Efficacy of Biological Therapies and Small Molecules in Patients with Refractory Ulcerative Proctitis

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Background

Ulcerative proctitis (UP) is often associated with disabling symptom. Most patients with UP can effectively be treated with conventional therapy. However, some patients, referred to as refractory UP, require advanced therapies (biological agents and small molecules). Evidence regarding the treatment of refractory UP with advanced treatment is scarce.

Aims

This study aimed to evaluate the effectiveness of first- and further-line biologics and small-molecule Janus kinase (JAK) inhibitors in refractory UP.

Methods

This is a retrospective cohort study of patients with UP at our referral center between September 2015 and June 2022. The study included adult patients with UP refractory to conventional treatment with a Mayo endoscopic subscore (MES) of ≥ 2 at inclusion before initiating advanced therapy and with a follow-up period of at least 24 weeks. The primary endpoint was corticosteroid-free clinical remission (CSFR) at the last follow-up visit, defined as partial Mayo Score (PMS) ≤2, with rectal bleeding subscore 0 and no use of corticosteroids within 90 days before the assessment timepoint. Secondary outcomes included biochemical remission (fecal calprotectin ≤250 µg/g), combined corticosteroid-free clinical and biochemical remission, endoscopic remission (MES of 0), and discontinuation rate.

Results

23 patients were included. The median follow-up duration was 33 months. In total, patients underwent 44 courses of advanced therapy for UP (14 infliximab, 16 adalimumab, 4 golimumab, 4 vedolizumab, 1 ustekinumab, 5 tofacitinib). 47.8% (11/23) of the patients received second-line treatment, 30.4% (7/23) 3rd-line, 9% (2/23) 4th-line, and 4.3% (1/23) 5th-line treatment (Table 1, Figure 1). 87% (20/23) of patients achieved CSFR. 78% (18/23) were in biochemical remission, 78% (18/23) were in combined clinical and biochemical remission, and 13% (8/13) were in endoscopic remission (Figure 2). The most common reason for treatment discontinuation was non-response, followed by side effects (Table 1). By the end of the follow up period, 12 (52%) patients were on advanced therapies.

Conclusion

Our findings indicate that advanced therapies are effiicacious in patients with rafractory UP.

Table 1. Characteristics per successive biologic period (1st – 5th)

Variable	First-line n=23 (%)	Second-line n=11 (%)	Third-line n=7 (%)	Fourth-line n=2 (%)	Fifth-line n=1 (%)
Anti-TNF agent					
Infliximab	11 (48)	3 (27)	0	0	0
Adalimumab	11 (48)	4 (36)	0	1 (50)	0
Golimumab	1 (4)	1 (9)	1 (14)	0	1 (100)
Non-anti-TNF agent					
Vedolizumab	0	2 (18)	2 (28)	0	0
Ustekinumab	0	0	0	1 (50)	0
Tofacitinib	0	1 (9)	4 (57)	0	0
Median duration of therapy, months					
Overall	12 (3-22)	24 (3-65)	17 (5-24)	9	
Anti-TNF agent	12 (3-22)	14 (3-117)	24	7	17
Non-anti-TNF agent	0	38 (24-52)	17 (5-26)	10	
Cessation due to primary non-response					
Overall	2 (9)	3 (25)	2 (29)	1 (50)	0
Anti-TNF agent	2 (9)	2 (25)	0	1 (100)	-
Non-anti-TNF agent	0	1 (33)	2 (33)	0	0
Cessation due to secondary non-response					
Overall	5 (22)	7 (64)			
Anti-TNF agent	5 (22)	5 (56)			
Non-anti-TNF agent	0	2 (66)			
Cessation due to side effects					
Overall	5 (22)	2 (17)	0	0	0
Anti-TNF agent	5 (25)	2 (22)	0	0	0

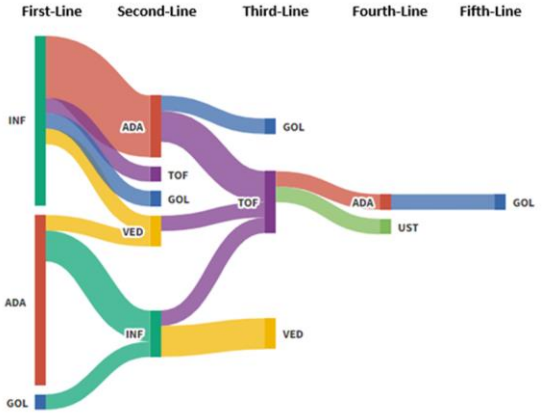

Figure 1. Sankey diagram of biologic switching patterns over the follow-up period, *ADA, adalimumab; GOL, golimumab; IFX, infliximab; TOF, tofacitinib; UC, UST, ustekinumab; VED, vedolizumab.*

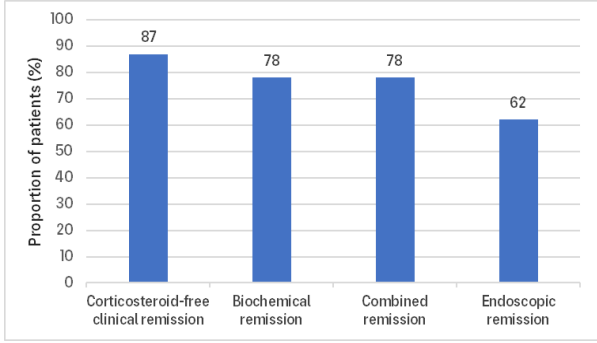

Figure 2. Corticosteroid-free clinical, biochemical, combined and endoscopic remission rates in UP patients treated with at least one advanced therapy.

VÄSTRA GÖTALANDSREGIONEN