BIOVAS Trial

The BIOVAS trial is now open for recruitment in Glasgow.

BIOVAS is a multi-centre, pragmatic, randomised double blind, placebo-controlled, modified-crossover phase 2B trial of infliximab, rituximab and tocilizumab for refractory NAAV in adults and children. The trial will test the hypothesis that biologics are superior to placebo in the control of refractory NAAV. Each of the three trial biologics (infliximab, rituximab and tocilizumab) will be compared to placebo in a sequential modified crossover, placebo-controlled design.

Main inclusion criteria

To be included in the trial the participant must:

1. Aged at least 5 years
2. Have given, or their parent/legal guardian aged ≥ 16 years old has given, written informed consent
3. Diagnosis of NAAV
4. Refractory disease defined by:
   - Active disease, BVAS v3-BIOVAS/ PVAS with ≥ 1 severe (new/worse) or ≥ 3 non-severe (new/worse) items despite 12 weeks of conventional therapy OR
   - Inability to reduce prednisolone below 15mg/day or (0.3mg/kg/day in case of children) without relapse in the 12 weeks prior to screening visit

Main exclusion criteria

Participants are excluded from the trial if any of the following criteria apply:

1. Previous treatment failure/contraindication to ≥ 2 active trial IMPs
2. Increase in the dose or frequency of background immunosuppressive (e.g. methotrexate) or anti-cytokine therapy within 30 days prior to screening visit
3. Use of plasma exchange or intravenous immunoglobulins within the 30 days, or cyclophosphamide or lymphocyte depleting biologic (e.g. rituximab) within 6 months of screening visit
4. Concomitant use of any biologic and/or anti-TNF agent other than the trial IMPs for the duration of the trial.
5. Have an active systemic bacterial, viral or fungal infection, or active/latent tuberculosis assessed/documented as per local clinical practice; this includes COVID19 testing if warranted and as per local routine practice.
6. Hepatitis B (HB) core antibody (Ab) or HB surface antigen positive or hepatitis C antibody positive or human immunodeficiency virus (HIV) antibody test positive
7. History of malignancy within five years prior to screening visit or any evidence of persistent malignancy, except fully excised basal cell or squamous cell carcinomas of the skin, or cervical carcinoma in situ which has been treated or excised in a curative procedure
8. Pregnant or breastfeeding, or inability/unwillingness to use a highly effective method of contraceptive if a woman of childbearing potential (WOCBP; Section 11.9)

9. Severe disease, which in the opinion of the physician prevents randomisation to placebo

10. Recent or upcoming major surgery within 45 days of screening visit

11. Leukocyte count < 3.5 x 109 cells/l, platelet count < 100 x 10_9 cells/l, neutrophil count of < 2 x 10_9 cells/l

12. 12. ALT or ALP > 3 times the upper limit of normal

13. Symptomatic congestive heart failure (NYHA class III/IV) requiring prescription medication within 90 days of screening visit

14. Demyelinating disorders

15. History or presence of any medical condition or disease which, in the opinion of the Investigator, may place the participant at unacceptable risk because of trial participation

16. Administration of live or live attenuated vaccines within 45 days of screening

17. Have received an investigational medicinal product (IMP) within 5 half-lives or 30 days prior to screening

18. Diagnosis of adenosine deaminase type 2 (DADA2)

19. Hypersensitivity to the active IMP substance or to any of the formulation excipients (unless IMP excluded for a particular patient pre-randomisation)