# OPTIMISE: Optimal Precision Therapies to Customise Care in Childhood and Adolescent Cancer

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## Goal

- OPTIMISE is a precision oncology platform study designed to leverage findings from ZERO and PROFYLE national sequencing initiatives to provide treatment options for patients with relapsed/refractory solid tumours and brain tumours

## Objectives

**Primary aims**

1. To use molecular sequencing to allocate children, adolescent and young adult (CAYA) patients with advanced solid tumours to specific treatment arms of molecularly-targeted agents;
2. To determine the recommended phase II dose of a novel single agent or combination in the CAYA patient population;
3. To determine the objective response rates (ORR; complete and partial response) in CAYA patients with advanced solid tumours with defined specific genomic alterations treated with molecularly-targeted agents.

**Secondary aims**

1. To estimate the overall clinical benefit rate (CBR; complete and partial response and stable disease) in CAYA patients with advanced solid tumours with defined specific genomic alterations treated with molecularly-targeted agents;
2. To estimate the progression free survival (PFS) in this CAYA patient population receiving molecularly-targeted agents;
3. To obtain information about the tolerability and safety of molecularly-targeted agents and/or novel combinations;
4. To obtain estimates of pharmacokinetics of molecularly-targeted agents and/or novel combinations in this CAYA patient population.

**Exploratory aims**

1. To explore correlation between symptoms reported by patients and/or caregivers and AEs reported by clinicians.
2. To assess the impact of study participation on symptoms reported by patients and/or their caregivers.
3. To explore engagement in self-reporting of symptoms by patients and/or caregivers

## Study method

- Multi-arm platform study open across Australia and Canada
- ANZCHOG is international sponsor with C17 Council regulatory coordinator for Canada
- Patient's must be pre-enrolled on ZERO, PROFYLE or equivalent comprehensive sequencing program
- Study arm-specific eligibility criteria apply

## Results

- Study is ongoing, no results currently publicly available

## Impact/outcomes

- Study activated in both Australia and Canada
- Hospital for Sick Children, CHU Ste Justine and BC Children's Hospital open for Arm A
- CHEO and Stollery in process of opening
- Planning to activate IWK for Arm A via CRAFT decentralised model
- Arm C activated in Australia, awaiting activation at SickKids and then other sites

## Project timelines

- Initial Australian Medical Research Future Fund Grant 2021
- Grants from Cancer Research Society and CIHR for Canada in 2022
- Initial regulatory approval from Health Canada September 2024
- Study is ongoing

## The challenge

TERRY FOX PROFYLE
PRECISION ONCOLOGY FOR YOUNG PEOPLE

**PROFYLE**
Comprehensive access to cancer sequencing across Canada for CAYA patients

- No 'built in' access to targeted therapeutic interventions
- Lack of available clinical trials
- Lack of access to clinical trials/targeted agents

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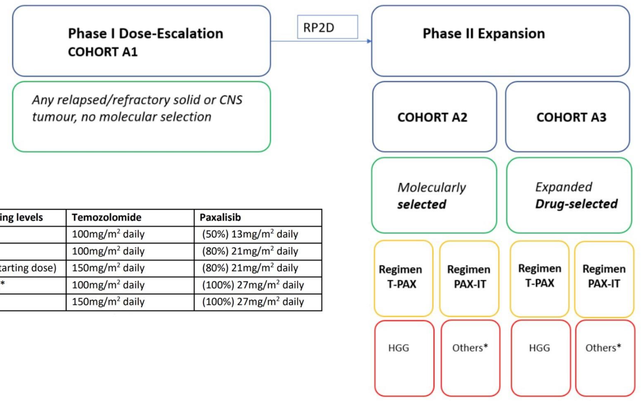
## Arm A: paxalisib plus chemotherapy

Paxalisib is a CNS-penetrant PI3K/mTOR inhibitor
Combination with temozolomide ± irinotecan

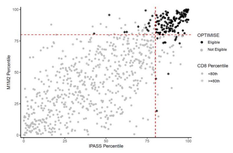



| Dosing levels | Temozolomide | Paxalisib |
|---|---|---|
| -2 | 100mg/m$^2$ daily | (50%) 13mg/m$^2$ daily |
| -1 | 100mg/m$^2$ daily | (80%) 21mg/m$^2$ daily |
| 0 (starting dose) | 150mg/m$^2$ daily | (80%) 21mg/m$^2$ daily |
| (1a)* | 100mg/m$^2$ daily | (100%) 27mg/m$^2$ daily |
| 1 | 150mg/m$^2$ daily | (100%) 27mg/m$^2$ daily |

## Arm C: nivolumab + relatlimab (Opduolag)

Combined PD1 and LAG3 inhibition

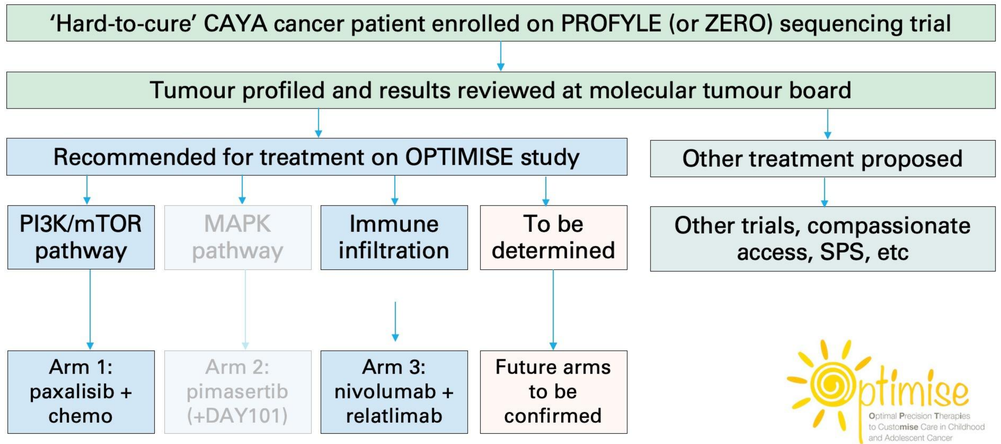
Cohort C1 Immune infiltrated
≥80$^{th}$ centile for 2 of 3 scores:
- CD8 T-cell
- M1/M2 macrophage
- iPASS




Cohort C2 RRD deficient
failed to respond or relapsed after anti-PD(L)1

- Combined PD1/LAG3 inhibition (Opduolag)
- Enrolment limited to patients able to receive fixed adult dose
- Patient selection based on immune infiltration determined by RNAseq
- Pre-screening through existing national sequencing programs in Canada and Australia (PROFYLE/ZERO)
- Pilot study for initial signal of efficacy (12 patients)
- Additionally allow enrolment of patients with RRD tumours previously treated with anti-PD1 monotherapy (≤12 patients)

## Overall study schema

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