PCL/24/06 - Endothelial Dysfunction as a Mechanism of Vascular Injury & Increased Cardiovascular Disease Risk in Large Vessel Vasculitis

Large vessel vasculitis (LVV) is a condition which involves inflammation of medium- and large-sized blood vessels. Over time, this inflammation can permanently damage the blood vessels leading to pain, vision loss, and blood vessel rupture. Treatment is usually effective in the short term. However, the disease is a lifelong condition, and relapse is common. Longer-term, affected patients have a high risk of heart disease, including heart attacks and strokes. Currently, little is known about why this is the case, and so little can be done to reduce this risk. The ‘endothelium’ is an important layer within blood vessels which controls their response to stress. If the endothelium is damaged, it can increase the risk of heart disease. My previous work has suggested that a damaged endothelium may be at least partly responsible for the increased heart disease risk in LVV. If this is the case, then drugs which improve the endothelium may also be able to reduce the risk of heart disease.

Therefore, in this proposal I plan to assess the function of the endothelium in detail in patients with LVV, and to see if this can be improved with currently available tablets. I will recruit a group of patients with well-controlled LVV and a separate group of similarly aged people without LVV. First, I will assess the function of the endothelium in both groups; next, half of the patients with LVV will either receive a medication (bosentan) that will hopefully improve endothelial function, and the other half will receive a ‘placebo’ for a period of 6 weeks. Following this, I will assess the function of the endothelium again. My scientific thinking is that patients with LVV will have poorly working endothelium compared to similarly aged people without LVV, and that this will improve after 6 weeks of the medication.