and are subject to ongoing review by the EMA safety committee, Prof D'Haens said.

Trials and real-world data

Prof Jonas Halfvarson, Sweden, then talked about the efficacy and safety profile for tofacitinib in UC.

– The OCTAVE Phase II trial demonstrate the efficacy of oral tofacitinib in patients with moderate-to-severely active UC, he established.

Symptom improvement, measured by stool frequency and rectal bleeding, was significant already at day 3,. Statistically significant improvements in IBD-Q (a quality of life instrument for IBD patients) and SF-36v2 (a generic quality of life questionnaire) scores were reported, Prof Halfvarson continued.

– A substantial proportion of patients – approximately 50 % – were anti-TNF experienced. And more than 50 % of those who failed induction, and then went into the open label arm of the study, had clinical response.

A dose-dependent risk of herpes zoster was observed. Prof Halfvarson underlined that the incidence did not increase over time.

Malignancies and non-melanoma skin cancer occurred infrequently in patients. The incidence rate did not increase with longer treatment duration. Venous thromboembolism events occurred in 5 patients, receiving tofacitinib 10 mg twice daily.

– Real world data are needed to ensure that trial data on efficacy and safety are maintained. More that 102,000 patients with RA have been treated with tofacitinib. In UC, a real-world study from the US and one from France, have shown that the results from clinical trials in UC are replicated in real life. So emerging real-world evidence for tofacitinib indicate effectiveness in the clinical setting, and a safety profile consistent with the OCTAVE clinical programme, Prof Halfvarson summarised.

Not a biologic

Prof D'Haens ended the symposium by talking about dosing and monitoring.

– A thorough work-up and screening is recommended prior to initiating tofacitinib in appropriate patients, he said.

Laboratory tests at baseline include lymphocytes, neutrophils and haemoglobin – then lipids after 4 - 8 weeks. Monitor for drug-induced liver injury, malignancy, infection and pulmonary embolism.

– Advise patients of the risk of herpes zoster infection, and to be vigilant for sign and symptoms of herpes zoster!

Tofacitinib is *not* a biologic, and is therefore not susceptible to changes in drug clearance due to the formation of neutralising anti-drug antibodies, Prof D'Haens pointed out.

– Assess patient response, and adjust dose accordingly. Routine monitoring of adverse events and/or laboratory abnormalities is recommended. Restarting tofacitinib after a treatment interruption can be considered, was his last message.

Per Lundblad