2024. PROFILE

RCT-OL/ Top-down vs Step up/ newly CD

A biomarker-stratified comparison of top-down versus accelerated step-up treatment strategies for patients with newly diagnosed Crohn's disease (PROFILE): a multicentre,open-label randomised controlled trial

Multicentre, open-label, biomarker-stratified, randomised controlled trial.
Patients with newly diagnosed CD (16-80y/o) were tested for a prognostic biomarker derived from T-cell transcriptional signatures and then were randomized to early top-down (early combined immunosuppression with infliximab and immunomodulator) vs step-up (conventional) strategy stratified by biomarker signature (IBDhi or IBDlo), endoscopic inflammation and extent.

Primary endpoint: Sustained steroid-free and surgery-free remission to week 48.

Results: N=386

- Median time from diagnosis to enrolment 12 days (0-191).
- There was no biomarker-treatment interaction effect.
- Sustained steroid-free and surgery-free remission was 79% in the top-down group vs 15%, p<0.0001
- There were fewer adverse events (including flares) and serious adverse events in the top-down strategy.

Conclusion:
Top-down treatment with combination IFX plus immunomodulator achieved substantially better outcomes at 1 year than accelerated step-up treatment. The biomarker did not show clinical utility. Top-down treatment should be considered standard of care for patients with newly diagnosed active Crohn's disease

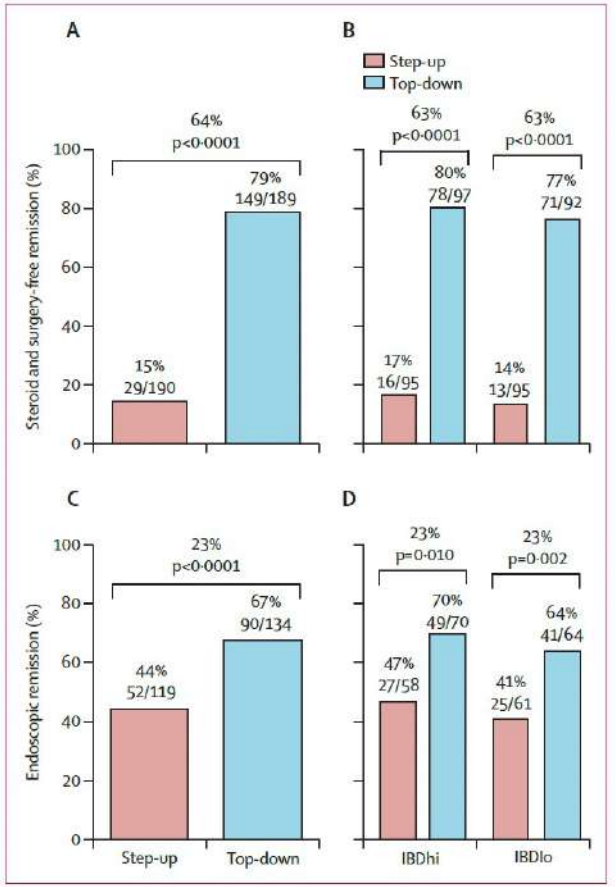

Figure 3: **Primary endpoint and key secondary endpoint**
(A) Sustained steroid-free and surgery-free remission until week 48 for treatment groups. (B) Sustained steroid-free and surgery-free remission until week 48 for biomarker-treatment subgroups. (C) Endoscopic remission (absence of ulceration) at week 48 for treatment groups. (D) Endoscopic remission (absence of ulceration) at week 48 for biomarker-treatment subgroups.

NM Noor, JC Lee et al. Lancet Gastroenterol Hepatol. 2024;