MES were 8.3 and 2.6, respectively. A significantly higher proportion of patients treated with APR30 achieved TMS clinical remission (Δ18%) and modified Mayo score (MMS) clinical remission (Δ25%) compared with PBO. A higher proportion of patients treated with APR30 and APR40 achieved a clinical response at Week 12 compared with PBO, but the result was only significant for the APR40 treatment group. At Week 12, a significantly higher proportion of patients treated with APR30 achieved a decrease of at least one point from baseline MES (Δ32%) and an MES ≤1 (Δ32%) compared with PBO. Both APR30 and APR40 treatment groups showed a trend for a higher proportion of patients achieving histological remission, defined as a Geboes score <2, compared with the PBO group. A significantly higher proportion of patients treated with APR30 achieved mucosal healing (MES ≤1 with Geboes score <2) (Δ18%) compared with PBO. Patients treated with APR30 achieved significant improvements in percent changes from baseline in hsCRP at Weeks 4, 8, and 12 and faecal calprotectin at Weeks 2, 4, and 8 compared with PBO. A similar safety profile was seen in patients treated with APR30 and APR40.

Conclusions: In this 12-week, phase 2 study, patients with active UC treated with APR30 had clinically meaningful improvements in symptoms, endoscopy, biomarkers, and mucosal healing compared with PBO. The observed adverse events were consistent with those expected in UC patients and were also consistent with the known safety profile of apremilast.

**Methods:** Serum samples were obtained from 31 UC patients (58% female, median age 35.6 years) both at baseline and after a median (IQR) of 14 (10–25) weeks. All patients had endoscopic disease activity prior to treatment (Mayo endoscopic subscore/MES ≥2) and MH was defined at follow-up endoscopy as MES ≤1. NGAL-MMP-9, LL-37, and CHI3L1 were measured with ELISA. Binary logistic regression analysis was used to combine multiple markers. ROC analysis was used to test the performance of individual and combined markers. Non-parametric tests were performed, and p-values of <0.05 were considered significant.

**Results:** Twenty-one patients (68%) achieved MH with ADM therapy. Compared with baseline, NGAL-MMP-9 levels significantly decreased in patients with MH (96.9 vs. 214.1 ng/ml, p = 0.002), whereas patients without MH had similar levels. Neutrophil count was significantly lower after ADM compared with baseline in patients with MH only (3.6 vs. 6.5 10⁹/l, p = 0.023). CRP levels significantly decreased after ADM in patients with MH (15 to 1.1 mg/l, p = 0.008) and were higher at baseline in patients with MH compared with without MH (15 vs. 2.4 mg/l, p = 0.004). LL-37 levels significantly increased in patients without MH post-ADM compared with baseline (29 vs. 19.3 ng/ml, p = 0.034) and were significantly higher compared with patients with MH post-ADM (29 vs. 18.7 ng/ml, p = 0.031). CHI3L1 levels significantly decreased after ADM in patients with MH only (47.4 to 21.6 pg/ml, p = 0.049). The performance of NGAL-MMP-9 (AUC=0.70), neutrophil count (AUC=0.58), CRP (AUC=0.56), LL-37 (AUC=0.79), and CHI3L1 (AUC=0.69) to discriminate MH post-ADM significantly increased when all markers were combined (AUC=0.86). The 5-marker panel was discriminative for MH with 75% sensitivity, 89% specificity, 67% positive predictive value, and 92% negative predictive value.

**Conclusions:** Neutrophil-related markers (NGAL-MMP-9, LL-37, and CHI3L1) as well as CRP and neutrophil count were significantly associated with MH after treatment with ADM. These data are in concordance with our previous findings in infliximab-treated patients. We therefore suggest a broad clinical utility of this panel for monitoring MH in UC patients under anti-TNF treatment.

**OP007 Detection of mucosal healing with a serum marker panel in adalimumab-treated patients with ulcerative colitis**

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**Background:** Surrogate markers that accurately detect mucosal healing (MH) in patients with ulcerative colitis (UC) are urgently needed. After infliximab therapy, neutrophil gelatinase B-associated lipocalin in complex with matrix metalloproteinase-9 (NGAL-MMP-9), cathelicidin LL-37 and chitinase 3-like 1 (CHI3L1), together with C-reactive protein (CRP) and neutrophil count were significantly associated with MH. We investigated whether these five markers were also associated with MH after treatment with adalimumab (ADM).

**OP008 α4β7 Integrin-dependent gut homing of non-classical monocytes is essential for intestinal wound healing mediated by M2 macrophages**

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**Background:** The anti-α4β7 integrin antibody Vedolizumab is successfully used for the treatment of IBD. Mechanistically, it is well established that it inhibits α4β7 integrin-dependent gut homing of pathogenic T lymphocytes to the inflamed gut. However, the impact of anti-α4β7 treatment on monocyte gut homing, which differentiate to macrophages regulating intestinal inflammation and tissue remodelling, has not been investigated so far.

**Methods:** Expression of gut homing integrins on peripheral blood monocyte and intestinal macrophage subsets from IBD patients and controls was analysed by flow cytometry and immunohistochemistry, respectively. Dynamic adhesion assays were used to investigate
monocyte adhesion to mucosal addressin vascular cell adhesion molecule (MAdCAM)-1 with or without vedolizumab treatment. Monocyte subset homing to the inflamed gut was studied in mice in vivo. Moreover, mouse models were used to assess intestinal wound healing with and without anti-α4β7 antibodies and the proportion of macrophage subsets was quantified by immunohistochemistry. Flow cytometric distribution of monocyte subsets was measured in patients treated with vedolizumab.

Abstract OP008 – Figure. (A) Expression of α4β7 integrin on human monocyte subsets. (B) Expression of α4β7 integrin on mouse monocyte subsets. (C) In vivo homing of mouse classical vs. non-classical monocytes. (D) Wound healing in mice treated with or without anti-α4β7.
Results: While the expression of α4β7 was low on overall monocytes, human CD16+ intermediate and non-classical monocytes and murine CX3CR1+ non-classical monocytes expressed high levels of α4β7 (Figure 1A and B) and other homing markers typically expressed by lymphocytes. Homing marker expression in classical monocytes and CD14+ intestinal macrophages was similar while the pattern observed in non-classical monocytes rather resembled that of CD163+ macrophages, thus supporting earlier reports indicating a preferential differentiation of non-classical monocytes to M2 macrophages. Anti-α4β7 treatment inhibited dynamic adhesion of human monocytes in vitro and gut homing of murine monocytes in vivo (Figure 1C). Intestinal wound healing in mice treated with anti-α4β7 antibodies (Figure 1D) and in β7−/− mice was impaired going along with reduced numbers of M2 macrophages. In IBD patients treated with vedolizumab, the proportion of CD16+ monocytes increased over the course of treatment.

Conclusions: In addition to blocking lymphocyte homing to the gut, anti-α4β7 treatment also impedes non-classical monocyte homing. This leads to reduced presence of M2 macrophages surrounding mucosal wounds and impaired intestinal wound healing potentially providing an explanation for the recent clinical observation of increased postoperative complications in vedolizumab-treated patients.

Disclosure: Support provided by Takeda.

OP009
A combination of clinical, serological, and genetic factors predicts complicated disease course in paediatric-onset Crohn’s disease: results from a population-based study

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Background: Identification of patients at high risk of progressing disease would be invaluable in guiding initial therapy in Crohn’s disease (CD). Clinical parameters at diagnosis are insufficient to predict a disabling course of CD. The objective of this study was to evaluate a combination of clinical, serological, and genetic factors to predict complicated disease course in paediatric-onset CD.

Methods: Paediatric-onset CD patients, diagnosed before 17 years between 1988 and 2004 and followed more than 5 years were extracted from the French population-based Epimad registry. Complicated disease course was defined by the evolution from an inflammatory (B1) to a complicated behaviour (stricturing B2, or penetrating B3); or an intestinal resection. Available data included clinical data at diagnosis, serological markers at inclusion (ASCA, ANCA, anti-OmpC, anti-Cbri1, anti-Fla2, anti-Flax) and 370 candidate single-nucleotide polymorphisms (SNP) associated with CD or other immune-mediated diseases or with a role in inflammation pathways, interaction with micro-organisms, or modulation of innate immunity. Lasso logistic regression models with stability selection were used to select variants associated with severe disease. A final logistic adaptive lasso regression model was performed including clinical, serological and selected variants.

Results: A total of 219 patients were included in this study with a median age at diagnosis of 14.3 years (IQR 11.9–16.0). One-third (n = 70) experienced an intestinal resection during the 5 years following diagnosis. Among the 156 patients with inflammatory disease (B1) at diagnosis, about one-third (n = 48) progressed to a complicated behaviour. Final model for resection included complicated behaviour (B2 or B3) at diagnosis, extra-intestinal manifestations at diagnosis and 23 SNPs. Final model for complicated behaviour included ANCA (protective effect) and Asca-IgG (negative effect) levels and 18 SNPs. In both models, half of SNPs were known as susceptibility loci of IBD or CD including NOD2 G908R missense mutation. Six variants were common between the two models. Area under the curve assessed by 5-fold cross-validation were, respectively, 0.84 (IC 95% [0.80–0.88]) and 0.89 (IC 95% [0.87–0.91]).

Conclusions: In this population-based paediatric-onset CD cohort, a combination of clinical, serotypic, and genotypic variables is able to predict disease progression with a high accuracy. After validation in an independent cohort, this prediction score will be helpful to identify patients needing early biological therapy.

Reference

OP010
Shallow whole-genome sequencing predicts the future cancer risk of low-grade dysplastic lesions arising in ulcerative colitis

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Background: The management of low-grade dysplasia (LGD) in UC is uncertain due to the variable risk of progression to colorectal cancer (CRC). Chromosomal copy number alterations (CNAs) occur in colonic epithelial cells of UC patients who have developed CRC. The burden of CNAs in precursor LGD relative to high-grade dysplasia (HGD)/CRC has not been defined, and the correlation between LGD CNA burden and future CRC risk is unknown. Shallow