



SESSION 4

Combination Therapy with Biologics: Does one size fit all?

WHY HAVE WE NOT FINALLY FIGURED OUT COMBINATION THERAPY?

Siew Ng, MBBS (Lond) PhD (Lond) FRCP (Lond) FRCP (Edin) AGAF FHKCP FHKAM (Med)

Presented by Jennifer Jones, MD MSc FRCPC

Biologic therapies—including anti-TNF antibodies (infliximab, adalimumab), anti-integrin inhibitors (vedolizumab) and anti-IL23 antibody (ustekinumab)—are mainstays of treatment for IBD. When added to infliximab, immunomodulators can reduce immunogenicity and infusion reactions, increase infliximab drug levels and improve outcomes. The SONIC trial in Crohn's disease and SUCCESS trial in ulcerative colitis showed that the combination of infliximab and azathioprine is superior to monotherapy with either agent alone at inducing clinical remission in treatment-naïve patients with moderate-to-severe disease. Studies with adalimumab have suggested that the presence of anti-drug antibodies is associated with low levels of trough adalimumab and lessened clinical effect, but there is a lack of evidence suggesting that using an immunomodulator concomitantly can prevent the development of these antibodies. Currently, we also lack prospective evidence addressing the role of combination therapy with vedolizumab or ustekinumab; however, subanalysis of clinical trials has shown that adding an immunomodulator to these biologics results in an overall lower level of anti-drug antibodies.

So why not treat all patients with combination therapy? First, the role of combination therapy in non-naïve patients and its optimal duration is unknown. Concerns about treatment cost and adverse events of combination therapy—especially opportunistic infection and malignancy (particularly lymphoma)—have also precluded widespread use. In patients with risk factors for disabling disease, complications or surgery, combination therapy should be a preferred strategy. While international guidelines recommend the use of combination therapy, its use should be preceded by a careful balance of the risks and benefits by the physician and patient, especially in situations where the strongest evidence for combination therapy may not directly apply.

References

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