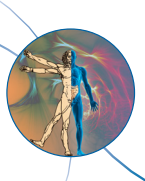

SESSION 2

THERAPEUTICS IN IBD: MANY NEW CHOICES, BUT WHO'S ON FIRST?

Relative Efficacy and Safety of Biologic Therapy

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Biologic therapy, starting with the introduction of specific antagonists to tumor necrosis factor alpha (TNFα), and advanced by the addition of several new drug classes, has greatly improved the management of IBD. Multiple biologics are now available to treat ulcerative colitis (UC) and Crohn's disease (CD), which raises critical questions regarding the relative therapeutic index of these agents and their positioning in treatment algorithms. In this talk, both safety and efficacy will be discussed for the TNF antagonists, the gut specific anti-integrin vedolizumab, and IL-12/23 antagonists.

This discussion needs to be grounded in the context of several general observations. First, a large unmet medical need still exists with respect to efficacy. Early initiation of biologics in high-risk patients is required to achieve optimal benefits with biologic therapy. Nevertheless, even when this paradigm is followed, remission rates remain less than ideal. For example, in the SONIC study that evaluated patients with active CD with an average disease duration of just two years and who were naïve to azathioprine and biologics, the endoscopic healing rate was only 45%. Importantly, endoscopic remission rates are considerably lower than this in long-duration disease and for patients who have failed at least one biologic. Second, safety is a very important consideration for patients and clinicians. The "second generation" monoclonal antibodies vedolizumab and ustekinumab have infection rates that are indistinguishable from placebo, which is a clear differentiator from the TNF antagonists. Third, payors are under enormous financial pressure from the high cost of biologic drugs. Biosimilar TNF antagonists have entered the marketplace amid several controversies regarding their role in management.

In this milieu, professional societies have developed treatment guidelines that are based upon the best evidence available. Unfortunately, these recommendations are not free from bias and constitutively lag behind data generated from trials. The current Canadian Association of Gastroenterology (CAG) guidelines for treatment of UC and CD will be reviewed and commented upon in the light of relevant new data from important trials, including the VARSITY and SERENE studies. Practical recommendations regarding choice of treatment will be offered.

Finally, some speculations regarding the future of IBD management will be made. Specifically, the relative potential of combined therapy and of precision medicine will be discussed and progress towards identification of optimal treatment targets outlined.

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