Letter to Editor

Tools for managing IBD in obese patients: Get JAK in the box!

Sir,

We read with interest the review article by Johnson and Loftus discussing the impact of obesity on inflammatory bowel disease (IBD) patients.[1] The authors discussed the negative impact obesity has on therapeutic response to monoclonal antibodies in this patient population, including the "TNF Sink," resulting in lower drug trough levels and suboptimal clinical response. However, the potential beneficial rule of small molecules in these patients warrants highlighting. The first class of these molecules to be used in IBD is the JAK inhibitors tofacitinib, the pharmacokinetics of which is not affected by the patient's body weight.[2] In a *post hoc* analysis of the OCTAVE clinical program, baseline body mass index (BMI) had no bearing on the proportion of patients achieving efficacy endpoints.[3] In practice, clinicians might be limited to prescribing tofacitinib to bio-naïve patients, as its current approval is for those in whom treatment with conventional therapy and monoclonal antibodies failed.

The situation may change with the introduction of other agents of this class. Filgotinib, a highly selective JAK1 inhibitor, showed good efficacy in ulcerative colitis (UC) patients in whom conventional therapy and/or biologics failed. Data from the phase III SELECTION trial showed a favorable safety profile.[4] Similar to filgotinib, upadacitinib showed promising results in the phase II trials in UC and Crohn's disease (CD), UACHIEVE, and CELEST.[5,6] The impact of body weight on the pharmacokinetics of these agents is expected to be similar to tofacitinib.[7] Other small molecules such as S1P modulators are also thought to be unaffected by body weight. In short, with the expanding therapeutic armamentarium in IBD and the move toward a personalized approach to treatment, clinicians could well consider the use of small molecules in obese IBD patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Access this article online	
Quick Response Code:	Website: www.saudijgastro.com
	DOI: 10.4103/sjg.sjg_439_21

How to cite this article: Alrammah HM, AlMubayedh H, AlAmeel T. Tools for managing IBD in obese patients: Get JAK in the box!. Saudi J Gastroenterol 2021;27:316.