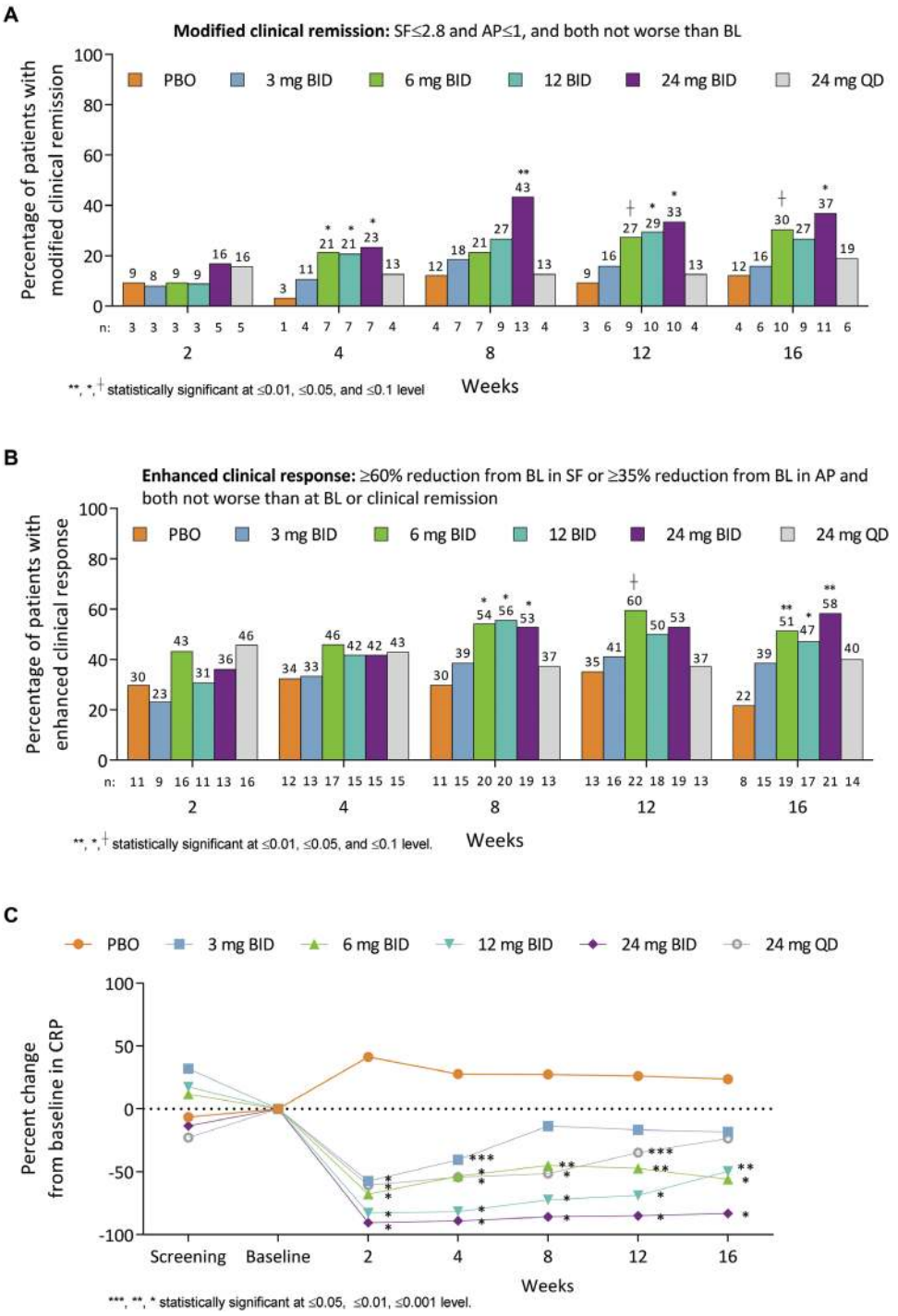

Abstract OP022 – Figure. Proportion of patients with (A) modified clinical remission; (B) enhanced clinical response; (C) mean change in hsCRP over time. Modified clinical remission was analysed in patients with SF ≥ 4, AP ≥ 2.0 at BL.

OP023

A phase 3b open-label multicentre study (VERSIFY) of the efficacy of vedolizumab on endoscopic healing in moderately to severely active Crohn's disease (CD)

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Background: Vedolizumab (VDZ) is a gut-selective humanised immunoglobulin G1 monoclonal antibody that prevents the trafficking of T-lymphocytes into the gastrointestinal submucosa by antagonising the interaction of alpha4beta7 integrin with its ligand, mucosal addressin cell adhesion molecule 1 (MAdCAM-1).[1] VDZ has demonstrated statistically significant differences in clinical remission from placebo in patients (patients) with moderately to severely active Crohn's disease (CD),[2] but endoscopic healing was not previously assessed. The present study evaluated the effect of VDZ on endoscopic remission and healing in patients with CD.

Methods: Patients with moderately to severely active CD (≥3 months; CD Activity Index [CDAI] 220-450; Simple Endoscopic Score for CD [SES-CD] ≥7; ≥1 mucosal ulceration on centrally read endoscopy) who had previously experienced treatment failure with corticosteroids, immunomodulators, and/or at least one tumour necrosis factor-alpha (TNF) antagonist were enrolled. Patients received VDZ 300 mg intravenously at weeks 0, 2, 6, and then every 8 weeks for 26 weeks, followed by a 26-week treatment extension period. The primary endpoint was endoscopic remission (SES-CD ≤4) at week 26, assessed by centrally read ileocolonoscopy. Key secondary endpoints included endoscopic response (SES-CD ≥50% reduction from baseline) and complete endoscopic healing (absence of ulcerations) at week 26. Subgroup analyses stratified by TNF antagonist exposure status were performed for all endpoints and by disease severity for endoscopic remission only.

Results: Of the 101 patients enrolled, 55% had previously failed at least one TNF antagonist (TNF-F), and 46% were categorised as having severe endoscopic activity at entry (SES-CD score of >15). Endoscopic remission rates at week 26 were 12% overall, 20% in TNF antagonist naïve (TNF-N), and 6% in TNF-F patients, respectively (Table 1). Endoscopic remission at week 26 was achieved in 17% of patients with moderate endoscopic activity (SES-CD score of 7–15) compared with 7% of patients with severe disease. Endoscopic response and complete endoscopic healing rates at week 26 are shown in Table 1.

Table 1. Endoscopic outcomes at week 26 by TNF antagonist status.

	Overall (N=101)	TNF-N (n=46)	TNF-F (n=55)
Endoscopic remission, %	12	20	6
Endoscopic response, %	25	28	22
Complete endoscopic healing, %	15	24	7

Abbreviations: TNF, tumour necrosis factor alpha; TNF-F, TNF antagonist failure; TNF-N; TNF antagonist naïve.

Conclusions: VDZ demonstrated the ability to induce endoscopic remission and healing in a refractory population. TNF-N patients were more likely to achieve endoscopic remission and healing than those with previous treatment failure to a TNF antagonist.

References

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OP024

Long-term safety and efficacy of the anti-MAdCAM monoclonal antibody SHP647 for the treatment of Crohn's disease: the OPERA II study

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Background: Despite available treatments, patients with Crohn's disease (CD) often experience symptoms and complications of uncontrolled intestinal inflammation. SHP647 is a fully human IgG2κ anti-MAdCAM monoclonal antibody, in development for induction and maintenance of remission in patients with CD and ulcerative colitis. OPERA II was a 72-week, multicentre, open-label, phase 2 extension study (NCT01298492), designed to assess the long-term safety and efficacy of SHP647 in patients with moderate to severe CD.

Methods: Included patients had completed 12 weeks' treatment (placebo or 22.5 mg, 75 mg or 225 mg s.c. SHP647) in OPERA I (NCT01276509), or had a clinical response (≥3-point decrease in Harvey Bradshaw Index [HBI] score) to 225 mg SHP647 in the open-label study, TOSCA (NCT01387594). Patients received SHP647 (75 mg, s.c.) every 4 weeks from baseline to week 72, and were followed up monthly for a further 6 months. Dose de-escalation to 22.5 mg owing to intolerance/AEs, or escalation to 225 mg owing to clinical deterioration/poor response, was allowed as judged by the investigator. Primary endpoints were frequency of AEs, AEs leading to withdrawal and SAEs. HBI scores were used to define remission (score <5) and assessed as exploratory efficacy measures.

Results: In total, 268 patients (mean age 36.5 years; 56.3% women) were enrolled and entered the treatment period; 149 completed the study. Mean ± SD HBI score at OPERA II baseline was 4.9 ± 3.01. A total of 1150 and 461 AEs were reported during the treatment and follow-up periods, respectively. The most common treatment-related AEs during treatment were nasopharyngitis (5.6%), arthralgia (6.0%), and headache (5.2%). No patient experienced progressive multifocal leukoencephalopathy. Eighty patients experienced SAEs; these were considered treatment-related in 10 patients. Among patients who had AEs leading to discontinuation (n = 54) the most common AE was CD flares. Two patients died: one (75 mg) of multiple organ failure after postoperative aspiration following a resection of the terminal ileum. The second (225 mg) died of metastatic neoplasm of unknown primary, with adenocarcinoma identified on cytology. Neither death was considered drug-related. HBI remission and response rates showed no unexpected decay over time (Figure 1).