Digestive and Liver Disease 56 (2024) 220–222

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Correspondence

Anti-IL23 in inflammatory bowel disease patients with dermatological indication: The shared gastroenterological-dermatological clinic experience

Dear Editor,

in the present letter we report our experience with anti-interleukin (IL)−23 drugs in patients with both inflammatory bowel disease (IBD) and psoriasis followed up in our shared outpatients clinic. Up to 50 % of patients with IBD have at least one extra-intestinal manifestation (EIM), mainly involving the skin (more than 10 % of patients with IBD) [1]. In particular, a significant association between psoriasis and IBD is widely reported in the literature. In fact, psoriasis and IBD share some of their immunogenetic pathway, specifically IL-23 [2].

Indeed, two anti-IL−23 drug (risankizumab and guselkumab) have been approved for treatment of psoriasis and one (risankizumab) [3] has recently been approved for treating Crohn's disease (CD).

Given the significant involvement of the skin in patients suffering from gastrointestinal diseases, in 2018 a shared gastroenterological-dermatological clinic was set up at the "San Lazzaro" unit of the "A.O.U. Città della Salute e della Scienza" hospital of Turin, Italy. This clinic was created with the aim to follow patients suffering from pathologies of both gastroenterological and dermatological interest in a multidisciplinary way in order to be able to optimize the therapeutic management of these patients and to adopt, where possible, shared therapeutic strategies. This shared approach to IBD and skin manifestations gave to gastroenterologist early access to new biological therapies before the official approval for IBD; conversely dermatologist can benefit of higher dosage of the shared drugs once approved for IBD, as usually IBD require higher dosage of the same drug.

In this context, we performed the first real world observational study of patients with IBD and skin disease, undergoing anti IL−23 drugs for dermatological indication. The study was conducted between February 2021 and May 2023. We selected all IBD patients who were prescribed anti−IL23 drug for dermatological indication. Of note, the drugs were administrered following dermatological schedule (risankizumab was 75 mg as 2 subcutaneous injections at week 0, week 4, and then every 12 week and guselkumab 100 mg as a single subcutaneous dose, followed by a further dose after 4 weeks and then 100 mg every 8 weeks).

We evaluated the clinical remission rate of IBD after 3, 6, and 12 months, defined as Harvey Bradshaw Index (HBI) < 5 or partial Mayo Score (pMAYO) < 2 without anti−IL23 discontinuation. Also, we evaluated steroid-free clinical remission at 3, 6, and 12 months and the trend of C reactive protein (CRP) and calprotectin values through follow up time. In addition, therapy retention during follow up was recorded, and we evaluated factors possibly influencing the outcome, including previous biological therapies and smoking habits.

In the period of interest, 17 patients affected by IBD and concomitant psoriasis were recruited because anti−IL23 therapy (9 risankizumab, 8 guselkumab) was started with dermatological indication: 10 (58.8 %) males, mean age 49.1 ± 12.4 years, 7 (41.2 %) current smokers. Baseline characteristics are described in Table 1.

At the time of enrollment, IBD was in remission in 2 out of 17 (11.7 %) patients vs 12 out of 17 (70.5 %) after 3 months ($p = 0.004$); among 14 patients with available 6 months follow up, 1 of 14 (7.1 %) was in clinical remission at T0 and 9 of 14 (64.3 %) T6 ($p = 0.008$); in the 13 patients who reached 12 months follow up, 2 (15.4 %) were in clinical remission at T0 and 8 (61.5 %) at T12 ($p = 0.03$). Steroid free remission was present in 2 of 17 (11.7 %) at T0 and 12 of 17 (70.5 %) at T3 ($p = 0.004$); of the 14 patients who had 6 month follow up, 1 (7.1 %) was in steroid-free remission at T0 and 8 (57.1 %) at T6 ($p = 0.02$); among the 13 patients who reached one year follow up, 2 of 13 (15.4 %) were in steroid-free remission at T0 and 7 (53.8 %) at T12 ($p = 0.12$) (Fig. 1).

As far as laboratory values are concerned, despite a trend in decreasing in calprotectin values, no significant differences were observed in calprotectin and CRP between the different timepoints.

At logistic regression, no predictors of clinical remission were found, including previous anti−IL12/23 failure (OR = 0.2, $p = 0.2$) or type of anti-IL23 (guselkumab OR = 0.09, $p = 0.07$; risankizumab = 4.5, $p = 0.2$).

Throughout the follow-up (mean 10 months ±3.9, maximum 22 months) a total of 4 patients (25.5 %) discontinued anti−IL23: 2 patients at T3, 1 due to side effects (arthralgia) and 1 due to IBD activity; 2 patients at T6, one due to side effects (arthralgia) and 1 due to IBD activity.

Two cases of arthralgias (11.8 %) and one case of fever with chills (5.9 %) were recorded. Of these, only the first two cases resulted in discontinuation of the drug.

It is important to underline that the dosage at which these drugs were administered was that on label in moderate-severe psoriasis, therefore, lower than the dosages with which the trial in IBD were conducted. Nonetheless, a statistically significant clinical remission rate compared to baseline was achieved at all timepoints. In particular, after 3 months the clinical remission was reached by 70.5 % of the patients ($p = 0.004$). The figure remained almost constant also at 6 (64.3 %, $p = 0.008$) and 12 months (61.5 %, $p = 0.03$). One possible explanation for the decrease in the rate of remission at 12 months compared to that observed at 3 months is that an intention-to-treat analysis was conducted whereby failure was considered even when the patient was lost to follow-up before 12 months. This result confirms the data from clinical trials. In fact, in the phase 2 GALAXI 1 study it was demonstrated that guselkumab in patients with CD allows to reach clinical remission rates at week 12 of around 50 % in CD and 60 % in

https://doi.org/10.1016/j.dld.2023.11.012

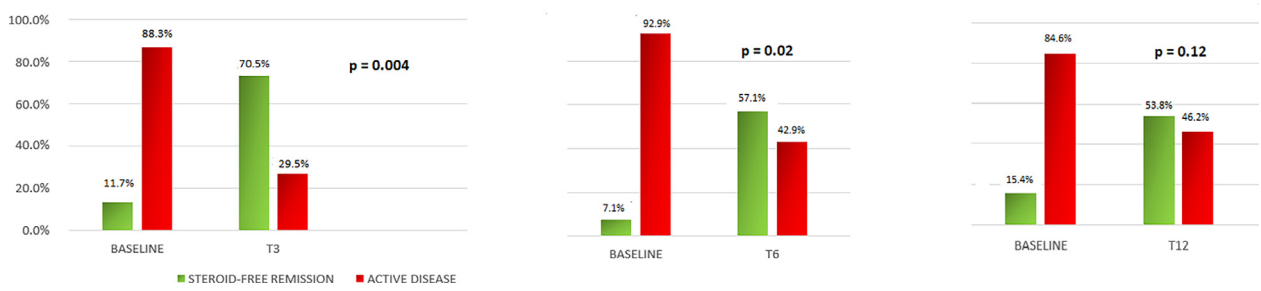

Fig. 1. Steroid-free inflammatory bowel disease clinical remission.

Table 1
Baseline characteristics of IBD patients treated with anti-IL23.

Type of IBD, n (%)	
CD	14 (82.4)
UC	3 (17.6)
IBD duration at T0, years (mean ± SD)	13.1 (12.0)
Age at IBD diagnosis, years (mean ± SD)	36.1 (13.8)
CD localization, n (%)	
Ileum (L1)	3 (21.4)
Ileum + colon (L3)	7 (50.0)
Ileum + upper gastrointestinal tract (L1+L4)	1 (7.2)
Ileum + colon + upper gastrointestinal tract (L3+L4)	3 (21.4)
UC localization, n (%)	
rectum (E1)	1 (33.3)
extensive colitis (E3)	2 (66.7)
CD clinical activity according to HBI, n (%)	
Remission (with steroids)	1 (7.1)
Mild	7 (50.0)
Moderate	5 (35.8)
Severe	1 (7.1)
UC clinical activity according to pMAYO, n (%)	
Remission (with steroids)	1 (33.3)
Moderate	2 (66.7)
Previous advanced therapies for IBD, n (%)	
Infliximab	2 (11.8)
Adalimumab	11 (64.7)
Golimumab	1 (5.9)
Vedolizumab	2 (11.8)
Ustekinumab	7 (41.2)
Drugs at T0, n (%)	
Mesalamine	11 (64.7)
Systemic steroids	4 (23.5)
Methotrexate	3 (17.6)
Adalimumab	4 (23.5)
Vedolizumab	1 (5.9)
Ustekinumab	4 (23.5)

IBD, inflammatory bowel disease; n, number; CD, Crohn's disease; UC, ulcerative colitis; SD; standard deviation; HBI, Harvey-Bradshaw index.

UC [4,5]. Regarding Risankizumab in CD, the ADVANCE trial found a clinical remission of about 40 % at week 12 [6]. As maintenance therapy at week 52, in the phase 3 FORTIFY study clinical remission was obtained in about 50 % of patients [7].

Regarding the safety profile, no serious side effects have been recorded. There were no unexpected safety events including malignancies and infections during the observation period. These data seem to confirm, at least in the short term, that treatment with anti–IL23 drugs is well tolerated and has a good safety profile. The data obtained in our study confirm the results presented in the literature deriving from clinical trials. In particular, the studies conducted revealed a reassuring safety profile for risankizumab even at a gastroenterological dosage. The ADVANCE study had a serious adverse event rate of 3.8 % [6]. Similarly, no new safety risks were identified in the phase 3 maintenance period of the FORTIFY study [7]. In the study by Feagan et al., the majority of adverse events recorded were exacerbation of CD, arthralgia (22 %), headache (20 %), and abdominal pain (18 %) [8]. The safety profile of guselkumab appears similar [4].

The limitations of our study are the low sample size which may have limited the interpretation of the results. On the other hand, ours is the first study in the world that provides clinical data on the efficacy and safety of anti–IL23 in the context of IBD in the real-world. Another limitation is the lack of endoscopic outcome, but being a real-world study, it was not possible to obtain this examination during the short follow-up, but we used fecal calprotectin as a surrogate biomarker for endoscopy. In addition, ours is an observational study and there is no control group. Finally, the dosages used are not those that will be approved in IBD as we have adhered to the dosages indicated for psoriasis which are much lower, but our patients were able to be treated with only 1 drug for both psoriasis and IBD, despite being a highly refractory population, with about 40 % of patients having already failed even anti–IL12/23.

In conclusion, anti–IL23 appear to be effective in inducing clinical remission in high refractory patients with IBD and psoriasis, with a good safety.

Conflict of interest

The author acting as the submission's guarantor must is Davide Giuseppe Ribaldone.

Source of funding

None declared.

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