JOURNAL ARTICLE

P759 Ustekinumab as rescue treatment in therapy-refractory or -intolerant ulcerative colitis FREE

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Journal of Crohn's and Colitis, Volume 12, Issue supplement_1, February 2018, Page S495, https://doi.org/10.1093/ecco-jcc/jjx180.886
Published: 16 January 2018

Abstract

Background

Ustekinumab is a monoclonal antibody targeting interleukins-12 and -23, commonly and successfully used in Crohn's disease. Pre-approval trials are on-going and so far no clinical observation data on the use of ustekinumab in ulcerative colitis (UC) is available. AIM: To assess the clinical outcomes achieved with ustekinumab as rescue treatment in therapy-refractory or -intolerant UC.

Methods

A retrospective data analysis was performed in 17 UC patients of our tertiary referral center who received ustekinumab between 2016 and 2017 as rescue therapy. All patients were intolerant or refractory to purine-analogues, TNF-antibody therapy, and the anti-integrin vedolizumab. To all patients ustekinumab was provided as a rescue treatment after colectomy had been offered to them as only other option. The primary outcome was achievement of clinical remission at 3 and 6 months. Clinical remission was defined as score of ≤5 points in the modified Truelove and Witts colitis activity index (CAI).

Results

A total of 17 UC patients were treated with ustekinumab. All patients (17/17) previously had been steroid-refractory or -dependant and had recently failed all of the following drugs: purine-analogues, anti-TNF-antibodies and anti-integrin-antibodies. Of those, 41% (7/17) had failed infliximab and either golimumab or adalimumab, and 29% (5/17) had also failed i.v. ciclosporine. At the start of the rescue therapy, 65% of patients (11/17) had moderately or severely active disease and 35% (6/17) were in remission, but had intolerable side effects under TNF- or integrin blocking treatment, which had to be stopped. Therefore, the CAI at the start of the therapy ranged between 1 and 11 with a median of 8. All patients received ustekinumab as approved for Crohn's disease (6 mg/kg body weight as an infusion and 90 mg ustekinumab as s.c. injection every 8 weeks). Median follow-up was 27 weeks (range: 15–40). In two patients therapy was stopped due to refractory disease at months 6 and 24 and in 1 patient, therapy was stopped due to drowsiness at week 4. All 3 patients underwent colectomy. Median CAI at 4 weeks was 5 points (range 1–8). Median CAI at 3 months was 4.5 points (range 0–9). Median CAI at 6 months was 2 points (range 0–7). Including the three drop-outs, clinical remission was achieved in 65% (11/17) at 1, 3, and 6 months, whereas only 35% (6/17) of patients were in remission at the start of the study.

Conclusions

Ustekinumab was effective as rescue medication in therapy-refractory or -intolerant UC in a large IBD referral center. It seems possible that large ongoing trials will confirm our findings and ustekinumab could become a new therapeutic option for refractory UC.

Topic: tumor necrosis factors, patient referral, integrins, colectomy, crohn's disease, inflammatory bowel disease, ulcerative colitis, monoclonal antibodies, colitis, follow-up, interleukins, purine nucleosides, steroids, antibodies, treatment outcome, irritable bowel syndrome, infliximab, drowsiness, adalimumab, ustekinumab, golimumab, infusion procedures, treatment resistant disorders, disease remission, vedolizumab, primary outcome measure

Issue Section: c. Clinical: Therapy and observation

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protocol and contraindications to vedolizumab. All patients provided a written consent. Data on clinical characteristics, treatment, disease activity and the short health scale (SHS) were recorded at baseline and prospectively, using an electronic Case Record Form, integrated with the Swedish National Quality Registry for IBD (SWIBREG). Data on the patients who had completed the 52 week follow-up are presented. The primary outcome at week 52 was clinical remission, defined as a Harvey Bradshaw Index (HBI) <5. Continuous data are presented as median (interquartile range). Differences between baseline and week 52 were assessed by the Wilcoxon-signed rank test.

Results: In total, 169 CD patients had been included by 19/09/2017. Clinical characteristics of patients (n = 104) who had completed the 52 week study period are shown in Table 1; 95/104 (91%) patients had failed prior anti-TNF therapy. At week 52, 71/104 (68%) were still on treatment with vedolizumab and 45/104 (43%) had achieved clinical remission. Among the 71 patients who had continued vedolizumab treatment, a decrease in the median HBI [6 (3–10) vs. 3 (2–5.5); n = 68; p < 0.001], median CRP [4.0 (2.0–10) g/l vs. 3.0 (1.4–5.0) g/l; n = 67; p = 0.01] and median f-Calprotectin [561 (139.5–830) vs. 232.5 (77.5–464) µg/g; n = 36; p = 0.09] was observed from baseline to week 52. Consistently, quality of life improved, defined by a significant reduction of the overall SHS score (n = 68; p < 0.001).

Table 1. Baseline demographics and clinical characteristics of patients with Crohn's disease (n=104) treated with vedolizumab

Median age yr. (IQR)	24 (19-35)
Sex; male no. (%)	51 (49)
Median disease duration yr. (IQR)	9 (4-20)
Current smoker no. (%)	12 (11.5)
Location–no. (%)	
Ileal (L1)	17 (16.3)
Colonic (L2)	30 (28.8)
Ileocolonic (L3)	56 (53.8)
Upper Gastrointestinal (L4) only	1 (1)
Behaviour–no. (%)	
Non-stricturing, non-penetrating (B1)	54 (51.9)
Stricturing (B2)	36 (34.6)
Penetrating (B3)	14 (13.5)
Perianal disease–no. (%)	25 (24)
Previous medications anti-TNF therapy – no. (%)	95 (91.3)
Reason for termination of last anti-TNF no. (%)*	
Primary non response	19 (20.0)
Secondary loss of response/Intolerance	63 (66.3)
Other reasons	9 (9.5)

*Information on reason for termination of last anti-TNF is missing in 4 patients

Conclusions: Vedolizumab treated patients represented a treatment-refractory group. Significant improvements in clinical- and inflammatory activity, as well as in quality of life, were observed in patients who continued treatment through to week 52. The study was financially supported by Takeda.

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Ustekinumab as rescue treatment in therapy-refractory or -intolerant ulcerative colitis

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Background: Ustekinumab is a monoclonal antibody targeting interleukins-12 and -23, commonly and successfully used in Crohn's disease. Pre-approval trials are on-going and so far no clinical observation data on the use of ustekinumab in ulcerative colitis (UC) is available. AIM: To assess the clinical outcomes achieved with ustekinumab as rescue treatment in therapy-refractory or -intolerant UC.

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Monitoring of laboratory parameters during thiopurine maintenance therapy in patients with inflammatory bowel disease: An unnecessary burden?

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