C87080, 2007-000830-38

CLINICAL STUDY REPORT SYNOPSIS

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Sponsor:

UCB Pharma S.A.

Allée de la Recherche 60

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Belgium

Official study title:

A Phase IIIB, Multi-centre Open Label, Follow-Up Study to Evaluate the Safety and Efficacy of Certolizumab Pegol Administered Concomitantly with DMARDs in Subjects with Active Rheumatoid Arthritis who Participated in the Study C87076

CLINICAL STUDY REPORT SYNOPSIS: C87080

Name of company: UCB Pharma S.A.	**Individual study table referring to part of the dossier:** Not applicable	*(For National Authority Use Only)*
Name of finished product: Cimzia®	**Volume**: Not applicable	
Name of active ingredient: Certolizumab pegol (CZP)	**Page:** Not applicable	

Title of study: A Phase IIIB, Multi-centre Open Label, Follow-Up Study to Evaluate the Safety and Efficacy of Certolizumab Pegol Administered Concomitantly with DMARDs in Subjects with Active Rheumatoid Arthritis who Participated in the Study C87076

Investigators: This was a multicenter study; 25 Investigators enrolled subjects

Study sites: Subjects were enrolled at 25 centers in 5 countries ([redacted] and [redacted])

Publication(s) (reference[s]): None

Study period: **First subject enrolled:** 27 Jan 2009 **Last subject completed:** 14 Dec 2012	**Phase of development:** Phase 3B

Objective(s): The primary objective of this study was to continue to assess the safety of certolizumab pegol (CZP) in combination with disease-modifying antirheumatic drug (DMARD) treatment.

The secondary objectives of this study were:

The following efficacy, pharmacokinetic (PK), and immunological variables assessed throughout the entire Treatment Period:

- Proportion of subjects in clinical remission defined as:
  - Disease activity score 28-joint count erythrocyte sedimentation rate (DAS28[ESR])
  - Clinical Disease Activity Index (CDAI)
  - Simplified Disease Activity Index (SDAI)
- Reduction of signs and symptoms of the disease as measured by the American College of Rheumatology (ACR) criteria
- Improvement in subject's physical function as measured by the Health Assessment Questionnaire-Disability Index (HAQ-DI)
- Relief in subject's pain, fatigue, and disease activity as measured by the Patient's Assessment of Arthritis Pain-visual analog scale (PtAAP-VAS), Fatigue Assessment Scale (FASCA), and

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Patient's Global Assessment of Disease Activity-visual analog scale (PtGADA-VAS)

- To assess the PK profile and immunogenicity of CZP in combination with DMARD(s)

Assessed at specific time points during the Treatment Period:

- To explore, at Week 0, subjects' willingness to self-inject CZP at home
- For subjects choosing to self-inject CZP, to explore the subjects' experience with self-injection (including injection site reactions) using the Self-Injection Assessment Questionnaire (SIAQ) version 2 at Weeks 0, 2, 4, 6, 8, 10, and 12
- For subjects not self-injecting CZP, to explore the burden of injection site reactions using the Injection Site Reaction Questionnaire (ISRQ) at Weeks 0, 2, 4, 6, 8, 10, and 12

Methodology: This was a Phase 3B, multicenter, open-label, follow-up study to C87076 (feeder study) designed to continue to assess the safety and efficacy of CZP. Subjects were treated with CZP every 2 weeks (Q2W) until CZP was commercially available for the indication of rheumatoid arthritis (RA) in the subject's country or region, or until further notice from UCB.

Two subject populations were eligible to enter the study from C87076:

Population 1: Those subjects who failed to achieve remission at Week 20 and/or Week 24 and who completed the Week 24 assessment of C87076. The Week 24 assessment of C87076 (Visit 14) was also the Entry assessment for C87080 (Week 0/Visit 1). This population received CZP 200mg Q2W. No induction phase was applied to ensure the blinding of C87076.

Population 2: Those subjects who achieved remission at both Week 20 and Week 24, flared up between Week 24 and Week 52, and completed the Week 52 assessment of C87076. The Week 52 assessment of C87076 (Visit 26) was also the Entry assessment for C87080 (Week 0/Visit 1). Subjects who flared prior to Week 48 in C87076 received CZP 200mg Q2W in C87080. Those who flared at Week 48 or Week 52, received CZP 400mg once or CZP 400mg Q2W 3 times, respectively, as part of the induction phase in C87080. Thereafter, subjects entered C87080 and received treatment with CZP 200mg Q2W. A flare in C87076 was defined as CDAI ≥11, which had to be confirmed at 2 consecutive visits 4 weeks apart. In the event a subject did not meet the CDAI ≥11 criterion at both visits, but the subject was re-treated at the site, the subject was considered as having flared.

Two weeks after the final dose of study medication, subjects returned to the study center for a Completion/Withdrawal Visit, and 12 weeks after the final dose of study medication, subjects returned to the study center for a 12-Week Safety Follow-Up Visit.

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Home administration:

For practical reasons, subjects had the opportunity to perform self-injections at home if they had the appropriate storage conditions available to keep the study medication, and were willing and able to perform the injection themselves. In these cases, study medication injections were performed at the following locations:

Hospital administration: Weeks 0, 2, 4, 8, and every 8 weeks thereafter

Home administration: Week 6, Weeks 10, 12, and 14, Weeks 18, 20, and 22, etc

To ensure proper administration of the study medication, subjects were trained at the study center to self-inject CZP during the first visits (Weeks 0, 2, and 4) in C87080. The subjects were asked to return all used and unused study medication at their next study center visit.

Subjects who did not have appropriate storage conditions at home or were not willing or able to perform the self-injection came to the study center for all scheduled visits Q2W and had the study medication injected by a nurse.

If a subject who started home self-injection was no longer willing to self-inject study medication, then s/he had the opportunity to switch back to hospital nurse administered injections.

Number of subjects (planned and analyzed): It was expected there would be a maximum of 132 subjects participating in this study (open-label extension study of C87076). A total of 131 subjects enrolled; 120 subjects had no prior remission (65 subjects previously treated with placebo [PBO]+DMARD and 55 subjects previously treated with CZP+DMARD) and 11 subjects had temporary remission during C87076.

Diagnosis and main criteria for inclusion: Subjects must have either failed to achieve remission in C87076 at Week 20 and/or Week 24 (CDAI >2.8), which was confirmed at Week 24, or must have achieved remission at Week 20, which was confirmed at Week 24, flared up between Week 24 and Week 52 and completed the entire C87076 study through Week 52.

Test product, dose(s) and mode of administration: Certolizumab pegol for subcutaneous (sc) injection was provided in individually packaged prefilled syringes, consisting of 1mL syringes with 25G needles containing an injectable volume of 1mL of liquid CZP (acetate pH 4.7) for single use at dosage strength of 200mg/mL.

Duration of treatment: All subjects received CZP 200mg Q2W during the study (the majority of subjects completed the study early due to approval of CZP for the treatment of RA in their country/region or after further notice from UCB). For subjects who flared at Week 48 or Week 52 of C87076, they received CZP 400mg Q2W 1 time or 3 times, respectively, as part of

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the induction phase. The actual duration of exposure to CZP in C87080 ranged from 14 to 950 days, with a median duration of exposure of 378.5 days.

Reference therapy, dose(s) and mode of administration: None

Criteria for evaluation:

Efficacy: As this was primarily a safety study, a primary efficacy variable was not defined.

The efficacy variables assessed were:

- Proportion of subjects in clinical remission defined as:
  - DAS28(ESR) remission (DAS28[ESR] <2.6) by visit
  - CDAI remission (CDAI ≤2.8) by visit
  - SDAI remission (SDAI ≤3.3) by visit
- ACR20, ACR50, and ACR70 responder rate by visit
- Change from Baseline in HAQ-DI by visit
- Change from Baseline in PtAAP-VAS, FASCA, and PtGADA-VAS by visit

The following efficacy variables were not formally planned in the protocol but were defined in the statistical analysis plan (SAP):

- Change from Baseline in other individual components of the ACR criteria, including tender joint count (TJC), swollen joint count (SJC), Physician's Global Assessment of Disease Activity-visual analog scale (PhGADA-VAS), C-reactive protein (CRP) ratio, and erythrocyte sedimentation rate (ESR) ratio
- Disease activity levels (remission rate, low disease activity [LDA], moderate disease activity [MDA], high disease activity [HDA]) for DAS28(ESR), CDAI, and SDAI scores

Pharmacokinetics: Plasma samples were collected for the determination of CZP concentrations at Week 0 and at 24-week intervals (through Week 120). For those subjects who flared at Week 52 of C87076, plasma samples were taken at Week 4 of C87080.

Immunologic: Plasma samples were collected for the determination of anti-CZP antibodies at Week 0 and at 24-week intervals (through Week 120). For those subjects who flared at Week 52 of C87076, plasma samples were taken at Week 4 of C87080.

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Safety: Safety variables included the following: extent of exposure, adverse events (AEs), laboratory evaluations (hematology, biochemistry, and urinalysis), physical examination (included tuberculosis [TB] testing), and vital signs.

Statistical methods: The Safety Set (SS) was used to summarize and analyze all safety variables. The Full Analysis Set (FAS) was used to summarize and analyze all background and efficacy data. The FAS was defined exactly the same as for the SS. For efficacy and safety data, unless otherwise specified, there were no adjustments for missing data; an observed analysis was performed. Baseline was defined as the Baseline value from C87076.

For exploratory purposes, the FAS/SS was further split into 2 subgroups of subjects, depending on the time they entered C87080:

- No prior remission: those who entered C87080 at Week 24 of C87076 (ie, nonremitters at both Week 20 and Week 24 of C87076)
- Temporary remission: those who entered C87080 at Week 52 of C87076 (ie, completed the Week 24 assessments of C87076 despite having lost remission and flared between Week 24 and Week 52)

The No prior remission subgroup was further split by randomized C87076 treatment group as follows:

- CZP 400mg Q2W ×3 followed by CZP 200mg Q2W plus DMARD (CZP+DMARD)
- Placebo (saline 0.9%) plus DMARD (PBO+DMARD)

The potential influence of mode of administration was also explored by splitting the FAS/SS into 2 subsets: Self-injection and Hospital nurse injection.

Efficacy analyses:

- The number and percentage of subjects in CDAI remission by visit was analyzed for the FAS. The actual and change from Baseline in CDAI score by visit were descriptively presented for the FAS. The number and percentage of subjects in remission, LDA, MDA, and HDA by visit were analyzed for the FAS.
- The number and percentage of subjects in DAS28(ESR) and SDAI remission by visit were analyzed for the FAS. The actual and change from Baseline in DAS28(ESR) and SDAI scores by visit were descriptively presented for the FAS. The number and percentage of subjects in DAS28(ESR) or SDAI remission, LDA, MDA, and HDA by visit were analyzed for the FAS.

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- Descriptive statistics of the percentage of subjects with ACR20, ACR50, and ACR70 responses by visit were presented for the FAS. For the ACR components:
  - CRP and ESR levels and CRP and ESR ratios to Baseline were summarized by descriptive statistics by visit for the FAS.
  - The actual and change from Baseline in the TJC and SJC by visit were descriptively presented for the FAS.
  - The actual and change from Baseline in HAQ-DI by visit were descriptively presented for the FAS.
  - The actual and change from Baseline in the PtAAP-VAS and PhGADA-VAS by visit were descriptively presented for the FAS.
- The actual and change from Baseline in the FASCA by visit were descriptively presented for the FAS.
- The number and percentage of subjects willing to self-inject at Week 0 were presented for the FAS.
- Descriptive statistics for the SIAQ PRE-Self-Injection and POST-Self-Injection domain scores were presented for the FAS.
- Descriptive statistics for the ISRQ domain score were presented for the FAS.

Pharmacokinetic and immunological analyses:

Pharmacokinetic analyses were performed on the SS. Plasma CZP concentrations were summarized for the overall group and by anti-CZP antibody status for the overall group.

Immunological analyses (presence of anti-CZP antibody) were performed on the SS and were presented for the overall group.

Safety analyses:

Safety analyses were performed on the SS and were presented for the overall group. All treatment-emergent AEs (TEAEs) were tabulated by providing the number of subjects reporting at least 1 event, the corresponding percentage of subjects in the SS, and the number of individual occurrences of the event by the Medical Dictionary for Regulatory Activities (MedDRA®) System Organ Class (SOC), high level term (HLT), and preferred term (PT). Additional summaries of TEAEs by severity, relationship to study medication, remission status, and mode of administration, as well as summaries for TEAEs leading to permanent discontinuation and

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serious AEs (SAEs) were presented.

Descriptive statistics for actual and change from Baseline values were presented for hematology and biochemistry laboratory values by visit, and shifts tables were produced for each hematology and biochemistry laboratory parameters. Actual and change from Baseline values were summarized for vital signs by visit. Extent of exposure was summarized by descriptive statistics.

Summary and conclusions:

Subject disposition: A total of 131 subjects enrolled in C87080, and 96 subjects (73.3%) completed the study. A total of 130 subjects were included in both the FAS and SS. The SS was identical to the FAS.

In the No prior remission subgroup, a similar percentage of subjects completed the study in the PBO+DMARD and CZP+DMARD groups (75.4% and 69.1% of subjects, respectively). In the PBO+DMARD group, compared with the CZP+DMARD group, a higher percentage of subjects discontinued due to AEs (15.4% and 7.3%, respectively), and a lower percentage of subjects discontinued due to lack of efficacy (7.7% and 16.4%, respectively).

In the Temporary remission subgroup, 81.8% of subjects completed the study. The most frequently reported reasons for discontinuing the study were due to AEs and withdrawal of consent for personal reasons (9.1% of subjects each). Due to the small number of subjects in the Temporary remission subgroup (11 subjects), useful comparisons with the No prior remission subgroup cannot be made.

Efficacy results: As this was primarily a safety study, a primary efficacy variable was not defined. A secondary objective of this long-term, open-label extension study was to continue to assess the efficacy of CZP 200mg Q2W in combination with DMARD treatment in subjects with RA. The efficacy parameters assessed the clinical signs and symptoms of RA.

The efficacy results were analyzed for all subjects (overall population) and also in subgroups of subjects who had no prior remission or temporary remission during C87076.

In the overall population, subjects showed improvement from Week 0 to Week 32 in all efficacy variables assessed; from Week 40 through the end of the study (Week 128), the improvements were maintained for subjects remaining in the study.

Subjects in the No prior remission subgroup (subjects who were not remitters at Week 24 of C87076) who received CZP in C87076 (CZP+DMARD group), showed some improvement from Baseline of C87076 in all efficacy variables assessed at entry into C87080, and showed further improvement with long term CZP treatment, which was maintained through the end of the study (Week 128) for subjects remaining in the study. Subjects in the No prior remission subgroup who

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received PBO in C87076 (PBO+DMARD group), showed slight worsening or no improvement from Baseline of C87076 in all efficacy variables assessed at entry into C87080, but quickly showed improvement such that by as early as Week 8, the improvement from Baseline of C87076 was similar to the CZP+DMARD group. The PBO+DMARD group showed further improvement similar to the CZP+DMARD group during the study, which was maintained through the end of the study (Week 128).

Although the sample size in the Temporary remission subgroup was very small (N=11), these subjects showed improvement from Baseline of C87076 in all efficacy variables assessed at entry into C87080, and these improvements were maintained with continued CZP treatment during C87080, through Week 16. After Week 16, most subjects in the Temporary remission subgroup had completed the study.

The results of the efficacy analyses are summarized below for subjects in the No prior remission subgroup who were previously treated with CZP (CZP+DMARD) versus placebo (PBO+DMARD) during the feeder study (C87076).

- At Week 0, no subjects (0%) in the No prior remission subgroup were CDAI remitters; the percentage of subjects who were CDAI remitters in both the PBO+DMARD and CZP+DMARD groups increased through Week 56 and was maintained from Week 64 through the end of the study (Week 128) for subjects remaining in the study.
- At Week 0 in the PBO+DMARD group, there were higher percentages of subjects with CDAI MDA and HDA, and a lower percentage of subjects with LDA, compared with the CZP+DMARD group. Over time, the percentage of subjects with CDAI MDA and HDA in both groups decreased and the percentage of subjects with CDAI remission and LDA increased. The percentage of subjects with CDAI MDA was low and relatively stable in both groups; during Weeks 40 to 128, no subject (0%) in either group had CDAI HDA.
- At Week 0, there was worsening from Baseline of C87076 in CDAI score in the PBO+DMARD group and improvement from Baseline of C87076 in the CZP+DMARD group. At Week 8, the improvement in CDAI score in the PBO+DMARD group was similar to the CZP+DMARD group, and both groups continued to show further similar improvement from Week 16 through the end of the study (Week 128).
- At Week 0, there was a lower percentage of subjects who were DAS28(ESR) or SDAI remitters in the PBO+DMARD group, compared with the CZP+DMARD group; however, the percentage of subjects who were DAS28(ESR) or SDAI remitters increased during the study in both groups and were similar through the end of the study.

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- At Week 0, there was a higher percentage of subjects in the PBO+DMARD group, compared to the CZP+DMARD, who had DAS28(ESR) or SDAI MDA and HDA; however, at Week 8, the percentage of subjects with DAS28(ESR) or SDAI MDA and HDA was similar in the PBO+DMARD and CZP+DMARD groups. Over time, the percentage of subjects with DAS28(ESR) or SDAI MDA and HDA in both groups decreased and the percentage of subjects with DAS28(ESR) or SDAI remission and LDA increased. During Weeks 40 to 128, no subject in either group had DAS28(ESR) or SDAI HDA.
- At Week 0, subjects in the PBO+DMARD group showed a slight improvement or slight worsening from Baseline of C87076 in DAS28(ESR) or SDAI scores, respectively, while the CZP+DMARD group showed some improvement from Baseline. At Week 8, the PBO+DMARD group showed larger improvements in both DAS28(ESR) and SDAI scores similar to the CZP+DMARD group. Both groups continued to show improvement from Baseline in DAS28(ESR) and SDAI scores that were maintained through the end of the study (Week 128).
- The percentage of subjects who were ACR20, ACR50, and ACR70 responders at Week 0 was lower in the PBO+DMARD group, compared with the CZP+DMARD group; however, at Week 8, the percentage of ACR20, ACR50, and ACR70 responders increased in the PBO+DMARD group and was similar to the CZP+DMARD group. In both groups, the percentage of subjects who were ACR20, ACR50, and ACR70 responders increased during the study.
- The individual ACR components (CRP, ESR, TJC, SJC, HAQ-DI, PtAAP-VAS, PtGADA VAS, and PhGADA-VAS) showed similar trends for the PBO+DMARD and CZP+DMARD groups as the ACR20, ACR50, and ACR70 responses; the PBO+DMARD group showed less improvement than the CZP+DMARD group at Week 0; showed similar improvement at Week 8 to the CZP+DMARD group, and both groups continued to improve and the improvements were maintained through the end of the study (Week 128).

In the overall population at Week 0, there was a small improvement from Baseline of C87076 in FASCA score, which continued to improve through Week 32. During Weeks 40 to 128, the improvements from Baseline in FASCA score were relatively stable.

The SIAQ results indicate the subjects' high level of comfort with self-injection of CZP in terms of feelings about injections, self-image, confidence, injection site reactions, ease of use, and satisfaction with the self-injection. The subjects' assessment of their experience with

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self-injection of CZP was stable or slightly improved from the first self-injection (at Week 0) to Week 12, with all domain scores >7.0 units (on a scale from 0 to 10) at Week 12.

Pharmacokinetic and immunologic results: Plasma CZP concentrations were determined at 24-week intervals from Week 24 to Week 120; geometric mean plasma CZP concentrations ranged from 17.091µg/mL to 25.569µg/mL.

A total of 13 subjects (10.0%) were anti-CZP antibody positive (defined as >2.4 units/mL) at any visit during C87076 or C87080. Geometric mean plasma CZP concentrations were lower in subjects who were anti-CZP antibody positive, as expected due to the increased PK clearance of CZP in subjects with anti-CZP antibodies.

Safety results: The primary objective of this long-term, open-label extension study was to continue to assess the safety of CZP 200mg sc Q2W in combination with DMARD treatment in subjects with RA.

The safety profile of long-term CZP treatment was in line with the anti-TNFα class of drugs. No new safety concerns were identified during this study in relation to the safety profile observed in the double-blind, placebo-controlled feeder study (C87076) and in previous long-term, open-label extension CZP studies (treatment duration up to 7.5 years) in subjects with RA.

For the overall population, the mean number of CZP doses received was 34.7, and the mean duration of exposure to CZP during C87080 was 499.1 days. The maximum duration of exposure during C87080 was 950 days (2.6 years).

- In the No prior remission subgroup, the mean number of doses received was similar for the PBO+DMARD and CZP+DMARD groups (38.0 and 35.3 doses, respectively), and in the Temporary remission subgroup, the mean number of doses received was 12.3 doses.
- Subjects in the Self-injection subset received a higher mean number of CZP doses (37.0), compared with the Hospital nurse injection subset (30.4 doses).

A total of 92 subjects (70.8%) reported 314 TEAEs during the study. The most frequently reported TEAE PTs were upper respiratory tract infection (12 subjects [9.2%]), nasopharyngitis (9 subjects [6.9%]), pharyngitis, urinary tract infection, and diarrhea (8 subjects [6.2%] each), and hypertension (7 subjects [5.4%]).

- In the No prior remission subgroup, the percentage of subjects with at least 1 TEAE and the incidences of the most frequently reported TEAE PTs were similar in the PBO+DMARD and CZP+DMARD groups.
- The incidence of TEAEs was similar in the Self-injection and Hospital nurse injection

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subsets.

Few subjects reported TEAEs of severe intensity (14 subjects [10.8%]).

A total of 51 subjects (39.2%) reported TEAEs that were judged by the Investigator to be related to study medication. The most frequently reported related TEAE PT was upper respiratory tract infection (6 subjects [4.6%]).

No deaths were reported during the study. A total of 25 subjects (19.2%) reported 37 treatment-emergent SAEs; the most frequently reported PTs were TB, dyspnoea, and myocardial ischaemia (2 subjects [1.5%] each).

- In the No prior remission subgroup, there was a higher incidence of treatment-emergent SAEs in the PBO+DMARD group, compared with the CZP+DMARD group (17 subjects [26.2%] reported 21 events, and 7 subjects [13.0%] reported 11 events, respectively). There was a higher incidence of the following SAE PTs in the PBO+DMARD group, compared with the CZP+DMARD group: myocardial ischemia, dyspnea, and TB (2 subjects [3.1%] and 0 subjects each, respectively). The incidence of other SAE PTs was similar in the 2 groups.

A total of 15 subjects (11.5%) reported TEAEs leading to permanent discontinuation, and 30 subjects (23.1%) reported TEAEs that led to temporary study medication discontinuation.

- In the No prior remission subgroup, the percentage of subjects reporting TEAEs that led to permanent study medication discontinuation was higher in the PBO+DMARD group, compared with the CZP+DMARD group (10 subjects [15.4%] and 4 subjects [7.4%], respectively). The percentage of subjects reporting TEAEs that led to temporary study medication discontinuation was similar in the PBO+DMARD and CZP+DMARD groups (17 subjects [26.2%] and 12 subjects [22.2%], respectively).

A total of 4 subjects (3.1%) reported 7 injection site reactions.

- The incidence of injection site reactions was slightly lower in the Self-injection subset, compared with the Hospital nurse injection subset (2 subjects [2.3%] reported 4 events and 2 subjects [4.5%] reported 3 events).

A total of 9 subjects (6.9%) reported 9 treatment-emergent SAEs in the Infections and infestations SOC. Tuberculosis, reported in 2 subjects (1.5%), was the only treatment emergent SAE reported in more than 1 subject. There were no reports of disseminated or extrapulmonary TB.

Serious AEs of lung neoplasm malignant and basal cell carcinoma were reported in 1 subject

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each (0.8%). No malignancies were reported in subjects ≤30 years of age.

There were no TEAEs of cardiac failure; 2 subjects (1.5%) reported SAEs of myocardial ischemia.

No new safety concerns were identified based on a review of events in the categories of infections, malignancies, cardiac, vascular, immune system, and neurologic events of interest. There were no reported events related to confirmed lupus diagnosis, sarcoidosis, or Wegener's granulomatosis, and no events indicative of serious bleeding events, bone marrow aplasia, or serious skin reactions.

None of the mean and median changes from Baseline of C87076 in hematology or biochemistry parameters were considered clinically significant. No clinically relevant shift patterns, based on change from Baseline to any post-Baseline visit were observed for any of the hematology or biochemistry parameters. There were few markedly abnormal hematology or biochemistry values; most were isolated findings and not considered clinically relevant.

None of the mean and median changes from Baseline of C87076 in vital signs (diastolic and systolic blood pressure, heart rate, and body temperature) were considered clinically significant.

Conclusions: The primary objective of this study was to assess the long-term safety of CZP 200mg Q2W with DMARD treatment in subjects with low to moderate RA. The results of this study demonstrated treatment with CZP was consistent with what would be expected with anti-TNFα drugs and with placebo-controlled studies and long-term studies with CZP. No new safety concerns were identified during this study.

The secondary objectives of this study were to assess the continuing long-term efficacy of CZP in the treatment of signs and symptoms of RA. Long-term use of CZP 200mg sc Q2W with DMARD treatment resulted in maintenance of robust improvements in measures of the clinical signs and symptoms of RA during this study (up to 2.5 years). Subjects in the No prior remission subgroup (who had received 26 weeks of treatment with either PBO or CZP during C87076 prior to entering C87080) showed additional improvement in the clinical signs and symptoms of RA with long-term CZP treatment.

Overall, considering both the safety and efficacy results, this study demonstrated a positive benefit-risk ratio of long-term treatment with CZP 200mg Q2W, confirming that this is an appropriate dose regimen for long-term treatment of subjects with active RA.

Report date: 08 Jul 2013