

LETTER TO THE EDITOR

Certolizumab pegol for plaque psoriasis in women of childbearing potential, pregnant or breastfeeding in clinical settings: One-year outcomes from the international noninterventional CIMREAL study

Dear Editor,

Psoriasis onset in women often overlaps with the peak reproductive age (18 and 45 years).¹ This presents unique challenges in the management of psoriasis in women of childbearing potential (WoCBP). Certolizumab pegol (CZP), a TNF inhibitor which lacks the Fc region of the IgG molecule resulting in no-to-minimal transfer across the placenta or into breast milk, is recommended for WoCBP, including those who are pregnant or breastfeeding.^{2,3} However, real-world data on its effectiveness and safety in these populations are limited.

In CIMREAL, a prospective, noninterventional study across nine countries in Europe and Canada (2019–2022), the effectiveness and safety of CZP were evaluated in patients with moderate to severe psoriasis. Out of 399 patients, 272 were women.⁴ This report here focuses on WoCBP ($n=193$), including pregnant patients ($n=24$) and breastfeeding patients ($n=12$), to provide real-world insights into these underreported populations.

Improvements in Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) outcomes were noted over a 1-year period in WoCBP, pregnant and breastfeeding women. These improvements were more pronounced in WoCBP and pregnant cohorts when adhering to the on-label CZP dosing. PASI and DLQI assessments were conducted for the full analysis set (Table 1). Despite the differences in BMI (6 with BMI >30, 9 with BMI >25), prior biologic exposure (11 with prior use and 6 exposed to two biologics during pregnancy) and initial CZP exposure in various stages of pregnancy (14 preconception, 1 in the first and 6 in the second trimester), consistent disease control, indicating drug effectiveness and treatment adherence was observed at all time points in the pregnant cohort.

In the WoCBP cohort, 36.3% experienced adverse events (AEs), with 13% having serious AEs. The most common AEs were related to drug ineffectiveness (10.9%), peri-pregnancy events (10.4%) and COVID-19 infection (5.2%). No new safety issues were reported.⁴

Of the 15 known pregnancy outcomes, 13 were live births (86.6%, including 3 preterm births), 1 was a spontaneous abortion and 1 an ectopic pregnancy. Existing literature shows a 2.5% higher risk of ectopic pregnancy in women with moderate to severe psoriasis.⁵ No congenital malformations or serious neonatal complications were reported. These data align with UCB pharmacovigilance data for CZP-exposed pregnancies, indicating similar outcomes to the general population.⁶ Table 2 provides details on individual patient characteristics and pregnancy outcomes.

Female sex is an established risk factor for treatment discontinuation in psoriasis.⁷ However, we observed a moderate to low discontinuation rate (20.2%) and a high cumulative probability of on-drug survival (87.5% by Kaplan–Meier analysis) in the WoCBP cohort at 1 year, suggesting that patients experienced sustained therapeutic benefit of CZP in a real-world setting. The pregnancy cohort had a slightly higher discontinuation rate (26.1%) than WoCBP, likely due to concerns about fetal harm. In contrast, the literature reports 77.6% discontinuation rate for biologic treatments during pregnancy,⁸ likely increasing the risk of disease flares⁹ or adverse pregnancy outcomes.¹⁰

Our study has limitations inherent in its exploratory nature. CIMREAL was not specifically designed for WoCBP, and subgroup analyses lacked adjustment for confounders. Incomplete data on pregnancy outcomes, a small sample size for pregnant and breastfeeding women and reliance on investigator-determined WoCBP and self-reported pregnancy may limit the generalizability and accuracy of the findings.

This analysis of the CIMREAL data is the first to demonstrate the effectiveness and safety of CZP in women of childbearing potential, including pregnant and breastfeeding patients. CZP provides effective psoriasis control with minimal fetal drug exposure during pregnancy and breastfeeding. Overall, these findings may facilitate informed discussions between physicians and patients

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TABLE 1 PASI and DLQI outcomes (full analysis set).

Outcomes	WoCBP ^a			Pregnancy ^b			Breastfeeding ^c		
	Baseline	Month 3	Month 12	Baseline	Month 3	Month 12	Baseline	Month 3	Month 12
PASI, mean ± SD	13.0 ± 8.5 [n = 178]	4.0 ± 4.5 [n = 150]	1.7 ± 2.7 [n = 135]	8.7 ± 5.6 [n = 23]	2.7 ± 4.0 [n = 18]	2.0 ± 2.0 [n = 15]	16.5 ± 8.9 [n = 10]	2.7 ± 2.1 [n = 9]	1.8 ± 2.7 [n = 7]
PASI 75 response (95% CI)	48.3 (40.6–56.0) [n = 150]	71.7 (64.4–79.0) [n = 135]	–	–	–	–	–	–	–
PASI 90 response (95% CI)	27.3 (20.4–35.2) [n = 150]	60.0 (51.2–68.3) [n = 135]	–	–	–	–	–	–	–
PASI ≤3 (95% CI)	54.7 (46.3–62.8) [n = 150]	82.2 (74.7–88.3) [n = 135]	66.7 (41.0–86.7) [n = 18]	73.3 (44.9–92.2) [n = 15]	55.6 (21.2–86.3) [n = 9]	85.7 (42.1–99.6) [n = 7]	–	–	–
PASI ≤3 adhering to CZP (95% CI)	61.8 (51.6–71.2) [n = 102]	86.9 (79.0–92.7) [n = 107]	70.0 (34.8–93.3) [n = 10]	100.0 (54.1–100) [n = 6]	60.0 (14.7–94.7) [n = 5]	66.7 (9.4–99.2) [n = 3]	–	–	–
PASI ≤2 (95% CI)	46.0 (37.8–54.3) [n = 150]	74.1 (65.8–81.2) [n = 135]	61.1 (35.7–82.7) [n = 18]	66.7 (38.4–88.2) [n = 15]	44.4 (13.7–78.8) [n = 9]	71.4 (29.0–96.3) [n = 7]	–	–	–
PASI ≤2 adhering to CZP (95% CI)	50.0 (39.9–60.1) [n = 102]	80.4 (71.6–87.4) [n = 107]	60.0 (26.2–87.8) [n = 10]	100.0 (54.1–100) [n = 6]	60.0 (14.7–94.7) [n = 5]	66.7 (9.4–99.2) [n = 3]	–	–	–
DLQI, mean ± SD	13.2 ± 7.3 [n = 164]	5.5 ± 5.5 [n = 143]	2.5 ± 3.7 [n = 125]	11.9 ± 8.2 [n = 23]	3.9 ± 4.4 [n = 18]	4.1 ± 4.2 [n = 14]	18.4 ± 8.5 [n = 10]	4.9 ± 5.7 [n = 9]	4.9 ± 7.6 [n = 7]
DLQI 0/1 (95% CI)	28.0 (20.8–36.1) [n = 143]	56.0 (46.8–64.9) [n = 125]	44.4 (21.5–69.2) [n = 18]	42.9 (17.7–71.1) [n = 14]	44.4 (13.7–78.8) [n = 9]	57.1 (18.4–90.1) [n = 7]	–	–	–
DLQI 0/1 adhering to CZP (95% CI)	27.8 (19.2–37.9) [n = 97]	58.2 (47.8–68.1) [n = 98]	44.4 (13.7–78.8) [n = 9]	50 (11.8–88.2) [n = 6]	40 (5.3–85.3) [n = 5]	66.7 (9.4–99.2) [n = 3]	–	–	–

Abbreviations: CI, confidence interval; CZP, certolizumab pegol; DLQI, Dermatology Life Quality Index; OC, observed cases; PASI, Psoriasis Area and Severity Index; SD, standard deviation; WoCBP, women of childbearing potential.

^aFull analysis set, all patients who received at least one dose of CZP, provided valid consent and had a valid baseline and at least one post-baseline PASI measurement; 178 of 193 WoCBP were included in the full analysis set.

^b23 of 24 women with reported pregnancy during the study were included in the full analysis set; one patient was not considered due to missing data. Of these, 19 pregnancies were reported prospectively and four retrospectively.

^c10 of 14 women with reported breastfeeding at baseline were included in the full analysis set. Two were excluded because they became pregnant during the study and were included in the pregnancy cohort and two were not considered due to missing data.

TABLE 2 Patient characteristics and pregnancy outcomes in individual patients (safety analysis set).

Patients	BMI (kg/m ²)	Age (years)/duration PSO (years)	Previous and ongoing medical conditions	Previous biologic	Maintenance dose (400 mg Q2W) ^a	CZP exposure			Pregnancy outcomes	Neonatal outcomes (weight)
						Pre-conceived	First trimester	Second trimester		
1 ^b	31.4	32/18	PsA	No	No	Yes	Yes	Yes	Live birth (39 weeks)	2680 g
2	21.1	29/17	HBV, bilateral kidney cyst	ETA, SEC	No	NA	NA	NA	NA	NA
3 ^{cd}	43.3	34/20	Hypertension	ADA	No	No	Yes	Yes	Pre-term live birth (34 weeks)	NA
4	26.8	25/10	Multiple allergies, depression, anxiety and back pain	ETA, ADA UST	Yes	Yes	NA	NA	NA	NA
5 ^b	27.2	30/3	Urticaria	GUS	Yes	Yes	NA	NA	NA	NA
6 ^{b,c,d}	54.1	34/1	GERD, PsA and GD	ADA	Yes	No	Yes	Yes	NA	NA
7	25.4	31/4	Oligomenorrhoea and PCOS	No	Yes	Yes	Yes	Yes	Pre-term live birth, (36 weeks)	1810 g
8	30.1	37/NA	No	No	No	NA	NA	NA	NA	NA
9 ^c	18.4	27/17	Prophylaxis COVID-19	BRO	No	Yes	Yes	Yes	NA	NA
10 (excluded from efficacy analysis)	23.3	26/16	Lower lip herpes and toes acrosyndrome	ADA, UST	No	Yes	Yes	Yes	Live birth (38 weeks)	3190 g
11	29.0	36/4	No	No	No	Yes	Yes	Yes	Live birth (39 weeks)	3500 g
12	15.8	31/6	No	No	No	Yes	Yes	Yes	Live birth (39 weeks)	3065 g
13 ^d	35.6	31/16	Hypothyroidism	No	No	Yes	NA	No	Ectopic pregnancy and induced abortion	NA
14	20.8	34/29	No	No	Yes	Yes	NA	No	NA	NA
15 ^c	25.6	35/18	No	IXE	No	No	Yes	Yes	Pre-term live birth, 35 weeks	2700 g
16	21.3	37/11	No	UST	No	Yes	Yes	Yes	Live birth (38 weeks)	3850 g
17 ^d	NA	35/0	Hypothyroidism and PsA ^e	No	No	Yes	Yes	No	Spontaneous abortion at 9 weeks 3d (not related to CZP)	NA
18	27.4	27/2	No	No	No	Yes	Yes	Yes	Live birth	3620 g
19	27.1	25/13	No	UST, ADA	No	Yes	Yes	Yes	Live birth (40 weeks)	2780 g

TABLE 2 (Continued)

Patients	BMI (kg/m ²)	Age (years)/duration PSO (years)	Previous and ongoing medical conditions	Previous biologic	Maintenance dose (400 mg Q2W) ^a	CZP exposure			Pregnancy outcomes	Neonatal outcomes (weight)
						Pre-conceived	First trimester	Second trimester		
20	24.6	26/15	Syringomyelia, scoliosis and acne	No	No	Yes	Yes	NA	NA	NA
21	24.1	33/10	No	No	No	Yes	Yes	NA	NA	NA
22	27.7	32/25	No	No	Yes	No	No	Live birth (39 weeks)	3492 g	
23 ^c	25.5	31/15	Charcot marie tooth disease, anxiety and depression	ADA, UST	Yes	No	Yes	Live birth (38 weeks)	2785 g	
24 ^c	39.9	25/20	PCOS	ETA, ADA, IFX, GUS	Yes	No	Yes	Live birth (40 weeks)	2290 g	

Note: Safety analysis set: all WoCBP patients who received at least one dose of CZP and provided valid consent; The green highlights reflect patients who reported receiving CZP during the entire pregnancy plus preconception.

Abbreviations: ADA, adalimumab; BMI, body mass index; BRO, brodalumab; COVID-19, coronavirus disease; CZP, certolizumab pegol; ETA, etanercept; GD, gestational diabetes; GERD, gastroesophageal reflux disease; GUS, guselkumab; HBV, hepatitis B virus; IFX, infliximab; IXE, ixekizumab; NA, not available; PCOS, polycystic ovary syndrome; PsA, psoriatic arthritis; PSO, plaque psoriasis; Q2W every 2 weeks; SEC, secukinumab; UST, ustekinumab.

^aMaintenance dose at baseline.

^bGestational diabetes during pregnancy, with two of them being obese and one overweight.

^cThese patients were switched to CZP during pregnancy.

^dPregnancy reported retrospectively.

^ePrevious and ongoing medical conditions were not reported at baseline but reported retrospectively.

regarding management of psoriasis during this sensitive period in a woman's life.

ACKNOWLEDGEMENTS

The authors and UCB express their gratitude to the patients, investigators and staff involved in this study. Thanks to Dr. Etomi Oseme for valuable insights and to SreeHarsha B. and Dhanya M. from Enago Life Sciences, India for medical writing support.

FUNDING INFORMATION

This study was funded in full by UCB Pharma.

CONFLICT OF INTEREST STATEMENT

TH received consultancy, speaker fees and/or research funding from AbbVie, Ammirall, Amgen, Biogen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer Inc., Roche, Sandoz, Sanofi and UCB Pharma. FL received consultancy, speaker fees and/or research funding from AbbVie, Amgen, Bausch Health, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer Inc., Sandoz, Sanofi, Sun Pharma and UCB Pharma. TB received consulting fees from Abbvie, Eli Lilly, Janssen, Leo Pharma, Novartis and Pfizer; participated in clinical studies for Abbvie, Amgen, Eli Lilly, Janssen, Leo Pharma, Novartis and Pfizer; participated in clinical studies for Abbvie, Amgen, Eli Lilly, Janssen, Leo Pharma, Novartis and UCB Pharma. LB received speaker, research grants and participation in advisory Board from Abbvie, Amgen, Biogen, Eli Lilly, Janssen, Novartis, Sanofi Genzyme and UCB Pharma. AF conducted clinical trials and acted as a speaker and consultant for Abbvie, Ammirall, Amgen, Celgene, Eli Lilly, Janssen, Kyowa Hakko Kirin, Leo Pharma, Novartis, Pfizer, Roche Farma, Sanofi, Sun Pharma, Takeda and UCB Pharma. AB received consultancy fees from Abbvie, Ammirall, Bristol Myers Squibb, Leo Pharma, Novartis, Pfizer and UCB; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Abbvie, Ammirall, Bristol Myers Squibb, Eli Lilly and Company, Janssen, Leo Pharma, Novartis, Pfizer, UCB and Thornton & Ross; support for attending recent Dermatology Congress (travel, accommodation and registration) from Ammirall, Lilly, Abbvie, Novartis, Janssen, Biofrontera and UCB. KA received honoraria for participation in advisory boards, consultation, clinical trials or as speaker from Abbvie, Ammirall, Antabio, Bayer, Brand Murray Fuller, Bristol Myers Squibb, Emeritipharma, Emphasis, Euroimmune, Galderma, Janssen, La Roche-Posay, Leo, L'Oréal, Novartis, Parexel International, Pierre Fabre, RG Pharma, Roxall, Sanofi Genzyme, TFS Trial Form Support and UCB Pharma. IDP, FF, JH and PW are employees and shareholders of UCB Pharma. EP reports no conflicts of interest in this work.

DATA AVAILABILITY STATEMENT



Underlying data from this manuscript are outside of UCB's data sharing policy and are not available for sharing.

ETHICAL APPROVAL

Reviewed and approved by the respective ethics committees of all participating centres.

ETHICS STATEMENT

CIMREAL was conducted in accordance with the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines and with the Helsinki Declaration of 1975, as revised in 1983. The patients in this manuscript have given written informed consent to the publication of their case details.

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[Correction added on 24 December 2024, after first online publication: Flórez Ángeles, Jackie Hee and Paulette Williams have been corrected to Flórez Menéndez Ángeles, Hee Jackie and Williams Paulette, respectively.]

[Correction added on 22 January 2025, after first online publication: the authors' surname and forename have been corrected.]