ICR The Institute of Cancer Research

Blood testing to improve treatment for children with cancer

Progress report for Abbie's Fund
Written in conjunction with Professor Louis Chesler

April 2019

We would like to express our gratitude to Abbie's Fund for your continued and generous support of our research. We are delighted to provide you with an update on some key advances we have made against the project's on-going objectives. We hope you are proud of the progress you have helped to make possible.

We are striving to get precision medicine to children with cancer. Precision therapies specifically target changes in a patient's DNA. By being targeted, toxic side effects can be reduced. This is vital for such young patients. Key to this is a program of rapid genetic sequencing for every UK child with a solid tumour. Excitingly, our work in this area is now moving forward in conjunction with the NHS.

Crucially, by building knowledge of the genetic variants associated with childhood tumours, we can also identify promising drugs already in clinical use.

Clinicians are now able to personalise treatment plans to maximise potential for cure and minimise adverse long-term toxic side-effects from the treatments. In order to continually make treatments more effective and accurate we are utilising feedback from clinical trials and using expert databases.

Professor Louis Chesler's current neuroblastomma research funded by Abbie's Fund is based on the use of tissue and blood samples collected from patients with newly diagnosed and relapsed solid tumours, and also from patients on active treatment with precision medicines.

Dr Louis Chesler

Increasingly, technology to test blood, rather than tumour tissue is becoming available. A simple blood test will offer a quicker, cheaper, less painful way to

analyse a child's tumour than taking biopsies or bone marrow samples. We are pleased to say that for the first time, in 2018, our initial blood-based testing was incorporated into clinical trials. The support of Abbie's Fund has been invaluable in making this progress possible.

Please find below some key points of progress made by Professor Louis Chesler, his team and colleagues, over the past year:

- Tumour and blood samples from newly diagnosed or relapsed patients at The Royal Marsden Hospital (RMH) are now being routinely sequenced – initially through our original single-site METEOR study and now through our national Stratified Medicine Paediatrics (SMPaeds) study. When we last updated you the number of patients analysed was 100 – it now stands at approximately 300. We have built a large-scale collaboration with Great Ormond Street Hospital (GOSH) to collect and sequence tumour tissue and blood serially from all of their solid tumour patients.

- Our panel-based testing was evaluated by NICR and is commissioned by NHS. More details can be found here:

  https://www.nice.org.uk/advice/mib133/resources/nextgeneration-sequencing-panel-for-solid-tumour-cancers-in-children-pdf-2285963394018757

- We are continuing our successful national molecular tumour board, having set up the first in this country. In these weekly conferences results of our sequencing activity are reported to physicians based at the Royal Marsden and GOSH, Oxford and Cambridge. Based on these conferences, clinical decisions are rendered for further care where other options are exhausted. We have now used this approach to treat several patients at RMH and GOSH, and increasingly at other national centres. This tumour board will began to issue formal clinical reports nationally as part of SMPaeds in February 2019, when the study formally opened. This study for the first time begun clinical testing of blood from patients with all relapsed solid tumours in February 2019, in a major achievement for us.

- We have again secured significant support from Children with Cancer UK and Cancer Research UK, to expand the blood-based analysis that you kick-started. Through this we will continue to be a core-funded genomics specialty hub for paediatric cancer, dedicated to development of further blood-based sequencing techniques through to 2020.

- As mentioned above, our formal testing of blood samples nationally began in February 2019. This will initially use a panel-based approach in the research setting, and then will extend to include formal clinical reporting of molecular-genetic changes in blood in mid-late-2019. If this data is robust we will commission this test through NICR for use in the NHS.

- Lastly, we were awarded a Wellcome-ICR PhD for a super student (Reda Stankaite), who is focusing completely on blood-based testing across all of these projects, together with Mike Hubank in the genome core, and Andrea Sottoriva, in our clonal evolution Centre.

We have now reached our implementation phase after more than 5 years of development work. We are now routinely implementing these tests in all NHS patients with relapsed solid tumours. We anticipate commissioning of blood-based testing later in the year and into 2020, a major achievement for us in a relatively short time.

We hope to now develop the data quite rapidly on what mutations occur in the blood and at what level, and aim to test whether a positive test in blood has sufficient clinical power to alter treatment decisions. We will also begin to see whether treatment with targeted precision medicines is constrained by development of resistance (to ALK inhibitors in neuroblastoma) and whether we can use the levels of ALK DNA in the blood of patients on treatment to predict their clinical response and/or remission.

We remain extremely grateful for the ongoing support from Abbie's Fund. Your funding has continued to allow Lou, together with Dr Jennifer Tall, Dr Sally George and Elisa Izquierdo Delgado to develop the blood and genomic tests described above. We hope you are proud that changes to clinical practice are resulting from your generous support.

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