REAL WORD LONG-TERM EFFICACY AND SAFETY OF VEDOLIZUMAB IN MANAGING ULCERATIVE COLITIS VERSUS CROHN'S DISEASE: RESULTS FROM "LONG VEDO" ITALIAN MULTICENTER STUDY

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Background


The NEW ENGLAND JOURNAL of MEDICINE

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Vedoliz… …aintenance Therapy …ative Colitis

Brian G. Feagan, M… …geerts, M.D., Ph.D., Bruce E. Sands, M.D., Stephen Hanauer, M.D., Jean-Frédéric Colombel, …, William J. Sandborn, M.D., Gert Van Assche, M.D., Ph.D., Jeffrey Axler, M.D., Hyo-Jong Kim, M.D., Ph.D., Silvio Danese, M.D., Ph.D., Irving Fox, M.D., Catherine Milch, M.D., Serap Sankoh, Ph.D., Tim Wyant, Ph.D., Jing Xu, Ph.D., and Asit Parikh, M.D., Ph.D., for the GEMINI 1 Study Group*

GEMINI 1


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Vedolizumab as … …nance …ease

William J. S… …M.D., Paul Rutgeerts, M.D., Ph.D., Stephen Ha… …ic Colombel, M.D., Bruce E. Sands, M.D., Milan Lu… …., Richard N. Fedorak, M.D., Scott Lee, M.D., Brian Bressler, … …ving Fox, M.D., Maria Rosario, Ph.D., Serap Sankoh, Ph.D., Jing Xu, Ph.D., Kristin Stephens, B.A., Catherine Milch, M.D., and Asit Parikh, M.D., Ph.D., for the GEMINI 2 Study Group*

GEMINI 2


Gastroenterology 2014;147:618–627

Effects of Vedolizumab Induct… …tor With Crohn's Disease i… …Antagonist Trea…

Bruce E. Sands,[1] Brian… …erts,[3] Jean-Frédéric Colombel,[1,4] William J. Sandborn,[5] R… …ert D'Haens,[7] Shomron Ben-Horin,[8] Jing Xu,[9] Maria Rosario,[9] Irving Fo… …arikh,[10] Catherine Milch,[9] and Stephen Hanauer[11]

GEMINI 3


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APT Alimentary Pharmacology & Therapeutics WILEY

Long-term safety of vedoli… …atory bowel disease

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GEMINI LTS

Background

Clinical trials in inflammatory bowel diseases rarely represent the real-world patient population, several real-world experience studies with Vedolizumab have been published to date and two systematic reviews[1-2] have confirmed the effectiveness and safety of vedolizumab in treating patients with UC and CD.

However, there are no data on long-term outcomes of patients with IBD treated with vedolizumab.

1. Engel T *et al.* Vedolizumab in IBD-lessons from real-world experience; a systematic review and pooled analysis *J Crohns Colitis.* 2018
2. Bressler B *et al.* Vedolizumab and anti-tumor necrosi factor alfa real-world outcomes in biologic-naive Inflammatory bowel disease patients: results from the EVOLVE study. *Journal of Crohn's and Colitis.* 2021

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Aim

The aim of the present study was to assess the long term effectiveness and safety of VDZ to treat a large IBD outpatient population in some Italian IBD centers after approval of their reimbursement for IBD by the Italian Regulatory Authorities. In addition, to evaluate any differences between UC and CD in terms of long-term outcomes

Research design and methods

This study ("LONG-VEDO" study) consisted of a retrospective, observational, multicenter study on pts affected by UC and CD treated with VDZ (Entyvio™) in 32 Italian IBD centers. We assessed patients enrolled from 1st January 2017 to 30th June 2022, who completed at least the induction treatment.

The primary endpoint was to compare the VDZ performances in UC patients versus CD patients in terms of the following:

- Induction of remission in patients naïve and previously exposed to biologics;
- Maintenance of remission in patients naïve and previously exposed to biologics,
- Safety of VDZ in UC and CD, defined as the absence of adverse events (AE) during treatment.

Research design and methods

The ***secondary goals*** were to evaluate if there was any difference between UC patients versus CD patients in terms of the following:

- ***Clinical response***, defined as a decrease of at least 2 points in the Mayo score in UC patients and at least 3 points in the HBI in CD patients;
- ***Mucosal healing***, defined as a Mayo subscore for endoscopy of ≤1 in UC and as SES-CD ≤2 in CD patients;
- ***Reduction of steroid use*** *during the study*;
- ***Maintenance of steroid-free remission*** during the study;
- ***Prevention of surgery*** (colectomy in UC and any surgical procedure related to the disease in CD)
- ***Optimization rate*** for the VDZ during the follow-up to reach or maintain remission.

Results_Demographics and disease characteristics

729 pts (from 1st January 2017 to 30th June 2022)
Median follow up 18 (IQR 6-36) months

475 patients with Ulcerative Colitis (UC)
254 patients with Crohn's Disease (CD)

Demographics, disease characteristics, and concomitant medications.

	Tot. (729 pts)	UC (475 pts)	CD (254 pts)	P*
Gender, male	406 (55.7)	265 (55.8)	141 (55.5)	0.943
Median (IQR) age, years	54 (41-66)	53 (41-65)	55 (39-67)	0.373^
Median (IQR) disease duration, years	9 (4-16)	9 (3-17)	10 (6-19)	0.924^
Smoke	191 (26.2)	115 (24.2)	76 (29.9)	0.095
Presence of comorbidities	328 (45.0)	214 (45.1)	114 (44.9)	0.965
Previous appendectomy	78 (10.7)	33 (6.9)	45 (17.7)	**<0.000**
Concomitant therapy				
Mesalazine	612 (84.0)	451 (94.9)	161 (63.4)	**<0.000**
Steroids	563 (77.2)	377 (79.4)	186 (73.2)	0.059
Tiopurine	216 (29.6)	143 (30.1)	73 (28.7)	0.070
Indication to therapy with VDL				
Steroid resistance	47 (6.4)	31 (6.5)	16 (6.3)	
Steroid dependency	290 (39.8)	209 (44.0)	81 (31.9)	
Primary failure to biologics	80 (11.0)	55 (11.6)	25 (9.8)	**0.002**
Secondary failure to biologics	227 (31.1)	137 (28.8)	90 (35.4)	
Others	85 (11.7)	43 (9.1)	42 (16.5)	
Naïve to biologics	294 (40.3)	196 (41.3)	98 (38.6)	0.482
Montreal classification of extent of UC				
Left-sided colitis		208 (43.8)	-	
Extensive colitis		267 (56.2)	-	
Montreal classification of CD				
Location				
Isolated ileal disease		-	106 (41.7)	
Isolated colonic disease		-	29 (11.4)	
Ileocolonic disease		-	111 (43.7)	
Isolated UGI disease		-	8 (3.1)	
Concomitant perianal disease		-	36 (14.2)	
Behaviour				
Non stricturing, non-penetrating		-	113 (44.5)	
Stricturing		-	105 (41.3)	
Penetrating		-	36 (14.2)	
Median (IQR) CRP, (mg/L)	5.0 (3-15)	5.0 (3-15	5.0 (3-16)	0.867^
Median (IQR) fecal calprotectin (µg/g)	355 (190-643)	390(201-425)	321 (187-685)	0.537^
Median (IQR) partial Mayo score		6 (4-7)	-	
Median (IQR) Mayo subscore for endoscopy		2 (2-3)	-	
Median (IRQ) HBI		-	8 (5-10)	
Median (IRQ) SES-CD		-	9 (6-12)	

Data are given as number (percentage) of patients unless otherwise indicated. IQR, interquartile range; CRP, C-reactive protein; HBI, Harvey-Bradshaw index; SES-CD, simple endoscopic score for Crohn's disease. *Chi-square test unless otherwise inidcated; ^Kruskal-Wallis test.

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Results_Induction of Clinical Remission (6 Months)

Factors influencing induction of clinical remission at univariate and multivariate analysis with logistic regression.

Variables	**Clinical remission**	**P***	**Hazard ratio (95% CI)**	***p***
Group				
Ulcerative colitis	286 (60.4)		-	
Crohn's disease	187 (73.6)	< 0.00	1.822 (1.304 to 2.546)	**<0.000**
Naïve to biologics				
Yes	185 (62.9)	0.330	0.868 (0.635 to 1.186)	0.373
No	289 (66.4)		-	
CU /Naïve to biologics	98 (53.5)	0.854		
CD /Naïve to biologics	87 (46.5)	-		
CU/Previously biologics	147 (50.9)	0.912		
CD/previously biologics	142 (49.1)	-		

Data are given as number (percentage) of patients unless otherwise indicated. * Chi-square test

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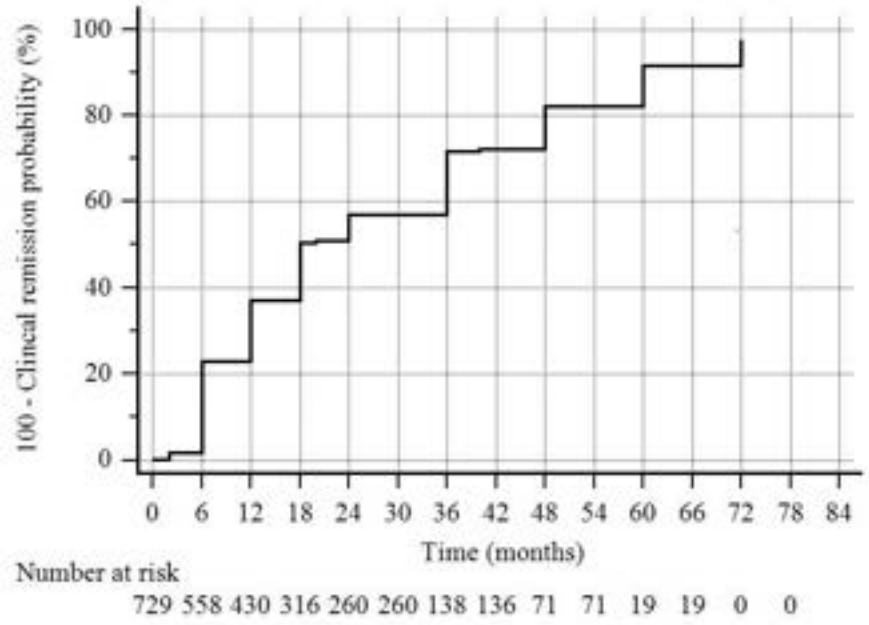
Results_Manteinance of Clinical Remission

Factors influencing manteinance of clinical remission at univariate and multivariate analysis with Cox proportional-hazard regressi

Variables	Clinical remission	P*	Hazard ratio (95% CI)	*p*
Group				
Ulcerative colitis	386 (70.3)	0.939	0.963 (0.813 to 1.142)	0.667
Crohn's disease	207 (69.3)		-	
Naïve to Biologics				
Yes	249 (84.7)	0.056	1.105 (0.938 to 1.301)	0.232
No	344 (79.1)		-	
Induction of clinical remission at 6 months				
Yes	437 (92.2)	<0.000	-	
No	156 (61.2)		0.550 (0.458 to 0.661)	**<0.000**

Data are given as number (percentage) of patients unless otherwise indicated. * Chi-square test



Results_Secondary Goals

Outcomes of secondary end-points during follow-up.

	Total (n=729 pts)	Ulcerative colitis (n=475 pts.)	Crohn's disease (n=254 pts.)	P*
Clinical response	642 (88.1)	428 (90.1)	214 (84.3)	**0.023**
Mucosal healing	76/187 (40.6)	48/114 (42.1)	28/73 (38.3)	0.265
Steroid-free remission	501 (68.7)	350 (73.6)	171 (67.3)	0.836
Optimization	48 (6.6)	35 (7.4)	13 (5.1)	0.072
Primary failure	22 (3.0)	18 (3.8)	4 (1.8)	0.138
Secondary failure	49 (6.7)	28 (5.9)	21 (8.3)	0.128
Surgery	21 (2.9)	8 (1.7)	13 (5.1)	**<0.05**

Data are given as number (percentage) of patients unless otherwise indicated. * Chi-square test

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Results _ safety

35 AEs in 729 pts (4,8%)

The rate of AEs reported in our cohort was extremely low.
It is probably due to the retrospective nature of the
study, so the minor AEs did not deserve medical intervention and were not reported in the
medical records (or managed by GP and not reported during follow-up visits

	Total (729pts)	UC (475pts)	CD (254pts)	p
Total AE	35 (4,8)	16 (3,4)	19 (7,4)	
Mild-Moderate AE	**23 (3,1)**	**10 (2,1)**	**13 (5,1)**	ns
- Herpes Zoster	2 (0,3)	-	2 (0,8)	
- Psoriatic arthritis	2 (0,3)	-	2 (0,8)	
- Thyroid adenoma	1 (0,1)	1 (0,2)	-	
- Churg Strauss vasculitis	1 (0,1)	-	1 (0,4)	
- Allergy	8 (1,1)	1 (0,2)	3 (1,2)	
- Alopecia	3 (0,4)	1 (0,2)	2 (0,8)	
- De Quervein thyroiditis	1 (0,1)	1 (0,2)	-	
- Pneumonia	2 (0,3)	1 (0,2)	1 (0,4)	
- Arthropathies	3 (0,4)	1 (0,2)	2 (0,8)	
Severe AE	**12 (1,6)**	**6 (1,3)**	**6(2,4)**	ns
- Lung Infection	1 (0,1)	1 (0,2)	-	
- Jejunal cancer	1 (0,1)	-	1 (0,4)	
- Allergy	2 (0,3)	1 (0,2)	1 (0,4)	
- Colon perforation	1 (0,1)	1 (0,2)	-	
- Prostatic cancer	1 (0,1)	1 (0,2)	-	
- Pulmonary embolism	1 (0,1)	-	1 (0,4)	
- Ovarian cancer	1 (0,1)	1 (0,2)	-	
- Cardiac failure	1 (0,1)	1 (0,2)	-	
- Hypertension	1 (0,1)	-	1 (0,4)	
- Adrenal Neoplasm	1 (0,1)	-	1 (0,4)	
- Anemia/leukopenia	1 (0,1)	-	1 (0,4)	
Death	**3 (0,4)**	**2 (0,4)**	**1 (0,4)**	ns
- SARS COV 2 infection	2 (0,3)	1 (0,2)	1 (0,4)	
- Cardiac Failure	1 (0,1)	1(0,2)	-	

Data are given as number (percentage) of patients.

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Conclusions

This large, real-life study found that:

• VDZ is able to obtain remission in both UC and CD patients, irrespective of their naïve-to-biologics status, and in CD patients we have a faster induction of remission than in CU patients;

• There are no differences between UC and CD patients in the rate of maintenance of the remission under VDZ, irrespective of the naïve-to biologics status;

• VDZ has a favorable safety profile, both in UC and CD;

• Clinical remission within the 6^{th} month of treatment is the stronger predictive factor to maintain a long-term remission.