Ustekinumab effective for Crohn’s disease after failure of anti-TNF therapy. In an industry-sponsored multi-center dose-ranging trial (CERTIFI) ustekinumab (UST) – an anti-IL-12/23 mAb - was evaluated in adults with moderate-severe Crohn’s disease who failed anti-TNF therapy. A total of 526 patients were randomized to receive 3 doses of UST IV (1, 3 or 6 mg/kg) or placebo. Response at week 6 was significantly higher in the 6 mg dose vs. placebo (40% vs. 23.5%). Remission rates favored UST but were not significantly different. UST responders at week 6 were then randomized to receive two additional doses of drug or placebo SQ at weeks 8 and 16. Maintenance data favored UST for both response (69.4% vs. 42.5%, P<0.001) and remission (41.7% vs. 27.4%, P=0.03) at 22 weeks. There was also a trend towards superior mucosal healing with UST. CRP was a predictor of response. Serious infections occurred more frequently in UST recipients but no internal cancers were detected.

Comments: Ustekinumab is already approved in the US for treatment of severe psoriasis. Interestingly, several recent case reports suggest that it may also be effective for palmo-plantar psoriasis induced by anti-TNF agents. The questions raised by these data are whether the drug should be used as first, second or third-line therapy (if it receives FDA clearance), whether IV and SQ forms are equivalent and whether combination therapy is beneficial. The members of our IBD club unanimously suggested they would use this agent as second line therapy (after anti-TNF failure and before natalizumab). (see Sandborn et al. – NEJM ‘12. Oct 18;367(16):1519-28.

Cyclosporin and infliximab equally effective for severe ulcerative colitis. Cyclosporine A (CsA) and infliximab (IFX) have both been shown to be effective for ulcerative colitis but which agent should be used first line for severe disease is not clear. In a multi-center European study coordinated by the French GETAID group, 115 patients with severe UC, refractory to steroids, were randomized to receive open-label CsA or IFX followed by azathioprine in responders. Treatment failure at 3 months occurred in 60% of patients given CsA and 54% given IFX (absolute risk difference 6%, non-significant). A similar proportion of patients underwent colectomy (17% vs. 21%). Nine patients in the CsA group and 14 in the IFX group had severe adverse events. The authors concluded that CsA and IFX have similar efficacy for steroid-refractory UC.

Comments: I think most IBD specialists, who have used CsA in the past, expected to see better results with CsA than IFX. Remarkably, the results of this study proved otherwise. That said, in clinical practice, IFX is far more extensively used by most gastroenterologists treating UC patients compared to CsA and has already won this battle. Another caveat is that the use of IFX and CsA in close succession is associated with a high risk of septic complications. IFX is FDA-approved for treatment of patients with active UC while CsA is not. (see also Laharie et al. – Lancet ’12, Oct 9.)