Results: We identified 9,284 pIBD patients enrolled between 2007 and 2016, 62% with Crohn’s disease. The mean age of the cohort was 13.7 years (SD, 4.2) and comprised of 47% females. The median follow-up was 24 months (IQR, 33). Twenty percent of this cohort were treated with an aTNF agent during follow-up and 38% with an immunomodulator (Thiopurine or Methotrexate). Nearly 8.5% were started on an aTNF agent while treated with an immunomodulator, of which 90% were Thiopurines. We identified 3 cases of lymphoma occurring over 25,413 person-years of follow-up (Incidence rate, 1.18 cases/100,000 person-years). The absolute risk of lymphoma in our pIBD sample was 0.3 x 10^{-3}. There were no cases of hepatosplenic T cell lymphoma observed. The medication exposure history for cases of lymphoma did not include treatment with an aTNF agent and/or an immunomodulator.

Conclusion: Among our cohort of pIBD, the overall incidence and absolute risk of lymphoma were extremely low. Treatment with aTNF agents and/or immunomodulators was not associated with an increased risk of malignancy. Our results would support prioritization of the clinical benefits of aTNF agents over the low risk for malignancy.

P100
REAL-WORLD COMPARISON OF ARTHRALGIAS WITH INFlixIMAB VS. VEDOLIZUMAB IN THE TREATMENT OF BIO-NAIVE INFLAMMATORY BOWEL DISEASE
Timothy Ritter, Chris Fourment, Samantha Kuten, Lucinda Van Anglen

Background: Both infliximab (IFX) and vedolizumab (VDZ) are approved for the treatment of inflammatory bowel disease (IBD) in adults. VDZ is gut-specific and thought to be less effective in controlling extraintestinal manifestations than IFX. The purpose of this study was to compare the incidence and timing of arthralgias between IFX and VDZ.

Methods: We performed a retrospective cohort study of bio-naive adult patients treated with IFX or VDZ for ulcerative colitis (UC) or Crohn’s disease (CD) at a large multispecialty gastroenterology private practice. Patients were case-matched 1:1 based on age, gender, diagnosis, and baseline disease severity using the partial Mayo (pMayo) for UC and the modified Harvey-Bradshaw Index (mHBI) for CD. Arthralgias were captured out to 12 months of therapy and classified as pre-existing or new-onset based on time to occurrence. Those with pre-existing arthralgias were excluded from new-onset arthralgias analyses. Rates of arthralgias and time to new-onset arthralgias were compared between IFX and VDZ patients.

Results: A total of 77 IFX (58 UC, 19 CD) and 77 VDZ (58 UC, 19 CD) case-matched pairs were generated. Baseline demographics were similar between IFX and VDZ groups: mean age 45±16.9 vs 46±16.2, male gender 60% vs 61%, Rates of pre-existing arthralgias were 13/77 (17%) and 12/77 (16%) in IFX and VDZ cohorts (p=0.83), respectively. Resolution of pre-existing arthralgias was also similar between groups (6/13 vs 7/12, p=0.70). Of the remaining 64 IFX and 65 VDZ patients without arthralgias at baseline, 16 (25%) IFX patients and 17 (26%) VDZ patients experienced new-onset arthralgias (p=1.0). Median time to new-onset arthralgias was 5.0 (IQR 3.4-7.0) months in IFX patients, compared to 3.3 (IQR 1.4-5.3) months in VDZ patients (p=0.15). While IFX patients appeared to develop new-onset arthralgias earlier, this was not significant (p=0.20) [Figure 1]. Of note, two IFX patients discontinued therapy due to suspected drug-induced lupus with arthralgias; there were no VDZ discontinuations due to arthralgias.

Conclusions: Our data suggests that resolution of pre-existing arthralgias and new-onset arthralgias are similar, despite the gut selectivity of VDZ compared to IFX. Continued therapy due to suspected drug-induced lupus with arthralgias; there were no cases of hepatosplenic T cell lymphoma observed. The medication exposure history for cases of lymphoma did not include treatment with an aTNF agent and/or an immunomodulator. Our data suggests that resolution of pre-existing arthralgias and new-onset arthralgias are similar, despite the gut selectivity of VDZ compared to IFX. Continued therapy due to suspected drug-induced lupus with arthralgias; there were no cases of hepatosplenic T cell lymphoma observed. The medication exposure history for cases of lymphoma did not include treatment with an aTNF agent and/or an immunomodulator.

P101
SARCOPENIA IS ASSOCIATED WITH INCREASED RISK OF INFECTION IN IBPOPATIENTS OLDER THAN 50 YEARS STARTING BIOLOGIC MEDICATIONS
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Background: The relationship between sarcopenia and clinical outcomes outside of the post-operative setting has not been well-studied in IBD patients. We aimed to characterize the prevalence of sarcopenia and its association with adverse events and clinical response in IBD patients starting on new biologic medications.

Methods: We identified a retrospective cohort of adult (≥18 years old) IBD patients at the University of Minnesota with an abdominal CT or MRI within 6 months prior to or one month after starting a new biologic medication. Baseline demographics, disease severity (based on Physician’s Global Assessment from GI encounters), laboratory values and clinical outcomes for one year after the start of medications were obtained from chart review. The primary endpoint was incidence of adverse events (defined as infection, need for surgery, or hospitalization) within one year after medication start. The secondary outcome was clinical response as assessed based on clinical, endoscopic, and radiographic follow-up. Skeletal muscle index (SMI) measures were obtained from CT/MRI images at the L3 vertebral level. Published cut-offs (SMI of 38.5 cm2/m2 for women and 52.4 cm2/m2 for men) were used to determine the presence of sarcopenia. Associations between sarcopenia and outcomes were analyzed using logistic regression and age stratification was performed.

Results: Ninety-four patients (74 CD, 20 UC, 47% male, mean age 38 years) were included in the analysis. The majority of patients had moderate disease severity, but not hospitalization. Examples included sinusitis, upper respiratory infections, periodontitis, urinary tract infection, herpes simplex, and two cases of C. difficile. Furthermore, when controlling for disease duration and concomitant steroid use, the association between sarcopenia and infection remained significant. In this age subgroup, there was no association between sarcopenia and clinical response to therapy.

Conclusions: In our cohort, sarcopenia was present in the majority of adult IBD patients starting new biologic medications. In patients ≥ 50 years old, sarcopenia was associated with an increased risk of infections. Further work is needed to validate these findings and to understand which patients may benefit from sarcopenia assessment prior to biologic start.
S-MER peptide specifically binds to serum amyloid A (SAA), a stress pro-inflammatory protein, which generates aggregated amyloid deposits in the IBD colon (de Villiers et al. Cytokine 12:1337-1347,2000). Our studies further provide in vitro evidence, strengthened by in vivo experiments, that SAA is a significant target of this pentamer. To this end, the S-MER peptide (but not the corresponding scrambled peptide) inhibits the release of the pro-inflammatory cytokines IL-6 and IL-1β from SAA-activated fibroblasts. Furthermore, the S-MER peptide was found to retard the early stages of amyloid-type aggregation of SAA in solution (Fig 2). Adopting the β-sheet conformation, MTADV would display opposing hydrophobic and hydrophilic faces that could interact with the β-sheet-forming amyloidogenic sequences in SAA. This suggests that the mechanism of action for the S-MER peptide in vivo may depend on its ability to slow the aggregation of SAA, thus reduce its contribution to chronic inflammation. Finally, using bioinformatics and qRT-PCR, we have found the pentamer up-regulates a set of genes involved in resistance to chronic inflammations. Hence, our study provides both a new potential drug (MTADV) and a new therapeutic target candidate (SAA) for IBD.

ICOS is a costimulatory receptor highly related to CD28, upregulated upon T cell activation and mediating costimulatory signals in post-activation T cells - suggesting ICOS may be more relevant in active disease. In contrast, CD28 predominates in non-inflammatory cytokine and flow analysis of blood was performed throughout the study. Clinical presence of colitis was assessed using a disease activity index based on weight loss and stool consistency. At end of study, colonies were measured and assessed histologically.

**Results:** ALPN-101 suppressed cytokine release (IFNγ, IL-2) from healthy or IBD patient PBMCs superior to single pathway inhibitors. In vivo, preventively or therapeutically, a single dose of ALPN-101 was efficacious to significantly improve multiple colitis readouts. Repeat dosing completely prevented onset of colitis. ALPN-101-treated mice gained weight and had colon weight-to-length ratios similar to the no-colitis cohort and demonstrated significant suppression of T cells and pro-inflammatory cytokines (e.g. TNFα, IL-12/23, IL-6). Mice treated from Day 0 to the end of study had no signs of colitis (D). None of the mice in these groups had their muscularis layer of colon affected by inflammation. Mice treated with a single dose at day 0 or day 14 had milder colitis than Fc control-treated mice, although the differences were not statistically significant.

**Conclusion:** Dual pathway inhibitor ALPN-101 is superior to single pathway inhibition in human in vitro and mouse in vivo translational studies and may be a novel therapeutic candidate for the treatment of IBD. Clinical trials for ALPN-101 in multiple inflammatory diseases are planned and underway.

**Alpn-101, a First-in-Class Dual ICOS/CD28 Antagonist, Demonstrates Efficacy in Patient-Derived PBMC in Vitro and in an In Vivo T Cell Transfer Model of Chronic Inflammatory Bowel Disease (IBD)**

Kristine Swiderek, Stacey Dillon, John Moore, Susan Bort, Sherri Mudri, Katherine Lewis, Mark Rixon, Jahnvi Bhandari, Stanford Peng

Background: T cell costimulation has been strongly implicated in the pathogenesis of IBD, yet CD28 costimulatory pathway inhibitors (e.g. abatacept, CTLA4-Fc) have not proven clinically efficacious, implicating an alternative costimulatory pathway.

AZD4205, a Selective, Gi Tract-Enriched Selective JAK1 Inhibitor for Crohn’s Disease: Preclinical Evidence and Phase I Data

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Background: AZD4205 is an oral, ATP-competitive, JAK1 selective inhibitor. Nonclinical data showed its higher drug concentration within the