Efficacy and Safety of Secukinumab in Patients With New Onset of Giant Cell Arteritis Who Are in Clinical Remission

Last Update: Nov 15, 2024

A Randomized, Parallel-group, Double-blind, Placebo-controlled, Multicenter Trial to Investigate the Efficacy and Safety of Subcutaneously Administered Secukinumab in Patients With New-onset of Giant Cell Arteritis (GCA) Who Are in Clinical Remission and Eligible for Treatment With Glucocorticoid-monotherapy

ClinicalTrials.gov Identifier:

NCT05380453

Novartis Reference Number:CAIN457R1DE01

See if you Pre-qualify

All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

The purpose of this study is to demonstrate the efficacy and safety of subcutaneously (s.c.) administered secukinumab 300 mg in combination with glucocorticoid taper regimen compared to placebo in combination with glucocorticoid taper regimen, in adult patients with new onset of giant cell arteritis (GCA) who are in clinical remission and who are eligible for treatment with glucocorticoid-monotherapy as per current clinical practice and treatment guidelines for the targeted participant population, thereby supporting health technology assessments (HTAs) of secukinumab in Germany. Recent scientific evidence identified an association between polymorphisms within the IL-17A locus and GCA, supporting a role for IL-17A in vasculitis pathophysiology. Analysis of the inflammatory processes in the aortic wall has indicated that inflammatory cytokines, such as IL-6 and IL-17A are involved in GCA pathogenesis. Elevated IL-17A mRNA levels are correlated with IL-6 and IL-23p19 mRNA levels indicating the involvement of the IL-23/Th17 axis in GCA. With its pleiotropic activity on many different cell types, IL-17A may actively contribute to the inflammatory processes in GCA. In addition, animal studies also support a role of IL-17A as a driver of vasculitis, since mice deficient in IRF-4 binding protein, which have increased IL-21 and IL-17A expression, spontaneously develop arthritis-like joint disease and large vessel vasculitis (LVV).

As secukinumab has already demonstrated a positive benefit/risk profile in the treatment of multiple chronic inflammatory diseases, including PsO, PsA and axSpA, and based on the scientific rationale for targeting the IL-17 pathway in GCA as well as on the basis of the currently ongoing Phase 2 Proof-of-Concept trial the which evaluates the efficacy, safety and tolerability of 300 mg secukinumab compared to placebo, in combination with a 26-week prednisolone taper regimen in adult subjects with GCA (EudraCT number: 2018-002610-12) (Venhoff, et al., 2021), inhibition of IL-17A by secukinumab has a potential therapeutic benefit for GCA patients.

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with glucocorticoid taper regimen, in adult patients with new onset of giant cell arteritis (GCA) who are in clinical remission and who are eligible for treatment with glucocorticoid-monotherapy as per current clinical practice and treatment guidelines for the targeted participant population, thereby supporting health technology assessments (HTAs) of secukinumab in Germany.

Condition
Giant Cell Arteritis
Phase
Phase3
Overall Status
Recruiting
Number of Participants
146
Start Date
Sep 21, 2022
Completion Date
Jul 13, 2026
Gender
All
Age(s)
50 Years - (Adult, Older Adult)

Interventions

Drug

Placebo to match Secukinumab, s.c.

Placebo will be administered as s.c. injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter.
Biological

Secukinumab 300 mg, s.c.

Secukinumab will be administered at a dose of 300 mg as s.c. injection at Baseline, Week 1,2,3,4 and then every 4 weeks thereafter.

Eligibility Criteria

Inclusion Criteria:

Participants eligible for inclusion in this study must meet all of the following criteria:

1. Signed informed consent must be obtained prior to participation in the study.
2. Participant must be able to understand and communicate with the investigator and comply with the requirements of the study.
3. Male or female participants at least 50 years of age.
4. Diagnosis of new-onset GCA, defined as GCA diagnosed within 6 weeks of baseline (BSL) visit, based on meeting all of the following criteria:

* Age at onset of disease ≥50 years.

* History of Erythrocyte Sedimentation Rate (ESR) ≥30 mm/hr or C-reactive protein (CRP) ≥10 mg/L attributable to active GCA.
* 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) AND/OR symptoms of limb ischemia (claudication).
* Temporal artery biopsy revealing features of GCA AND/OR evidence of vasculitis in cranial or extracranial arteries by angiography or cross-sectional imaging study such as ultrasound, magnetic resonance angiography (MRA), computed tomography angiography (CTA), positron emission tomography - computed tomography (PET-CT)
5. Participants must be in clinical remission at BSL:

- Definition of clinical remission: absence of signs and symptoms attributable to active GCA as determined by the investigator.
6. Participants with no relapsing GCA at BSL:

- Definition of relapsing GCA: occurrence of clinical relapse after clinical remission.
7. Prednisolone or equivalent dose (oral) of 20-60 mg/day or equivalent dose of other glucocorticoids (GCs) at BSL.

Exclusion Criteria:

Participants meeting any of the following criteria are not eligible for inclusion in this study.

3. Participants not eligible for glucocorticoid monotherapy due to known increased risk for or presence of GC-related adverse-effects or complications and/or intolerance to GCs, such as osteoporosis, diabetes mellitus, cardiovascular disease and glaucoma as assessed at the investigator's discretion (see Appendix 15.2).

4. Previous exposure to secukinumab or another biologic drug directly targeting IL-17 or IL-17 receptor.

5. Participants 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).

6. Previous participation in clinical trials for GCA 7. Participants who have been treated with inhibitors directly targeting IL-12 and/or IL-23 (such as ustekinumab, guselkumab, tildrakizumab, risankizumab), IL-1 or IL-1 receptor (such as anakinra or canakinumab), or abatacept within 4 weeks or within 5 half-lives of the drug (whichever is longer) prior to BSL.

8. Treatment with tocilizumab, other IL-6/IL6-R inhibitor or JAK inhibitor within 12 weeks or within 5 half-lives of the drug (whichever is longer) prior to BSL, or if participant did not respond to or experienced a clinical relapse during treatment any time before BSL.

9. Any treatment received for GCA other than GCs and participant did not respond to treatment or experienced a clinical relapse during treatment any time before BSL.

10. Any other biologics within 4 weeks or within 5 half-lives of the drug (whichever is longer) prior to BSL.

11. Participants treated with i.v. immunoglobulins or plasmapheresis within 8 weeks prior to BSL.

12. Participants treated with cyclophosphamide, tacrolimus, everolimus hydroxychloroquine, cyclosporine A, azathioprine, sulfasalazine, mycophenolate mofetil within 6 months prior to BSL.

13. Participants treated with methotrexate (MTX), within 4 weeks prior to BSL. 14. Participants treated with

leflunomide within 8 weeks prior to BSL unless a cholestyramine washout has been performed in which case the participant must be treated within 4 weeks of BSL.

15. Participants treated with an alkylating agent within 5 years prior to Baseline, unless specified in other exclusion criteria.

16. Participants requiring systemic chronic glucocorticoid therapy for any other reason than GCA at Screening.

17. Receipt of \> 100 mg daily intravenous methylprednisolone pulse therapy within 6 weeks prior to BSL.

18. Participants requiring chronic (i.e., not occasional "prn") high potency opioid analgesics for pain management.

19. Participants treated with any investigational agent within 4 weeks or within 5 half-lives of the drug (whichever is longer) prior to BSL.

20. Contraindication or hypersensitivity to secukinumab. 21. Active ongoing inflammatory diseases other than GCA that might confound the evaluation of the benefit of secukinumab therapy, including inflammatory bowel disease or uveitis.

22. Active ongoing diseases which in the opinion of the investigator immunocompromises the participant and/or places the participant at unacceptable risk for treatment with immunomodulatory therapy.

23. 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 immunocomprises the participant and/or places the participant at unacceptable risk for participation in an immunomodulatory therapy.

24. Major ischemic event (e.g., myocardial infarction, stroke, etc.) or transient ischemic attack (TIA) (except ischemia-related vision loss), related or unrelated to GCA, within 12 weeks of screening.

25. Confirmed diagnosis of any primary form of systemic vasculitis, other than GCA.

26. Active systemic infections during the last 2 weeks (exception: common cold) prior to BSL.

32. History of ongoing, chronic or recurrent infectious disease or evidence of tuberculosis infection as defined by a positive QuantiFERON TB-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 tuberculosis. If presence of latent tuberculosis is established, then treatment according to local country guidelines must be initiated prior to BSL.

35. Live vaccinations within 6 weeks prior to BSL or planned live vaccination during study participation until 12 weeks after last study treatment administration.

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