J Gastroenterol (2018) 53:799–800
https://doi.org/10.1007/s00535-018-1458-y

The Japanese Society of Gastroenterology

LETTER TO THE EDITOR

A proposed treatment algorithm for mild to moderate ulcerative colitis—with an emphasis on budesonide foam and mucosal healing

Juris Pokrotnieks[1,2] · **Stanislav Sitkin**[3,4]

Received: 15 November 2017 / Accepted: 26 December 2017 / Published online: 3 April 2018

We read with great interest the paper recently published by Naganuma et al. [1] on the budesonide foam in mild to moderate ulcerative colitis (UC). Indeed, second-generation corticosteroids, such as budesonide, can become a reliable "intermediate layer" between mesalazine and systemic corticosteroids in the UC treatment pyramid. In this regard, we would like to supplement the current treatment algorithm considering data from rectal budesonide studies [1–6].

Earlier, two large studies have shown similar efficacy and safety of budesonide foam compared with hydrocortisone foam [2], as well as compared with budesonide enema in patients with distal UC [3]. Furthermore, in the second study, most patients (84%) preferred foam because of its better tolerability and easier application [3].

More recently, two large, randomized, placebo-controlled, phase 3 studies demonstrated that a significantly greater percentage of patients with active, mild to moderate ulcerative proctitis or proctosigmoiditis receiving budesonide foam achieved remission at week 6 compared with placebo (41.2 vs. 24.0%) [4, 5]. Furthermore, budesonide foam was significantly better than placebo in terms of rectal bleeding resolution and endoscopic improvement.

Budesonide foam has also demonstrated efficacy in achieving mucosal healing (MH) in UC. A study performed by Naganuma et al. [6] showed that twice-daily budesonide foam induced complete MH in almost half of patients with mild to moderate distal UC. In the next study [1], 32.8% of UC patients including those with left-sided colitis and pancolitis achieved complete MH of distal lesions in the budesonide foam group as compared with 3.2% in the placebo group. Furthermore, complete MH of distal lesions promoted clinical remission not only in proctitis, but also in left-sided colitis and pancolitis, suggesting that budesonide foam may be an effective therapeutic option in UC patients with various disease extents [1]. It seems clinically important, given that MH is now considered as a major therapeutic goal in UC [7]. Because complete MH contributes to the long-term clinical outcomes in UC, budesonide foam can be effectively used prior to escalation therapy (systemic corticosteroids, immunosuppressants, biologics) in patients with distal active inflammation.

An additional benefit of budesonide foam is that its effectiveness does not depend on the response to 5-aminosalicylic acid (5-ASA) [2, 4, 5]. A recent study [1] clearly indicates the potential efficacy of budesonide foam in patients with 5-ASA failure. In the subgroup that had received previous treatment with rectal 5-ASA, 33.3% of patients achieved clinical remission, and 18.2% achieved complete MH of distal lesions. Similarly, clinical remission and complete MH of distal lesions were obtained also in about a third of patients receiving high doses of oral 5-ASA.

Given the current data on the efficacy and safety of budesonide rectal foam, we propose to integrate this drug

This comment refers to the article available at https://doi.org/10.1007/s00535-017-1376-4.

✉ Stanislav Sitkin
drsitkin@gmail.com

[1] Department of Internal Diseases, Rīga Stradiņš University, Riga, Latvia

[2] Centre of Gastroenterology, Hepatology and Nutrition, Pauls Stradiņš Clinical University Hospital, Riga, Latvia

[3] Department of Internal Diseases, Gastroenterology and Dietetics, North-Western State Medical University named after I.I. Mechnikov, St. Petersburg, Russia

[4] State Research Institute of Highly Pure Biopreparations, St. Petersburg, Russia

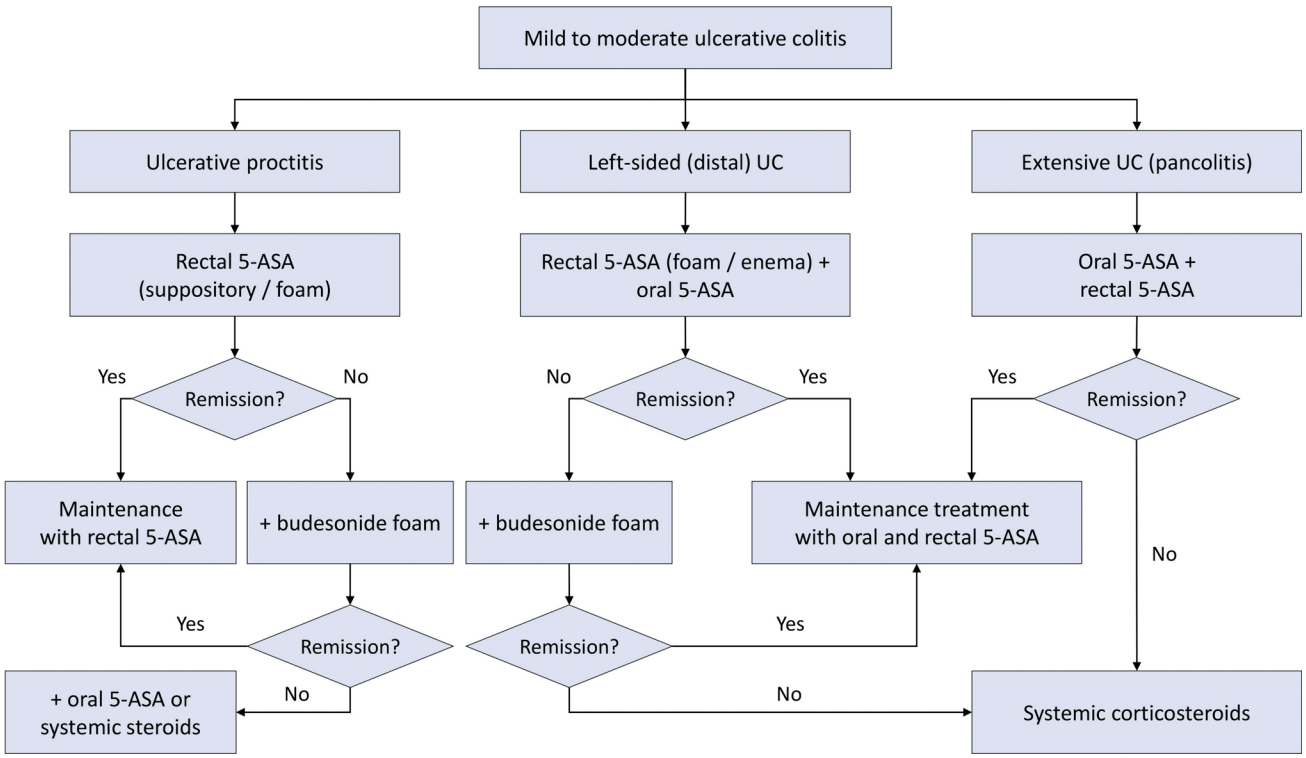

Fig. 1 A proposed algorithm that integrates budesonide foam into mild to moderate UC treatment. *5-ASA* 5-Aminosalicylic acid, *UC* ulcerative colitis

into the treatment algorithm for induction of remission in mild to moderate UC. Budesonide foam can be added to the existing 5-ASA therapy and before starting systemic corticosteroids (Fig. 1). In ulcerative proctitis, if symptoms persist despite adequate rectal 5-ASA therapy, budesonide foam should first be added before switching to a combination with oral 5-ASA. In left-sided (distal) UC, in the case of oral or rectal 5-ASA treatment failure, budesonide foam can be added to the ongoing 5-ASA therapy, before systemic steroids [1–6]. In extensive UC systemic corticosteroids should generally be administered after combined oral and rectal 5-ASA therapy failure, because there is limited evidence of budesonide's efficacy in pancolitis.

In conclusion, budesonide foam, as having sufficient efficacy and a more favorable safety and tolerability profile, can serve as a reasonable alternative to systemic corticosteroids as an intermediate step in the current treatment algorithm for mild to moderate UC.

Compliance with ethical standards

Conflict of Interest The authors declare that they have no conflict of interest. Authors must indicate whether or not they have/had a financial relationship (within the last 3 years) with any organization that sponsored the research. They should also confirm that they have full control of all primary data and they agree to allow the journal to review their data if requested.

References

1. Naganuma M, Aoyama N, Tada T, et al. Complete mucosal healing of distal lesions induced by twice-daily budesonide 2-mg foam promoted clinical remission of mild-to-moderate ulcerative colitis with distal active inflammation: double-blind, randomized study. J Gastroenterol. 2018;53(4):494–506. https://doi.org/10.1007/s00535-017-1376-4.
2. Bar-Meir S, Fidder HH, Faszczyk M, et al. Budesonide foam vs. hydrocortisone acetate foam in the treatment of active ulcerative proctosigmoiditis. Dis Colon Rectum. 2003;46(7):929–36.
3. Gross V, Bar-Meir S, Lavy A, et al. Budesonide foam versus budesonide enema in active ulcerative proctitis and proctosigmoiditis. Aliment Pharmacol Ther. 2006;23:303–12.
4. Sandborn WJ, Bosworth B, Zakko S, et al. Budesonide foam induces remission in patients with mild to moderate ulcerative proctitis and ulcerative proctosigmoiditis. Gastroenterology. 2015;148(4):740–50.e2.
5. Bosworth BP, Sandborn WJ, Rubin DT, Harper JR. Baseline oral 5-ASA use and efficacy and safety of budesonide foam in patients with ulcerative proctitis and ulcerative proctosigmoiditis: analysis of 2 phase 3 studies. Inflamm Bowel Dis. 2016;22:1881–6.
6. Naganuma M, Aoyama N, Suzuki Y, et al. Twice-daily budesonide 2-mg foam induces complete mucosal healing in patients with distal ulcerative colitis. J Crohns Colitis. 2016;10(7):828–36.
7. Shah SC, Colombel JF, Sands BE, Narula N. Mucosal healing is associated with improved long-term outcomes of patients with ulcerative colitis: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2016;14(9):1245–55.e8.