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Efficacy and Safety of Two Doses of Anifrolumab Compared to Placebo in Adult Subjects With Active Systemic Lupus Erythematosus

Sponsor: AstraZeneca
Collaborator: PRA Health Sciences
Protocol # D3461C00005
ClinicalTrials.gov Identifier: NCT02446912

Brief Title	Efficacy and Safety of Two Doses of Anifrolumab Compared to Placebo in Adult Subjects With Active Systemic Lupus Erythematosus
Official Title	A Multicentre, Randomised, Double-blind, Placebo-controlled, Phase 3 Study Evaluating the Efficacy and Safety of Two Doses of Anifrolumab in Adult Subjects With Active Systemic Lupus Erythematosus
Brief Summary	The purpose of this study is to evaluate the efficacy and safety of an intravenous treatment regimen of two doses of anifrolumab versus placebo in adult subjects with moderately to severely active, autoantibody-positive systemic lupus erythematosus (SLE).
Detailed Description	This is a Phase 3, multicentre, multinational, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of an intravenous treatment regimen of two doses of anifrolumab versus placebo in subjects with moderately to severely active, autoantibody-positive systemic lupus erythematosus (SLE) while receiving standard of care (SOC) treatment. The study will be performed in adult subjects aged 18 to 70 years of age.

Eligibility

Ages Eligible for Study: 18 Years to 70 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

1. Aged 18 through 70 years at the time of screening
2. Diagnosis of paediatric or adult SLE with a diagnosis of SLE according to the ACR 1982 revised criteria ≥24 weeks prior to signing the Informed Consent form (ICF)
3. Currently receiving at least 1 of the following:
    a. A dose of oral prednisone (≤40 mg/day) for a minimum of 2 weeks prior to signing of the ICF.
    b. Any of the following medications administered for a minimum of 12 weeks prior to signing the informed consent, and at a stable dose for a minimum of 8 weeks prior to signing the informed consent and until Day 1:

(i) Azathioprine ≤200 mg/day (ii) Antimalarial (eg, chloroquine, hydroxychloroquine, quinacrine) (iii) Mycophenolate mofetil ≤2 g/day or mycophenolic acid ≤1.44 g/day (iv) Oral, subcutaneous (SC), or intramuscular methotrexate ≤25 mg/week (v) Mizoribine ≤150 mg/day

4. Fulfils at least 4 of the 11 ACR modified 1982 classification criteria for SLE, at least 1 of which must be:
    a. Positive antinuclear antibody (ANA) test at screening by immunofluorescent assay (IFA) at the central laboratory with titre ≥1:80; OR
    b. Elevated anti-dsDNA antibodies OR anti-Smith (anti-Sm) antibody at screening as determined by the central laboratory
5. At Screening, Disease Activity Adjudication Group confirmation of:

    SLEDAI-2K Criteria: SLEDAI-2K score ≥6 points and "Clinical" SLEDAI-2K score ≥4 points. The "Clinical" SLEDAI-2K is the SLEDAI-2K assessment score without the inclusion of points attributable to any urine or laboratory results including immunologic measures:

6. Must not have active or latent TB on either chest radiograph or by quantiferon gold test
7. Day 1 "Clinical" SLEDAI-2K score ≥4 points
8. OCS dose stable for at least 2 weeks
9. Stable SLE SOC treatment
10. Women of child-bearing potential must have a negative serum β-hCG test at screening and negative urine pregnancy test prior to administration of investigational product

Exclusion Criteria:

1. Receipt of any investigational product (small molecule or biologic agent) within 4 weeks or 5 half-lives prior to signing of the ICF, whichever is greater
2. Receipt of any of the following: Intra-articular, intramuscular or IV glucocorticosteroids within 6 weeks prior to Day 1
3. History of, or current diagnosis of, a clinically significant non SLE-related vasculitis syndrome.
4. Active severe or unstable neuropsychiatric SLE
5. Active severe SLE-driven renal disease 6. Diagnosis (within 1 year of signing the ICF) of mixed connective tissue disease or any history of overlap syndromes of SLE or SSc.
6. History of, or current, inflammatory joint or skin disease other than SLE
7. History of any non-SLE disease that has required treatment with oral or parenteral corticosteroids for more than 2 weeks within the 24 weeks prior to enrollment
8. Confirmed positive test for hepatitis B or hepatitis C
9. Any severe herpes infection at any time prior to Week 0 (Day 1)
10. Opportunistic infection requiring hospitalisation or parenteral antimicrobial treatment within 3 years prior to randomization
11. History of cancer, apart from: Squamous or basal cell carcinoma of the skin that has been successfully treated OR Cervical cancer in situ that has been successfully treated