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Subcutaneous infliximab (CT-P13 SC) for ulcerative colitis: 2-year extension results of the LIBERTY-UC study

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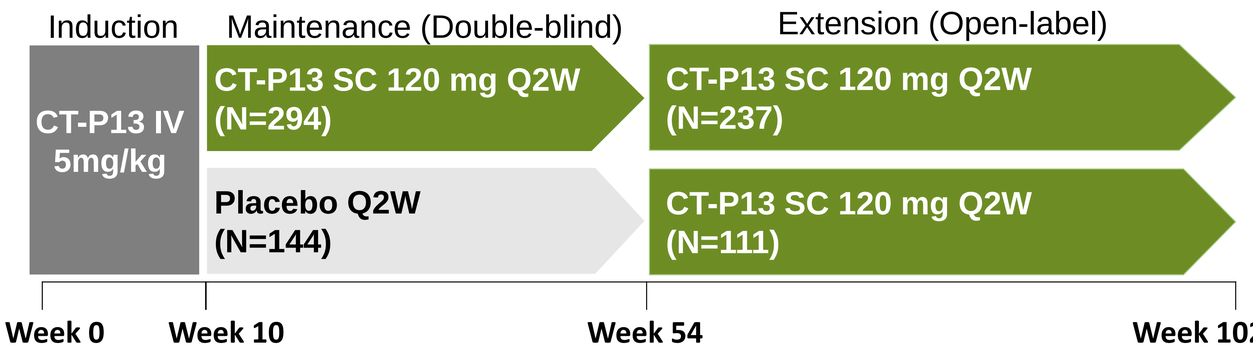
Background

- Superiority of CT-P13 subcutaneous (SC) infliximab formulation over placebo in maintenance therapy was demonstrated in both ulcerative colitis[1] and Crohn's disease[2].
- We now present the efficacy and safety results up to Week 102 of CT-P13 SC 120 mg group in the LIBERTY-UC study (NCT04205643).

1. Sands et al., J Crohns Colitis, 2023.17.Supplement_1, i623-i624.
2. Colombel et al., J Crohns Colitis, 2023.17.Supplement_1: i161-i162

Method

Figure 1. Study design



Key eligibility criteria

- Patients with moderately to severely active UC (modified Mayo score [MMS] 5 to 9 with endoscopic subscore of ≥ 2 points).
- Failure of Conventional therapy (corticosteroids alone or in combination with immunomodulator).
- Previously received less than 2 biologic agents, 2 Janus kinase (JAK) inhibitors, or 2 of both biologic agents and JAK inhibitors.

Definition of efficacy endpoint

- Clinical remission: stool frequency ≤ 1, rectal bleeding 0 and endoscopic subscore ≤ 1.
- Clinical response: decrease in MMS from baseline of at least 2 points and at least 30%, decrease in the rectal bleeding subscore of ≥ 1 or an absolute rectal bleeding subscore ≤ 1.
- Endoscopic-histologic mucosal improvement: endoscopic subscore ≤ 1 and a Robarts Histopathology Index score ≤ 3 with a lamina propria neutrophils and neutrophils in epithelium subscore = 0.
- Corticosteroid-free remission: Achieves clinical remission without corticosteroid for at least 8 weeks at Week 54 or 102, among the patients who used oral corticosteroids at baseline.

Study design

- Patients who received adjusted dose of CT-P13 240 mg during maintenance phase continued receiving CT-P13 240 mg in the extension phase
- ADA was detected based on an electrochemiluminescence affinity capture elution method which is new-generation, high-sensitivity, drug-tolerant assays that were validated according to the regulatory guideline[3,4]

3. Guideline on Immunogenicity assessment of therapeutic proteins (EMEA/CHMP/BMWP/14327/2006 Rev. 1.
4. Guidance for Industry: Assay Development for Immunogenicity Testing of Therapeutic Proteins (FDA, 2019).

Demographics and safety

Table 1. Demographics

		CT-P13 SC 120mg (N=237)
Age, median (range)	Years	37.0 (18-73)
Sex, n(%)	Male	136 (57.4)
Race, n(%)	White	232 (97.9)
Weight at baseline, median (range)	Kg	71.30 (42.1-130.2)
MMS at baseline, mean(SD)	Score	7.0 (5-9)
UC disease duration, median (range)	Years	3.74 (0.1-31.4)
Biologics and/or JAK inhibitors history, n(%)	Used	24 (10.1)
Immunomodulators at baseline, n(%)	Used	57 (24.1)
Oral corticosteroids at baseline, n(%)	Used	96 (40.5)

JAK, Janus kinase; MMS, Modified Mayo score; SC, subcutaneous; SD, standard deviation

- No new safety signal was seen during maintenance and extension phase (Table 2).
- ADA incidence in the CT-P13 SC groups were shown in Table 3.

Table 2. Safety results in maintenance and extension phase

Number of Patients (%)		CT-P13 SC 120mg (N'=241)
TEAEs	Total	193 (80.1)
	Related	66 (27.4)
TESAEs	Total	26 (10.8)
	Related	1 (0.4)
Systemic injection reaction	Total	13 (5.4)
Delayed hypersensitivity	Total	1 (0.4)
Localized injection site reaction	Total	14 (5.8)
Infection	Total	102 (42.3)
	Related	15 (6.2)
Study drug discontinuation due to TEAE	Total	5 (2.1)
	Related	4 (1.7)
Malignancy	Total	0

SC, subcutaneous; TEAE, Treatment-emergent adverse event, TESAE, Treatment-emergent serious adverse event.
N', The number of patients who treated in extension phase among safety population.
The adverse events occurred in Maintenance and Extension phase are included. For patients with dose adjustment, all data collected regardless of dose adjustment are included in this summary.

Table 3. Immunogenicity in treatment period

Number of Patients (%)	CT-P13 SC 120mg (N'=241)
Positive Conversion in ADA, n*/N#(%)	179/234 (76.5)

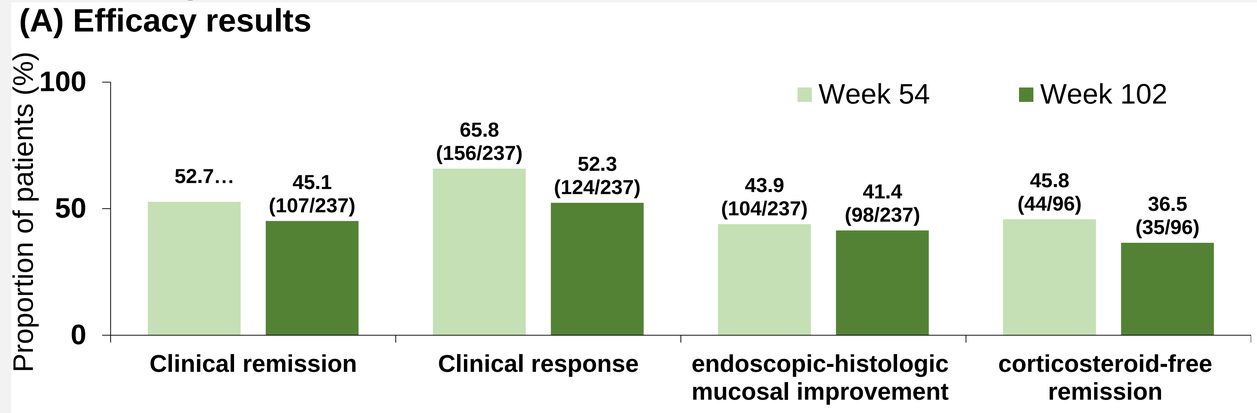
ADA, Anti-drug antibody; SC, subcutaneous;
N', The number of patients who treated in extension phase among safety population.
Number of patients who have at least one ADA result (including not reported result) after Week 0 study drug administration and have not any ADA positive result before Week 0 study drug administration
* Number of patients who reported at least one ADA/NAb positive after Week 0 study drug administration (regardless of dose adjustment for both treatment groups) during Treatment Period

Efficacy

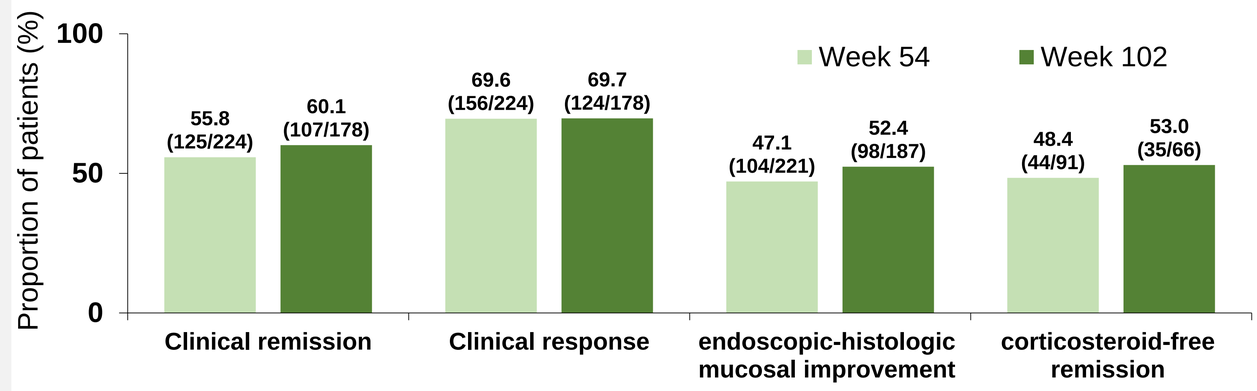
- Compared to the W54, efficacy results of patients treated extension phase in the CT-P13 SC arm were generally maintained at Week 102 in both non-responder imputation analysis for missing or invalid data (Figure 2A) and no imputation for missing or invalid data (Figure 2B).
- Partial Mayo score are maintained lower level from Week 10 to Week 102 (Figure 3).
- Among patient who achieved efficacy endpoints at Week 54, high proportion of patients retain efficacy endpoints at Week 102 (Table 4).

Figure2. Efficacy results for randomized patients who treated in extension phase

(A) Efficacy results

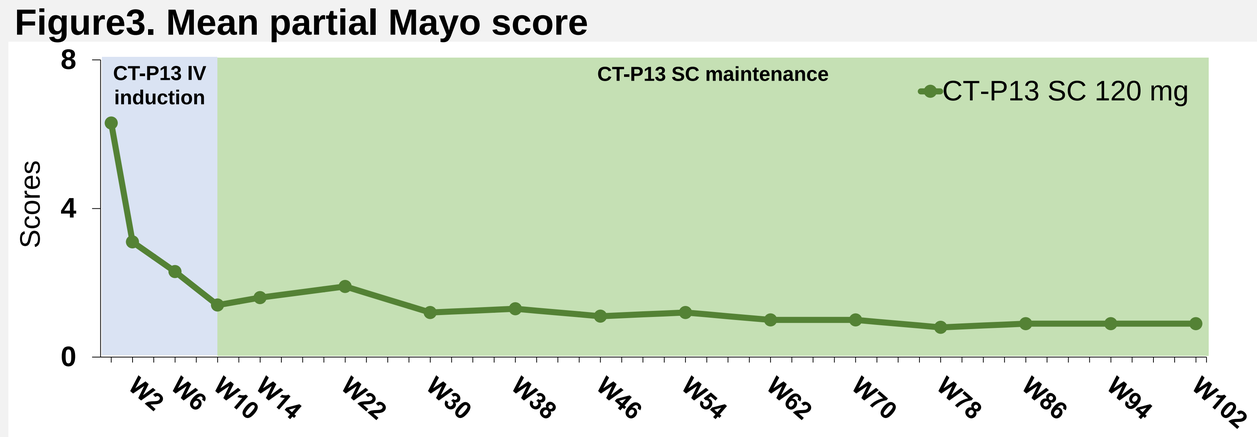


(B) Efficacy results by Observed analysis



Patients with dose adjustment to CT-P13 SC 240mg prior to Week 54 are considered as not achieving each endpoints.

Figure3. Mean partial Mayo score



For patients with dose adjustment, data collected before initiation of dose adjustment for both treatment groups are included in this summary

Table 4. Proportion of patients retaining efficacy endpoints at Week 102

Number of Patients (%)	CT-P13 SC 120mg (N=237)
Clinical remission	86/125 (68.8)
Clinical response	116/156 (74.4)
Endoscopic-histologic mucosal improvement	71/104 (68.3)
Corticosteroid-free remission	27/44 (61.4)

Percentages are calculated using the number of patients treated in Extension Phase and achieved each efficacy endpoints at Week 54 as denominator.
Patients with dose adjustment to CT-P13 SC 240mg prior to Week 54 are considered as not achieving each endpoints.

CONCLUSIONS

- The efficacy of CT-P13 SC 120 mg in UC patients was maintained through 2 years.
- No new safety concerns were found during 2-years of CT-P13 SC treatment.
- These results indicate that long term use of CT-P13 SC can maintain clinical benefit as well as safety with the convenience of SC administration for patient with moderately to severely active UC.

DISCLOSURE: BTherapeutics, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Calibr, Celltrion, ClostraBio, Connect Biopharm, Cytoki Pharma, Eli Lilly and Company, Enthera, Evommune, Ferring, Fresenius Kabi, Galapagos, Gilead Sciences, Genentech, Glaxo SmithKline, Gossamer Bio, HMP Acquisition, Imhotex, Immunic, InDex Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Ironwood Pharmaceuticals, Janssen, Johnson & Johnson, Kaleido, Kalyope, Merck, MiroBio, Morphic Therapeutic, MRM Health, OSE Immunotherapeutics, Pfizer, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, RedHill Biopharma, Sun Pharma Global, Surrozen, Synlogic Operating Company, Takeda, Target RWE, Theravance Biopharma R&D, TLL Pharmaceutical, USWM Enterprises, Ventyx Biosciences, Viela Bio, and stock options from Ventyx Biosciences S.B. Hanauer: Consultancy from AbbVie, Allergan, Amgen, Arena, Astra Zeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cosmos, Catalys Pacific, Covance, Genentech, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Progenity, Prometheus, Receptos, Salix, Samsung Bioepis, Seres Therapeutics, Sorriso, Takeda, TLL, UCB, Vhsquared. Clinical Research for AbbVie, Allergan, Amgen, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Prometheus, Receptos, Takeda, UCB. Speaker for AbbVie, Bristol Myers Squibb, Janssen, Pfizer, Takeda. Independent Data Monitoring Conference for Arena, Boehringer Ingelheim, Bristol Myers Squibb, Gossamer, Prometheus, Protagonist. J.F. Colombel: Receiving payment for lectures from AbbVie, Amgen, Allergan, Inc. Ferring Pharmaceuticals, Shire, and Takeda. 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Sandborn:research grants from Abbvie, Abivax, Arena Pharmaceuticals, Boehringer Ingelheim, Celgene, Genentech, Gilead Sciences, Glaxo Smith Kline, Janssen, Lilly, Pfizer, Prometheus Laboratories, Seres Therapeutics, Shire Pharmaceuticals, Takeda, Theravance Biopharma; consulting fees from Abbvie, Abivax, Admirx, Alfasigma, Alimentiv, Alivio Therapeutics, Allakos, Amgen, Arena Pharmaceuticals, AstraZeneca, Atlantic Pharmaceuticals, Bausch Health (Salix), Beigene, Bellatrix Pharmaceuticals, Biora (Progenity), Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Meyers Squibb, Celgene, Celltrion, Clostrabio, Codexis, Equillium, Forbion, Galapagos, Genentech, Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Immunic (Vital Therapies), Index Pharmaceuticals, Inotrem, Intact Therapeutics, Iota Biosciences, Janssen, Kiniksa Pharmaceuticals, Kyverna Therapeutics, Landos Biopharma, Lilly, Morphic Therapeutics, Novartis, Ono Pharmaceuticals, Oppilan Pharma (now Ventyx Biosciences), Otsuka, Pandion Therapeutics, Pfizer, Pharm Olam, Polpharm, Prometheus Biosciences, Protagonist Therapeutics, PTM Therapeutics, Quell Therapeutics, Reistone Biopharma, Seres Therapeutics, Shanghai Pharma Biotherapeutics, Shoreline Biosciences, Sublimity Therapeutics, Surrozen, Takeda, Theravance Biopharma, Thetis Pharmaceuticals, Tillotts Pharma, Vedanta Biosciences, Ventyx Biosciences, Vimalan Biosciences, Vivelix Pharmaceuticals, Vividion Therapeutics, Vivreon Gastrosciences, Xencor, Zealand Pharma; stock or stock options from Allakos, BeiGene, Biora (Progenity), Gossamer Bio, Oppilan Pharma (now Ventyx Biosciences), Prometheus Biosciences, Prometheus Laboratories, Protagnoists Therapeutics, Shoreline Biosciences, Ventyx Biosciences, Vimalan Biosciences, Vivreon Gastrosciences; and employee at Shoreline Biosciences and Ventyx Biosciences. Spouse: Iveric Bio - consultant, stock options; Progenity - stock; Oppilan Pharma (now Ventyx Biosciences) - stock; Prometheus Biosciences - employee, stock, stock options; Prometheus Laboratories – stock, stock options, consultant, Ventyx Biosciences –stock, stock options; Vimalan Biosciences – stock. S. Schreiber: Consultancy and personal fees from AbbVie, Arena, BMS, Biogen, Celltrion, Celgene, Falk, Ferring, Fresenius, Gilead, HIKMA, IMAB, Janssen, MSD, Morphic, Pfizer, Protagonist, Provention Bio, Sandoz, Takeda, and Theravance. S. Danese: Consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, Applied Molecular Transport, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Dr Falk Pharma, Eli Lilly, Enthera, Ferring Pharmaceuticals Inc., Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, Morphic, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, Teladoc Health, TiGenix, UCB Inc., Vial, Vifor. 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