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HISTOLOGIC REMISSION IN UC: ARE WE READY? INSIGHTS FROM VARSITY

The next step in the evolution of treatment goals for ulcerative colitis (UC) may be "complete remission".

This includes histologic healing and the potential goal of further changing the course of the disease.

At a satellite symposium, sponsored by Takeda, the role of histology in UC was discussed.

Prof Jean-Frédéric Colombel, USA, who was the Chair, began by reviewing our current understanding of histologic remission. He underlined that evidence for more stringent treatment targets has continued to accumulate in ulcerative colitis (UC), since the publication of *Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE)*.

Histologic remission predictive of better outcome

In 2015, STRIDE established targets for clinical and endoscopic remission – but evidence for histologic remission was lacking. Between 2016 and 2018 multiple studies showed histologic remission to be associated with reduced risk for relapse in patients achieving endoscopic improvement and remission, he continued.

– The vocabulary may be confusing. Previously, many studies have defined mucosal healing as endoscopic outcomes only. But today, mucosal healing reflects both endoscopic *and* histologic outcomes.

A meta-analysis published 2016, showed that mucosal healing at the first endoscopic evaluation after initiation of UC therapy was associated with improved long-term outcomes. Another meta-analysis with results from 44 studies, published 2019, had investigated the correlation between pooled endoscopic and histologic remission. It found that in general, histologic remission may be achieved in fewer patients than endoscopic remission.

– Endoscopic remission and histologic

remission do not completely correlate in UC. Nevertheless, histologic remission may be more predictive of positive outcomes in UC than endoscopic remission, Prof Colombel summarised.

Scores

So what *is* histologic healing?

– Several definitions of histologic remission in UC have been proposed – however the most appropriate goal is yet to be determined. An example could be: "No architectural abnormalities and no increase in inflammatory cells in lamina propria", Prof Laurent Peyrin-Biroulet, France, said.

Differences in scoring methodology and definitions of histologic outcomes highlight the need for standardisation in UC, he continued.

– In UC, I think that mucosal healing should involve both endoscopic and histologic outcomes.

Prof Peyrin-Biroulet continued by presenting scores for assessment of histologic inflammation in UC (there are several). The Nancy histological index (NHI) and the Robarts histological index (RHI) have undergone the most profound validation – through testing of four operating properties: Reliability, content validity, construct validity (i.e. hypothesis testing) and criterion validity.

– Differences in scoring methodology and definitions of histologic outcomes highlight the need for standardisation in UC, Prof Peyrin-Biroulet continued.

He concluded his talk by looking into the future.

– There is ongoing work in ECCO for a consensus on standardisation of histology in UC. I also think artificial intelligence is going to replace the pathologist, and faecal calprotectin to replace biopsies. Then maybe one day we will be talking about molecular healing?

Standardisation needed

Prof Silvio Danese, Italy, presented data from the VARSITY trial. It is a Phase IIIb randomised, double blind, multicentre study on UC in which patients were randomised to either adalimumab or vedolizumab. Endoscopies were performed at baseline, week 14 and week 52.

– At week 14, significantly more patients on vedolizumab (37,3 %) had minimal histologic disease activity, compared to those on adalimumab (24,4 %). Week 52 the figures for vedolizumab and adalimumab were 42,3 % versus 25,6 % respectively.

So VARSITY showed that with vedolizumab therapy, achieving minimal histologic disease is possible in up to 42 % of UC patients, Prof Danese underlined.

In his summary, Prof Colombel said that currently histology is not a treatment target – but histologic healing is associated with favourable outcomes.

– If it is going to be an endpoint in clinical practice, standardisation of biopsy collection and pathology reporting is needed, he pointed out.

Per Lundblad