

CCLG: The Children & Young People's Cancer Association research: Investigating clinical trial samples to predict how atypical teratoid rhabdoid tumours will respond to treatment

Project title: Molecular Biological Profiling for the SIOP-ATRT-01 Trial

Project stage: Ongoing (started March 2023, planned end February 2026)

Funded by: CCLG and CCLG Special Named Funds including Joel Prince Starlight Fund and Our Buoy Hugo's Fund

Led by: Dr Daniel Williamson, Newcastle University



About the project

Atypical teratoid rhabdoid tumours (ATRT) are a rare but aggressive type of childhood cancer that starts in the brain or spinal cord. Patients are usually very young and current treatments are often ineffective or have a high risk of damaging long-term effects. For many other childhood cancers, biological profiling is used to find out which patients are likely to respond well to treatment and those who won't. In this way, doctors can avoid using too strong treatments that have lots of side-effects on patients that are low-risk, and find which patients need different and newer treatments. Biological profiling has not yet been used for children with ATRT, in part because of the rarity of the disease and the lack of clinical trials.

Dr Daniel Williamson's lab team at Newcastle University, along with others, have shown that there might be a link between a tumour's genetics and its response to therapy by analysing samples from ATRT patients. Using state-of-the-art genetic testing that looks at tens of thousands of genes and their expression, the researchers found at least three subtypes of ATRT which appear to affect patient survival.

Using the genetic testing results, the team could then use artificial intelligence techniques to find biological patterns which, when a child is diagnosed, could predict how likely they are to respond to treatment. Whilst these techniques are promising, researchers have not been able to gather enough evidence and data yet because of the rarity of ATRT.

Alongside the new international SIOP-ATRT-01 clinical trial, Dr Williamson will use the state-of-the-art genetic testing to analyse the UK patients' samples. This will create a valuable set of data that includes differences in tumours' molecular biology and how the patients responded to standardised treatments. Teams in other countries will also be using the same techniques to create datasets, which will be pooled at the end of the trial. Dr Williamson hopes that the internationally pooled data will help show whether biology predicts response to therapy, and therefore can be used to direct future treatments for patients with ATRT.

Progress

From their analysis of over 50 ATRT samples so far, the team have created a tool that can produce a 'risk score' based on the molecular features of the tumour (such as genetics and protein levels). This score could, in the future, guide treatment decisions. The tool has shown that around a quarter of patients show signs of responding particularly well to treatment. If the tool can be translated into clinical practice, it could allow these children to have gentler treatments – and show which patients should be prioritised for newer, more targeted treatments. This tool, and all of the data the team have gathered so far, have been made freely available to other researchers to help speed up improvements for patients.

What's next?

Over the next year, the researchers will continue to analyse ATRT patient samples. They're working with partners across Europe to make sure that every child enrolled in the SIOP-ATRT-01 clinical trial has access to their molecular testing. They are also developing more user-friendly versions of the tools that can make it easier for doctors and researchers to understand a patient's cancer.

Dr Williamson has applied for a number of project grants to continue their work on clinical trial samples after this project ends. This could help validate their tools, and gather more valuable ATRT insights.



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