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TRISH MULTIPLE SCLEROSIS RESEARCH FOUNDATION FELLOWSHIP

The 5-year \$500,000 Trish Multiple Sclerosis Research Foundation Fellowship, which will commence January 2024, has been awarded to Dr Chao Zhu, Monash University. Dr Zhu will be working with Associate Investigators Professor Helmut Butzkueven and A/Prof Anneke van der Walt.

For people living with multiple sclerosis, high-efficacy disease-modifying therapies provide almost complete freedom from new lesions and relapses and also greatly reduce disability progression, including conversion to secondary progressive MS. If not treated, multiple sclerosis becomes progressive. Most patients present with relapsing remitting MS, but without treatment their MS will become progressive. However, long-term exposure to these high-efficacy disease-modifying therapies can increase the risk of severe infections and cancer. With increasing age, MS disease activity declines, while the risk of infection and cancer increases. Therefore, whether and when MS patients can safely de-escalate to say, a lower efficacy disease-modifying therapy or discontinue these therapies is extremely important. The topic is of such great interest that ECTRIMS convened a specific Focussed Workshop in March 2023, to which Professor Butzkueven was invited.

High-efficacy disease-modifying therapies will be a most important part of MS management for many years into the future. Dr Zhu's important work will make the use of these treatments safer and allow changes in their use to be made based on clear information as to the safety of such changes. Currently people living with MS risk disease recurrence when these changes are made. Dr Zhu's work is translational research; it is clearly aimed at improving therapy and hence the patient's well-being.

Dr Zhu, Professor Butzkueven and A/Prof van der Walt's team have compared specific treatment switch/de-escalation scenarios, however they have not examined the hazards and benefits of disease-modifying therapy discontinuation.

Dr Zhu and his team will leverage the MSBase Database (93,800 patient records from 171 clinics in 43 countries around the world), the only global MS registry. A simple risk score will be developed for predicting outcomes following the de-escalation/discontinuation of various high-efficacy disease-modifying therapies. The risk score will be validated using internal MSBase data sets and external data sets from France, Denmark, Sweden, and Italy registries, with whom a strong collaboration has been established.

A user-friendly online platform/APP will be developed and freely made available globally for clinicians and patients to display scenario-specific risk scores, making it easy to implement study findings into clinical care and ensure treatment decisions are highly personalised.

Dr Zhu's collaborator, Professor Butzkueven said, *"We are now preventing progressive and disabling MS in most people whose disease starts with relapses. This transformation has taken place because of the widespread use of highly effective treatments."*

Australia is getting older. In 2023, there are 4.6 million Australians over 65, this will rise to over 7 million over the next 20 years. But as people with MS age, treatments increase the risk of cancer and serious infections. As a person with MS, if you have had a melanoma removed or just been in hospital with a bad pneumonia, is it better to scale back the MS treatment or keep going? This is a really complicated question- on the one hand, we want to stop progression of MS, on the other hand we want to be safe. Because the answer is complex, and depends very much on personal circumstances, we need to develop a personalised, individual way to recommend the best overall course of action.

With this Trish Fellowship, Dr Zhu will work with over 93,000 patient records from MSBase and over 250,000 from Denmark, Sweden, Italy and France to develop and test a score-based individualised treatment recommendation, before developing an APP to make the score generally available and continue to refine its accuracy. This research will maximise prevention of progression and disability while improving safety, especially in the many older people with MS.

We thank the Trish Foundation for their incredible commitment to preventing MS progression globally, by supporting this ambitious plan and fund an incredibly talented early career researcher for a full five years."