#157 - Designing a hybrid type III effectiveness-implementation, multi-model trial in Precision Oncology

Presenting Author:
Kim An[1]

Affiliation
1. Parkville Familial Cancer Centre, Peter \MacCallum Cancer Centre, Australia

Country of residence
Australia

Objectives/aims
Precision oncology aims to match the right treatment to the right person, based on a genetic or molecular understanding of their cancer. With the rapid emergence of effective molecularly targeted therapies, there is heightened interest in available tests that detect actionable variants in a patient's cancer and help identify individualised treatment options. Complex genomic profiling (CGP) has such potential. It can identify hundreds of variants across many cancers using circulating tumour DNA (ctDNA) from the bloodstream. However, access to this test is currently inequitable in Victoria, Australia and assistance in interpreting results is not standardised and not specific to a patient's context.

As genomic profiling becomes more clinically significant in cancer care, it is important to assess how it can best be delivered to Victorians with cancer, regardless of their location or the health service they are using. To help inform the current study, somatic tumour-based profiling was offered to patients at metropolitan oncology services in Victoria to explore the experiences of oncologists involved. This evidence-based research and theoretical frameworks guided the development of three models of care. The implementation of these models will be evaluated in this trial but ctDNA, instead of traditionally used archival tumour tissue, will be utilised for CGP as a non-invasive alternative that can be provided by smaller clinical sites, supporting wider-spread implementation.

This lends itself to an effectiveness-implementation hybrid type III design that takes a dual focus a priori in assessing the clinical effectiveness of an intervention and,

concurrently, the implementation. The primary aim is to evaluate the implementation of CGP for patients with advanced cancer within three models of care in regional and metropolitan oncology services in Victoria. Secondarily, the utility of ctDNA to detect actionable variants and treatment changes, relative to standard of care testing, will be monitored. We intend to present the design of this hybrid type III trial and how outcomes will be measured.

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Methods

The hybrid type III design uses an exploratory, sequential mixed methods approach and prioritises the implementation focus, with effectiveness as the secondary aim.

The evaluation of implementing the models of care is underpinned by the Consolidated Framework of Implementation Research (CFIR), Theoretical Domains Framework (TDF) and Proctor's Implementation Outcomes Framework to examine the barriers, enablers, acceptability, feasibility and sustainability of deploying CGP. Data will be collected from the perspectives of patients, healthcare professionals and the implementation process outcomes involved - via surveys and interviews - at key timepoints throughout the clinical pathways of care. The cost of implementing these novel pathways will also be quantified.

The effectiveness of CGP using ctDNA – compared to standard of care testing – will be assessed using clinical data for each patient to identify the proportion where a clinically actionable somatic variant is detected and the proportion for whom this somatic information changes their treatment.

Main findings

Patients with advanced cancer will be offered ctDNA CGP via one of three models of care in this hybrid type III trial. Each model will be implemented in one regional and one metropolitan oncology setting in Victoria and will include private and public hospital sites. Process maps have been developed to visualise the intervention's clinical processes and evaluation timepoints. These maps highlight the key differences between the models and specifies when and how data will be collected to assess implementation and effectiveness.