Efficacy and Safety of Candidate Biosimilar CT-P43 Versus Originator Ustekinumab in Moderate to Severe Plaque Psoriasis: 28-Week Results of a Randomised, Active-Controlled, Double-Blind, Phase III study

Supplementary Materials

BioDrugs

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Supplementary methods

Supplementary Table 1. Study centres and IRBs/IECs.

Country	Study centre	IRB/IEC
Estonia	North Estonia Medical Centre Foundation, Tallinn	Research Ethics Committee of the National Institute for Health Development, Tallinn
	Clinical Research Centre Ltd, Tartu	
Poland	Centrum Medyczne AMED Warszawa Targowek, Warszawa	Komisja Bioetyczna przy Okregowej Izbie Lekarskiej w Rzeszowie, Rzeszów
	REUMA RESEARCH Anna Boryczka-Trefler, Warszawa	
	Centrum Badan Klinicznych PI-House Sp. z o. o., Gdansk	
	‘ZDROWIE OSTEO-MEDIC’ s.c. Lidia i Artur Racewicz, Agnieszka i Jerzy Supronik, Białystok	
	Klinika Dermatologii, Kliniczny Szpital Wojewodzki nr 1 im Fryderyka Chopina w Rzeszowie, Rzeszów	
	Wromedica I. Bielicka, A. Strzalkowska S. C., Wrocław	
	Specjalistyczny Gabinet Dermatologiczny Aplikacyjno-Badawczy, Marek Brzewski, Pawei Brzewski SC, Krakow	
	DermoDent Centrum Medyczne Aldona	

	Czajkowska Rafal Czajkowski S.C., Osielsko	
	MICS Centrum Medyczne Warszawa, Warszawa	
	Centrum Medyczne Reuma Park NZOZ, Warsaw	
	ClinicMed Daniluk, Nowak Spółka Jawna, Białystok	
	Klinika Ambroziak Sp. Z o.o., Ambroziak Dermatologia Kosiarzy, Warsaw	
	Centrum Medyczne AMED Oddział w Łodzi, Łódź	
	ETYKA Osrodek Badan Klinicznych, Olsztyn	
	Clinical Best Solutions Sp. Z o.o. Sp. K., Warszawa	
	Dermoklinika Centrum Medyczne s.c., Łódź	
	Pratia MCM Krakow, Krakow	
	dermMedica Sp. z o.o, Wrocław	
	Cityclinic Przychodnia Lekarsko Psychologiczna Matusiak Spółka Partnerska, Wrocław	
Republic of Korea	Inje University Ilsan Paik Hospital, Goyang	Inje University Ilsan Paik Hospital IRB, Goyang
	Pusan National University Hospital, Busan	Pusan National University Hospital IRB, Busan
	CHA Bundang Medical Center, CHA University, Seongnam	CHA Bundang Medical Center, CHA University IRB, Seongnam

	Seoul National University Bundang Hospital, Seongnam	Seoul National University Bundang Hospital IRB, Seongnam
	Seoul National University Hospital, Seoul	Seoul National University Hospital, Seoul
	Konkuk University Medical Center, Seoul	Konkuk University Medical Center IRB, Seoul
	The Catholic University of Korea, Bucheon St. Mary's Hospital, Bucheon	Bucheon St. Mary's Hospital IRB, Bucheon
Ukraine	Therapeutic Department, Military Hospital (Military Unit A3309) of Military-Medical Clinical Center of Eastern Region, Zaporizhzhia	Ethics Committee of Military Hospital (Military Unit A3309) of Military-Medical Clinical Centre of Eastern Region, Zaporizhzhia
	Medical Center of LLC Academic Medical Group, Lviv	Ethics Committee of Medical Center of LLC Academic Medical Group, Lviv
	Outpatient Department, Treatment and Diagnostic Center of Private Enterprise 'Asklepiy', Uzhhorod	Ethics Committee at Treatment and Diagnostic Centre of Private Enterprise 'Asklepiy', Uzhhorod
	Department #1, Treatment and Diagnostic Center of Private Enterprise 'Asklepiy', Lviv	Ethics Committee at Treatment and Diagnostic Centre of Private Enterprise 'Asklepiy', Lviv
	Department of General Therapy, Medical Clinical Research Center of Medical Center LLC Health Clinic, Vinnytsia	Ethics Committee of Medical Centre LLC Health Clinic, Vinnytsia

	Clinical Consultative Department, Medical Center of LLC Medical Center ‘Consilium Medical’, Kyiv	Ethics Committee at LLC Medical Centre Consilium Medical, Kyiv

IEC, institutional ethics committee; IRB, institutional review board.

Protocol amendments

Key protocol amendments during the study period are listed below.

Global protocol amendment (5 July 2021)

- Updates related to the planned numbers of patients, study centres and countries were made to sections of the protocol regarding selection of study patients and treatment assignment, owing to the number of enrolled patients exceeding expectations.
- Revisions to exclusion criteria and prior and concomitant medications section to improve clarity and allow patients who had received stable doses of drugs that might aggravate psoriasis for at least 4 weeks prior to first study drug administration to be enrolled, if psoriasis had not been exacerbated.
- Details of the statistical analyses changed to delete categories for the covariate of body weight in ANCOVA analyses, to revise information about tipping point analyses to align with the statistical analysis plan, and to include statistical testing for secondary efficacy endpoints.
- Addition of recommendation that if the patients were receiving concomitant cytochrome P450 substrates, there should be monitoring for therapeutic effect or drug concentration, with adjustment of the co-administered drug dose as needed, considering ustekinumab characteristics.
- Clarification of the definition of adverse events to exclude disease progression of psoriasis and psoriatic arthritis, given the study enrolled patients with concomitant psoriatic arthritis, which may also be treated with ustekinumab.
- Addition of information regarding follow-up for patients with hepatitis B reactivation at Week 16.
- Supplemented detail for the definitions of major protocol deviations.

United States-specific protocol amendment (14 July 2021)

- Analysis set definitions, statistical assumptions (including the equivalence margin and analysis set) and missing data handling methods were revised following comments from the US Food and Drug Administration.

Korea-specific protocol amendment (22 July 2021)

- Further revisions to protocol sections regarding the planned number of study centres/countries, sample size calculations and selection of study patients, given the number of enrolled patients exceeded expectations and the screening failure rate was lower than expected.

- Clarification of the method of handling missing data in relation to sensitivity analysis for the primary efficacy endpoint.

Inclusion and exclusion criteria

Inclusion criteria

Each patient had to meet all of the following criteria to be enrolled in the study:

1. Male or female patients aged ≥18 and ≤80 years of age.
2. Diagnosed with plaque psoriasis for ≥24 weeks before first study drug administration.
3. Stable moderate to severe chronic plaque psoriasis, with or without PsA, at screening and at the time of first study drug administration, defined as a PASI score ≥12, involved body surface area ≥10% and an sPGA score ≥3.
4. Patient was a candidate for phototherapy or systemic therapy.
5. Patient had adequate renal and hepatic function at screening, defined as:
    - Serum creatinine levels ≤1.5 x upper limit of normal (ULN) or an estimated creatinine clearance level >50 mL/min (Cockcroft-Gault formula)
    - Serum alanine aminotransferase or aspartate aminotransferase ≤2.5 x ULN
    - Serum total bilirubin ≤1.5 ULN.

6. Haemoglobin level ≥10 g/dL, absolute neutrophil count ≥1.5 x 10^3 cells/µL and platelet count ≥100 x 10^3 cells/µL at screening.

7. Patient or legal guardian, if applicable, was informed of the full nature and purpose of the study, including possible risks and side effects, and given ample time and opportunity to read and understand this information. Patient or legal guardian signed and dated consent form before participation in the study.

8. Female patients of childbearing potential agreed to use a highly effective method of contraception consistent with local regulations during the study and for ≥15 weeks after study drug discontinuation. Male patients with a sexually active female partner agreed to use a highly effective method of contraception consistent with local regulations during the study and for ≥15 weeks after study drug discontinuation. If a patient or their partner had been surgically sterilised <24 weeks prior to the date of signing the informed consent form, they agreed to use a highly effective method of contraception.

Exclusion criteria

Patients meeting any of the following criteria were excluded from the study:

1. Patients with forms of psoriasis other than plaque-type (such as erythrodermic, pustular, guttate or medication-induced psoriasis) or other skin conditions (such as eczema) that could interfere with efficacy assessments, at the time of screening.

2. Patient previously received ustekinumab (or biosimilar) or any other drug that targets IL-12 or IL-23.

3. Prior exposure to ≥2 biologic agents approved for the treatment of psoriasis. Patients with exposure to one prior biologic could be enrolled, after a sufficient washout period (the longer of 12 weeks or 5 half-lives) prior to first study drug administration.

4. Concurrent/chronic inflammatory or autoimmune disease/symptoms other than psoriasis or PsA that might confound study evaluations.

5. History of allergies to the active substance or any study drug excipients, or hypersensitivity to immunoglobulin products, latex or rubber.

6. Received live or live-attenuated vaccine within 4 weeks prior to first study drug administration, during the study or ≤15 weeks after the last study drug dose.

7. Received Bacillus Calmette–Guérin vaccination within 1 year prior to first study drug, during the study or ≤1 year after the last study drug dose.

8. Concurrent/history of infection, as follows:

    a. Concurrent or past history of infection with human immunodeficiency virus, or concurrent hepatitis B virus or hepatitis C infection. Resolved past infection with hepatitis B virus or hepatitis C virus was permitted.

    b. Concurrent or past history of serious infection requiring hospitalisation or parenteral injection of antibiotics within 8 weeks prior to first study drug administration.

    c. Herpes zoster infection within 8 weeks prior to first study drug administration.

    d. Concurrent/history of granulomatous infections or other severe, chronic or recurrent infections (such as sepsis, abscess, opportunistic infections, invasive fungal infections [e.g., histoplasmosis, non-tuberculous mycobacterial infection], infected skin wounds or ulcers). Patients with sufficient documentation of complete resolution of such infections could be enrolled.

9. Concurrent/history of tuberculosis, as follows:

    a. Concurrent/history of active tuberculosis, even if complete resolution was documented.

    b. Signs or symptoms suggestive of active tuberculosis.

c. Exposure to a person with active tuberculosis, such as first-degree family members or co-workers, within 16 weeks prior to first study drug administration.

d. History of latent tuberculosis, unless sufficient documentation of completion of tuberculosis prophylaxis or receipt of ≥3 weeks of country-specific tuberculosis prophylaxis prior to first study drug administration (with the intention to complete the entire course).

e. Concurrent diagnosis of latent tuberculosis at screening, defined as a positive interferon-γ release assay (IGRA) result and negative chest X-ray at screening. If the result of the IGRA was indeterminate at screening, one retest was allowed during the screening period. Patients could be enrolled if results of the repeat IGRA were negative; if results were positive, patients could be enrolled if they had received ≥3 weeks of country-specific tuberculosis prophylaxis prior to first study drug administration (with the intention to complete the entire course). Patients with repeat indeterminate results could not be enrolled.

10. One or more of the following medical conditions:

a. Diabetes mellitus considered by the investigator to be clinically significant and uncontrolled.

b. Uncontrolled hypertension (systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥100 mmHg).

c. Any malignancy within 5 years prior to first study drug administration, except adequately treated non-metastatic squamous carcinoma of the uterine cervix, cutaneous basal cell carcinoma, or cutaneous squamous cell carcinoma with no evidence of recurrence for ≥12 weeks prior to first study drug administration.

d. Current/history of severe uncontrolled cardiac disease (such as unstable angina or clinically significant electrocardiogram abnormalities) or myocardial infarction ≤24 weeks prior to first study drug administration.

e. History of organ transplantation (except corneal transplantation) within 12 weeks prior to first study drug administration.

f. Clinically significant respiratory disease, as determined by the investigator (including chronic obstructive pulmonary disease, asthma or pleural effusion).

g. Any major surgical procedure within 12 weeks prior to first study drug administration or planned during the study.

h. History/evidence of a clinically significant medical or psychiatric condition considered by the investigator to pose a risk to patient safety or to impede study evaluations, procedures or completion.

11. Patient receiving or planning to receive any of the following prohibited medications or treatments that could affect psoriasis:

    a. Topical treatments for psoriasis within 2 weeks prior to first study drug administration. Salicylic acid shampoo use was permitted, other than on the mornings of study visits, including efficacy assessments. Low-potency topical corticosteroids were permitted for the face and intertriginous areas, other than within 12 hours prior to study visits, including PASI or sPGA assessments.

    b. Ultraviolet A phototherapy (with or without oral psoralen) or ultraviolet B phototherapy, within 4 weeks prior to first study drug administration.

    c. Systemic steroids or non-biologic systemic therapies within 4 weeks prior to first study drug administration.

    d. Any investigational drug within the longer of 4 weeks or 5 half-lives prior to first study drug administration.

    e. Initiation or dose modification of drugs that might aggravate psoriasis (e.g., beta-blockers, lithium, antimalarials) within 4 weeks prior to first study drug administration. Patients receiving stable doses for ≥4 weeks prior to first study drug administration, without exacerbation of

psoriasis, could be enrolled provided the same dose was maintained throughout the study.

f. Herbal treatments within 2 weeks prior to first study drug administration.

12. Patient was pregnant, breastfeeding, or planning to be pregnant or to breastfeed within 15 weeks of the last study drug dose; or planning to father a child or donate sperm within 15 weeks of the last study drug dose.

13. Unwilling to limit ultraviolet light exposure (e.g., excessive sun exposure and/or use of tanning devices) during the study period.

14. History or current abuse of alcohol or drugs within 1 year prior to screening.

15. Vulnerable patients (e.g., employees of the clinical trial site or any other individuals involved in the conduct of the study, immediate family members of such individuals, individuals in prison or institutionalised by law enforcement).

16. Patients who, in the opinion of the investigator, should not participate in the study.

Supplementary Table 2. Schedule of procedures and assessments.

	Screening	Treatment Period I					Treatment Period II			EOS
Week	**–6**	**0**	**2**	**4**	**8**	**12**	**16**	**28**	**40**	**52**
Day	**–42 to –1**	**1**	**15**	**29**	**57**	**85**	**113**	**197**	**281**	**365**
Screening/baseline assessments										
Informed consent, demographics, medical history, hepatitis C and HIV tests, chest X-ray	X									
Inclusion/exclusion criteria, % BSA involvement	X	X								
Randomisation		X					X			
Hepatitis B	X						(X)			(X)
Serum pregnancy test	X									X
Interferon-γ release assay	X						X			
Study drug-related procedures and assessments										
Study drug administration		X		X			X	X	X	

Hypersensitivity/ISR/local injection-site pain (VAS) monitoring		X			X			X	X	X	
Efficacy assessments											
PASI, sPGA	X	X	X	X	X	X	X	X	X	X	X
DLQI		X	X	X	X	X	X	X	X	X	X
Patient pain VAS and global assessment VAS (patients with PsA)		X				X	X	X	X		X
PK/immunogenicity assessments											
PK and immunogenicity sampling		X			X		X	X	X	X	X
Biomarker sampling[a]		X									
Safety assessments											
Vital signs, body weight, physical examination, clinical laboratory test	X	X			X	X	X	X	X	X	X
Urine pregnancy test		X			X			X	X	X	
ECG	X						X		X		X

Monitoring of prior and concomitant medications, tuberculosis and AEs	X

[a]Only for patients signing a separate informed consent form.

AE, adverse event; BSA, body surface area; DLQI, Dermatology Life Quality Index; ECG, electrocardiogram; EOS, end of study; HIV, human immunodeficiency virus; ISR, injection-site reaction; PASI, Psoriasis Area and Severity Index; PK, pharmacokinetic; sPGA, static Physician's Global Assessment; VAS, visual analogue scale.

Analysis sets

Analysis sets were defined as follows:

- ITT: all randomised patients.
- mITT, for analyses using FDA assumptions: all patients who were randomised and received study drug.
- Full analysis set (FAS), for analyses using EMA assumptions: all patients who were randomised and received a full dose of study drug.
- Per-protocol set: all randomised patients who received a full dose of study drug at Weeks 0 and 4, underwent PASI assessment at baseline and Week 12, and did not have any major protocol deviation.
- PK set: all patients who were randomised, received one full dose of study drug and had at least one measurable post-treatment PK reading.
- Safety set: all patients who received study drug.

Data subsets were also analysed by Treatment Period, as follows:

- ITT – Treatment Period II subset: all patients in the ITT set who were randomised to study drug prior to dosing at Week 16.
- mITT – Treatment Period II subset, for analyses using FDA assumptions: all patients in the mITT set who were randomised to study drug prior to dosing at Week 16 and received study drug on or after Week 16.
- FAS – Treatment Period II subset, for analyses using EMA assumptions: all patients in the FAS set who were randomised to study drug prior to dosing at Week 16 and received a full dose of study drug on or after Week 16.
- PK – Treatment Period II subset: all patients in the PK set who received at least one full dose of study drug and had at least one measurable post-treatment PK result on or after Week 16.
- Safety – Treatment Period II subset: all patients in the safety set who received study drug on or after Week 16.

Missing data and sensitivity analyses

Primary efficacy endpoint analyses using FDA assumptions were conducted using an ANCOVA model. Missing data were handled using multiple imputation with a ‘missing at random’ assumption. Sensitivity analyses were conducted using ‘best-worst case’ and ‘worst-best case’ scenarios.

Sensitivity analyses using EMA assumptions assessed the impact of missing data via multiple imputation with an ANCOVA model and were conducted using ‘best-worst case’ and ‘worst-best case’ scenarios.

Supplementary results

Supplementary Table 3. Patient demographics, disease characteristics and stratification factors (ITT – Treatment Period II subset).

	Continued CT-P43 (N=253)	**Continued originator ustekinumab (N=125)**	**Switched to CT-P43 (N=124)**
Baseline patient demographics and disease characteristics			
Age (years), median (range)	41 (18–74)	42 (18–77)	41 (18–76)
Sex, n (%)			
Male	161 (63.6)	86 (68.8)	83 (66.9)
Female	92 (36.4)	39 (31.2)	41 (33.1)
Race, n (%)			
Asian	23 (9.1)	10 (8)	11 (8.9)
White	230 (90.9)	115 (92.0)	113 (91.1)
Ethnicity, n (%)			
Hispanic or Latino	1 (0.4)	1 (0.8)	0
Non-Hispanic or non-Latino	252 (99.6)	124 (99.2)	124 (100)
Height (cm) at screening, median (range)	174 (151.7–213.0)	173 (149.2–195.0)	175 (141.0–189.0)
Body weight (kg) at baseline, median (range)	85.00 (41.0–168.0)	86.00 (46.1–142.8)	85.00 (48.0–151.5)
Body mass index (kg/m^2) at baseline, median (range)	27.580 (15.82–46.54)	28.380 (18.21–44.26)	27.215 (15.85–48.36)
Involved body surface area (%), mean (SD)	26.1 (14.2)	23.2 (12.2)	25.5 (14.2)
Time since plaque-type psoriasis diagnosis (years), mean (SD)	17.86 (12.197)	15.69 (11.457)	15.60 (11.808)
Concomitant PsA, n (%)	80 (31.6)	44 (35.2)	39 (31.5)

PASI score, mean (SD)	21.5 (7.97)	19.9 (6.56)	22.1 (9.17)
DLQI score, mean (SD)	13.2 (7.11)	11.6 (6.52)	12.1 (6.76)
sPGA score, mean (SD)	3.2 (0.38)	3.2 (0.36)	3.2 (0.40)
Prior use of non-biologic systemic agents, n (%)	152 (60.1)	72 (57.6)	72 (58.1)
Prior use of systemic steroids, n (%)	27 (10.7)	11 (8.8)	9 (7.3)
Stratification factors (first randomisation)			
Country, n (%)			
Estonia	5 (2.0)	3 (2.4)	3 (2.4)
Poland	188 (74.3)	91 (72.8)	95 (76.6)
Republic of Korea	23 (9.1)	10 (8.0)	11 (8.9)
Ukraine	37 (14.6)	21 (16.8)	15 (12.1)
Baseline body weight category, n (%)			
≤100 kg	195 (77.1)	98 (78.4)	97 (78.2)
>100 kg	58 (22.9)	27 (21.6)	27 (21.8)
Use of prior biologic approved for psoriasis treatment, n (%)			
Yes	38 (15.0)	21 (16.8)	23 (18.5)
No	215 (85.0)	104 (83.2)	101 (81.5)
Stratification factors (second randomisation)			
Dose at Week 16, n (%)			
45 mg	194 (76.7)	98 (78.4)	97 (78.2)
90 mg	59 (23.3)	27 (21.6)	27 (21.8)

DLQI, Dermatology Life Quality Index; ITT, intent-to-treat; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; SD, standard deviation; sPGA, static Physician Global Assessment.

Supplementary Table 4. 'Best-worst case' and 'worst-best case' sensitivity analyses of the primary endpoint (FDA and EMA approaches; mITT and FAS).

Protocol (analysis set)	Treatment group	n	LS mean (SE)	Treatment difference (CI)
FDA (mITT)	Best-worst case[a]			90% CI
	CT-P43	256	78.00 (1.985)	3.64 (1.08, 6.19)
	Originator ustekinumab	253[b]	74.37 (1.949)	
	Worst-best case[c]			90% CI
	CT-P43	256	77.98 (1.773)	1.67 (−0.61, 3.96)
	Originator ustekinumab	253[b]	76.31 (1.740)	
EMA[d] (FAS)	Best-worst case[a]			95% CI
	CT-P43	198	78.57 (2.335)	2.86 (−0.78, 6.51)
	Originator ustekinumab	199[b]	75.71 (2.321)	
	Worst-best case[c]			95% CI
	CT-P43	198	78.23 (2.056)	0.48 (−2.72, 3.69)
	Originator ustekinumab	199[b]	77.75 (2.044)	

An ANCOVA was performed with the treatment as a fixed effect and country, baseline body weight, prior biologic use approved for psoriasis treatment and baseline PASI score as covariates.

[a]Analysis used ANCOVA and 'best-worst case' assumptions, meaning that missing values for the CT-P43 group were imputed as 100% (thus PASI scores at Week 12 were all reduced to 0) and missing values in the originator ustekinumab group were imputed as 0% (thus PASI scores at Week 12 were unchanged from baseline).

[b]Data were missing for five patients.

[c]Analysis used ANCOVA and 'worst-best case' assumptions, meaning that missing values for the CT-P43 group were imputed as 0% (thus PASI scores at Week 12 remained unchanged from baseline) and missing values in the originator ustekinumab group were imputed as 100% (thus PASI scores at Week 12 were all reduced to 0).

[d]Per EMA statistical analysis plan, only patients who received ≥1 full 45 mg dose of study drug and did not receive any 90 mg doses in Treatment Period I were analysed.

ANCOVA, analysis of covariance; CI, confidence interval; EMA, European Medicines Agency; FAS, full analysis set; FDA, Food and Drug Administration; LS, least squares; mITT, modified intent-to-treat; PASI, Psoriasis Area and Severity Index; SE, SE, standard error.

Supplementary Table 5. Mean PASI score at each study visit during Treatment Period I (mITT/FAS).

	CT-P43 (N=256)	**Originator ustekinumab (N=253)**
Week 2		
n	252	251
Mean (SD)	17.48 (7.625)	17.21 (7.637)
Week 4		
n	254	249
Mean (SD)	12.91 (6.476)	13.08 (6.884)
Week 8		
n	255	250
Mean (SD)	6.14 (4.794)	6.49 (5.493)
Week 12		
n	256	248
Mean (SD)	2.98 (3.412)	3.44 (4.362)
Week 16		
n	254	248
Mean (SD)	2.02 (2.942)	2.61 (3.943)

FAS, full analysis set; mITT, modified intent-to-treat; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

Supplementary Table 6. Mean PASI score at each study visit during Treatment Period II (mITT/FAS – Treatment Period II subset).

	Continued CT-P43 (N=253)	**Continued originator ustekinumab (N=125)**	**Switched to CT-P43 (N=124)**
Week 16			
n	253	124	124
Mean (SD)	2.03 (2.946)	2.40 (3.500)	2.81 (4.346)
Week 28			
n	251	124	124
Mean (SD)	1.12 (2.124)	1.51 (2.776)	1.68 (2.719)

FAS, full analysis set; mITT, modified intent-to-treat; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

Supplementary Table 7. Proportion of PASI 50/75/90/100 responders at each study visit during Treatment Period I (mITT/FAS).

	CT-P43 (N=256)	**Originator ustekinumab (N=253)**
PASI 50, n (%)		
Week 2	16 (6.3)	13 (5.1)
Week 4	78 (30.5)	68 (26.9)
Week 8	213 (83.2)	195 (77.1)
Week 12	247 (96.5)	240 (94.9)
Week 16	251 (98.0)	240 (94.9)
PASI 75, n (%)		
Week 2	7 (2.7)	4 (1.6)
Week 4	17 (6.6)	20 (7.9)
Week 8	122 (47.7)	117 (46.2)
Week 12	212 (82.8)	187 (73.9)
Week 16	226 (88.3)	209 (82.6)
PASI 90, n (%)		
Week 2	2 (0.8)	0
Week 4	4 (1.6)	8 (3.2)
Week 8	50 (19.5)	43 (17.0)
Week 12	129 (50.4)	127 (50.2)
Week 16	171 (66.8)	154 (60.9)
PASI 100, n (%)		
Week 2	0	0
Week 4	2 (0.8)	1 (0.4)
Week 8	12 (4.7)	15 (5.9)
Week 12	47 (18.4)	48 (19.0)
Week 16	76 (29.7)	61 (24.1)

FAS, full analysis set; mITT, modified intent-to-treat; PASI 50/75/90/100, Psoriasis Area and Severity Index 50/75/90/100% improvement from baseline.

Supplementary Table 8. Proportion of PASI 50/75/90/100 responders at each study visit during Treatment Period II (mITT/FAS – Treatment Period II subset).

	Continued CT-P43 (N=253)	**Continued originator ustekinumab (N=125)**	**Switched to CT-P43 (N=124)**
PASI 50, n (%)			
Week 16	250 (98.8)	120 (96.0)	120 (96.8)
Week 28	250 (98.8)	121 (96.8)	123 (99.2)
PASI 75, n (%)			
Week 16	225 (88.9)	104 (83.2)	105 (84.7)
Week 28	244 (96.4)	116 (92.8)	116 (93.5)
PASI 90, n (%)			
Week 16	170 (67.2)	80 (64.0)	74 (59.7)
Week 28	205 (81.0)	98 (78.4)	98 (79.0)
PASI 100, n (%)			
Week 16	75 (29.6)	28 (22.4)	33 (26.6)
Week 28	116 (45.8)	46 (36.8)	45 (36.3)

FAS, full analysis set; mITT, modified intent-to-treat; PASI 50/75/90/100, Psoriasis Area and Severity Index 50/75/90/100% improvement from baseline.

Supplementary Table 9. Proportions of patients with an sPGA score of 0 or 1 at each study visit during Treatment Period I (mITT/FAS).

Patients, n (%)	CT-P43 (N=256)	Originator ustekinumab (N=253)
Week 2	11 (4.3)	10 (4.0)
Week 4	45 (17.6)	38 (15.0)
Week 8	165 (64.5)	158 (62.5)
Week 12	219 (85.5)	201 (79.4)
Week 16	228 (89.1)	208 (82.2)

FAS, full analysis set; mITT, modified intent-to-treat; sPGA, static Physician Global Assessment.

Supplementary Table 10. Proportions of patients with an sPGA score of 0 or 1 at each study visit during Treatment Period II (mITT/FAS – Treatment Period II subset).

Patients, n (%)	Continued CT-P43 (N=253)	Continued originator ustekinumab (N=125)	Switched to CT-P43 (N=124)
Week 16	227 (89.7)	104 (83.2)	104 (83.9)
Week 28	232 (91.7)	111 (88.8)	113 (91.1)

FAS, full analysis set; mITT, modified intent-to-treat; sPGA, static Physician Global Assessment.

Supplementary Table 11. Change from baseline in DLQI scores at each study visit during Treatment Period I (mITT/FAS).

	CT-P43 (N=256)	**Originator ustekinumab (N=253)**
Week 2		
n	252	251
Mean (SD)	−3.7 (4.75)	−3.1 (4.44)
Week 4		
n	254	249
Mean (SD)	−5.5 (5.71)	−5.0 (5.40)
Week 8		
n	255	249
Mean (SD)	−8.5 (6.49)	−7.6 (6.09)
Week 12		
n	255	248
Mean (SD)	−9.7(6.74)	−8.5 (6.67)
Week 16		
n	253	248
Mean (SD)	−9.9 (7.13)	−8.5 (6.65)

DLQI, Dermatology Life Quality Index; FAS, full analysis set; mITT, modified intent-to-treat; SD, standard deviation.

Supplementary Table 12. Change from baseline in DLQI scores at each study visit during Treatment Period II (mITT/FAS – Treatment Period II subset).

	Continued CT-P43 (N=253)	**Continued originator ustekinumab (N=125)**	**Switched to CT-P43 (N=124)**
Week 16			
n	252	124	124
Mean (SD)	−9.9 (7.14)	−8.4 (6.85)	−8.6 (6.46)
Week 28			
n	250	124	124
Mean (SD)	−10.9 (7.20)	−8.8 (6.95)	−9.4 (6.66)

DLQI, Dermatology Life Quality Index; FAS, full analysis set; mITT, modified intent-to-treat; SD, standard deviation.

Supplementary Table 13. Serum ustekinumab concentrations (μg/mL) over time during Treatment Period I (PK set).

	CT-P43 (N=256)		Originator ustekinumab (N=248)	
	45 mg	**90 mg**	**45 mg**	**90 mg**
Week 0				
n	198	58	194	54
Mean (SD)	0 (NC)	0 (NC)	0 (NC)	0.00 (0.01)
Week 4				
n	196	58	193	53
Mean (SD)	2.41 (0.81)	3.40 (1.23)	2.22 (0.87)	2.70 (1.16)
Week 12				
n	198	58	192	54
Mean (SD)	1.40 (0.63)	1.82 (0.78)	1.16 (0.74)	1.35 (0.78)
Week 16				
n	195	58	192	54
Mean (SD)	0.56 (0.32)	0.66 (0.34)	0.45 (0.37)	0.49 (0.39)

NC, not calculable; PK, pharmacokinetic; SD, standard deviation.

Supplementary Table 14. Serum ustekinumab concentrations (μg/mL) over time during Treatment Period II (PK set – Treatment Period II subset).

	Continued CT-P43 (N=244)		**Continued originator ustekinumab (N=117)**		**Switched to CT-P43 (N=114)**	
	45 mg	**90 mg**	**45 mg**	**90 mg**	**45 mg**	**90 mg**
Week 16						
n	187	57	90	26	88	26
Mean (SD)	0.58 (0.31)	0.67 (0.33)	0.48 (0.35)	0.53 (0.42)	0.49 (0.37)	0.49 (0.36)
Week 28						
n	185	57	90	26	88	26
Mean (SD)	0.43 (0.26)	0.51 (0.30)	0.38 (0.28)	0.42 (0.34)	0.41 (0.26)	0.44 (0.33)

PK, pharmacokinetic; SD, standard deviation.

Supplementary Table 15. TEAEs ≥Grade 3 in intensity during Treatment Period I (safety set) and Treatment Period II (safety set – Treatment Period II subset), by system organ class and preferred term.

System organ class Preferred term	Treatment Period I		Treatment Period II		
	CT-P43 (N=256)	Originator ustekinumab (N=253)	Continued CT-P43 (N=253)	Continued originator ustekinumab (N=125)	Switched to CT-P43 (N=124)
Patients with ≥1 Grade ≥3 TEAE, n (%)	15 (5.9)	13 (5.1)	4 (1.6)	3 (2.4)	7 (5.6)
Study drug related	3 (1.2)	0	0	0	1 (0.8)
Blood and lymphatic system disorders, n (%)					
Leukopenia	0	0	1 (0.4)	0	0
Neutropenia	4 (1.6)	4 (1.6)	0	1 (0.8)	1 (0.8)
Gastrointestinal disorders, n (%)					
Gastrointestinal inflammation	1 (0.4)	0	0	0	0
Infections and infestations, n (%)					
COVID-19 pneumonia	2 (0.8)	1 (0.4)	0	0	0
Study drug related	1 (0.4)	0	0	0	0
Latent tuberculosis	0	0	2 (0.8)	0	0
Injury, poisoning and procedural complications, n (%)					
Ligament sprain	0	1 (0.4)	0	0	0
Investigations, n (%)					
Alanine aminotransferase increased	0	0	0	0	1 (0.8)

Study drug related	0	0	0	0	1 (0.8)
Aspartate aminotransferase increased	0	0	0	0	1 (0.8)
Study drug related	0	0	0	0	1 (0.8)
Blood cholesterol increased	0	1 (0.4)	0	0	0
Blood creatine phosphokinase increased	1 (0.4)	0	0	0	0
Study drug related	1 (0.4)	0	0	0	0
Blood potassium decreased	0	0	0	0	1 (0.8)
Blood triglycerides increased	0	1 (0.4)	0	0	1 (0.8)
Gamma-glutamyl transferase increased	0	1 (0.4)	0	0	0
Muscle enzyme increased	1 (0.4)	0	0	0	0
Neutrophil count decreased	0	1 (0.4)	0	2 (1.6)	2 (1.6)
White blood cell count decreased	0	1 (0.4)	0	0	1 (0.8)
Metabolism and nutrition disorders, n (%)					
Hypertriglyceridemia	3 (1.2)	2 (0.8)	1 (0.4)	0	0
Nervous system disorders, n (%)					
Headache	2 (0.8)	0	0	0	0
Study drug related	1 (0.4)	0	0	0	0
Subarachnoid haemorrhage	0	1 (0.4)	0	0	0
Pregnancy, puerperium and perinatal conditions, n (%)					
Spontaneous abortion	0	1 (0.4)	0	0	0
Psychiatric disorders, n (%)					

Bipolar disorder	1 (0.4)	0	0	0	0
Reproductive system and breast disorders, n (%)					
Menstrual disorder	0	1 (0.4)	0	0	0

COVID-19, coronavirus disease 2019; TEAE, treatment-emergent adverse event.

Supplementary Table 16. TEAEs reported for ≥3% of patients in any treatment group during either Treatment Period, displayed for Treatment Period I (safety set) and Treatment Period II (safety set – Treatment Period II subset).

System organ class Preferred term	Treatment Period I		Treatment Period II		
	CT-P43 (N=256)	Originator ustekinumab (N=253)	Continued CT-P43 (N=253)	Continued originator ustekinumab (N=125)	Switched to CT-P43 (N=124)
Infection and infestations, n (%)					
COVID-19	11 (4.3)	12 (4.7)	0	0	1 (0.8)
Latent tuberculosis	0	0	7 (2.8)	4 (3.2)	4 (3.2)
Upper respiratory tract infection	3 (1.2)	8 (3.2)	4 (1.6)	0	2 (1.6)

COVID-19, coronavirus disease 2019; TEAE, treatment-emergent adverse event.

Supplementary Table 17. Summary of immunogenicity findings during the overall Treatment Period (safety set).

Patients, n (%)	**Treatment Period I**		**Treatment Period II**		
	CT-P43 (N=256)	**Originator ustekinumab (N=253)**	**Continued CT-P43 (N=253)**	**Continued originator ustekinumab (N=125)**	**Switched to CT-P43 (N=124)**
Week 0					
ADA positive	4 (1.6)	3 (1.2)	4 (1.6)	2 (1.6)	1 (0.8)
NAb positive[a]	0	0	0	0	0
ADA negative	251 (98.0)	249 (98.4)	248 (98.0)	122 (97.6)	123 (99.2)
Week 4					
ADA positive	11 (4.3)	18 (7.1)	11 (4.3)	8 (6.4)	9 (7.3)
NAb positive[a]	1 (0.4)	5 (2.0)	1 (0.4)	3 (2.4)	1 (0.8)
ADA negative	243 (94.9)	231 (91.3)	241 (95.3)	116 (92.8)	114 (91.9)
Week 12					
ADA positive	21 (8.2)	57 (22.5)	21 (8.3)	26 (20.8)	31 (25.0)
NAb positive[a]	8 (3.1)	24 (9.5)	8 (3.2)	10 (8.0)	14 (11.3)
ADA negative	235 (91.8)	191 (75.5)	232 (91.7)	99 (79.2)	92 (74.2)
Week 16					
ADA positive	26 (10.2)	61 (24.1)	26 (10.3)	27 (21.6)	34 (27.4)
NAb positive[a]	15 (5.9)	31 (12.3)	15 (5.9)	11 (8.8)	20 (16.1)

ADA negative	227 (88.7)	187 (73.9)	227 (89.7)	97 (77.6)	90 (72.6)
Week 28					
ADA positive	26 (10.2)	43 (17.0)	26 (10.3)	21 (16.8)	22 (17.7)
NAb positive[a]	15 (5.9)	20 (7.9)	15 (5.9)	11 (8.8)	9 (7.3)
ADA negative	225 (87.9)	205 (81.0)	225 (88.9)	103 (82.4)	102 (82.3)

[a]NAb evaluations were conducted in patients with confirmed ADA-positive results.

ADA, anti-drug antibody; NAb, neutralising antibody.

Supplementary Table 18. Percentage improvement from baseline in PASI score at Week 12, by ADA status (mITT set/FAS).

	CT-P43	Originator ustekinumab
ADA positive[a]		
n	21	57
Mean (SD)	84.86 (20.50)	80.39 (21.25)
ADA negative[b]		
n	235	191
Mean (SD)	86.16 (14.27)	85.06 (16.10)

[a]Patients with positive ADA result at Week 12.

[b]Patients with negative ADA result at Week 12.

ADA, anti-drug antibody; FAS, full analysis set; mITT, modified intent-to-treat; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

Supplementary Table 19. Serum ustekinumab concentrations (μg/mL) during Treatment Period I, by ADA status (PK set).

	CT-P43		Originator ustekinumab	
	45 mg	**90 mg**	**45 mg**	**90 mg**
ADA positive[a]	**N=29**		**N=74**	
Week 0				
n	24	5	54	20
Mean (SD)	0	0	0	0.00 (0.02)
Week 4				
n	24	5	53	20
Mean (SD)	2.33 (0.89)	2.04 (1.57)	1.99 (0.89)	2.53 (1.27)
Week 12				
N	24	5	54	20
Mean (SD)	1.08 (0.74)	0.85 (0.84)	0.79 (0.60)	1.23 (0.86)
Week 16				
N	24	5	53	20
Mean (SD)	0.32 (0.33)	0.22 (0.25)	0.27 (0.30)	0.39 (0.37)
ADA negative[b]	**N=227**		**N=174**	
Week 0				
n	174	53	140	34
Mean (SD)	0	0	0	0
Week 4				
n	172	53	140	33
Mean (SD)	2.43 (0.80)	3.53 (1.13)	2.30 (0.85)	2.80 (1.11)
Week 12				
n	174	53	138	34
Mean SD	1.45 (0.61)	1.91 (0.72)	1.31 (0.73)	1.42 (0.73)
Week 16				
n	171	53	139	34
Mean (SD)	0.59 (0.31)	0.70 (0.32)	0.52 (0.37)	0.55 (0.40)

[a]Patients with positive ADA result at Week 12.

[b]Patients with negative ADA result at Week 12.

ADA, anti-drug antibody; PK, pharmacokinetics; SD, standard deviation.

Supplementary Table 20. Summary of TEAEs during Treatment Period I, by ADA status (safety set).

	CT-P43	**Originator ustekinumab**
ADA positive[a]	**N=29**	**N=76**
Total number of TEAEs	19	36
Patients with ≥1 TEAE, n (%)	12 (41.4)	24 (31.6)
Related to study drug	3 (10.3)	4 (5.3)
Total number of TESAEs	0	1
Patients with ≥1 TESAEs, n (%)	0	1 (1.3)
Related to study drug	0	0
Total number of TEAEs leading to study discontinuation	0	0
Total number of TEAEs classified as infections	5	10
Patients with ≥1 TEAEs classified as infections, n (%)	4 (13.8)	10 (13.2)
Related to study drug	0	2 (2.6)
Total number of TEAEs classified as ISRs	2	1
Patients with ≥1 TEAEs classified as ISRs	2 (6.9)	1 (1.3)
Related to study drug	2 (6.9)	1 (1.3)
Total number of TEAEs classified as hypersensitivity reactions	0	0
Total number of TEAEs classified as malignancies	0	0
Total number of deaths	0	0
ADA negative[b]	**N=227**	**N=175**
Total number of TEAEs	139	71
Patients with ≥1 TEAE, n (%)	83 (36.6)	50 (28.6)
Related to study drug	15 (6.6)	11 (6.3)
Total number of TESAEs	4	3
Patients with ≥1 TESAEs, n (%)	4 (1.8)	3 (1.7)

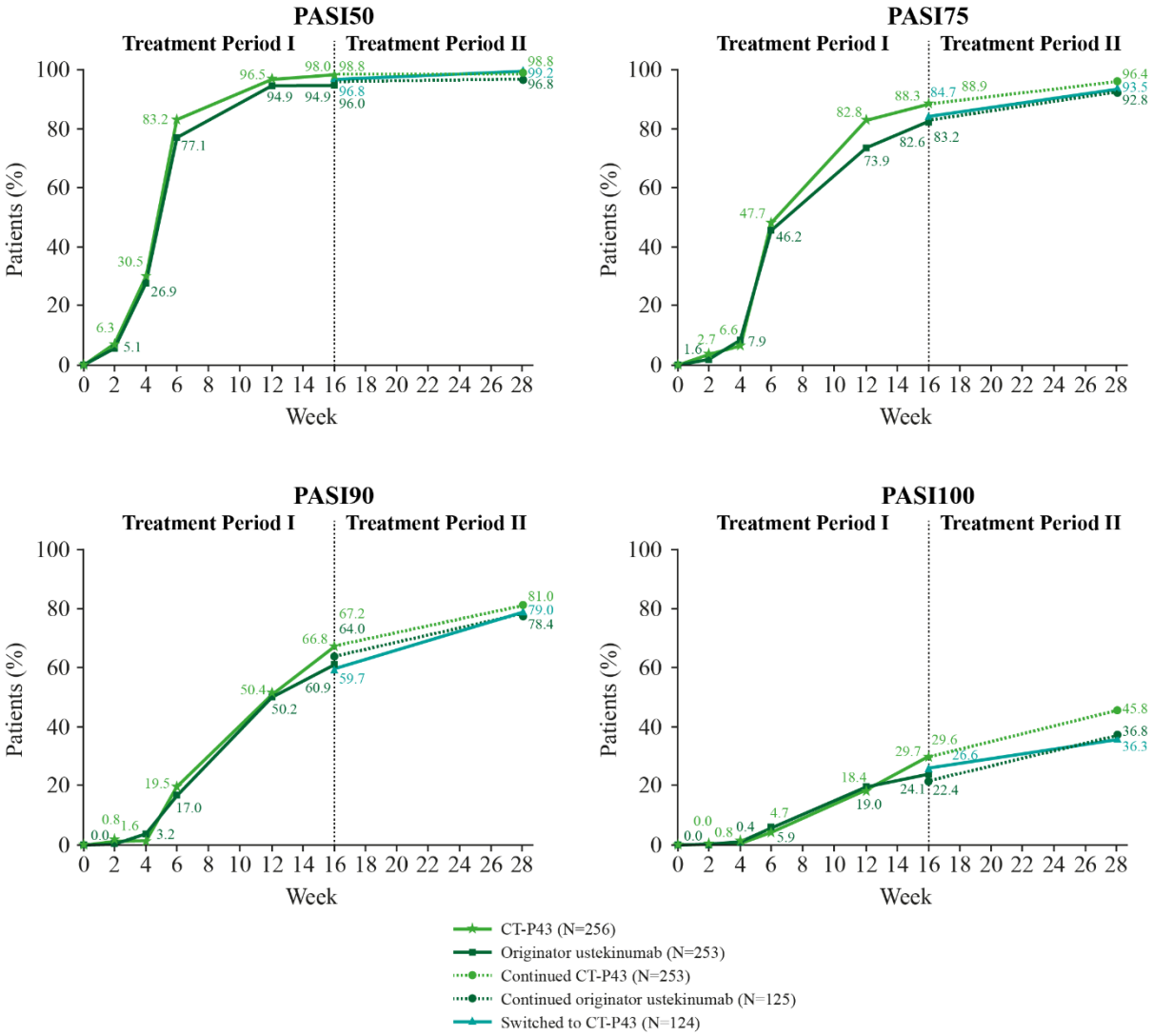
Related to study drug	1 (0.4)	0
Total number of TEAEs leading to study discontinuation	0	0
Total number of TEAEs classified as infections	34	25
Patients with ≥1 TEAEs classified as infections, n (%)	30 (13.2)	22 (12.6)
Related to study drug	9 (4.0)	6 (3.4)
Total number of TEAEs classified as ISRs	1	1
Patients with ≥1 TEAEs classified as ISRs	1 (0.4)	1 (0.6)
Related to study drug	1 (0.4)	1 (0.6)
Total number of TEAEs classified as hypersensitivity reactions	0	0
Total number of TEAEs classified as malignancies	0	0
Total number of deaths	0	0

[a]Patients with positive ADA result at Week 12.

[b]Patients with negative ADA result at Week 12.

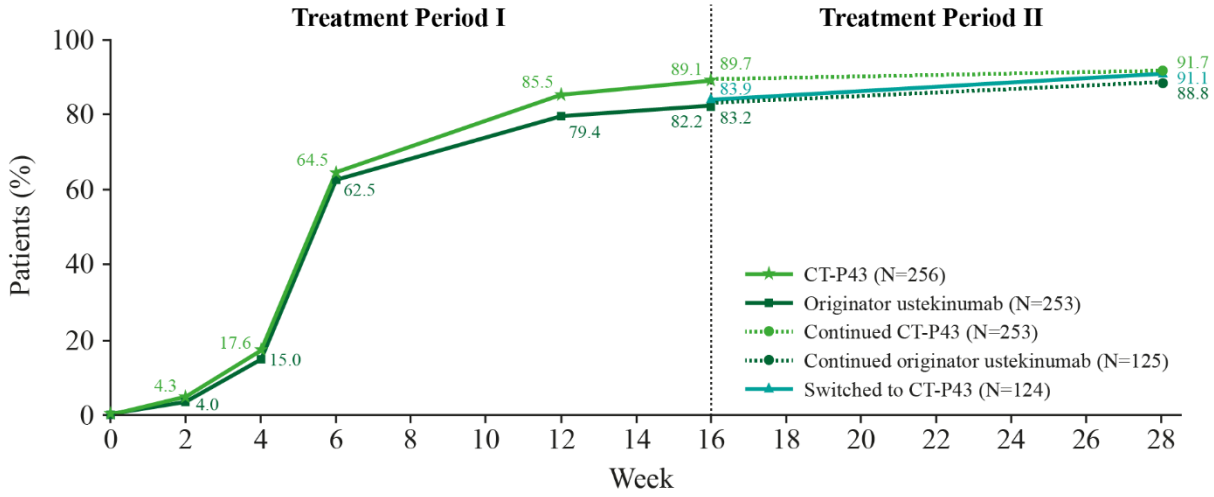
ADA, anti-drug antibody; ISR, injection-site reaction; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

Supplementary Figure 1. Proportion of PASI 50/75/90/100 responders at each study visit during Treatment Periods I and II (mITT/FAS).



FAS, full analysis set; mITT, modified intent-to-treat; PASI, Psoriasis Area and Severity Index

Supplementary Figure 2. Proportions of patients with an sPGA score of 0 or 1 at each study visit during Treatment Periods I and II (mITT/FAS).



FAS, full analysis set; mITT, modified intent-to-treat; sPGA, static Physician Global Assessment.