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EDITORIAL

Refractory ulcerative colitis: Upadacitinib versus other biologics

Said G Farhat, Jessy G Fadel

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Said G Farhat, Jessy G Fadel, Department of Gastroenterology Research, Saint George University of Beirut, Beirut 00000, Lebanon

Said G Farhat, Dr. Sulaiman Al Habib Hospital, Dubai 00000, United Arab Emirates

Corresponding author: Said G Farhat, MD, Associate Professor, Department of Gastroenterology Research, Saint George University of Beirut, Rmeil Street, Ashrafieh, Beirut 00000, Lebanon. saidfarhat@hotmail.com

Abstract

In this editorial we comment on an article published in *World Journal of Clinical Cases* in 2024, in which a case of refractory ulcerative colitis (UC) was discussed based on the response to different lines of biologics. Different studies showed that different classes of biologics have their advantages and disadvantages in the treatment of refractory UC. Certain classes are superior to others and if tried earlier on would lead to a possible change in the outcome.

Key Words: Refractory; Ulcerative colitis; Upadacitinib; Ustekinumab; Vedolizumab

Core Tip: Ulcerative colitis (UC), a major type of inflammatory bowel disease whose treatment is sometimes challenging and some patients do not respond well to the available therapies. We discuss the case of a patient diagnosed with refractory UC, with primary non-response to infliximab and vedolizumab (VDZ). The patient experienced recurrent symptoms after receiving mesalazine, prednisone, azathioprine, infliximab, and VDZ for more than four years. Through maximizing the upadacitinib (UPA) treatment, UC remission was achieved. This report suggests that the small-molecule UPA may be a new treatment option that requires further research.

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INTRODUCTION

Over the past decade, advancements in medical treatments regarding inflammatory bowel disease (IBD) have taken place [1]. As a result, clinical remission has been achieved in patients with refractory ulcerative colitis (UC). Pro-inflammatory cytokines, such as tumor necrosis factor-α and interleukin-2, along with the cell-surface adhesive molecule integrin α4β7, have been proposed as mediators of inflammation in UC[1]. Upadacitinib (UPA), within the class of JAK inhibitors, has shown a favorable benefit-risk profile in patients experiencing moderately to severely active UC. It was shown that during induction treatment of UC, UPA achieved higher clinical efficacy and similar safety compared to 5-(tetradecyloxyl)-2-furoic acid[2]. In order to achieve mucosal deep remission, combination therapy would be an effective and potent management approach.

DISCUSSION

To find a definitive treatment, several studies and ongoing research are focused on refractory UC. By definition, UPA is a highly selective competitive inhibitor of the adenosine triphosphate binding pocket in JAK1. Cellular assays have demonstrated UPA's selectivity for JAK1 over JAK2, JAK3, and TYK2. As well, it has been approved for managing moderate to severe UC. Trials have shown UPA's superiority over placebo with regard to all primary and secondary endpoints, including clinical, endoscopic, and histological outcomes, using 45 mg orally once daily during induction and either 30 mg or 15 mg daily in maintenance[3]. From a safety perspective, UPA has been proven to be a safe and well-tolerated medication across immune-mediated diseases, with manageable adverse risks[3]. Compared to patients taking ustekinumab (UST), several studies indicated that a greater proportion of patients taking UPA achieved a clinical response and steroid-free clinical remission at 8-16 wk and endoscopic remission within 52 wk[4]. In comparison to UST, UPA was associated with a significantly higher clinical response and endoscopic remission[4]. Conversely to vedolizumab (VDZ), UPA is more efficient, addressing the slow onset defect of VDZ induction. However, the safety of UPA in situations such as infections and tumors is inferior to that of VDZ, and long-term use requires testing for risks of adverse events such as deep vein thrombosis[5]. As a consequence, in case of the prolonged onset of action, VZD should not have been selected or could have been combined with UPA for an efficacious response. Additionally, it was shown that patients who received UST had a shorter duration of treatment and achieved steroid-free response on induction compared to those on VDZ. This study suggested that using UST as a first line compared to VDZ, would have changed the consequence of events and resulted in a better outcome[6]. Furthermore, studies showed that combined therapy of tofacitinib twice daily with UST resulted in clinical improvement[7]. Therefore, using UST alone or in combination with JAK inhibitors instead of VZD would have achieved a more efficient response.

CONCLUSION

In conclusion, refractory UC remains a highly debated topic, driving experts to continually search for a definitive treatment. Different classes of biologics have been tested, each with its own advantages and disadvantages. JAK inhibitors, particularly in combination with UST, have shown promising results. Ongoing research holds promise for managing moderate to severe refractory UC and should be followed for future treatment advancements. Additionally, developing new molecules targeting novel pathways would be highly valuable in IBD research.

FOOTNOTES

Author contributions: Farhat SG and Fadel JG contributed to this paper; Farhat SG designed the overall concept; Fadel JG contributed to the writing, discussion, and editing of the manuscript, and literature review; all authors have read and approved the final manuscript.

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Country of origin: Lebanon

ORCID number: Said G Farhat 0000-0002-8071-4681.

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