BACKGROUND: IBD comprises Crohn’s disease (CD) and ulcerative colitis (UC), both are characterized by unpredictable exacerbations and remissions. The incidence is highest in adolescent and early adulthood, and alike other chronic diseases, can have a considerable impact on patients’ HRQoL. Few studies assessing HRQoL have been performed in adolescents and young adults (AYA) patients. Our objectives were to assess HRQoL and this behavior. This study evaluated a cohort of patients with moderately-to-severely active CD submitted to anti-TNF therapy in order to compare the exercise capacity and physical activity in daily life before and after anti-TNF-therapy induced remission. We hypothesised that patients who achieved an remission present significant improvement in the previous levels of exercise capacity and PA in daily life.

METHODS: In this prospective longitudinal study conducted between March 2015 and June 2018, 44 adult outpatients with active CD were evaluated at two different moments: before infliximab (IFX) administration and 24 weeks after infliximab therapy. We included patients with CD, aged ≥ 18 years and under 65 years, with a 3-month history of active disease, defined as a Harvey-Bradshaw index (HBI) score of 6 or higher and a serum level of C-reactive protein of more than 5.0 mg per liter, with indication for anti-tumor necrosis factor alpha therapy, i.e., refractory disease unresponsive to conventional therapies or steroid-dependent and those presenting with aggressive disease or features of poor prognosis definition, such as extensive bowel disease, complex fistulizing disease, or severe endoscopic lesion as defined by the presence of deep and extensive ulcers. Eligible patients received induction therapy consisting of intravenous injections of 5 mg/kg of IFX at week 0, 2, and 6 followed by maintenance infusion (5 mg/kg) at weeks 14 and 22. Participants were followed until week 24. Patients were evaluated for PA in daily life using accelerometer, exercise capacity, physical muscle strength, anthropometry, and body composition. The primary endpoint was an increase in the total number of steps/day in daily life at week 24 in CD patients achieving IFX-induced remission. Secondary endpoints included improvement in the shuttle walking test (SWT), the grip strength (HS), active time, and inactive time.

RESULTS: Thirty-eight (86.4%) patients achieved infliximab-induced remission at the end of 24 weeks and presented a significant increase from baseline in number of steps taken of 1092 (7400 ± 2890 vs. 6348 ± 3177, respectively; P = 0.006). The inactive time was significantly reduced when compared to baseline period (454 ± 1063 vs. 427 ± 978, respectively; P = 0.033). There was no difference in the distance walked before and after IFX infusion.

CONCLUSION: Infliximab-induced remission followed by maintenance therapy has shown to be effective for increasing PA levels in daily life as shows by increase in the number of steps taken per day as well as by reduced inactive time on patients with moderately-to-severely active CD. Given the important role of PA for patients with CD, anti-TNF therapy may be useful therapeutic strategy along with targeted PA recommendations for increasing PA levels. Furthermore, strategies of treatment associated with an exercise program must be considered for this population.

Ozanimod Reduced Fecal Calprotectin Levels in Patients with Ulcerative Colitis in the Phase 3 True North Study

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BACKGROUND: Ozanimod (oz) is a highly selective, orally available, sphingosine-1-phosphate (SIP) receptor modulator that binds with high affinity to SIP1 and SIP3 receptor subtypes. Ozanimod demonstrated efficacy and safety for up to 52 weeks of treatment in patients with moderately-to-severely active ulcerative colitis (UC) in the double-blind, randomized, phase 3 True North study. Fecal calprotectin (FCP), which occurs as a consequence of neutrophil in the gastrointestinal tissue from an inflammatory process, is strongly correlated with endoscopic activity in UC. The aim of this analysis was to assess the change in FCP in a prespecified biomarker analysis of patients in the True North study.

METHODS: True North was a randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of oral ozanimod HCl 1 mg/day (equivalent to ozanimod 0.92 mg) vs placebo once daily over a 10-week induction period and a 42-week maintenance period in patients with moderately-to-severely active UC. In the induction period, patients in Cohort 1 were randomized to receive double-blind ozanimod or placebo and patients in Cohort 2 received open label ozanimod. Patients in either cohort who responded to ozanimod at week 10 were re-randomized to receive double-blind ozanimod or placebo for the maintenance period up to week 52. FCP was assessed at baseline, week 10, and week 52. The proportion of patients with FCP response stratified by baseline FCP was evaluated at weeks 10 and 52.

RESULTS: At baseline, mean FCP levels were 2509 μg/g in patients randomized to ozanimod (n = 422) and 3440 μg/g in those randomized to placebo (n = 214) in Cohort 1. A total of 451 patients who responded to ozanimod in the induction period (Cohort 1 and Cohort 2) were re-randomized in the maintenance period and had FCP data; 226 continued to receive ozanimod (mean baseline FCP, 2284 μg/g) and 225 received placebo (mean baseline FCP, 2987 μg/g). FCP levels were significantly improved with ozanimod vs placebo in both induction and maintenance periods. Mean (SD) change in FCP from baseline of ozanimod vs placebo was -470.2 (1609.7) μg/g vs 21.1 (7918.3) μg/g at week 10 (P = 0.002) and -155.17 (4427.9) μg/g vs -463.7 (3770.6) μg/g at week 52 (P = 0.019). Of patients with elevated FCP at baseline using cutoffs of >50 and >150 μg/g, significantly more patients had reduced FCP levels below those respective cutoffs at week 10 with ozanimod vs placebo: 21% vs 6% and 33% vs 5% respectively (P = 0.008 and P = 0.002). The proportion of patients with elevated FCP at baseline who remained on ozanimod were significantly more likely to have FCP levels below these cutoffs vs those clinical responders re-randomized to placebo, 46% vs 24% and 57% vs 38% for baseline FCP >50 and >150 respectively (P < 0.01, both).

CONCLUSION: In patients with moderately-to-severely active UC, ozanimod led to significant reductions in FCP during induction and maintenance therapy, with a greater proportion of patients achieving FCP response with ozanimod vs placebo across multiple baseline FCP cutoffs. These results are consistent with the inhibition of inflammation in the gut by ozanimod in patients with moderate-to-severe UC.

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