Inflammatory bowel disease: How should psoriasis patients be managed with concomitant inflammatory bowel disease?

Narrative review of the existing literature and an assessment of approval status of psoriasis therapies for Crohn's disease and ulcerative colitis were conducted. Existing guidelines were consulted [1-3].

Results/Answer:

We recommend working in collaboration with the treating gastroenterologist when prescribing a systemic therapy in psoriasis patients with concomitant chronic inflammatory bowel disease.	↑↑	STRONG CONSENSUS[1]  EXPERT CONSENSUS
In patients with psoriasis and active IBD or a history of IBD, we **recommend** to preferentially use approved targeted therapies with a documented efficacy in these conditions: *Crohn's disease:* anti-TNF (infliximab, adalimumab, certolizumab) and anti-IL-12/23p40 (ustekinumab). *Ulcerative colitis:* anti-TNF (infliximab, adalimumab) and anti-IL-12/23p40 (ustekinumab).	↑↑	
If these first-choice treatments cannot be used, **we suggest** the following treatments to be considered as second choice targeted treatment options in patients with psoriasis and IBD: *Crohn's disease:* Anti-IL-23p19 (preferred risankizumab, guselkumab; also possible: tildrakizumab) *Ulcerative colitis:* Anti-IL-23p19 (preferred risankizumab, guselkumab; also possible: tildrakizumab)	↑	
If these first-choice treatments cannot be used, we **suggest** the following treatments to be considered as second choice oral treatment options in patients with psoriasis and IBD *Crohn's disease:* Methotrexate *Active ulcerative colitis:* Ciclosporine (preferred), apremilast (also possible)	↑	
In combination with other treatments, we **suggest** acitretin as an adjunct therapy for patients with IBD and psoriasis, especially in cases with mild paradoxical psoriasis	↑	
We suggest against the use of anti IL 17 antibodies in patients with inflammatory bowel disease.	↓	

[1] due to personal-financial conflict of interest 4 abstentions

Likely due to an overlap in the pathophysiology and genetic background of psoriasis and Crohn's disease, the risk of psoriasis patients developing Crohn's disease is approximately two- to threefold higher compared to the general population [4,5].

The IL-17A antibody secukinumab and the IL-17RA antibody brodalumab have failed in studies in Crohn's disease, with some patients experiencing worsening of their disease during treatment [6,7]. Cases of newly onset Crohn's disease and ulcerative colitis have been observed during treatment of psoriasis patients with IL-17 inhibitors. The observed signal is, however, low, and it is presently unclear if the rate exceeds the rate expected in a psoriasis population [8]. In a recent summary of the safety observed in clinical trials of secukinumab in psoriasis, for example, the event-rate per 100 patient-years of exposure was 0.05 (95% confidence interval 0.02-0.1) for Crohn's disease (approximately one case per 2000 patients treated for one year) and 0.1 (0.07-0.2) for ulcerative colitis (approximately one case per 1000 patients treated for one year) [9]. Since anti-TNF antibodies and ustekinumab, and possibly anti-IL-23 antibodies, are effective in treating Crohn's disease[10], the use of these biologics in psoriasis may decrease the occurrence of new onset Crohn's disease cases in psoriasis patients. [11]

The prescription information for bimekizumab, ixekizumab and secukinumab include a warning regarding the use of these drugs in patients with inflammatory bowel disease, while active Crohn's disease is a contraindication for the use of brodalumab.

In contrast, ustekinumab, adalimumab, infliximab, and certolizumab are all targeted therapies approved not only for the treatment of psoriasis, but also for the treatment of Crohn's disease and, in the case of adalimumab, infliximab and ustekinumab, ulcerative colitis. Notably, the anti-TNF fusion protein etanercept failed in clinical trials in Crohn's disease (reviewed in Whitlock SM et al. 2018 [12]).

There is an ongoing phase II/III clinical development program for the IL-23p19 inhibitors guselkumab and risankizumab in Crohn's disease and ulcerative colitis. In the case of risankizumab, positive clinical effects have been published for the induction and long term treatment of patients with Crohn's disease [10,13] and are supported by immunological findings in the intestinal mucosa of patients with Crohn's disease receiving the drug [14]. There are several published case reports on the successful use of guselkumab in patients with Crohn's disease [15,16].

Due to their intestinal side effect profile with a relatively frequent induction of abdominal pain, loose stools and diarrhoea, fumarates should not be used in patients with inflammatory bowel disease. Severe gastrointestinal diseases are listed as contraindication in the prescription information of Fumaderm® and Skilarence®.

Inhibition of PDE4 with apremilast has shown positive effects in a phase 2 trial with ulcerative colitis [17].

Methotrexate has limited efficacy in Crohn's disease [18,19] and probably even less in ulcerative colitis [20,21], but there is a considerable body of experience and no signal for a worsening of these conditions.

Acitretin may be considered neutral in patients with psoriasis and inflammatory bowel disease and has been used in the treatment of patients with inflammatory bowel disease that developed psoriasiform lesions (including cases of so called paradoxical psoriasis) during treatment with TNF antagonist [22].

Cyclosporine is frequently used in the treatment of steroid-refractory ulcerative colitis and has demonstrated long term outcomes similar to those of infliximab [23].

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