ANZCHOG
Australian & New Zealand Childrens Haematology/Oncology Group

TRIAL UPDATE: A Pilot Study of Nivolumab in Paediatric Patients with Hypermutant Cancers

The international trial "A Pilot Study of Nivolumab in Paediatric Patients with Hypermutant Cancers" (the Hypermutant Cancers Study) has closed to recruitment, with preliminary results indicating a potential benefit of immune checkpoint inhibitors not previously detected in clinical trials with paediatric patients diagnosed with solid tumours.

The National Principal Investigator, Professor David Ziegler, highlighted the importance of these findings. "Immune checkpoint inhibitors have produced extraordinary results in a range of highly aggressive adult cancers, however, prior to this trial, they have been ineffective for childhood cancers. This has been disappointing, as it was hoped that these inhibitors would provide a new treatment option for children, particularly for tumours where we have struggled to improve survival rates."

Results from the adult clinical trials demonstrated that cancers that respond well to immune checkpoint inhibitors are "hypermutant" – they have a high number of tumour mutations. Collectively, cancers that occur in childhood have a low mutational burden, which may explain the disappointing results in previous trials. Based on this information, the Hypermutant Cancers Study specifically targeted patients who had an increased tumour mutation burden and/or replication repair deficiency to receive the immune checkpoint inhibitor, nivolumab.

The trial was developed by colleagues at the Hospital for Sick Children (Toronto, Canada) and involved patients from Canada, USA, Europe, Middle East and Australia. Three sites in Australia opened the study, however, due to small patient numbers, only two patients were enrolled. A total of 11 patients were enrolled worldwide during the recruitment period of three and a half years, with a range of tumour types (5 glioblastoma (GBM), 2 anaplastic astrocytoma (AA), 2 neuroblastoma, 1 colorectal adenocarcinoma (CRC) and 1 adrenocortical carcinoma).

Preliminary results from the pilot study were presented at the 2021 American Society Clinical Oncology (ASCO) Annual Meeting and showed evidence of impressive clinical benefit particularly for relapsed GBM/AA patients for whom median survival is otherwise only about 6 months.

"These results are very exciting, and we will continue to monitor these patients to analyse the longer-term impact of nivolumab treatment," said Professor Ziegler. "As a pilot study, this trial has provided an opportunity for Australian children to access an innovative investigational agent as a part of an international trial. It has provided valuable information about the role of checkpoint inhibition and will guide the development of future clinical trials. It has also built on our collaboration with our Canadian colleagues in Toronto, and we are working with them to undertake an umbrella trial, OPTIMISE (Optimal Precision Therapies to CustoMISE Care in Childhood and Adolescent Cancer), which will test multiple, novel targeted combination therapies for children with a range of low survival cancers.

We would like to thank the following organisations for partnering with ANZCHOG to enable access to this trial for Australian children:

- Bristol-Myers Squibb
- Cure Brain Cancer Foundation
- Australian Brain Cancer Mission
- Cancer Institute NSW

Relevant links:

- https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.15_suppl.10011
- https://clinicaltrials.gov/ct2/show/NCT02992964?term=nivolumab+hypermutant&draw=2&rank=1

ANZCHOG is a non-profit organisation committed to ensuring Australian and New Zealand children receive world-class cancer care. We are the peak professional body for paediatric oncologists and health professionals who care for children with cancer, spearheading national initiatives to enhance clinical care through communication, research, networking and education. We are also the national cooperative clinical trials group for childhood cancer, actively working with trial consortia around the globe to ensure Australian and New Zealand children have the opportunity to access the latest promising cancer treatments.

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