European Crohn's and Colitis Organisation

Vedolizumab in combination with steroids for induction therapy in Crohn's disease: An exploratory analysis of the GEMINI 2 and GEMINI 3 studies

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Disclosures

- **B.E. Sands** — Research funding: Pfizer, Janssen, MedImmune, Takeda; Consultancy: Takeda, Janssen, AbbVie, Pfizer, Shire, Lilly, Amgen
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Background & Methods

- CS are a first-line induction therapy for IBD, but long-term use is limited
  - Vedolizumab, a gut-selective $\alpha_4\beta_7$ integrin antagonist, can be used after conventional treatment for moderately to severely active CD
- Limited data have been reported in support of using a combination of CS and a biologic agent as induction therapy

Objective: To assess the efficacy and safety of vedolizumab and CS as induction therapy in patients with moderately to severely active CD*

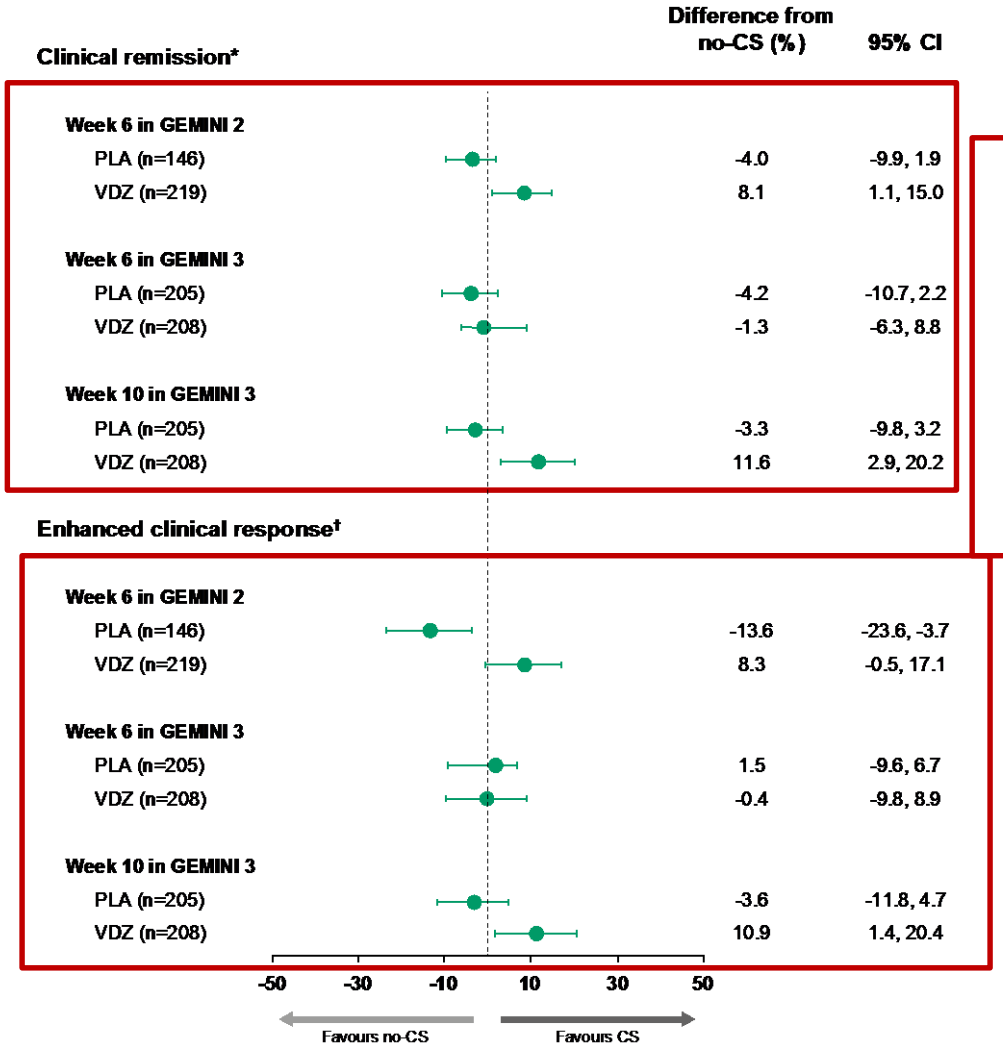
- A *post hoc* exploratory analysis of efficacy and safety of CS use on vedolizumab vs placebo
  - GEMINI 2 (NCT00783692): 6-week induction period
  - GEMINI 3 (NCT01224171): 10-week induction period
- Study endpoints
  - Efficacy: Clinical remission and enhanced response (on CDAI)
  - Safety: Number and incidence of AEs

*Patients had moderately to severely active CD, a score of 220 to 450 on the Crohn's Disease Activity Index (CDAI), and no response to or unacceptable side effects from one or more of the following: glucocorticoids, immunosuppressive agents, or anti-tumor necrosis factor alpha (anti-TNFα) agents.

AE, adverse event; CD, Crohn's disease; CDAI, Crohn's disease activity index; CS, corticosteroids; VDZ, vedolizumab.

1. Gomollón F, et al. *J Crohns Colitis.* 2017;11:3-25; 2. Ford AC, et al. *Am J Gastroenterol.* 2011;106:590-599; 3. Irving PM, et al.

Clinical remission and enhanced clinical response stratified by treatment arm

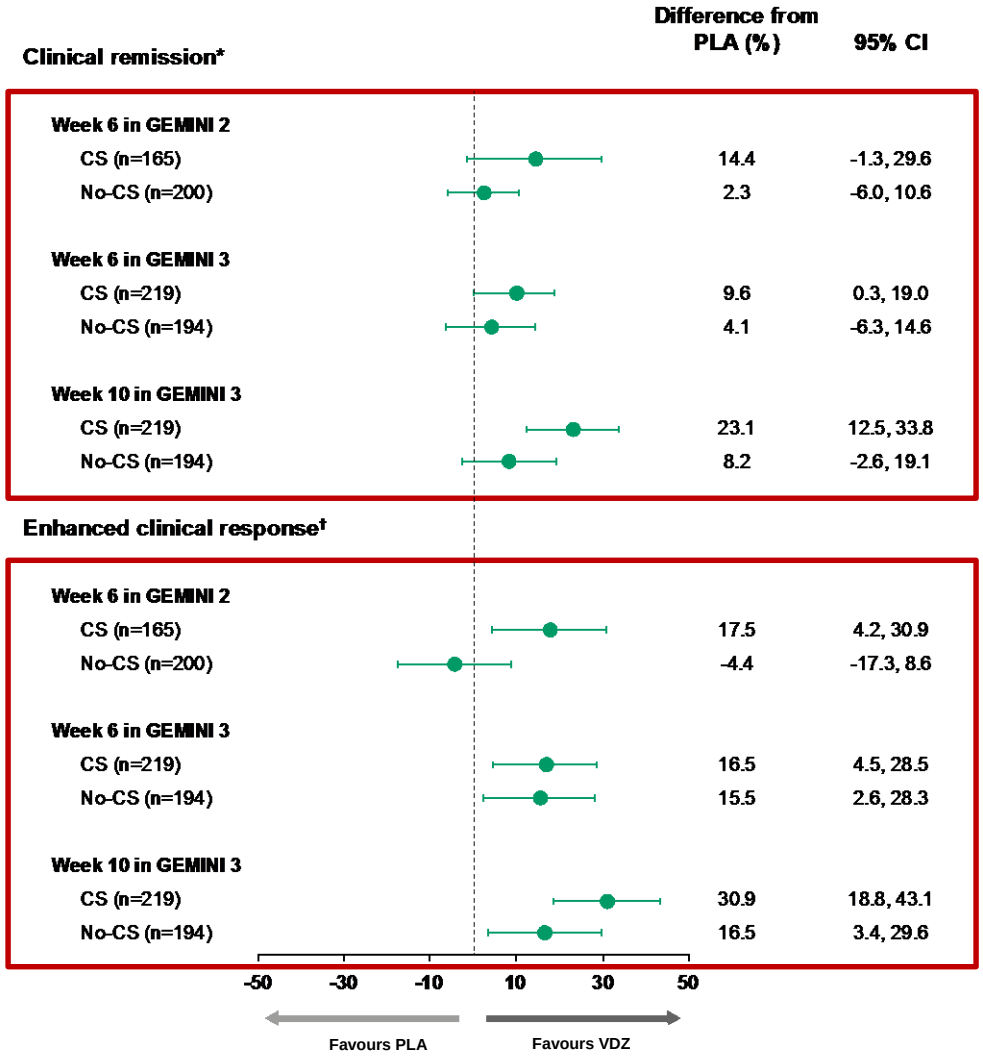


- Baseline characteristics were comparable across treatment groups and CS subgroups
- VDZ treatment arm
  - More patients in the CS subgroup‡ achieved **clinical remission*** than in the no-CS subgroup
    - Week 6 in GEMINI 2: 19.0% vs 10.9%
    - Week 10 in GEMINI 3: 34.2% vs 22.7%
- Higher rates of **enhanced clinical response†** were also achieved in the CS subgroup‡ than in the no-CS subgroup at Week 10 in GEMINI 3 (53.2% vs 42.3%)
- Vedolizumab plus CS induction therapy improves clinical outcomes
  - CS alone is insufficient

*Clinical remission: CDAI score of ≤150 points.
†Enhanced clinical response: decrease of ≥100 points in CDAI score from baseline.
‡Continued stable CS dosing (≤30 mg/day of prednisone or equivalent) was permitted.

CDAI, Crohn's Disease Activity Index; CI, confidence interval; CS, corticosteroid; PLA, placebo; VDZ, vedolizumab.

Clinical remission and enhanced clinical response stratified by CS subgroup



- CS subgroup‡
  - VDZ was associated with a higher rate of **clinical remission** than PLA at Week 6 (19.0% vs 4.6%) in GEMINI 2 and Week 6 (19.8% vs 10.2%) and Week 10 (34.2% vs 11.1%) in GEMINI 3

- **Enhanced clinical response** rates‡ were also higher with VDZ than PLA
  - Week 6 GEMINI 2: 36.0% vs 18.5%
  - Week 6 GEMINI 3: 38.7% vs 22.2%
  - Week 10 GEMINI 3: 53.2% vs 22.2%

*Clinical remission: CDAI score of ≤150 points.
†Enhanced clinical response: decrease of ≥100 points in CDAI score from baseline.
‡Continued stable CS dosing (≤30 mg/day of prednisone or equivalent) was permitted.

CDAI, Crohn's Disease Activity Index;
CI, confidence interval; CS, corticosteroid;
PLA, placebo; VDZ, vedolizumab.

Overview of adverse events during induction therapy

	GEMINI 2				GEMINI 3			
	PLA		VDZ		PLA		VDZ	
	CS (n = 65)	No CS (n = 81)	CS (n = 100)	No CS (n = 119)	CS (n = 108)	No CS (n = 97)	CS (n = 111)	No CS (n = 97)
Any AEs,* n (%)	41 (63)	45 (56)	59 (59)	64 (54)	62 (57)	62 (64)	61 (55)	57 (59)
Drug-related AEs, n (%)	10 (15)	19 (23)	24 (24)	26 (22)	17 (16)	17 (18)	21 (19)	13 (13)
AEs resulting in discontinuation, n (%)	4 (6)	5 (6)	4 (4)	5 (4)	6 (6)	2 (2)	2 (2)	2 (2)
Serious AEs, n (%)	5 (8)	4 (5)	11 (11)	8 (7)	3 (3)	13 (13)	6 (5)	8 (8)

- AE incidence was similar across groups
- No new safety signals were observed

*No deaths occurred in either study.

AE, adverse event; CS, corticosteroid; PLA, placebo; VDZ, vedolizumab.

Conclusions

- Continuing CS use during vedolizumab induction therapy may have synergistic benefits in moderately to severely active CD
  - Higher rates of clinical remission and enhanced clinical response
  - Similar safety/tolerability profile
- Further prospective randomised studies designed and powered to assess combined vedolizumab and CS vs CS alone are warranted and should confirm the current insight

CD, Crohn's disease; CS, corticosteroids; VDZ, vedolizumab.