PrevANZ Vitamin D MS Prevention Trial

Progress report

March 2014

Background

PrevANZ is a world-first clinical trial that will test whether oral vitamin D supplementation can prevent MS in those at risk of developing the disease.

The Phase IIb randomised, double blind, placebo-controlled trial will focus on the possibility of using oral vitamin D supplementation to prevent a diagnosis of MS following a person's presentation with a first episode of symptoms – **people with CIS or clinically isolated syndrome**.

PrevANZ will also test appropriate dosage levels and safety. Vitamin D3 will be administered at doses of 0 (placebo), 1000 international units (I.U), 5000 I.U., and 10,000 I.U. daily for 48 weeks. Patients will be monitored by clinical and MRI measures to determine if oral vitamin D supplementation can delay or prevent a second clinical or radiological event that would result in a diagnosis of clinically definite MS. The trial will take four years to complete.

The need for the PrevANZ trial has arisen from a now significant body of evidence for the role that vitamin D deficiency plays in MS. However, to date there has not been a clinical trial to provide the necessary evidence on the benefits that can be expected from vitamin D supplementation or the correct dose.

This is an area in which the expertise in Australia and New Zealand can contribute significantly to the prevention and better treatment of MS globally.

Progress

Project Governance

The working group (contract research organisation, MSRA, PrevANZ Prinicipal Investigators) continue to hold fortnightly teleconferences to coordinate all logistical aspects of the trial, monitor recruitment and address enquires and any issues as they arise. The Steering Committee will meet again in March.

The Data Safety Monitoring Board (DSMB), comprised of three independent physicians with expertise in endocrinology, statistics and clinical trials has held its first quarterly meeting. The DSMB monitor the accrual of data and all reports of adverse events and serious adverse events to ensure patient safety throughout the trial.

Trial sites - Initiation

19 trial sites (14 in Australia, 5 in New Zealand) are now initiated and recruiting participants. A full list of trial sites can be viewed here.

An application for ethics approval has been made to the Human Research Ethics Committee at the Wesley Hospital, Brisbane with the outcome expected later this month and other logistical arrangements with the trial site are underway.

Patient enrolment

With the majority of trial sites now active, enrolments are now beginning to increase. 19 patients are now enrolled in the trial at sites as shown in the table below, with a further 7 patients currently undergoing eligibility screening at a number of sites.

Trial site	No. patients
Australian Neuromuscular Research Institute (WA)	3
Box Hill Hospital (Vic)	1
Royal Melbourne Hospital (Vic)	1
Royal Hobart Hospital (Tas)	5
Waikato (NZ)	1
Gold Coast (QLD)	3
John Hunter Hospital (NSW)	1
Austin Health (Vic)	1
Auckland Hospital (NZ)	2
Christchurch Hospital (NZ)	1

Patient enrolment will occur until October 2015 and each patient will be 'on drug' and monitored for 48 weeks. We anticipate that the last patients will complete the trial in October 2016. Data analysis will occur in early 2017 with the final trial outcome expected by June 2017.

Recruitment and promotion of the trial

With the majority of sites now initiated the main focus is now on ramping up recruitment. Primary routes for trial promotion at this stage are through the colleague referral networks of the site investigators including Ophthalmologists (where many cases of optic neuritis will present). Flyers were also placed in satchels at the conference of the Royal Australian New Zealand College of Ophthalmologists in October 2013 and sent out through the Australian New Zealand Association of Neurologists (ANZAN) mailing list. Further promotion of the trial will occur at the ANZAN Conference in May 2014.

The recruitment rate is continuously monitored and additional methods for recruitment will be enacted as required as the trial progresses.

While at this stage the trial is not being actively promoted to individuals, those who have been newly diagnosed with a first demyelinating event (Clinically Isolated Syndrome) can be informed of the trial and referred to their local site for further information and screening. The window of eligibility is 120 days from the onset of the first demyelinating event. Details of the trial, with information on eligibility and site contact details can be found at www.mstrials.org.au/PrevANZ-Trial

Quarterly newsletters are being sent to neurologists and study coordinators at the sites containing updates on trial recruitment and reminders about logistical and clinical processes.

Funding

Contributions from Foundation 5 Million+, Trish MS Research Foundation, the John T Reid Charitable Trusts, MS Societies of WA, Tasmania and Queensland, Clayton Utz Foundation and other private donations have been received for the trial.

The total trial budget stands at almost $2.8 million dollars. Efforts continue at MSRA to raise a further $800,000 to achieve a fully enrolled trial of 240 patients for a statistically robust and conclusive result to the trial.