Efficacy and safety of biosimilar CT-P13 compared with originator infliximab in patients with active Crohn’s disease: an international, randomised, double-blind, phase 3 non-inferiority study

RobotReviewer report

Risk of bias table

trial	design	n	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Byong D, 2019	RCT	?? ?	+	+	?	+

Characteristics of studies

Byong D, 2019

Population	1. Briefly, patients were aged 18,Äì75 years; had a disease duration of 12 weeks or more before randomisation and a CDAI of 220,Äì450 points; and had not responded to, were intolerant of, or had contraindications for, non-biological treatments for active Crohn's disease. 2. This study investigated whether CT-P13 is non-inferior to infliximab in patients with Crohn's disease who were naive to biological therapy. 3. Added value of this study This study provides the first high-level evidence of the non-inferior efficacy of CT-P13 to infliximab in anti-tumour necrosis factor (TNF) agent-naive patients with active Crohn's disease.
Intervention	1. 12 Per regulatory guidelines, approval of CT-P13 was based on proof of biosimilarity versus infliximab in physicochemical , in-vitro, and clinical studies,Äîincluding randomised controlled trials (RCTs) in patients with ankylosing spondylitis or rheumatoid arthritis,Äîthat established equivalence of the drugs in terms of pharmacokinetics and efficacy, as well as similarity in terms of safety and immunogenicity. 2. Randomisation and masking Patients were randomly assigned (1:1:1:1) to receive CT-P13 followed by CT-P13 at week 30 (CT-P13,ÄìCT-P13 group); CT-P13 followed by infliximab at week 30 (CT-P13,Äì infliximab group); infliximab followed by infliximab at week 30 (infliximab,Äìinfliximab group); and infliximab followed by CT-P13 at week 30 (infliximab,ÄìCT-P13 group). 3. The aims of this study were to establish non-inferior efficacy of CT-P13 compared with infliximab in patients with active Crohn's disease who were naive to biological therapy, at week 6 using the Crohn's Disease Activity Index (CDAI), 17 as well as to assess endoscopy findings, inflammation biomarkers, pharmacokinetics, safety, and immunogenicity up to week 54 after switching or continued treatment at week 30.

Outcomes	1. Tertiary efficacy end points were CDAI-100 response at weeks 6, 14, 30, and 54, steroidfree remission (defined as a CDAI <150 points at week 30 without the use of corticosteroids in the Statistical analysis

Bias	Judgement	Support for judgement
Random sequence generation	low	1. Randomisation and masking Patients were randomly assigned (1:1:1:1) to receive CT-P13 followed by CT-P13 at week 30 (CT-P13,ÄìCT-P13 group); CT-P13 followed by infliximab at week 30 (CT-P13,Äì infliximab group); infliximab followed by infliximab at week 30 (infliximab,Äìinfliximab group); and infliximab followed by CT-P13 at week 30 (infliximab,ÄìCT-P13 group). 2. Results Between Aug 20, 2014, and Feb 15, 2017, 308 patients were screened, of whom 220 were randomly assigned to receive CT-P13 (n=111; 56 in the CT-P13,ÄìCT-P13 group and 55 in the CT-P13,Äìinfliximab group) or infliximab (n=109; 54 in the infliximab,Äìinfliximab group and 55 in the infliximab,ÄìCT-P13 group) at week 0. 3. Randomisation was stratified by region (European or non-European); history of treatment with immunomodulators (eg, azathioprine, 6-mercaptopurine, or meth otrexate); and disease duration (<3 years or ,â•3 years).
Allocation concealment	low	1. Randomisation and masking Patients were randomly assigned (1:1:1:1) to receive CT-P13 followed by CT-P13 at week 30 (CT-P13,ÄìCT-P13 group); CT-P13 followed by infliximab at week 30 (CT-P13,Äì infliximab group); infliximab followed by infliximab at week 30 (infliximab,Äìinfliximab group); and infliximab followed by CT-P13 at week 30 (infliximab,ÄìCT-P13 group). 2. All data, including safety and efficacy data, were monitored by an independent data monitoring committee throughout the study period. 3. The sponsor was involved in study conception and design, and data collection, analysis, and interpretation.
Blinding of participants and personnel	high/unclear	1. The sponsor was involved in study conception and design, and data collection, analysis, and interpretation. 2. All data, including safety and efficacy data, were monitored by an independent data monitoring committee throughout the study period. 3. The primary endpoint was analysed using StatXact PROCs 11.0 for SAS 9.2,Äì9.3, and all other analyses were performed using SAS software version 9.2 and Enterprise guide 7.1.
Blinding of outcome assessment	low	1. All data, including safety and efficacy data, were monitored by an independent data monitoring committee throughout the study period. 2. The sponsor was involved in study conception and design, and data collection, analysis, and interpretation. 3. Acknowledgments The authors thank all patients, staff, and investigators involved in this study.