INTRODUCTION: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of UC. Efficacy and safety of tofacitinib were evaluated in randomized, placebo-controlled Phase (P2) (NCT00787202) and P3 (NCT01465563; NCT01485891; NCT01438574) studies, and in an ongoing, open-label, long-term extension (OLE) study (NCT01740612) (1–3). We report updated tofacitinib safety analyses from the tofacitinib UC clinical program, with exposure up to 6.8 years.

METHODS: Two cohorts were analyzed: P3 Maintenance (N = 592; patients [pts] receiving placebo, tofacitinib 5 or 10 mg twice daily [BID]) and Overall (N = 1,157; pts receiving tofacitinib 5 or 10 mg BID in P2/P3/OLE studies; data as of May 2019, database not locked). Proportions and incidence rates (IRs; unique pts with events per 100 pt-years [PY] of exposure) were evaluated for adverse events (AEs) of special interest. Opportunistic infections (OIs), malignancies, major adverse cardiovascular events (MACE), and gastrointestinal (GI) perforations were reviewed by independent adjudication committees.

RESULTS: Demographic, clinical characteristics, and safety data are shown in the Table. In the Overall Cohort, 1,157 pts received ≥ 1 dose of tofacitinib 5 or 10 mg BID; most pts (N = 959, 83%) received an average dose of 10 mg BID. Median treatment duration was 623 (range 1–2,549) days. 2,531 PY of exposure. IRs (95% confidence interval) for AEs of special interest were: deaths, 0.19 (0.06, 0.44); serious infections, 1.79 (1.24, 2.77); herpes zoster (non-serious and serious), 3.48 (2.79, 4.30); OIs, 1.07 (0.71, 1.55); malignancies (excl. non-melanoma skin cancer [NMSC]), 0.75 (0.46, 1.14); NMSC, 0.73 (0.44, 1.13); MACE, 0.26 (0.11, 0.54); deep vein thrombosis, 0.04 (0.00, 0.21); pulmonary embolism, 0.15 (0.04, 0.38); GI perforations, 0.11 (0.02, 0.33). Results in the Overall Cohort as per the previous Nov 2017 data cut are presented for context (4).

CONCLUSION: The safety profile of tofacitinib in pts with UC was manageable and consistent with that of other UC therapies incl. biologics. Overall, IRs for AEs of interest have generally remained consistent with previous data cuts (2,581.3 PY of exposure). IRs (95% confidence interval) for AEs of special interest have generally remained the same or decreased. Incidence rates (IRs; unique pts with events per 100 pt-years [PY] of exposure) were evaluated for adverse events (AEs) of special interest. Opportunistic infections (OIs), malignancies, major adverse cardiovascular events (MACE), and gastrointestinal (GI) perforations were reviewed by independent adjudication committees.

REFERENCES

S0704

Treatment Outcome of Tofacitinib Dose Reduction to 5 mg BID vs Remaining on 10 mg BID in Patients With UC Who Were in Stable Remission on 10 mg BID: 6-Month Data From the Double-Blind, Randomized RIVETING Study

Séverine Vermeire, MD, PhD1, Chinyu Su, MD2, Nervin Lawendy, PharmD2, Haiying Zhang, PhD2, Wenjin Wang, PhD2, Julian Panés7.
1University of California San Diego, La Jolla, CA; 2Icahn School of Medicine at Mount Sinai, New York, NY; 3University of Copenhagen, Copenhagen, Denmark; 4University of California San Diego, La Jolla, CA; 5Inflammatory Bowel Disease Center, Academic Medical Centre, Amsterdam, Noord-Holland, Netherlands; 6Eli Lilly and Company, Indianapolis, IN; 7Hospital Clínico de Barcelona, IDRRAPs, CIBERehd, Barcelona, Catalonia, Spain.

Table 1. Treatment Effect of Mirikizumab vs Placebo in Reducing Crohn’s Disease Activity Index [705]

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Mirikizumab vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 24</td>
<td>-5.7 (0.1, 11.3)</td>
</tr>
<tr>
<td>Week 48</td>
<td>-7.9 (1.7, 14.2)</td>
</tr>
</tbody>
</table>

RESULTS:

In total, 140 pts were randomized (1:1) to tofacitinib 5 or 10 mg BID. 77.1% and 90.0% of pts were in remission based on modified Mayo score at Mo6 (primary endpoint) in the 5 and 10 mg BID groups, respectively (adjusted difference 12.9%; 95% CI 0.5, 25.0); when analyzed by subgroup (baseline endoscopic subclass, prior TNFi treatment failure), differences ranged from 3% to 21%. Consistent dosing group differences were seen for the secondary endpoints of remission and clinical response, according to total Mayo score, and mucosal healing. Rates of AEs and SAEs were similar across dose groups. AEs of special interest included: serious infections (5 mg BID, n = 2; herpes zoster (5 mg BID, n = 1; 10 mg BID, n = 3; all non-serious); pulmonary embolism (10 mg BID, n = 1). There were no cases of deep vein thrombosis or death.

CONCLUSION: These 6-mo data from RIVETING showed that most pts in stable remission on tofacitinib 10 mg BID maintenance therapy, maintained remission after dose reduction to 5 mg BID. Differences between dose groups were 11.4%–12.9% for various efficacy endpoints, favoring the 10 mg BID group. For pts who reduced dose to 5 mg BID, pts with baseline endoscopic subclass 0 and those without prior TNFi failure were more likely to maintain remission vs pts with subclass 1 and pts with prior TNFi failure, respectively. No new safety risks were identified in this limited dataset.

REFERENCES

S0705
Presidential Poster Award

Evaluation of Symptom Improvement During Induction in Patients With Crohn’s Disease Treated With Mirikizumab

William J. Sandborn, MD, FACC8, Bruce E. Sands, MD, MS, FACC8, Peter C. Hanauer9,20,21, Monika Fischer, MD, MSc4, Kim Isaacs5, April N. Nagel, DPhil, MPH8, Debra Miller11, Elias GoumaValdes4, Noah Agada6, Paul Dellon22, Robert D’Haens, MD, PhD9.
1University of California San Diego, La Jolla, CA; 2Icahn School of Medicine at Mount Sinai, New York, NY; 3University of Göttingen, Göttingen, Germany; 4Indiana University School of Medicine, Indianapolis, IN; 5University of North Carolina at Chapel Hill, Chapel Hill, NC; 6Hill and Company, Indianapolis, IN; 7Inflammatory Bowel Disease Centre, Academic Medical Centre, Amsterdam, Noord-Holland, Netherlands.

INTRODUCTION: Mirikizumab (mri), a humanized, IgG4 monoclonal antibody that targets IL-23a, has shown efficacy for fistulizing, stricture, and fecal urgency symptoms in fistulizing Crohn’s disease colitis. In a phase 2, randomized, parallel-arm, placebo-controlled study, symptom improvement was evaluated in patients with moderately-to-severely active CD after intravenous induction treatment with mri (NCT02891226).

METHODS: Entry criteria for enrollment included an average daily stool frequency (SF; ≥ 4) and/or the average daily occurrence of abdominal pain (AP; ≥ 2) from the Crohn’s Disease Activity Index (CDAI), and a Simple Endoscopic Score for CD ≥ 7 in patients with ileal- or colonic- or ≥ 4 in patients with isolated ileal disease. Patients were randomised 2:1:1:2 to receive intravenous mri (200 mg, 600 mg, or 1,000 mg) or placebo at weeks 0, 4, and 8. Endpoints in this analysis included changes from baseline in CDAI, SF, and AP at weeks 4, 8, and 12. A mixed effects model for repeated measures analysis was conducted to compare mean changes from baseline across treatment groups for the all-patient cohort and for the biologic-experienced subgroup. Factors in the analysis included treatment, geographic region, baseline score, prior biologic CD therapy (all-patient cohort), visit, and treatment by visit interaction as fixed effects. An unstructured variance covariance was used.

RESULTS: A total of 191 patients were randomised at baseline, which included biologic naive (n = 71) and biologic-experienced patients (n = 120). Changes in CDAI, SF, AP at weeks 4, 8, and 12 compared to baseline are shown in the Table. In the all-patient cohort, statistically significant

[Table 1. Treatment Effect of Mirikizumab vs Placebo in Reducing Crohn’s Disease Activity Index, Stool Frequency, and Abdominal Pain Over Time]

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Mirikizumab vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 24</td>
<td>-5.7 (0.1, 11.3)</td>
</tr>
<tr>
<td>Week 48</td>
<td>-7.9 (1.7, 14.2)</td>
</tr>
</tbody>
</table>

Downloaded from https://www.amjgastro.com/ by B2DMf5ePHKbH4TTImqenVA+lpWIIBvonhQl60Etgtdnn9T1vLQWJq/+R2O4Kjt58on06/20/2021
Published on behalf of The American Gastroenterological Association
improvement in CDAI was observed with mini 600 mg and in SF with mini 200 mg compared to placebo at early week 4 (Table). Improvement in CDAI and SF occurred with all mini doses (200 mg, 400 mg, 1,000 mg) at week 8 and 12 and in AP at week 8 and 12 with all mini doses. Compared to placebo, the subgroup of biologic-experienced patients showed statistically significant improvement in CDAI at week 4 (mini 600 mg) and at weeks 8 and 12 with all three doses. Further, significant improvement was observed in SF at week 12 (mini 600 mg and mini 1,000 mg) and in AP at week 8 (mini 600 mg) and week 12 (mini 600 mg and mini 1,000 mg).

CONCLUSION: Treatment with mini induced early improvement in clinical symptoms and disease activity in patients with moderately-to-severely active CD.

The Outcome of Inflammatory Bowel Disease in Patients With Colon Cancer: A Propensity-Based Nationwide Inpatient Sample Study
Amrendra Mandal, MD1, Rajan Kanth, MD2, Vijay Gayam, MD2. 1SUNY Upstate Medical University, Syracuse, NY; 2Interfaith Medical Center, Brooklyn, NY.

INTRODUCTION: Studies have discovered the relationship between inflammatory bowel disease (IBD) and colon cancer. However, to our knowledge, there are no previous Nationwide Inpatient Sample (NIS) data regarding the outcome of IBD in a patient with colon cancer. In the present NIS study, we aimed to analyze the characteristic pattern and its impact on the length of stay, hospital cost, morbidity, and mortality of patients with IBD and a co-diagnosis of Colon cancer in the United States.

METHODS: We analyzed hospitalized patients with a diagnosis of IBD and a co-diagnosis of colon cancer. VS. IBD without colon cancer as a control using data from the NIS from 2016 to 2017 to determine the characteristics and in-patients’ outcomes among patients with IBD with colon cancer. For baseline characteristics, we used patient demographics (age, race, and sex), the Charlson Comorbidity Index, insurance status, hospital characteristics, and relevant comorbidities as shown as per ICD-10-CM/PCS codes. A propensity score matching model was developed to derive two matched groups for comparative outcome analysis from accounting for potential confounding factors and reducing the effect of selection bias.

RESULTS: Of the 8063 cases of LT identified from 2016 to 2017 admitted with the diagnosis of IBD. Of these total admissions, 181,560 were IBD without colon cancer, and 465 were IBD with colon cancer. There was no statistically significant difference observed with the in-hospital mortality. There were higher odds of AKI (OR 1.5, 95% CI 1.6–9.8; P = 0.00), colectomy (OR 1.2, 95% CI 1.3–2.3; P = 0.00) and lower gastrointestinal bleeding (LIGB) (OR 1.6, 95% CI 1.8–3.7; P = 0.00). A longer length of stay (7.1–6.9 vs. 5.0–5.6, P = 0.00) and higher mean total charge ($20283 vs. 12166, P = 0.00) were observed in the IBD with colon cancer. The factors affecting the length of stay in IBD with colon cancer were intestinal perforation, peritonitis, sepsis, diabetes mellitus, and dyslipidemias.

CONCLUSION: Patients with IBD-associated Colon cancer appear to have higher complications rate, higher costs, and more extended hospital stay. Therefore, early identification and management of complications related to IBD among patients with colon cancer are particularly crucial to reduce morbidity as well as hospital cost.

The Use of Combination Vedolizumab and Ustekinumab in Crohn’s Disease: A Retrospective Cohort Study
Kerry Glassion, DO1, Lin Wang, PhD2, Chika Ezana, MD, MS3, Stephen Wong, PhD, PEI, Rency P. Abraham, MD, MS3. 1Houston Methodist Hospital, Houston, TX; 2Houston Methodist Hospital Research Institute, Houston, TX.

INTRODUCTION: There is limited data on the use of more than one biologic in the treatment of patients with inflammatory bowel disease (IBD). The aim of our study was to determine the effectiveness and safety of combining vedolizumab (VDZ) and ustekinumab (UST) in patients with Crohn’s disease (CD).

METHODS: We collected data on 30 patients with CD who received treatment with a combination of VDZ and UST from 2015 to 2019 for persistent disease activity or concomitant rheumatologic or dermatologic disease. Clinical scoring and laboratory markers (ESR, CRP, albumin, and vitamin D) were collected at baseline (prior to starting combination therapy) and at follow up (after at least two months on combination therapy). Endoscopic data was collected within 6 months prior to initiation of combination therapy and at follow up (after at least two months on combination therapy). Adverse events were documented. The primary outcome was effectiveness defined by improvement in laboratory parameters, clinical, and endoscopic scoring, the secondary outcome was safety.

RESULTS: The mean age was 37 (+/-12.2) years, 63% were female, 73% Caucasian, with a disease duration of 14 (+/-10.6) years. Patients had failed therapy with a median of 2 (2-3) previous biologic medications. The mean ESR decreased 42.8 vs 27.3, P = 0.04, and mean albumin improved, 3.4 vs 4.0, P = 0.0005. The median HBI score improved from 7 to 5, P = 0.004 at follow up. There was no significant improvement in endoscopic score at follow up, however 50% of the group did not have follow up available. There were 5 serious adverse events (SAE), and no deaths. On multivariate analysis, immunomodulator use, longer disease duration, increasing age, and albumin were found to be risk factors for serious infection.

CONCLUSION: Combination biologic therapy with VDZ and UST may be an effective option for CD patients with refractory disease or concomitant autoimmune disease inadequately controlled by biologic monotherapy. There appears to be an increased risk of serious infection compared to biologic monotherapy, however this risk might be minimized by discontinuing immunomodulators prior to the initiation of combination therapy. Larger prospective studies are needed to confirm these findings.

The Postoperative Outcomes of Patients With Inflammatory Bowel Disease Undergoing Liver Transplant: A Nationwide Analysis
David U. Lee, MD1, Gregory H. Fan, BA2, Raj B. Karagozian, MD2. 1Tufts Medical Center, Boston, MA.

INTRODUCTION: Due to the shared liver etiologies and metabolic risk factors, patients with IBD develop end-stage liver disease that require liver transplant therapy (LT). It is therefore important to assess the effect of IBD on the postoperative outcomes in patients undergoing LT.

METHODS: Patients who underwent LT were selected from the 2011-2017 National Inpatient Sample and were stratified by the presence of IBD (a combination of Crohn’s disease and ulcerative colitis). The endpoints included mortality, length of stay, hospitalization costs, and postoperative outcomes.

RESULTS: Of the 8063 cases of LT identified from the database, 277 cases had IBD. Compared to the IBD-absent cohort, the IBD cohort was younger (47.1 vs 52.3 y, P < 0.01) and more likely to be