



The TiNT Trial

Trametinib in paediatric, adolescent and young adult patients with Neurofibromatosis Type 1 associated plexiform neurofibromas or progressive optic pathway gliomas

2022

MAY UPDATE



Background

Neurofibromatosis type 1 (NF1) is a common genetic condition, affecting 1 in 3000 Australians, which can cause a number of medical issues ranging in severity. Some children and young adults with NF1 develop tumours, called low grade optic pathway gliomas (OPG) or plexiform neurofibromas (PN).

Although survival is high, many patients with OPG or PN suffer from visual loss, pain, disfigurement and brain impairments. These life-long and highly debilitating effects suffered by NF1 patients motivated Australian and New Zealand researchers to develop the TiNT study. The trial will evaluate the use of trametinib, a MEK inhibitor that reduces tumour growth in adults diagnosed with melanoma, and has shown promising results in preliminary studies with neurofibromatosis tumours.

The TiNT trial is the first trial in the world to comprehensively examine if treatment with trametinib can reduce tumour growth in children and adolescents experiencing NF-associated tumours. Other Quality of Life (QoL) aspects will also be measured, including pain, vision and memory. Additional data will be gathered on safety, event-free and overall survival.

The TiNT trial will be available at every children's cancer centre throughout Australia and New Zealand. ANZCHOG is the national sponsor for TiNT at all participating sites, with ANZCHOG's National Trials Centre providing central coordination and oversight for the trial. The Murdoch Children's Research Institute (MCRI) will lead the neuro-psychology and statistical elements of the trial.

Associate Professor Geoffrey McCowage and Dr Andrew Dodgshun jointly lead the TiNT trial. A/Prof McCowage is an experienced oncologist at the Children's Hospital at Westmead and Dr Dodgshun is a paediatric cancer specialist at Christchurch Hospital, New Zealand. Associate Professor Johnathan Payne is the lead neuropsychologist for the neurocognitive and quality of life (QoL) components of the trial.

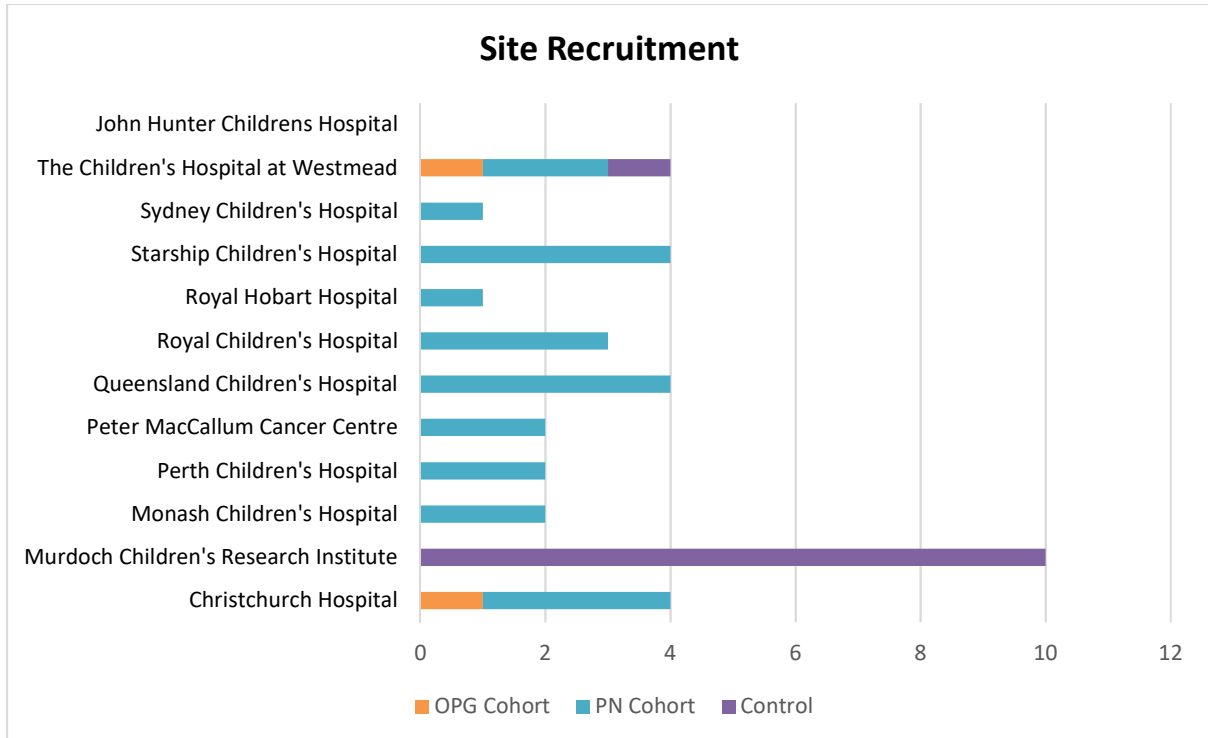


Trial Update

TINT is recruiting at twelve centres across Australia and New Zealand with the final site to open in the coming months.

We are aiming to recruit 120 participants in total, with 60 patients to receive trametinib in two treatment arms equally distributed between PN and OPG participants, and 60 control participants. Thus far:

- **24 participants with PN have been enrolled and are receiving trametinib**
- **2 participants with OPG have been enrolled and are receiving trametinib**
- **11 participants have been enrolled on the control arm.**





The last 12 months (May 2021 – May 2022) has been focused on the **Recruitment and Treatment** phase of the trial.



Essential activities undertaken during this period were:

- ✓ **Additional sites have been activated** at Murdoch Children's Research Institute, Royal Hobart Hospital, John Hunter Children's Hospital and Peter MacCallum Cancer Centre
- ✓ **Peter MacCallum Cancer Centre (PMCC)** is unique in that it is a satellite site to Royal Children's Hospital. Recruitment at PMCC enables the study to capture Adolescent and Young Adult (AYA) participants up to 25 years of age. Allowing these participants to be treated in a facility that is suited to their age and not in a paediatric setting. Recruitment has been good since site activation in early 2022.
- ✓ **Yearly Anticipated Recruitment** has been met for the PN cohort however slower recruitment of the OPG cohort.
- ✓ **Control patients** are slightly below expected recruitment target for this trial. Control patients must be age-matched so recruitment of these patients will follow recruitment to the treatment arms. COVID pandemic health directives have caused some issues with patients being able to attend sites for appointments/assessments which has had an impact on recruiting control patients.
- ✓ **Remote monitoring** has occurred for all sites with enrolled patients. Due to the impacts of COVID-19 an extensive remote monitoring plan has been implemented.
- ✓ **End of treatment remote monitoring** has occurred for 2 participants who met the parameters to come off protocol therapy early. Reasons include disease progression and ongoing toxicity.
- ✓ **Quarterly Data Review** has been undertaken and reported.
- ✓ **Central safety and Quality tasks** have been completed and reported.
- ✓ **Data Safety Board Meetings** have taken place.



The TiNT Trial is open at:

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Sites Activated

Queensland Children's Hospital

Brisbane, QLD

Royal Children's Hospital

Melbourne, VIC

Monash Children's Hospital

Clayton, VIC

Perth Children's Hospital

Perth, WA

Starship Hospital

Auckland, NZ

**The Children's Hospital at
Westmead**

Westmead, NSW

Royal Hobart Hospital

Hobart, TAS

Christchurch Hospital

Christchurch, NZ

Sydney Children's Hospital

Randwick, NSW

John Hunter Children's Hospital

Newcastle, NSW

**Murdoch Children's
Research Institute**

Melbourne, VIC

**Peter MacCallum Cancer
Centre**

Melbourne, VIC

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Sites Pending Activation

Women's and Children's Hospital

Adelaide, SA

Acknowledgements

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