Key learnings from Rare Disease Project ECHO®

Series 3: Session 3 (7 November 2024) – Innovative clinical trials access models

Opening presentation

This session was presented by Professor David Coman, a clinical geneticist, metabolic physician and consultant paediatrician. The presentation was about innovative approaches to clinical trials in rare disease.

Rare disease presentation

Ataxia Telangiectasia (A-T) is a rare progressive, degenerative disease with complex symptoms similar to cerebral palsy and cystic fibrosis, with an increased risk of developing cancer. Children are born asymptomatic but develop progressive motor symptoms from the age of 2-3 years, with normal intellect.

Prof Coman and his team recently conducted a randomised Phase 2a/b clinical trial aimed at improving mitochondrial dysfunction in people with A-T using a re-purposed disease modifying treatment. Trial endpoints were developed in collaboration with families to ensure outcomes were meaningful for families, and included laboratory assessments, ataxia ratings, MRI imaging, lung function testing, and speech and language assessments.

Assessments were conducted every 2 months in Brisbane; this schedule was determined in consultation with families, recognising the often-complex logistical challenges associated with travelling to Brisbane and the physical impact of the travel and testing on individuals with A-T.

Prof Coman emphasised the importance of partnerships with various stakeholders including the local health service, hospital, pharmaceutical companies, and, importantly, individuals and families with A-T, to facilitate effective collaboration, gain valuable input into trial design, and ensure expectations of trial outcomes are managed.

The trial enrolled 16 children and 15 adults across Australia and was run during the Covid-19 pandemic, which made conducting the trial challenging. The trial was very successful, with significant improvements in a range of endpoints, including ataxia scores and nasal cell markers. The most significant improvements were in speech and language, important outcomes for individuals and their families.

Due to complex factors, access to the trial treatment was stopped after 12 months, after which clinicians and families negotiated with the supplier for further treatment. An open-label extension arm eventually started for a further 12 months. Although most clinical gains had been lost during the period without treatment, some benefits are now being observed.

Discussion with the community of clinical learning practice

The group discussion covered:

- The benefit of mature data and tight clinical trial design when applying for MRFF funding for trials, and effective lobbying with local members of parliament to raise awareness and gain support.
- The importance of natural history data in acting as an untreated control.
- The value of providing patients and their families with resources to help them understand their diagnosis, and to offer a follow-up appointment to allow further discussion.
- Funding is challenging to obtain, and pharmaceutical and biotech companies often need to see a return on investment. The MRFF helped to fund a number of investigator-initiated trials that would otherwise not have been run.
- A lack of clinical trial infrastructure is a stumbling block for trials being conducted outside of the major capital cities.
- The importance of equity and being person-centred when conducting clinical trials, flexibility when individuals are unable to attend scheduled visits and listening to families' needs.
- Health professionals can reach out to the RARE Helpline for guidance.

Key recommendations that Project ECHO® participants and experts shared relating to conducting clinical trials in rare disease were:

- The importance of being patient centred, and designing and conducting clinical trials in collaboration with individuals and families
- Partnerships with other health organisations are also critical
- The importance of designing clinical trial endpoints in consultation with patients and families to ensure the outcomes captured are meaningful to people with the rare condition

Useful resources for clinicians and patients discussed this session were:

- RARE Portal
- Rare Disease 101 Australia
- National Recommendations for Rare Disease Health Care
- Australian Clinical Trials
- ClinicalTrials.org (US and global clinical trials)
- Advanced Therapies Handbook
- Mental health and wellbeing support for Australians living with a rare disease
- RARE Helpline