EVIDENCE-BASED GI
AN ACG PUBLICATION

Subcutaneous Infliximab for Maintenance of IBD Remission: Added Convenience With Potential for Improved Efficacy?

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IBD

This summary reviews Hanauer SB, Sands BE, Schreiber S et al. Subcutaneous infliximab (CT-P13 SC) as maintenance therapy for inflammatory bowel disease: Two randomized Phase 3 trials (LIBERTY). *Gastroenterology*. 2024;167:919–933.

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Keywords: Crohn's Disease, Ulcerative colitis, infliximab, maintenance, subcutaneous, biosimilar

STRUCTURED ABSTRACT

Question: Is the subcutaneous (subq) CT-P13 infliximab (IFX) biosimilar efficacious as maintenance therapy for patients with moderate-to-severe Crohn's disease (CD) or ulcerative colitis (UC)?

Design: Two randomized, placebo-controlled, multicenter and international clinical trials (LIBERT-CD AND LIBERTY-UC).

Setting: There were 148 clinical sites in 26 countries for the CD study, and 104 clinical sites in 14 countries for the UC study.

Patients: Adult patients with moderate-to-severe CD or UC who are IFX naïve

and have never had any intolerance or inadequate response to any other anti-TNF biologic.

Intervention: During the induction phase, all patients received the intravenous (IV) formulation of CT-P13 IFX at 5 mg/kg at 0, 2 and 6 weeks. At week 10, clinical responders were randomized into the maintenance phase to receive either the subq formulation of CT-P13 IFX at 120 mg every 2 weeks or a placebo until week 54. At week 22, dose escalation of subq CT-P13 IFX to 240 mg was permitted for patients who initially responded and subsequently lost response. Concomitant use of stable doses of immunomodulators and 5-ASA agents was also permitted.

Outcomes: A primary efficacy outcome at week 54 was clinical remission: absolute Crohn's Disease Activity Index (CDAI) score of <150 points for CD patients and stool frequency and endoscopic subscores of 0–1 points and rectal bleeding subscore of 0 points for UC patients. A co-primary outcome for the CD study was endoscopic response (50% decrease in Simple Endoscopic Score for Crohn's Disease [SES-CD] from baseline). Secondary outcomes included endoscopic remission, corticosteroids-free remission, pharmacokinetics, immunogenicity and safety evaluations by monitoring treatment-emergent adverse events.

Data analysis: Intention-to-treat analysis. A Cochran–Mantel–Haenszel chi-square test was used for the outcomes.

Funding: Celltrion, Inc, a global pharmaceutical company based in South Korea who manufactures CT-P13 IFX biosimilar

Results: Among the 343 patients who were randomized for the CD study, 58% were male, median age was 36 years, 91% White, mean diagnosis duration was 4.3 years, mean CDAI was 312, and mean SES-CD was 11.5, with 43% receiving corticosteroids at week 0 and 75% of them achieved clinical remission at week 10. Study completion rate was 85% of randomized patients in treatment arm. Among the 438 patients who were randomized for the UC study, 55% were male, median age was 37 years, 98% White, mean diagnosis duration was 6.1 years, mean total Mayo was 8.8, and mean modified Mayo was 6.6, with 41% receiving corticosteroids at week 0 and 49% of them achieved clinical remission at week 10. Study completion rate was 82% of randomized patients in treatment arm.

Subq CT-P13 IFX showed superior efficacy over placebo for all primary and secondary outcomes for both studies (Table 1). These results remained valid for patients requiring dose escalation at week 22. The mean pre-dose serum concentration maintained a consistent and therapeutic level up to week 54 in both studies for patients receiving CT-P13 SC. In the CD study, 65.1% of patients receiving subq CT-P13 IFX had positive conversion in anti-drug antibodies, while 76.2% in the placebo group. In the UC study, these numbers were 63.8% in the treatment group vs 91.8% in the placebo group.

Adverse events were similar in both arms of both studies, and most were considered not related to the study drug.

	For the CD Study		For the UC Study	
	Subq CT-P13 (n=231)	Placebo (n=112)	Subq CT-P13 (n=294)	Placebo (n=144)
Clinical remission	62.3%	32.1%	43.2%	20.8%
Endoscopic response	51.1%	17.9%	-	-
Clinical response	65.8%	38.4%	53.7%	31.3%
Endoscopic remission	34.6%	10.7%	35.7%	16.7%
Corticosteroid-free remission	40.4%	22.7%	36.7%	18.0%

Table 1. Primary and secondary outcomes for both studies at week 54.
CD, Crohn's disease; Subq, subcutaneous; UC, ulcerative colitis.

COMMENTARY

Why Is This Important?

One of the main strengths of this study is that it provides updated outcomes for an established medication. Unlike the original IFX studies that were used to approve IFX for moderate to severe inflammatory bowel disease (IBD) patients,[1,2] this trial uses not only clinical remission but also endoscopic remission and endoscopic response, which are the current and updated standards of practice in evaluating therapy options for IBD patients. Nonetheless, when it comes to patient-oriented outcomes, the results of this study are rather comparable to the early pivotal studies.

The benefit of subq formulations of IFX biosimilars is increased convenience for patients who no longer need to plan

their schedule around timing of intravenous administration of infliximab. Furthermore, subq formulation of IFX is associated with fewer sub-therapeutic serum trough levels of IFX versus IV administration. It's possible that subq administration would produce more consistent therapeutic serologic concentrations of IFX, which could translate to increased efficacy compared to maintenance of IBD remission with IV administration of IFX.

Key Study Findings

These trials demonstrated superiority of subq CT-P13 IFX biosimilar vs placebo for maintenance of remission in both moderately to severely active CD and moderately to severely active UC.

Both studies met their (co-) primary end points and key secondary end points at week 54, and improvements were also seen in additional efficacy and biomarker results. Biweekly dosing of CT-P13 SC was well tolerated, with no new safety signals, and provided consistent serum IFX concentrations.

Caution

This is a placebo-controlled trial, not a head-to-head trial comparing maintenance of IV and subq formulation of the CT-P13 medication. However, the subq formulation has been on the market in Europe since 2020, and there is literature on comparing both formulations for specific outcomes.[3,4] Also, given the spectrum of effective and safe medications for IBD, placebo-controlled trials may be an undue hardship on IBD patients and an active control may be preferable whether the trial is designed as a superiority or non-inferiority trial.

My Practice

Anti-tumor necrosis factor (TNF) medications remain the first-line regimen for a good number of IBD patients. With this new subq formulation being FDA approved, insurers are now starting to cover it, and it will become more available to our patients. In my practice, whenever I am recommending an anti-TNF (when clinically indicated), I go over the different options available, including the subq formulation of new and established medications. The appeal of injectable medications for certain patients are flexibility, ability to travel or work remotely, not being tethered to an infusion center(which proved to increase safety and compliance during the COVID-19 pandemic[5]), among others.

Some potential barriers are inability to maneuver the injection in patients with limited fine motor skills, the need for stable housing to keep the medication refrigerated, and the lack of safety data in some special populations such as pregnant patients.[6,7] I will engage with my patient to help them get to a well-informed decision on their IBD care plan. This study ushers in a new era for one of the most established medications and its biosimilars, while we also have new oral medications competing with

infusions and injectables at various efficacies and safety profiles.

For Future Research

As we have increased the options of IBD medications to our patients with a new formulation of a well-known and well-studied drug, I look forward to additional real-world evidence to validate the efficacy in special populations such as pregnant patients, long-term safety and utilization patterns of this SC formulation from the United States and the world.

Conflict of Interest

Dr. Al Kazzi reports no conflicts of interest.

The authors of this study are active on social media. Tag them on X to discuss their work and this EBGI summary.

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