Study Results Synopsis for Public Disclosure

Name of product: Secukinumab (AIN457) 125 mg/5 mL solution for infusion

Protocol identification number: Protocol number CAIN457E22101, EU CT no. 2023-507667-19-00 and Clinicaltrials.gov nº. NCT06130540

Title of study: An open-label, multicenter study to evaluate the pharmacokinetics, safety and tolerability of intravenous secukinumab infusion in adults with giant cell arteritis (GCA) or polymyalgia rheumatica (PMR).

Study center(s): This study was conducted at 19 sites across 6 countries: Czech Republic (2 sites, 2 participants), Italy (2 sites, 3 participants), Portugal (1 site, 4 participants), Spain (3 sites, 7 participants), Switzerland (3 sites, 19 participants), United States (8 sites, 30 participants).

Publication (reference): None

Study period:

Study initiation date: 27-Mar-2024 (first participant first visit)

Study completion date: 02-Apr-2025 (last participant last visit)

Phase of development (phase of this clinical study): Ib

Objectives: The objectives and endpoints are presented below:

Table 0-1 Objectives and related endpoints

Objective(s)	Endpoint(s)
Primary objective(s)	**Endpoint(s) for primary objective(s)**
To determine the steady state Pharmacokinetics (PK) of secukinumab after multiple intravenous (i.v.) doses in patients with GCA or PMR	PK parameters: Steady-state maximum concentration (Cmax,ss), Area under the curve during the dosing interval at steady-state (AUCtau,ss) and average concentration at steady-state (Cavg,ss (=AUCtau,ss/tau), Steady-state minimum concentration (Cmin,ss)
Secondary objective(s)	**Endpoint(s) for secondary objective(s)**
To assess the safety and tolerability of secukinumab i.v. in patients with GCA or PMR	Safety and tolerability demonstrated by assessing: • Adverse events (AEs) and serious adverse events (SAEs) (incidence, severity, and relationship to study drug) • Changes in clinical laboratory measures and vital signs
Further PK Characterization	Clearance (CL) and volume of distribution at steady state (Vss)

Study design and methodology: This was a 12-week, open-label, multicenter, basket design study followed by an up to 8-week follow-up period in 2 cohorts of participants, one cohort with GCA and another cohort with PMR.

Post trial access (PTA) to secukinumab, where available, was offered for those participants who completed the 12-week treatment period and who, in the opinion of the Investigator, have

benefited from continued treatment with secukinumab, and when in accordance with local laws and regulations. The roll-over to PTA was possible at any time from Week 12 up to Week 20.

Participants who discontinued the treatment prematurely performed the end of treatment (EOT) visit at 4 weeks post last dose administration and a final end of study (EOS) post-treatment safety follow-up. A total of 65 participants were enrolled with 34 participants in GCA cohort and 31 participants in PMR cohort. All were included in safety set. Fifty-five participants (GCA cohort: 28 participants; and PMR cohort: 27 participants) were included in the PK analysis set.

Diagnosis and main criteria for inclusion:

The study population comprised male or non-pregnant, non-lactating female participants at least 50 years of age.

For GCA:

- Diagnosis of GCA based on meeting all of the following criteria:
  - Age at onset of disease ≥ 50 years
  - Unequivocal cranial symptoms of GCA (e.g., new-onset localized headache, scalp or temporal artery tenderness, permanent or temporary ischemia-related vision loss, or otherwise unexplained mouth or jaw pain upon mastication), and/or unequivocal symptoms of PMR (defined as shoulder and/or hip girdle pain associated with inflammatory morning stiffness) and/or symptoms of limb ischemia (claudication)
  - Temporal artery biopsy (TAB) revealing features of GCA and/or cross-sectional imaging study such as ultrasound (e.g., cranial or axillary), MRI/MRA, CTA, or PET-CT with evidence of vasculitis.
- Active GCA disease within 6 months prior to Baseline as defined by meeting both of the following:
  - Presence of signs or symptoms attributed to active GCA and not related to prior damage (e.g., vision loss that occurred without new findings)
  - Elevated erythrocyte sedimentation rate (ESR) ≥ 30 mm/hr or CRP ≥ 10 mg/L attributed to active GCA or active GCA on TAB or on imaging study.

For PMR:

- Diagnosis of PMR according to the provisional American college of rheumatology / European alliance of associations for rheumatology (ACR/EULAR) classification criteria: Participants ≥ 50 years of age with a history of bilateral shoulder pain accompanied by elevated CRP concentration (≥10 mg/L) and/or elevated ESR (≥ 30 mm/hr) who scored at least 4 points from the following optional classification criteria:
  - Morning stiffness > 45 min (2 points)
  - Hip pain or restricted range of motion (1 point)
  - Absence of rheumatoid factor and/or anti-citrullinated protein antibodies (2 points)
  - Absence of other joint involvement (1 point).
- Active PMR disease within 6 months prior to Baseline as defined by signs and symptoms attributable to PMR meeting the following:

- Bilateral shoulder girdle and/or bilateral hip girdle pain associated with inflammatory stiffness with or without additional symptoms, indicative of a PMR relapse (such as constitutional symptoms) that are in the opinion of the Investigator not due to other diseases that may mimic PMR such as osteoarthritis in shoulders or hips, polyarticular calcium pyrophosphate deposition disease, rotator cuff disease, adhesive capsulitis (frozen shoulder) or fibromyalgia.

Diagnosis and main criteria for exclusion:

For GCA:

- History of hypersensitivity or contraindication to any of the study treatments or its excipients or to drugs of similar chemical classes.
- History of clinically significant liver disease or liver injury as indicated by clinically significantly abnormal liver function tests (LFTs), such as SGOT (AST), SGPT (ALT) and serum bilirubin. The Investigator should be guided by the following criteria:
  - AST (Aspartate Aminotransferase) and ALT (Alanine Aminotransferase) may not exceed 3 x the upper limit of normal (ULN)
  - Total bilirubin concentration may not exceed 1.5 x ULN.

  Any one of these parameters, if elevated above ULN, should be re-checked once more as soon as possible, and in all cases, at least prior to enrollment, to rule-out laboratory error.
- Active infections or history of ongoing, chronic or recurrent infectious disease including but not limited to below:
  - Active infections during the last 2 weeks prior to baseline
  - Known infection with human immunodeficiency virus (HIV), hepatitis B (HBV) or hepatitis C (HCV) at screening or baseline, except for HCV successfully treated and cured, according to local/global guidelines
  - Evidence of tuberculosis (TB) infection as defined by a positive QuantiFERON TB-Gold Plus test. Participants with a positive test may participate in the study if further work-up (according to local practice/guidelines) establishes conclusively that the participant has no evidence of active TB. If the test result is indeterminate, the Investigator may repeat the test once or may proceed directly to perform the work-up for TB as per local procedures. If presence of latent TB is established, then treatment must be initiated prior to baseline (both treatment and timing prior to baseline according to local country guidelines).
- Active inflammatory bowel disease or active uveitis.
- Active ongoing diseases which in the opinion of the Investigator immuno-compromises the participant and/or places the participant at unacceptable risk for treatment with immunomodulatory therapy.
- Current severe progressive or uncontrolled disease, which in the judgment of the Investigator renders the participant unsuitable for the trial, including but not limited to below:
  - Major ischemic event (e.g., myocardial infarction, stroke, etc.) or transient ischemic attack (TIA) within 12 weeks of screening

  - Significant medical conditions or diseases, including but not limited to the following: uncontrolled hypertension, congestive heart failure (New York Heart Association (NYHA) status of class III or IV) and uncontrolled diabetes mellitus
  - Any other current severe progressive or uncontrolled diseases per the Investigator's discretion
- Confirmed diagnosis of any primary form of systemic vasculitis, other than GCA.

For PMR:

- History of hypersensitivity or contraindication to any of the study treatments or its excipients or to drugs of similar chemical classes.
- History of clinically significant liver disease or liver injury as indicated by clinically significantly abnormal liver function tests (LFTs), such as SGOT (AST), SGPT (ALT) and serum bilirubin. The Investigator should be guided by the following criteria:
  - AST (Aspartate Aminotransferase) and ALT (Alanine Aminotransferase) may not exceed 3 x the upper limit of normal (ULN)
  - Total bilirubin concentration may not exceed 1.5 x ULN.

  Any one of these parameters, if elevated above ULN, should be re-checked once more as soon as possible, and in all cases, at least prior to enrollment, to rule-out laboratory error.
- Active infections or history of ongoing, chronic or recurrent infectious disease including but not limited to below:
  - Active infections during the last 2 weeks prior to baseline.
  - Known infection with human immunodeficiency virus (HIV), hepatitis B (HBV) or hepatitis C (HCV) at screening or baseline, except for HCV successfully treated and cured, according to local/global guidelines.
  - Evidence of TB infection as defined by a positive QuantiFERON TB-Gold Plus test. Participants with a positive test may participate in the study if further work-up (according to local practice/guidelines) establishes conclusively that the participant has no evidence of active TB. If the test result is indeterminate, the Investigator may repeat the test once or may proceed directly to perform the work-up for TB as per local procedures. If presence of latent TB is established, then treatment must be initiated prior to baseline (both treatment and timing prior to baseline according to local country guidelines).
- Active inflammatory bowel disease or active uveitis.
- Active ongoing diseases which in the opinion of the Investigator immuno-compromises the participant and/or places the participant at unacceptable risk for treatment with immunomodulatory therapy.
- Current severe progressive or uncontrolled disease, which in the judgment of the Investigator renders the participant unsuitable for the trial, including but not limited to below:
  - Major ischemic event (e.g., myocardial infarction, stroke, etc.) or transient ischemic attack (TIA) within 12 weeks of screening.

  - Significant medical conditions or diseases, including but not limited to the following: uncontrolled hypertension, congestive heart failure (New York Heart Association (NYHA) status of class III or IV) and uncontrolled diabetes mellitus.
  - Any other current severe progressive or uncontrolled diseases per the Investigator's discretion.
- Evidence of GCA as indicated by typical (cranial) symptoms (e.g., persistent or recurrent localized headache, temporal artery or scalp tenderness, jaw claudication, blurry or loss of vision, symptoms of stroke), extremity claudication, imaging and/or temporal artery biopsy result.
  - Note: Imaging and/or temporal artery biopsy are not standard of care for PMR management and diagnosis and are therefore not mandated as part of the screening; Patients with PMR symptoms only who have a temporal artery biopsy in line with GCA and/or radiologic signs of vasculitis may be eligible for the GCA cohort.
- Concurrent rheumatoid arthritis or other inflammatory arthritis or other connective tissue diseases, such as but not limited to systemic lupus erythematosus, systemic sclerosis, vasculitis, myositis, mixed connective tissue disease, and ankylosing spondylitis.
- Concurrent diagnosis or history of neuropathic muscular diseases including fibromyalgia.
- Inadequately treated hypothyroidism (e.g., persistence of symptoms, lack of normalization of serum thyroid stimulation hormone (TSH) despite regular hormonal replacement treatment).

Test and reference therapies, dose and mode of administration, batch number:

Secukinumab liquid in vial (LIVI) for i.v. infusion provided in glass vials, each containing 125 mg/5 mL secukinumab concentrate for solution for infusion. Participants were given all the secukinumab infusions by the site staff on site during the Treatment Period (last dose at Week 8). Each participant was administered the doses as indicated in Table 2-2.

Table 0-2 Dose and treatment schedule

Investigational drug (name and strength)	Dose	Frequency and/or regimen
Secukinumab (AIN457) 125 mg/5 mL	4 mg/kg	Baseline
Secukinumab (AIN457) 125 mg/5 mL	2 mg/kg	Week 4 and Week 8

No auxiliary medicinal products (AxMPs) were defined or reference therapy was administered in this study.

Protocol amendments and other changes to study conduct:

This CSR describes the conduct of the study according to protocol amendment v01. The key features of amendment are given in the table below.

Table 0-3 Protocol Amendments

Version and date	Summary of key changes
Amendment v01, 10-Sep-2024	The main purpose of this global Amendment 01 was to address the conditions included in the initial approval of this study under the EU-Clinical Trial Regulation (CTR) process. • Addition of the approximate number of centers participating in the study Additional clarifications and updates have been made: • Clarification of the instructions for Investigators to report potential Hy's law cases as serious adverse events • Removal of bilateral tubal ligation from the list of methods exempting women from pregnancy testing • Revision of adverse event monitoring period from '12 weeks following the last dose of study treatment' and serious adverse event monitoring period from 'until 30 days after last study visit or 12 weeks from last dose (whichever is later)' to 'until End of Study visit/12 weeks after last dose of study treatment (whichever is later)' • Revision of the reporting period of SAEs suspected to be causally related to study treatment per Investigator's judgement to Novartis Safety from '12-week period after the last study treatment/30 days after last patient visit (whichever is later)' to 'after End of Study visit/12 weeks after last dose of study treatment (whichever is later)'

Criteria for evaluation

Efficacy assessments: Not measured in this study.

Pharmacokinetics assessments:

PK samples were collected at the pre and end of infusion at Baseline, Week 4 and Week 8; and at any time during Weeks 9, 10, 11, 12, 16 and 20. An electrochemiluminescence method was used for bioanalytical analysis of secukinumab in serum with a lower limit of quantification (LLOQ) of 50.0 ng/mL.

Concentrations below the LLOQ were reported as "zero," and missing data were appropriately labeled as such in the Bioanalytical data report.

Phoenix WinNonlin software (Version 6.4 or higher) was utilized to determine the following PK parameters using the actual recorded sampling times: Cmax,ss, Cmin,ss, AUCtau,ss, Cavg,ss, and CLss. Individual serum concentrations were reported in µg/mL. Vss could not be determined with the actual PK dataset available.

Safety assessments: Safety assessment included AEs, SAEs monitoring, laboratory evaluations (hematology, clinical chemistry, and urinalysis), physical examination, vital signs, height and weight, immunogenicity, and pregnancy and assessment of fertility.

Statistical methods:

The statistical analysis was performed by Novartis using SAS 9.4.

<u>Analysis sets</u>

The safety analysis set (SAF) included all participants who received at least 1 dose of study treatment of secukinumab.

The pharmacokinetic analysis set (PAS) included all participants who provided an evaluable PK profile. A profile was considered evaluable if following conditions were satisfied: Participant received all planned secukinumab doses, and participant provided at least 1 primary PK parameter.

The number (%) of participants in each analysis set by cohort (GCA and PMR) were summarized and presented. Participants excluded from the PAS were listed using SAF.

Analysis of the primary endpoint:

PK parameters for secukinumab were determined using no-compartmental methods Phoenix WinNonlin v8 or higher (Pharsight, Mountain View, CA, USA). The primary PK parameters were the Cmax,ss AUCtau,ss, Cavg,ss (=AUCtau,ss/tau) and Cmin,ss resulting from secukinumab 2 mg/kg q4w i.v. with 4 mg/kg loading i.v. regimen in participants with GCA and participants with PMR, respectively. Further, the clearance at steady-state, CLss, was also determined.

The PK analysis was based on the PK analysis set.

Descriptive summary statistics of PK parameters were provided by cohort. Summary statistics of PK parameters included n, m (number of non-zero concentrations), mean, CV%, SD, median, geometric mean, geometric CV%, minimum, Q1, Q3 and maximum. PK parameters were listed by cohort and participant number.

Analysis of the secondary endpoint:

For all safety analyses, the SAF was used. All listings and tables were presented by cohort.

Adverse events

Treatment emergent AEs were summarized with number (and percentage) by cohort with primary system organ class (SOC), preferred term (PT) and maximum severity.

Separate summaries were provided for death, SAEs and AEs leading to study treatment discontinuation, AE suspected to be related to study drug.

Safety topics of interest (STI) defined in the Program Case Retrieval Sheet was reported..

Laboratory evaluations

Descriptive summary statistics for the change from baseline to each study visit were presented. These descriptive summaries were presented by test group and laboratory test. Change from baseline was summarized only for participants with both baseline and post baseline values.

For each parameter, the maximum change from baseline was analyzed analogously.

In addition, shift tables were provided for all parameters based on Common Terminology Criteria for Adverse events (CTCAE).

Vital signs

Analysis of the vital sign measurements using summary statistics for the change from baseline for each post-baseline visit was performed. These descriptive summaries were presented by

vital sign. Change from baseline was only be summarized for participants with both baseline and post-baseline values.

Summary - Results

Disposition: A total of 65 participants were treated at 19 sites across 6 countries, divided into either GCA (N=34) or PMR (N=31) cohorts. The majority of participants (95.4%, 62/65) completed the study treatment period (GCA cohort: 94.1%, 32/34; and PMR cohort: 96.8%, 30/31).

Four participants (6.2%) were discontinued from the study, out of which:

- Three discontinued the study treatment (GCA cohort: 1 due to cardiac arrest (fatal event), 1 due to AE of limb injury which was caused by an animal scratch; and PMR cohort: 1 due to subject decision).
- One participant (GCA cohort) discontinued from the study after treatment completion due to physician decision.

Data sets analyzed: All the 65 enrolled participants were included in the Safety set. Fifty-five participants (84.6%) were included in the PK analysis set (GCA cohort: 82.4%, 28/34; and PMR cohort: 87.1%, 27/31).

Demographics: Of the 65 participants enrolled in the study, 60.0% (39) participants were female (GCA cohort: 67.6%, 23/34; and PMR cohort: 51.6%, 16/31). A majority of the participants (96.9%) were White (GCA cohort: 97.1%; and PMR cohort: 96.8%), predominantly of Not Hispanic or Latino ethnicity (98.5% overall; GCA cohort: 97.1% and PMR cohort: 100.0%).

Overall, the mean age of participants was 72.2 years (range: 54-86 years), 72.2 years (range: 55-86 years) in the GCA and 72.1 years (range: 54-86 years) in the PMR cohort. The overall mean body weight was 75.9 kg (range: 43.4 to 116.3 kg) and more than 10 kg difference in mean weight was reported in the GCA (70.8 kg) vs. the PMR cohort (81.4 kg). There were more former smokers in the PMR cohort (35.5%, 11/31) vs. the GCA cohort (17.6%, 6/34). Other demographics were generally similar between the two cohorts.

Baseline disease characteristics: Of the 34 participants in GCA cohort, 64.7% (22) were newly diagnosed with GCA and 35.3% (12) had relapsing GCA. Of the 31 participants in PMR cohort, 29 had relapsing PMR and 2 were newly diagnosed with PMR.

The mean time since the first diagnosis to baseline was 1.09 years in GCA and 3.99 years in PMR cohort, the mean age of first disease onset was 71.2 years in GCA and 68.3 years in PMR cohort. The mean time since the most recent relapse/new onset to baseline was 2.41 months in GCA and 2.65 months in PMR cohort. All 65 participants (34 in GCA and 31 in PMR), had at least one relevant medical history and currently ongoing medical condition.

Except for notable differences (≥20%) between the GCA vs. PMR cohort in participants with SOCs Endocrine disorders (14.7% vs. 38.7%), General disorders and administration site (8.8% vs. 29.0%) and Skin and subcutaneous tissue disorders (8.8% vs. 29.0%), baseline disease characteristics reported were generally similar between the two cohorts.

Exposure: The median duration of exposure was 12.14 weeks (12.29 weeks in the GCA cohort; and 12.14 weeks in PMR cohort). All participants 100.0% (65) were on ≥4 weeks of exposure

and 16.9% (11) of participants were on ≥20 weeks of exposure. A majority of participants (96.9%, 63) were administered all 3 doses of study treatment (GCA cohort: 94.1%, 32/34; and PMR cohort: 100.0%, 31/31).

Pharmacokinetic results:

PK - Predose concentrations at steady state (Cmin,ss) were between 23 and 27 µg/mL with a moderate inter-participant variability ≤ 25%. Due to the higher body weight in PMR than in GCA and in line with PK theory, Cmax,ss was 9.7% higher in PMR than in GCA, i.e., 79.3 µg/mL vs. 72.3 µg/mL. In line with initial model predictions, the observed Cmin,ss, Cavg,ss and Cmax,ss values were in the expected range. With a loading dose of 4 mg/kg at Baseline and maintenance with 2 mg/kg i.v. at Weeks 4 and 8, steady-state was reached from Week 4 onwards. AUCtau,ss and Cavg,ss exhibited moderate inter-participant variability with a coefficient of variation of < 25% in the GCA and PMR cohorts and in the combined study population. CLss was similar in GCA and PMR, i.e, 0.135 L/day and 0.153 L/day, respectively.

Despite the difference in mean body weight and body weight distribution across the GCA and PMR populations in this study, PK behavior was similar in both cohorts.

Safety results:

- Overall, a total of 70.8% participants (GCA cohort: 79.4% and PMR cohort: 61.3%) reported at least one treatment-emergent AE (TEAE). Of these, most frequently reported TEAEs (≥15% overall) were reported under the SOC Infections and infestations (29.2% overall) which was numerically higher in proportion in GCA cohort than PMR cohort (32.4% vs. 25.8%), followed by SOC Musculoskeletal and connective tissue disorders (26.2% overall, and 29.4% vs. 22.6% in GCA and PMR cohort, respectively) and SOC Injury, poisoning and procedural complications (16.9% overall) which was also higher in proportion for GCA compared to PMR cohort (23.5% vs. 9.7%). In Infections and infestations SOC, only PTs upper respiratory tract infection, COVID-19, oral candidiasis, and urinary tract infection were reported in 2 or more participants.
- Most frequently reported TEAEs (>5 %) by PTs in GCA cohort were giant cell arteritis (11.8%, 4/34), animal scratch, arthralgia, facial pain, muscle spasm, myalgia, oral candidiasis and upper respiratory tract infection (5.9%, 2/34 each). For PMR cohort the most frequently reported TEAEs by PTs were polymyalgia rheumatica (9.7%, 3/31), COVID-19, hyperparathyroidism and lymphocyte count decreased (6.5%, 2/31 each).
- The majority of the TEAEs were reported of mild to moderate severity in both cohorts. The overall number of severe AEs reported was low, occurring only in 3 participants (4.6%). These included PTs cardiac arrest and giant cell arteritis in the GCA cohort (2 participants) and PT suicidal ideation in the PMR cohort (one participant). They were all reported as SAEs.
- A total of 15.4% participants reported at least one AE considered as treatment-related by the Investigator (GCA cohort: 23.5%; and PMR cohort: 6.5%). The majority of the study treatment-related AEs were reported from SOC Infections and infestations (6.2% overall) and all were in the GCA cohort. Each participant reported one of the following contributing PTs: oral candidiasis, oral fungal infection, respiratory tract infection, and upper respiratory tract infection. However, in the PMR cohort, 6.5% reported one

treatment-related AE each, classified under SOC Injury poisoning and procedural complications and SOC Skin and subcutaneous tissue disorders (PTs: infusion related reaction and urticaria each).

- Overall, five participants with at least one SAE including one fatal case (7.7%) were reported in the study (GCA cohort: 11.8% and PMR cohort: 3.2%). None of the SAEs were assessed as treatment-related by the Investigator. Except for one participant who reported 2 SAEs (PTs: colitis microscopic and hypertension), none of these SAEs occurred in more than 1 participant each. Three of the SAEs were of severe intensity (PTs: cardiac arrest [fatal], giant cell arteritis and suicidal ideation), three were of moderate intensity (PT: leukoencephalopathy, hypertension and colitis microscopic). The SAE of worsening of hypertension occurred when the SAE of worsening of colitis microscopic was resolving in the same participant. One participant in the GCA cohort died due to cardiac arrest. The cause of death was tachycardic atrial fibrillation, attributed to coronary and hypertensive heart disease, as well as type 2 diabetes mellitus, and it was not considered as treatment-related by the Investigator. All the SAEs were reported under GCA cohort, except for suicidal ideation under PMR cohort.
- Only one participant discontinued the study treatment and the study due to AE in addition to the aforementioned fatal case. This was a participant in the GCA cohort with AE of limb injury which was caused by an animal scratch. Adverse events (PT diarrhea and PT upper respiratory tract infection in 1 participant each) that required study treatment interruptions with dosing visit postponed were reported in the GCA cohort.
- The most commonly reported TEAEs of STIs were from SOC Infections and infestations (29.2%) overall, numerically higher (32.4%) in the GCA compared to PMR cohort (25.8%). Most contributing PT in this SOC included upper respiratory tract infection (4.6%). Additional infections included Fungal Infectious Disorders (high level group term [HLGT], PTs: Oral candidiasis, Fungal infection, and Oral fungal infection) which was overall reported in 4 (6.2%) participants (3 in GCA and 1 in PMR cohort), and Infections of Skin Structures (Novartis MedDra Queries [NMQ], PTs: balanoposthitis, infected bite, and erysipelas) which was overall reported in 3 participants, and they were all in GCA cohort. Hypersensitivity (SMQ, narrow) was overall reported in 3 participants with the PTs included infusion related reaction, eye swelling, and urticaria (1 in GCA and 2 in PMR cohort). Two STIs were reported in severe severity, and both were considered as serious adverse events. One MACE event (NMQ) was reported with the PT cardiac arrest, fatal event in GCA cohort and one Suicide/self-injury (SMQ) with the PT Suicidal ideation in PMR cohort. All other STIs were reported in either mild or moderate severity.
- Most participants had hematology and chemistry parameters within normal range at baseline and post-baseline with no notable clinical significant laboratory changes.
- One participant in the GCA cohort had worsening in liver enzymes with the maximum value reported ALT >10×ULN (from local lab), and AST value >5×ULN. The transaminase levels returned to normal after discontinuing the concomitant medication of Cemidon B6 to treat current history of latent TB without any change to the study treatment. The Investigator assessed the AE (PT: hypertransaminasemia) as not related

to the study treatment but due to Cemidon B6 per the clinical query. No other significant liver enzyme-related abnormalities were reported.

- One participant had a newly occurring or worsening vital sign abnormality with the highest reported blood pressure of 200/80 mmHg on study Day 85 which was considered as SAE (PT: hypertension) and it occurred during the hospitalization to manage the SAE of worsening of colitis microscopic. No vital sign abnormality led to discontinuation of the study treatment.

Conclusions

The steady state PK for secukinumab was achieved in participants within both the cohorts at Week 4 as expected and PK parameters such as Cmin,ss (pre-infusion) and Cavg,ss are similar in GCA and PMR cohorts. Cmax,ss is 9.7% higher in PMR than in GCA cohort due to the higher body weight in PMR than in GCA cohort. PK behavior was very similar in both cohorts.

Secukinumab was considered safe and well tolerated, and the safety profile observed in this study is in line with the already known safety profile of secukinumab and showed no new safety signals with i.v. formulation administered in adult participants with GCA or PMR.