BIOVAS: a clinical trial in Non-ANCA vasculitis
Plain English Summary

The vasculitis diseases occur when the body's immune system attacks the walls of blood vessels, causing injury to the vessel and the part of the body it supplies with blood. Vasculitis is rare, there are a number of different types, and they affect both children and adults. We treat vasculitis with steroids and other drugs aiming to damp down the activity of the immune system, but the drugs often cause side effects. Some patients do not improve with this treatment, or cannot tolerate it and their vasculitis worsens (refractory vasculitis). Such patients are at high risk of health complications from the disease and its therapy and are in need of newer treatments with fewer side effects.

Biologics are expensive drugs manufactured from biological sources. They are designed to the target immune system more precisely compared to older drugs. Although biologics have been used for some years to treat vasculitis, for many types of vasculitis we do not have good data to guide the correct choice of biologic, and when to use it. Two biologics have been fully tested and are now licensed for the more common forms of vasculitis. We want to establish whether biologics are effective and represent value for money for patients with refractory vasculitis.

BIOVAS will look at three different biologics, infliximab (INF), tocilizumab (TCZ) and rituximab (RTX), chosen for scientific reasons and because there is already some experience of their use in vasculitis. We will recruit 140 patients (children & adults) with refractory vasculitis and compare each drug to a placebo (dummy) treatment. Patients will have the following types of vasculitis: giant cell arteritis, Takayasu's arteritis, polyarteritis nodosa, cerebral vasculitis, Cogan's syndrome, relapsing polychondritis, IgA vasculitis, non-infective cryoglobulinaemic vasculitis. Patients will not be able to take part if they have recently received a biologic drug, have a serious infection, or are pregnant.

Treatments will be decided by a process called randomisation (like "flipping a coin"). Patients will be assigned to a treatment sequence (e.g. one sequence may be TCZ, then INF, then placebo, then RTX). They will start on the first allocated treatment and stay on it as long as it is helping them; if the treatment does not work, or stops working, they will move to the next treatment in the sequence. Neither the doctor nor the patient will be aware of the treatment they are on unless there is an emergency. All treatments are given as a drip into a vein in the patient's arm. TCZ and INF are given

monthly whilst RTX is given as two doses two weeks apart every six months.

All patients will be seen in clinic at the start of the trial and again every four months to see how they are doing. These visits will check whether the treatment is working or not. Patients will be asked to complete questionnaires about how they feel the disease is affecting their lives, as well as recording side effects. The study will estimate the treatment costs to the NHS, costs the patient experience due to the disease and whether the disease is affecting their job or schooling/education.

We will use statistical tests to analyse all the information before we draw any conclusions. The BIOVAS study team includes experts in vasculitis and patient representatives. This is a pragmatic study with the aim of establishing the benefits and costs of these drugs on patient's health and quality of life. This will help patients in the future to receive the best possible treatment for their conditions.