Supporting Information

Additional Supporting Information may be found in the online version of this article:

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Table S1. Primary outcome measures in patients with UC aged <65 years and ≥65 years

Outcome	Age	Patients, n/N (%)			%-Point difference from PBO (95% CI)	
Week 6		**PBO (n=149)**	**VDZ (n=225)**		**VDZ**	
Clinical response[a]	<65 years	37/142 (26)	103/217 (48)		21.4 (11.6, 31.2)	
	≥65 years	1/7 (14)	3/8 (38)		23.2 (-26.3, 67.5)	
Week 52		**VDZ/PBO[b] (n=126)**	**VDZ/VDZ (Q8W)[c] (n=122)**	**VDZ/VDZ (Q4W)[d] (n=125)**	**VDZ/VDZ (Q8W)[c]**	**VDZ/VDZ (Q4W)[d]**
Clinical remission[e]	<65 years	19/121 (16)	50/117 (43)	54/119 (45)	27.0 (16.0, 38.1)	29.7 (18.6, 40.7)
	≥65 years	1/5 (20)	1/5 (20)	2/6 (33)	0.0 (-62.6, 62.6)	13.3 (-45.1, 66.7)

CI, confidence interval; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; UC, ulcerative colitis; VDZ, vedolizumab.

[a]Defined as reduction in complete Mayo score of ≥3 points and ≥30% from baseline with an accompanying decrease in rectal bleeding subscore of ≥1 point or absolute rectal bleeding subscore of ≤1 point.

[b]Patients received VDZ during induction and PBO during maintenance.

[c]Patients received VDZ during induction and VDZ Q8W during maintenance.

[d]Patients received VDZ during induction and VDZ Q4W during maintenance.

[e]Defined as complete Mayo score of ≤2 points and no individual subscore >1 point.

Table S2. Primary outcome measures in patients with CD aged <65 years and ≥65 years

Outcome	Age	Patients, n/N (%)			%-Point difference from PBO (95% CI)	
Week 6		**PBO (n=148)**	**VDZ (n=220)**		**VDZ**	
Clinical remission[a]	<65 years	9/142 (6)	31/218 (14)		7.9 (1.8, 14.0)	
	≥65 years	1/6 (17)	1/2 (50)		33.3 (-53.4, 90.6)	
Enhanced clinical response[b]	<65 years	37/142 (26)	68/218 (31)		5.1 (-4.3, 14.6)	
	≥65 years	1/6 (17)	1/2 (50)		33.3 (-53.4, 90.6)	
Week 52		**VDZ/PBO[c] (n=153)**	**VDZ/VDZ (Q8W)[d] (n=154)**	**VDZ/VDZ (Q4W)[e] (n=154)**	**VDZ/VDZ (Q8W)[d]**	**VDZ/VDZ (Q4W)[e]**
Clinical remission[a]	<65 years	30/149 (20)	58/151 (38)	56/152 (37)	18.3 (8.2, 28.4)	16.7 (6.7, 26.7)
	≥65 years	3/4 (75)	2/3 (67)	0/2 (0)	-8.3 (-75.5, 63.4)	-75.0 (-99.4, 22.9)

CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; CI, confidence interval; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; VDZ, vedolizumab.

[a]Defined as CDAI score ≤150.

[b]Defined as a ≥100-point reduction in CDAI score from baseline.

[c]Patients received VDZ during induction and PBO during maintenance.

[d]Patients received VDZ during induction and VDZ Q8W during maintenance.

[e]Patients received VDZ during induction and VDZ Q4W during maintenance.

Table S3. Mean change from baseline CRP levels at week 6 in CD induction ITT patients

	Age <35 years		Age 35 to <55 years		Age ≥55 years	
	PBO (n = 67)	**VDZ (n = 111)**	**PBO (n = 63)**	**VDZ (n = 96)**	**PBO[a] (n = 18)**	**VDZ (n = 13)**
Patients with CRP data, n	67	111	62	96	18	13
Mean change from baseline serum CRP, mg/L (SD)	-3.2 (33.9)	-3.0 (15.8)	-2.2 (27.2)	-2.7 (17.7)	-10.3 (24.0)	-4.3 (7.8)

CD, Crohn's disease; CRP, C-reactive protein; ITT, intent-to-treat; PBO, placebo; SD, standard deviation; VDZ, vedolizumab.

Table S4. Adverse events by age <65 years and ≥65 years

Adverse event[a]	Patients, n (%)			
	Age <65 years		Age ≥65 years	
	PBO/PBO[b] (n = 284)	VDZ/VDZ[c] (n = 1400)	PBO/PBO[b] (n = 13)	VDZ/VDZ[c] (n = 34)
Nasopharyngitis	19 (7)	177 (13)	2 (15)	3 (9)
Headache	28 (10)	171 (12)	4 (31)	6 (18)
Crohn's disease	33 (12)	161 (12)	3 (23)	3 (9)
Arthralgia	26 (9)	158 (11)	3 (23)	8 (24)
Pyrexia	21 (7)	127 (9)	1 (8)	0
Nausea	22 (8)	126 (9)	1 (8)	2 (6)
Dizziness	7 (2)	45 (3)	1 (8)	3 (9)
Edema peripheral	9 (3)	35 (3)	3 (23)	3 (9)

PBO, placebo; VDZ, vedolizumab.
[a]Only adverse events occurring in ≥9% of vedolizumab-treated patients in any group are listed.
[b]Patients received PBO during induction and maintenance periods.
[c]Patients received VDZ during induction and maintenance periods.

Table S5. Adverse hematological events in patients with UC and CD

Adverse hematological event[a]	Patients, n (%)					
	Age <35 years		Age 35 to <55 years		Age ≥55 years	
	PBO/PBO[b] (n = 120)	VDZ/VDZ[c] (n = 688)	PBO/PBO[b] (n = 141)	VDZ/VDZ[c] (n = 599)	PBO/PBO[b] (n = 36)	VDZ/VDZ[c] (n = 147)
Any hematological AE	**6 (5)**	**28 (4)**	**4 (3)**	**16 (3)**	**0**	**3 (2)**
Lymphopenia	4 (3)	14 (2)	2 (1)	11 (2)	0	1 (<1)
Lymphocyte count decreased	2 (2)	7 (1)	0	3 (<1)	0	1 (<1)
Leukopenia	0	4 (<1)	0	1 (<1)	0	1 (<1)
Monocytopenia	0	1 (<1)	0	0	0	0
Neutropenia	0	1 (<1)	0	0	0	0
Febrile neutropenia	0	1 (<1)	0	0	0	0
Thrombocytopenia	0	1 (<1)	0	0	0	0
White blood cell count decreased	1 (<1)	2 (<1)	0	2 (<1)	0	0
Cyclic neutropenia	0	0	0	0	0	0
Neutrophil count decreased	1 (<1)	0	2 (1)	1 (<1)	0	0

AE, adverse event; CD, Crohn's disease; PBO, placebo; UC, ulcerative colitis; VDZ, vedolizumab.
[a]Ranked from highest to lowest incidence in patients aged <35 years who were treated with VDZ.
[b]Patients received PBO during induction and maintenance periods.
[c]Patients received VDZ during induction and maintenance periods.

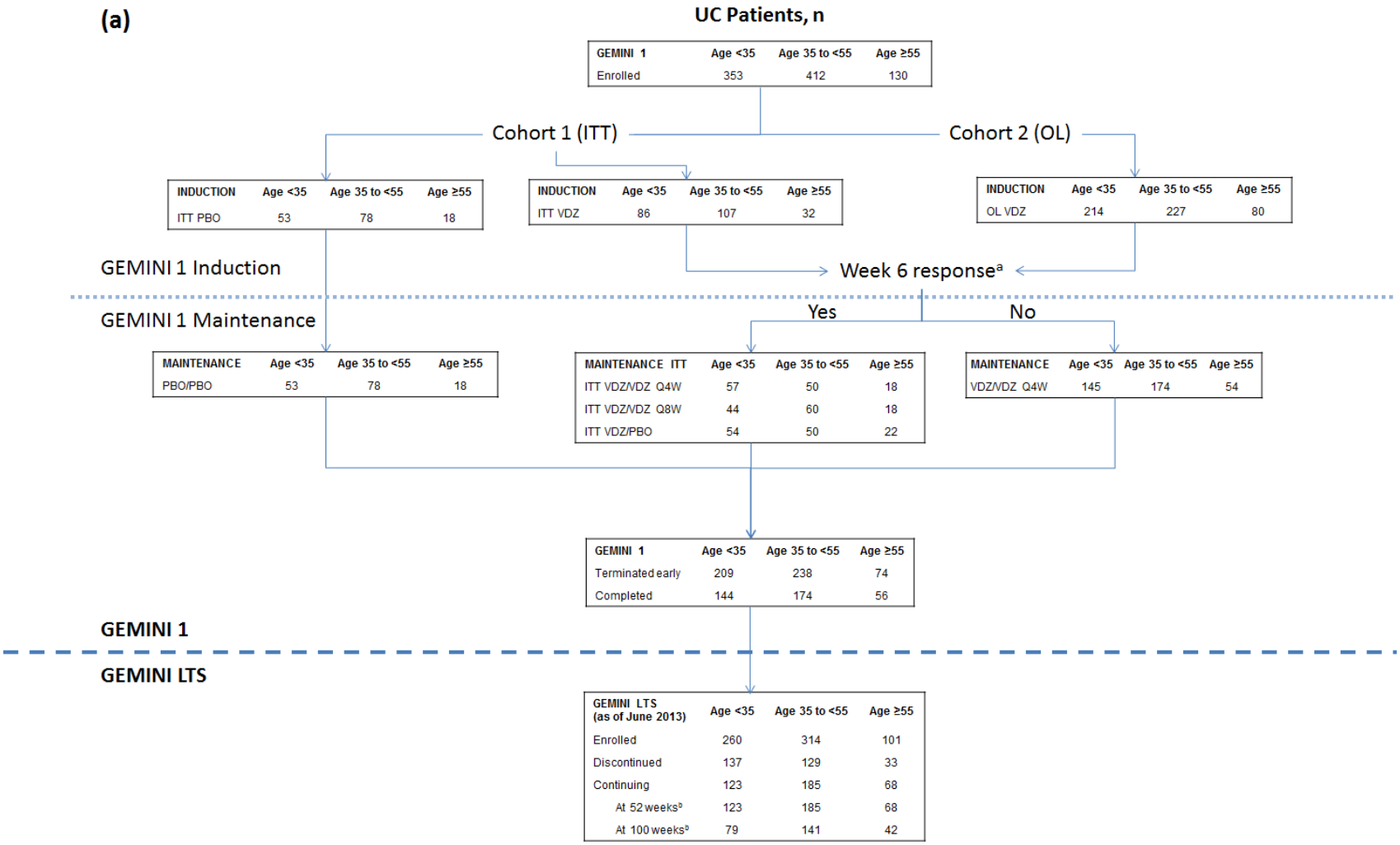
Table S6. Deaths reported in patients with UC and CD

Age	No. of events	Age/ Sex	Indications	Cause of death (preferred term[a])	Treatment group (induction/ maintenance)	No. of VDZ doses
<35 years	3	23/M	CD	Myocarditis	VDZ/VDZ (Q4W)	2
		28/M	CD	CD, sepsis	VDZ/VDZ (Q8W)	8
		30/M	CD	Septic shock	VDZ/VDZ (Q4W)	4
35 to <55 years	1	46/F	CD	Intentional overdose	VDZ/VDZ (Q4W)	5
≥55 years	2	66/M	UC	Arteriosclerosis coronary artery	Cohort 2 VDZ (induction only)	1
		75/M	CD	Bronchopneumonia	PBO/PBO	0

CD, Crohn's disease; ITT, intent-to-treat; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; UC, ulcerative colitis; VDZ, vedolizumab.

[a]Medical Dictionary for Regulatory Activities preferred term.

Figure S1.


(a)
UC Patients, n
GEMINI 1 | Age <35 | Age 35 to <55 | Age ≥55
Enrolled | 353 | 412 | 130
Cohort 1 (ITT)
Cohort 2 (OL)
INDUCTION | Age <35 | Age 35 to <55 | Age ≥55
ITT PBO | 53 | 78 | 18
INDUCTION | Age <35 | Age 35 to <55 | Age ≥55
ITT VDZ | 86 | 107 | 32
INDUCTION | Age <35 | Age 35 to <55 | Age ≥55
OL VDZ | 214 | 227 | 80
GEMINI 1 Induction
Week 6 response[a]
GEMINI 1 Maintenance
Yes
No
MAINTENANCE | Age <35 | Age 35 to <55 | Age ≥55
PBO/PBO | 53 | 78 | 18
MAINTENANCE ITT | Age <35 | Age 35 to <55 | Age ≥55
ITT VDZ/VDZ Q4W | 57 | 50 | 18
ITT VDZ/VDZ Q8W | 44 | 60 | 18
ITT VDZ/PBO | 54 | 50 | 22
MAINTENANCE | Age <35 | Age 35 to <55 | Age ≥55
VDZ/VDZ Q4W | 145 | 174 | 54
GEMINI 1 | Age <35 | Age 35 to <55 | Age ≥55
Terminated early | 209 | 238 | 74
Completed | 144 | 174 | 56
GEMINI 1
GEMINI LTS
GEMINI LTS (as of June 2013) | Age <35 | Age 35 to <55 | Age ≥55
Enrolled | 260 | 314 | 101
Discontinued | 137 | 129 | 33
Continuing | 123 | 185 | 68
At 52 weeks[b] | 123 | 185 | 68
At 100 weeks[b] | 79 | 141 | 42

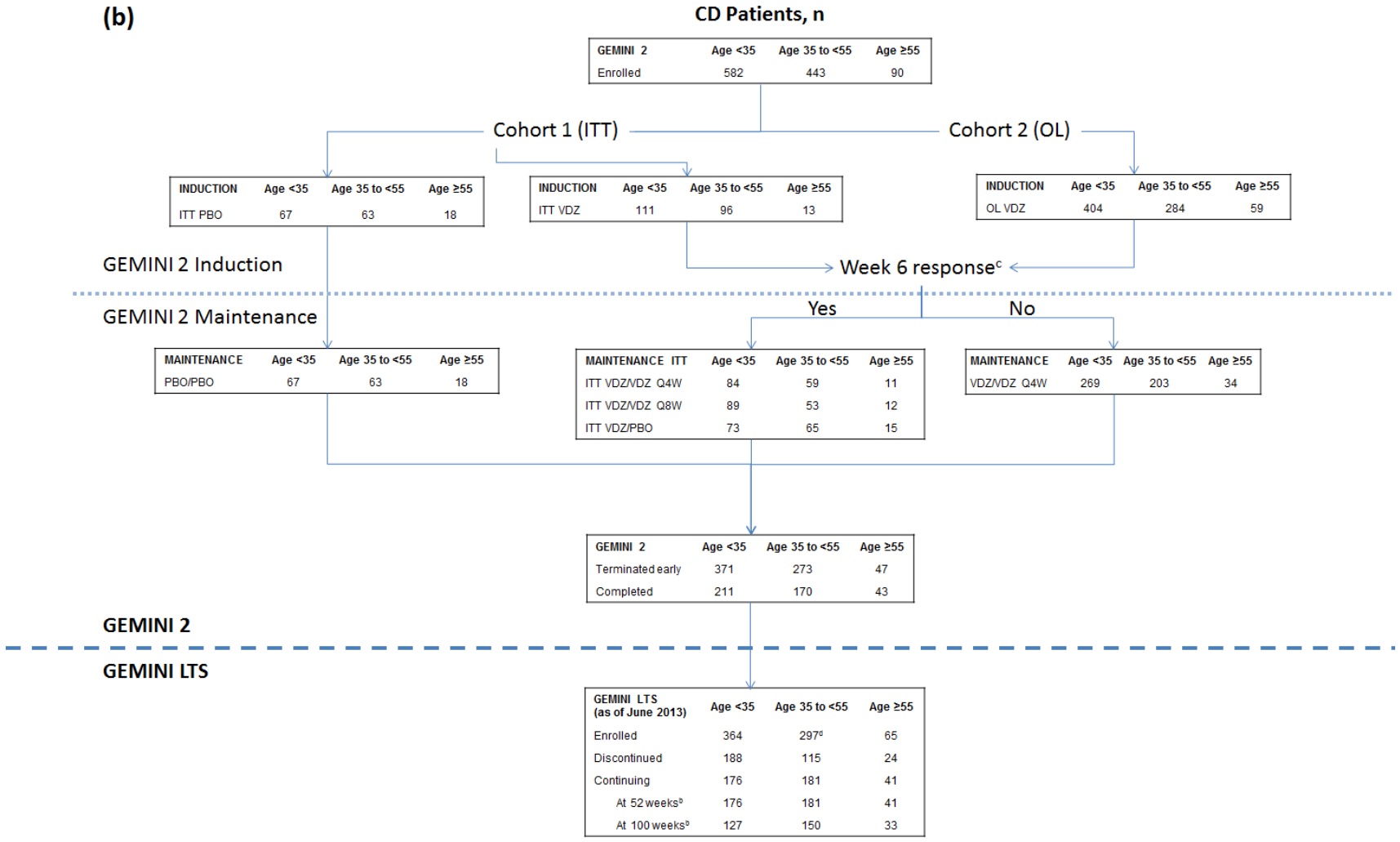


Figure S1. Disposition of UC and CD patients in the GEMINI studies. Patients were randomized for **(A)** GEMINI 1 and **(B)** GEMINI 2 induction therapy to receive intravenous vedolizumab (300 mg, ITT VDZ) or placebo (ITT PBO). An additional

group of patients were enrolled in the open-label vedolizumab (300 mg) treatment group (OL VDZ). Patients who demonstrated clinical response to vedolizumab at week 6 were randomly assigned to receive vedolizumab (300 mg) every 4 weeks (ITT VDZ/VDZ Q4W) or every 8 weeks (ITT VDZ/VDZ Q8W) or placebo (ITT VDZ/PBO) for up to 52 weeks beginning from week 6. Patients who did not achieve a clinical response at week 6 received vedolizumab (300 mg) every 4 weeks (VDZ/VDZ Q4W). Patients who received placebo during induction continued to receive placebo throughout the maintenance study (PBO/PBO). Patients enrolled in GEMINI LTS received open-label vedolizumab (300 mg) every 4 weeks.

CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; ITT, intent-to-treat; LTS, Long-Term Safety; OL, open-label; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; UC, ulcerative colitis; VDZ, vedolizumab.

[a]Clinical response at week 6 was defined as a reduction from baseline (week 0) in the Mayo Clinic score of ≥3 points and ≥30%, with an accompanying decrease of ≥1 point in the rectal bleeding subscore or an absolute rectal bleeding subscore of 0 or 1.

[b]Time from baseline (week 0) of the GEMINI LTS trial.

[c]Clinical response at week 6 was defined as a ≥70-point decrease from baseline CDAI score.

[d]One patient completed study.

Figure S2.

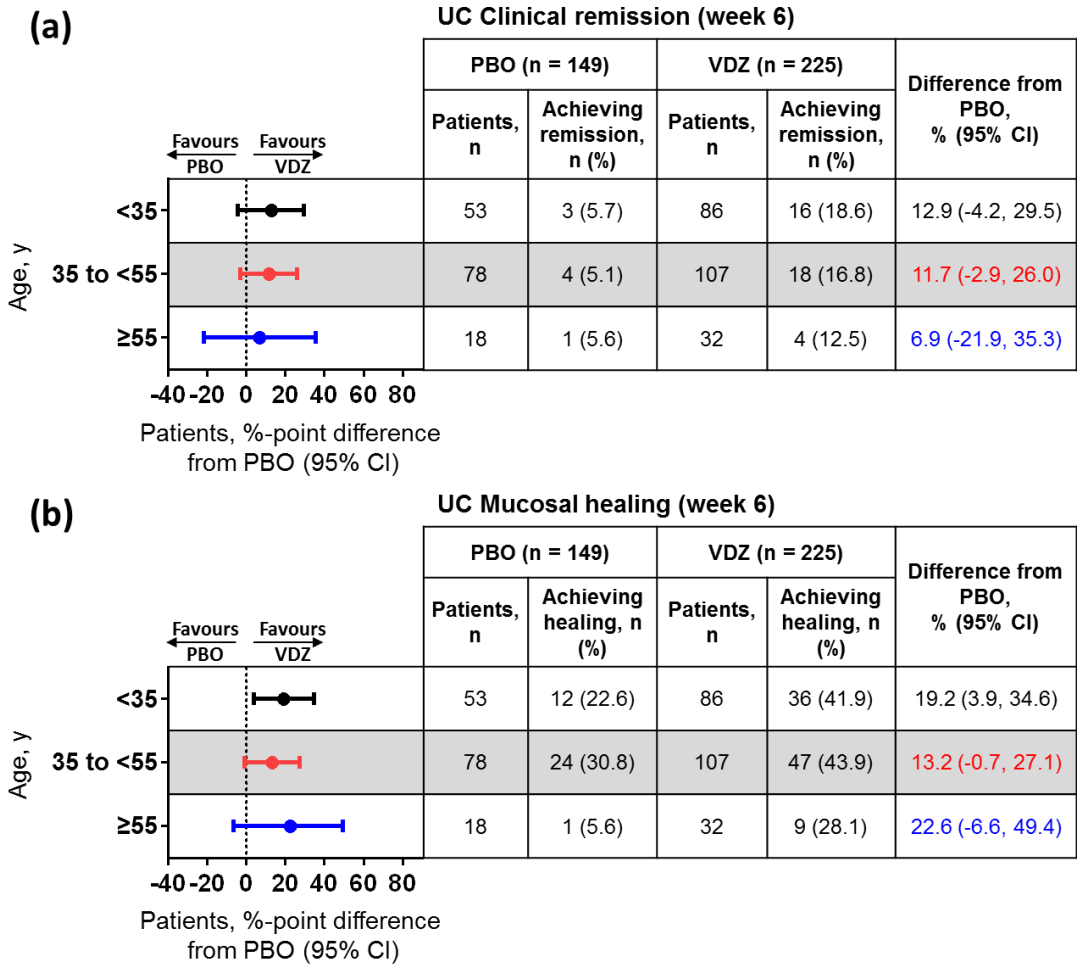


Figure S2. Secondary endpoints in the UC induction phase. **(A)** Clinical remission and **(B)** mucosal healing at week 6 in the induction ITT population.

CI, confidence interval; ITT, intent-to-treat; PBO, placebo; UC, ulcerative colitis; VDZ, vedolizumab.

Figure S3.

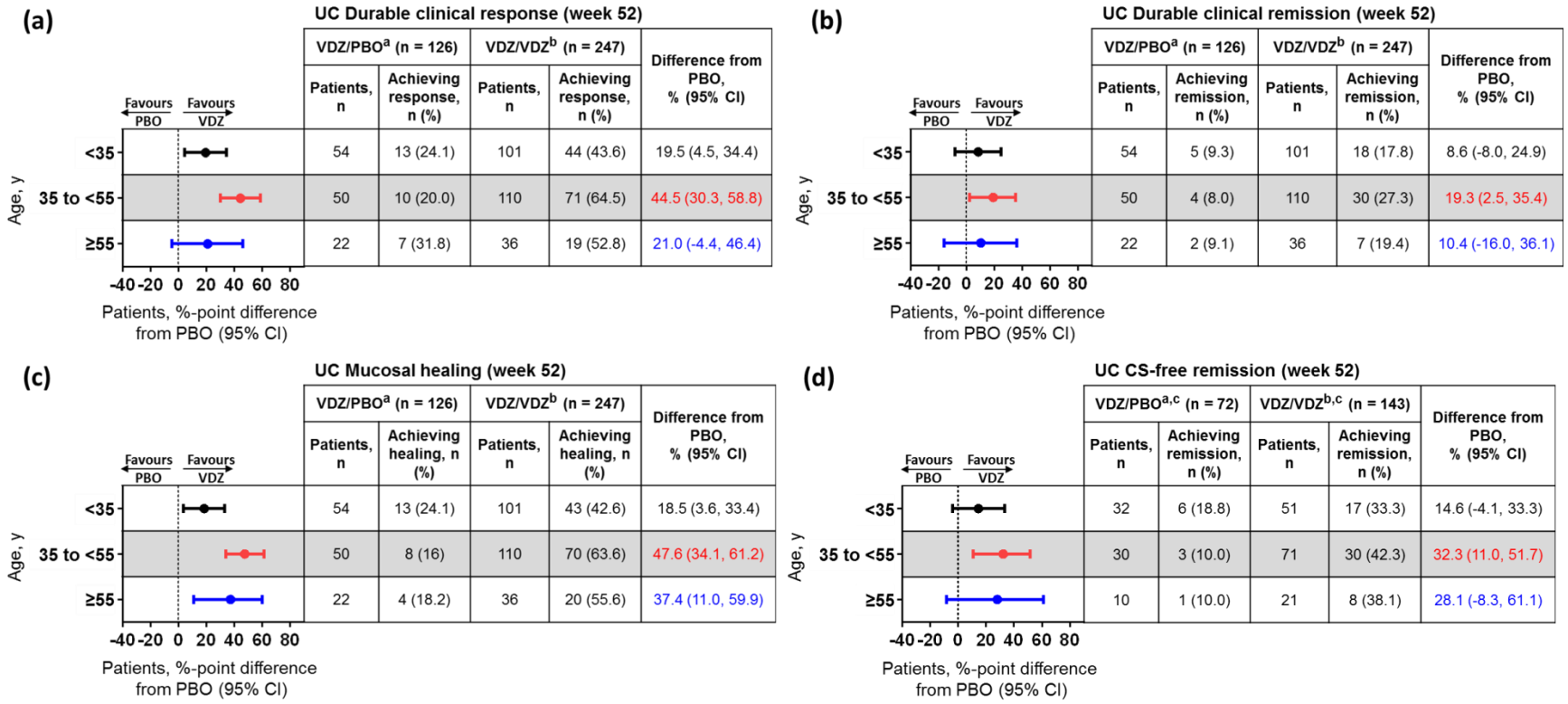


Figure S3. Secondary endpoints in the UC maintenance phase. **(A)** Durable clinical response, **(B)** durable clinical remission, **(C)** mucosal healing, and **(D)** corticosteroid-free remission at week 52 in the maintenance ITT population.

CI, confidence interval; CS, corticosteroid; ITT, intent-to-treat; PBO, placebo; UC, ulcerative colitis; VDZ, vedolizumab.

[a]Patients received VDZ during induction and PBO during maintenance.

[b]Patients received VDZ during induction and VDZ every 4 weeks or every 8 weeks during maintenance.

[c]Patients were receiving concomitant CS at study enrolment.

Figure S4.

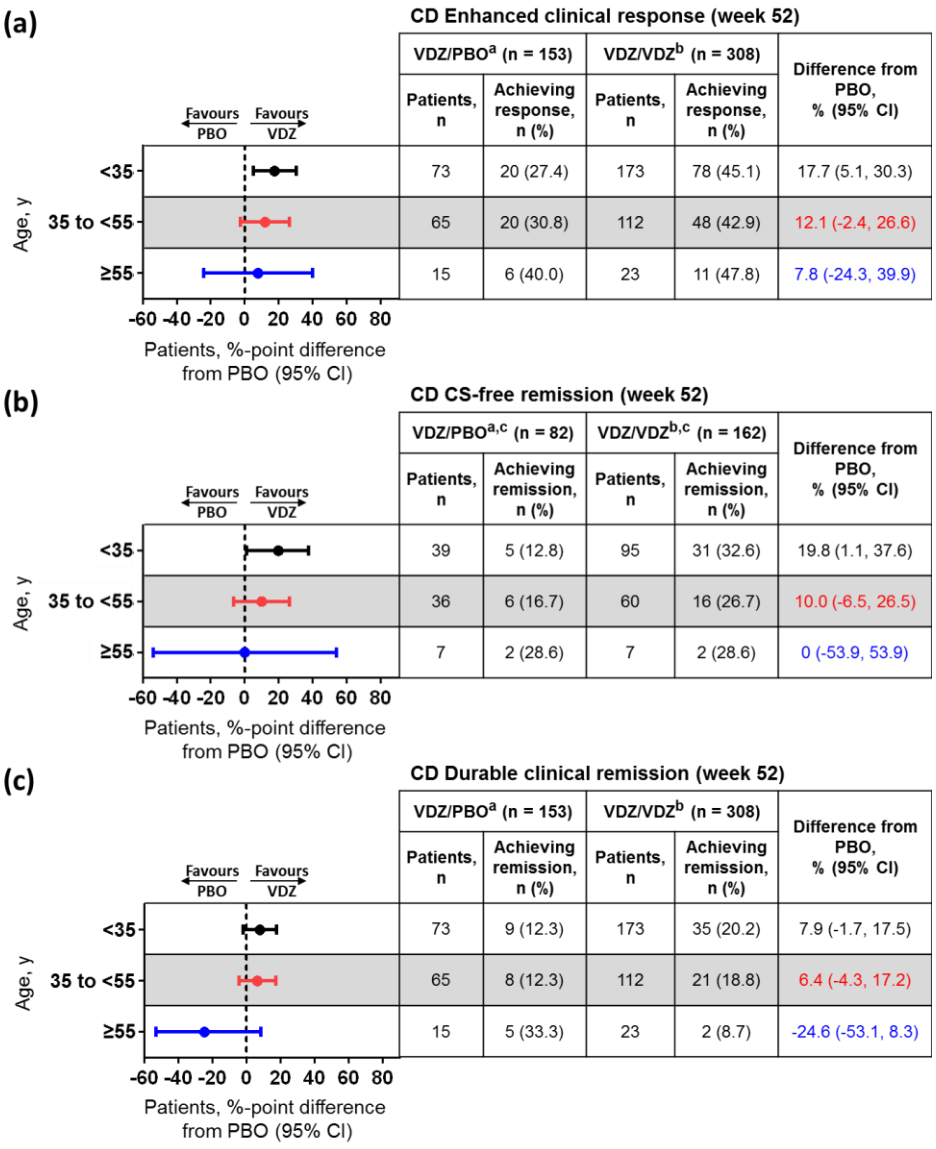


Figure S4. Secondary endpoints in the CD maintenance phase. **(A)** Enhanced clinical response, **(B)** corticosteroid-free remission, and **(C)** durable clinical remission at week 52 in the maintenance ITT population.

CD, Crohn's disease; CI, confidence interval; CS, corticosteroid; ITT, intent-to-treat; PBO, placebo; VDZ, vedolizumab.

[a]Patients received VDZ during induction and PBO during maintenance.

[b]Patients received VDZ during induction and VDZ every 4 weeks or every 8 weeks during maintenance.

[c]Patients were receiving concomitant CS at study enrolment.