Anti-TNF-α and Immunomodulatory Combination Therapy

- High serum levels of infliximab and adalimumab - ↑ clinical remission[1,2]
  - ↑ Risk of anti-TNF-α failure with presence of anti-drug antibodies (ADAs)
- Combination therapy with anti-TNF-α and immunomodulatory therapy
  - Immunomodulatory therapy reduces formation of ADAs, improving anti-TNF-α short- and long-term efficacy[3]
  - Clinical trial results:
    - ↑ Corticosteroid-free remission with INFLIXIMAB + AZATHIOPRINE than either alone in anti-TNF-α naïve patients, for both CD and UC[4,5]
    - INFLIXIMAB + METHOTREXATE no more effective than infliximab monotherapy[6]
- Safety considerations[3]
  - Risk of infections or malignancies with combination therapy was similar to anti-TNF-α monotherapy in most clinical studies

1. Kennedy A, et al. *Lancet Gastroenterol Hepatol*. 2019;4(5):341-53; 2. Berends SE, et al. *Clin Pharmacokinet*. 2019;58(1):15-37; 3. Hashash J, et al. *Ann Gastroenterol*. 2021;34(5):612-24; 4. Colombel JF, et al. *N Engl J Med*. 2010;362(15):1383-95; 5. Panaccione R, et al. *Gastroenterology*. 2014;146(2):392-400.e3; 6. Feagan BG, et al. *Gastroenterology*. 2014;146(3):681-8.e1.

Anti-TNF-α and Immunomodulatory Co-Therapy – Guideline Recommendations

- ACG and AGA guidelines recommend immunomodulatory co-therapy for patients with moderate-to-severe CD or UC receiving anti-TNF-α therapy[1-4]
  - Strongest recommendation is for the specific combination of infliximab and a thiopurine[1-4]
  - Combining vedolizumab or ustekinumab with thiopurines or methotrexate should also be considered[2,3]
- Although both ACG and AGA consider combination therapy as a "strong recommendation," the AGA guidelines for moderate-to-severe UC add:
  - "Patients, particularly those with less severe disease, who place higher value on the safety of biologic monotherapy and lower value on the efficacy of combination therapy may reasonably choose biologic monotherapy."[3]

ACG, American College of Gastroenterology; AGA, American Gastroenterological Association.

1. Rubin DT, et al. *Am J Gastroenterol*. 2019;114(3):384-413; 2. Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113(4):481-517; 3. Feurstein JD, et al. *Gastroenterology.* 2020;158(5):1450-61; 4. Feurstein JD, et al. *Gastroenterology*. 2021;160(7):2496-2508.

Anti-TNF-α and IL-23 Inhibitor

- Other combinations of therapies may also be more beneficial than monotherapy
- VEGA - proof-of-concept phase 2 trial
  - Treatment groups
    - Golimumab (anti-TNF-α) 200 mg IV
    - Guselkumab (IL-23) 100-200 mg SC
    - Combination therapy was statistically more effective for some clinical and endoscopic endpoints than either monotherapy, but not for all endpoints
  - Safety
    - Rates of serious infection were similar among the 3 groups
    - Small trial (N = 214) and combination therapy was limited to the 12-week induction period

Feagan BG, et al. *Lancet Gastroenterol Hepatol*. 2023;8(4):307-20.