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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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 2010,3 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 a cumulative safety data over 96 weeks in the CZP in PsO phase 3 clinical development programs.

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 (NCT02322672), and CIMPACT (NCT02456420) 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.
- Exclusion criteria: previous treatment with CZP or ≥2 biologics; previous treatment with etanercept (ETN) (TNF inhibitor 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 the study drug; 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 systemic PSO therapy, phototherapy, and/or photochemotherapy).
- Exclusion criteria: previous treatment with CZP or ≥2 biologics; previous treatment with etanercept (ETN) (TNF inhibitor 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 the study drug.

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).

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CZP 200 mg Q2W (N=726)</th>
<th>CZP 400 mg Q2W (N=726)</th>
<th>CZP 200 mg Q4W (N=995)</th>
<th>Flexera</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.8 (7.0)</td>
<td>51.1 (6.8)</td>
<td>51.4 (6.9)</td>
<td>51.0 (6.8)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>57.5</td>
<td>56.7</td>
<td>58.5</td>
<td>62.7</td>
</tr>
<tr>
<td>Psoriasis disease duration (years)</td>
<td>12.6 (7.7)</td>
<td>12.7 (7.7)</td>
<td>12.6 (7.7)</td>
<td>12.7 (7.7)</td>
</tr>
<tr>
<td>Prior systemic therapy (%)</td>
<td>46.2</td>
<td>47.8</td>
<td>49.6</td>
<td>58.4</td>
</tr>
<tr>
<td>Anticoagulant therapy (%)</td>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Exposed to methotrexate (%)</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>Total AEs, IR (95% CI)</th>
<th>Serious AEs, IR (95% CI)</th>
<th>Discontinuations due to AEs, IR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 16</td>
<td>122 (12.3)</td>
<td>9 (0.9)</td>
<td>4 (0.4)</td>
</tr>
<tr>
<td>Week 48</td>
<td>254 (28.3)</td>
<td>20 (2.1)</td>
<td>7 (0.7)</td>
</tr>
<tr>
<td>Week 96</td>
<td>342.6 (36.5)</td>
<td>29 (3.0)</td>
<td>9 (0.9)</td>
</tr>
</tbody>
</table>

Table 3. Overview of AEs and SAEs to Week 96

- 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 who 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


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

- AB: Consulting honoraria and clinical investigator: AbbVie, Actis, Akros, Allergan, Almirall, Avenger, Boehringer Ingelheim, Bristol-Myers Squibb/GlaxoSmithKline, Celgene, Dermirva, Dermira, Eli Lilly, Galderma, Genentech/Roche, GSK, Janssen, LEO Pharma, Meijl, Merck, Novartis, Pfizer, Purdue Pharma, Regeneron, Sanofi, Sun Pharma, UCB Pharma, Valeant, Vidac. Speaker’s fees: Eli Lilly, Janssen, Regeneron, Sanofi/Genevy; BS: Consulting fees and/or other honoraria: AbbVie, Amirial, Amgen, AstreZeneca, Boehringer Ingelheim, Celgene, Dermirva Inc., Janssen, Eli Lilly, LEO Pharma, Medac, Meno Therapeutics, Novartis. Pfizer, GSK, UCB, Pharma, Sun Pharma, Ortho Dermatologici/ Valeant, Regeneron, Sanofi Genzyme; CORRONA Psoriasis Registry; Grant Support to the University of Connecticut for Fellowship Program (to the University of Connecticut, not BS); AbbVie, Janssen, RL: Consulting fees and/or other honoraria: AbbVie, Amgen, Boehringer Ingelheim International GmbH, Centocor, Pfizer, Janssen, LEO Pharma, El Lilly, Valenta, SK, CA, MB; Employes of UCB Pharma; ML, Consultant for Allergan, Aqua, LEO Pharma, Promius. Employee of Mount Sinai which receives research funds from Abbvie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen/Johnson & Johnson, Kadmon, Medimmune/Astra Zeneca, Novartis, Pfizer, Valeant, Vidac; KR; Advisor and/or paid speaker and/or clinical investigator for AbbVie, Abbttle, Amgen, Biogen, Biokin, Boehringer Ingelheim, Celgene, Centocor/Covegen, Forward Pharma, GSK, Janssen/Cliaq, Nyqua Kirin, LEO Pharma, El Lilly, Medac, Marck, Sharp & Dohme Corp, Novartis, Ocean Pharma, Pfizer, Regeneron, Samsung Bioepis, Sanofi, Takeda, UCB Pharma, Xanadot. Acknowledgements

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