Clostridium difficile infection in ulcerative colitis: Data from the tofacitinib clinical program and an insurance claims database

BACKGROUND: Patients with inflammatory bowel disease (IBD), particularly ulcerative colitis (UC), have a higher risk of Clostridium difficile infection (CDI) than the general population (1). The incidence of CDI is increasing among patients with IBD, and certain UC treatments may be associated with greater risk (1). We report CDI events in the tofacitinib UC clinical program, and the incidence of the number of patients receiving other treatments for UC.

METHODS: For the tofacitinib UC program, rates of CDI patients (with an adverse event [AE] of CDI, Clostridium difficile colitis, or Clostridium test-positive, plus concomitant oral metronidazole or vancomycin) was counted once per cohort for the induction cohort (patients from an 8-week Phase 1b trial) and for the week 6-24 phase 1b/2 extension study (patients from an NCT01465756). For contextualization, we calculated as number of unique patients with events per 100 patient-years (PY). For contextualization, we used data from the Truven MarketScan® Database, an administrative healthcare claims database

RESULTS: Among patients receiving other UC medications were obtained from a retrospective cohort study utilizing data from the Truven MarketScan® Database, an administrative healthcare claims database (as of December 2016; NCT01470612). Positive CDI risk factors were identified using an exclusion criterion for program entry. Overall incidence rate (IR) was calculated as number of unique patients with events per 100 patient-years (PY). For contextualization, CDI rates among patients receiving other UC medications was obtained from a retrospective cohort study utilizing data from the Truven MarketScan® Database, an administrative healthcare claims database (as of December 2016; NCT01470612). Positive CDI risk factors were identified using an exclusion criterion for program entry. Overall incidence rate (IR) was calculated as number of unique patients with events per 100 patient-years (PY). For contextu

CONCLUSION(S): In patients with UC, prior TNF/immunosuppression failure did not preclude benefit from tofacitinib induction or maintenance therapy. Prior TNF inhibition was associated with greater risk for HZ and NMDC. HZ cases in the UC program were typically non-complicated and manageable with standard antiviral therapy (2).

REFERENCES
predispose to chronic inflammation in affected patients, who are usually treated with biological agents such as anti-tumor necrosis factor-α (TNF-α). Despite that, even during clinical remission periods, Crohn’s disease (CD) patients may still present endoscopic disease activity and possibly a residual systemic inflammatory response. Therefore, in this study we aimed to evaluate the responsiveness and immune profile of peripheral blood mononuclear cells (PBMC) of infliximab-treated patients, as well as the relationship between the altered responses and the clinical disease presentation.

METHODS: We enrolled 20 healthy controls (HC) and 39 CD patients, which were classified according to the Harvey-Bradshaw Index (HBI) and Simple Endoscopic Score for Crohn’s Disease (SES-CD). All were using anti-TNF-α therapy (infliximab), including 61.5% in combination with Azathioprine.

RESULTS: Although 94% of the patients were in clinical remission, 53.1% presented disease mucosal activity. Considering the Montreal classification, 12.8% had colonic disease, while 33.4% had ileal and 33.4% ileocolonic disease. Most the patients developed complications, being 20.3% stenosis and 35.9% structuring disease, while 9% had perianal disease. The immunophenotyping identification of PBMC by flow cytometry showed increased CD4+ and CD14+CD16+ monocytes in CD, indicating a tendency towards an inflammatory response because of the increased CD16 expression, along with augmented NK and decreased NK cells and B lymphocytes.

CONCLUSION(S): Even in the clinical remission, CD patients had relevant systemic inflammatory response together with increased inflammatory population, probably elicited in an attempt to achieve immune-regulation after biological therapy. Financial support: Fapesp # 2017/0861-1.

P039
Efficacy and safety of ustekinumab in patients with refractory Crohn's disease: data from a real world study in Brazil
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BACKGROUND: Ustekinumab (UST) is a fully human monoclonal antibody against IL-12/23. UST induced a clinical response and maintained a higher rate of response than placebo in patients with Crohn’s disease (CD). UST was approved in Brazil in November 2017. Real world data regarding efficacy and safety to UST in CD is lacking in our country. We report our experience of use of UST in patients with CD refractory to anti-TNF therapy.

METHODS: An open-label prospective not controlled study was performed including patients from 4 academic medical centers with severely active, refractory CD starting on UST (IV infusions followed by scheduled subcutaneous [SC] injections) between November 2017 and August 2018. We evaluated clinical response and remission (based on Harvey-Bradshaw index [HBI]), C-reactive protein (CRP) and faecal calprotectin (FC) levels. Clinical response and remission (based on Harvey-Bradshaw index [HBI]), C-reactive protein (CRP) and faecal calprotectin (FC) levels. Clinical response and remission were defined by HBI decrease ≥3 and HBI ≤3, respectively. Patients were evaluated by HBI from baseline until week 32. CRP and FC were evaluated from baseline and at week 16.

RESULTS: Thirty-seven patients were treated with UST during the study period. The mean age was 37.5 years (IQR: 22–29), disease duration 10.7 years (IQR: 1–29), 76.8% had previous surgeries, 54% had perianal disease, 68.5% had anaemia. Mean HBI at baseline was 10.5 (IQR: 5–19). At baseline mean CRP was 25.9 mg/l and mean FC was 1,134.6 mg/kg (IQR: 150–3,175). At week 8, 81.1% achieved clinical response and 40.5% achieved clinical remission. At second SC injection (week 16 or 20), 63.3% of individuals achieved clinical remission (18/30). After the third SC injection (week 24 or 32), 66.7% of patients presented clinical remission (14/21). CRP decreased to 15.9 mg/l at week 8 and to 10.8 mg/l at week 16. Mean FC at week 16 was 996.2 mg/kg (IQR: 5–3,262), exhibiting a decrease of 138.4 mg/kg from baseline. One patient stopped UST due to non-response. No new safety signals were observed.

CONCLUSION(S): UST therapy was successful for inducing clinical remission and improving laboratory biomarkers of disease activity in patients with refractory CD. Both UST induction and maintenance regimens until week 32 were well tolerated. This result support a favorable safety profile.

P040
Vasculitis in a patient with refractory Crohn’s disease
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BACKGROUND: Crohn’s disease (CD) is associated with a variety of cutaneous manifestations, many of which parallel disease activity. Leukocytoclastic vasculitis (LV) is a rare and underdiagnosed cutaneous manifestation of CD.

CASE: A twenty-year old woman presented to our unit with a rash affecting her lower extremities seven days after intravenous and ileostomy and ileostomy for refractory CD. Her past medical history included the diagnosis of penetrating CD for 3-years (anti-TNF refractory). Investigations revealed: normal full blood count and electrolytes, negative serologies (HSV, HIV, HBV, syphilis, HCV), normal C-reactive protein (CRP), negative rheumatoid factor, negative antinuclear antibodies (ANA), positive antimembranous granulomata antibody (ANCA).

Skin biopsy diagnosed LV, characterized by angiocentric neutrophilic infiltrate with normal epithelium and no granulomas or fibrinoid necrosis.

DISCUSSION: LV is an immune-complex syndrome characterized by palpable purpura containing in the lower end of vessel. It is a rare skin manifestation of CD. Lesions range from 1 mm to several centimeters. The condition may also present as urticarial papules, nodules, vesicles, plaques, hemorrhagic bullae and necrotic ulcers. Fever, arthralgia, myalgia and ankle swelling may be present. It is often associated with active intestinal disease. It is believed that direct exposure of immune cells of inflamed intestinal mucosa to fecal antigens may lead to formation of immune complexes, deposited in vessel walls causing vasculitis. LV may also be triggered by medications, infections, surgery, chemicals and other autoimmune diseases. Our patient improved spontaneously after few weeks of surgery. During follow-up, she had no signs of skin lesions or intestinal flares.

CONCLUSION: LV is rare a small-vasculitis that may be observed in inflammatory bowel disease patients. Treatment of the predisposing condition is essential in patients with skin-limited disease.

P041
Increased healthcare utilization by Medicaid patients with inflammatory bowel disease at a tertiary care center
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BACKGROUND: Low socioeconomic status has been linked to numerous poor health outcomes, but there is little data regarding the impact of insurance status on inflammatory bowel disease (IBD) outcomes. We aimed to characterize utilization of healthcare resources by patients with IBD based on health insurance status, using Medicaid enrollment as a proxy for low socioeconomic status.

METHODS: We retrospectively identified adult patients with IBD engaged in a colorectal cancer surveillance colonoscopy program from July 2007 to June 2017. Our primary outcomes included emergency department (ED) visits, inpatient hospitalizations, biologic infusions, and steroid exposure, stratified by insurance status. We compared patients who had ever been enrolled in Medicaid to all other patients.

RESULTS: Of 947 patients with IBD, 221 (23%) ever had Medicaid. Compared to other insurances, Medicaid patients had significantly higher rates of ever being admitted to the hospital (22% vs 43.6%, P < 0.0001) or visiting the ED (90.5% vs 38.4%, P < 0.0001). When adjusted for sex, age at first colonoscopy, race, and ethnicity, Medicaid patients had a higher rate of inpatient hospitalizations (Rate ratio [RR] 2.95; 95% CI 2.59–3.36) and ED visits (RR 4.24; 95% CI 3.82–4.70) compared to patients with other insurance. Medicaid patients had significantly higher prevalence of requiring steroids (62.4% vs 37.7%, P < 0.0001) and after adjusting for the same factors, the odds of requiring steroids in the Medicaid population was increased (OR 3.77; 95% CI 2.53–5.62).

CONCLUSION(S): Medicaid insurance was an significant predictor of IBD care and outcomes. Patients with Medicaid may have less engagement in IBD care and seek emergency care more often.

P042
Inflammatory bowel disease is no longer a contraindication for radiation therapy: A systematic review of outcomes with modern RT techniques
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BACKGROUND: Inflammatory bowel disease (IBD) continues to be considered a contraindication to the use of Radiation Therapy (RT). Oncologists are often unwilling to deliver RT, due to a perceived increased risk of severe bowel toxicity, or IBD exacerbation. Modern precision RT techniques allow significant reduction in dose to normal organs, and several studies have reported low toxicity rates. We performed a systematic review of recent studies to summarize the current evidence regarding RT toxicity in cancer patients with IBD.

METHOD: MEDLINE and EMBASE databases were searched, using combinations of key terms, for relevant studies published over the past 10 years (2008-2018). Reference lists of eligible articles were also hand-searched. A total of 278 articles were screened, and 9 studies met our search criteria to be included in this review.

RESULTS: From the 9 relevant studies, 198 patients with IBD, treated using radiation therapy, and with outcome data available, were included. The reported median follow-up was 55.2 months. The majority of patients (n = 148, 75%) were male; 113 (57%) had Ulcerative Colitis, 81 (41%) had Crohn’s Disease, and 4 patients had IBD NOS. Nineteen patients (9.5%) were reported to have active IBD within 6–12 months prior to starting RT. Colo-rectal cancer was the most common malignancy (n = 91, 46%), followed by prostate cancer (n = 93, 42%), anal-canal (n = 10, 5%), and gynecological malignancies (n = 6, 3%). External beam RT was used as part of treatment for 173 patients (87%), while 25 received brachytherapy alone. About 28% (n = 55) also received concurrent