FIGHT MND.

Lead Investigator.
PROF JULIAN GOLD

Clinical Trial Name.
THE EFFICACY AND SAFETY OF TRIUMEQ IN PATIENTS WITH ALS. THE LIGHTHOUSE II TRIAL

Prof Julian Gold holding a package containing the medication Triumeq, which is highly effective against HERV-K.

Where do you work?

I am Director of the Albion Centre HIV service which is the largest service in Australia and one of the longest established services in the world. We are also the Regional WHO Collaborating Centre. The clinic is a facility of the NSW Health Department. I work for 2-3 months a year in the UK at The Royal London Hospital and at King's College where I focus on MND.

Can you give us a summary of your training and background?

I completed my medical degree at University of Sydney and post-graduate studies at University College Hospital in London. After that I worked for the U.S. Centers for Disease Control, the New York City Health Department, and then at WHO in Geneva. After returning to Australia, I worked at the Commonwealth Institute of Health and St Vincent's Hospital before joining the Albion Centre which is part of Prince of Wales Hospital.

What got you interested in MND research?

After treating people with HIV/AIDS for almost 25 years I became interested in the possibility that these wonderful drugs may be used for other conditions. Professor Avindra Nath and others observed that MND may be caused by a retrovirus which is in the same family as HIV. I had a personal contact with MND and then started to treat the person with Triumeq, which seemed to show some effect. We were fortunate to receive funding from FightMND to conduct an initial trial to determine the safety and tolerability of Triumeq in 40 patients with MND. This study was a collaboration between eminent neurologists in Sydney and Melbourne and many international colleagues.

Can you describe the work your team is currently pursuing?

The results of the initial trial were encouraging enough to plan a definitive clinical trial in Europe, Australia and the UK. This trial will involve more than 350 patients and use an innovative design which will enable more patients to participate and, hopefully get a result as soon as possible. Currently, we are doing preliminary studies as the Triumeq has to be crushed and put into capsules. If this work is successful, the trial should start in early 2020.

Describe your thoughts when you identified Triumeq as a potential treatment for MND?

Triumeq may be the ideal drug to test for MND. It is three active drugs in a single tablet which is taken once daily. There is huge global experience with Triumeq as a treatment for HIV and we know it has very good brain penetration.

What excites you about Triumeq?

The potential for repurposing Triumeq is very exciting, but it will all depend on the science of the clinical trial. There have been so many drugs with potential to treat MND that have failed in clinical trials. It is important that we are both optimistic and scientific at the same time. As Triumeq is already licenced and available (for HIV), it can be made available for treating MND if the trial is successful.

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What will this funding enable you to achieve?

Funding from FightMND is crucial to enable this trial to go ahead. The funding will be for the Australian and international aspects of the trial as we will need to work together to achieve a result as soon as we can. The FightMND funding will supplement funding we have from many sources in Australia and Europe as this investigator-initiated trial needs collaboration from everybody involved and a strong partnership between patients, clinicians and funders.

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We have shown previously that an ancient virus, hidden in the genome, may be responsible for MND/ALS, becoming activated and leading to the death of motor neurons. This type of virus, called a HERV (human endogenous retrovirus), is in the same class of viruses as HIV. More recently, a specific HERV, known as HERV-K, has been shown to be the likely culprit in MND/ALS. A common combination antiviral drug for HIV, Triumeq, is highly effective against HERV-K, and importantly, can cross into the nervous system. In the Lighthouse Study, a recent Australian clinical trial supported by FightMND, Triumeq was shown to be safe and well tolerated in 40 MND/ALS patients. Even though the study was not designed to look for benefits/effectiveness, the clinical responses were very promising. Therefore, there is an urgent need to confirm the efficacy of Triumeq as compared to placebo in a large, innovative, randomised trial.

The Lighthouse II trial will be conducted in 17 centres across Australia, Europe and the UK, enrolling 363 patients, and aims to show a clinically important benefit of Triumeq on survival time. The design is highly innovative, with a unique patient selection and advanced clinical trial methodology that involves 2:1 randomisation and monitoring schemes designed to stop the trial if the drug proves effective. The trial is predicted to provide a definite answer about the efficacy of Triumeq within 24-36 months after enrolling the first patient. The design ensures optimal use of time, minimal patient burden and wide inclusion criteria to speed-up enrolment rates. In addition, we will collect blood and urine at each visit to measure markers of disease progression. If there is a positive effect, we will apply for licensing for treating MND/ALS. As Triumeq is already licensed for treating HIV, this repurposing for MND/ALS may be an important factor in getting approval if it proves effective.

OBJECTIVES/OUTCOMES:

- Demonstrate the benefit of Triumeq on MND/ALS patient survival time.
- Assess if Triumeq reduces HERV-K expression in motor neurons.
- Determine the effect of Triumeq on the expression of known biomarkers that measure the progression of MND/ALS.
- Definite answer about the efficacy of Triumeq for treating MND/ALS within 24-36 months.