OBJECTIVE
To report cumulative three-year safety data in plaque psoriasis.

BACKGROUND
Cer tolizumab pegol (CZP) is an Fc-free, PEGylated, anti-tumor necrosis factor (TNF) biologic, which has been approved by the FDA and EMA for moderate to severe plaque psoriasis (PASI).11
CZP has shown a safety profile consistent with the anti-TNF class in adults with PASO over 96 weeks in phase 3 trials.3
Given that PSO is a chronic disease that can require management over much of a patient’s lifetime, it is important to establish the long-term safety profile of treatments.4
Here, we report cumulative safety data, pooled from three CZP phase 3 trials over 144 weeks, from a total of 995 patients.

METHODS
Patients and Study Design
Pooled safety data are presented for patients who received ≥1 dose of CZP during the 144 weeks of the CIMPASI-1 (NCT0232698), CIMPASI-2 (NCT0232672), or CIMPACT (NCT02546240) phase 3 studies (Figure 1).
Only 11 placebo-randomized patients continued on placebo after Week 16; placebo data are presented to Week 16 only.
Inclusion criteria: ≥18 years of age with PASO for ≥6 months with PASI Area and Severity Index (PASI) ≥12; ≥10% body surface area (BSA) affected, physician’s global assessment (PGA) >0 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, history of or current, chronic or recurrent viral, bacterial or fungal infections.

Safety Assessments
Safety data were analyzed for the dose–combined CZP-treated group (All CZP) and separately for each CZP dose.
For patients exposed to both doses of CZP over the course of the studies, treatment-emergent adverse events (TEAEs) were attributed to the dose being received at the time of onset, but each patient was counted in the All CZP group only.3
TEAEs and serious TEAEs were classified using MedDRA version 18.1.
Serious TEAEs were defined as those meeting one or more of the following criteria: life-threatening, leading to death, hospitalization, congenital anomalies/birth defects, medically significant (based upon medical judgement), infections requiring intravenous antibiotics, or leading to persistent or significant disability.
Incidence rates (IR) were calculated as the number of new cases per 100 patient-years (PY).

RESULTS
Patient Population
Across all three studies, a total of 995 patients received ≥1 dose CZP through Weeks 0–144.
Baseline characteristics were well balanced between the two treatment groups (Table 1).
Incidence of TEAEs
At Week 144, the IR of TEAEs and serious TEAEs was comparable between CZP dose groups (Table 2).
The most common TEAEs reported in >10% of patients, were nasopharyngitis (IR: 14.2; 95% CI: 12.5, 16.0) and upper respiratory tract infection (IR: 7.9; 95% CI: 6.7, 9.3).
The IR of TEAEs for CZP-treated patients did not increase with longer exposure (Table 3).
Selected TEAEs and Serious TEAEs of Interest
At Week 144 the overall incidences of selected TEAEs of interest and serious TEAEs of interest were low and were comparable between dose groups (Table 4).
There were 7 deaths, 2 of which were assessed by the investigator as related to the study drug (Table 2).
The IRs of serious infections and malignancies were low, and were comparable between dose groups (Table 4).
There was 1 case of active tuberculosis (TB) in a patient who lived in a country with a high TB prevalence (Table 4).
There were no reports of serious skin disorders or hypersensitivity reactions, and no cases of lupus or lupus-like events.

CONCLUSIONS
No new safety signals were identified compared to previous studies in CZP.
The risk of TEAEs did not increase with longer or higher CZP exposure.
The safety profiles of the two CZP dose groups were similar.

References
2. Gisondi P. Incidence rates (IR) were calculated as the number of persistent or significant disability.
3. Patients exposed to both doses of CZP over the course of the studies, treatment-emergent adverse events (TEAEs) were attributed to the dose being received at the time of onset, but each patient was counted in the All CZP group only.
4. There were 7 deaths, 2 of which were assessed by the investigator as related to the study drug.
5. The IR of TEAEs for CZP-treated patients did not increase with longer exposure.
6. No new safety signals were identified compared to previous studies in CZP.
7. The risk of TEAEs did not increase with longer or higher CZP exposure.
8. The safety profiles of the two CZP dose groups were similar.

Author Contributions
Substantial contributions to study conception/design, acquisition/analysis/interpretation of data: AB, CB, GL, AG, AC, RO, CH, MR, RL. Drafting of the manuscript, or revising critically for important intellectual content: AB, CB, GL, AG, AC, RO, CH, MR, RL. Final approval of the manuscript: AB, CB, GL, AG, AC, RO, CH, MR, RL.

Author Disclosures
All authors: No relationships relevant to the submitted work. This article does not contain any identified individual patient data. The authors have no conflicts of interest to disclose.

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