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- Patient identifiers within text, tables, or figures
- By-patient data listings

Anonymized patient data may be made available subject to an approved research proposal submitted. Information which is considered intellectual property or company confidential was also redacted.

# 1.0 ABSTRACT

## Study Title

Long term outcomes of Drug Program for biological treatment in adult patients with ulcerative colitis in Poland.

## Keywords

Relapse, ulcerative colitis, vedolizumab durability of response/remission

## Background and Rationale

At the time of the study initiation, inclusion/exclusion criteria in Drug Program (DP, reimbursement program authorized by MoH to grant patients access to highly specialized therapies) for ulcerative colitis with infliximab or vedolizumab in Poland were in line with their approved labels but the treatment needed to be ceased after 54 weeks of therapy with vedolizumab or after 52 weeks of therapy with infliximab, regardless of the actual status of the disease (response/remission) at this time point. There was a data gap with regards to evaluation of real-life durability of response/remission after forced discontinuation of biologic treatment.

The aim of this non-interventional study (NIS) was to assess outcomes of the treatment introduced in the scope of DP for ulcerative colitis after biological treatment cessation, describing relapse rate in this cohort in consecutive periods of time.



## Research Question(s) and Objective(s)

Primary objective

To assess relapse rate in week 26 after withdrawal of biologic treatment with infliximab or vedolizumab in UC patients who completed DP with response/remission.

Secondary objectives

1. To assess relapse rate in week 52, 78 and 104 after withdrawal of biologic treatment with infliximab or vedolizumab in UC patients who completed DP with response/remission.
2. To evaluate need for steroid therapy in week 26, 52, 78 and 104 as a result of relapse.
3. To evaluate need for biologic treatment in week 26, 52, 78 and 104 as a result of relapse.
4. To assess real-life effectiveness of biologic treatment with infliximab or vedolizumab in UC patients in DP (effectiveness in induction, effectiveness in maintenance therapy, use of steroids or immunomodulators).
5. To assess real-life safety of biologic treatment with infliximab or vedolizumab in UC patients in DP.

Exploratory objectives

[redacted]

**Study Design**

Multicenter, non-interventional study with retrospective data collection and prospective follow-up in UC patients aged 18 years or older who received biologic treatment (infliximab or vedolizumab) in the scope of DP and who completed DP with response/remission.

**Setting**

The study was based on data collection from UC patients treated in DP. Individuals willing to participate in the study who completed the full course of treatment in DP (52 weeks for infliximab, 54 weeks for vedolizumab) with response or remission were enrolled in the prospective data collection. The first prospective assessment of UC symptoms (relapse rate) was performed in week 26 after last infusion of the biologic agent used in DP. Patients who maintained remission or response were followed up prospectively up to week 104 after the last infusion, the follow-up ended either when the patient relapsed or at V4 (104 weeks after the last infusion). Patients willing to participate in the study who did not complete the full course of treatment in DP were enrolled in the retrospective data collection (only data generated during the treatment in DP).

**Study Population: Subjects and Study Size, Including Dropouts**

Assuming that the relapse rate after 26 weeks of biologic treatment discontinuation would be equal to 20%, it was calculated that minimum of 25 patients should be enrolled. However, to increase precision of estimation (i.e. narrow down a width of confidence interval for relapse rate estimation) it was decided that approx. 70 patients who completed DP with response/remission would be enrolled. Total number of patients enrolled in the study was higher due to the fact that data were collected also from patients who lost response before treatment completion in DP.

**Data Sources and Data Collection**

Patients' medical records were the source of all data recorded in the eCRF. Therefore, only data available and already existing in patient files were recorded. No additional patient data, assessments, laboratory tests or visits except those collected/performed as a routine clinical practice were required for the purpose of this non-interventional study.



**Data Analysis**

In order to compare quantitative variables between visits, t-test (in case of normality) or Wilcoxon test (otherwise) was carried out. Normality assumptions were tested by Shapiro-Wilk test. Chi-square or Fisher test were used to compare categorical variables between subgroups. Proportion of responders and patients in remission were compared between visits using a proportion test. Where appropriate, 95% confidence intervals calculated using Wilson method were provided. Kaplan-Meier method was used to calculate the median time to event. 95% confidence intervals (CI) for this median were calculated using Hall-Wellner method.

[redacted]

Statistical significance was equal to 0.05 and p-value was reported with an accuracy of three decimal places (values lower than 0.001 were reported as <0.001).

For comparisons between subgroups (bio-naïve vs bio-failures and bio-naïve vs bio-exposed) Holm-Bonferroni correction was used for testing each outcome.

Descriptive statistics, such as mean, standard deviation, median, quantiles, minimum and maximum, were used to summarize quantitative variables. For categorical variables, frequency tables were presented.

The numerical results were rounded to one decimal place more than the precision of the initial data. In case of percentages, they were presented with accuracy of one decimal place.

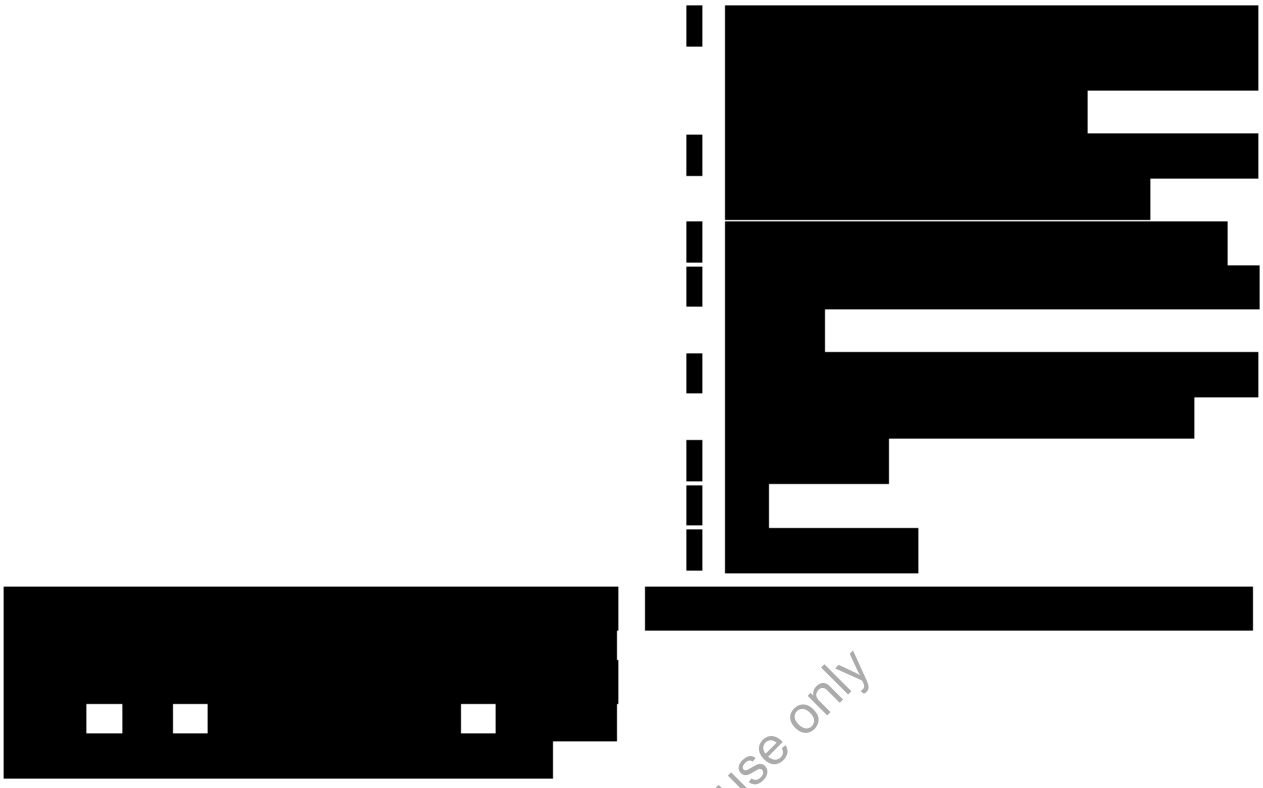
Unless otherwise specified, continuous variables were presented as boxplot displaying median, lower and higher quartile as well as minimum and maximum for each subgroup. If both variables were continuous, a scatter plot was presented instead. Proportions were shown as forest plots (with a dot representing a proportion and whiskers representing a 95% CI). Data on time to outcome (relapse, hospitalization, colectomy, biologic treatment, steroid therapy, immunotherapy) were presented in the form of Kaplan-Meier plots.

**Variables (Exposures, Outcomes and/or Endpoints)**

The following variables were considered in the study:

| Objective | Variable |
|---|---|
| To assess relapse rate in week 26 after withdrawal of biologic treatment with infliximab or vedolizumab in UC patients who completed DP with response/remission | Assessment of response at Visit 1 (26 weeks after the end of DP) |
| To assess relapse rate in week 52, 78 and 104 after withdrawal of biologic treatment with infliximab or vedolizumab in UC patients who completed DP with response/remission. | Assessment of response at Visit 2, 3 and 4 (weeks 52, 78 and 104 after the end of DP) |
| To evaluate need for steroid therapy in week 26, 52, 78 and 104 as a result of relapse. | Use of steroid therapy since previous visit |
| To evaluate need for biologic treatment in week 26, 52, 78 and 104 as a result of relapse. | Use of biologic treatment since previous visit (with name and dose collected). |
| To assess real-life effectiveness of biologic treatment with infliximab or vedolizumab in UC patients in DP (effectiveness in induction, effectiveness in maintenance therapy, use of steroids or immunomodulators). | Data collected during retrospective visit:<br>• response to induction treatment<br>• response or remission at the end of DP<br>• use of corticosteroids at the start and at the end of DP<br>• use of immunomodulatory drugs at the start and at the end of DP |
| To assess real-life safety of biologic treatment with infliximab or vedolizumab in UC patients in DP. | Adverse events collected for period during and after DP. |

[redacted]



**Results (Data Analysis)**

In total, between 13th July 2020 (first visit of the first subject) to 11th January 2024 (last visit of the last subject), of 99 patients screened in the study, 84 (84.8%) subjects met the criteria of the Full Analysis (FAS) population, while 78 (78.8%) subjects met the criteria of inclusion in the Per Protocol population (PP). 43 (51.2%) patients attended Visit 2 (Week 52 after the last infusion in DP), 31 (36.9%), respectively, attended Visit 3 (Week 78 after the last infusion in DP). 26 (31.0%) subjects completed the study (attended Visit 4 at Week 104 after the last infusion in DP). 58 (69.0%) patients terminated the study prematurely, the vast majority (N = 54, 93.1%) due the disease relapse.

The median age of 84 patients in the FAS population was 37.0 (range 20.0-84.0) years, with no difference between the cohorts treated in DP with infliximab (N = 35) and with vedolizumab (N = 49). Most patients were males (N = 50, 59.5%), also in the DP infliximab and vedolizumab cohorts. The median height of patients was 174.0 (range 151.0-200.0) cm, the median weight was 72.0 (range 42.0-121.0) kg, the median BMI score was 23.9 (range 16.4-43.6). In the infliximab and vedolizumab cohorts, the respective values were: 172.0 (range 151.0-200.0) cm, 65.0 (range 42.0-121.0) kg, 23.1 (range 17.0-39.1) and 176.0 (range 156.0-193.0) cm, 73.0 (range 45.0-115.0) kg, 25.2 (16.4-43.6). Non-smokers accounted for three-quarters of patients (N = 62, 73.8%), 13 (15.5%) patients were ex-smokers.

Disease extent at DP start in the FAS population was mostly left-sided (E 2), in 47 (56.0%) patients (N = 17, 48.6% and N = 30, 61.2% patients in the infliximab and vedolizumab DP cohorts, respectively). Extensive UC (E 3) was recorded in 35 (41.7%) patients in the overall population (N = 16, 45.7% patients and N = 19, 38.8% patients in the DP cohorts, respectively). In 2 (2.4%) patients ulcerative proctitis (E 1) was recorded, in the infliximab DP cohort only (Per Protocol population). The median time from the UC diagnosis in the overall population was 8.0 (range 1.0-23.0) years, in the infliximab and vedolizumab DP cohorts 7.0 (range 1.0-21.0) years and 8.0 (range 3.0-23.0) years, respectively.

At the end of DP, the median partial Mayo scores were 0.0 (range 0.0-9.0), 0.0 (range 0.0-7.0) and 0.0 (range 0.0-9.0) in the overall study population and the DP cohorts treated with infliximab or vedolizumab, respectively. The endoscopic outcomes were available in only 30 (35.7%) patients in the overall study population, in 14 (40.0%) patients and 16 (32.7%) patients in the DP cohorts treated with infliximab or vedolizumab, respectively. The median full Mayo scores were 2.5 (range 0.0-12.0), 1.0 (range 0.0-8.0) and 4.0 (range 0.0-12.0), respectively.

Prior to DP start, 56% (N = 47) of patients in the FAS population were exposed to biologic treatment. The most frequently biologic agent used was infliximab (87.3%, N = 41, including its biosimilar form). Vedolizumab accounted for the second most frequently used biologic agent (19.1%, N = 9). In the cohort treated in DP with infliximab, bio-exposed patients accounted for 37.1% (N = 13), in the cohort treated with vedolizumab they accounted for 69.4% (N = 34) of patients. Among patients who used infliximab in DP, the biologic agent most frequently used previously was infliximab (61.6%, N = 8), with the second most frequent treatment being vedolizumab (46.2%, N = 6). Among patients treated in DP with vedolizumab, the vast majority previously received infliximab (97.0%, N = 33). Half of patients (N = 23, 48.9%) were bio-failures, most frequently due to primary lack of response (N = 9, 39.1%) or loss of previous response (N = 8, 34.8%). Treatment intolerance was recorded in a quarter of patients (N = 6, 26.1%). In the Per Protocol population, prior to DP 45 (57.7%) patients were previously exposed to biologic therapy, mostly to infliximab (66.6%, N = 39, including its biosimilar form), or vedolizumab (20%, N = 9). 23 (48.9%) patients were bio-failures, primary lack of response and loss of previous response were equally represented as the reasons ( N = 8, 38.1%). Intolerance to biologic agent used was recorded in 5 (23.8%) patients.

Of 84 patients in the FAS population, 78 (92.9%) patients completed the entire DP treatment. Of 35 patients treated with infliximab, the entire treatment of 52 weeks was completed by 32 (91.4%) patients. Of 49 patients treated in DP with vedolizumab, 46 (93.9%) patients completed the entire treatment of 54 weeks. The reason for not completing the entire treatment in all patients was loss of response. The median no. of infliximab doses administered in DP in the Full Analysis population was 8.0 (range 5.0-10.0), the median no. of vedolizumab doses was 9.0 (range 4.0-13.0). In most of patients (N = 55, 70.5%) who completed the full DP treatment, both in the infliximab cohort (N = 24, 75.0%) and the vedolizumab cohort (N = 31, 67.4%), remission at DP completion was observed. Response was observed in 29.5% (N=23) of all patients who completed the full DP treatment, in 8 (25.0%) patients in the infliximab DP cohort and in 15 (32.6%) patients in the vedolizumab cohort. Steroid-free remission was achieved in 27.3% (N=15) of patients with remission after DP, with similar rates (N = 6, 25.0%) in the infliximab DP cohort and N = 9, 29.0% in the vedolizumab DP cohort. Mucosal healing was observed in more than three-quarters of patients who completed the full DP treatment (N = 56, 71.8%), more frequently (N = 25, 78.1%) in patients in the infliximab DP cohort than in the vedolizumab DP cohort (N = 31, 67.4%).

At DP start, more than two-thirds of patients in the FAS population used corticosteroids (N = 59, 70.2%) with the median dose of 30.0 (range 5.0-100.0) mg/day of prednisolone equivalents, in the infliximab cohort and in the vedolizumab cohort there were 24 (68.6%) patients and 35 (71.4%) patients treated with corticosteroids, respectively, with the median doses of prednisolone equivalents of 30.0 (range 15.0-100.0) mg/day and 25.0 (range 5.0-50.0) mg/day, respectively. At DP end, corticosteroids were used in 10 (11.9%) patients only, with the median dose of prednisolone equivalents of 15.0 (range 10.0-30.0) mg/day. In the DP cohorts, corticosteroids were used in 1 (2.9%) patient and in 9 (18.4%) patients, respectively, with the median doses of prednisolone equivalents of 30.0 mg/day and 10.0 (range 10.0-30.0) mg/day, respectively. Immunomodulators at DP start were used in half of patients (N = 43, 51.2%), in more patients in the infliximab cohort (N

= 23, 65.7%) than in the vedolizumab cohort (N = 20, 40.8%). In three-quarters of patients (N = 33, 76.7%), azathioprine was used as the prevalent immunomodulator [the median dose of 100.0 (range 50.0-200.0) mg/day], in the DP cohorts it was used in 19 (82.6%) patients and 14 (70.0%) patients, respectively. At DP end, immunomodulators were used in less than half of patients (N = 39, 46.4%) patients, in more patients in the infliximab cohort (N = 21, 60.0%) than in the vedolizumab cohort (N = 18, 36.7%).

Of 78 patients who completed DP with response/remission, the relapse at week 26 reached 43.6% (95% CI: 32.6% – 55.3%, N = 34). The median time from DP end to loss of response was 12.1 (range 0.1-24.0) weeks. In patients treated in DP with infliximab, the relapse rate at week 26 accounted for 43.8% (95% CI: 26.8% – 62.1%, N = 14). The median time to loss of response reached 13.5 (range 1.6-24.0) weeks. In the vedolizumab cohort, the relapse rate at week 26 accounted for 43.5% (95% CI: 29.2% - 58.8%, N = 20). The median time to loss of response reached 11.9 (range 1.6-24.0) weeks. The decline in the response/remission durability was observed in patients in the subsequent weeks of the follow-up. At week 52, the relapse rate in the overall study population reached 58.4% (95% CI: 46.6% - 69.4%), by week 104, it reached 73.7% (95% CI: 62.1% - 82.8%). The overall relapse rate after discontinuation of biologic treatment reached 71.8% (95% CI: 60.3% - 81.1%). In patients treated in DP with infliximab, the relapse rates recorded at week 52 and 104 accounted for 53.1% (95% CI: 35.0% - 70.5%) and 68.8% (95% CI: 49.9% - 83.3%). The overall relapse rate in this cohort reached 68.8% (95% CI: 49.9% - 83.3%). The corresponding relapse rates in the vedolizumab cohort were higher, accounting for 62.2% (95% CI: 46.5% - 75.8%) and 77.3% (95% CI: 61.8% - 88.0%), respectively. The overall relapse rate in this cohort reached 73.9% (95% CI: 58.6% - 85.2%). The median time to relapse reached 15.6 (range 0.0-96.4) weeks and was shorter in the infliximab DP cohort (14.6, range 0.0-94.4 weeks) than in the vedolizumab cohort (17.8, range 0.0-96.4 weeks).



After discontinuation of treatment in DP, biologic therapy was resumed in 48.2% (95% CI: 34.8% - 61.8%, N = 27) of patients who lost response thereafter, mostly by week 26 (35.7%, 95% CI: 23.7% - 49.7%, N = 20). In the subsequent weeks (52, 78, 104) the declining rates of resuming biologic therapy were recorded, in 22.7% (95% CI: 8.7% - 45.8%, N = 5), 18.2% (95% CI: 3.2% - 52.2%, N = 2) and 16.7% (95% CI: 0.9% - 63.5%, N = 1) of patients, respectively. The median time to resume biologic treatment was 15.6 (range 0.9-95.9) weeks. In the DP cohorts, the resumption of biologic therapy was recorded in half of patients (50.0%, 95% CI: 30.7% - 69.3%, N= 11) in the infliximab cohort and in almost half of patients (47.1%, 95% CI: 30.2% - 64.6%, N = 16) in the vedolizumab cohort. In the infliximab cohort, the highest resumption rate was recorded by week 26 (40.9%, 95% CI: 21.5% - 63.3%, N = 9). No resumption was recorded after week 78. In the vedolizumab cohort, similar rates were recorded by week 26 and from week 78 to week 104 (32.4%, 95% CI: 18.0% - 50.6%, N = 11 and 33.3%, 95% CI: 1.8% - 87.5%, N = 1), the resumption rates at week 52 and 78 gradually declined (21.4%, 95% CI: 5.7% - 51.2%, N = 3 and 16.7%, 95% CI: 0.9% - 63.5%, N = 1, respectively). The median time to resuming the biologic therapy was shorter in the infliximab DP cohort (13.1, range 0.9-76.0 weeks) than in the vedolizumab DP cohort (16.4, range 8.7-95.9 weeks).

Overall, after DP end in two-thirds of patients (N = 38, 67.9%) corticosteroids were introduced, in three-quarters of patients (N = 25, 73.5%) in the vedolizumab DP cohort and more than half (N = 13, 59.1%) of patients in the infliximab DP cohort. There was no clear pattern regarding the rates of corticosteroids introduction in the respective observation timepoints in neither of the groups, the overall median time to introducing corticosteroid therapy was 18.6 (range 1.9-96.6) weeks, 18.0 (range 4.9-96.6) weeks in the infliximab DP cohort and 20.7 (range 1.9-96.4) weeks in the vedolizumab DP cohort. Immunomodulatory therapy after the end of DP was initiated in 3 patients,

in 2 (9.1%) patients (one bio-naïve and one bio-exposed) in the infliximab DP cohort and in 1 (2.9%) bio-exposed patient in the vedolizumab DP cohort. The overall median time to initiate the immunomodulatory treatment was 53.3 (range 21.0-78.0) weeks. In the infliximab cohort, one patient initiated it within 53 weeks after the end of the DP, while the other within 78 weeks after the end of the DP. In one patient treated in DP with vedolizumab, immunomodulatory therapy was initiated within 21 weeks after the end of DP.

During the follow-up after DP end, overall 14 (25.0%) patients required hospital treatment due to UC exacerbation, 2 (9.1%) patients in the infliximab DP cohort (by week 26, the median time to admission was 16.1 (range 12.7-19.4) weeks) and 12 (35.3%) patients in the vedolizumab DP cohort, with the median time to hospital admission of 20.9 (range 9.6-92.6) weeks. The overall median time to the hospital admission was 19.1 (range 9.6-92.6) weeks.

The median number of stools with visible blood on the previous day and stool frequency above the norm on the previous day during the prospective follow-up in the cohort treated in DP with infliximab in all time points was equal to zero. In patients in the vedolizumab DP cohort, the median numbers were 1.0 (range 0.0-6.0) and 1.5 (range 0.0-4.0) in weeks 26 and 52, respectively. In other time points, the median number of stools with visible blood on the previous day and the frequency of stools above the norm on the previous day was equal to zero.

After DP end, 14 AEs were recorded, of those 9 were experienced by week 26 and 5 by week 101 of biologic treatment discontinuation. 11 AEs (incidence 17.5/100 patient-years) were considered serious. 9 SAEs were experienced by patients treated with vedolizumab (incidence 25.4/100 patient-years), 2 SAEs by patients treated with infliximab (incidence 7.3/100 patient-years). The most frequent AEs were exacerbation of ulcerative colitis, recorded in 8 patients treated with vedolizumab and in 2 patients treated with infliximab. In 1 patient treated with vedolizumab, bladder tumor was recorded (incidence 2.8/100 patient years), considered not related to the treatment.

**Discussion**

The relapse rate at week 26 reached 43.6% (95% CI: 32.6% – 55.3%, N = 34), the median time from DP end to loss of response was 12.1 (range 0.1-24.0) weeks. In patients treated in DP with infliximab, the relapse rate at week 26 accounted for 43.8% (95% CI: 26.8% – 62.1%, N = 14), with the median time to loss of response of 13.5 (range 1.6-24.0) weeks. In the vedolizumab DP cohort, the relapse rate at week 26 accounted for 43.5% (95% CI: 29.2% - 58.8%, N = 20), the median time to loss of response reached 11.9 (range 1.6-24.0) weeks. The decline in the response/remission durability was observed in patients in the subsequent weeks of the follow-up, by week 104, it reached 73.7% (95% CI: 62.1% - 82.8%) in the overall study population. The overall relapse rate after discontinuation of biologic treatment reached 71.8% (95% CI: 60.3% - 81.1%). The overall relapse rate in the cohort of patients treated in DP with infliximab reached 68.8% (95% CI: 49.9% - 83.3%), in the cohort treated with vedolizumab reached 73.9% (95% CI: 58.6% - 85.2%). The median time to relapse reached 15.6 (range 0.0-96.4) weeks, 14.6 weeks in the infliximab cohort (14.6, range 0.0-94.4 weeks) ad 17.7 weeks in the vedolizumab cohort (17.8, range 0.0-96.4 weeks). The studies reporting the outcomes

of IBD patients after discontinuation of anti-TNF showed the risk of relapse after anti-TNF withdrawal of ca. 30-40% at 1 year, and greater than 50% beyond 2 years. In a systematic review of effects of therapy withdrawal, the cumulative probability of relapse after anti-TNF discontinuation varied from 35% to 45%, with median times of follow-up between 16 and 29 months. In a systematic review and meta-analysis of the risk of relapse after discontinuation of anti-TNF in IBD patients, which included 27 studies [21 infliximab, 6 infliximab/adalimumab], the overall risk of UC relapse after discontinuation of anti-TNF therapy was 38%; 28% of patients relapsed at 12 months and 36% at medium term, e.g. 12-24 months after the discontinuation. Data on response durability after vedolizumab discontinuation in UC patients in clinical remission is scarce. In a single retrospective observational study including patients treated with vedolizumab for at least 6 months who discontinued it after at least 3 months of stable steroid-free clinical remission, relapse rate was 64% after a median of 11.2 months. The median time to relapse was 13.2 months. In a study under Taiwan reimbursement policy which required patients to discontinue biologic treatment after one year of treatment, the percentage of relapse after biologic discontinuation reached 47.0%, 41.4%, and 40.0% for 1st, 2nd and 3rd biologic treatment cycle, respectively. Overall, the study results regarding the relapse rate in patients treated with infliximab or vedolizumab in whom biologic treatment was withdrawn seem to replicate the literature data on the biologic treatment withdrawal in UC and indicate that if followed for long enough, most patients in whom the therapy has been stopped relapse regardless of the biologic agent used. The mucosal healing at treatment discontinuation may be considered a beneficial factor in terms of the lower probability of relapse as mucosal healing at DP end was more pronounced in patients who were treated with infliximab, with corresponding improved inflammatory status (CRP level) in this cohort in comparison to patients treated in DP with vedolizumab. A significant association between CRP levels and the risk of relapse in patients with CD or UC was reported in the literature.

After biologic treatment had been discontinued, it was re-initiated in half of patients who lost the response. The highest rate of retreatment, reaching 35.7%, was observed by week 26, the median time to restarting biologic treatment was 15.6 weeks following the end of DP. The rate of retreatment by week 26 was comparable in patients treated with infliximab (40.9%) and with vedolizumab (32.4%) and continued to be comparable by week 78 (20% vs. 16.7%). In patients treated in DP with infliximab, biologic treatment was re-initiated earlier (median 13.1 weeks) than in those treated in DP with vedolizumab (16.4 weeks). A favorable outcome following retreatment in relapsing patients after transient discontinuation of maintenance therapy with anti-TNF drugs was reported earlier. In a meta-analysis of the relapse after discontinuation of anti-TNF therapy, the efficacy of retreatment was 85%. In other systematic reviews and meta-analyses to evaluate the efficacy and safety of retreatment in patients with IBD, remission rate following infliximab reinduction was 78%. Unfortunately, none of these studies provided details on the rate and time of biologics reintroduction after prior discontinuation. In the only prospective observational study, biological therapy needed to be reintroduced in 59% of patients after a median 7.5 months of earlier discontinuation. Response was achieved in 54% of patients within an average of 8 weeks after the reintroduction of the therapy. Detailed data on the rate and time of vedolizumab reintroduction are lacking. The literature data imply high vedolizumab effectiveness at retreatment, similarly to the high efficacy of retreatment with anti-TNFs. The results of the current study may suggest that the need for biologic retreatment after non-elective treatment withdrawal is more pronounced if patients were treated with infliximab than with vedolizumab. This observation warrants further research. Unfortunately, collection of the data on the efficacy of biologics reintroduction remained beyond the scope of the study.

Of 84 patients enrolled in the study, all (100%) responded to induction with infliximab (N = 35) or vedolizumab (N = 49). More than 90% of patients completed the full DP treatment (N = 32, 91.4%

in the infliximab DP cohort, N = 46, 93.9% in the vedolizumab DP cohort). In most patients (N = 55, 70.5%) who completed the full DP treatment, both in the infliximab cohort (N = 24, 75.0%) and the vedolizumab cohort (N = 31, 67.4%), remission at DP completion was observed. Response was observed in 29.5% (N=23) of all patients who completed the full DP treatment, in 8 (25.0%) patients in the infliximab DP cohort and in 15 (32.6%) patients in the vedolizumab cohort. Steroid-free remission rate reached 29% in the vedolizumab DP cohort and 25% in the infliximab cohort. The clinical remission and steroid-free remission rates shown in this study after 52 weeks of biologic treatment need to be considered with caution. The study results may be skewed by the study design which focused on enrolling patients who completed DP with response/remission and included the retrospective data collection regarding the outcomes of treatment in DP. This resulted in a preselection of patients which in consequence might have impacted drug effectiveness data in the study cohort.

Important treatment goals in UC are to achieve and then sustain corticosteroid-free clinical remission, allowing patients to benefit from short-term corticosteroid use while avoiding the safety issues associated with longer-term corticosteroid use. According to literature reviews, after initial exposure to corticosteroids, around two-third of patients will require their reintroduction, and one-third will become steroid-dependent over time. The study results showed high effectiveness of biologic therapy in assuring corticosteroid-free disease course in UC patients. At DP start, two-thirds of patients in the study population were treated with corticosteroids, with comparable rate in the vedolizumab cohort (69.6%) and in the infliximab cohort (65.6%). The median prednisolone dose equivalents at DP start were 30 mg/day. At DP end, the rate of corticosteroids non-users reached almost 90%, it was higher in patients treated with infliximab, in whom only one patient used corticosteroids, than in individuals treated with vedolizumab, however in this cohort it exceeded 80%. The median dose equivalents were reduced to 15 mg/day. Studies have shown anti-TNF therapy to be effective in achieving corticosteroid-free remission (in about 30%) in patients with moderate-to-severe UC.



After cessation of biologic treatment, corticosteroids were re-introduced in two-thirds patients who relapsed. Their use was required in around 40% of patients already at week 26, in 41.2% of patients in the vedolizumab cohort and 36.4% of patients in the infliximab cohort. Over the entire study period, three-quarters of patients treated in DP with vedolizumab and more than half of patients treated with infliximab were on corticosteroids by week 104. The median time to corticosteroids initiation was 18.6 weeks, it was comparable in patients treated in DP with infliximab (18.0 weeks) and with vedolizumab (20.7 weeks). The data show that initiation of corticosteroids was more frequent after vedolizumab withdrawal than after infliximab withdrawal. However, any inference regarding the corticosteroid reintroduction resulting from the specific biologic agent used is burdened with significant limitations. To some extent, these findings correspond with the observation on the relapse rates in both groups. The small size of the DP groups may partly impact the results.

Retrospective data has reported that steroid dependency in UC patients ranges between 11% and 38%. The steroid-dependent cohort in this study reached 50%. The population included in the study followed the inclusion criteria of DP and, therefore, included patients in whom immunosuppressive treatment had failed, and corticosteroid dependency was high. Additionally the vedolizumab cohort included more steroid-dependent patients (more than half of the cohort) than the infliximab one (more than a third). Therefore, the inclusion criteria of DP can explain the high percentage of patients with corticosteroid dependence in this study. Furthermore, the differences in the clinical characteristics of study subjects at baseline between the infliximab and vedolizumab cohorts, including disease extent or CRP value, or in biologic treatment prior to the DP start and primary lack of response to the treatment prior to DP start need also to be taken into account as the confounding factors. Higher rates

of steroid dependency and a high need for early corticosteroids reintroduction may reflect a more severe UC population which could partly explain why the rate of corticosteroid users in the study diverges from those in the literature.

[redacted]

During DP, 5 AEs were recorded (incidence 5.8/100 patient years). 2 of them (*Clostridium difficile* infection, of mild severity, and arthrtalgia, of moderate severity, incidence 2.9/100 patient-years each were assessed as related with infliximab use). One SAE (GI obstruction, incidence 1.2/100 patient-years) was considered serious but not related to the treatment used (infliximab). No AEs related to

its use, nor SAEs were reported for vedolizumab. No statistical analysis was made for the AEs recorded in the current study, it seems unlikely, however, that if it had been provided, it would have implied any changes to the well-known safety profiles of both biologic agents.

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