Effectiveness and Safety of JAK-inhibitors in inflammatory Bowel Diseases: A single-Center real-life experience.

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BACKGROUND-AIMS
The therapeutic landscape for IBD has expanded with the introduction of a new class of drugs targeting the JAK-STATpathway. Janus kinase inhibitors (JAKi) are small molecules, including tofacitinib and filgotinib(approved for ulcerative colitis[UC]), and upadacitinib (approved for both UC and Crohn's disease[CD]).Given their favourable efficacy and safety profiles, the JAKi offer an additional therapeutic option for IBD patients who have experienced failure with previous lines of biologics.The aim of this study was to evaluate the effectiveness and safety of the JAKi in a cohort of IBD patients with prior failure of biologic therapies, in a real-world clinical setting.
METHODS
This is a retrospective, observational, single-center study conducted at our IBD unit.We enrolled consecutive adult patients with a diagnosis of UC-CD, treated with JAKi. For each patient, demographic data (including prior and concomitant therapies),clinical disease activity (assessed using the partial Mayo score for UC and the Crohn's Disease Activity Index[CDAI]for CD), and laboratory tests—including faecal calprotectin(FC)—were collected.Clinical response was evaluated at week 8for UC and at week 12 forCD, while steroid-free clinical remission was assessed at week 24for both conditions.Steroid-free clinical remission was defined as a partial Mayo score<2 for UC and a Harvey-Bradshaw Index(HBI)<5for CD. Adverse events occurring during the observational period were also recorded.All variables underwent descriptive statistical analysis using SPSS software.
RESULTS
A total of 140 IBD patients were included in the study:89(63%) with UCand 51(37%)with CD. Among the UC patients,45 were treated with tofacitinib,12 with filgotinib, and32 with upadacitinib.All 51CD patients received upadacitinib.JAK inhibitors were initiated in 23 patients(16%)due to steroid dependence and non-response to anti-TNFα therapy.In the remaining 117 patients(84%),therapy was started due to steroid dependence and failure of both anti-TNFα and additional advanced therapies(third-line treatment).Clinical response was observed in 90 of the 140 patients(64%):59 UCpatients(66%)and 31 CDpatients(68%).Steroid-free clinical remission at week 24 was achieved in

77patients(55%):47 UC patients(52%)and 30 CD patients(58%).Mean FC levels decreased significantly, from1375 µg/g at baseline to 478 µg/g at the 6-month follow-up(p<0.01).Regarding safety,12 adverse events(8%)were reported during the short- to medium-term follow-up:11cases involved infectious complications, and 1 case presented as general malaise. JAK inhibitor therapy was discontinued in 2 patients (1%)due to adverse events, both of which involved atypical and severe herpes simplex virus infections.

CONCLUSIONS

This real-world observational study confirms the effectiveness of JAKinhibitors in IBD patients with prior biologic therapy failure. The JAKi demonstrated a favourable safety profile, with no significant serious adverse events reported.

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