Safety of Certolizumab Pegol in Plaque Psoriasis: Pooled 96-Week Data from Three Phase 3, Multicenter, Randomized, Placebo-Controlled Studies (CIMPASI-1, CIMPASI-2 and CIMPACT)

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OBJECTIVE

- To report cumulative 96-week safety data from three phase 3 trials of certolizumab pegol in plaque psoriasis.

BACKGROUND

- Plaque psoriasis (PSO) is an immune-mediated, inflammatory disease that affects around 3% of adults in the United States.[1,2]
- The Fc-free, PEGylated, anti-tumor necrosis factor (TNF) biologic certolizumab pegol (CZP) was approved by the FDA for moderate to severe PSO in 2018,[3] and has shown a safety profile consistent with the anti-TNF class in adults with PSO over 48 weeks in phase 3 trials.[4,5]
- Here, we report cumulative safety data over 96 weeks from the CZP in PSO phase 3 clinical development program.

METHODS

Patients and Study Design

- Safety data, pooled across studies, are presented for patients who received ≥1 dose of CZP during the first 96 weeks of the CIMPASI-1 (NCT02326298), CIMPASI-2 (NCT02326272), and CIMPACT (NCT02346240) phase 3 studies **(Figure 1)**.
- Only 11 placebo-randomized patients continued on placebo after Week 16; placebo data are presented to Week 16 only.
- Patient inclusion criteria: ≥18 years of age, moderate to severe PSO ≥6 months with Psoriasis Area Severity Index (PASI) ≥12, ≥10% body surface area (BSA) affected, Physician's Global Assessment (PGA) ≥3 on a 5-point scale; candidates for systemic PSO therapy, phototherapy, and/or photochemotherapy.
- Exclusion criteria: previous treatment with CZP or >2 biologics; previous treatment with etanercept (ETN) (CIMPACT only); treatment with ETN within the first 12-weeks of enrolment (CIMPASI-1 and CIMPASI-2 only); history of primary failure to any biologic or secondary failure to >1 biologic; erythrodermic, guttate or generalized PSO types; current or history of chronic or recurrent viral, bacterial or fungal infections.

Safety Assessments

- Adverse events (AEs) and serious adverse events (SAEs) were classified using MedDRA version 18.1.
- An SAE was defined as an AE meeting one or more of the following criteria: leading to death, life-threatening, leading to significant or persistent disability/incapacity, congenital anomalies/birth defects, an important medical event (based upon medical judgement) or leading to initial or prolonged inpatient hospitalization.
- Incidence rates (IR) were calculated as incidence of new cases per 100 patient-years (PY).

RESULTS

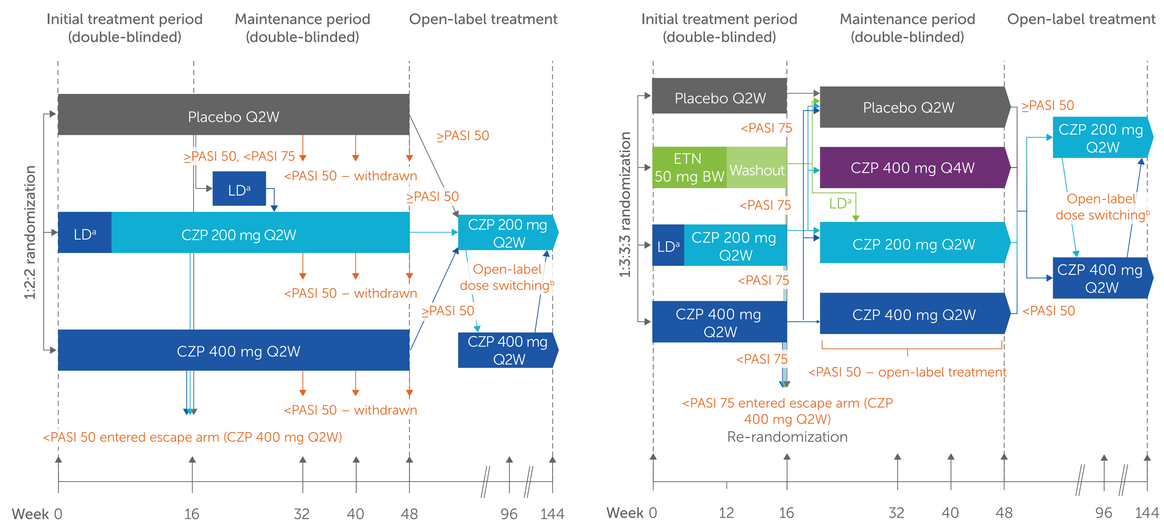
Patient Population

- Across all 3 studies, 995 patients received ≥1 dose CZP through Weeks 0–96.
- Total exposure to CZP was 1,471 PY.
- Baseline characteristics were well-balanced between treatment groups **(Table 1)**.

Incidence of AEs and SAEs

- At Week 16, the IR of AEs within both the CZP 400 mg every two weeks (Q2W) and CZP 200 mg Q2W dose groups was comparable to that of placebo **(Table 2)**.

Figure 1. CIMPASI-1, CIMPASI-2 and CIMPACT study design



[a]Loading dose of CZP 400 mg Q2W at Weeks 0, 2 and 4 or Weeks 16, 18 and 20; [b]Depending on PASI response, any dose adjustments were either mandatory or at the discretion of the Investigator. BW: twice per week; CZP: certolizumab pegol; ETN: etanercept; LD: loading dose; PASI: Psoriasis Area Severity Index; Q2W: every two weeks; Q4W: every four weeks.

Table 1. Pooled demographics and baseline characteristics for patients who received ≥1 dose CZP through Weeks 0–96

	All CZP[a] (N=995)	CZP 400 mg Q2W (N=711)	CZP 200 mg Q2W (N=726)
Patient and disease characteristics			
Age, years, mean ± SD	45.6 ± 13.2	45.7 ± 13.0	45.3 ± 13.1
Male, n (%)	652 (65.5)	463 (65.1)	487 (67.1)
BMI, kg/m², mean ± SD	30.4 ± 7.0	30.7 ± 7.2	30.2 ± 6.7
Disease duration, years, mean ± SD	18.2 ± 12.5	18.3 ± 12.4	18.5 ± 12.6
PASI, mean ± SD	20.2 ± 7.8	20.2 ± 7.7	20.2 ± 7.8
Prior treatment			
Biologic therapy, n (%)	299 (30.1)	219 (30.8)	219 (30.2)
Anti-TNF	122 (12.3)	87 (12.2)	91 (12.5)
Anti-IL-17	149 (15.0)	106 (14.9)	109 (15.0)
Anti-IL-12/IL-23	49 (4.9)	42 (5.9)	30 (4.1)
Prior systemic therapy for psoriasis, n (%)	714 (71.8)	519 (73.0)	526 (72.5)

[a]Patients who received both CZP 200 mg Q2W and CZP 400 mg Q2W are only included once in the population count for the 'All CZP' group. BMI: body mass index; CZP: certolizumab pegol; IL: interleukin; PASI: Psoriasis Area Severity Index; Q2W: every two weeks; SD: standard deviation; TNF: tumor necrosis factor.

Table 2. Cumulative AEs over time at Weeks 16, 48 and 96

	n/N (%) IR (95% CI)			
	All CZP[a]	CZP 400 mg Q2W	CZP 200 mg Q2W	Placebo
Week 16	414/692 (59.8) 319.1 (289.1, 351.4)	217/342 (63.5) 348.3 (303.5, 397.9)	197/350 (56.3) 292.1 (252.8, 335.9)	97/157 (61.8) 342.6 (277.8, 417.9)
Week 48	709/962 (73.7) 219.6 (203.7, 236.4)	444/627 (70.8) 228.6 (207.8, 250.9)	321/460 (69.8) 221.2 (197.6, 246.7)	-
Week 96	820/995 (82.4) 172.7 (161.1, 184.9)	528/711 (74.3) 186.4 (170.9, 203.0)	514/726 (70.8) 161.4 (147.8, 176.0)	-

[a]Patients who received both CZP 200 mg Q2W and CZP 400 mg Q2W are only included once in the population count for the 'All CZP' group. AE: adverse event; CI: confidence interval; CZP: certolizumab pegol; IR: incidence rate per 100 patient-years; Q2W: every two weeks.

Table 3. Overview of AEs and SAEs to Week 96

	All CZP[a] (N=995)	CZP 400 mg Q2W (N=711)	CZP 200 mg Q2W (N=726)
Exposure (PY)	1,471	700	772
Total AEs, IR (95% CI)	172.7 (161.1, 184.9)	186.4 (170.9, 203.0)	161.4 (147.8, 176.0)
Total SAEs, IR (95% CI)	9.2 (7.7, 10.9)	10.8 (8.5, 13.7)	7.7 (5.9, 10.0)
Most commonly reported AEs (≥10% patients),[b] IR (95% CI)			
Nasopharyngitis	19.0 (16.6, 21.6)	21.8 (18.3, 25.9)	19.4 (16.2, 23.1)
Upper respiratory tract infection	10.3 (8.6, 12.2)	11.9 (9.4, 14.9)	9.6 (7.4, 12.1)
Selected AEs and SAEs of interest, IR (95% CI)			
Serious infections	1.7 (1.1, 2.5)	1.7 (0.9, 3.0)[c]	1.6 (0.8, 2.7)[d]
Active tuberculosis	0.1 (0.0, 0.4)	0.1 (0.0, 0.8)	0.0
Primary progressive multiple sclerosis	0.1 (0.0, 0.4)	0.1 (0.0, 0.8)	0.0
Congestive heart failure	0.1 (0.0, 0.4)	0.1 (0.0, 0.8)	0.0
Malignancies (excluding non-melanoma skin cancer)	0.5 (0.2, 1.1)	0.6 (0.2, 1.5)[e]	0.7 (0.2, 1.5)[f]
Non-melanoma skin cancer	0.2 (0.0, 0.6)	0.4 (0.1, 1.3)[g]	0.0
Discontinuations due to AEs, IR (95% CI)	4.3 (3.3, 5.5)	5.5 (3.9, 7.5)	3.4 (2.2, 5.0)
Severe AEs, IR (95% CI)	7.4 (6.0, 9.0)	8.6 (6.5, 11.1)	6.6 (4.8, 8.7)
AEs leading to death, IR (95% CI)	0.3 (0.1, 0.7)	0.3 (0.0, 1.0)[h]	0.3 (0.0, 0.9)[i]

[a]Patients who received both CZP 200 mg Q2W and CZP 400 mg Q2W are only included once in the population count for the 'All CZP' group; [b]Other commonly reported AEs (≥5% patients) included arthalgia, headache, psoriasis and hypertension; [c]Two each of pneumonia, erysipelas, and one each of abdominal abscess, appendicitis, *Escherichia* sepsis, endophthalmitis, ovarian abscess, *Klebsiella* pneumonia, bronchitis, bacteraemia, sepsis, tuberculosis, pyelonephritis, haematoma infection; [d]Two cellulitis events and one each of gastroenteritis, pancreas infection, Borrelia infection, Bartholin's abscess, Varicella, infected bite, pneumonia, bronchitis, pyoderma, urinary tract infection; [e]One each of adenocarcinoma of the colon, anaplastic oligodendroglioma, prostate cancer, clear cell renal cell carcinoma; [f]One each of breast cancer, glioblastoma, Hodgkin's disease, laryngeal cancer, prostate cancer; [g]Two basal cell carcinoma, one keratoacanthoma; [h]One craniocerebral injury and one multiple injuries, both assessed as unrelated to study drug; [i]One chronic obstructive pulmonary disease assessed as unrelated to study drug, one patient experienced distributive shock, cardiac arrest, hepatic failure and disseminated intravascular coagulation and death was assessed as related to the study drug by the Investigator. AE: adverse event; CI: confidence interval; CZP: certolizumab pegol; IR: incidence rate; PY: patient-years; Q2W: every two weeks; SAE: serious adverse event; TNF: tumor necrosis factor.

- The IR of AEs did not increase over time to Week 96 for patients receiving CZP **(Table 2)**.
- At Week 96, the IR of SAEs was comparable between the two CZP dose groups **(Table 3)**.

Selected AEs and SAEs of Interest

- At Week 96, the overall incidence of selected AEs and SAEs of interest was low **(Table 3)**.
- There were 4 deaths, 1 of which in the CZP 200 mg Q2W dose group was assessed by the Investigator as related to the study drug **(Table 3)**.
- There were no reports of serious skin disorders such as Steven Johnson or Lupus.

CONCLUSIONS

- The overall incidence of AEs and SAEs of interest was low and the IR of SAEs was comparable between the two dose groups.
- Risk did not increase with longer exposure.
- No new safety signals were identified compared with previous studies in CZP.
- The safety profile of CZP dosed at both 400 mg and 200 mg Q2W was consistent with the anti-TNF class in PSO.

References

1. Kurd SK and Gelfand JM. JAAD 2009;60:218–24; **2.** Rachakonda TD. *et al.* 2014;70:512–6; **3.** Certolizumab Pegol Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125160s270lbl.pdf [Last accessed: May 2019]; **4.** Gottlieb AB. *et al.* JAAD 2018;79:302–14.e6; **5.** Lebwohl M. *et al.* JAAD 2018;79:266–76.e5.

Author Contributions

Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: AB, BS, RL, SK, CA, MB, ML, KR; Drafting of the publication, or revising it critically for important intellectual content: AB, BS, RL, SK, CA, MB, ML, KR; Final approval of the publication: AB, BS, RL, SK, CA, MB, ML, KR.

Author Disclosures

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