SESSION 2
ADVANCED MEDICAL THERAPIES FOR IBD

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Objectives

- Review the current treatment armamentarium for inflammatory bowel disease (IBD)
- Review best evidence for sequencing of advanced therapies
- Review combination therapy as an emerging strategy

Abstract

The history of inflammatory bowel disease (IBD) therapeutics has evolved remarkably over the past century. Early approaches were limited to supportive care, as the underlying disease mechanisms of the disease were poorly understood and no effective medications existed, resulting in substantial morbidity for affected individuals. The first breakthrough was in the 1940s when sulfasalazine was found to be effective in treating ulcerative colitis (UC), with subsequently, 5-aminosalicylic acid (5-ASA) identified as the active therapeutic component of sulfasalazine. By 1955, Truelove and Witts reported the first blinded, controlled trial demonstrating that corticosteroids reduced mortality in UC. The 1950–1970s saw the development of immunomodulators, including methotrexate, 6-mercaptopurine and azathioprine (prodrug of 6-mercaptopurine). The approval of infliximab in 1998 for Crohn's Disease (CD), a monoclonal antibody targeting the pro-inflammatory cytokine tumor necrosis factor alpha (TNFα), hailed the beginning of a new era of monoclonal antibodies that transformed management and led to disease modification and reduced surgeries. Subsequent advancements led to the development of other monoclonal antibodies with alternative mechanisms of action, specifically vedolizumab, an anti-integrin α4β7 agent, the interleukin (IL) inhibitor ustekinumab (targeting IL-12 and IL-23), followed by risankizumab, mirikizumab, and guselkumab (targeting IL-23). In parallel, from the mid-2010s to 2020, advanced small molecules emerged with the approval of Janus kinase (JAK) inhibitors and sphingosine-1-phosphate (S1P) receptor modulators. Despite this plethora of therapeutic options, a therapeutic ceiling has been reached necessitating the development of agents targeting alternative pathways, as well as the promise of combination biologics with the results of the DUET trials targeting anti-TNF and IL-23 eagerly awaited.

References

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