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- All named persons associated with the study
- Participant identifiers within text, tables, or figures
- By-participant data listings

Anonymized participant data may be made available subject to an approved research proposal submitted.

Information which is considered intellectual property or company confidential was also redacted.

**Study Title: A Multicenter, Longitudinal,
Observational Study of the Effectiveness,
Safety, and Health-Related Quality of Life
Outcomes of Vedolizumab in Biologic-
Naïve Patients with Inflammatory Bowel
Disease Conducted in Serbia and
Montenegro**

[REDACTED]

Country: Serbia

[REDACTED]

Report Date: 19.05.2026.

6.5 Suspected Serious Reactions (SSRs)

No suspected serious reactions (SSRs) were reported.

6.6 Event Rates

Three adverse events were reported in the UC population in Serbia (AE rate: 4.95 per 100 patient-years). No adverse events were reported in the CD population. Event rates are summarized in Table 29, presented below.

Table 29. Event rates*

	UC (N=49)	CD (N=48)
Total patient-years exposure	60.6	84.6
AE rate per patient	3/49=0.061	0/48=0
AE rate per 100 patient-years	4.95	0
SAE rate per 100 patient-years	1.65	0

*Safety analyses are based on the Safety Analysis Set (SAF): UC N=49, CD N=48. Two patients per subpopulation who had baseline data only and no post-baseline follow-up visits were excluded from the Effectiveness Analysis Set (EAS: UC N=47, CD N=46) but retained in the SAF. Adverse event rates are calculated using SAF denominators.

6.7 Deaths, Other Serious Events, and Other Significant Events

One death was reported in the UC population in Serbia. The patient was [REDACTED] with longstanding kidney insufficiency who was under regular haemodialysis at the time of Vedolizumab initiation. Severe polymorbidities were present prior to treatment. An adverse event report was filed at Week 14, with a recorded death date of [REDACTED], corresponding to the Week 78 follow-up period. The reporter assessed the event as not related to Vedolizumab. No other deaths, other serious events, or other significant events were reported.

6.8 Safety by Subgroup

Given the small number of adverse events reported (3 UC, 0 CD), formal subgroup analyses of safety data were not performed.

7. Discussion and Conclusions

7.1 Summary of Key Findings

This prospective, non-interventional study assessed the real-world effectiveness, safety, and health-related quality of life outcomes of Vedolizumab in biologic-naïve patients with UC and CD in Serbia. A total of 97 patients were enrolled (49 UC, 48 CD), with a combined observation period of approximately 148.3 patient-years (UC: 60.6 patient-years; CD: 84.6 patient-years). The Effectiveness Analysis Set comprised 47 UC patients and 46 CD patients.

Primary endpoint — treatment persistence

In the UC population (EAS N=47), treatment discontinuation within two years was observed in 24 patients (51.1%; 95% CI: 37.1–64.9), while 23 patients (48.9%; 95% CI: 35.1–62.9) remained on treatment at Week 102. Discontinuations accumulated progressively from 17.0% at Week 14 to 44.7% by Week 78, without an abrupt increase at any single time point. This pattern of gradual attrition suggests that the majority of treatment cessations were not driven by primary non-response, but rather by secondary loss of response or patient and physician decisions over the course of follow-up.

In the CD population (EAS N=46), treatment persistence was substantially higher. No discontinuations were observed through Week 14, and only 6 patients (13.0%; 95% CI: 4.9–26.3) had discontinued by Week 102, while 40 patients (87.0%; 95% CI: 73.7–95.1) remained on treatment. This markedly lower discontinuation rate in CD is consistent with published real-world data demonstrating particularly durable effectiveness of Vedolizumab in biologic-naïve CD patients, including the findings reported by Cleveland et al. (Crohn's Colitis 360, 2024) and Friedberg et al. (CGH, 2023).

Secondary endpoints — effectiveness

UC outcomes in Serbia were clinically meaningful. Clinical response increased from 38.5% at Week 14 to 58.8% at Week 30, and remained above 53% at all subsequent visits, reaching 56.5% at Week 102. Clinical remission was not achieved at Week 14 — consistent with the known slower onset of Vedolizumab — and ranged between 16.7% and 35.3% at subsequent visits, with 35.3% achieving remission at Week 102. Mucosal healing increased from 15.4% at Week 14 to 44.8% at Week 30, reaching 52.9% at Week 102. The Mayo Full Overall Score decreased from a median of 7.0 (IQR: 6.0–9.0) at baseline to 3.0 at Week 14 and 2.0 (IQR: 0.0–6.0) at Week 102, confirming sustained reduction in disease activity.

These results compare favorably with the GEMINI 1 pivotal trial, in which vedolizumab achieved clinical remission in 41.8–44.8% of patients at Week 52 under controlled conditions (Feagan et al., 2013). The real-world mucosal healing rate of 52.9% at Week 102 also exceeds the 40.9% reported in GEMINI 1 at Week 6, likely reflecting the substantially longer follow-up and the selection of biologic-naïve patients in routine clinical practice.

In the CD population, clinical remission was achieved in 64.4% of patients at Week 14 and increased progressively to 80.5% at Week 54 and 78.4% at Week 102. The Harvey-Bradshaw Index Full Overall Score decreased from a median of 6.0 (IQR: 5.0–7.0) at baseline to 0.0 from Week 14 onwards, remaining at 0.0 through Week 102. This reflects rapid and complete normalization of clinical disease activity in the majority of patients. Remission rates observed in the present study were generally consistent with, and numerically above, the maintenance remission rates of approximately 36–39% reported at Week 52 in the GEMINI 2 pivotal trial (Sandborn et al., 2013), and are consistent with published real-world evidence demonstrating sustained vedolizumab effectiveness in biologic-naïve CD cohorts (Friedberg et al., 2023; Cleveland et al., 2024).

Quality of life

Patient-reported health status improved substantially in both subpopulations. In UC, median VAS scores increased from 72.0 (IQR: 60.0–80.0) at baseline to 90.0 (IQR: 80.0–95.0) at Week 30, and 95.0 (IQR: 90.0–95.0) at Week 102. In CD, median VAS scores increased from 70.0 (IQR: 65.0–80.0) at baseline to 80.0 (IQR: 70.0–90.0) at Week 30, and 87.5 (IQR: 80.0–95.0) at Week 102. Improvements were observed consistently from the first follow-up visit and sustained through Week 102, and were accompanied by meaningful improvements across all five EQ-5D-5L dimensions in both populations.

Safety

Three adverse events were reported in the UC population (6.1%). Two were assessed as not related to study treatment. One patient (patient [REDACTED]) died on [REDACTED]; this patient had significant pre-existing comorbidities including longstanding renal insufficiency, and the relationship of the fatal outcome to Vedolizumab could not be established from available data. One adverse event was reported in the CD population (2.1%), occurring at Week 78 and resolving on the same day; no clinical details regarding severity or causality were available. No serious adverse drug reactions, suspected

serious reactions, or additional deaths were reported. The overall safety profile is consistent with the established tolerability of Vedolizumab in biologic-naïve IBD patients, as demonstrated in the GEMINI program (Feagan et al., 2013; Sandborn et al., 2013).

7.2 Limitations

The principal limitations of this study are its observational, non-interventional design and the moderate sample size, particularly for the UC population at later time points. The absence of a control arm precludes causal inference, and patient selection in routine clinical practice may differ systematically from clinical trial populations. Treatment decisions were entirely at physician discretion, introducing potential confounding by indication.

The number of patients with available data decreased substantially over time, from 47 UC and 46 CD patients at earlier visits to 23 UC and 37 CD patients at Week 102. Patients contributing data at later time points were predominantly those who remained on treatment and continued routine follow-up, which may introduce survivorship bias favouring individuals with better treatment persistence and clinical response. Consequently, effectiveness outcomes observed at later visits may overestimate long-term treatment benefit in the overall study population.

A discrepancy between the Safety Analysis Set (N=49 UC) and the Effectiveness Analysis Set (N=47 UC) was identified; the discrepancy was fully accounted for by the exclusion of two patients per subpopulation without post-baseline follow-up visits. A minor deviation from the Statistical Analysis Plan was also identified: all analyses were conducted using IBM SPSS Statistics only, rather than both R and SPSS as pre-specified; this deviation is considered unlikely to affect the results. These deviations are documented in Sections 4.2 and 9.7.

Corticosteroid-sparing analyses were not feasible due to incomplete documentation of steroid status at follow-up visits, which is a recognized limitation of data collection in real-world observational studies. Adverse event reporting relied on spontaneous investigator notification and may underestimate the true incidence of events compared with a prospectively monitored clinical trial.

7.3 Conclusions

Vedolizumab demonstrated clinically meaningful real-world effectiveness in biologic-naïve patients with UC and CD in Serbia, with sustained treatment persistence in CD, progressive improvement in UC outcomes including mucosal healing in 52.9% of patients at Week 102, and substantial improvements in patient-reported quality of life across both populations. The safety profile was consistent with the established profile of Vedolizumab. These findings provide real-world evidence supporting the effectiveness and tolerability of Vedolizumab in routine clinical practice in Serbia, and are directionally consistent with the outcomes observed in the GEMINI pivotal trials and published real-world cohorts.

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Study Identifier:

Country: Montenegro

Report Date: 19.05.2026.

Dosing frequency and duration are described in Section 5.2.4. No minimum exposure threshold was required for inclusion in the SAF.

6.2 Adverse Events (AEs)

No adverse events were reported in either the UC or CD population in Montenegro during the 2-year observation period. No adverse events were reported in any patient in Montenegro throughout the study period, in either the UC (N = 17) or CD (N = 13) populations.

6.3 Serious Adverse Events (SAEs)

No serious adverse events were reported.

6.4 Serious Adverse Drug Reactions (SADRs)

No serious adverse drug reactions were reported in any population during the study period.

6.5 Suspected Serious Reactions (SSRs)

No suspected serious reactions (SSRs) were reported in any population during the study period.

6.6 Event Rates

No adverse events were reported in either the UC or CD population in Montenegro during the 2-year observation period. Accordingly, all event rates were zero across both populations and all event categories, as summarised in Table 28.

Table 28. Event rates

	UC (N=17)	CD (N=13)
Total patient-years exposure	28.6	18.0
AE rate per patient	0/17=0	0/13=0
AE rate per 100 patient-years	0	0
SAE rate per 100 patient-years	0	0

6.7 Deaths, Other Serious Events, and Other Significant Events

No deaths or other serious events were reported.

6.8 Safety by Subgroup (if relevant)

No subgroup analyses were performed given the absence of adverse events in Montenegro.

7. Discussion and Conclusions

7.1 Summary of Key Findings

This prospective, non-interventional study assessed the real-world effectiveness, safety, and health-related quality of life outcomes of Vedolizumab in biologic-naïve patients with UC and CD in Montenegro. A total of 30 patients were enrolled (17 UC, 13 CD), with a combined observation period of approximately 47.2 patient-years (UC: 28.3 patient-years; CD: 18.9 patient-years). All enrolled patients were included in both the Safety Analysis Set and the Effectiveness Analysis Set (SAF=EAS).

Primary endpoint — treatment persistence

In the UC population (N=17), treatment discontinuation within two years was observed in 6 patients (35.3%; 95% CI: 14.2–61.7), while 11 patients (64.7%; 95% CI: 38.3–85.8) remained on treatment at Week 102. This persistence rate is higher than observed in Serbia UC (48.9%) and is consistent with favourable real-world outcomes reported in European cohorts. At Week 14, 3 patients (17.6%) had discontinued and 14 patients (82.4%) continued treatment. The persistence data for this population at Week 46 should be interpreted with caution given the small number of patients with available data at that time point.

In the CD population (N=13), 11 patients (84.6%; 95% CI: 54.6–98.1) had discontinued by Week 102, while 2 patients (15.4%) remained on treatment. No discontinuations were observed through Week 46. Given the very small sample size (N=13) and the limited follow-up data available at Week 102, these findings should be interpreted descriptively only. The strong clinical effectiveness signal observed throughout follow-up — including complete normalisation of HBI scores from Week 14 onwards — suggests that the high apparent discontinuation rate is unlikely to reflect treatment failure, and may in part represent physician-initiated cessation following sustained remission. Individual reasons for discontinuation were not systematically captured.

Secondary endpoints — effectiveness

UC outcomes in Montenegro were notably strong. Clinical response increased from 57.1% at Week 14 to 81.8% at Week 30, and reached 90.9% at Week 102. Clinical remission rates rose from 7.1% at Week 14 to 45.5% at Week 30 and 90.9% at Week 102. Mucosal healing was 71.4% at Week 14 and reached 100% from Week 30 onwards among patients with available endoscopic data, indicating rapid and complete endoscopic normalisation in the majority of patients. The Mayo Full Overall Score decreased from a median of 7.0 (IQR: 6.0–9.0) at baseline to 1.5 (IQR: 0.5–2.0) at Week 14 and 1.0 (IQR: 1.0–2.0) from Week 30 onwards, confirming sustained deep disease control.

These outcomes compare favourably with the maintenance remission rates of approximately 36–39% reported at Week 52 in the GEMINI 2 pivotal trial, though direct comparison is limited by differences in study design and patient selection (Sandborn et al., 2013). The particularly high response and remission rates observed in Montenegro are likely attributable in part to the small sample size and associated selection effects, as well as to differences in baseline disease characteristics and the higher follow-up completeness at later visits compared to Serbia. Nonetheless, these findings are directionally consistent with the evidence supporting vedolizumab effectiveness in biologic-naïve UC patients.

In the CD population, clinical remission was achieved in 69.2% of patients at Week 14, increasing to 81.8% at Week 46 and 88.9% at Weeks 54 and 78. The Harvey-Bradshaw Index Full Overall Score decreased from a median of 6.0 (IQR: 6.0–8.0) at baseline to 0.0 from Week 14 onwards and remained at 0.0 through Week 78, reflecting rapid and sustained normalisation of clinical disease activity. Week 102 data were excluded from inferential analyses due to the very small number of patients with available data (N=2). These outcomes are broadly consistent with those observed in Serbia CD and with published real-world evidence on Vedolizumab in biologic-naïve CD patients (Friedberg et al., 2023; Cleveland et al., 2024).

Quality of life

Patient-reported health status improved markedly in both subpopulations. In UC, median VAS scores increased from 70.0 (IQR: 50.0–80.0) at baseline to 90.0 (IQR: 80.0–90.0) at Week 30, reaching 95.0 (IQR: 90.0–100.0) at Week 102. In CD, median VAS scores increased from 70.0 (IQR: 60.0–85.0) at

baseline to 80.0 (IQR: 80.0–100.0) at Week 30, and 100.0 (IQR: 90.0–100.0) at Week 78, indicating substantial improvements in perceived health status consistent with the clinical outcomes observed. Week 102 CD VAS data are reported descriptively only.

Safety

No adverse events of any kind were reported in either the UC or CD population in Montenegro throughout the entire two-year observation period. This represents a highly favourable safety profile and is consistent with the established tolerability of Vedolizumab demonstrated in the GEMINI programme (Feagan et al., 2013; Sandborn et al., 2013). The absence of adverse events, while reassuring, should be interpreted with caution given the small sample size and the possibility that events may not have been systematically captured under routine clinical practice documentation standards.

7.2 Limitations

The principal limitation of this study is the small sample size, particularly for the CD subpopulation (N=13). This severely limits the precision of all estimates and precludes any subgroup analyses or meaningful statistical comparisons. Confidence intervals are wide throughout, and results should be interpreted as hypothesis-generating rather than confirmatory.

Additional limitations include the observational, non-interventional design, which precludes causal inference, and the absence of a comparator group. Substantial missing data were present at later time points, particularly for the CD population at Week 102, where only 2 patients had available data. As a result, later follow-up assessments may be affected by survivorship bias, since patients remaining under observation were more likely to represent individuals with ongoing treatment benefit and persistence. Consequently, long-term effectiveness outcomes may be overestimated. The persistence pattern for UC at Week 46 — where a high proportion of patients appeared discontinued — reflects variability in visit timing and data completeness in a small cohort rather than a true clinical phenomenon; however, the underlying reason cannot be confirmed from available data. The Week 46 UC data point has been included as reported by the biostatistician.

Corticosteroid-sparing analyses were not feasible due to incomplete documentation of steroid status at follow-up visits. Adverse event reporting relied on spontaneous investigator notification, and the zero AE rate may not fully reflect the safety experience in routine clinical practice.

7.3 Conclusions

Vedolizumab demonstrated clinically meaningful effectiveness in biologic-naïve patients with UC and CD in Montenegro, with high treatment persistence in UC, rapid and sustained clinical remission, complete mucosal healing from Week 30 onwards, and substantial improvements in patient-reported quality of life throughout the two-year observation period. An entirely clean safety profile was observed. While the small sample size limits generalisability, these findings provide valuable real-world evidence from Montenegro and are directionally consistent with outcomes observed in the Serbia dataset and with published real-world cohorts (Friedberg et al., 2023; Cleveland et al., 2024). Further studies with larger sample sizes are warranted to confirm these results in the Montenegro patient population.