**Sponsor**

Novartis Pharmaceuticals

**Generic Drug Name**

***Instruction:*** *Do not use trade/commercial names.*

***Example:*** *Valsartan*

**Trial Indication(s)**

***Instruction:*** *This information is usually found on the clinical study report (CSR) title page. Please record all indications being studied in this protocol.*

**Protocol Number**

CAIN457ADE11C

**Protocol Title**

A randomized, parallel-group, double-blind, placebo-controlled, multicenter phase 2 trial to investigate the safety and efficacy of secukinumab (AIN457) in patients with giant cell arteritis (TitAIN)

**Clinical Trial Phase**

Phase 2

**Phase of Drug Development**

***Instruction:*** *Stage of the drug in development. This is not the trial phase. For example a Phase I drug-drug interaction trial can be conducted during Phase 3 drug development.*

*Example: Phase I, II, III, IV*

**Study Start/End Dates**

Study Start Date: January 2019 (Actual)

Primary Completion Date: June 2021 (Actual)

Study Completion Date: June 2021 (Actual)

**Reason for Termination (If applicable)**

**Study Design/Methodology**

***Instruction:*** *This information is found in the CSR synopsis and should, at a minimum, contain the type of study conducted with a description of the treatment periods. Adjust verb tense to past*

*tense as necessary.*

***Definition:*** *Specific information about how the trial was conducted*

***Example:*** *Multicenter, multinational, randomized, double-blind, parallel-group, efficacy*

**Centers**

Germany(11)

**Objectives:**

***Instruction:*** *This information can be found in the CSR Synopsis. Objectives should align with the Outcome Measures.*

**Test Product (s), Dose(s), and Mode(s) of Administration**

***Instruction:*** *This information can be found in the CSR synopsis.*

***Definition****: Name, dose, and route of administration of study drug. Do not include preparation instructions of product.*

***Example:*** *Oral tablets of xyz 160 mg*

**Statistical Methods**

***Instruction*** *: Do not include the statistical methodology applied to exploratory outcome measures.*

***Definition****: Statistical methodology applied to the data. This section should be copied directly from the statistical methods section of the CSR Synopsis. If the stats methodology does not align with the primary and secondary outcome measures (results) than edit the statistical methodology section to ensure alignment with the primary and secondary results.*

***Example:*** *Unless otherwise specified, all statistical tests were conducted against a 2-sided alternative hypothesis, employing a significance level of 0.05.*

**Study Population: Key Inclusion/Exclusion Criteria**

Inclusion Criteria:
  
  
  
 Diagnosis of GCA classified according to the following criteria:
  
 •Age at onset of disease ≥ 50 years.
  
 •History of ESR ≥ 30 mm/hr or CRP ≥ 10 mg/L.
  
 •Unequivocal cranial symptoms of GCA (new-onset localized headache, scalp or temporal artery tenderness, ischemia-related vision loss, or otherwise unexplained mouth or jaw pain upon mastication)
  
AND/OR
  
symptoms of polymyalgia rheumatica (PMR) defined as shoulder and/or hip girdle pain associated with inflammatory morning stiffness
  
 •Temporal artery biopsy revealing features of GCA
  
AND/OR
  
 •evidence of large-vessel vasculitis by angiography or cross-sectional imaging study such as magnetic resonance angiography (MRA), computed tomography angiography (CTA), positron emission tomography-computed tomography (PET CT), or ultrasound
  
  
 Patients with new onset GCA or relapsing GCA
  
(Definition new onset: diagnosis of GCA within 6 weeks of Baseline Visit; Definition relapsing GCA: diagnosis of GCA (in accordance with inclusion criterion no. 4) > 6 weeks before Baseline Visit and in the meantime achieved remission (absence of signs and symptoms attributable to GCA and normalization of ESR (< 30 mm/hr) and CRP (<10.0mg/L) included) including previous treatment with ≥ 25 mg/day prednisolone equivalent for ≥ 2 weeks.)
  
  
 Active disease as defined by the presence of signs and symptoms of GCA (cranial or PMR) and elevated ESR ≥ 30 mm/hr, or CRP ≥ 10 mg/L, attributed to active GCA within 6 weeks of Baseline.
  
  
Prednisolone dose of 25-60 mg/day at Baseline.
  
  
  
Exclusion Criteria:
  
  
Previous exposure to secukinumab or other biologic drug directly targeting Interleukin(IL)-17 or IL-17 receptor.
  
  
Patients treated with any cell-depleting therapies including but not limited to anti-CD20 or investigational agents (e.g. anti-CD3, anti-CD4, anti-CD5 or anti-CD19).
  
  
Patients who have previously been treated with any biologic agent including but not limited to tocilizumab, sirukumab, abatacept, or tumor necrosis factor alpha (TNFα) inhibitors (infliximab, adalimumab, etanercept, certolizumab, golimumab).
  
  
Patients who have previously been treated with tofacitinib or baricitinib.
  
  
Patients treated with i.v. immunoglobulins or plasmapheresis within 8 weeks prior to Baseline.
  
  
Patients treated with cyclophosphamide, tacrolimus or everolimus within 6 months prior to Baseline.
  
  
Patients treated with hydroxychloroquine, cyclosporine A, azathioprine, sulfasalazine or mycophenolate mofetil within 4 weeks of Baseline.
  
  
Patients treated with leflunomide within 8 weeks of Baseline unless a cholestyramine washout has been performed in which case the patient must be treated within 4 weeks of Baseline.
  
  
Patients treated with an alkylating agent except for cyclophosphamide as mentioned above.
  
  
Patients requiring systemic chronic glucocorticoid therapy for any other reason than GCA.
  
  
Chronic systemic glucocorticoid therapy over the last 4 years or longer; or inability, in the opinion of the investigator, to withdraw glucocorticoid therapy through protocol-defined taper regimen due to suspected or established adrenal insufficiency.
  
  
Patients requiring chronic (i.e. not occasional “prn”) high potency opioid analgesics for pain management.
  
  
Active ongoing inflammatory diseases or underlying metabolic, hematologic, renal, hepatic, pulmonary, neurologic, endocrine, cardiac, infectious or gastrointestinal conditions, which in the opinion of the investigator immunosuppressed the patient and/or places the patient at unacceptable risk for participation in an immunomodulatory therapy.
  
  
History of renal trauma, glomerulonephritis, or patients with one kidney only, or a serum creatinine level exceeding 1.8 mg/dL (159.12 μmol/L).
  
  
Screening total white blood cell (WBC) count < 3000/μL, or platelets < 100 000/μL or neutrophils < 1500/μL or hemoglobin < 8.3 g/dL (83 g/L).
  
  
Major ischemic event, unrelated to GCA, within 12 weeks of screening.
  
  
Known infection with human immunodeficiency virus (HIV), hepatitis B or hepatitis C at screening or randomization.
  
  
Life vaccinations within 6 weeks prior to Baseline or planned vaccination during study participation until 12 weeks after last study treatment administration.

**Participant Flow Table**

|  |  |  |
| --- | --- | --- |
| **Overall Study** | | |
|  | **Secukinumab** | **Placebo** | **Total** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |  |
| **Started** | **27** | **25** | **52** |
| **Completed** | **22** | **17** | **39** |
| **Not Completed** | **5** | **8** | **13** |
| **Subject decision** | **2** | **3** | **5** |
| **Physician Decision** | **2** | **4** | **6** |
| **Death** | **0** | **1** | **1** |
| **Lost to Follow-up** | **1** | **0** | **1** |

**Baseline Characteristics**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Secukinumab** | **Placebo** | **Total** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |  |
| **Number of Participants [units: participants]** | **27** | **25** | **52** |
| **Age Continuous(units: years) Mean ± Standard Deviation** | | |
|  | **76.4±5.31** | **69.6±8.02** | **73.1±7.52** |
| **Sex: Female, Male(units: participants) Count of Participants (Not Applicable)** | | |
| **Female** | **17** | **18** | **35** |
| **Male** | **10** | **7** | **17** |
| **Race/Ethnicity, Customized(units: participants) Count of Participants (Not Applicable)** | | |
| **White** | **27** | **25** | **52** |

***Instruction****: This information can usually be found in Section 11 of the CSR. Do not include in-text table numbers, post-text table numbers, or appendix numbers from the CSR. Do not include figures or graphics. Do not include written descriptions.*

***Definition:*** *Outcome Measures tables should match what is in the CSR. Titles, Tables and Footnotes should be copied/pasted under Primary and Secondary Outcome Measure results. All Primary and Secondary Outcome Measures should be reported. If there is a corresponding Clinicaltrials.gov record, ensure the number and variable of Outcome Measures matches ClinicalTrial.gov. Formatting may differ.*

**Primary Outcome Result(s)**

**Percentage of GCA participants in sustained remission until Week 28(Time Frame: Until week 28)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Percentage of GCA participants in sustained remission until Week 28(units: percentage of participants)Median (95% Confidence Interval)** |
|  | **0.70(0.52 to 0.85)** | **0.20(0.12 to 0.30)** |

**Statistical Analysis**

|  |  |  |
| --- | --- | --- |
| **Groups** | **Secukinumab,Placebo** | **Odds Ratio** |
| **Odds Ratio (OR)** | **9.31** |  |
| **95% Confidence Interval2-Sided** | **3.54 to 26.29** |  |

**Statistical Analysis**

|  |  |  |
| --- | --- | --- |
| **Groups** | **Secukinumab,Placebo** | **Risk Difference** |
| **Risk Difference (RD)** | **0.50** |  |
| **95% Confidence Interval2-Sided** | **0.29 to 0.67** |  |

**Statistical Analysis**

|  |  |  |
| --- | --- | --- |
| **Groups** | **Secukinumab,Placebo** | **Risk ratio** |
| **Risk Ratio (RR)** | **3.43** |  |
| **95% Confidence Interval2-Sided** | **2.10 to 5.87** |  |

**Secondary Outcome Result(s)**

**Percentage of participants at remission at Week 12(Time Frame: Week 12)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Percentage of participants at remission at Week 12(units: percentage of participants)** |
|  | **81.5** | **48.0** |

**Time to first GCA flare after clinical remission(Time Frame: Up to Week 52 (included))**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Time to first GCA flare after clinical remission(units: days)Median (95% Confidence Interval)** |
|  | **NA(NA to NA) [1]** | **197.0(101.0 to 280.0)** |

[1] NA: not reached, why?

**Total cumulative prednisolone dose over 28 and 52 weeks(Time Frame: Over 28 and 52 weeks)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Total cumulative prednisolone dose over 28 and 52 weeks(units: total cumulative prednisolone)Mean ± Standard Deviation** | | |
| **Baseline to Week 28** | **2689.70 ± 935.860** | **2693.74 ± 1241.907** |
| **Baseline to Week 52** | **2841.26 ± 1116.192** | **3375.58 ± 1720.978** |

**Percentage of participants with GCA who had sustained remission until Week 52(Time Frame: Until Week 52)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Percentage of participants with GCA who had sustained remission until Week 52(units: Percentage of participants)** |
|  | **59.3** | **8.0** |

**Percentage of participants on prednisolone dose ≤ 5mg/day(Time Frame: Week 19, Week 28, Week 52)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Percentage of participants on prednisolone dose ≤ 5mg/day(units: Percentage of participants)** | | |
| **Week 19 (n = 25, 20)** | **88.0** | **50.0** |
| **Week 28 (n = 23, 20)** | **82.6** | **45.0** |
| **Week 52 (n = 21, 17)** | **90.5** | **76.5** |

**Physicians global assessment (PhGA) of disease activity: Change from Baseline Score via visual analogue scale (VAS)(Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 44 & 52)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Physicians global assessment (PhGA) of disease activity: Change from Baseline Score via visual analogue scale (VAS)(units: scores on a scale)Mean ± Standard Error** | | |
| **Week 4 (n = 27, 23)** | **-4.8 ± 14.43** | **-3.2 ± 18.45** |
| **Week 8 (n = 26, 21)** | **-5.8 ± 12.77** | **2.1 ± 18.94** |
| **Week 12 (n = 25, 20)** | **-3.4 ± 21.93** | **-3.1 ± 10.81** |
| **Week 16 (n = 25, 20)** | **-4.1 ± 15.62** | **0.7 ± 13.97** |
| **Week 20 (n = 24, 20)** | **-6.9 ± 14.78** | **-1.5 ± 14.32** |
| **Week 24 (n = 23, 20)** | **-4.3 ± 15.92** | **2.2 ± 17.22** |
| **Week 28 (23, 19)** | **-5.4 ± 15.61** | **3.9 ± 21.47** |
| **Week 36 (21, 19)** | **-8.7 ± 18.45** | **0.7 ± 17.45** |
| **Week 44 (n = 21, 16)** | **-5.5 ± 16.87** | **1.1 ± 15.20** |
| **Week 52 (n = 21, 16)** | **-9.5 ± 16.72** | **4.0 ± 21.24** |

**Patients global assessment (PGA) of disease activity: Change from Baseline via visual analogue scale (VAS)(Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 44 & 52)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Patients global assessment (PGA) of disease activity: Change from Baseline via visual analogue scale (VAS)(units: scores on a scale)Mean ± Standard Deviation** | | |
| **Week 4 (n = 27, 23)** | **-15.8 ± 28.17** | **-0.5 ± 23.58** |
| **Week 8 (n = 26, 21)** | **-15.8 ± 27.61** | **-10.8 ± 27.64** |
| **Week 12 (n = 25, 20)** | **-8.0 ± 29.43** | **-11.9 ± 31.46** |
| **Week 16 (n = 25, 20)** | **-18.6 ± 19.39** | **-8.8 ± 31.43** |
| **Week 20 (n = 24, 20)** | **-19.18 ± 30.68** | **-6.9 ± 31.94** |
| **Week 24 (n = 23, 20)** | **-14.9 ± 28.84** | **-7.0 ± 30.61** |
| **Week 28 (n = 23, 19)** | **-14.4 ± 25.46** | **-8.0 ± 31.31** |
| **Week 36 (n = 21, 19)** | **-20.9 ± 22.31** | **-8.6 ± 29.90** |
| **Week 44 (n = 21, 16)** | **-21.7 ± 27.35** | **-9.4 ± 30.58** |
| **Week 52 (n = 21, 16)** | **-19.2 ± 27.35** | **-15.9 ± 24.04** |

**Change from Baseline in FACIT-Fatigue scale(Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 44 & 52)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Change from Baseline in FACIT-Fatigue scale(units: scores on a scale)Mean ± Standard Deviation** | | |
| **Week 4 (n = 27, 23)** | **2.11 ± 9.613** | **-0.96 ± 7.358** |
| **Week 8 (n = 26, 21)** | **2.19 ± 10.190** | **0.81 ± 7.498** |
| **Week 12 (n = 25, 20)** | **0.96 ± 11.175** | **-0.25 ± 10.047** |
| **Week 16 (n = 25, 20)** | **2.12 ± 8.876** | **-0.36 ± 8.884** |
| **Week 20 (n =24, 20)** | **3.42 ± 8.617** | **0.05 ± 10.318** |
| **Week 24 (n = 23, 20)** | **2.91 ± 10.409** | **-3.10 ± 11.281** |
| **Week 28 (n = 23, 19)** | **3.61 ± 11.044** | **0.42 ± 9.203** |
| **Week 36 (n = 21, 19)** | **3.90 ± 7.245** | **1.84 ± 8.719** |
| **Week 44 (n = 21, 16)** | **2.67 ± 5.986** | **0.31 ± 10.928** |
| **Week 52 (n = 21, 16)** | **19.63 ± 43.792** | **5.51 ± 27.259** |

**Change from Baseline in Short-Form (SF)-36 questionnaire(Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 44 & 52)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Change from Baseline in Short-Form (SF)-36 questionnaire(units: scores on a scale)Mean ± Standard Deviation** | | |
| **Week 4: Physical Functioning (PF) (n = 27, 23)** | **44.36 ± 11.226** | **43.98 ± 10.159** |
| **Week 8: PF (n = 26 ,21)** | **-0.44 ± 8.849** | **0.18 ± 4.987** |
| **Week 12: PF (n = 25, 20)** | **0.38 ± 6.322** | **-0.38 ± 8.750** |
| **Week 16: PF (n = 25, 20)** | **-0.00 ± 8.646** | **-0.86 ± 6.814** |
| **Week 20: PF (n = 24, 20)** | **0.80 ± 8.098** | **-0.10 ± 6.495** |
| **Week 24: PF (n = 22, 20)** | **0.52 ± 5.702** | **-2.11 ± 8.667** |
| **Week 28: PF (n = 23, 19)** | **1.25 ± 5.276** | **-0.40 ± 6.460** |
| **Week 36: PF (n = 21, 19)** | **1.37 ± 5.778** | **-1.31 ± 6.631** |
| **Week 44: PF (n = 21, 16)** | **1.00 ± 6.674** | **-0.36 ± 8.065** |
| **Week 52: PF (n = 21, 16)** | **2.46 ± 4.770** | **0.12 ± 5.696** |
| **Week 4: Role-Physical (R-P) (n =27, 23)** | **3.49 ± 7.886** | **0.49 ± 10.616** |
| **Week 8: R-P (n =26, 21)** | **3.80 ± 9.628** | **-0.75 ± 10.515** |
| **Week 12: R-P (n = 25, 20)** | **3.32 ± 9.3301** | **1.01 ± 9.539** |
| **Week 16: R-P (n = 25, 20)** | **4.58 ± 8.947** | **-1.12 ± 8.847** |
| **Week 20: R-P (n = 24, 20)** | **4.40 ± 9.538** | **-0.45 ± 8.163** |
| **Week 24: R-P (n = 22, 20)** | **3.37 ± 7.458** | **-0.00 ± 10.094** |
| **Week 28: R-P (n = 23, 19)** | **5.96 ± 10.034** | **1.77 ± 8.553** |
| **Week 36: R-P (n = 21, 19)** | **5.99 ± 6.444** | **0.24 ± 10.121** |
| **Week 44: R-P (n = 21, 16)** | **5.13 ± 6.515** | **0.70 ± 11.262** |
| **Week 52: R-P (n = 21, 16)** | **6.20 ± 6.659** | **1.40 ± 9.126** |
| **Week 4: Bodily Pain (BP) (n = 27, 23)** | **8.03 ± 13.272** | **7.68 ± 11.235** |
| **Week 8: BP (n = 26, 21** | **5.80 ± 14.475** | **9.68 ± 10.485** |
| **Week 12: BP (n = 25, 20)** | **6.92 ± 13.426** | **6.84 ± 11.674** |
| **Week 16: BP (n = 25, 20)** | **7.69 ± 14.841** | **4.50 ± 13.560** |
| **Week 20: BP (n = 24, 20)** | **6.10 ± 14.072** | **8.63 ± 12.457** |
| **Week 24: BP (n = 22, 20)** | **5.97 ± 12.689** | **3.93 ± 11.952** |
| **Week 28: BP (n = 23, 19)** | **6.47 ± 12.643** | **6.32 ± 13.149** |
| **Week 36: BP (n = 21, 19)** | **7.20 ± 13.724** | **7.81 ± 10.794** |
| **Week 44: BP (n = 21, 16)** | **8.01 ± 15.378** | **9.00 ± 7.910** |
| **Week 52: BP (n = 21, 16)** | **5.49 ± 12.328** | **8.39 ± 11.866** |
| **Week 4: General Health (GH) ( n = 27, 23)** | **3.49 ± 9.207** | **0.23 ± 6.761** |
| **Week 8: GH (n = 26, 21)** | **2.74 ± 8.119** | **0.18 ± 6.758** |
| **Week 12: GH (n = 25, 20** | **2.22 ± 7.383** | **0.62 ± 8.158** |
| **Week 16: GH (n = 25, 20)** | **2.28 ± 8.235** | **-0.74 ± 7.858** |
| **Week 20: GH (n = 24, 20)** | **4.50 ± 6.774** | **-0.38 ± 7.933** |
| **Week 24: GH (n = 22, 20)** | **2.85 ± 7.149** | **-0.19 ± 9.031** |
| **Week 28: GH (n = 23, 19)** | **3.53 ± 7.285** | **1.18 ± 7.837** |
| **Week 36:GH (n = 21, 19)** | **3.42 ± 6.680** | **-0.47 ± 7.833** |
| **Week 44: GH (n = 21, 16)** | **1.02 ± 8.127** | **-0.30 ± 9.597** |
| **Week 52: GH (n = 21, 16)** | **3.03 ± 6.733** | **0.15 ± 10.277** |
| **Week 4: Vitality (n = 27, 23)** | **4.07 ± 8.607** | **-1.42 ± 7.699** |
| **Week 8: Vitality (n = 26, 21)** | **2.17 ± 7.952** | **0.71 ± 8.185** |
| **Week 12: Vitality (n = 25, 20)** | **3.57 ± 7.477** | **-0.30 ± 9.241** |
| **Week 16: Vitality (n = 25, 20)** | **4.28 ± 7.431** | **-0.45 ± 7.847** |
| **Week 20: Vitality (n = 24, 20)** | **4.70 ± 8.445** | **0.45 ± 9.652** |
| **Week 24: Vitality (n = 22, 20)** | **3.78 ± 7.112** | **-1.93 ± 11.697** |
| **Week 28: Vitality (n = 23, 19)** | **6.20 ± 7.489** | **0.16 ± 6.679** |
| **Week 36: Vitality (n = 21, 19)** | **7.07 ± 7.060** | **1.41 ± 5.635** |
| **Week 44: Vitality (n = 21, 16)** | **6.08 ± 8.375** | **-0.93 ± 12.497** |
| **Week 52: Vitality (n = 21, 16)** | **7.21 ± 8.690** | **0.37 ± 11.474** |
| **Week 4: Social Functioning (SF) (n = 27, 23)** | **3.71 ± 7.939** | **1.74 ± 7.499** |
| **Week 8: SF (n = 26, 21)** | **4.82 ± 8.327** | **2.63 ± 9.979** |
| **Week 12: SF (n = 25, 20)** | **4.01 ± 9.154** | **1.76 ± 7.325** |
| **Week 16: SF (n = 25, 20)** | **5.21 ± 11.069** | **0.75 ± 7.325** |
| **Week 20: SF (n = 24, 20)** | **4.81 ± 10.080** | **3.51 ± 8.150** |
| **Week 24: SF (n = 22, 20)** | **4.56 ± 8.602** | **0.00 ± 10.912** |
| **Week 28: SF (n = 23, 19)** | **3.49 ± 8.476** | **3.17 ± 9.631** |
| **Week 36: SF (n = 21, 19)** | **7.16 ± 10.703** | **5.01 ± 7.285** |
| **Week 44: SF (n = 21, 16)** | **6.45 ± 8.988** | **0.63 ± 11.561** |
| **Week 52: SF (n = 21, 16)** | **7.16 ± 8.621** | **2.82 ± 9.681** |
| **Week 4: Role-Emotional (RE) (n = 27, 23)** | **-0.77 ± 12.454** | **3.48 ± 12.985** |
| **Week 8: RE (n = 26, 21)** | **3.08 ± 11.457** | **1.99 ± 13.239** |
| **Week 12: RE (n = 25, 20)** | **-0.42 ± 12.076** | **0.52 ± 13.188** |
| **Week 16: RE (n = 25, 20)** | **3.76 ± 10.586** | **-0.00 ± 11.465** |
| **Week 20: RE (n = 24, 20)** | **3.48 ± 11.058** | **0.35 ± 11.569** |
| **Week 24: RE (n = 22, 20)** | **2.85 ± 11.753** | **-1.22 ± 16.025** |
| **Week 28: RE (n = 23, 19)** | **3.63 ± 11.853** | **1.10 ± 11.725** |
| **Week 36: RE (n = 21, 19)** | **5.47 ± 10.066** | **0.73 ± 16.518** |
| **Week 44: RE (n = 21, 16)** | **4.15 ± 12.293** | **3.26 ± 16.354** |
| **Week 52: RE (n = 21, 16)** | **6.14 ± 11.385** | **0.43 ± 19.234** |
| **Week 4: Mental Health (MH) (n = 27, 23)** | **3.0 ± 8.514** | **0.57 ± 8.420** |
| **Week 8: MH (n = 26, 21)** | **2.82 ± 10.643** | **1.49 ± 6.950** |
| **Week 12: MH (n = 25, 20)** | **3.14 ± 10.786** | **4.45 ± 7.690** |
| **Week 16: MH (n = 25, 20)** | **4.29 ± 8.337** | **5.36 ± 6.379** |
| **Week 20: MH (n = 24, 20)** | **3.49 ± 10.926** | **6.41 ± 7.984** |
| **Week 24: MH (n = 22, 20)** | **2.62 ± 8.730** | **2.61 ± 13.149** |
| **Week 28: MH (n = 23, 19)** | **2.84 ± 9.816** | **6.06 ± 7.350** |
| **Week 36: MH (n = 21, 19)** | **5.98 ± 8.111** | **5.64 ± 8.988** |
| **Week 44: MH (n = 21, 16)** | **4.11 ± 8.969** | **1.14 ± 11.891** |
| **Week 52: MH (n = 21, 16)** | **5.73 ± 7.473** | **4.25 ± 11.257** |

**Change from Baseline in EQ (EuroQol)-5D-5L questionnaire(Time Frame: Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 36, 44 & 52)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **27** | **25** |
| **Change from Baseline in EQ (EuroQol)-5D-5L questionnaire(units: scores on a scale)Mean ± Standard Deviation** | | |
| **Week 4 (n = 27, 23)** | **11.26 ± 16.819** | **1.87 ± 21.467** |
| **Week 8 (n = 26, 21)** | **5.58 ± 16.650** | **5.52 ± 29.646** |
| **Week 12 (n = 25, 20)** | **4.64 ± 19.598** | **3.30 ± 22.850** |
| **Week 16 (n = 25, 20)** | **7.000 ± 19.530** | **4.40 ± 27.354** |
| **Week 20 (n = 24, 20)** | **7.88 ± 19.077** | **6.30 ± 25.041** |
| **Week 24 (n = 23, 20)** | **6.39 ± 17.598** | **-1.00 ± 29.902** |
| **Week 28 (n = 23, 19)** | **4.43 ± 17.840** | **10.37 ± 21.670** |
| **Week 36 (n = 21, 19)** | **6.90 ± 17.972** | **5.32 ± 28.825** |
| **Week 44 (n = 21, 16)** | **6.38 ± 19.505** | **12.69 ± 21.941** |
| **Week 52 (n = 21, 16)** | **11.62 ± 16.877** | **10.81 ± 24.109** |

**Change from Baseline in Erythrocyte Sedimentation Rate (ESR)(Time Frame: Baseline, Week 28, Week 52)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **19** | **6** |
| **Change from Baseline in Erythrocyte Sedimentation Rate (ESR)(units: mm/hr)Mean ± Standard Deviation** | | |
| **Week 28** | **4.158 ± 17.3630** | **9.667 ± 21.0206** |
| **Week 52 (n = 17, 5)** | **-4.647 ± 11.1296** | **13.000 ± 6.2450** |

**Change from Baseline in C-Reactive Protein (CRP) Level(Time Frame: Baseline, Week 28, Week 52)**

|  |  |  |
| --- | --- | --- |
|  | **Secukinumab** | **Placebo** |
| **Arm/Group Description** | **Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** | **Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen.** |
| **Number of Participants Analyzed [units: participants]** | **19** | **6** |
| **Change from Baseline in C-Reactive Protein (CRP) Level(units: mg/L)Mean ± Standard Deviation** | | |
| **Week 28** | **3.968 ± 8.7463** | **3.417 ± 4.4459** |
| **Week 52 (n = 17, 5)** | **-0.759 ± 2.7803** | **12.720 ± 24.0632** |

***Instruction:*** *This information can usually be found in the CSR*

***Definition: Safety tables for Company Clinical Trial Results template: by system organ class,***

***By preferred term and death/SAE/discontinuations***

**Safety Results**

**All-Cause Mortality**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **SecukinumabN = 27** | **PlaceboN = 25** | **All ParticipantsN = 52** |
| **Arm/Group Description** | Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen. | Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen. | All participants who participated in the study. |
| **Total participants affected** | 1 (3.70%) | 1 (4.00%) | 2 (3.85%) |

**Serious Adverse Events by System Organ Class**

|  |  |
| --- | --- |
| **Time Frame** | Adverse Events were reported from first dose of study treatment until end of treatment plus 30 days, up to a maximum duration of 573 days (543 days maximum exposure plus 30 days post treatment) for midostaurin and up to a maximum duration of 416 days (386 days maximum exposure plus 30 days post treatment) for placebo. |
| **Additional Description** | Adverse Event (AE): Any sign or symptom that occurs during treatment plus 30 days post treatment. |
| **Source Vocabulary for Table Default** | MedDRA (24.0) |
| **Assessment Type for Table Default** | Systematic Assessment |

|  |  |  |  |
| --- | --- | --- | --- |
|  | **SecukinumabN = 27** | **PlaceboN = 25** | **All ParticipantsN = 52** |
| **Arm/Group Description** | Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen. | Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen. | All participants who participated in the study. |
| **Total participants affected** | 6 (22.22%) | 11 (44.00%) | 17 (32.69%) |
| **Cardiac disorders** |  |  |  |
| **Atrial fibrillation** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Atrial tachycardia** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Cardiac failure** | 1 (3.70%) | 1 (4.00%) | 2 (3.85%) |
| **Tachyarrhythmia** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Gastrointestinal disorders** |  |  |  |
| **Faecaloma** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Gastrointestinal pain** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Melaena** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Noninfective sialoadenitis** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **General disorders and administration site conditions** |  |  |  |
| **General physical health deterioration** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Pyrexia** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Infections and infestations** |  |  |  |
| **Arthritis bacterial** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Erysipelas** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Urinary tract infection** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Injury, poisoning and procedural complications** |  |  |  |
| **Face injury** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Fall** | 1 (3.70%) | 1 (4.00%) | 2 (3.85%) |
| **Femur fracture** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Fibula fracture** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Pelvic fracture** | 1 (3.70%) | 1 (4.00%) | 2 (3.85%) |
| **Spinal compression fracture** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Investigations** |  |  |  |
| **Inflammatory marker increased** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Metabolism and nutrition disorders** |  |  |  |
| **Fluid retention** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Musculoskeletal and connective tissue disorders** |  |  |  |
| **Spinal stenosis** | 1 (3.70%) | 1 (4.00%) | 2 (3.85%) |
| **Neoplasms benign, malignant and unspecified (incl cysts and polyps)** |  |  |  |
| **Squamous cell carcinoma of lung** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Nervous system disorders** |  |  |  |
| **Cerebrovascular accident** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Dizziness** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Facial paralysis** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Intracranial aneurysm** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Neurological symptom** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Syncope** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Respiratory, thoracic and mediastinal disorders** |  |  |  |
| **Asphyxia** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Aspiration** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Chronic obstructive pulmonary disease** | 0 (0.00%) | 1 (4.00%) | 1 (1.92%) |
| **Pulmonary embolism** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Vascular disorders** |  |  |  |
| **Deep vein thrombosis** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |
| **Haematoma** | 1 (3.70%) | 0 (0.00%) | 1 (1.92%) |

**Other Adverse Events by System Organ Class**

|  |  |
| --- | --- |
| **Time Frame** | Adverse Events were reported from first dose of study treatment until end of treatment plus 30 days, up to a maximum duration of 573 days (543 days maximum exposure plus 30 days post treatment) for midostaurin and up to a maximum duration of 416 days (386 days maximum exposure plus 30 days post treatment) for placebo. |
| **Additional Description** | Adverse Event (AE): Any sign or symptom that occurs during treatment plus 30 days post treatment. |
| **Source Vocabulary for Table Default** | MedDRA (24.0) |
| **Assessment Type for Table Default** | Systematic Assessment |
| **Frequent Event Reporting Threshold** | 5% |

|  |  |  |  |
| --- | --- | --- | --- |
|  | **SecukinumabN = 27** | **PlaceboN = 25** | **All ParticipantsN = 52** |
| **Arm/Group Description** | Participants received secukinumab at a dose of 300 milligrams (mg) as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen. | Participants received placebo as subcutaneous (s.c.) injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter through to week 48 along with a 26-week prednisolone tapering regimen. | All participants who participated in the study. |
| **Total participants affected** | 25 (92.59%) | 23 (92.00%) | 48 (92.31%) |
| **Endocrine disorders** |  |  |  |
| **Cushingoid** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Eye disorders** |  |  |  |
| **Glaucoma** | 2 (7.41%) | 2 (8.00%) | 4 (7.69%) |
| **Vision blurred** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Gastrointestinal disorders** |  |  |  |
| **Dental caries** | 2 (7.41%) | 0 (0.00%) | 2 (3.85%) |
| **Diarrhoea** | 2 (7.41%) | 2 (8.00%) | 4 (7.69%) |
| **Haemorrhoidal haemorrhage** | 0 (0.00%) | 2 (8.00%) | 2 (3.85%) |
| **Nausea** | 0 (0.00%) | 2 (8.00%) | 2 (3.85%) |
| **General disorders and administration site conditions** |  |  |  |
| **Fatigue** | 2 (7.41%) | 1 (4.00%) | 3 (5.77%) |
| **Oedema peripheral** | 2 (7.41%) | 4 (16.00%) | 6 (11.54%) |
| **Infections and infestations** |  |  |  |
| **Gastroenteritis** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Nasopharyngitis** | 5 (18.52%) | 5 (20.00%) | 10 (19.23%) |
| **Oral candidiasis** | 4 (14.81%) | 1 (4.00%) | 5 (9.62%) |
| **Respiratory tract infection** | 2 (7.41%) | 1 (4.00%) | 3 (5.77%) |
| **Rhinitis** | 2 (7.41%) | 0 (0.00%) | 2 (3.85%) |
| **Urinary tract infection** | 4 (14.81%) | 2 (8.00%) | 6 (11.54%) |
| **Injury, poisoning and procedural complications** |  |  |  |
| **Bone contusion** | 2 (7.41%) | 0 (0.00%) | 2 (3.85%) |
| **Fall** | 2 (7.41%) | 0 (0.00%) | 2 (3.85%) |
| **Rib fracture** | 2 (7.41%) | 0 (0.00%) | 2 (3.85%) |
| **Skin laceration** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Thoracic vertebral fracture** | 0 (0.00%) | 2 (8.00%) | 2 (3.85%) |
| **Tooth fracture** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Investigations** |  |  |  |
| **Blood pressure increased** | 0 (0.00%) | 2 (8.00%) | 2 (3.85%) |
| **C-reactive protein increased** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Gamma-glutamyltransferase increased** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Metabolism and nutrition disorders** |  |  |  |
| **Diabetes mellitus** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Musculoskeletal and connective tissue disorders** |  |  |  |
| **Arthralgia** | 3 (11.11%) | 3 (12.00%) | 6 (11.54%) |
| **Back pain** | 0 (0.00%) | 5 (20.00%) | 5 (9.62%) |
| **Bursitis** | 3 (11.11%) | 1 (4.00%) | 4 (7.69%) |
| **Muscle spasms** | 4 (14.81%) | 1 (4.00%) | 5 (9.62%) |
| **Osteoarthritis** | 3 (11.11%) | 2 (8.00%) | 5 (9.62%) |
| **Osteoporosis** | 2 (7.41%) | 1 (4.00%) | 3 (5.77%) |
| **Nervous system disorders** |  |  |  |
| **Dizziness** | 3 (11.11%) | 0 (0.00%) | 3 (5.77%) |
| **Headache** | 4 (14.81%) | 3 (12.00%) | 7 (13.46%) |
| **Polyneuropathy** | 2 (7.41%) | 0 (0.00%) | 2 (3.85%) |
| **Sciatica** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Tension headache** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Skin and subcutaneous tissue disorders** |  |  |  |
| **Alopecia** | 2 (7.41%) | 1 (4.00%) | 3 (5.77%) |
| **Rash** | 2 (7.41%) | 2 (8.00%) | 4 (7.69%) |
| **Skin ulcer** | 2 (7.41%) | 0 (0.00%) | 2 (3.85%) |
| **Vascular disorders** |  |  |  |
| **Giant cell arteritis** | 1 (3.70%) | 2 (8.00%) | 3 (5.77%) |
| **Haematoma** | 1 (3.70%) | 3 (12.00%) | 4 (7.69%) |
| **Hypertension** | 6 (22.22%) | 8 (32.00%) | 14 (26.92%) |

**Other Relevant Findings**

***Definition:*** *Important finding not meeting the criteria for efficacy/safety results (ie, notable change in laboratory or drug trough values that posed no safety issue, but is of medical interest).*

***Example:*** *Mean (SD) parameters of company product*

**Conclusion:**

***Instruction: This should be copied from the CSR Synopsis. Please read carefully:***

* ***Ensure that the conclusion refers to only primary and secondary outcome measures***
* ***No exploratory outcome measures***
* ***Spell out all acronyms***
* ***Remove any company specific terminology***

**Date of Clinical Trial Report**

***Definition:*** *e-signature date*