



SESSION 1

BIOLOGICS: MATCHING DRUGS TO PATIENTS

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The concept of matching drugs to patients with inflammatory bowel disease (IBD) includes sequencing of available drugs, incorporation of new agents, and the use of individual therapies (precision medicine). Strategies that can inform thinking regarding the sequencing of individual therapies include network meta-analyses and head-to-head trials. For ulcerative colitis (UC), network meta-analyses have suggested that infliximab and vedolizumab may be the most effective agents in patients who are naïve to biologic therapy, and that tofacitinib and ustekinumab may be the most effective agents in patients who have failed biologic therapy.¹ The superiority of vedolizumab over adalimumab was confirmed in a head-to-head trial.² For Crohn's disease (CD), network meta-analyses have suggested that infliximab and adalimumab may be the most effective agents in patients who are naïve to biologic therapy, and that ustekinumab may be the most effective agent in patients who have failed biologic therapy.³ Head-to-head trials comparing ustekinumab to adalimumab, guselkumab to ustekinumab, and others are underway. There are multiple early- and late-stage new agents that are being evaluated for IBD. Those that are in Phase 3 clinical trials include: Janus kinase (JAK) inhibitors such as filgotinib and upadacitinib; anti-p19 (interleukin-23) antibodies such as risankizumab, mirikizumab, guselkumab, and brazikumab; and sphingosine-1-phosphate (S1P) modulators such as ozanimod and etrasimod. Many—if not all—of these drugs will reach the approval stage over the next several years. Among the new agents are also a number of agents in Phase 2 that specifically target local delivery to the GI tract. Combination therapy with dual biologic agents and/or advanced small molecules is of increasing interest, and initial trials are underway. Finally, precision medicine, which includes clinical decision support tools, therapeutic drug monitoring, and companion diagnostic testing is making its way into clinical practice in IBD. IBD specialists will need to be familiar with sequencing an ever-increasing number of IBD therapeutics and be able to use combination therapy and precision medicine to maximize patient outcomes.

References

1. Singh S, Murad MH, Fumery M, et al. First- and Second-Line Pharmacotherapies for Patients With Moderate to Severely Active Ulcerative Colitis: An Updated Network Meta-Analysis. *Clin Gastroenterol Hepatol*. 2020;18:2179–91e6.
2. Sands BE, Peyrin-Biroulet L, Loftus EV, Jr., et al. Vedolizumab versus Adalimumab for Moderate-to-Severe Ulcerative Colitis. *N Engl J Med*. 2019;381:1215–26.
3. Singh S, Fumery M, Sandborn WJ, et al. Systematic review and network meta-analysis: first- and second-line biologic therapies for moderate-severe Crohn's disease. *Aliment Pharmacol Ther*. 2018;48:394–409.