PrevANZ Vitamin D MS Prevention Trial

Progress report

December 2013

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 enquries and any issues as they arise. The full PrevANZ Steering Committee held a teleconference in October 2013.

Site Investigators, members of the Steering Committee and the CRO met face-to-face at the Progress in MS Research conference in November 2013. This was a very productive meeting, with most sites now initiated, allowing early queries and minor problems to be addressed.

Logistics

The electronic Case Report Form (eCRF) for gathering clinical data at patient visits is running smoothly. Data for the first patients has been entered and feedback on the system from the sites' Study Coordinators is very positive, with only a few minor glitches detected and resolved.

12 Month stability results on the vitamin D capsules have come in from both the manufacturer and the independent chemical analysis laboratory and show the study drug continues to be stable. Analysis will be repeated at 18 months and 24 months.

Trial sites - Initiation

19 trial sites (14 in Australia, 5 in New Zealand) are now initiated and recruiting participants.

Following the withdrawal of the Royal Brisbane and Women's Hospital from the trial, Dr Pam McCombe and the Wesley Hospital, Brisbane, have been approached to join the trial. Dr McCombe

and her colleague Dr Noel Saines, are very keen to participate in the trial and will refer patients to the highly experienced clinical trials unit at the Wesley. Contracts and ethical and regulatory approvals are underway.

The Royal North Shore Hospital in Sydney has experienced some delays, but is now going through the Regulatory Approvals process.

Patient enrolment

13 patients are now enrolled in the trial at sites as shown below. Patients are also undergoing screening at several of the other sites.

2—Australian Neuromuscular Research Institute (WA)
1— Box Hill Hospital (Vic)
5—Royal Hobart Hospital (Tas)
1— Waikato (NZ)
2—Gold Coast (QLD)
1—John Hunter Hospital (NSW)
1—Austin Health (Vic)

Patient enrolment will occur over the next 2.5 years and each patient will be 'on drug' and monitored for 48 weeks. We anticipate that the last patients will complete the trial in December 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 referral networks of the site investigators. The investigators are discussing the trial and where possible presenting to their colleagues within their hospitals and other local hospitals (such as eye hospitals 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 and were sent out through the Australian New Zealand Association of Neurologists mailing list.

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

While at this stage the trial is not being actively promoted to individuals with MS, those who have been newly diagnosed with a 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. This is a relatively wide window to facilitate recruitment. Details of the trial, with information on eligibility and site contact details can be found at www.mstrials.org.au/PrevANZ-Trial

The second quarterly newsletter has been 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.