GEMINI LTS Clinical Trial Factsheet

Moderately to severely active ulcerative colitis or Crohn's disease

GEMINI Long-Term Safety Study

Study design: a phase 3, single-arm, open-label, multinational study[1]. Data were collected from approximately 400 study sites in 39 countries between May 2009 and October 2017

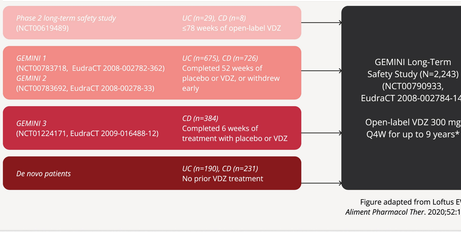


Figure adapted from Loftus EV, et al. *Aliment Pharmacol Ther*. 2020;52:1353-65

PRIMARY OBJECTIVE[1]

- Patients were evaluated at visits at least every 4 weeks; vital signs, concomitant medications, AEs, and SAEs (including signs and symptoms of PML) were recorded

EXPLORATORY OBJECTIVES[1]

- Efficacy as measured by clinical remission and clinical response
  - ***Clinical response in UC:*** reduction in the partial Mayo score of ≥2 points and ≥25% from baseline, with a decrease in the rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of ≤1 point
  - ***Clinical remission in UC:*** defined by a partial Mayo score of ≤2 with no individual subscore of >1
  - ***Clinical response in CD:*** defined as ≥3-point decrease from baseline in the HBI score, and clinical remission was defined by an HBI score of ≤4

KEY INCLUSION CRITERIA

- ✓ 18–80 years of age[2-4]
- ✓ Previous treatment in Phase 2 long-term safety study (NCT00619489) or one of the three Phase 3 GEMINI studies: GEMINI 1 (NCT00783718), GEMINI 2 (NCT00783692), or GEMINI 3 (NCT01224171) that, in the opinion of the investigator, was well tolerated[1,5]
- ✓ Moderately to severely active UC or CD that has not been previously treated with vedolizumab[1]

KEY EXCLUSION CRITERIA

- ✕ Development of any new, unstable, or uncontrolled disease[3]

*Treatment duration varied by patient and continued if there was sustained clinical benefit or until loss to follow-up for any reason, including vedolizumab approval and access to commercially available drug, or the presence of an expanded-access program at the local study site.

AE, adverse event; **CD**, Crohn's disease; **EudraCT**, European Union Drug Regulating Authorities Clinical Trials Database; **HBI**, Harvey-Bradshaw Index; **LTS**, long-term safety; **PML**, progressive multifocal leukoencephalopathy; **Q4W**, every 4 weeks; **SAE**, serious adverse event; **UC**, ulcerative colitis; **VDZ**, vedolizumab.

References

1. Loftus EV, et al. *Aliment Pharmacol Ther*. 2020;52:1353-65
2. Feagan BG, et al. *N Engl J Med*. 2013;369:699–710
3. Sandborn WJ, et al. *N Engl J Med*. 2013;369:711–21
4. Sands BE, et al. *Gastroenterology*. 2014;147:618-27.e3
5. Loftus EV, et al. *Aliment Pharmacol Ther*. 2020;52:1353-65 (supplementary appendix)

PRIMARY ENDPOINT[1]

Safety overview

ADVERSE EVENTS	Ulcerative colitis (n=894) n (%)	Ulcerative colitis (n=894) Incidence/1,000 person-years*	Crohn's disease (n=1,439) n (%)	Crohn's disease (n=1,439) Incidence/1,000 person-years*
Any TEAE	829 (92.7)	1220.5	1295 (96.0)	1799.2
Severity of AE				
Mild	163 (18.2)	N/A	223 (16.5)	N/A
Moderate	451 (50.4)	N/A	656 (48.6)	N/A
Severe	451 (50.4)	N/A	656 (48.6)	N/A
Treatment-related AE	335 (39.7)	N/A	623 (46.2)	N/A
Treatment withdrawn due to AE	137 (15.3)	N/A	229 (17.0)	N/A
SAEs	227 (31.0)	90.9	548 (40.6)	146.5
Treatment-related SAEs	37 (4.1)	N/A	79 (5.9)	N/A
AESIs				
Total infections	591 (66.1)	388.9	937 (69.5)	492.1
Deaths	4 (<1)[f]	N/A	6 (<1)[g]	N/A
Treatment-related death	1 (<1)[h]	N/A	1 (<1)[i]	N/A

Table adapted from Loftus EV, et al. *Aliment Pharmacol Ther*. 2020;52:1353-65

[f]Respiratory failure, acute stroke, West Nile virus encephalitis, pulmonary embolism.
[g]Traumatic intracranial hemorrhage, hepatocellular carcinoma, suicide, pneumonia, septicemia, leiomyosarcoma.
[h]One patient who received long-term vedolizumab therapy subsequently died because of West Nile virus encephalitis. However, based on the mechanism of action of vedolizumab and available information, there is no known association between this event and vedolizumab therapy. There are also no other safety signals linking vedolizumab to the West Nile virus. Therefore, although this event was recorded by the principal investigator as treatment-related, there is no evidence to support this association.
[i]Death of one patient with Crohn's disease (hepatocellular carcinoma) was considered treatment-related by the treating physicians.

- Inclusive of prior vedolizumab trials and GEMINI LTS, treatment-emergent EIMs occurred in 172 patients with UC (19.2%) and 443 patients with CD (32.8%)
- Benign or malignant neoplasms occurred in 58 patients with UC (6.5%) and 92 patients with CD (6.8%)
- The most common benign neoplastic events were skin papillomas (<1% UC, 1.2% CD) and melanocytic nævus (<1% in UC and CD)
- The most common malignant neoplasm in patients with UC or CD was basal cell carcinoma (<1% in UC and CD)

Incidence of treatment-emergent extraintestinal manifestations in patients with UC or CD

ADVERSE EVENTS	Ulcerative colitis (n=894) n (%)	Ulcerative colitis (n=894) Incidence/1,000 person-years (95% CI)*	Crohn's disease (n=1,439) n (%)	Crohn's disease (n=1,439) Incidence/1,000 person-years (95% CI)*
Any extraintestinal manifestation	172 (19.2)	70.6 (59.3–81.9)	443 (32.8)	157.5 (140.6 –174.5)
Arthralgia	120 (13.4)	47.0 (38.2–55.8)	269 (19.9)	84.1 (73.2 –94.9)

Incidence of treatment-emergent gastrointestinal manifestations in patients with UC or CD

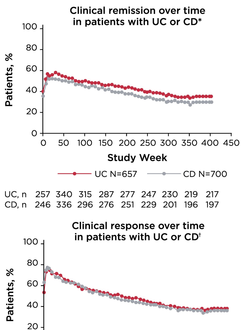
ADVERSE EVENTS	Ulcerative colitis (n=894) n (%)	Ulcerative colitis (n=894) Incidence/1,000 person-years (95% CI)*	Crohn's disease (n=1,439) n (%)	Crohn's disease (n=1,439) Incidence/1,000 person-years (95% CI)*
Gastrointestinal infections of special interest*	122 (13.6)	46.9 (38.3–55.6)	162 (12.0)	46.1 (38.8–53.4)
Abdominal and gastrointestinal infections (pathogen unspecified)*	92 (10.3)	34.9 (27.6–42.3)	141 (10.5)	39.6 (32.9–46.3)

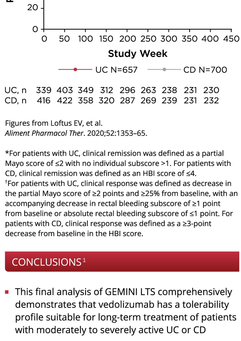
**Gastrointestinal infections of special interest included pathogen-unspecified abdominal or gastrointestinal infections.
[j]MedDRA preferred terms: gastroenteritis, diarrhea infectious, gastrointestinal infection, enteritis infectious, enterocolitis infectious, and gastric infection.

Tables adapted from Loftus EV, et al. *Aliment Pharmacol Ther*. 2020;52:1353-65.

EXPLORATORY ENDPOINTS[1]

- At 400 weeks of treatment, 217 of 658 (33.0%) patients with UC and 197 of 700 (28.1%) patients with CD were in clinical remission and 230 of 657 (35.0%) and 232 of 700 (33.1%), respectively, had a clinical response
- 142 patients with UC (16.8%) experienced ≥1 UC-related hospitalization, colectomy, or UC-related procedure
- 365 patients with CD (28.1%) experienced ≥1 CD-related hospitalization, bowel resection, or CD-related procedure
- These events were more frequent among patients who had previously failed TNFα antagonist therapy versus those who had not (23% versus 12% UC, 30% versus 24% CD)
- Of all hospitalizations, the most common reasons for admission of patients with UC were UC (34.4%), abdominal/GI infection (4.5%), and abdominal/GI pain (3.0%)





Figures from Loftus EV, et al. *Aliment Pharmacol Ther*. 2020;52:1353–65.

*For patients with UC, clinical remission was defined as a partial Mayo score of ≤2 with no individual subscore >1. For patients with CD, clinical remission was defined as an HBI score of ≤4.
†For patients with UC, clinical response was defined as decrease in the partial Mayo score of ≥2 points and ≥25% from baseline, with an accompanying decrease in rectal bleeding subscore of ≥1 point from baseline or absolute rectal bleeding subscore of ≤1 point. For patients with CD, clinical response was defined as a ≥3-point decrease from baseline in the HBI score.

CONCLUSIONS[1]

- This final analysis of GEMINI LTS comprehensively demonstrates that vedolizumab has a tolerability profile suitable for long-term treatment of patients with moderately to severely active UC or CD
- This is an important consideration for the management of UC and CD, which are chronic conditions requiring lifelong therapy

*Time-adjusted incidence rate per 1,000 patient-years = (number of patients experiencing an AE of interest/total person time in years) × 1,000.

AE, adverse event; **AESI**, adverse event of special interest; **CD**, Crohn's disease; **CI**, confidence interval; **EIM**, extraintestinal manifestation; **HBI**, Harvey Bradshaw Index; **LTS**, long-term safety; **MedDRA**, Medical Dictionary for Regulatory Activities; **SAE**, serious adverse event; **TEAE**, treatment-emergent adverse event; **TNFα**, tumor necrosis factor-alpha; **UC**, ulcerative colitis.

References

1. Loftus EV, et al. *Aliment Pharmacol Ther*. 2020;52:1353–65

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