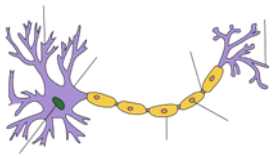
NEW ZEALAND MND REGISTRY

MND REGISTRY NEWSLETTER WINTER 2021

Welcome to our bi-annual newsletter for the New Zealand Motor Neuron Disease Registry. I hope you are keeping well in the current lockdown and safe within your bubbles. I understand it can be a stressful and changeling time for many.

The purpose of these newsletters is to keep our participants updated on what is happening in the Registry and any exciting research news that is emerging in MND research. I acknowledge the frustration some people are experiencing with the lack of clinical trials in New Zealand. I want to assure you that the Registry is proactively reaching out to principal investigators of studies and recent communications with some pharmaceutical research companies have increased awareness of New Zealand as a potential clinical trial site.



These efforts are beginning to pay off as a clinical trial site for the Wave Life Sciences study has been approved in Auckland and Christchurch. This is a milestone for MND research in New Zealand and the MND Registry assisted in the early stage negotiations of this proposal. You can read more about this study on page 3.

The Registry recently received enquiries from three international studies. These studies are gathering data using online questionnaires. You should have received an email inviting you to participate. If not you can read about these studies in this newsletter. Even though this type of research may not make a difference to you it is contributing towards a greater understanding of how MND affects individuals and is assisting in the development of services that may help future generations. The researchers of these studies thank you in advance for taking the time to participate.

As a participant in the New Zealand MND Registry, you will be informed about any research or clinical studies in New Zealand that you are eligible to participate in. To ensure your details remain up to date please contact us if you have a change in diagnosis, receive genetic test results, or change your contact details.

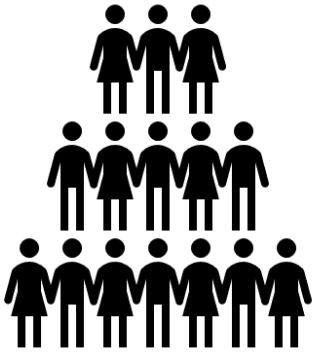
In this newsletter, you can read about the ongoing studies in New Zealand and some international clinical trials that are showing promising results. If you know someone with MND who is not on the Registry please share this newsletter with them.

Kia kaha Dympna Mulroy (Curator)

HOW ARE WE DOING!

Registry has facilitated recruitment to 11 research studies

Registry approached 20 studies to consider NZ as a research site



305 People enrolled in Registry

192

Active Participants

4 = studies currently inviting NZ participants

1 = supporting recruitment for 1 upcoming clinical trial in NZ

COLLABORATION WITH RESEARCHERS

THE REGISTRY HAS ASSISTED RECRUITMENT TO THE FOLLOWING STUDIES:

- Swallowing Skill Training
- Thought-assistive technology
- Stigma in MND
- Remote wheelchair assessment
- ALS Quest
- Prevalence of sleep disorders

CURRENT COLLABORATIONS:

- **WAVE LIFE SCIENCES, WVE-004-001 STUDY, FOR PATIENTS WITH C9ORF72-ASSOCIATED AMYOTROPHIC LATERAL SCLEROSIS (ALS) OR FRONTOTEMPORAL DEMENTIA (FTD). – CLINICAL TRIAL SITES AUCKLAND & CHRISTCHURCH**
  - This is a multicentre, randomised, double-blind, placebo-controlled study to evaluate the safety and tolerability, of intrathecal wve-004 in adult patients with motor neurone disease (MND) or frontotemporal dementia (FTD), caused by C9orf72. To participate in the study, patients must have a documented gene mutation and display symptoms of MND. Due to the strict inclusion criteria, only a small number of people on the Registry are eligible. If you have a diagnosis of MND or FTD and have a positive genetic test result, please ensure your details are up to date on the Registry. Contact will be made with known eligible participants in the coming months.

- **GENETIC SCREENING IN MOTOR NEURON DISEASE – UNIVERSITY OF AUCKLAND**
  - The purpose of this study is to understand the genetic causes of MND in New Zealanders. In addition, the study aims to test how certain MND gene mutations affect human cells. People with MND (familial or sporadic), and people with no MND and no family history of MND are invited to participate. If you are interested in participating in this study, please contact the Registry. You can read more about this study on page 5.

- **USING MRI TO INVESTIGATE BLOOD-BRAIN BARRIER LEAKAGE IN MND - UNIVERSITY OF AUCKLAND**
  - The blood-brain barrier is an important structure that controls the entry of substances from the blood into the brain and vice versa. When this barrier is broken, it can contribute to neurodegeneration. Some evidence suggests there is blood-brain barrier breakdown in MND however, it is unclear how this happens and when in disease progression it occurs. The investigators of this study would like to develop and validate a new, non-invasive method to investigate the blood-brain barrier function of the human brain using MRI. Eligibility criteria must be met to enrol in this study. For more information, please contact the Registry.

- **EARSWITCH PROJECT – UNIVERSITY OF BATH, UNITED KINGDOM**
  - This study is collecting preliminary information by questionnaire about whether people living with MND could benefit from a new communication/assistive device located in earphones. It is investigating the new AAC switch access site using a small muscle in the ear. They are recruiting 2000 healthy people and 2000 people with neurological conditions. Participants need to complete a brief survey to help understand more about this ear muscle and to ultimately further this technology. Anyone with MND can participate. Information about the study and how to participate is available here.

- **PSYCHOLOGICAL IMPACTS OF MND & PREDICTIVE GENETIC TESTING – MACQUARIE UNIVERSITY, NSW**
  - This study is investigating the psychological factors that determine whether someone undergoes predictive genetic testing for MND/ALS. They are also seeking to understand the impact of familial MND and (where relevant) the impact of undergoing testing amongst those who receive a positive or negative result. This will be the first study to quantitatively assess the impact of genetic testing and familial MND on at-risk relatives.

    To participate you must meet all the following criteria:

    - At risk of MND e.g., have a history of familial MND
    - 18 years or older
    - Asymptomatic for MND/ALS or frontotemporal dementia (FTD)

    The researchers are looking for people who have either not been tested or have received a negative test result. They have reached their target enrolment number of participants who have a positive genetic test result. Participating in this study involves completing a survey. Click on this link to access the survey or to read more about the study.

UNDERSTANDING THE GENETICS OF MND

MND research is becoming increasingly focused on the role that genes play in the development of the disease and how gene therapies may provide more personalised treatment options for people with MND in the future. A recent study by Brown et al (2021) conducted a literature review to identify population-based studies reporting MND prevalence and/or incidence rates. They found studies from 22 different countries in Europe, North America, Latin America and Asia. The results suggest that although the proportions of SOD1 and C9orf72 are higher among those with familial MND, the majority of SOD1 and C9orf72 MND cases are found among those with sporadic MND. This suggests that classification of familial MND based on reported family history does not capture the full

picture of MND of genetic origin. This relates to an opinion piece written in 2017 by Dr Ammar Al-Chalabi, who is a well-renowned researcher in MND. Dr Ammar Al-Chalabi challenges the use of the terms 'familial MND' and 'sporadic MND' and states that finding the underlying cause for a person's MND is vital. This includes the importance of genetic testing even when there is no known family history. Click here to read this article in full.

More locally Dr Emma Scotter, head of the Motor Neuron Disease Lab at the University of Auckland's Centre for Brain Research, and Dr Richard Roxburgh, a neurologist and neuro-geneticist at Auckland City Hospital and Associate Professor at the university, are running the largest study to date on the genetics of MND in New Zealand. Inherited cases of MND account for some 10% of patients. In practice, genetic testing is not routinely offered to people with MND unless they have a known family history of the disease. This study aims to enrol 300 participants with a diagnosis of MND including those with a sporadic or familial form. Identifying the genetic cause of a person's MND may help them in accessing clinical drug trials as more treatments are being tested targeting genetic forms of MND. An example is the Tofersen drug that targets the SOD1 gene, discussed below. You can read more about the New Zealand genetic study in a recent article published by The University of Auckland.

If you are interested in taking part in Dr Scotters study on 'Genetic Screening in MND'please contact the Registry and we will put you in contact with her research team.

INTERNATIONAL CLINICAL TRIALS UPDATE

TOFERSEN (BIIB067) BIOGEN; ADULTS WITH SYMPTOMATIC SOD1

Tofersen is an experimental antisense oligonucleotide (ASO) designed to reduce SOD1 protein in people with MND caused by SOD1 gene mutations. The treatment is a DNA-based molecule that binds the SOD1 mRNA — a blueprint of the gene that leaves the nucleus and is read by the cell's protein-making machinery to make SOD1 protein — blocking the production of this protein. A placebo-controlled clinical study started in 2016 and is due to be completed shortly. Biogen recently announced a two-part plan for early access to treatment following the completion of this trial.

1. Participants on the placebo drug will transition to active therapy, and before the safety and efficacy of tofersen are established, compassionate use access will be allowed for a subset of the SOD1-MND population with the most rapidly progressive disease.

2. If results from the study indicate that tofersen is safe and effective, and if no further studies are required, Biogen will initiate an early access program for the broad SOD1-MND population in countries where this is permitted by local regulations.

TOFERSEN (BIIB067) BIOGEN; PRESYMPTOMATIC ADULTS WITH SOD1 MUTATION.

Leading on from the anticipated success of Tofersen (BIIB067) for symptomatic SOD1, a study for clinically presymptomatic adults with SOD1 mutation was recently announced. Individuals must have a SOD1 variant known to cause rapidly progressive MND and be clinically presymptomatic for MND. Levels of a blood protein (measured in the blood which reflects neural cell damage) must also be low.

The development of drugs for presymptomatic adults of MND highlights the importance of current studies investigating the genetic causes and associations of MND and early identification of individuals with a genetic form of MND.

EDARAVONE

Edaravone is an antioxidant drug that protects nerve cells by mopping up 'free radicals in the body. Our cells usually have effective ways of dealing with free radicals, but these become less efficient with age. When neurones are damaged, as happens with neurodegenerative diseases, then more free radicals are produced and the body becomes less effective at eliminating them. This drug has been approved in Japan, South Korea, Canada, the USA, Switzerland, and China. In May 2019 the submission in Europe was withdrawn after the demand for an additional long-term study. Edaravone has not been approved by Medsafe in New Zealand. There are currently four ongoing trials with Edaravone and one yet to recruit. The Registry made contact with the company regarding a trial site in New Zealand, but this was not approved. Trials are still ongoing in the USA, Canada, France, Italy, Switzerland, and Japan to evaluate the long-term safety and tolerability of oral edaravone in subjects with MND over 24 and 48 weeks.

CONTACT DETAILS

The New Zealand MND Registry is run by Assoc Prof Richard Roxburgh (Principal Investigator) and Dympna Mulroy (Study Coordinator) with advice from the MND Registry Board composed of MND neurologists, MND scientists and MND Association reps. The MND Registry is sponsored by MND New Zealand.

If you would like any information about the Registry, please don't hesitate to contact us.

Email: mndregistry@adhb.govt.nz

Phone: 0800 MND REGISTRY or 027 561 7332

Website: https://mnd.org.nz/registry/

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