Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks from 2 phase 3, multicenter, randomized, double-blinded, placebo-controlled studies (CIMPASI-1 and CIMPASI-2)

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Background: Certolizumab pegol, the only Fc-free, PEGylated anti–tumor necrosis factor biologic, demonstrated clinically meaningful improvements suggestive of a positive risk-benefit balance in phase 2 studies in adults with moderate-to-severe chronic plaque psoriasis.

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Conflicts of interest: Dr Gottlieb has consulted and/or received other fees from Janssen Inc, Celgene Corp, Bristol-Myers Squibb Co, Beiersdorf Inc, AbbVie, UCB, Novartis, Incyte, Eli Lilly, Reddy Labs, Valeant, Dermira Inc, Allergan, and Sun Pharmaceutical Industries; and has received research or educational grants (paid to Tufts Medical Center) from Janssen Incyte, Lilly, Novartis, Allergan, and LEO Pharma. Dr Blauvelt has received honoraria or fees for consulting, being a clinical investigator, and/or speaker for AbbVie, Aclaris, Allergan, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dermavant, Dermira Inc, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Janssen, LEO Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB Pharma, Valeant, and Vidac. Dr Leonardi has received fees or honoraria for consulting, speaking, or serving on the advisory board for AbbVie, Actavis, Amgen, Boehringer Ingelheim Pharma, Celgene, Coherus, Corrona, Dermira Inc, Eli Lilly, Galderma, Glenmark, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Sandoz, Stiefel, UCB Pharma, Vitae, and Wyeth. Dr Poulin has received research grants as an investigator for AbbVie, Baxter, Boehringer Ingelheim Pharma, Celgene, Centocor/Janssen, Eli Lilly, EMD Serono, GlaxoSmithKline, LEO Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Takeda, and UCB Pharma; and has received honoraria speaking for AbbVie, Celgene, Janssen, Eli Lilly, LEO Pharma, Novartis, Regeneron, and Sanofi Genzyme. Dr Reich has received speaker's fees or honoraria from and/or served on the advisory board for AbbVie, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Eli Lilly, Medac, Merck Sharp & Dohme, Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB Pharma, and Xenoport. Dr Thaçi has received research support from AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, Dignity, Eli Lilly, Forward-Pharma, GlaxoSmithKline, LEO Pharma, Janssen-Cilag, Maruho, Merck Sharp & Dohme, Mitsubishi Pharma, Novartis, Pfizer, Roche, Regeneron, and Sandoz; received honoraria from AbbVie, Biogen, Celgene, Janssen, LEO Pharma, Pfizer, Roche-Possay, Novartis, and Mundipharma; served as a consultant for AbbVie, Biogen, Celgene, Dignity, Galapagos, Maruho, Mitsubishi, Novartis, Pfizer, and Xenoport; and sat on the scientific advisory boards for AbbVie, Amgen, Biogen, Celgene, Eli Lilly, GlaxoSmithKline, LEO Pharma, Pfizer, Novartis, Janssen, Mundipharma, and Sandoz. Ms Drew and Dr Burge have received stock options from Dermira Inc. Mr Peterson owns stock in UCB Inc. Dr Arendt owns stock in and has received stock options from UCB Inc.

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Objective: Assess certolizumab efficacy and safety versus placebo in phase 3 studies.

Methods: Patients with moderate-to-severe chronic plaque psoriasis were randomized 2:2:1 to certolizumab 400 mg, certolizumab 200 mg, or placebo every 2 weeks. At week 16, certolizumab-treated patients achieving a 50% reduction in Psoriasis Area and Severity Index continued treatment through week 48. Coprimary endpoints were week 16 responder rates, defined as a 75% reduction in Psoriasis Area and Severity Index and Physician's Global Assessment 0/1 (clear/almost clear) and ≥2-point improvement. Safety was assessed by treatment-emergent adverse events.

Results: Week-16 endpoints were significantly greater for both doses of certolizumab versus placebo, and the responses were maintained through week 48. For most measures, improvement was numerically greater for certolizumab 400 mg. No unexpected safety signals were identified.

Limitation: There was no active comparator.

Conclusion: Treatment with either certolizumab 400 mg or 200 mg every 2 weeks was associated with significant and clinically meaningful improvements in moderate-to-severe psoriasis. The 400-mg dose could provide additional clinical benefit. The safety profile was consistent with the therapeutic class. (J Am Acad Dermatol 2018;79:302-14.)

Key words: anti-TNF; anti—tumor necrosis factor; certolizumab pegol; chronic plaque psoriasis; CIMPASI-1; CIMPASI-2; phase 3 trial.

CAPSULE SUMMARY

- Certolizumab pegol is an Fc-free, PEGylated anti—tumor necrosis factor biologic.
- In these phase 3 psoriasis studies, certolizumab pegol 200 mg and 400 mg every 2 weeks demonstrated statistically significant and clinically meaningful improvements versus placebo; no new safety signals were observed.
- Certolizumab pegol affords additional psoriasis treatment options.

Psoriasis is a common chronic, immune-mediated inflammatory disease with significant psychosocial and emotional effects, such as fatigue, frustration, increased self-consciousness, and depression.[1-3] Patients with more severe psoriasis are often treated with systemic medications, phototherapy, and biologic agents, but not all patients tolerate or respond to currently available therapies, and some might have contraindications. In addition, loss of response can occur over time, necessitating additional treatment options.[4] Indeed, over half of patients with severe psoriasis report being dissatisfied with available treatments, and as many as 30% of these patients are receiving treatment that is not in accordance with accepted treatment guidelines.[5,6]

Certolizumab pegol (CZP) is the only Fc-free, PEGylated anti—tumor necrosis factor (TNF) biologic. Unlike other anti-TNF biologics, CZP does not bind the neonatal Fc receptor (FcRn) because it lacks the IgG Fc. Consequently, it is not expected to undergo FcRn-mediated transfer across the placenta,[7] showing minimal placental transfer of CZP from mothers to infants.[8] PEGylation increases the half-life of CZP to 14 days.[9]

CZP has previously demonstrated promising results in treatment of psoriasis in phase 2 trials[10] and treatment of psoriatic arthritis in a phase 3 trial.[11] The objective of each of the 2 phase 3 trials reported here, CIMPASI-1 and CIMPASI-2, was to evaluate the efficacy and safety of CZP compared with placebo in the treatment of moderate-to-severe chronic plaque psoriasis.

METHODS

Study design

CIMPASI-1 (NCT02326298) and CIMPASI-2 (NCT02326272) are ongoing, replicate, phase 3, randomized, double-blinded, multicenter, 144-week studies in outpatient clinics in North America and Europe (Fig 1). CIMPASI-1 and CIMPASI-2 began December 18, 2014, and December 22, 2014, respectively, and the week-48 cutoff dates were October 20, 2016, and August 16, 2016, respectively. Results from the first 48 weeks of double-blind treatment are reported here; the open-label safety extension is ongoing.

At the baseline visit, an interactive voice web response system was used to assign patients to subcutaneous treatment with CZP 400 mg every 2 weeks, CZP 200 mg every 2 weeks (after loading

Abbreviations used:

CZP:	certolizumab pegol
DLQI:	Dermatology Life Quality Index
FcRn:	neonatal Fc receptor
PASI:	Psoriasis Area and Severity Index
PASI 50:	≥50% reduction in PASI from baseline PASI
PASI 50-75:	≥50% but <75% reduction in PASI from baseline PASI
PASI 75:	≥75% reduction in PASI from baseline PASI
PASI 90:	≥90% reduction in PASI from baseline PASI
PGA:	Physician's Global Assessment
TEAE:	treatment-emergent adverse event
TNF:	tumor necrosis factor

dose of CZP 400 mg at weeks 0, 2, and 4), or placebo every 2 weeks until week 16 (initial treatment period) according to the randomization schedule produced by an independent biostatistician (2:2:1, stratified by site). The loading dose administered to patients randomized to the CZP 200-mg every 2 weeks group is consistent with approved labeling for CZP in other indications.

At week 16, CZP-treated PASI 50 responders (patients with a ≥50% reduction in Psoriasis Area and Severity Index [PASI] from their baseline PASI) and placebo-treated PASI 75 responders (patients with a ≥75% reduction in PASI from their baseline PASI) continued receiving their respective treatments through week 48 (the maintenance period). Placebo-treated patients who were PASI 50 responders but PASI 75 nonresponders (≥50% but <75% reduction in PASI from baseline PASI) at week 16 received CZP 200 mg every 2 weeks (after loading doses of CZP 400 mg at weeks 16, 18, and 20). PASI 50 nonresponders at week 16 entered the escape arm of the study and received open-label CZP 400 mg every 2 weeks. PASI 50 nonresponders at weeks 32, 40, or 48 were withdrawn from the study. Injections during the first 48 weeks of each study were administered by study personnel who were not involved in any other study procedures.

During the study, PASI 90 (≥90% reduction in PASI from baseline PASI) responder rate at week 16 was added as a secondary endpoint via protocol amendment; there were no other important changes to the protocol after study commencement. CIMPASI-1 and CIMPASI-2 were approved by local institutional review boards or independent ethics committees (quorum institutional review board numbers 29985 and 29986; EudraCT numbers 2014-003513-28 and 2014-003486-14) on November 11, 2014, and were carried out in accordance with good clinical practice requirements[12] and the Declaration of Helsinki.[13] Informed consent was obtained from participants and documented.

Study participants

Eligible patients were ≥18 years of age with plaque psoriasis for ≥6 months with baseline PASI ≥12, body surface area affected ≥10%, and a Physician's Global Assessment (PGA) ≥3 on a 5-point scale. All participants were candidates for systemic therapy, phototherapy, or photochemotherapy.

Patients were excluded if they had previous treatment with CZP or >2 biologics (including other anti-TNF biologics); had a history of primary failure to any biologic (ie, no response within the first 12 weeks of treatment) or secondary failure to >1 biologic (ie, patient initially responded and then stopped treatment due to loss of response after week 12); had erythrodermic, guttate, or generalized pustular psoriasis; had a history of current, chronic, or recurrent viral, bacterial, or fungal infections; had known active or latent tuberculosis infection (assessed by using an interferon-γ release assay) or at high risk for a tuberculosis infection; had congestive heart failure; had a history of lymphoproliferative disorder; had a history of or suspected to have demyelinating disease of the central nervous system; or were breastfeeding, pregnant, or planned to become pregnant within 3 months of last dose of study drug.

Efficacy and safety assessments

Coprimary efficacy endpoints assessed at week 16 were PASI 75 and PGA 0/1 (clear/almost clear with a ≥2-point improvement from baseline) responder rates. Secondary endpoints included week-16 PASI 90 responder rate, change in Dermatology Life Quality Index (DLQI) between baseline and week 16, and PASI 75 and PGA 0/1 responder rates at week 48. Other efficacy variables included PASI 90 responder rate at week 48 and PASI 100 (100% reduction in PASI from baseline PASI) and DLQI 0/1 (no/small impact of psoriasis on patient's quality of life[14]) responder rates at week 16 and week 48. Safety was assessed via treatment-emergent adverse events (TEAEs).

Groups for efficacy analyses during the 16-week initial treatment period were based on randomization at baseline, and analyses during the maintenance period (weeks 16-48) were based on the treatment group assigned at week 16.

Statistical analysis

Assumptions for the week-16 PGA 0/1 responder rate for CZP 200 mg every 2 weeks (50%) and

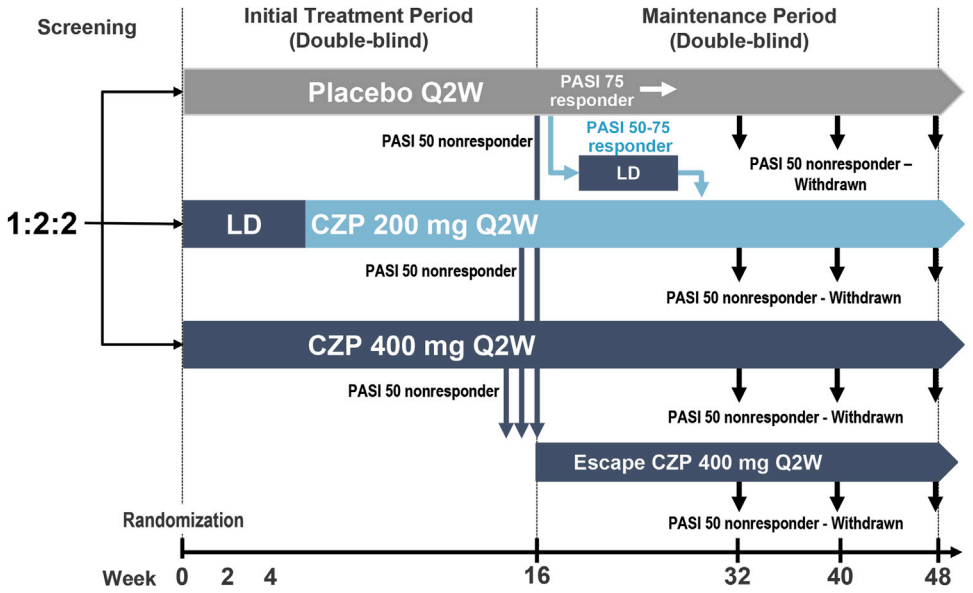

Fig 1. Study design. *CZP*, Certolizumab pegol; *LD*, loading dose CZP 400 mg at weeks 0, 2, and 4 or weeks 16, 18, and 20; *PASI*, Psoriasis Area and Severity Index; *PASI 50*, ≥50% reduction in PASI from baseline PASI; *PASI 50-75*, ≥50% but <75% reduction in PASI from baseline PASI; *PASI 75*, ≥75% reduction in PASI from baseline PASI; *Q2W*, every 2 weeks.

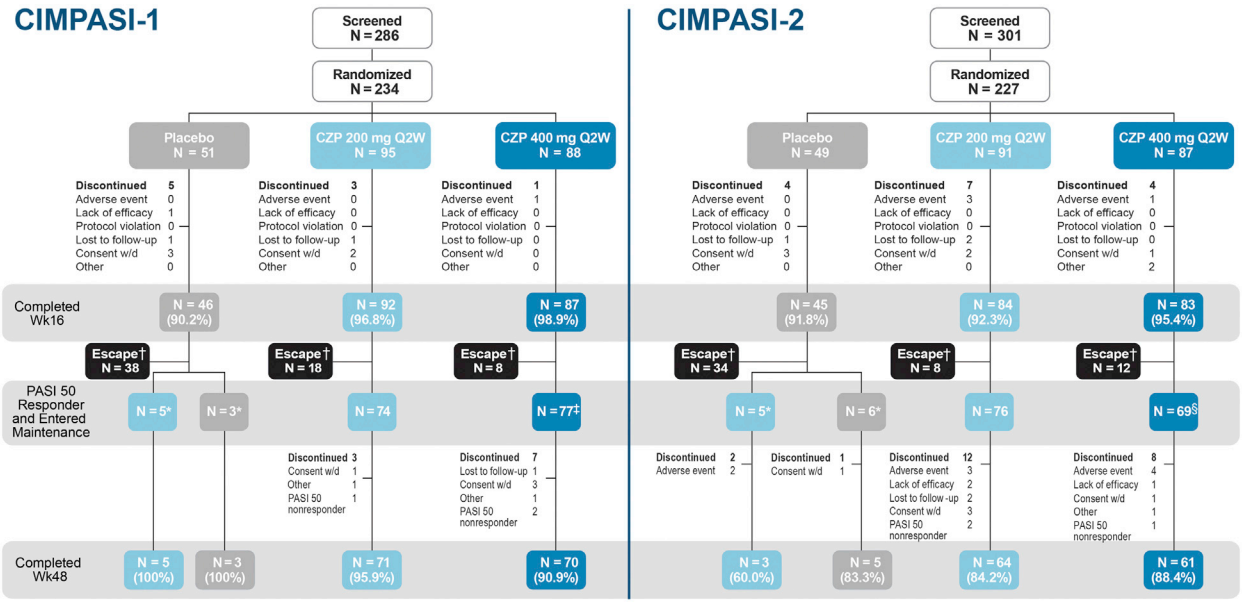

Fig 2. Patient disposition to week 48. *Upon entering maintenance period, placebo-treated PASI 75 responders (≥75% reduction in PASI from baseline PASI) continued blinded placebo treatment; PASI 50-75 responders (≥50% but <75% reduction in PASI from baseline PASI) received CZP 200 mg every 2 weeks. †PASI 50 nonresponders at week 16 received open-label CZP 400 mg every 2 weeks in the escape arm of the study. ‡Two patients completed week 16 but did not enter maintenance period due to adverse events. §Two patients completed week 16 but did not enter maintenance period: 1 was lost to follow-up and 1 withdrew consent. Patients randomized to CZP 200 mg every 2 weeks received a loading dose of CZP 400 mg at weeks 0, 2, and 4. *CZP*, Certolizumab pegol; *PASI*, Psoriasis Area and Severity Index; *PASI 50*, ≥50% reduction in PASI from baseline PASI; *Q2W*, every 2 weeks; *w/d*, withdrawn.

Table I. Patient demographics and baseline disease characteristics of randomized patients

Characteristic	CIMPASI-1			CIMPASI-2			Pooled		
	Placebo, N = 51	CZP 200 mg Q2W, N = 95	CZP 400 mg Q2W, N = 88	Placebo, N = 49	CZP 200 mg Q2W, N = 91	CZP 400 mg Q2W, N = 87	Placebo, N = 100	CZP 200 mg Q2W, N = 186	CZP 400 mg Q2W, N = 175
Demographics									
Age, y, mean ± SD	47.9 ± 12.8	44.5 ± 13.1	43.6 ± 12.1	43.3 ± 14.5	46.7 ± 13.3	46.4 ± 13.5	45.7 ± 13.8	45.6 ± 13.2	45.0 ± 12.9
Male, n (%)	35 (68.6)	67 (70.5)	60 (68.2)	26 (53.1)	58 (63.7)	43 (49.4)	61 (61.0)	125 (67.2)	103 (58.9)
White, n (%)	45 (88.2)	87 (91.6)	79 (89.8)	44 (89.8)	86 (94.5)	81 (93.1)	89 (89.0)	173 (93.0)	160 (91.4)
Geographic region, n (%)									
North America	26 (51.0)	49 (51.6)	45 (51.1)	35 (71.4)	61 (67.0)	61 (70.1)	61 (61.0)	110 (59.1)	106 (60.6)
Europe	25 (49.0)	46 (48.4)	43 (48.9)	14 (28.6)	30 (33.0)	26 (29.9)	39 (39.0)	76 (40.9)	69 (39.4)
Weight, kg, mean ± SD	95.2 ± 19.5	92.6 ± 21.0	92.2 ± 21.7	87.1 ± 26.4	97.8 ± 25.6	91.8 ± 27.7	91.3 ± 23.4	95.1 ± 23.4	92.0 ± 24.8
BMI, kg/m^2, mean ± SD	32.2 ± 6.8	31.1 ± 7.3	30.7 ± 6.7	30.2 ± 8.0	32.8 ± 8.3	31.7 ± 8.9	31.2 ± 7.4	32.0 ± 7.8	31.2 ± 7.9
Baseline disease characteristics									
Duration of psoriasis at screening, y, mean ± SD	18.5 ± 12.9	16.6 ± 12.3	18.4 ± 12.9	15.4 ± 12.2	18.8 ± 13.5	18.6 ± 12.4	17.0 ± 12.6	17.7 ± 12.9	18.5 ± 12.6
Concurrent self-reported PsA, n (%)	4 (7.8)	10 (10.5)	15 (17.0)	9 (18.4)	22 (24.2)	26 (29.9)	13 (13.0)	32 (17.2)	41 (23.4)
PASI, mean ± SD	19.8 ± 7.5	20.1 ± 8.2	19.6 ± 7.9	17.3 ± 5.3	18.4 ± 5.9	19.5 ± 6.7	18.6 ± 6.6	19.2 ± 7.2	19.6 ± 7.3
DLQI, mean ± SD	13.9 ± 8.3	13.3 ± 7.4	13.1 ± 6.5	12.9 ± 7.3	15.2 ± 7.2	14.2 ± 7.2	13.4 ± 7.8	14.2 ± 7.4	13.7 ± 6.9
BSA, %, mean ± SD	26.1 ± 16.1	25.4 ± 16.9	24.1 ± 16.6	20.0 ± 9.5	21.4 ± 12.2	23.1 ± 11.6	23.1 ± 13.6	23.5 ± 14.9	23.6 ± 14.3
PGA score, n (%)									
3: moderate	35 (68.6)	62 (65.3)	65 (73.9)	37 (75.5)	66 (72.5)	61 (70.1)	72 (72.0)	128 (68.8)	126 (72.0)
4: severe	16 (31.4)	33 (34.7)	23 (26.1)	12 (24.5)	25 (27.5)	26 (29.9)	28 (28.0)	58 (31.2)	49 (28.0)
Any systemic psoriasis treatment, n (%)	36 (70.6)	66 (69.5)	61 (69.3)	36 (73.5)	65 (71.4)	63 (72.4)	72 (72.0)	131 (70.4)	124 (70.9)
Prior biologic use, n (%)*	15 (29.4)	30 (31.6)	29 (33.0)	14 (28.6)	32 (35.2)	30 (34.5)	29 (29.0)	62 (33.3)	59 (33.7)
Type									
Anti—TNF-α	10 (19.6)	19 (20.0)	17 (19.3)	9 (18.4)	22 (24.2)	22 (25.3)	19 (19.0)	44 (23.7)	39 (22.3)
Anti—IL-17A	3 (5.9)	8 (8.4)	4 (4.5)	2 (4.1)	8 (8.8)	4 (4.6)	5 (5.0)	16 (8.6)	8 (4.6)
Number used†									
1 therapy	13 (25.5)	22 (23.2)	22 (25.0)	11 (22.4)	22 (24.2)	21 (24.1)	24 (24.0)	44 (23.7)	43 (24.6)
2 therapies	2 (3.9)	8 (8.4)	7 (8.0)	3 (6.1)	10 (11.0)	8 (9.2)	5 (5.0)	18 (9.7)	15 (8.6)

BMI, Body mass index; *BSA*, body surface area; *CZP*, certolizumab pegol; *DLQI*, Dermatology Life Quality Index; *IL*, interleukin; *PASI*, Psoriasis Area and Severity Index; *PGA*, Physician's Global Assessment; *PsA*, psoriatic arthritis; *Q2W*, every 2 weeks; *SD*, standard deviation; *TNF*, tumor necrosis factor.

*Patients may have had exposure to >1 prior biologic but ≤2, per exclusion criteria.

†One patient in the CZP 400-mg Q2W group in CIMPASI-2 had prior exposure to ≥3 biologics, which was a protocol violation.

Table II. Primary and secondary endpoints

Endpoint	CIMPASI-1			CIMPASI-2			Pooled		
	Placebo, N = 51	CZP 200 mg Q2W, N = 95	CZP 400 mg Q2W, N = 88	Placebo, N = 49	CZP 200 mg Q2W, N = 91	CZP 400 mg Q2W, N = 87	Placebo, N = 100	CZP 200 mg Q2W, N = 186	CZP 400 mg Q2W, N = 175
Coprimary									
Week 16									
PASI 75 responder rate, %*	6.5	66.5	75.8	11.6	81.4	82.6	9.9	76.7	82.0
OR vs placebo		29.0	45.7		33.4	36.2		30.0	41.5
(97.5% CI)		(7.0 to 120.4)	(10.7 to 195.6)		(10.0 to 112.0)	(10.7 to 122.7)		(12.0 to 74.9)	(16.3 to 105.7)
P value		<.0001	<.0001		<.0001	<.0001		<.0001	<.0001
PGA 0/1 responder rate, %*	4.2	47.0	57.9	2.0	66.8	71.6	2.7	56.8	65.3
OR vs placebo		20.1	31.1		106.2	133.2		48.7	69.5
(97.5% CI)		(3.7 to 109.4)	(5.7 to 170.5)		(9.6 to 1178.8)	(11.9 to 1489.6)		(11.7 to 203.3)	(16.5 to 292.0)
P value		<.0001	<.0001		<.0001	<.0001		<.0001	<.0001
Secondary									
Week 16									
PASI 90 responder rate, %*	0.4	35.8	43.6	4.5	52.6	55.4	2.5	45.9	52.2
OR vs placebo		36.7	50.6		24.3	27.2		34.3	44.1
(97.5% CI)		(5.7 to 235.2)	(7.9 to 325.0)		(4.4 to 134.4)	(4.9 to 151.2)		(6.7 to 175.7)	(8.6 to 226.5)
P value		<.0001	<.0001		<.0001	<.0001		<.0001	<.0001
DLQI change from baseline, mean ± SD†	−3.3 ± 6.9	−8.9 ± 8.5	−9.6 ± 6.5	−2.9 ± 6.6	−11.1 ± 7.8	−10.0 ± 7.6	−3.1 ± 6.7	−10.0 ± 8.2	−9.8 ± 7.0
Adjusted mean difference vs placebo		−6.0	−6.8		−6.6	−6.2		−6.3	−6.5
(97.5% CI)		(−8.2 to −3.8)	(−9.1 to −4.6)		(−8.9 to −4.4)	(−8.5 to −3.9)		(−7.8 to −4.7)	(−8.1 to −4.9)
P value		<.0001	<.0001		<.0001	<.0001		<.0001	<.0001
Week 48									
PASI 75 responder rate, % (95% CI)‡	NA	67.2 (57.1 to 77.4)	87.1 (79.8 to 94.5)	NA	78.7 (68.9 to 88.5)	81.3 (71.9 to 90.7)	NA	70.7 (60.6 to 80.7)	83.6 (75.9 to 91.3)
PGA 0/1 responder rate, % (95% CI)‡	NA	52.7 (42.0 to 63.3)	69.5 (59.2 to 79.8)	NA	72.6 (61.2 to 83.9)	66.6 (54.4 to 78.9)	NA	61.0 (50.3 to 71.8)	68.9 (58.7 to 79.1)

CI, Confidence interval; *CZP*, certolizumab pegol; *DLQI*, Dermatology Life Quality Index; *NA*, not applicable; *OR*, odds ratio; *PASI*, Psoriasis Area and Severity Index; *PASI 50*, ≥50% reduction in PASI from baseline PASI; *PASI 75*, ≥75% reduction in PASI from baseline PASI; *PASI 90*, ≥90% reduction in PASI from baseline PASI; *PGA 0/1*, Physician's Global Assessment clear/almost clear, with ≥2-category improvement from baseline; *SD*, standard deviation; *Q2W*, every 2 weeks.

*On the basis of the logistic regression model, with factors for treatment, region, prior biologic exposure (yes/no), study (pooled only), and interaction terms for study by region (pooled only) and study by prior biologic exposure (pooled only) using Markov chain Monte Carlo method for multiple imputation.

†On the basis of the analysis of covariance model, with factors for treatment group, region, prior biologic exposure (yes/no), study (pooled only), and interaction terms for study by region (pooled only) and study by prior biologic exposure (pooled only) and baseline DLQI score as a covariate, using last observation carried forward imputation.

‡On the basis of the logistic regression model, where week-16 PASI 50 nonresponders were imputed as nonresponders at all subsequent time points and all other missing data were imputed via multiple imputation.

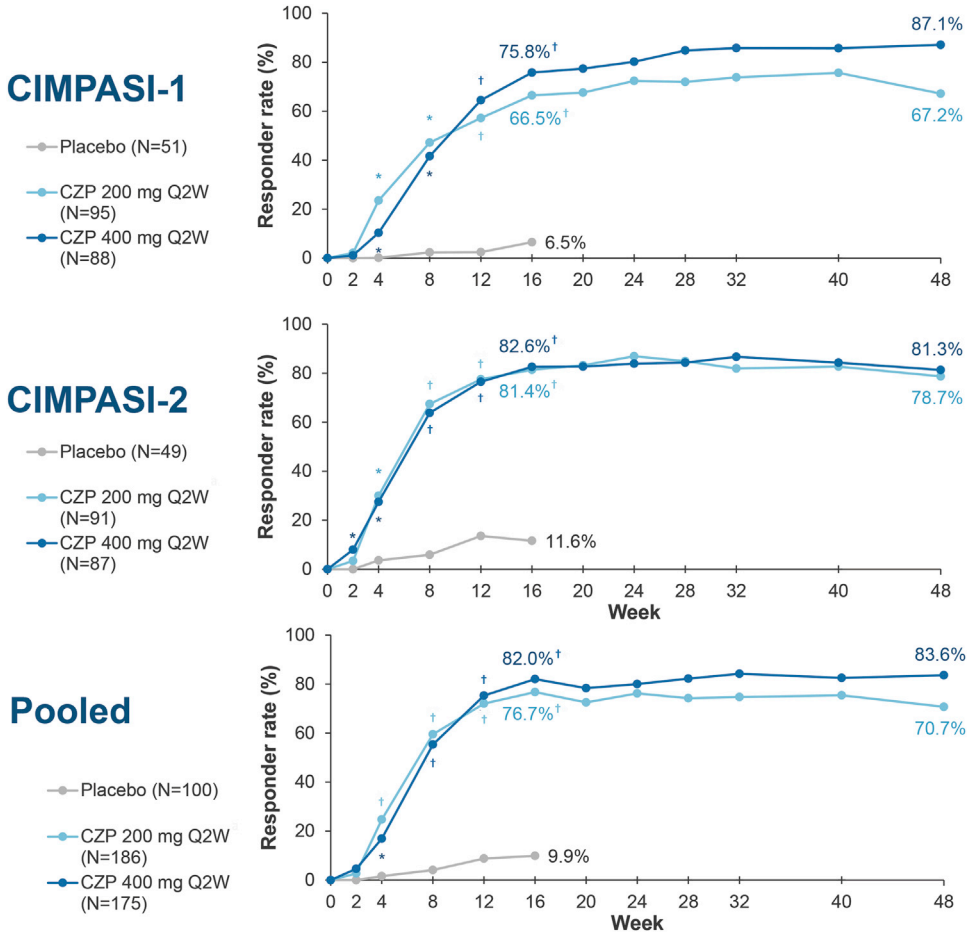

Fig 3. PASI 75 responder rates of randomized patients through week 48, by visit. Patients randomized to CZP 200 mg every 2 weeks received loading doses of CZP 400 mg at weeks 0, 2, and 4. The responder rate analysis was based on the logistic regression model. *$P < .05$ versus placebo (controlled for multiplicity at week 16 in CIMPASI-1 and CIMPASI-2). †$P < .0001$ versus placebo (controlled for multiplicity at week 16 in CIMPASI-1 and CIMPASI-2). *CZP*, Certolizumab pegol; *PASI*, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction in PASI from baseline PASI; *Q2W*, every 2 weeks.

placebo (5%) were based on data collected in the phase 2 trials evaluating CZP in patients with plaque psoriasis.[10] Under these assumptions, a sample size of 225 (allocated 2:2:1 to CZP 400 mg, CZP 200 mg, and placebo, respectively) was calculated to provide >99% power to detect a difference between CZP 200 mg and placebo with a 2-sided alpha level of 0.025.

Efficacy analyses were performed on the randomized set (all randomized patients). Logistic regression models with fixed effects for treatment group, region, and prior biologic exposure (yes/no) were used to analyze week-16 PASI 75, PGA 0/1, and PASI 90 responder rates. The Markov chain Monte Carlo method for multiple imputation was used to account for missing data. Participants who did not achieve week-16 PASI 50 responses were considered nonresponders for all subsequent time points. All other missing data in the maintenance period were handled via multiple imputation. An analysis of covariance model with treatment group, region, and prior biologic exposure (yes/no) as factors and baseline DLQI score as a covariate was used to analyze DLQI change from baseline at week 16; last observation carried forward was used to account for imputation of missing DLQI data. Participants who did not achieve a PASI 50 response at week 16 had their week-16 DLQI value carried forward to all subsequent time points, while all other missing data in the maintenance period were imputed via last observation carried forward. Multiplicity was controlled via a fixed sequence testing procedure split by dose (the overall alpha of 0.05 was allocated as 0.025 to each dose). A full

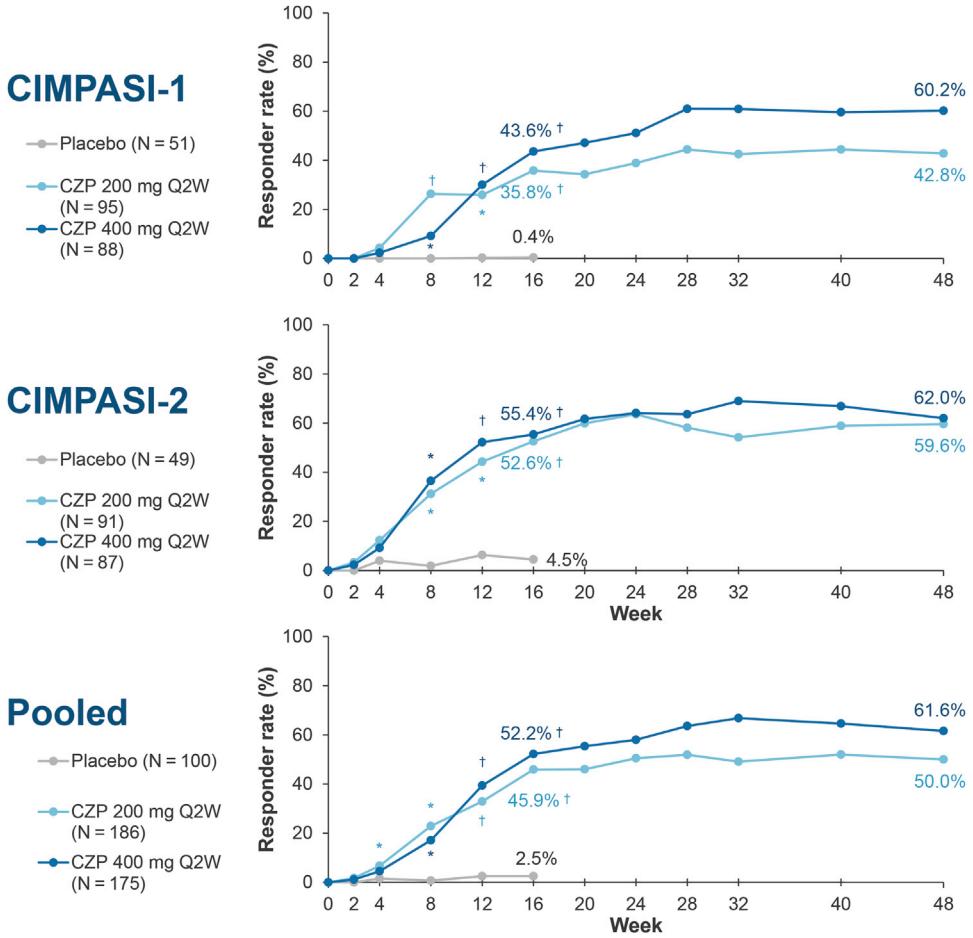

Fig 4. PASI 90 responder rates of randomized patients through week 48, by visit. Patients randomized to CZP 200 mg every 2 weeks received loading doses of CZP 400 mg at weeks 0, 2, and 4. The responder rate analysis was based on the logistic regression model.*$P < .05$ versus placebo (controlled for multiplicity at week 16 in CIMPASI-1 and CIMPASI-2). †$P < .0001$ versus placebo (controlled for multiplicity at week 16 in CIMPASI-1 and CIMPASI-2). *CZP*, Certolizumab pegol; *PASI*, Psoriasis Area and Severity Index; *PASI 90*, ≥90% reduction in PASI from baseline PASI; *Q2W*, every 2 weeks.

description of this procedure can be found in the Supplementary Appendix (available at http://www.jaad.org).

Week-16 safety assessments were performed on the safety set (all randomized patients who received ≥1 dose of study medication). Week-48 safety assessments were performed on the set of patients treated with CZP (randomized patients who received ≥1 dose of CZP). TEAEs were attributed to the medication being taken at the time the event occurred.

RESULTS

Patient disposition, demographics, and baseline characteristics

Of 587 participants screened for both studies, 234 were randomized in CIMPASI-1 and 227 were randomized in CIMPASI-2. Week-16 and week-48 completion rates were high and similar between treatments and between studies (Fig 2). Demographics and baseline disease characteristics were similar across treatment groups and between CIMPASI-1 and CIMPASI-2 (Table I), except for sex (CIMPASI-1 had a higher percentage of males than CIMPASI-2) and geographic region (CIMPASI-2 had a higher percentage of North American patients than CIMPASI-1). In addition, a larger proportion of patients in CIMPASI-2 than CIMPASI-1 self-reported concurrent psoriatic arthritis.

Efficacy through week 16 and week 48

At week 16, significantly higher PASI 75 responder rates were observed for CZP 400 mg (CIMPASI-1, 75.8%; CIMPASI-2, 82.6%) and CZP 200 mg (CIMPASI-1, 66.5%; CIMPASI-2, 81.4%) than placebo (CIMPASI-1, 6.5%; CIMPASI-2, 11.6%; $P < .0001$ for

Table III. Safety overview and TEAEs of interest through week 16 and week 48

	CIMPASI-1			CIMPASI-2		
Baseline to week 16 (safety set)	**Placebo, N = 51**	**CZP 200 mg Q2W, N = 95**	**CZP 400 mg Q2W, N = 88**	**Placebo, N = 49**	**CZP 200 mg Q2W, N = 90**	**CZP 400 mg Q2W, N = 87**
TEAEs, n (%) [incidence rate, new cases/100 patient-years]						
All	28 (54.9) [279.1]	52 (54.7) [292.3]	57 (64.8) [375.9]	33 (67.3) [388.9]	54 (60.0) [308.7]	60 (69.0) [405.7]
Drug-related*	4 (7.8)	7 (7.4)	15 (17.0)	4 (8.2)	17 (18.9)	15 (17.2)
Serious	1 (2.0) [6.8]	2 (2.1) [6.9]	5 (5.7) [19.0]	0	2 (2.2) [7.4]	4 (4.6) [15.3]
Discontinuations due to TEAE, n (%)	0	0	2 (2.3)	0	3 (3.3)	1 (1.1)
Deaths, n (%)	0	0	0	0	0	0
Other TEAEs of interest, n (%) [incidence rate, new cases/100 patient-years]						
Infections and infestations	16 (31.4) [126.9]	30 (31.6) [125.0]	39 (44.3) [194.5]	15 (30.6) [123.8]	26 (28.9) [111.2]	34 (39.1) [158.1]
Latent tuberculosis	0	0	0	0	0	0
Candida infections	0	0	0	0	1 (1.1) [3.7]†	0
Oral fungal infection	0	0	0	0	0	1 (1.1) [3.8]
Fungal skin infection	0	0	1 (1.1) [3.7]	0	0	0
Herpes zoster	0	0	0	1 (2.0) [6.9]	1 (1.1) [3.7]	0
Herpes dermatitis	0	0	0	0	0	1 (1.1) [3.7]
Epstein-Barr viral infection	0	0	0	0	1 (1.1) [3.7]	0
Nasopharyngitis	7 (13.7) [49.5]	18 (18.9) [68.5]	18 (20.5) [77.0]	5 (10.2) [36.2]	8 (8.9) [31.0]	6 (6.9) [23.0]
Upper respiratory tract infection	3 (5.9) [20.5]	7 (7.4) [25.0]	8 (9.1) [31.7]	2 (4.1) [14.0]	4 (4.4) [15.0]	5 (5.7) [19.2]
Serious infections	0	0	0	0	0	1 (1.1) [3.8]‡
Malignancy	0	0	0	0	0	1 (1.1) [3.8]§
IBD flare	0	0	0	0	0	0
Depression	0	0	1 (1.1) [3.7]	0	1 (1.1) [3.7]	1 (1.1) [3.8]

Baseline to week 48 (treated with CZP set)	**CZP 200 mg Q2W, N = 100**	**CZP 400 mg Q2W, N = 144**	**CZP 200 mg Q2W, N = 95**	**CZP 400 mg Q2W, N = 129**
TEAEs, n (%) [incidence rate, new cases/100 patient-years]				
All	72 (72.0) [217.5]	111 (77.1) [257.6]	73 (76.8) [235.6]	103 (79.8) [277.5]
Drug-related*	14 (14.0)	28 (19.4)	24 (25.3)	27 (20.9)
Serious	4 (4.0) [5.3]	11 (7.6) [10.4]	7 (7.4) [9.7]	7 (5.4) [7.5]
Discontinuations due to TEAE, n (%)	0	5 (3.5)	8 (8.4)	8 (6.2)
Deaths, n (%)	0	1 (0.7)	0	0
Other TEAEs of interest, n (%) [incidence rate, new cases/100 patient-years]				
Infections and infestations	50 (50.0) [102.2]	76 (52.8) [115.9]	48 (50.5) [97.8]	68 (52.7) [111.2]
Latent tuberculosis	0	1 (0.7) [0.9]	0	0
Candida infections	1 (1.0) [1.3]‖	0	1 (1.1) [1.4]†	2 (1.6) [2.1]†¶

Oral fungal infection	0	0	0	1 (0.8) [1.0]
Fungal skin infection	0	1 (0.7) [0.9]	0	0
Nasopharyngitis	28 (28.0) [46.4]	40 (27.8) [46.9]	17 (17.9) [26.4]	25 (19.4) [29.0]
Upper respiratory tract infection	12 (12.0) [17.2]	13 (9.0) [12.8]	11 (11.6) [16.1]	13 (10.1) [14.5]
Serious infections	0	1 (0.7) [0.9][#]	0	1 (0.8) [1.0][‡]
Malignancy	0	1 (0.7) [0.9][§§]	0	1 (0.8) [1.0][§§]
IBD flare	0	0	0	0
Depression	0	2 (1.4) [1.8]	1 (1.1) [1.4]	2 (1.6) [2.1]

Patients who switched doses could be counted in both CZP doses. Total exposure for all CZP patients from baseline to week 48 was 356.57 patient-years (CIMPASI-1 = 186.65; CIMPASI-2 = 169.92).
CZP, Certolizumab pegol; *IBD*, inflammatory bowel disease; *Q2W*, every 2 weeks; *TEAE*, treatment-emergent adverse event.
*Incidence rate not calculated.
†Vulvovaginal candidiasis.
‡Abdominal abscess and hematoma infection (bicycle accident).
§Basal cell carcinoma.
‖Oral candidiasis.
¶Nail *Candida*.
#Erysipelas.

all), and responses were maintained through week 48 for both CZP doses (Table II; Fig 3). Higher PASI 75 responder rates occurred in the CZP 400-mg group than the CZP 200-mg group in the CIMPASI-1 trial and in the pooled data sets at weeks 16 and 48. Little difference between doses was noted in the CIMPASI-2 data set.

At week 16, significantly higher PGA 0/1 responder rates were observed for CZP 400 mg (CIMPASI-1, 57.9%; CIMPASI-2, 71.6%) and CZP 200 mg (CIMPASI-1, 47.0%; CIMPASI-2, 66.8%) than placebo (CIMPASI-1, 4.2%; CIMPASI-2, 2.0%; $P < .0001$ for all); responses were maintained through week 48 for both CZP doses (Table II; Supplemental Fig 1; available at http://www.jaad.org). PGA 0/1 responder rates were higher in the CZP 400-mg group than the CZP 200-mg group in the CIMPASI-1 trial and the pooled data set at week 16 and week 48, with little difference observed between doses in the CIMPASI-2 data set.

In the pooled data set through week 48, PASI 75 responder rates in patients with and without prior anti-TNF biologic use were 66.7% and 75.0%, respectively, for the CZP 400-mg group and 61.4% and 63.4%, respectively, for the CZP 200-mg group. Through week 48, the PGA 0/1 responder rates in patients with and without prior anti-TNF biologic use were 53.8% and 59.6%, respectively, for the CZP 400-mg group and 50.0% and 53.5%, respectively, for the CZP 200-mg group.

At week 16, CZP-treated patients achieved significantly higher PASI 90 responder rates than placebo-treated patients in the CIMPASI-1 and CIMPASI-2 trials and in the pooled data set ($P < .0001$ for all); responses were maintained through week 48 (Table II; Fig 4). Similar to other assessments, PASI 90 responder rates at week 16 and week 48 showed a more prominent dose-response relationship in the CIMPASI-1 data set and the pooled data set than in the CIMPASI-2 data set. Pooled PASI 100 responder rates are discussed in the Supplementary Appendix.

The change in DLQI at week 16 was significantly greater for CZP (either dose) than placebo in the CIMPASI-1 and CIMPASI-2 trials and in the pooled data set ($P < .0001$ for all), and the response was maintained through week 48 (Table II; Supplemental Fig 2; available at http://www.jaad.org). Similarly, the proportion of week-16 DLQI 0/1 responders was greater for CZP (either dose) than placebo, and this response was maintained through week 48 (Supplemental Fig 3; available at http://www.jaad.org). Through 48 weeks, the CZP 400-mg dose was associated with greater DLQI 0/1 responder rates than the CZP 200-mg dose in each individual study and the pooled analysis.

Safety

In CIMPASI-1, TEAEs incidence rates per 100 patient-years were 375.9 for CZP 400 mg—treated patients, 292.3 for CZP 200 mg—treated patients, and 279.1 for placebo-treated patients through week 16 (Table III). These rates decreased by week 48 for the CZP 400 mg—treated and CZP 200 mg—treated patients to 257.6/100 patient-years and 218.3/100 patient-years, respectively. CIMPASI-2 TEAEs incidence rates per 100 patient-years were 405.7, 308.7, and 388.9 for patients treated with CZP 400 mg, CZP 200 mg, and placebo, respectively, through week 16. These rates decreased by week 48 for the CZP 400 mg—treated and CZP 200 mg—treated patients to 277.5/100 patient-years and 236.0/100 patient-years, respectively.

After 48 weeks of treatment, the most common TEAEs occurring in all CZP-treated patients were nasopharyngitis and upper respiratory tract infection (Table IV). In pooled data, there were 18 serious TEAEs reported for the CZP 400 mg—treated patients and 11 for the CZP 200 mg—treated patients (Supplemental Table I; available at http://www.jaad.org). One serious infection was reported in the CZP 400-mg group in the CIMPASI-1 trial (erysipelas), and another was reported in the 400-mg group in the CIMPASI-2 trial (abdominal abscess and hematoma infection from bicycle accident). No opportunistic infections were reported. One death due to a motor vehicle accident was reported in the CIMPASI-1 trial.

DISCUSSION

The results from CIMPASI-1 and CIMPASI-2 indicate that treatment with CZP 400 mg or 200 mg every 2 weeks led to significantly greater PASI 75, PGA 0/1, and PASI 90 responder rates at week 16 than treatment with placebo in patients with moderate-to-severe chronic plaque psoriasis. These rates were maintained through week 48 for both CZP doses. Compared with treatment with placebo, treatment with either CZP dose was also associated with significant and clinically meaningful improvements in health-related quality of life through week 16, which was maintained through week 48. With a recent study indicating that over half of severe psoriasis patients are dissatisfied with their current treatment[5] and the well-documented correlation between psoriasis severity and decreased quality of life,[15-18] these efficacy results are encouraging. Furthermore, the safety profile observed for CZP was consistent with previous reports for CZP and the known and established safety profile associated with anti-TNF therapy.[10,19] Importantly, the incidence and distribution of TEAEs through week 48 were comparable between each CZP dose. The incidence of TEAEs of interest was comparable to that of other anti-TNF agents.[20,21]

The week-16 PASI 75 responder rate observed for patients treated with placebo was higher than expected (11.6%) in CIMPASI-2. However, the CZP treatment effect was similar between the 2 studies, and the higher than expected placebo rate could be explained by the variable course of psoriasis and small patient numbers. Although CIMPASI-1 showed a dose-response relationship for PASI 75, PGA 0/1, and PASI 90 responder rates, CIMPASI-2 results were generally similar between the CZP 400-mg and 200-mg doses. Several demographic and baseline clinical characteristic differences were observed between the 2 studies; however, there is no clear evidence to indicate these differences affected clinical outcomes across the studies.

It has been suggested that biologic efficacy is lower in patients with previous exposure to biologics.[22-24] In this report, however, PASI 75 and PGA 0/1 week-48 responses were similar in patients with and without prior anti-TNF use. This is consistent with clinical trial data of CZP treatment in psoriatic arthritis,[25] where both skin and joint responses were similar in patients with and without prior anti-TNF exposure. It is also notable that these improvements occurred in a population with a mean body mass index >30, since high body mass index has been an observed negative predictor of biologic response.[24]

There are several limitations in the CIMPASI studies. No active comparator arm was included in the trials, and patients were excluded from the study for having a history of primary failure to biologic therapy. In addition, sample sizes are smaller than other phase 3 psoriasis trials, making it difficult to discern whether observed study variations are simply a consequence of patient numbers. However, these data are still generalizable to the broader psoriasis patient population, given that the demographics of the study group were typical of that for psoriasis phase 3 programs, efficacy of this study was similar to that of the phase 2 studies of CZP in psoriasis,[10] and the results mirror what has been seen in clinical practice.[26]

In conclusion, the results provide confirmation that treatment of moderate-to-severe chronic plaque psoriasis with either CZP 400 mg or 200 mg every 2 weeks was associated with significant, clinically meaningful improvements in efficacy and quality of life that were maintained over time, regardless of previous anti-TNF exposure, with the expected safety profile for this class of drug. Although the study was not powered to detect significant

Table IV. Most frequently (≥5% in any group) reported TEAEs

	CIMPASI-1				CIMPASI-2		
Baseline to week 16 (safety set)	**Placebo, N = 51**	**CZP 200 mg Q2W, N = 95**	**CZP 400 mg Q2W, N = 88**	**Baseline to week 16 (safety set)**	**Placebo, N = 49**	**CZP 200 mg Q2W, N = 90**	**CZP 400 mg Q2W, N = 87**
Nasopharyngitis	7 (13.7) [49.5]	18 (18.9) [68.5]	18 (20.5) [77.0]	Nasopharyngitis	5 (10.2) [36.2]	8 (8.9) [31.0]	6 (6.9) [23.0]
URTI	3 (5.9) [20.5]	7 (7.4) [25.0]	8 (9.1) [31.7]	URTI	2 (4.1) [14.0]	4 (4.4) [15.0]	5 (5.7) [19.2]
Back pain	4 (7.8) [28.1]	1 (1.1) [3.4]	0	Pruritus	5 (10.2) [37.5]	1 (1.1) [3.7]	6 (6.9) [23.6]
Headache	0	5 (5.3) [17.8]	8 (9.1) [31.6]	Psoriasis	3 (6.1) [21.4]	2 (2.2) [7.4]	3 (3.4) [11.5]
Cough	0	1 (1.1) [3.4]	5 (5.7) [18.9]	Cough	1 (2.0) [6.9]	1 (1.1) [3.7]	4 (4.6) [15.4]
Baseline to week 48 (treated with CZP set)		**CZP 200 mg Q2W, N = 100**	**CZP 400 mg Q2W, N = 144**	**Baseline to week 48 (treated with CZP set)**		**CZP 200 mg Q2W, N = 95**	**CZP 400 mg Q2W, N = 129**
Nasopharyngitis		28 (28.0) [46.4]	40 (27.8) [46.9]	Nasopharyngitis		17 (17.9) [26.4]	25 (19.4) [29.0]
URTI		12 (12.0) [17.2]	13 (9.0) [12.8]	URTI		11 (11.6) [16.1]	13 (10.1) [14.5]
Arthralgia		6 (6.0) [8.2]	2 (1.4) [1.8]	Hypertension		5 (5.3) [7.1]	8 (6.2) [8.6]
Headache		6 (6.0) [8.2]	12 (8.3) [11.7]	Urinary tract infection		5 (5.3) [7.1]	5 (3.9) [5.3]
				Pruritus		2 (2.1) [2.8]	8 (6.2) [8.8]
				Pharyngitis		6 (6.3) [8.5]	3 (2.3) [3.2]
				Bronchitis		2 (2.1) [2.7]	7 (5.4) [7.5]

Values are n (%) [incidence, new cases/100 patient-years]. Patients who switched doses could be counted in both CZP doses. Total exposure for all CZP patients from baseline to week 48 was 356.57 patient-years (CIMPASI-1 = 186.65; CIMPASI-2 = 169.92).

CZP, Certolizumab pegol; *Q2W*, every 2 weeks; *TEAE*, treatment-emergent adverse event; *URTI*, upper respiratory tract infection.

differences between the CZP treatment groups, for most outcome measures, improvement was numerically greater in the 400-mg group than in the 200-mg group, suggesting heightened efficacy at the higher dose. These studies show that CZP, a unique anti-TNF biologic, affords a novel treatment option for psoriasis patients.

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SUPPLEMENTARY APPENDIX. METHODS

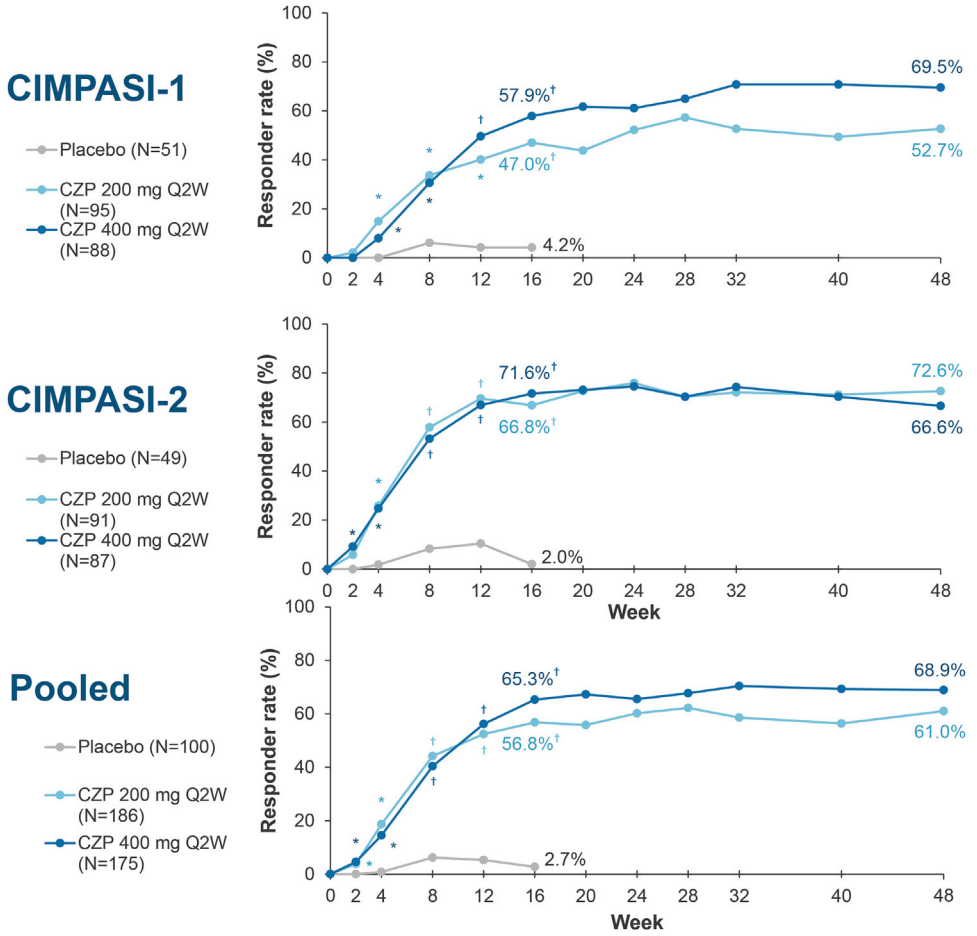
Multiple comparisons/multiplicity

The statistical analysis of the coprimary and secondary efficacy variables accounted for multiplicity and controlled the familywise type I error rate at a 2-sided alpha level of 0.05 by using a fixed-sequence testing procedure (Supplemental Fig 4). The hypotheses were mapped into 2 sets (H_1, H_3, H_5, and H_7; H_2, H_4, H_6, and H_8) such that the hypotheses within each set corresponded to the same certolizumab pegol (CZP) dose, and the type I error was split equally between CZP 400 mg every 2 weeks and CZP 200 mg every 2 weeks, such that each dose was tested at a 2-sided alpha level of 0.025.

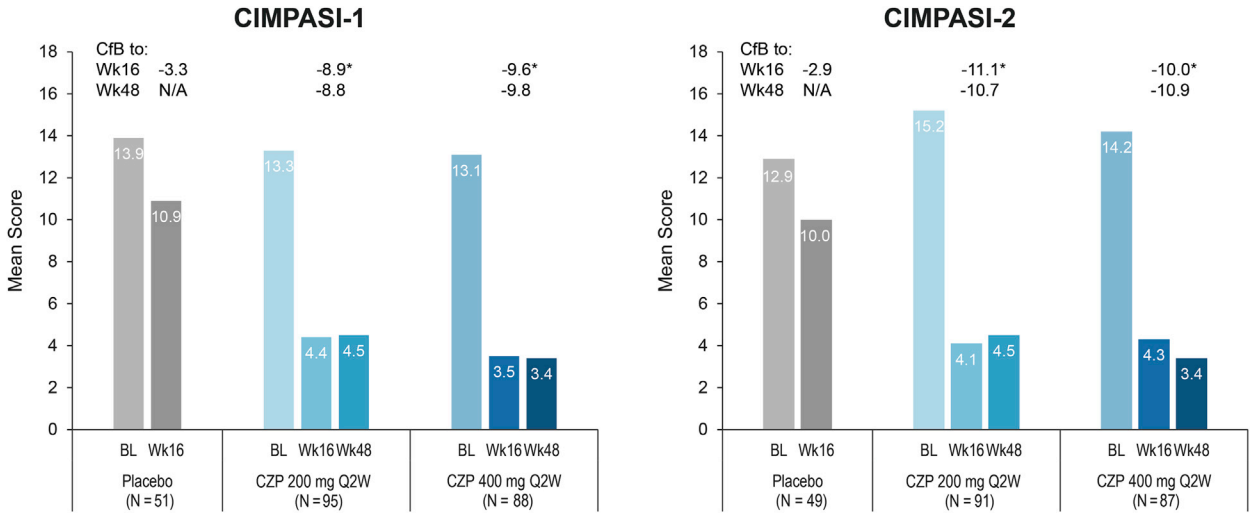
The first 2 hypotheses for each dose (H_1 and H_3 for CZP 400 mg every 2 weeks, and H_2 and H_4 for CZP 200 mg every 2 weeks) tested whether the given CZP dose was superior to placebo for PASI 75 (≥75% reduction in Psoriasis Area and Severity Index [PASI] from baseline PASI) response and Physician's Global Assessment (PGA) response at week 16. If both were rejected at a 2-sided alpha level of 0.025, then that alpha was passed to the next test in the sequence, allowing the procedure to proceed. The hypotheses associated with the subsequent tests were for the secondary efficacy endpoints and were based on testing for superiority relative to placebo. If all hypotheses within 1 set of hypotheses (either CZP 400 mg every 2 weeks or CZP 200 mg every 2 weeks) were rejected, the corresponding type I error probability was passed on to the other set of hypotheses and that set was retested, if necessary, at a 2-sided alpha level of 0.05.

RESULTS

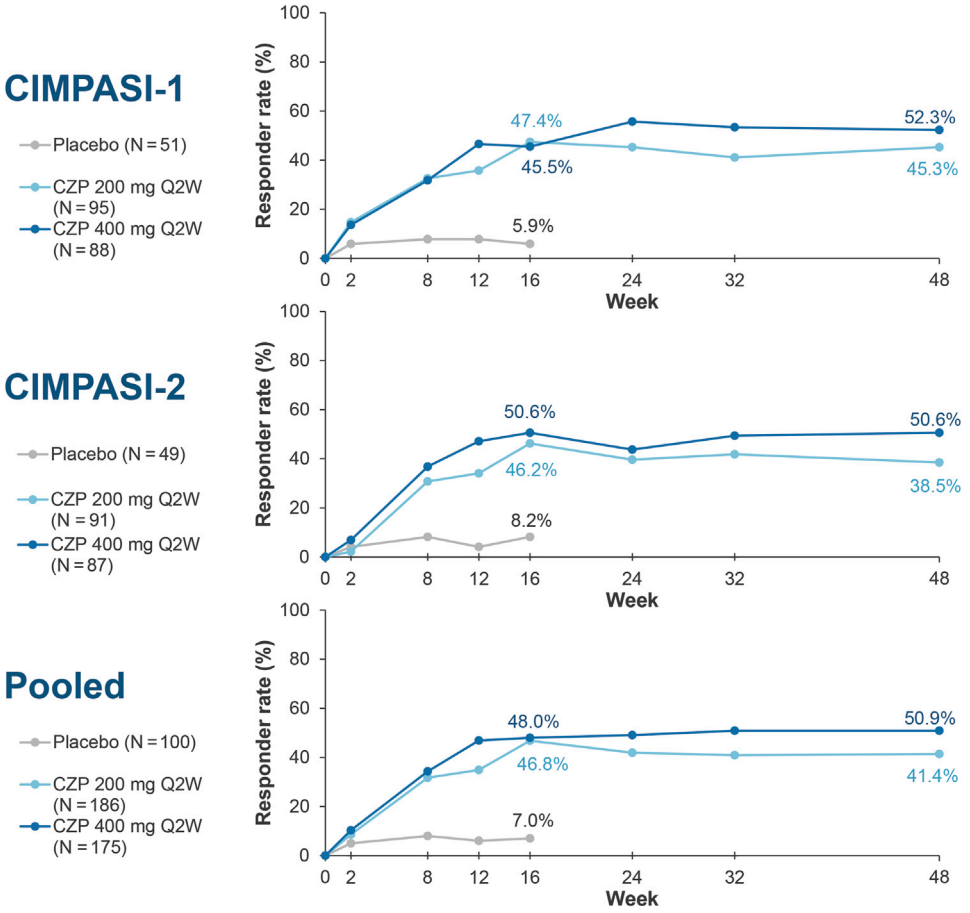
At week 16 in CIMPASI-1, PASI 100 (100% reduction in PASI from baseline PASI) responder rates were 12.7% for CZP 400 mg every 2 weeks, 13.7% for CZP 200 mg every 2 weeks, and 0.2% for placebo. By week 48, the responder rates for patients taking CZP 400 mg every 2 weeks and CZP 200 mg every 2 weeks improved to 23.6% and 21.8%, respectively. At week 16 in CIMPASI-2, PASI 100 responder rates were 18.8% for CZP 400 mg every 2 weeks, 15.4% for CZP 200 mg every 2 weeks, and 1.8% for placebo, and by week 48, they improved to 38.3% and 31.4% for CZP 400 mg every 2 weeks and CZP 200 mg every 2 weeks, respectively. Pooled data for PASI 100 showed responder rates of 14.4% for CZP 400 mg every 2 weeks, 12.7% for CZP 200 mg every 2 weeks, and 0.9% for placebo through week 16. At week 48, PASI 100 response rates in the pooled population were 34.5% for CZP 400 mg every 2 weeks and 28.5% for CZP 200 mg every 2 weeks.



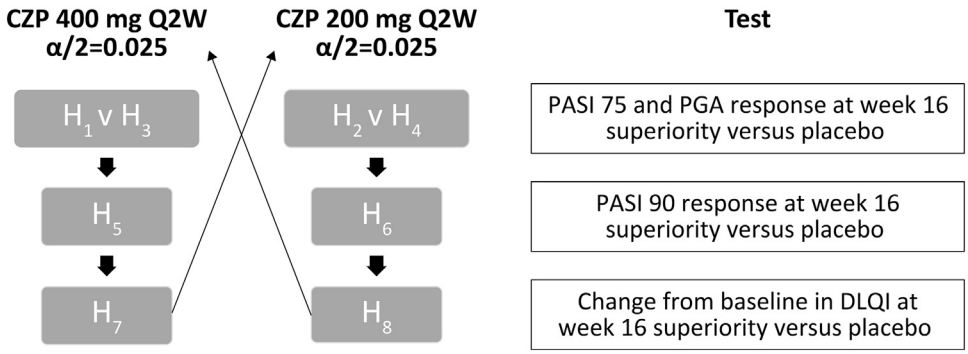
Supplemental Fig 1. PGA 0/1 responder rates of randomized patients through week 48, by visit. Patients randomized to CZP 200 mg every 2 weeks received loading doses of CZP 400 mg at weeks 0, 2, and 4. Responder rates were based on the logistic regression model.*$P < .05$ versus placebo (controlled for multiplicity at week 16 in CIMPASI-1 and CIMPASI-2). †$P < .0001$ versus placebo (controlled for multiplicity at week 16 in CIMPASI-1 and CIMPASI-2). *CZP*, Certolizumab pegol; *PGA 0/1*, Physician's Global Assessment clear/almost clear with ≥2-category improvement from baseline; *Q2W*, every 2 weeks.



Supplemental Fig 2. Change in DLQI of randomized patients at weeks 16 and 48. Patients randomized to CZP 200 mg every 2 weeks received loading doses of CZP 400 mg at weeks 0, 2, and 4. The analysis of covariance model was used. *$P < .0001$ vs placebo (controlled for multiplicity at week 16). *BL*, Baseline; *CfB*, change from baseline; *CZP*, certolizumab pegol; *DLQI*, Dermatology Life Quality Index; *Q2W*, every 2 weeks.



Supplemental Fig 3. DLQI 0/1 responder rates through week 48. Patients randomized to CZP 200 mg every 2 weeks received loading doses of CZP 400 mg at weeks 0, 2, and 4. Responder rates were based on the percentage of participants with DLQI 0/1 at each given time point (no modeling performed). *CZP*, Certolizumab pegol; *DLQI*, Dermatology Life Quality Index; *Q2W*, every 2 weeks.



Supplemental Fig 4. Fixed-sequence testing procedure. *CZP*, Certolizumab pegol; *DLQI*, Dermatology Life Quality Index; *PASI*, Psoriasis Area and Severity Index; *PASI 75*, ≥75% reduction in PASI from baseline PASI; *PASI 90*, ≥90% reduction in PASI from baseline PASI; *PGA*, Physician's Global Assessment; *Q2W*, every 2 week.

Supplemental Table I. Serious TEAEs, by dose, study phase, and trial (CIMPASI-1 and CIMPASI-2)

	CIMPASI-1			CIMPASI-2		
Category	Placebo, N = 51	CZP 200 mg Q2W, N = 100	CZP 400 mg Q2W, N = 144	Placebo, N = 49	CZP 200 mg Q2W, N = 95	CZP 400 mg Q2W, N = 129
Any serious TEAE, n (%) [incidence rate, new cases/100 patient-years]	1 (2.0) [6.8]	4 (4.0) [5.3]	11 (7.6) [10.4]	0	7 (7.4) [9.7]	7 (5.4) [7.5]
Baseline to week 16	Cholelithiasis	Splenic hematoma, rib fracture, hallucination, and hemothorax*; gastrointestinal necrosis and strangulated hernia*	Anaphylactoid reaction; injection site reaction; osteoarthritis; concussion; lymphadenitis		Depression; increase in transaminases	Basal cell carcinoma; abdominal abscess, hematoma infection, contusion, penile swelling, and scrotal swelling*; skin ulcer; chest X-ray abnormal
Week 16 to 48		Hand fracture; intervertebral disc protrusion	Basal cell carcinoma; tendon rupture; erysipelas; multiple nonsite-specific injuries; radius fracture; psoriasis		Blood count abnormal; migraine; transient ischemic attack; joint swelling; drug-induced liver injury and psoriatic arthropathy*	Benign salivary gland neoplasm; cardiac failure congestive; laryngeal cyst

CZP, Certolizumab pegol; *Q2W*, every 2 weeks; *TEAE*, treatment-emergent adverse event.
*Group of TEAEs occurred in the same patient.