



## Clinical trial results:

### A Phase 3, Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo- and Active-Controlled Study Followed by a Placebo-Controlled Maintenance Period and Open-Label Follow-Up to Evaluate the Efficacy and Safety of Certolizumab Pegol in Subjects With Moderate to Severe Chronic Plaque Psoriasis

#### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2014-003492-36          |
| Trial protocol           | GB DE HU CZ NL PL BG FR |
| Global end of trial date | 17 December 2018        |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1              |
| This version publication date  | 01 January 2020 |
| First version publication date | 01 January 2020 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | PS0003 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02346240 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | UCB Biopharma SPRL  |
| Sponsor organisation address | Allée de la Recherche 60, Brussels, Belgium, B-1070                               |
| Public contact               | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |
| Scientific contact           | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 11 February 2019 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 17 December 2018 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To compare the efficacy of certolizumab pegol (CZP) administered subcutaneously (sc) at the doses of CZP 400 mg every 2 weeks (Q2W) and CZP 200 mg Q2W after a loading dose of CZP 400 mg Q2W at Weeks 0, 2, and 4 to placebo in the treatment of moderate to severe chronic plaque psoriasis (PSO).

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Background therapy/concomitant medication was permitted as defined in the study protocol.

Evidence for comparator:

Etanercept (ETN) is a fusion protein consisting of the fragment crystallizable (Fc) fragment of Immunoglobulin G1 (IgG1) with the Type 2 soluble Tumor Necrosis Factor (TNF) alpha receptor. ETN is specific for TNF alpha and lymphotoxin alpha. ETN was the first TNF alpha inhibitor approved for the treatment of psoriasis and is part of the standard armamentarium. The approved initial dose is 50 milligrams (mg) twice weekly. The safety and efficacy profile of ETN is well established. The first approval worldwide for ETN was in the United States in 1998 for the treatment of rheumatoid arthritis and in 2004 for psoriasis. All of these factors make ETN an ideal active comparator in this study.

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 11 February 2015 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Bulgaria: 25       |
| Country: Number of subjects enrolled | Czech Republic: 80 |
| Country: Number of subjects enrolled | France: 14         |
| Country: Number of subjects enrolled | Germany: 63        |
| Country: Number of subjects enrolled | Hungary: 25        |
| Country: Number of subjects enrolled | Netherlands: 3     |
| Country: Number of subjects enrolled | Poland: 233        |
| Country: Number of subjects enrolled | United Kingdom: 24 |
| Country: Number of subjects enrolled | United States: 92  |
| Worldwide total number of subjects   | 559                |
| EEA total number of subjects         | 467                |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 519 |
| From 65 to 84 years                       | 40  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

This study started to enroll participants in February 2015, from multiple sites in Europe and United States and concluded in December 2018. 559 participants are included in the Randomized Set (RS) shown in the Participant Flow.

### Pre-assignment

Screening details:

The study included a Screening Period, an Initial Treatment Period up to Week 16, a Maintenance Treatment Period up to Week 48, an Open-Label Extension Treatment Period up to Week 144 and a Safety Follow-up Period up to Week 157. The Participants Flow refers to the Randomized Set, the Maintenance Set and the Open Label Set.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Initial Period (Baseline to Week 16)   |
| Is this the baseline period? | Yes                                    |
| Allocation method            | Randomised - controlled                |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

Blinding implementation details:

CZP and placebo treatments were administered in a double-blind fashion (the sponsor, subject, and blinded site staff remained blinded to treatment assignment during the first 16 weeks of the study). Etanercept treatments were administered in a single-blind fashion (the sponsor and the blinded site staff remained blinded, but the subject and unblinded study staff knew the treatment assignment during the first 16 weeks of the study).

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | Placebo Q2W |

Arm description:

Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.

Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.

|  |  |
|--|--|
| Arm type                               | Placebo                                      |
| Investigational medicinal product name | Placebo                                      |
| Investigational medicinal product code | PBO  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Etanercept |
|------------------|------------|

Arm description:

Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.

- PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

|          |                   |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

|   |  |
|---|--|
| Investigational medicinal product name      | Etanercept                                   |
| Investigational medicinal product code      | ETN  |
| Other name                                  |  |
| Pharmaceutical forms                        | Solution for injection in pre-filled syringe |
| Routes of administration                    | Subcutaneous use                             |
| Dosage and administration details:          |  |
| Subcutaneous injections: 50 mg twice weekly |  |
| <b>Arm title</b>                            | CZP 200 mg Q2W                               |

Arm description:

CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment: •PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

|   |  |
|---|--|
| Arm type  | Experimental                                 |
| Investigational medicinal product name                            | Certolizumab pegol                           |
| Investigational medicinal product code                            | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:                                |  |
| Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W |  |
| <b>Arm title</b>  | CZP 400 mg Q2W                               |

Arm description:

CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment: •PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

|   |  |
|---|--|
| Arm type  | Experimental                                 |
| Investigational medicinal product name                            | Certolizumab pegol                           |
| Investigational medicinal product code                            | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:                                |  |
| Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W |  |

| <b>Number of subjects in period 1</b>    | Placebo Q2W | Etanercept | CZP 200 mg Q2W |
|--|-------------|------------|----------------|
| Started                                  | 57          | 170        | 165            |
| Completed Week 16                        | 55          | 159        | 159            |
| Finished Wk16 started Maintenance Period | 55          | 159        | 159            |

|                              |    |     |     |
|------------------------------|----|-----|-----|
| Completed                    | 55 | 159 | 159 |
| Not completed                | 2  | 11  | 6   |
| Consent withdrawn by subject | 1  | 2   | 3   |
| Subject missed 3 visits      | -  | -   | 1   |
| Adverse event, non-fatal     | -  | 4   | 1   |
| Non-compliance               | -  | 1   | -   |
| Lost to follow-up            | 1  | 2   | 1   |
| Lack of efficacy             | -  | 1   | -   |
| Protocol deviation           | -  | 1   | -   |

| Number of subjects in period 1           | CZP 400 mg Q2W |
|--|----------------|
| Started                                  | 167            |
| Completed Week 16                        | 162            |
| Finished Wk16 started Maintenance Period | 160            |
| Completed                                | 160            |
| Not completed                            | 7              |
| Consent withdrawn by subject             | 2              |
| Subject missed 3 visits                  | -              |
| Adverse event, non-fatal                 | 1              |
| Non-compliance                           | 1              |
| Lost to follow-up                        | 3              |
| Lack of efficacy                         | -              |
| Protocol deviation                       | -              |

## Period 2

|                              |   |
|------------------------------|---|
| Period 2 title               | Maintenance Period (Week 16 to Week 48) |
| Is this the baseline period? | No                                      |
| Allocation method            | Randomised - controlled                 |
| Blinding used                | Double blind                            |
| Roles blinded                | Subject, Investigator, Assessor, Carer  |

Blinding implementation details:

Participants who entered the escape arms of the study received open-label CZP 400 mg every 2 weeks. Participants who relapsed were removed from the placebo-controlled Maintenance Period and entered the OLE Period.

## Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|   |  |
|---|--|
| <b>Arm title</b>  | Placebo/Placebo Q2W                          |
| Arm description:  |  |
| This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI75 response at Week 16 and continued to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).                    |  |
| Arm type  | Placebo                                      |
| Investigational medicinal product name  | Placebo                                      |
| Investigational medicinal product code  | PBO  |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:  |  |
| Subcutaneous injections every 2 weeks (Q2W)   |  |
| <b>Arm title</b>  | Etanercept/Placebo Q2W                       |
| Arm description:  |  |
| This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).        |  |
| Arm type  | Placebo                                      |
| Investigational medicinal product name  | Placebo                                      |
| Investigational medicinal product code  | PBO  |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:  |  |
| Subcutaneous injections every 2 weeks (Q2W)   |  |
| Investigational medicinal product name  | Etanercept                                   |
| Investigational medicinal product code  | ETN  |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:  |  |
| Subcutaneous injections: 50 mg twice weekly   |  |
| <b>Arm title</b>  | Etanercept/CZP 200 mg Q2W                    |
| Arm description:  |  |
| This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). |  |
| Arm type  | Experimental                                 |
| Investigational medicinal product name  | Certolizumab pegol                           |
| Investigational medicinal product code  | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:  |  |
| Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W   |  |
| Investigational medicinal product name  | Etanercept                                   |
| Investigational medicinal product code  | ETN  |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |

**Dosage and administration details:**

Subcutaneous injections: 50 mg twice weekly

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | CZP 200 mg Q2W/Placebo Q2W |
|------------------|----------------------------|

**Arm description:**

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

|  |  |
|--|--|
| Arm type                               | Placebo                                      |
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

|  |  |
|--|--|
| Investigational medicinal product name | Placebo                                      |
| Investigational medicinal product code | PBO  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

Subcutaneous injections every 2 weeks (Q2W)

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | CZP 200 mg Q2W/CZP 200 mg Q2W |
|------------------|-------------------------------|

**Arm description:**

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | CZP 200 mg Q2W/CZP 400 mg Q4W |
|------------------|-------------------------------|

**Arm description:**

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q4W in the Maintenance Period (Week 16 to Week 48).

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | CZP 400 mg Q2W/Placebo Q2W |
|------------------|----------------------------|



**Arm description:**

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

|  |  |
|--|--|
| Arm type                               | Placebo                                      |
| Investigational medicinal product name | Placebo                                      |
| Investigational medicinal product code | PBO  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

Subcutaneous injections every 2 weeks (Q2W)

|  |  |
|--|--|
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | CZP 400 mg Q2W/CZP 200 mg Q2W |
|------------------|-------------------------------|

**Arm description:**

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | CZP 400 mg Q2W/CZP 400 mg Q2W |
|------------------|-------------------------------|

**Arm description:**

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q2W in the Maintenance Period (Week 16 to Week 48).

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

**Dosage and administration details:**

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | Placebo Q2W/Escape CZP 400 mg Q2W |
|------------------|-----------------------------------|

**Arm description:**

This arm consisted of participants initially randomized in the Placebo arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |  |
|--|--|
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

|  |  |
|--|--|
| Investigational medicinal product name | Placebo                                      |
| Investigational medicinal product code | PBO  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Subcutaneous injections every 2 weeks (Q2W)

|                  |                                  |
|------------------|----------------------------------|
| <b>Arm title</b> | Etanercept/Escape CZP 400 mg Q2W |
|------------------|----------------------------------|

Arm description:

This arm consisted of participants initially randomized in the Etanercept arm, who did not achieve a PASI75 response at Week 16 escaped from the treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Etanercept                                   |
| Investigational medicinal product code | ETN  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Subcutaneous injections: 50 mg twice weekly

|  |  |
|--|--|
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

|                  |                                      |
|------------------|--------------------------------------|
| <b>Arm title</b> | CZP 200 mg Q2W/Escape CZP 400 mg Q2W |
|------------------|--------------------------------------|

Arm description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

|                  |                                      |
|------------------|--------------------------------------|
| <b>Arm title</b> | CZP 400 mg Q2W/Escape CZP 400 mg Q2W |
|------------------|--------------------------------------|

Arm description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two

weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Certolizumab pegol                           |
| Investigational medicinal product code | CZP  |
| Other name                             | Cimzia                                       |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W

| <b>Number of subjects in period 2</b>   | Placebo/Placebo Q2W | Etanercept/Placebo Q2W | Etanercept/CZP 200 mg Q2W |
|---|---------------------|------------------------|---------------------------|
| Started                                 | 2                   | 24                     | 50                        |
| Completed Maintenance Period            | 2                   | 23                     | 48                        |
| Finished Wk48 entered Open-label Period | 2                   | 23                     | 48                        |
| Completed                               | 2                   | 23                     | 48                        |
| Not completed                           | 0                   | 1                      | 2                         |
| Moved out of state                      | -                   | -                      | 1                         |
| Consent withdrawn by subject            | -                   | 1                      | 1                         |
| Adverse events and alcohol problem      | -                   | -                      | -                         |
| Withdrawn by Sponsor                    | -                   | -                      | -                         |
| Adverse event, non-fatal                | -                   | -                      | -                         |
| Patient's decisions                     | -                   | -                      | -                         |
| Sponsor decision due to non-compliance  | -                   | -                      | -                         |
| Unavailability due to business trip     | -                   | -                      | -                         |
| Lost to follow-up                       | -                   | -                      | -                         |
| Patient request due to non-compliance   | -                   | -                      | -                         |
| Lack of efficacy                        | -                   | -                      | -                         |
| Did not achieve PASI50                  | -                   | -                      | -                         |

| <b>Number of subjects in period 2</b>   | CZP 200 mg Q2W/Placebo Q2W | CZP 200 mg Q2W/CZP 200 mg Q2W | CZP 200 mg Q2W/CZP 400 mg Q4W |
|---|----------------------------|-------------------------------|-------------------------------|
|   |                            |                               |                               |
| Started                                 | 22                         | 44                            | 44                            |
| Completed Maintenance Period            | 20                         | 40                            | 43                            |
| Finished Wk48 entered Open-label Period | 20                         | 40                            | 43                            |
| Completed                               | 20                         | 40                            | 43                            |
| Not completed                           | 2                          | 4                             | 1                             |
| Moved out of state                      | -                          | -                             | -                             |
| Consent withdrawn by subject            | 1                          | 1                             | -                             |
| Adverse events and alcohol problem      | -                          | -                             | 1                             |

|  |   |   |   |
|--|---|---|---|
| Withdrawn by Sponsor                   | - | - | - |
| Adverse event, non-fatal               | 1 | 2 | - |
| Patient's decisions                    | - | - | - |
| Sponsor decision due to non-compliance | - | 1 | - |
| Unavailability due to business trip    | - | - | - |
| Lost to follow-up                      | - | - | - |
| Patient request due to non-compliance  | - | - | - |
| Lack of efficacy                       | - | - | - |
| Did not achieve PASI50                 | - | - | - |

| Number of subjects in period 2          | CZP 400 mg<br>Q2W/Placebo Q2W | CZP 400 mg<br>Q2W/CZP 200 mg<br>Q2W | CZP 400 mg<br>Q2W/CZP 400 mg<br>Q2W |
|---|-------------------------------|-------------------------------------|-------------------------------------|
|   |                               |                                     |                                     |
| Started                                 | 25                            | 50                                  | 49                                  |
| Completed Maintenance Period            | 23                            | 47                                  | 49                                  |
| Finished Wk48 entered Open-label Period | 23                            | 47                                  | 49                                  |
| Completed                               | 23                            | 47                                  | 49                                  |
| Not completed                           | 2                             | 3                                   | 0                                   |
| Moved out of state                      | -                             | -                                   | -                                   |
| Consent withdrawn by subject            | 1                             | 2                                   | -                                   |
| Adverse events and alcohol problem      | -                             | -                                   | -                                   |
| Withdrawn by Sponsor                    | -                             | -                                   | -                                   |
| Adverse event, non-fatal                | -                             | -                                   | -                                   |
| Patient's decisions                     | 1                             | -                                   | -                                   |
| Sponsor decision due to non-compliance  | -                             | 1                                   | -                                   |
| Unavailability due to business trip     | -                             | -                                   | -                                   |
| Lost to follow-up                       | -                             | -                                   | -                                   |
| Patient request due to non-compliance   | -                             | -                                   | -                                   |
| Lack of efficacy                        | -                             | -                                   | -                                   |
| Did not achieve PASI50                  | -                             | -                                   | -                                   |

| Number of subjects in period 2          | Placebo Q2W/Escape<br>CZP 400 mg Q2W | Etanercept/Escape<br>CZP 400 mg Q2W | CZP 200 mg<br>Q2W/Escape CZP<br>400 mg Q2W |
|---|--------------------------------------|-------------------------------------|--|
|   |                                      |                                     |  |
| Started                                 | 53                                   | 85                                  | 49   |
| Completed Maintenance Period            | 46                                   | 71                                  | 36   |
| Finished Wk48 entered Open-label Period | 45                                   | 68                                  | 35   |
| Completed                               | 45                                   | 68                                  | 35   |
| Not completed                           | 8                                    | 17                                  | 14   |
| Moved out of state                      | -                                    | -                                   | -  |
| Consent withdrawn by subject            | 2                                    | 5                                   | 2  |
| Adverse events and alcohol problem      | -                                    | -                                   | -  |

|  |   |   |   |
|--|---|---|---|
| Withdrawn by Sponsor                   | - | 1 | - |
| Adverse event, non-fatal               | 1 | 4 | 1 |
| Patient's decisions                    | - | - | - |
| Sponsor decision due to non-compliance | 1 | 1 | - |
| Unavailability due to business trip    | - | 1 | - |
| Lost to follow-up                      | - | 1 | - |
| Patient request due to non-compliance  | - | 1 | - |
| Lack of efficacy                       | 1 | - | 3 |
| Did not achieve PASI50                 | 3 | 3 | 8 |

| <b>Number of subjects in period 2</b>   | CZP 400 mg<br>Q2W/Escape CZP<br>400 mg Q2W |
|---|--|
| Started                                 | 36   |
| Completed Maintenance Period            | 30   |
| Finished Wk48 entered Open-label Period | 29   |
| Completed                               | 29   |
| Not completed                           | 7  |
| Moved out of state                      | -  |
| Consent withdrawn by subject            | 1  |
| Adverse events and alcohol problem      | -  |
| Withdrawn by Sponsor                    | -  |
| Adverse event, non-fatal                | 2  |
| Patient's decisions                     | -  |
| Sponsor decision due to non-compliance  | -  |
| Unavailability due to business trip     | -  |
| Lost to follow-up                       | -  |
| Patient request due to non-compliance   | -  |
| Lack of efficacy                        | -  |
| Did not achieve PASI50                  | 4  |

### Period 3

|                              |   |
|------------------------------|---|
| Period 3 title               | Open-Label Period (Week 48 to Week 144) |
| Is this the baseline period? | No                                      |
| Allocation method            | Randomised - controlled                 |
| Blinding used                | Not blinded                             |

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|   |  |
|---|--|
| <b>Arm title</b>  | Placebo/CZP 200 mg Q2W OLE                   |
| Arm description:<br>This arm consisted of participants from the Placebo-controlled Maintenance Period, who achieved PASI50 response (had no relapse) at Week 48 and entered the 96-Weeks OLE Period receiving CZP 200 mg Q2W. |  |
| Arm type  | Experimental                                 |
| Investigational medicinal product name  | Placebo                                      |
| Investigational medicinal product code  | PBO  |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:<br>Subcutaneous injections every 2 weeks (Q2W)   |  |
| Investigational medicinal product name  | Certolizumab pegol                           |
| Investigational medicinal product code  | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:<br>Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W   |  |
| <b>Arm title</b>  | CZP 200 mg Q2W/CZP 200 mg Q2W OLE            |
| Arm description:<br>This arm consisted of participants who received CZP 200 mg Q2W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE.                                     |  |
| Arm type  | Experimental                                 |
| Investigational medicinal product name  | Certolizumab pegol                           |
| Investigational medicinal product code  | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:<br>Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W   |  |
| <b>Arm title</b>  | CZP 400 mg Q4W/CZP 200 mg Q2W OLE            |
| Arm description:<br>This arm consisted of participants who received CZP 400 mg Q4W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE on the CZP 200mg Q2W dose.           |  |
| Arm type  | Experimental                                 |
| Investigational medicinal product name  | Certolizumab pegol                           |
| Investigational medicinal product code  | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:<br>Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W   |  |
| <b>Arm title</b>  | CZP 400 mg Q2W/CZP 200 mg Q2W OLE            |
| Arm description:<br>This arm consisted of participants who received CZP 400 mg Q2W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE on the CZP 200mg Q2W dose.           |  |
| Arm type  | Experimental                                 |

|   |  |
|---|--|
| Investigational medicinal product name                            | Certolizumab pegol                           |
| Investigational medicinal product code                            | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:                                |  |
| Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W |  |
| <b>Arm title</b>  | Esc CZP 400 mg Q2W/CZP 400 mg Q2W OLE        |

Arm description:

This arm consisted of participants who received open-label CZP 400mg Q2W in the Maintenance Period and entered OLE.

|   |  |
|---|--|
| Arm type  | Experimental                                 |
| Investigational medicinal product name                            | Certolizumab pegol                           |
| Investigational medicinal product code                            | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:                                |  |
| Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W |  |
| <b>Arm title</b>  | Placebo/CZP 400 mg Q2W OLE                   |

Arm description:

This arm consisted of participants from the Placebo-controlled Maintenance Period, who did not achieve PASI50 response (had relapse) and entered the 96-weeks OLE Period receiving CZP 400 mg Q2W.

|   |  |
|---|--|
| Arm type  | Experimental                                 |
| Investigational medicinal product name                            | Placebo                                      |
| Investigational medicinal product code                            | PBO  |
| Other name  |  |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:                                |  |
| Subcutaneous injections every 2 weeks (Q2W)                       |  |
| Investigational medicinal product name                            | Certolizumab pegol                           |
| Investigational medicinal product code                            | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:                                |  |
| Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W |  |
| <b>Arm title</b>  | Any CZP/CZP 400 mg Q2W OLE                   |

Arm description:

This arm consisted of participants who relapsed on CZP 200 mg Q2W, CZP 400 mg Q4W and 400 mg Q2W.

|   |  |
|---|--|
| Arm type  | Experimental                                 |
| Investigational medicinal product name                            | Certolizumab pegol                           |
| Investigational medicinal product code                            | CZP  |
| Other name  | Cimzia                                       |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe |
| Routes of administration  | Subcutaneous use                             |
| Dosage and administration details:                                |  |
| Subcutaneous injections: 200 mg every 2 weeks (Q2W) or 400 mg Q2W |  |

| Number of subjects in period 3  | Placebo/CZP 200 mg<br>Q2W OLE | CZP 200 mg<br>Q2W/CZP 200 mg<br>Q2W OLE | CZP 400 mg<br>Q4W/CZP 200 mg<br>Q2W OLE |
|---------------------------------|-------------------------------|---|---|
|                                 |                               |   |   |
| Started                         | 34                            | 122                                     | 41                                      |
| Completed                       | 31                            | 105                                     | 34                                      |
| Not completed                   | 3                             | 17                                      | 7                                       |
| Adverse event, serious fatal    | -                             | 1                                       | 1                                       |
| Consent withdrawn by subject    | -                             | 4                                       | 1                                       |
| Adverse event, non-fatal        | 1                             | 6                                       | 2                                       |
| Lost to follow-up               | 2                             | 2                                       | 3                                       |
| No PASI50 response              | -                             | 2                                       | -                                       |
| No efficacy of study medication | -                             | 1                                       | -                                       |
| Lack of efficacy                | -                             | 1                                       | -                                       |
| Protocol deviation              | -                             | -                                       | -                                       |

| Number of subjects in period 3  | CZP 400 mg<br>Q2W/CZP 200 mg<br>Q2W OLE | Esc CZP 400 mg<br>Q2W/CZP 400 mg<br>Q2W OLE | Placebo/CZP 400 mg<br>Q2W OLE |
|---------------------------------|---|---|-------------------------------|
|                                 |   |   |                               |
| Started                         | 48                                      | 177   | 34                            |
| Completed                       | 45                                      | 146   | 27                            |
| Not completed                   | 3                                       | 31  | 7                             |
| Adverse event, serious fatal    | -                                       | 1   | -                             |
| Consent withdrawn by subject    | -                                       | 10  | 1                             |
| Adverse event, non-fatal        | 3                                       | 13  | 3                             |
| Lost to follow-up               | -                                       | 1   | 1                             |
| No PASI50 response              | -                                       | 4   | 2                             |
| No efficacy of study medication | -                                       | -   | -                             |
| Lack of efficacy                | -                                       | 1   | -                             |
| Protocol deviation              | -                                       | 1   | -                             |

| Number of subjects in period 3  | Any CZP/CZP 400<br>mg Q2W OLE |
|---------------------------------|-------------------------------|
| Started                         | 16                            |
| Completed                       | 8                             |
| Not completed                   | 8                             |
| Adverse event, serious fatal    | -                             |
| Consent withdrawn by subject    | 1                             |
| Adverse event, non-fatal        | 3                             |
| Lost to follow-up               | 1                             |
| No PASI50 response              | 3                             |
| No efficacy of study medication | -                             |
| Lack of efficacy                | -                             |



|                    |   |
|--------------------|---|
| Protocol deviation | - |
|--------------------|---|

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Placebo Q2W |
|-----------------------|-------------|

#### Reporting group description:

Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.

Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.

|                       |            |
|-----------------------|------------|
| Reporting group title | Etanercept |
|-----------------------|------------|

#### Reporting group description:

Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.

- PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

|                       |                |
|-----------------------|----------------|
| Reporting group title | CZP 200 mg Q2W |
|-----------------------|----------------|

#### Reporting group description:

CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

|                       |                |
|-----------------------|----------------|
| Reporting group title | CZP 400 mg Q2W |
|-----------------------|----------------|

#### Reporting group description:

CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

| Reporting group values  | Placebo Q2W | Etanercept | CZP 200 mg Q2W |
|-------------------------|-------------|------------|----------------|
| Number of subjects      | 57          | 170        | 165            |
| Age categorical         |             |            |                |
| Units: Subjects         |             |            |                |
| <=18 years              | 0           | 1          | 0              |
| Between 18 and 65 years | 53          | 156        | 153            |
| >=65 years              | 4           | 13         | 12             |
| Age continuous          |             |            |                |
| Units: years            |             |            |                |
| arithmetic mean         | 46.5        | 44.6       | 46.7           |
| standard deviation      | ± 12.5      | ± 14.1     | ± 13.5         |

|                                       |    |     |     |
|---------------------------------------|----|-----|-----|
| Gender categorical<br>Units: Subjects |    |     |     |
| Female                                | 23 | 43  | 52  |
| Male                                  | 34 | 127 | 113 |

|                                       |                |       |  |
|---------------------------------------|----------------|-------|--|
| <b>Reporting group values</b>         | CZP 400 mg Q2W | Total |  |
| Number of subjects                    | 167            | 559   |  |
| Age categorical<br>Units: Subjects    |                |       |  |
| <=18 years                            | 2              | 3     |  |
| Between 18 and 65 years               | 154            | 516   |  |
| >=65 years                            | 11             | 40    |  |
| Age continuous<br>Units: years        |                |       |  |
| arithmetic mean                       | 45.4           |       |  |
| standard deviation                    | ± 12.4         | -     |  |
| Gender categorical<br>Units: Subjects |                |       |  |
| Female                                | 60             | 178   |  |
| Male                                  | 107            | 381   |  |

### Subject analysis sets

|                            |                  |
|----------------------------|------------------|
| Subject analysis set title | Placebo Q2W (RS) |
| Subject analysis set type  | Full analysis    |

Subject analysis set description:

Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.

Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.

Participants formed the Randomized Set (RS).

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Etanercept (RS) |
| Subject analysis set type  | Full analysis   |

Subject analysis set description:

Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.

- PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Participants formed the Randomized Set (RS).

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | CZP 200 mg Q2W (RS) |
| Subject analysis set type  | Full analysis       |

Subject analysis set description:

CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Participants formed the Randomized Set (RS).

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | CZP 400 mg Q2W (RS) |
| Subject analysis set type  | Full analysis       |

Subject analysis set description:

CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Participants formed the Randomized Set (RS).

|                            |                              |
|----------------------------|------------------------------|
| Subject analysis set title | Placebo/Placebo Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                |

Subject analysis set description:

This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI75 response at Week 16 and continued to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                                 |
|----------------------------|---------------------------------|
| Subject analysis set title | Etanercept/Placebo Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                   |

Subject analysis set description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                                    |
|----------------------------|------------------------------------|
| Subject analysis set title | Etanercept/CZP 200 mg Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                      |

Subject analysis set description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                                     |
|----------------------------|-------------------------------------|
| Subject analysis set title | CZP 200 mg Q2W/Placebo Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                       |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |  |
|----------------------------|--|
| Subject analysis set title | CZP 200 mg Q2W/CZP 200 mg Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                          |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |  |
|----------------------------|--|
| Subject analysis set title | CZP 200 mg Q2W/CZP 400 mg Q4W (WK16RS) |
| Subject analysis set type  | Full analysis                          |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q4W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                                     |
|----------------------------|-------------------------------------|
| Subject analysis set title | CZP 400 mg Q2W/Placebo Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                       |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |  |
|----------------------------|--|
| Subject analysis set title | CZP 400 mg Q2W/CZP 200 mg Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                          |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |  |
|----------------------------|--|
| Subject analysis set title | CZP 400 mg Q2W/CZP 400 mg Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                          |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                      |
|----------------------------|----------------------|
| Subject analysis set title | CZP 200 mg Q2W (TCS) |
| Subject analysis set type  | Safety analysis      |

Subject analysis set description:

This arm consisted of all participants who received CZP 200 mg at any time during the study.

|                            |                      |
|----------------------------|----------------------|
| Subject analysis set title | CZP 400 mg Q2W (TCS) |
| Subject analysis set type  | Safety analysis      |

Subject analysis set description:

This arm consisted of all participants who received CZP 400 mg at any time during the study.

| Reporting group values                | Placebo Q2W (RS) | Etanercept (RS) | CZP 200 mg Q2W (RS) |
|---------------------------------------|------------------|-----------------|---------------------|
| Number of subjects                    | 57               | 170             | 165                 |
| Age categorical<br>Units: Subjects    |                  |                 |                     |
| <=18 years                            | 0                | 1               | 0                   |
| Between 18 and 65 years               | 53               | 156             | 153                 |
| >=65 years                            | 4                | 13              | 12                  |
| Age continuous<br>Units: years        |                  |                 |                     |
| arithmetic mean                       | 46.5             | 44.6            | 46.7                |
| standard deviation                    | ± 12.5           | ± 14.1          | ± 13.5              |
| Gender categorical<br>Units: Subjects |                  |                 |                     |
| Female                                | 23               | 43              | 52                  |
| Male                                  | 34               | 127             | 113                 |

| Reporting group values                | CZP 400 mg Q2W (RS) | Placebo/Placebo Q2W (WK16RS) | Etanercept/Placebo Q2W (WK16RS) |
|---------------------------------------|---------------------|------------------------------|---------------------------------|
| Number of subjects                    | 167                 | 2                            | 24                              |
| Age categorical<br>Units: Subjects    |                     |                              |                                 |
| <=18 years                            | 2                   | 0                            | 0                               |
| Between 18 and 65 years               | 154                 | 2                            | 24                              |
| >=65 years                            | 11                  | 0                            | 0                               |
| Age continuous<br>Units: years        |                     |                              |                                 |
| arithmetic mean                       | 45.4                | 41.5                         | 47.2                            |
| standard deviation                    | ± 12.4              | ± 26.2                       | ± 13.5                          |
| Gender categorical<br>Units: Subjects |                     |                              |                                 |
| Female                                | 60                  | 2                            | 6                               |
| Male                                  | 107                 | 0                            | 18                              |

| Reporting group values | Etanercept/CZP 200 | CZP 200 mg | CZP 200 mg |
|------------------------|--------------------|------------|------------|
|------------------------|--------------------|------------|------------|

|                                       | mg Q2W (WK16RS) | Q2W/Placebo Q2W (WK16RS) | Q2W/CZP 200 mg Q2W (WK16RS) |
|---------------------------------------|-----------------|--------------------------|-----------------------------|
| Number of subjects                    | 50              | 22                       | 44                          |
| Age categorical<br>Units: Subjects    |                 |                          |                             |
| <=18 years                            | 0               | 0                        | 0                           |
| Between 18 and 65 years               | 47              | 21                       | 43                          |
| >=65 years                            | 3               | 1                        | 1                           |
| Age continuous<br>Units: years        |                 |                          |                             |
| arithmetic mean                       | 43.3            | 47.3                     | 43.2                        |
| standard deviation                    | ± 12.9          | ± 14.9                   | ± 12.4                      |
| Gender categorical<br>Units: Subjects |                 |                          |                             |
| Female                                | 13              | 7                        | 14                          |
| Male                                  | 37              | 15                       | 30                          |

| <b>Reporting group values</b>         | CZP 200 mg Q2W/CZP 400 mg Q4W (WK16RS) | CZP 400 mg Q2W/Placebo Q2W (WK16RS) | CZP 400 mg Q2W/CZP 200 mg Q2W (WK16RS) |
|---------------------------------------|--|-------------------------------------|--|
| Number of subjects                    | 44                                     | 25                                  | 50                                     |
| Age categorical<br>Units: Subjects    |  |                                     |  |
| <=18 years                            | 0                                      | 1                                   | 1                                      |
| Between 18 and 65 years               | 38                                     | 24                                  | 45                                     |
| >=65 years                            | 6                                      | 0                                   | 4                                      |
| Age continuous<br>Units: years        |  |                                     |  |
| arithmetic mean                       | 49.4                                   | 42.9                                | 43.3                                   |
| standard deviation                    | ± 15.1                                 | ± 9.7                               | ± 11.9                                 |
| Gender categorical<br>Units: Subjects |  |                                     |  |
| Female                                | 14                                     | 11                                  | 18                                     |
| Male                                  | 30                                     | 14                                  | 32                                     |

| <b>Reporting group values</b>         | CZP 400 mg Q2W/CZP 400 mg Q2W (WK16RS) | CZP 200 mg Q2W (TCS) | CZP 400 mg Q2W (TCS) |
|---------------------------------------|--|----------------------|----------------------|
| Number of subjects                    | 49                                     | 373                  | 412                  |
| Age categorical<br>Units: Subjects    |  |                      |                      |
| <=18 years                            | 0                                      | 2                    | 3                    |
| Between 18 and 65 years               | 45                                     | 346                  | 377                  |
| >=65 years                            | 4                                      | 25                   | 32                   |
| Age continuous<br>Units: years        |  |                      |                      |
| arithmetic mean                       | 44.6                                   | 45.3                 | 45.8                 |
| standard deviation                    | ± 13.0                                 | ± 13.0               | ± 13.2               |
| Gender categorical<br>Units: Subjects |  |                      |                      |
| Female                                | 17                                     | 115                  | 131                  |
| Male                                  | 32                                     | 258                  | 281                  |



## End points

### End points reporting groups

|  |                            |
|--|----------------------------|
| Reporting group title  | Placebo Q2W                |
| Reporting group description:<br>Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:<br>•PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.<br>Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.  |                            |
| Reporting group title  | Etanercept                 |
| Reporting group description:<br>Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.<br>•PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.<br>Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.   |                            |
| Reporting group title  | CZP 200 mg Q2W             |
| Reporting group description:<br>CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:<br>•PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.<br>Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions. |                            |
| Reporting group title  | CZP 400 mg Q2W             |
| Reporting group description:<br>CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:<br>•PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.<br>Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.  |                            |
| Reporting group title  | Placebo/Placebo Q2W        |
| Reporting group description:<br>This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI75 response at Week 16 and continued to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).   |                            |
| Reporting group title  | Etanercept/Placebo Q2W     |
| Reporting group description:<br>This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).   |                            |
| Reporting group title  | Etanercept/CZP 200 mg Q2W  |
| Reporting group description:<br>This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).  |                            |
| Reporting group title  | CZP 200 mg Q2W/Placebo Q2W |



Reporting group description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | CZP 200 mg Q2W/CZP 200 mg Q2W |
|-----------------------|-------------------------------|

Reporting group description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | CZP 200 mg Q2W/CZP 400 mg Q4W |
|-----------------------|-------------------------------|

Reporting group description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q4W in the Maintenance Period (Week 16 to Week 48).

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | CZP 400 mg Q2W/Placebo Q2W |
|-----------------------|----------------------------|

Reporting group description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48).

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | CZP 400 mg Q2W/CZP 200 mg Q2W |
|-----------------------|-------------------------------|

Reporting group description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48).

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | CZP 400 mg Q2W/CZP 400 mg Q2W |
|-----------------------|-------------------------------|

Reporting group description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q2W in the Maintenance Period (Week 16 to Week 48).

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Placebo Q2W/Escape CZP 400 mg Q2W |
|-----------------------|-----------------------------------|

Reporting group description:

This arm consisted of participants initially randomized in the Placebo arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

|                       |                                  |
|-----------------------|----------------------------------|
| Reporting group title | Etanercept/Escape CZP 400 mg Q2W |
|-----------------------|----------------------------------|

Reporting group description:

This arm consisted of participants initially randomized in the Etanercept arm, who did not achieve a PASI75 response at Week 16 escaped from the treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | CZP 200 mg Q2W/Escape CZP 400 mg Q2W |
|-----------------------|--------------------------------------|

Reporting group description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | CZP 400 mg Q2W/Escape CZP 400 mg Q2W |
|-----------------------|--------------------------------------|

Reporting group description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who did not achieve a PASI75 response at Week 16 escaped from the blinded treatment and received CZP 400 mg every two weeks. Participants who did not achieve PASI50 after 16 weeks of unblinded treatment were withdrawn from the study.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Placebo/CZP 200 mg Q2W OLE |
|-----------------------|----------------------------|

Reporting group description:

This arm consisted of participants from the Placebo-controlled Maintenance Period, who achieved PASI50 response (had no relapse) at Week 48 and entered the 96-Weeks OLE Period receiving CZP 200 mg Q2W.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | CZP 200 mg Q2W/CZP 200 mg Q2W OLE |
|-----------------------|-----------------------------------|

Reporting group description:

This arm consisted of participants who received CZP 200 mg Q2W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | CZP 400 mg Q4W/CZP 200 mg Q2W OLE |
|-----------------------|-----------------------------------|

Reporting group description:

This arm consisted of participants who received CZP 400 mg Q4W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE on the CZP 200mg Q2W dose.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | CZP 400 mg Q2W/CZP 200 mg Q2W OLE |
|-----------------------|-----------------------------------|

Reporting group description:

This arm consisted of participants who received CZP 400 mg Q2W in the Maintenance Period, who achieved a PASI50 response (had no relapse) at Week 48 and entered OLE on the CZP 200mg Q2W dose.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Esc CZP 400 mg Q2W/CZP 400 mg Q2W OLE |
|-----------------------|---------------------------------------|

Reporting group description:

This arm consisted of participants who received open-label CZP 400mg Q2W in the Maintenance Period and entered OLE.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Placebo/CZP 400 mg Q2W OLE |
|-----------------------|----------------------------|

Reporting group description:

This arm consisted of participants from the Placebo-controlled Maintenance Period, who did not achieve PASI50 response (had relapse) and entered the 96-weeks OLE Period receiving CZP 400 mg Q2W.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Any CZP/CZP 400 mg Q2W OLE |
|-----------------------|----------------------------|

Reporting group description:

This arm consisted of participants who relapsed on CZP 200 mg Q2W, CZP 400 mg Q4W and 400 mg Q2W.

|                            |                  |
|----------------------------|------------------|
| Subject analysis set title | Placebo Q2W (RS) |
|----------------------------|------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Placebo subcutaneous (sc) injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 continued to receive blinded Placebo. PASI75 non-responders at Week 16 were removed from blinded study medication and escaped to Certolizumab pegol (CZP) 400 mg Q2W. Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study.

Participants could enter a 96-week open-label extension period after completing the Maintenance Period (Weeks 16-48) and receive CZP under certain conditions.

Participants formed the Randomized Set (RS).

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Etanercept (RS) |
|----------------------------|-----------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Etanercept (ETN) 50 mg subcutaneous (sc) injections twice per week throughout Week 11.5.

- PASI75 responders at Week 16 were re-randomized to either CZP (loading dose of 400 mg at Weeks 16, 18, and 20 followed by 200 mg Q2W) or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Participants formed the Randomized Set (RS).

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | CZP 200 mg Q2W (RS) |
|----------------------------|---------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

CZP 400 mg injections at Weeks 0, 2, 4, followed by CZP 200 mg every 2 weeks (Q2W) from Week 6 to Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 were re-randomized to receive either CZP 200 mg Q2W or CZP 400 mg every 4 weeks (Q4W); with Placebo administered on alternate dosing weeks to maintain the blind) Or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Participants formed the Randomized Set (RS).

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | CZP 400 mg Q2W (RS) |
| Subject analysis set type  | Full analysis       |

Subject analysis set description:

CZP 400 mg injections every 2 weeks (Q2W) through Week 14. Treatment received from Week 16-48 is based on initial treatment and response to treatment:

- PASI75 responders at Week 16 were re-randomized to CZP 200 mg Q2W or CZP 400 mg Q2W or Placebo Q2W. Participants who did not achieve a PASI75 response at Week 16 were removed from blinded study medication and escaped to CZP 400 mg Q2W.

Participants who received unblinded CZP 400 mg Q2W for 16 weeks and did not achieve a PASI50 response were withdrawn from the study. Participants could enter a 96-week open-label extension period after completing the Maintenance Period and receive CZP under certain conditions.

Participants formed the Randomized Set (RS).

|                            |                              |
|----------------------------|------------------------------|
| Subject analysis set title | Placebo/Placebo Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                |

Subject analysis set description:

This arm consisted of participants initially randomized in the Placebo arm, who achieved a PASI75 response at Week 16 and continued to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                                 |
|----------------------------|---------------------------------|
| Subject analysis set title | Etanercept/Placebo Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                   |

Subject analysis set description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                                    |
|----------------------------|------------------------------------|
| Subject analysis set title | Etanercept/CZP 200 mg Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                      |

Subject analysis set description:

This arm consisted of participants initially randomized in the Etanercept arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                                     |
|----------------------------|-------------------------------------|
| Subject analysis set title | CZP 200 mg Q2W/Placebo Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                       |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |  |
|----------------------------|--|
| Subject analysis set title | CZP 200 mg Q2W/CZP 200 mg Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                          |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |  |
|----------------------------|--|
| Subject analysis set title | CZP 200 mg Q2W/CZP 400 mg Q4W (WK16RS) |
| Subject analysis set type  | Full analysis                          |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 200 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q4W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                                     |
|----------------------------|-------------------------------------|
| Subject analysis set title | CZP 400 mg Q2W/Placebo Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                       |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded Placebo in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |  |
|----------------------------|--|
| Subject analysis set title | CZP 400 mg Q2W/CZP 200 mg Q2W (WK16RS) |
| Subject analysis set type  | Full analysis                          |

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75

response at Week 16 and were re-randomized to receive blinded CZP 200 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |  |
|----------------------------|--|
| Subject analysis set title | CZP 400 mg Q2W/CZP 400 mg Q2W (WK16RS) |
|----------------------------|--|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

This arm consisted of participants initially randomized in the CZP 400 mg arm, who achieved a PASI75 response at Week 16 and were re-randomized to receive blinded CZP 400 mg Q2W in the Maintenance Period (Week 16 to Week 48). Participants formed the Week 16 Randomized Set (WK16RS).

|                            |                      |
|----------------------------|----------------------|
| Subject analysis set title | CZP 200 mg Q2W (TCS) |
|----------------------------|----------------------|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

This arm consisted of all participants who received CZP 200 mg at any time during the study.

|                            |                      |
|----------------------------|----------------------|
| Subject analysis set title | CZP 400 mg Q2W (TCS) |
|----------------------------|----------------------|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

This arm consisted of all participants who received CZP 400 mg at any time during the study.

## Primary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 12

|                 |   |
|-----------------|---|
| End point title | Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 12 |
|-----------------|---|

End point description:

The PASI75 response assessments are based on at least 75% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person's affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 12

| End point values                  | Placebo Q2W (RS)     | Etanercept (RS)      | CZP 200 mg Q2W (RS)  | CZP 400 mg Q2W (RS)  |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed       | 57                   | 170                  | 165                  | 167                  |
| Units: percentage of participants |                      |                      |                      |                      |
| number (not applicable)           | 5.0                  | 53.3                 | 61.3                 | 66.7                 |

## Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|                   |  |
|-------------------|--|
| Comparison groups | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
|-------------------|--|

|   |  |
|---|--|
| Number of subjects included in analysis | 224                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Estimated difference in responder rate |
| Point estimate                          | 61.6                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 52.1                                   |
| upper limit                             | 71.2                                   |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis 2                 |
| Statistical analysis description:  |  |
| The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups  | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis  | 222                                    |
| Analysis specification   | Pre-specified                          |
| Analysis type  | superiority                            |
| Method   | Regression, Logistic                   |
| Parameter estimate   | Estimated difference in responder rate |
| Point estimate   | 56.2                                   |
| Confidence interval  |  |
| level  | 95 %                                   |
| sides  | 2-sided                                |
| lower limit  | 46.4                                   |
| upper limit  | 66                                     |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis 3                 |
| Statistical analysis description:  |  |
| The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups  | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis  | 224                                    |
| Analysis specification   | Pre-specified                          |
| Analysis type  | superiority                            |
| P-value  | < 0.0001 <sup>[1]</sup>                |
| Method   | Regression, Logistic                   |
| Parameter estimate   | Odds ratio (OR)                        |
| Point estimate   | 37.988                                 |
| Confidence interval  |  |
| level  | 95 %                                   |
| sides  | 2-sided                                |
| lower limit  | 11.312                                 |
| upper limit  | 127.576                                |

Notes:

[1] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO.

| Statistical analysis title  | Statistical Analysis 4                 |
|---|--|
| Statistical analysis description:<br>The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups   | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis   | 222                                    |
| Analysis specification  | Pre-specified                          |
| Analysis type   | superiority                            |
| P-value   | < 0.0001 <sup>[2]</sup>                |
| Method  | Regression, Logistic                   |
| Parameter estimate  | Odds ratio (OR)                        |
| Point estimate  | 30.023                                 |
| Confidence interval   |  |
| level   | 95 %                                   |
| sides   | 2-sided                                |
| lower limit   | 8.971                                  |
| upper limit   | 100.481                                |

Notes:

[2] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO.

| Statistical analysis title  | Statistical Analysis 5                 |
|---|--|
| Statistical analysis description:<br>The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups   | Etanercept (RS) v CZP 400 mg Q2W (RS)  |
| Number of subjects included in analysis   | 337                                    |
| Analysis specification  | Pre-specified                          |
| Analysis type   | superiority                            |
| Method  | Regression, Logistic                   |
| Parameter estimate  | Estimated difference in responder rate |
| Point estimate  | 13.4                                   |
| Confidence interval   |  |
| level   | 95 %                                   |
| sides   | 2-sided                                |
| lower limit   | 2.7                                    |
| upper limit   | 24.1                                   |

| Statistical analysis title  | Statistical Analysis 6                |
|---|---------------------------------------|
| Statistical analysis description:<br>The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |                                       |
| Comparison groups   | Etanercept (RS) v CZP 200 mg Q2W (RS) |

|   |  |
|---|--|
| Number of subjects included in analysis | 335                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Estimated difference in responder rate |
| Point estimate                          | 8                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -2.9                                   |
| upper limit                             | 18.9                                   |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 7 |
|-----------------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |                                       |
|---|---------------------------------------|
| Comparison groups                       | Etanercept (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis | 337                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.0152 <sup>[3]</sup>               |
| Method                                  | Regression, Logistic                  |
| Parameter estimate                      | Odds ratio (OR)                       |
| Point estimate                          | 1.756                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 1.114                                 |
| upper limit                             | 2.768                                 |

Notes:

[3] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. ETN.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |                                       |
|---|---------------------------------------|
| Comparison groups                       | Etanercept (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis | 335                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.1523 <sup>[4]</sup>               |
| Method                                  | Regression, Logistic                  |
| Parameter estimate                      | Odds ratio (OR)                       |
| Point estimate                          | 1.388                                 |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 0.886                                 |
| upper limit                             | 2.175                                 |

Notes:

[4] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. ETN

### Secondary: Proportion of subjects who achieve a Physician's Global Assessment (PGA) Clear or Almost Clear response (with at least 2 category improvement) at Week 12

|                 |   |
|-----------------|---|
| End point title | Proportion of subjects who achieve a Physician's Global Assessment (PGA) Clear or Almost Clear response (with at least 2 category improvement) at Week 12 |
|-----------------|---|

End point description:

The Investigator assessed the overall severity of Psoriasis (PSO) using the following 5-point scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

| End point values                  | Placebo Q2W (RS)     | Etanercept (RS)      | CZP 200 mg Q2W (RS)  | CZP 400 mg Q2W (RS)  |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed       | 57                   | 170                  | 165                  | 167                  |
| Units: percentage of participants |                      |                      |                      |                      |
| number (not applicable)           | 1.9                  | 39.2                 | 39.8                 | 50.3                 |

### Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis | 224                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Estimated difference in responder rate |
| Point estimate                          | 48.5                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 39.33                                  |
| upper limit                             | 57.63                                  |

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables



accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis | 222                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Estimated difference in responder rate |
| Point estimate                          | 37.9                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 28.88                                  |
| upper limit                             | 46.96                                  |

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Statistical Analysis 3                 |
| Statistical analysis description:<br>The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups   | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis   | 224                                    |
| Analysis specification  | Pre-specified                          |
| Analysis type   | superiority                            |
| P-value   | < 0.0001 <sup>[5]</sup>                |
| Method  | Regression, Logistic                   |
| Parameter estimate  | Odds ratio (OR)                        |
| Point estimate  | 56.129                                 |
| Confidence interval   |  |
| level   | 95 %                                   |
| sides   | 2-sided                                |
| lower limit   | 7.787                                  |
| upper limit   | 404.555                                |

Notes:

[5] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Statistical Analysis 4                 |
| Statistical analysis description:<br>The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups   | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis   | 222                                    |
| Analysis specification  | Pre-specified                          |
| Analysis type   | superiority                            |
| P-value   | = 0.0004 <sup>[6]</sup>                |
| Method  | Regression, Logistic                   |
| Parameter estimate  | Odds ratio (OR)                        |
| Point estimate  | 36.566                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 5.061   |
| upper limit         | 264.196 |

Notes:

[6] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

## Secondary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI90) response at Week 12

|                 |   |
|-----------------|---|
| End point title | Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI90) response at Week 12 |
|-----------------|---|

End point description:

The PASI90 response assessments are based on at least 90% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person's affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

| End point values                  | Placebo Q2W (RS)     | Etanercept (RS)      | CZP 200 mg Q2W (RS)  | CZP 400 mg Q2W (RS)  |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed       | 57                   | 170                  | 165                  | 167                  |
| Units: percentage of participants |                      |                      |                      |                      |
| number (not applicable)           | 0.2                  | 27.1                 | 31.2                 | 34.0                 |

## Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis | 224                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Estimated difference in responder rate |
| Point estimate                          | 33.8                                   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 20.68   |
| upper limit         | 46.98   |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis | 222                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Estimated difference in responder rate |
| Point estimate                          | 31                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 18.18                                  |
| upper limit                             | 43.8                                   |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis | 224                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | < 0.0001 <sup>[7]</sup>                |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 39.949                                 |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 8.407                                  |
| upper limit                             | 189.828                                |

Notes:

[7] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis | 222                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | < 0.0001 <sup>[8]</sup>                |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 35.084                                 |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 7.363                                  |
| upper limit                             | 167.179                                |

Notes:

[8] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

### Secondary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 16

|                 |   |
|-----------------|---|
| End point title | Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 16 |
|-----------------|---|

End point description:

The PASI75 response assessments are based on at least 75% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person's affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 16

| End point values                  | Placebo Q2W (RS)     | CZP 200 mg Q2W (RS)  | CZP 400 mg Q2W (RS)  |  |
|-----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed       | 57                   | 165                  | 167                  |  |
| Units: percentage of participants |                      |                      |                      |  |
| number (not applicable)           | 3.8                  | 68.2                 | 74.7                 |  |

### Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|                   |  |
|-------------------|--|
| Comparison groups | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
|-------------------|--|

|   |  |
|---|--|
| Number of subjects included in analysis | 224                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Estimated difference in responder rate |
| Point estimate                          | 70.9                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 62.15                                  |
| upper limit                             | 79.59                                  |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis | 222                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Estimated difference in responder rate |
| Point estimate                          | 64.4                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 55.12                                  |
| upper limit                             | 73.63                                  |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis | 224                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | < 0.0001 <sup>[9]</sup>                |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 76.277                                 |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 17.952                                 |
| upper limit                             | 324.094                                |

Notes:

[9] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Statistical Analysis 4                 |
| Statistical analysis description:<br>The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups   | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis   | 222                                    |
| Analysis specification  | Pre-specified                          |
| Analysis type   | superiority                            |
| P-value   | < 0.0001 <sup>[10]</sup>               |
| Method  | Regression, Logistic                   |
| Parameter estimate  | Odds ratio (OR)                        |
| Point estimate  | 55.413                                 |
| Confidence interval   |  |
| level   | 95 %                                   |
| sides   | 2-sided                                |
| lower limit   | 13.135                                 |
| upper limit   | 233.782                                |

Notes:

[10] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

### **Secondary: Proportion of subjects who achieve a Physician's Global Assessment (PGA) Clear or Almost Clear response (with at least 2 category improvement) at Week 16**

|  |   |
|--|---|
| End point title  | Proportion of subjects who achieve a Physician's Global Assessment (PGA) Clear or Almost Clear response (with at least 2 category improvement) at Week 16 |
| End point description:<br>The Investigator assessed the overall severity of Psoriasis (PSO) using the following 5-point scale:<br>0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Week 16  |   |

| <b>End point values</b>           | Placebo Q2W (RS)     | CZP 200 mg Q2W (RS)  | CZP 400 mg Q2W (RS)  |  |
|-----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed       | 57                   | 165                  | 167                  |  |
| Units: percentage of participants |                      |                      |                      |  |
| number (not applicable)           | 3.4                  | 48.3                 | 58.4                 |  |

### **Statistical analyses**

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 1 |
|-----------------------------------|------------------------|

|  |  |
|--|--|
| Statistical analysis description:  |  |
| The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups  | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis  | 224                                    |
| Analysis specification   | Pre-specified                          |
| Analysis type  | superiority                            |
| Method   | Regression, Logistic                   |
| Parameter estimate   | Estimated difference in responder rate |
| Point estimate   | 55                                     |
| Confidence interval  |  |
| level  | 95 %                                   |
| sides  | 2-sided                                |
| lower limit  | 45.59                                  |
| upper limit  | 64.35                                  |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis 2                 |
| Statistical analysis description:  |  |
| The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups  | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis  | 222                                    |
| Analysis specification   | Pre-specified                          |
| Analysis type  | superiority                            |
| Method   | Regression, Logistic                   |
| Parameter estimate   | Estimated difference in responder rate |
| Point estimate   | 44.9                                   |
| Confidence interval  |  |
| level  | 95 %                                   |
| sides  | 2-sided                                |
| lower limit  | 35.39                                  |
| upper limit  | 54.49                                  |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis 3                 |
| Statistical analysis description:  |  |
| The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups  | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis  | 224                                    |
| Analysis specification   | Pre-specified                          |
| Analysis type  | superiority                            |
| P-value  | < 0.0001 <sup>[11]</sup>               |
| Method   | Regression, Logistic                   |
| Parameter estimate   | Odds ratio (OR)                        |
| Point estimate   | 40.717                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 9.741   |
| upper limit         | 170.198 |

Notes:

[11] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis | 222                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | < 0.0001 <sup>[12]</sup>               |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 27.165                                 |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | 6.504   |
| upper limit | 113.453 |

Notes:

[12] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

### **Secondary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI90) response at Week 16**

|                 |   |
|-----------------|---|
| End point title | Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI90) response at Week 16 |
|-----------------|---|

End point description:

The PASI90 response assessments are based on at least 90% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person's affected skin for the respective section. The minimum possible PASI score is 0= no disease, the maximum score is 72= maximal disease.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 16



| End point values                  | Placebo Q2W (RS)     | CZP 200 mg Q2W (RS)  | CZP 400 mg Q2W (RS)  |  |
|-----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed       | 57                   | 165                  | 167                  |  |
| Units: percentage of participants |                      |                      |                      |  |
| number (not applicable)           | 0.3                  | 39.8                 | 49.1                 |  |

## Statistical analyses

| Statistical analysis title  | Statistical Analysis 1                 |
|---|--|
| Statistical analysis description:<br>The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups   | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis   | 224                                    |
| Analysis specification  | Pre-specified                          |
| Analysis type   | superiority                            |
| Method  | Regression, Logistic                   |
| Parameter estimate  | Estimated difference in responder rate |
| Point estimate  | 48.8                                   |
| Confidence interval   |  |
| level   | 95 %                                   |
| sides   | 2-sided                                |
| lower limit   | 34.22                                  |
| upper limit   | 63.41                                  |

| Statistical analysis title  | Statistical Analysis 2                 |
|---|--|
| Statistical analysis description:<br>The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure. |  |
| Comparison groups   | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis   | 222                                    |
| Analysis specification  | Pre-specified                          |
| Analysis type   | superiority                            |
| Method  | Regression, Logistic                   |
| Parameter estimate  | Estimated difference in responder rate |
| Point estimate  | 39.5                                   |
| Confidence interval   |  |
| level   | 95 %                                   |
| sides   | 2-sided                                |
| lower limit   | 25.58                                  |
| upper limit   | 53.38                                  |

| Statistical analysis title | Statistical Analysis 3 |
|----------------------------|------------------------|
|----------------------------|------------------------|

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**Statistical analysis description:**

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 400 mg Q2W (RS) |
| Number of subjects included in analysis | 224                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | < 0.0001 <sup>[13]</sup>               |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 72.278                                 |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 14.65                                  |
| upper limit                             | 356.602                                |

Notes:

[13] - The p-value is evaluated at a 2-sided significance level for CZP 400 mg vs. PBO

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|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

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**Statistical analysis description:**

The statistical analysis of the co-primary efficacy variables and key secondary efficacy variables accounted for multiplicity by using a fixed sequence testing procedure.

|   |  |
|---|--|
| Comparison groups                       | Placebo Q2W (RS) v CZP 200 mg Q2W (RS) |
| Number of subjects included in analysis | 222                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | superiority                            |
| P-value                                 | < 0.0001 <sup>[14]</sup>               |
| Method                                  | Regression, Logistic                   |
| Parameter estimate                      | Odds ratio (OR)                        |
| Point estimate                          | 49.527                                 |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | 10.002                                 |
| upper limit                             | 245.256                                |

Notes:

[14] - The p-value is evaluated at a 2-sided significance level for CZP 200 mg vs. PBO

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**Secondary: Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 48 for those achieving PASI75 at Week 16**

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|                 |   |
|-----------------|---|
| End point title | Proportion of subjects who achieve a Psoriasis Activity and Severity Index (PASI75) response at Week 48 for those achieving PASI75 at Week 16 |
|-----------------|---|

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**End point description:**

The PASI75 response assessments are based on at least 75% improvement in the PASI score from Baseline. This is a scoring system that averages the redness, thickness, and scaliness of the psoriatic lesions (on a 0-4 scale), and weights the resulting score by the area of skin involved. Body divided into 4 areas: head, arms, trunk to groin, and legs to top of buttocks. Assignment of an average score for the redness, thickness, and scaling for each of the 4 body areas with a score of 0 (clear) to 4 (very marked). Determining the percentage of skin covered with PSO for each of the body areas and converting to a 0 to 6 scale. Final PASI= average redness, thickness, and scaliness of the psoriatic skin lesions, multiplied by the involved psoriasis area score of the respective section, and weighted by the percentage of the person's affected skin for the respective section. The minimum possible PASI score is

0= no disease, the maximum score is 72= maximal disease.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 48              |           |

| End point values                  | Placebo/Placebo Q2W (WK16RS) | Etanercept/Placebo Q2W (WK16RS) | Etanercept/CZP 200 mg Q2W (WK16RS) | CZP 200 mg Q2W/Placebo Q2W (WK16RS) |
|-----------------------------------|------------------------------|---------------------------------|------------------------------------|-------------------------------------|
| Subject group type                | Subject analysis set         | Subject analysis set            | Subject analysis set               | Subject analysis set                |
| Number of subjects analysed       | 2                            | 24                              | 50                                 | 22                                  |
| Units: percentage of participants |                              |                                 |                                    |                                     |
| number (not applicable)           | 100                          | 8.3                             | 82.0                               | 45.5                                |

| End point values                  | CZP 200 mg Q2W/CZP 200 mg Q2W (WK16RS) | CZP 200 mg Q2W/CZP 400 mg Q4W (WK16RS) | CZP 400 mg Q2W/Placebo Q2W (WK16RS) | CZP 400 mg Q2W/CZP 200 mg Q2W (WK16RS) |
|-----------------------------------|--|--|-------------------------------------|--|
| Subject group type                | Subject analysis set                   | Subject analysis set                   | Subject analysis set                | Subject analysis set                   |
| Number of subjects analysed       | 44                                     | 44                                     | 25                                  | 50                                     |
| Units: percentage of participants |  |  |                                     |  |
| number (not applicable)           | 79.5                                   | 88.6                                   | 36.0                                | 80.0                                   |

| End point values                  | CZP 400 mg Q2W/CZP 400 mg Q2W (WK16RS) |  |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                   |  |  |  |
| Number of subjects analysed       | 49                                     |  |  |  |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           | 98.0                                   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from Baseline (Week 0) until Week 144.

Adverse event reporting additional description:

At Week 16, most PBO-randomized participants escaped to CZP 400 mg Q2W and all ETN-randomized participants switched to PBO or CZP, leading to a significantly lower exposure in PBO/ETN arms than in CZP arms. Considering the limitations of such comparison, AEs reported while the participants were on PBO or ETN are not included in this summary.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

### Reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | CZP 200 mg Q2W (TCS) |
|-----------------------|----------------------|

Reporting group description:

This arm consisted of all participants who received CZP 200 mg at any time during the study.

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | CZP 400 mg Q2W (TCS) |
|-----------------------|----------------------|

Reporting group description:

This arm consisted of all participants who received CZP 400 mg at any time during the study.

| Serious adverse events  | CZP 200 mg Q2W (TCS) | CZP 400 mg Q2W (TCS) |  |
|---|----------------------|----------------------|--|
| Total subjects affected by serious adverse events                   |                      |                      |  |
| subjects affected / exposed   | 37 / 373 (9.92%)     | 51 / 412 (12.38%)    |  |
| number of deaths (all causes)                                       | 2                    | 1                    |  |
| number of deaths resulting from adverse events                      | 1                    | 0                    |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                      |                      |  |
| Anaplastic oligodendroglioma  |                      |                      |  |
| subjects affected / exposed   | 0 / 373 (0.00%)      | 1 / 412 (0.24%)      |  |
| occurrences causally related to treatment / all                     | 0 / 0                | 0 / 1                |  |
| deaths causally related to treatment / all                          | 0 / 0                | 0 / 0                |  |
| Glioblastoma  |                      |                      |  |
| subjects affected / exposed   | 1 / 373 (0.27%)      | 0 / 412 (0.00%)      |  |
| occurrences causally related to treatment / all                     | 0 / 1                | 0 / 0                |  |
| deaths causally related to treatment / all                          | 0 / 0                | 0 / 0                |  |
| Hodgkin's disease   |                      |                      |  |
| subjects affected / exposed   | 1 / 373 (0.27%)      | 0 / 412 (0.00%)      |  |
| occurrences causally related to treatment / all                     | 0 / 1                | 0 / 0                |  |
| deaths causally related to treatment / all                          | 0 / 0                | 0 / 0                |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Laryngeal cancer                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Clear cell renal cell carcinoma                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Benign neoplasm of bladder                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vascular disorders                              |                 |                 |  |
| Hypertensive crisis                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Peripheral arterial occlusive disease           |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pregnancy, puerperium and perinatal conditions  |                 |                 |  |
| Abortion  |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Abortion missed                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pregnancy with contraceptive                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| General disorders and administration site conditions |                 |                 |  |
| Inflammation   |                 |                 |  |
| subjects affected / exposed                          | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Systemic inflammatory response syndrome              |                 |                 |  |
| subjects affected / exposed                          | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Nodule   |                 |                 |  |
| subjects affected / exposed                          | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Vascular stent thrombosis                            |                 |                 |  |
| subjects affected / exposed                          | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Immune system disorders                              |                 |                 |  |
| Sarcoidosis  |                 |                 |  |
| subjects affected / exposed                          | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| House dust allergy                                   |                 |                 |  |
| subjects affected / exposed                          | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Reproductive system and breast disorders             |                 |                 |  |
| Cervical polyp                                       |                 |                 |  |
| subjects affected / exposed                          | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Ovarian cyst   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 373 (0.27%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Uterine cyst                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Endometrial hyperplasia                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Uterine polyp                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Dyspnoea  |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Chronic obstructive pulmonary disease           |                 |                 |  |
| subjects affected / exposed                     | 2 / 373 (0.54%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Nasal septum deviation                          |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pulmonary embolism                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psychiatric disorders                           |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| Bipolar I disorder                               |                 |                 |  |
| subjects affected / exposed                      | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Depression                                       |                 |                 |  |
| subjects affected / exposed                      | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Investigations                                   |                 |                 |  |
| Mycobacterium tuberculosis complex test negative |                 |                 |  |
| subjects affected / exposed                      | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Blood creatine phosphokinase increased           |                 |                 |  |
| subjects affected / exposed                      | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications   |                 |                 |  |
| Meniscus injury                                  |                 |                 |  |
| subjects affected / exposed                      | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Concussion                                       |                 |                 |  |
| subjects affected / exposed                      | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Craniocerebral injury                            |                 |                 |  |
| subjects affected / exposed                      | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 1           |  |
| Extradural haematoma                             |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Wrist fracture                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 2 / 412 (0.49%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Foot fracture                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Forearm fracture                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lower limb fracture                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Radius fracture                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ulna fracture                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ligament rupture                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Laceration                                      |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Facial bones fracture                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Rib fracture                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Intracardiac mass                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Coronary artery disease                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac failure                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute coronary syndrome                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute myocardial infarction                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0           |  |
| Angina pectoris                                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |
| Migraine  |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 2 / 412 (0.49%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Primary progressive multiple sclerosis          |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ear and labyrinth disorders                     |                 |                 |  |
| Vestibular disorder                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tympanic membrane perforation                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Eye disorders                                   |                 |                 |  |
| Cataract  |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Retinal detachment                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Large intestine polyp                           |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Crohn's disease                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Abdominal pain                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Haemorrhoids                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Inguinal hernia                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper gastrointestinal haemorrhage              |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Peptic ulcer                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Umbilical hernia                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Cholecystitis                                   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Liver disorder                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute hepatic failure                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatitis                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin and subcutaneous tissue disorders          |                 |                 |  |
| Erythrodermic psoriasis                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Guttate psoriasis                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psoriasis                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pustular psoriasis                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Purpura   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin ulcer                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Urinary bladder haemorrhage                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute kidney injury                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nephrolithiasis                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal cyst                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Sacroiliitis                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Spinal pain                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Chondropathy                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Polymyalgia rheumatica                          |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Mobility decreased                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Compartment syndrome                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Osteoarthritis                                  |                 |                 |  |
| subjects affected / exposed                     | 3 / 373 (0.80%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psoriatic arthropathy                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Appendiceal abscess                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Appendicitis perforated                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancreas infection                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Rectal abscess                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cellulitis                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Osteomyelitis                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Escherichia sepsis                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Endophthalmitis                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia klebsiella                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 373 (0.27%) | 2 / 412 (0.49%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchitis                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bacteraemia                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sepsis  |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pyoderma  |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Subcutaneous abscess                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 373 (0.27%) | 0 / 412 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Erysipelas                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tuberculosis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pyelonephritis                                  |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Obesity   |                 |                 |  |
| subjects affected / exposed                     | 0 / 373 (0.00%) | 1 / 412 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | CZP 200 mg Q2W (TCS) | CZP 400 mg Q2W (TCS) |  |
|---|----------------------|----------------------|--|
| Total subjects affected by non-serious adverse events |                      |                      |  |
| subjects affected / exposed                           | 150 / 373 (40.21%)   | 159 / 412 (38.59%)   |  |
| Vascular disorders                                    |                      |                      |  |
| Hypertension  |                      |                      |  |
| subjects affected / exposed                           | 20 / 373 (5.36%)     | 24 / 412 (5.83%)     |  |
| occurrences (all)                                     | 21                   | 24                   |  |
| Musculoskeletal and connective tissue disorders       |                      |                      |  |
| Arthralgia  |                      |                      |  |
| subjects affected / exposed                           | 17 / 373 (4.56%)     | 18 / 412 (4.37%)     |  |
| occurrences (all)                                     | 20                   | 20                   |  |
| Infections and infestations                           |                      |                      |  |
| Bronchitis  |                      |                      |  |
| subjects affected / exposed                           | 18 / 373 (4.83%)     | 18 / 412 (4.37%)     |  |
| occurrences (all)                                     | 21                   | 19                   |  |
| Nasopharyngitis                                       |                      |                      |  |
| subjects affected / exposed                           | 57 / 373 (15.28%)    | 66 / 412 (16.02%)    |  |
| occurrences (all)                                     | 84                   | 83                   |  |
| Upper respiratory tract infection                     |                      |                      |  |
| subjects affected / exposed                           | 39 / 373 (10.46%)    | 45 / 412 (10.92%)    |  |
| occurrences (all)                                     | 58                   | 64                   |  |
| Viral upper respiratory tract infection               |                      |                      |  |
| subjects affected / exposed                           | 23 / 373 (6.17%)     | 11 / 412 (2.67%)     |  |
| occurrences (all)                                     | 38                   | 13                   |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment   |
|---------------|---|
| 20 April 2015 | <p>Global Protocol Amendment 1 incorporated the country-specific amendments in the UK (Amendments 0.1 and 0.5), the Czech Republic (Amendment 0.2), Germany (Amendment 0.3), and France (Amendment 0.4).</p> <p>In addition, the following changes were made:</p> <ul style="list-style-type: none"><li>•Updated study contact information.</li><li>•The treatment received in Period 3 was based on initial treatment and response to treatment at Week 16. All CZP and Placebo (PBO) treatments were to be administered by dedicated unblinded site personnel at site visits.<ul style="list-style-type: none"><li>-Subjects initially randomized to CZP 200 mg Q2W were rerandomized (2:2:1) to receive either CZP 200 mg Q2W or CZP 400 mg Q4W (with PBO administered on alternate dosing weeks to maintain the blind) or PBO</li></ul></li><li>•Etanercept (ETN) treatments were allowed to be administered by trained study staff on site or outside of the study center (to allow flexibility around self-administration). If ETN was self-administered, compliance was to be recorded on a drug administration log by the subject and data were to be entered into the electronic Case Report form (eCRF) by study personnel. The percentage of doses missed (2 or more doses changed to 25% or more of the doses) was updated; ETN was administered more frequently than CZP or placebo during the Initial Treatment Period.</li><li>•The number of planned sites was increased (from 50 to 67) and Australia and Canada were removed.</li><li>•Exclusion Criterion #6 was clarified to include latex hypersensitivity.</li><li>•Changes were made to drug accountability to allow for on-site destruction with prior Sponsor approval.</li><li>•Secukinumab was added as a prohibited concomitant treatment.</li><li>•Stratification across sites based on prior biologic use was eliminated.</li><li>•Text describing the modified Nail Psoriasis Severity Index (mNAPSI) was updated.</li><li>•Elispot testing for tuberculosis was removed. The chest x-ray required at screening was not needed if an x-ray had already been performed within 3 months of screening.</li><li>•A center-by-treatment interaction analysis was added and described.</li></ul> |

|                  |   |
|------------------|---|
| 23 December 2015 | <p>Global Protocol Amendment 2 included the following changes:</p> <ul style="list-style-type: none"> <li>•CIMPACT (name of the PS0003 protocol) was added.</li> <li>•Updated study contact information.</li> <li>•Having at least a 90% reduction from Baseline in Psoriasis Area and Severity Index (PASI90) at Weeks 12 and 16 were added as secondary efficacy variables and PASI90 at Week 12 was included in the sequential testing procedure for the efficacy analysis.</li> <li>•Added time to onset of PASI90 as an efficacy variable. Deleted time to loss of PASI75 response at Week 16. Added EQ-5D-Visual Analog Scale (VAS) (inadvertently omitted in previous protocol).</li> <li>•Clarified the dosing period during the Initial Treatment Period, assessments performed, and use of unblinded study staff for drug administration.</li> <li>•Clarified study medication administration in Open-label Extension (OLE) Treatment Period.</li> <li>•Added secukinumab 24 weeks prior to the Baseline Visit as an exclusion for prior treatment.</li> <li>•Clarified the withdrawal criteria and addition of a withdrawal criterion to be consistent with the study population. See Exclusion Criterion #6.</li> <li>•Text was added to clarify that the unblinded team at the site was to transition their activities once the Week 48 visits (blinded Maintenance Treatment Period) were completed.</li> <li>•Clarified prohibited concomitant medications and therapies.</li> <li>•Added a window for the Safety Follow-Up (SFU) Visit (10 weeks after final dose); the visit should have occurred no more than 3 days prior to the scheduled visit date and within 14 days after the scheduled visit date (-3 days/+14 days).</li> <li>•Addition of a "Treated with CZP Set" (TCS) to further assess the safety of CZP in subjects with PSO. Addition of a Maintenance Set (MS) to further assess the efficacy and safety of CZP in long-term treatment of PSO.</li> </ul> |
|------------------|---|

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported

## Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29660425>