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BACKGROUND

- Ulcerative colitis (UC) is a chronic relapsing inflammatory disorder affecting the colon
- A hallmark of UC is increased immune cell activity and dysregulated extracellular matrix (ECM) remodelling, particularly of the mucosal collagens type III and IV, leading to mucosal damage
- Anti-TNF agents have significantly improved the management of UC—still, up to 40% of patients experience treatment failure, with the anti- α 4 β 7 integrin agent vedolizumab (VDZ) being frequently initiated following anti-TNF failure
- There is an unmet need for biomarkers enabling early assessment of treatment success

AIM

We investigated whether biomarkers of neutrophil activity, type III, and IV collagen remodelling could serve as early indicators of VDZ failure in anti-TNF experienced patients with UC

RESULTS

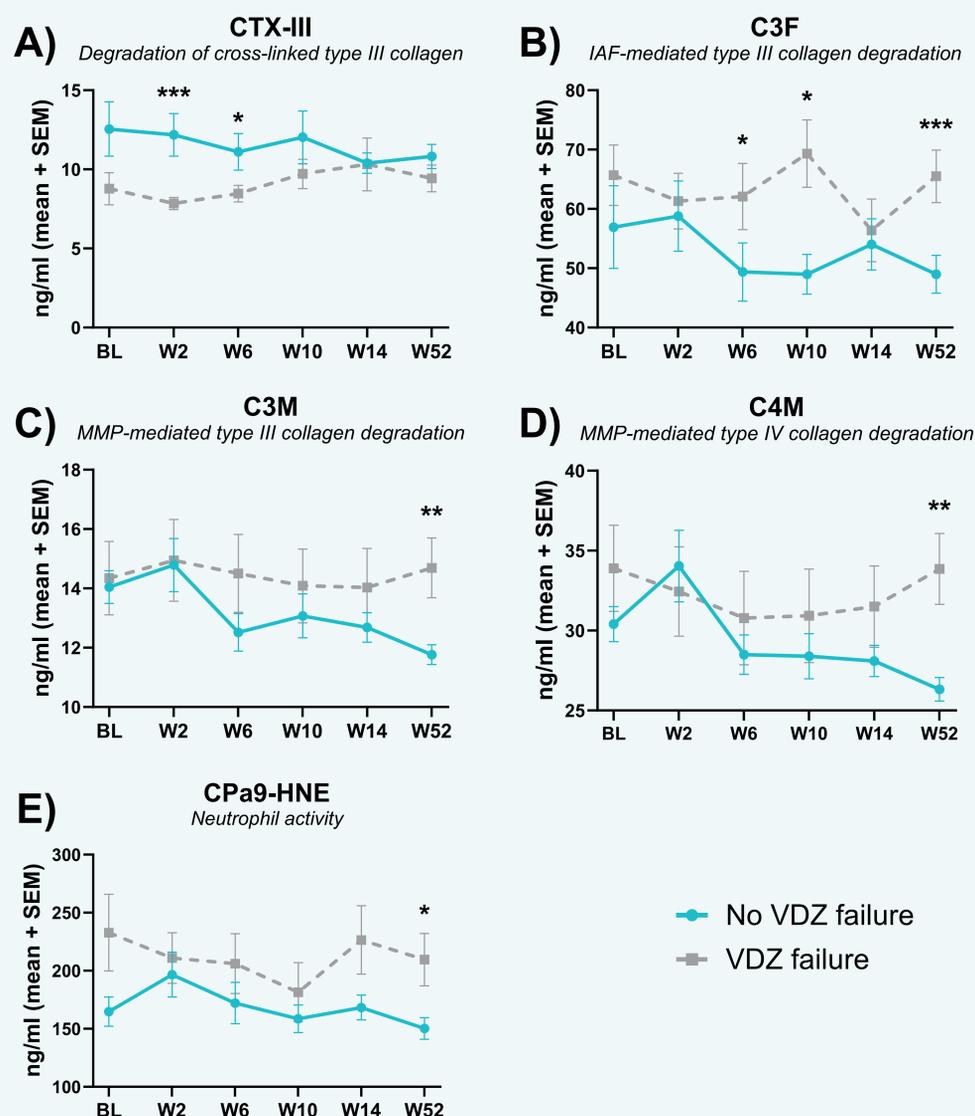


Figure 1. (A) CTX-III was significantly elevated at weeks 2 and 6 in patients who did not fail VDZ, with superior discriminative ability at week 2 (AUC [95%]: 0.84 [0.68–0.94]). (B) At weeks 6, 10, and 52, C3F was significantly higher in patients who failed VDZ than those without treatment failure, with superior discriminative ability at week 10 (AUC [95%]: 0.82 [0.65–0.93]). (C&D) C3M and C4M were significantly elevated in patients who failed VDZ at week 52 (AUC [95%]: 0.70 [0.58 to 0.81] & 0.72 [0.60 to 0.82]). (E) CPa9-HNE was significantly elevated at week 52 among patients failing VDZ. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$.

METHODS

- The cohort included 71 anti-TNF-experienced patients with UC switching to VDZ as second mode of pharmacological action
- Serum was drawn at baseline, weeks 2, 6, 10, 14, and 52– or until VDZ discontinuation
- Biomarkers of cross-linked type III collagen release (CTX-III), collagen type III and IV degradation (C3M, C4M), inflammatory associated fibroblast (IAF)-mediated degradation of type III collagen (C3F), and neutrophil activity (CPa9-HNE) were measured in serum for all timepoints
- The study outcome was VDZ failure <1 year (due to non-response, loss of response, adverse events, or absence of clinical remission at 1 year)

BASELINE DEMOGRAPHIC DATA

	No VDZ failure	VDZ failure
Patients, n	40	27
Age, years (range)	25 (11-63)	30 (15-68)
Female, n (%)	20 (50)	14 (52)
Male, n (%)	20 (50)	13 (48)
Smoking, n (%)		
Yes	1 (2)	3 (11)
No	27 (68)	19 (70)
Previous	12 (30)	5 (19)
Fecal calprotectin μg/g (range)	1370 (99-3000)	1845 (189-3130)
CRP, mg/L (range)	0 (0-33)	5 (0-71)
Montreal Extent, n (%)		
Proctitis (E1)	9 (23)	5 (19)
Left-sided (E2)	12 (30)	5 (19)
Pancolitis (E3)	19 (47)	17 (62)

CONCLUSIONS

Early increase in CTX-III, reflecting resolution of fibrosis, was associated with the absence of VDZ failure

Increased neutrophil activity (CPa9-HNE), IAF-mediated collagen type III degradation (C3F) and mucosal damage (C3M, C4M) associated with the failure of VDZ

Biomarkers reflecting neutrophil activity and inflammatory events in the mucosa are promising tools for early and dynamic assessment of later VDZ treatment outcomes in anti-TNF experienced patients with UC