RESULTS: Overall, IRR were infrequent—4.0% and 1.9% of all patients in UNITI 1 & 2, respectively, expe-
renced infusion reactions to the single IV dose. There were no differences in IRR between PRO & UST, or
between UST doses (UNITI 1 IRRs in 2.0%, PRO and 4.5% UST 130mg and 3.6%, UST 6-8 mg/kg, UNITI 2 IRRs in 3.0%, PRO and 4.5% UST 130mg and 1.5%, UST 6-8 mg/kg). During IM UNITI, in non-rand-
omized patients who were non-responders to placebo induction and received a 130mg IV injection, IRR to
PRO and PRO were similar and infrequent (2.5% and 1.8%, respectively). There were no anaphylactic or
delayed reaction events attributable to any IV dose. After SC administration, IRRs were not different across groups. In the combined (randomized and non- randomized) population, ISRs were 1.7% (6/373) in the Phase 2 and 3 CD clinical studies. Patients who received IV ustekinumab (doses included: 130mg flat dose and 1.3, 4.5, 6.6 mg/kg, during the placebo-controlled induction period (Week 0-8) were pooled from 2 Phase (C0379T07 & CERTIFI) and 2 Phase 3 (UNITI-1 and 2) clinical studies (total sample size = 1,886). For maintenance, SC UST (combining 90mg q12w and q14w) and PRO were pooled and compared in the randomized responder populations (ie responders to IV ustekinumab) from the maintenance phase of the 2 Phase 2 CERTIFI (Week 8 to Week 22) and Phase 3 4-UNITI (Week 22 to Week 44) studies (total sample size = 514).

RESULTS: No death occurred in either the induction or maintenance phases in any groups. Through 8
weeks of induction, the percentages of patients with AEs, SAEs, and infections were similar between
UST and PRO both on and off IMM and CS across all 4 subgroups, for UST, 58-63% had AEs, 47% had SAEs,
and 19-23% had infections and for PRO, 56-66% had AEs, 5-9% had SAEs, and 21-26% had infections. In
maintenance, proportions of patients experiencing AEs, SAEs, and infections were generally similar
between UST and PRO groups both on and off IMM and CS, across all 4 subgroups, for UST, 72-82%
had AEs, 9-10% had SAEs, and 41-43% had infections and for PRO, 77-88% had AEs, 9-13% had SAEs,
and 37-49% had infections. Proportions of patients on CS in both the UST and PRO groups experienced
slightly higher rates of AEs compared with those not on CS (UST, 82 vs 74%, respectively, PRO, 87% vs
76%, respectively). However, no significant differences in CDAI were observed between PRO & UST patients with
similar reported expected safety profile of UST in moderate to severe CD patients, although concomitant CS
did result in slightly higher rates of events during maintenance, par-
ticularly in the PRO group.

P-103

RAPIDITY OF SYMPTOMATIC IMPROVEMENT WITH UDENOLIZUMAB THERAPY FOR ACTIVE CD: A GEMINI POST HOC ANALYSIS

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POST HOC ANALYSIS

METHODS: Patients with active, moderate to severe CD were randomized to receive placebo (PRO) or
UDENOLIZUMAB (UDE) at weeks 0 and 2 during the 6-wk induction phase. The two patient-reported components
of the Crohn’s disease activity index (CDAI score)—abdominal pain subscores (APS) and number
of liquid or very soft stools subscore, or stool frequency (SF)—were evaluated at 0, 2, 4, and 8 wks. Mean
changes from baseline at wks 2, 4, and 8 were -12.3(-18.6, -6.8), -23.5(31.5, -15.7) and -25.0(31.4, -18.3) respectively for UDE and 4.6(14.2, 1.5), 9.9(19.5, 0.5),
and 12.4(20.8, 4.8) respectively for PRO. Similarly, a numerically greater percentage decrease in BL in PRO was
seen in PRO vs PRO, reaching statistical significance at wk 6 in both anti-TNF naïve and previously treated patients. Percent change from baseline was greater with UDE vs PRO with a percent change in RBS=0 at wk 2 (22.2% higher with 95%CI of 12.6-31.8%) than with PRO. A composite of SFS≤1 and RBS=0 was achieved in a significantly
greater proportion of patients with UDE vs PRO at all time points for both anti-TNF naïve and overall populations
with treatment differences of 15.7% and 9.0% at Week 2.

CONCLUSION: Udenolizumab therapy was well tolerated and improved CD symptoms in Udenolizumab
was well tolerated and achieved significant symptomatic improvement in comparison with PRO in this post hoc analysis.

P-105

ETRULIZUMAB TREATMENT IMPROVES HISTOLOGIC ACTIVITY AS ASSESSED BY BOTH THE ROBARTS HISTOPATHOLOGY AND NANCY HISTOLOGICAL INDICES

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BACKGROUND: Etrulizumab, an anti-β7 monoclonal antibody, showed efficacy and safety during 10 weeks of induction in patients with moderate-to-severely active ulcerative colitis (UC). Relief of rectal bleeding (RB) and stool frequency (SF) remain important treatment goals for pts and 2-3 months of infusion with physicians. We aimed to characterize early symptomatic response with VDZ, specifically evaluating the timing of RB and SF improvement.

METHODS: We assessed symptomatic improvement with VDZ through post-hoc analysis of GEMINI 1. Pts with active, moderate-to-severely UC were randomized to receive double-blind placebo (PRO) or VDZ (wk 0) and 2 during the 6-wk induction phase. Mayo clinic SF subcores (SFS) and RB score (IRB) were evaluated at 0, 2, 4, 6 wk. Mean subcores and mean percent change from baseline (BL) were reported for the overall population and in those who were tumor necrosis factor antagonist (anti-TNF) naïve. The percentages of pts who reached SFS<1 and/or IRB<0 were also determined.

RESULTS: In anti-TNF-naïve pts, greater percentage decreases in mean SFS from BL were observed with VDZ. Following statistical significance was reached at wk 2 for both anti-TNF naïve and previously treated patients. Percent change from baseline was greater with VDZ vs PRO with a percent change in RBS=0 at wk 2 (22.2% higher with 95%CI of 12.6-31.8%) than with PRO. A composite of SFS<1 and RBS=0 was achieved in a significantly greater proportion of patients with VDZ vs PRO at all time points for both anti-TNF naïve and overall populations with treatment differences of 15.7% and 9.0% at Week 2.

CONCLUSION: Early symptomatic improvement was achieved with VDZ as early as wk 2, with greater differences from PRO observed in anti-TNF-naïve pts. These results highlight the rapid onset of VDZ in terms of reducing symptoms and for those who exhibit a more gradual response should be used to inform clinical practice.
Abstracts

P-107
Long, Non-coding RNA Gene Expression Signatures to Distinguish Irritable Bowel Syndrome and Inflammatory Bowel Disease

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BACKGROUND: lncRNAs play critical roles in the regulation gene activity. This extends to genes whose protein products are critical for mounting both innate and adaptive immune responses. Our understanding of the functional role of lncRNAs in human diseases, including gastrointestinal disease, is in its infancy. No blood-based lncRNA biomarkers have been made commercially available to distinguish IBS from ID or identify individual inflammatory conditions. Here we sought to develop machine learning classifiers using long, non-coding RNA (lncRNA) gene expression data from blood to distinguish irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).

METHODS: Peripheral whole blood collected into PAXgene tubes was obtained from healthy control patients (n=115), and patients diagnosed with irritable bowel syndrome (n=128), Crohn’s disease (n=89), and ulcerative colitis (n=84). Patients diagnosed with celiac disease (n=39) were recruited as additional inflammatory bowel disease control group for classifiers capable of distinguishing IBS from Crohn’s disease or ulcerative colitis. RNA sequencing was performed using a subset of healthy control, celiac, Crohn’s disease, and ulcerative colitis patient samples to define differentially expressed lncRNA gene targets. To validate sequencing findings, RT-PCR was performed on all patients recruited in the study (n=469). Gene expression datasets generated were used to train and independently validate machine learning classifiers capable of distinguishing IBS and IBD from other subjects in the each cohort.

RESULTS: lncRNAs measured by RT-PCR exhibit high degrees of differential expression across healthy control, IBS, and IBD cohorts. Unlike previous studies of mRNAs, lncRNA expression differences were frequently 4-fold or greater in case/control comparisons. lncRNAs exhibit a high degree of discriminative power and can be used to generate predictions with accuracy exceeding 90% for classifiers capable of discriminating irritable bowel syndrome from other inflammatory conditions and healthy controls.

CONCLUSION(S): Gene expression data derived from peripheral whole blood analyzed using machine learning approaches produced high degrees of differential expression of irritable bowel syndrome and inflammatory bowel disease. Use of this information may provide clinically actionable information for healthcare providers.

P-108
Therapeutic Drug Monitoring of the Biosimilar SB2 (RENFLIXIS®, Infliximab-ada) Using LabCorp Infliximab Assays for Drug Level and Anti-drug Antibodies

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BACKGROUND: Therapeutic drug monitoring (TDM) of infliximab (IFX) concentration and anti-infliximab antibody (ADA) titer has helped physicians make informed clinical decisions in the management of inflammatory bowel disease (IBD). A TDM approach to treating IBD patients has been used to improve clinical efficacy of anti-TNF agents. The LabCorp IFX TDM test (drug and ADA levels) has been validated in peer-reviewed literature and is widely used by clinicians to help maximize treatment response. Recently approved by the FDA for treatment of IBD, RENFLIXIS (SB2, infliximab-ada) is a biosimilar of the originator infliximab (TNF alpha inhibitor). The aim of this study was to validate the LabCorp IFX TDM test for the quantification of serum SB2 concentrations and ADA. METHODOLOGY: To demonstrate ability to measure RENFLIXIS using the LabCorp IFX TDM test, SB2-specific immunoassays were developed SB2 calibrators and SB2-conjugated key reagents were used to construct SB2-specific immunoassays. Analytic performance including accuracy, precision, spike, recovery, specificity and sensitivity was evaluated. Exogenous SB2 was spiked into donor serum to assess recovery using the IFX drug assay. 124 IFX-treated IBD patients were split-tested using SB2 and IFX drug and ADA assays to assess equivalency and inter-laboratory variability.

RESULTS: Both SB2 drug level and ADA showed excellent agreement to IFX drug level and ADA respectively. SB2 assay accuracy (<11% bias) and precision (<7% bias) were equivalent to IFX assay accuracy (<5% bias) and precision (<10% CV) across the range of the assay. More importantly, spike and recovery of RENFLIXIS using the IFX drug assay was equivalent to the recovery of reference product IFX using the IFX drug assay. SB2 was spiked into the donor serum pool to generate 0.25, 0.5, 1.0, 2.0, 4.0, 5.0, 6.0, and 8.0 μg/mL targets. The same target concentrations were generated for IFX. Both sets of targets were used the IFX drug assay. Percent recovery of SB2 ranged from 87% to 114%; IFX recovery was 83% to 133%. Average spike and recovery was 99% for both SB2 and IFX using the IFX drug assay. Both the SB2 drug assay and IFX drug assay were used to analyze 59 serum samples of IBD patients treated with reference product IFX. The calculated linear regression between the two methods was Y=1.11x+0.13 and R² = 0.92. The IFX drug assay was specific and sensitive enough to be cross-reactive to the reference product IFX ADA assay in terms of precision (<10% CV), accuracy (<11% bias), linearity, drug tolerance and sensitivity. The LabCorp SB2 drug assay results were comparable to the reference IFX drug assay results. Antibody titer values were compared. Linear regressions of Y=1.99+0.87, R²=0.09 were obtained.

CONCLUSION(S): This study demonstrates complete cross-reactivity of RENFLIXIS (infliximab-ada) in LabCorp IFX TDM assay. Healthcare providers can confidently use LabCorp IFX TDM test to monitor RENFLIXIS (infliximab-ada) drug levels and serum ADA titers in their patients.

P-109
Use of Therapeutic Drug Monitoring (TDM) to Aid Treatment Decision Making: A Retrospective View From a Large Community Practice

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BACKGROUND: Traditionally, when a patient’s inflammatory bowel disease (IBD) symptomology worsens, physicians make a decision to either change the current therapy based on perceived loss of response or continue on the same therapy, adjusting either dose or frequency. Consequently, many patients are discontinued from effective therapies too soon, while others remain on ineffective therapies in the hopes that the clinical outcome will eventually improve. We aimed to provide insight into the usage of therapeutic drug monitoring (TDM) in a large community practice.

METHODS: We conducted a retrospective analysis of patients receiving infliximab (IFX) infusions who had TDM assays drawn between August 1st, 2016 and July 31st, 2017. We documented serum IFX and anti-infliximab (ATI) levels, achieving 4 categories of lab values (C-reactive protein, sedimentation rate, albumin, fecal calprotectin) and 3 categories of patient clinical symptoms (bowel movements, abdominal pain, rectal bleeding) to measure overall patient symptomology. We then examined the physicians’ response to TDM and the impact it had on patient symptoms and lab values.

RESULTS: A total of 67 IBD patients received a serum IFX level result lower than 4 μg/mL (34 MD, 13 CD). 23 patients had an undetectable serum IFX level (34.9%), 50 patients had an undetectable ATI level at the dose level at which they were tested. 10 patients had an ATI level greater than 200 ng/mL (14.9%), and 7 patients had an undetectable level of both serum IFX and ATI (10.4%). 17 patients changed therapy following the TDM result with 3 patients (17.6%) changing therapy more than once, 24 patients changed the dosage and/or frequency of Remicade infusions (35.8%), with 1 being taken off therapy altogether. 55 of 26 patients (88%) had no change in therapy despite low or undetectable drug levels.

CONCLUSION(S): Therapeutic Drug Monitoring in a large community practice enabled the practice to appropriately manage therapy in a majority of patients. However, in many patients the information received was not optimally interpreted or utilized. This suggests that further physician education or possibly automatic drug management protocols are needed to optimize patient outcomes.

P-110
Diagnostic Performance of Zinc Protoporphyrin/Heme Ratio in Screening of Anemia and Non-anemic Iron Deficiency in Patients With Inflammatory Bowel Disease

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BACKGROUND: Anemia in inflammatory bowel disease (IBD) is related to the chronic inflammatory nature of the disease and is commonly associated with iron deficiency (ID). However, the diagnosis of iron deficiency by means of currently available laboratory parameters is hampered by the lack of a gold standard and is even more complex and nonspecific in the presence of concomitant inflammatory conditions. Ferritin, in particular, as an acute-phase protein, may be strongly influenced by active inflammation. Zinc protoporphyrin (ZPP) has been identified as a promising screening method for ID, even in the presence of inflammation. Increase in ZPP to heme ratio has been demonstrated to be associated with other parameters related to inflammation. We aim to investigate and compare the diagnostic performance of ZPP in ID, iron deficiency anemia (IDA), anemia of chronic disease (ACD) and combined ACD/IDA.

(n=6), 100% experienced histologic response as assessed by RHI (5/9 with RHI nonmissing at week 10), and 83% (5/6) by NIH. Mean (SD) RHI changes were −19.2 (10.0) in patients with an ES ≤ 1 at week 10 versus −4.4 (10.1) in patients with an ES > 1. Mean (SD) NIH changes were −2.5 (1.5) in patients with ≤ 0.5 at week 10 versus −0.7 (1.0) in patients with >0.5 at week 10. Pearson correlation coefficients for RHI and NIH were 0.82 at baseline and 0.91 at week 10, while both histologic scores were similarly correlated with ES (0.25±0.28 as a baseline and 0.38±0.04 at week 10).

CONCLUSION(S): Histologic assessment of both RHI or NIH demonstrates improvement after week 10 with etrolizumab treatment and was greater in ATN-naive patients. Importantly, RHI or NIH reductions were associated with improved ES at week 10.

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