Breakthrough science provides hope for lupus patients

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Today the prestigious *New England Journal of Medicine* (*NEJM*) publishes research led by Monash University Professor Eric Morand that offers the first real hope for the treatment of lupus, a disease which affects 1.5 million people in the US and more than 5 million globally, 90% women and for which there is no cure.

The results are of an international, three-year, Phase 3 trial of a potential new drug that treats this autoimmune disease (also known as systemic lupus erythematosus (SLE)).

Lupus is an autoimmune disease in which the immune system attacks healthy parts of the body. It is particularly insidious disease as it has a ten-year mortality of 10%, "which if you are diagnosed in your early twenties is a terrible outcome," according to Professor Morand, who oversaw the global trial in over 360 people with SLE.

The trial, called TULIP 2, evaluated AstraZeneca's anifrolumab and achieved a statistically-significant and clinically-meaningful reduction in disease activity versus placebo, with both arms receiving standard of care.

Professor Morand has also been key in developing new lupus assessment criteria—which because the disease involves a number of organs in the body—can be difficult to both diagnose and monitor.

According to Professor Morand, there has only been one new treatment approved for the disease in the last 60 years, which is not available on the Pharmaceutical Benefits Scheme in Australia.

Between 60% and 80% of adults with SLE show increased interferon-induced genes, which reflect overproduction of the immune protein Type 1 interferon. While previous attempts to block this protein in lupus have failed, the potential new treatment, anifrolumab, works by blocking the receptor on all cells in the body, aiming to reverse the triggering of lupus symptoms.

Professor Morand said that interferon is associated with other autoimmune diseases such as Scleroderma and Sjogren's disease "so there may be potential for using anifrolumab in the treatment of other

interferon related diseases as well."

In the TULIP 2 trial, eligible patients received a fixed-dose intravenous infusion of anifrolumab or placebo every four weeks. TULIP 2 assessed the effect of anifrolumab in reducing disease activity—noting a significant effect in global disease activity measures.

The trial, from 2015 to 2018, involved 362 patients receiving either 300 mg of the drug or a placebo intravenously once every four weeks for 48 weeks. Benefit was measured using a defined clinical assessment of improvement in all organs as well as the number of flare ups (which see the patient experiencing fever, painful or swollen joints, fatigue, rashes or sores or ulcers in the mouth or nose). The volunteers were aged between 18 and 70 and had moderate to severe disease despite standard treatments. Patients with SLE typically die of organ failure.

The study found that—52 weeks after the trial started—significantly more patients on the drug than the placebo had:

- A reduction in overall disease activity in all active organs
- improvement in lupus skin disease
- A reduction in steroid drug doses
- Reduced annual rate of flares

The TULIP 2 trial followed on from the TULIP 1 trial which failed to meet its primary outcome. The second trial, published in the *NEJM*, used a different endpoint. "Measurement of treatment response in SLE has been very problematic and this represents a kind of second breakthrough of this trial," Professor Morand said.

AstraZeneca will now work with regulators, to bring anifrolumab, a potential new medicine, to patients. The study was done in collaboration with colleagues in Japan, the UK, the US, France and South Korea.

Provided by Monash University