This report may include approved and non-approved uses, formulations, or treatment regimens. The results reported may not reflect the overall profile of a product. Before prescribing any product mentioned in this report, healthcare professionals should consult local prescribing information for the product approved in their country.

SPONSOR is committed to publicly disclosing all medical research results that are significant to patients, health care providers or payers-whether favorable or unfavorable to the SPONSOR product-in an accurate, objective and balanced manner in order for our customers to make more informed decisions about our products.
Personally identifiable information (PII) within this document is either removed or redacted (i.e., specific content is masked irreversibly from view with a black bar) to protect personal privacy. Personally identifiable information includes:

- All named persons associated with the study
- 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.

Non-Interventional Study (NIS) Synopsis

Title	Observational Study of the Effectiveness of Vedolizumab on Treatment Outcomes and HRQoL in biologic naïve Patients with Inflammatory Bowel Diseases in Greece – the TROVE Study
PASS	No
EU PAS register number	EUPAS23580
Active substance	L04AG05 (vedolizumab)
Medicinal product	Entyvio®
Procedure number	Not applicable
Joint PASS	Not applicable
Country(-ies) of study:	Greece
Version/Date	V 0.1 / 14 October 2025
Page 1 of 11	

Title of the study	Observational Study of the Effectiveness of Vedolizumab on Treatment Outcomes and HRQoL in biologic naïve Patients with Inflammatory Bowel Diseases in Greece – the TROVE Study
Short title of the study	Vedolizumab in biologic naïve patients with IBD in Greece
Keywords	Ulcerative colitis, Crohn's disease, treatment persistence, HRQoL, vedolizumab, real-world, Greece
Rationale and background	Inflammatory bowel disease (IBD) poses significant challenges not only in its clinical management but also in addressing its broader impacts on patients' health-related quality of life (HRQoL). While vedolizumab has demonstrated clinical effectiveness in controlled clinical trials, real-world evidence, particularly in biologic-naïve populations, remains limited. This study aimed to address this gap by evaluating the long-term clinical benefits of vedolizumab in the Greek biologic-naïve IBD population, focusing on drug discontinuation rates, disease control through clinical indices such as the Full or Partial Mayo Score (FMS/PMS) for ulcerative colitis (UC) and the Harvey-Bradshaw Index (HBI) for Crohn's disease (CD), and patient-reported outcomes (PROs), as well as its impact on HRQoL.
Research question and objectives	***Primary objective*** • To assess the long-term clinical benefit for the biologic-naïve patients with IBD on treatment with vedolizumab. ***Secondary objectives*** • To assess the effectiveness of vedolizumab on HRQoL. • To evaluate clinical and endoscopic remission in patients on treatment with vedolizumab in real-world clinical practice. • To evaluate patient satisfaction with treatment. • To evaluate the role of laboratory tests (biological activity markers such as C-reactive protein [CRP] and faecal calprotectin [FCP]) as an adjunctive measure in disease management and vedolizumab treatment in clinical practice. • To assess the safety of vedolizumab.
Study design	TROVE was a prospective, observational (non-interventional), multicentre, cohort study designed primarily to assess the long-term clinical benefit in bio-naïve UC or CD patients initiating treatment with vedolizumab and being followed over a 2-year period in real-world clinical practice in Greece.
Setting	The study was conducted across 22 public and private gastroenterology and internal medicine departments/clinics across hospitals located in major cities of Greece. Investigators/sites were requested to consecutively enrol UC or CD patients initiating treatment with vedolizumab as per routine clinical practice, up to a predefined target based on site capacity; sites with low recruitment rates could be compensated by others. Recruitment spanned

	approximately two years, from 02 Nov 2018 (First Patient In; FPI) to 19 Jan 2021 (Last Patient In; LPI). Participating physicians followed each enrolled patient for up to 2 years after vedolizumab treatment initiation or until treatment discontinuation, whichever occurred first. Data collection occurred at Baseline (i.e., most recent assessments prior to vedolizumab treatment initiation) and thereafter during routine follow-up visits performed within the context of clinical practice, closest to the following timepoints: Week 14, Week 30, Week 46, Week 54, Week 78, and Week 102. Patients discontinuing vedolizumab before completing the 2-year follow-up were permanently withdrawn from the study.
Subjects and study size, including dropouts	A total of 182 adult patients (≥18 years of age) with moderately to severely active UC or CD, who had an inadequate response to, lost response to, or were intolerant to conventional therapy, and who were biologic-naïve and initiated treatment with vedolizumab, were enrolled in the study from 02 Nov 2018 to 19 Jan 2021. The cohort comprised 70 patients with CD and 112 with UC. Overall, 106 patients (58.24%) completed the two-year follow-up period of the study (67.14% in the CD and 52.68% in the UC subgroup). A total of 76 patients (41.76%) discontinued from the study, with the most common primary reasons for discontinuation being treatment secondary failure (23 patients; 29.87%), treatment primary failure (14 patients; 18.18%), or other reasons (15 patients; 19.48%).
Variables and data sources	This study mainly involved primary data collection using an electronic case report form (eCRF). Data were obtained within the context of routine clinical practice through clinical and laboratory assessments, medical chart abstraction, and patient self-reports. No additional diagnostic, monitoring or therapeutic procedures beyond those of routine clinical practice were performed. Patients' baseline sociodemographic and anthropometric characteristics, disease history and status at baseline, prior or concomitant non-biologic therapies, extraintestinal manifestations and relevant comorbid medical conditions, as well as laboratory assessments, were abstracted from patients' medical records. Treatment details and adverse events (AEs) were recorded as they occurred. Data on disease activity for both UC and CD were collected through routine clinical assessments performed by the treating physician, incorporating PROs. For UC, the FMS/PMS was used, along with standalone 2-item PROs (PRO2; stool frequency and rectal bleeding over the past 3 days). For CD, the HBI and PRO2 (abdominal pain and number of liquid or soft stools over the past 3 days) were used. Data on diagnostic evaluations, including both endoscopic and non-endoscopic imaging procedures, were recorded, if performed.

Additional PROs, such as the SIBDQ, the EQ-5D, and the TSQM-9 questionnaire, were completed by patients themselves or with assistance from the study physician when needed.

Primary outcome:

The primary outcome of the study was the drug discontinuation rate in UC patients and CD patients under treatment with vedolizumab during the two-year follow-up period and the reason(s) for discontinuation.

Secondary outcomes:

- Changes from baseline in SIBDQ and EQ-5D questionnaire scores for UC and CD patients at 30, 46, 54, 78, and 102 weeks of treatment.
- Changes from baseline in the PMS for UC patients and the HBI score for CD patients at 14, 30, 46, 54, 78, and 102 weeks of treatment.
- Rate of dose intensification (from Q8W to every six weeks [Q6W] or Q4W) among UC and CD patients over the two-year follow-up period.
- Proportion of UC and CD patients on steroids (steroid-sparing effect) at baseline, Week 6, and Week 14.
- Impact of treat-to-target treatment with vedolizumab, as assessed by changes from baseline in PROs of the PMS for UC patients and of the HBI for CD patients (rectal bleeding and stool frequency for UC, and abdominal pain and liquid or soft stools for CD) at 14, 30, 46, 54, 78, and 102 weeks of treatment, taking into consideration the average of the last 3 days.
- Endoscopic disease activity at baseline and Week 52 using the Mayo Endoscopic Score in UC patients and the Simple Endoscopic Score for Crohn's Disease (SES-CD) in CD patients.

  Note: Regarding UC, the majority of clinical trials define endoscopic remission and mucosal healing as a Mayo Endoscopic Score of 0 or 1. Regarding CD, endoscopic remission is defined as a SES-CD score between 0 and 2.
- Changes from baseline in the TSQM-9 score for UC and CD patients at 14, 30, 46, 54, 78, and 102 weeks of treatment.
- Effects of biological parameters as an adjunctive measure for monitoring inflammation, assessed by changes from baseline in CRP and FCP levels in UC and CD patients at 14, 30, 46, 54, 78, and 102 weeks of treatment.
- Clinical response, endoscopic response, CRP and FSP changes at Week 52 and Week 102, as well as changes of haemoglobin at week 14.
- Number of serious adverse events (SAEs), non-serious related AEs

	and special situation reports (SSRs).
Results	Of the 182 enrolled patients, 166 had at least one post-baseline clinical and/or endoscopic assessment and thus were included in the Full Analysis Set (FAS). This cohort served as the basis for all primary and secondary outcome analyses and was further divided into FAS-CD (N=65) and FAS-UC (N=101). **Baseline demographic characteristics, disease history and status at baseline** The mean ± SD age of the total cohort (FAS) at baseline (VDZ treatment initiation) was 47.44 ± 17.305 years, with just over half being male (53.61%) and the vast majority (98.80%) White/Caucasian. Nearly half of the patients were non-smokers (46.39%), while 27.11% were former smokers, and 24.10% were current smokers. The FAS-CD and FAS-UC subgroups exhibited a similar profile to that of the overall FAS population. At the time of CD diagnosis, the mean ± SD age of patients was 41.88 ± 19.474 years. According to the Montreal classification, most patients had either ileocolonic (L3; 35.38%) or ileal disease, with or without limited caecal involvement (L1; 33.85%), and exhibited non-stricturing, non-penetrating disease behaviour (B1) (67.68%). Active fistulae were present in 6.15% of patients, primarily anal or perianal. The mean ± SD age of UC patients at the time of diagnosis was 40.15 ± 16.448 years. Based on the Montreal classification, nearly half of these patients (47.52%) had extensive colitis (E3), while 42.57% had left-sided colitis (E2). In CD patients, the mean baseline HBI score was 7.08 ± 4.45, with moderate disease activity present in 38.46% of patients, remission in 33.85%, mild activity in 23.08%, and severe activity in 4.62%. For patients with a Crohn's Disease Activity Index (CDAI) assessment available (N=34), the mean ± SD score was 192.25 ± 102.628, while for patients with a SES-CD assessment available (N=41), the mean ± SD score was 12.24 ± 9.518, with severe endoscopic activity in 31.71% of patients, moderate and mild activity in 31.71% each, and remission in 4.88%. In UC patients, the mean baseline FMS was 7.04 ± 2.76, with moderate disease activity in 62.38%, mild activity in 20.79%, severe activity in 8.91%, and remission in 7.92%. **VDZ treatment initiation details** The most common primary reason for initiating VDZ within the overall study population was lack of or incomplete response to prior non-biologic therapy, reported in 53.61% of cases (44.62% in CD and 59.41% in UC). At the time of VDZ treatment initiation, most patients (45.18%) were neither steroid-dependent nor steroid-intolerant (56.92% in CD and 37.62% in UC), 31.33% were steroid-dependent (24.62% in CD and 35.64% in UC), and 6.02% were steroid-intolerant (4.62% in CD and 6.93% in UC).

Primary outcome: VDZ discontinuation rate

During the 2-year follow-up period, 36.14% of patients discontinued VDZ treatment (95% CI: 28.94% – 44.00%), translating to a treatment persistence rate of 63.86%. Discontinuation rates were higher among UC patients (41.58%; 95% CI: 31.99% – 51.82%) compared to CD patients (27.69%; 95% CI: 17.65% – 40.39%). Secondary treatment failure (37.70%) and primary treatment failure (19.67%) were the leading primary reasons for discontinuation. In UC patients, secondary failure accounted for 34.88% of discontinuations, followed by primary failure (23.26%). Similarly, in CD patients, secondary failure was the leading cause (44.44%), while other reasons contributed to 16.67%.

Secondary outcomes

HRQoL

SIBDQ

The mean ± SD SIBDQ total score at baseline was 44.38 ± 13.117, indicating moderate impact on HRQoL. Significant improvements were observed throughout the treatment period, with progressively larger increases in SIBDQ scores from baseline. By Week 14, the mean increase (i.e., improvement) was 9.45 points (95% CI: 7.29–11.60, $p<0.001$), reaching 12.96 points by Week 102 (95% CI: 10.52–15.40, $p<0.001$). Improvements were significant across all subdomains and timepoints ($p<0.001$).

EQ-5D

The mean ± SD EQ VAS score at baseline was 66.91 ± 20.372, indicating a moderate level of perceived health status. Significant improvements were observed throughout the treatment period, with the LS mean EQ VAS score increasing (i.e., improving) by 9 points at Week 14 and reaching an increase of 14.2 points by Week 102 ($p<0.001$ for all timepoints).

According to EQ-5D-5L responses at baseline, the majority of patients (76.40%) had no problems walking, while only 9.93% had moderate to severe problems. Nearly all patients (93.17%) also reported no issues with self-care, and almost half (48.45%) reported no problems performing usual activities. Regarding pain or discomfort, 35.40% of patients reported no pain, while 34.78% experienced slight pain, whereas anxiety or depression was common, with 59.0% of patients experiencing moderate, severe or extreme levels of anxiety/depression (36.02%, 15.53%, and 7.45%, respectively).

Disease activity

FMS/PMS for UC patients

Disease activity assessed by the Mayo score (FMS or PMS) demonstrated significant improvements throughout the treatment period. Remission rates

increased from 7.92% at baseline to 61.39% by Week 14, with further improvements observed by Week 102, where 89.66% of patients were at remission.

Shifts in disease activity categories further highlight the positive impact of treatment over time. By Week 14, 75.25% of patients showed improvements from their baseline condition, 22.77% remained stable, and only 1.98% deteriorated. Improvements persisted at later timepoints, with 72.28% improving by Week 30 and 50.50% by Week 102. Stability rates declined as more patients transitioned to better disease control, while deterioration remained rare, observed in 1.98% of patients at Week 54 and none at Week 78. Statistical analysis of these shifts confirmed significant changes in disease activity across all timepoints ($p < 0.001$).

HBI for CD patients

Disease activity assessed by the HBI also demonstrated significant improvements over the course of treatment, with the mean HBI score decreasing from 7.08 ± 4.45 at baseline to 1.87 ± 1.55 by Week 102. Accordingly, remission rates increased from 33.85% at baseline to 75.00% by Week 14, and further to 93.33% by Week 102.

Shifts in disease activity categories from baseline further reflect these improvements. By Week 14, 38.46% of patients improved, 23.08% remained stable, and no deterioration was observed. At Week 30, 36.92% improved, 16.92% remained stable, and 1.54% deteriorated. Improvement rates remained consistent at later time points: 36.92% by Week 30, 35.38% by Week 46, 36.92% by Week 54, and 32.31% by Week 78. By Week 102, 27.69% of patients improved, with only 1.54% deteriorating at Weeks 30 and 102. Statistical analysis confirmed significant changes in disease activity across all timepoints ($p < 0.001$).

PROs

Rectal bleeding for UC patients

At baseline, 35.64% of patients reported a rectal bleeding score of 2 (obvious blood with stool most of the time), 33.66% a score of 0 (no visible blood in stools) and 29.70% a score of 1 (streaks of blood with stool less than half of the time). Over time, the percentage of patients with a score of 0 improved substantially, increasing to 85.15% by Week 14 and 94.83% by Week 102.

Stool frequency for UC patients

At baseline, the majority of patients (59.40%) had stool frequency scores of 2 or 3 (21.78% and 37.62%, respectively). A score of 0 was observed in 19.80% of patients at baseline, which increased to 56.44% by Week 14 and 93.10% by Week 102. Accordingly, the proportion of patients with a score

of 2 or 3 decreased to 10.89% and 4.95% by Week 14, respectively, with no patients reporting such scores by Week 102.

Abdominal pain for CD patients

At baseline, 41.53% of patients reported moderate or severe abdominal pain (35.38% with a score of 2 and 6.15% with a score of 3), which decreased to 7.69% by Week 14 (6.15% with a score of 2 and 1.54% with a score of 3) and further to 2.13% by Week 102 (no patients with a score of 2 and 2.13% with a score of 3). Conversely, patients reporting no abdominal pain (score of 0) increased from 16.92% at baseline to 67.69% at Week 14 and 87.23% by Week 102.

Number of liquid or soft stools within CD patients

The mean ± SD number of liquid or soft stools at baseline was 4.26 ± 3.43. Significant reductions were observed across all study visits, with LS mean changes from baseline ranging between -2.34 (95% CI: -2.76 – -1.92) at Week 14 and -2.62 (95% CI: -3.05 – -2.18) at Week 102 ($p < 0.001$ for all timepoints).

Clinical response and remission

Among UC patients, clinical response rates, defined as a decrease of at least 2 points from baseline in the PMS score, were 76.29%, 75.28%, 79.17%, 81.54%, 84.48%, and 87.27%, at weeks 14, 30, 54, 78, and 102, respectively. Clinical remission rates, defined as the concurrent occurrence of a PMS <3 and PRO2 scores of 0 for rectal bleeding and 0 or 1 for stool frequency, increased from 16.83% at baseline to 71.13%, 79.78%, 77.78%, 83.08%, 91.38%, and 94.55%, respectively, at weeks 14, 30, 54, 78, and 102, respectively.

Among CD patients, clinical response rates, defined as a concurrent occurrence of a 3-point reduction in the HBI and a >50% decrease in the PRO2 scores of abdominal pain scores and number of liquid or soft stools, were 55.00%, 63.89%, 64.71%, 69.44%, 64.71%, and 63.33% at weeks 14, 30, 54, 78, and 102, respectively. Clinical remission rates, defined as either an HBI score <5 or a PRO2 score of 0 or 1 for abdominal pain score of 0 or 1 and a number of liquid or soft stools ≤3, increased from 20.00% at baseline to 67.50%, 80.56%, 97.06%, 94.44%, 85.29%, and 93.33% at Weeks 14, 30, 54, 78, and 102, respectively.

Steroid-sparing effect

In CD patients, steroid use showed a decline from 50.77% at baseline to 46.15% at Week 6 and 43.08% at Week 14. In UC patients, steroid use declined more substantially from 56.44% at baseline to 48.51% at Week 6 and 40.59% at Week 14. While results suggest a potential steroid-sparing effect, the absence of statistical analysis limits definitive conclusions.

Endoscopic disease activity (endoscopic mucosal healing/endoscopic response and remission)

Among UC patients, the majority (52.48%) had moderate endoscopic activity (a score of 2) at baseline, followed by those having severe activity (33.66%; a score of 3), whereas only 1.98% of the patients were at endoscopic remission (a score of 0). The limited number of patients undergoing endoscopic assessments at subsequent timepoints precluded the evaluation of endoscopic response and remission rates.

Among CD patients, baseline findings revealed that 46.88% of patients exhibited many aphthoid ulcers (<0.5 cm), and larger ulcerations (>0.5 cm) were present in 56.25% of cases. Inflammation of the mucosa was observed in 82.81% of patients, and 29.69% had evidence of narrowings. The limited number of patients undergoing endoscopic assessments, along with the absence of SES-CD scores, at subsequent timepoints, limited the ability to fully evaluate endoscopic response and remission rates.

Treatment satisfaction

TSQM-9

At baseline, the mean ± SD TSQM-9 total score was 38.59 ± 8.707, reflecting a moderate level of treatment satisfaction. Subdomain scores were 55.74 ± 21.412 for effectiveness, 65.68 ± 19.644 for convenience, and 55.20 ± 21.01 for global satisfaction. Significant improvements from baseline were observed in the total score across all study visits during treatment with VDZ. By Week 102, the total score had increased by an LS mean of 8.30 points (95% CI: 6.62 – 9.99; p<0.001). Similarly, significant improvements were observed across all TSQM-9 subdomains at each study visit. The effectiveness domain exhibited the greatest improvement, with an LS mean increase of 21.77 points (95% CI: 17.52 – 26.01; p<0.001). Global satisfaction also demonstrated a substantial increase of 19.88 points (95% CI: 15.68 – 24.08; p<0.001), while the convenience domain showed a meaningful improvement of 9.21 points (95% CI: 5.32 – 13.10; p<0.001).

Biological biomarkers

CRP and FCP

Baseline CRP levels were elevated in both CD and UC patients, reflecting active inflammation. In CD patients, the baseline mean ± SD CRP was 10.26 ± 16.751 mg/L (median: 4 mg/L), while in UC patients, it was 11.21 ± 19.534 mg/L (median: 3.65 mg/L).

Throughout the two-year follow-up period, CRP levels in CD patients showed small fluctuations but remained relatively stable, with a mean ± SD change of -0.69 ± 8.875 mg/L at Week 102. In contrast, UC patients demonstrated consistent reductions in CRP over time, with the largest decrease observed by Week 102 (mean change: -10.81 ± 23.482 mg/L).

Baseline FCP levels were also elevated, indicating intestinal inflammation. CD patients had a baseline mean ± SD FCP of 568.87 ± 548.464 µg/g

	(median: 337.00 μg/g), whereas UC patients exhibited highly variable FCP levels with a mean of 32,617.83 ± 116,394.43 μg/g (median: 93.00 μg/g), driven by extreme values. Over the treatment course, a limited number of patients had FCP data at subsequent visits, limiting the ability to draw robust conclusions about trends.
Discussion	This study provides the first real-world evidence on the long-term benefits of vedolizumab in a Greek cohort of biologic-naïve patients with UC or CD. Over two years of follow-up, high treatment persistence was observed (63.86%), with higher rates observed in CD compared to UC patients. These findings were generally consistent with previously reported two-year persistence rates in biologic-naïve populations, with some likely attributable to differences in clinical practices, patient populations, and healthcare systems. Treatment persistence serves as a valuable surrogate for long-term therapeutic benefit and safety, particularly in chronic conditions like UC and CD. Accordingly, in this study, vedolizumab demonstrated robust clinical effectiveness, with high clinical response rates achieved by Week 14 and sustained through Week 102. Similarly, remission rates improved as early as Week 14 and were further increased and sustained the two-year period, underscoring vedolizumab's ability to achieve and sustain disease control in biologic-naïve IBD patients. An important aspect of this study was the incorporation of both clinical indices and PROs to assess treatment outcomes comprehensively. Standalone 2-item PROs (PRO2), such as rectal bleeding and stool frequency for UC, and abdominal pain and stool frequency for CD, accurately reflected the therapeutic benefit of vedolizumab and closely aligned with remission rates assessed by clinical indices like the Mayo score and HBI, demonstrating their potential utility in clinical practice for disease follow-up and management. High clinical response and remission rates translated into significant HRQoL improvements, as evidenced by meaningful increases in IBD-specific SIBDQ and generic EQ VAS scores. Additionally, improvements in TSQM-9 total and subdomain scores, including effectiveness, global satisfaction, and convenience, further highlighted positive patient experiences with vedolizumab. In conclusion, this study contributes to the growing real-world evidence supporting vedolizumab as a first-line biologic for IBD. The high treatment persistence, along with substantial clinical response and remission rates, translating into meaningful improvements in HRQoL and treatment satisfaction, observed over two years align with the treat-to-target paradigm in IBD management, underscoring vedolizumab's effectiveness in achieving sustained disease control and enhancing patients' quality of life,

	reinforcing its role as a key therapeutic option for the long-term management of IBD.
Names and affiliations of principal investigators	[redacted]