There is a need to identify which patients will respond to targeted agents, according to their molecular profile. Establishing a mechanism to offer personalised treatment is rational. The number and range of molecular aberrations current gold standard for tumour characterisation is on archival or fresh tumour biopsy. Circulating tumour DNA (ctDNA) provides a contemporaneous and minimally invasive liquid surrogate. The ctDNA may better capture tumour heterogeneity, providing a more complete profile than a single biopsy.

Stratification to early phase trials of targeted therapy is a rational approach to drug development. The Tumour chAracterisation to Guide Experimental Targeted Therapy Trial (TARGET) will test the hypothesis that ctDNA molecular profiling helps to select experimental medicine and monitor response.

**Background:**
- There is a need to identify which patients will respond to targeted agents, according to their molecular profile, to inform treatment selection and thereby improve patient outcomes.
- Stratification to early phase trials of targeted therapy is a rational approach to drug development.
- Currently, the gold standard for tumour characterisation is on archival or fresh tumour biopsy.
- Circulating tumour DNA (ctDNA) provides a contemporaneous and minimally invasive liquid surrogate.
- ctDNA may better capture tumour heterogeneity, providing a more complete profile than a single biopsy.
- The Tumour chAracterisation to Guide Experimental Targeted Therapy Trial (TARGET) will test the hypothesis that ctDNA molecular profiling helps to select experimental medicine and monitor response.

**Methods:**
- Blood Sample
- ctDNA and germline DNA
- Targeted Next Generation Sequencing (NGS)
- Molecular Tumour Board
- Stratification to an appropriate Phase I trial of a relevant targeted therapy matched to an actionable molecular alteration

**STUDY PLAN**

<table>
<thead>
<tr>
<th>PART A1</th>
<th>PART A2</th>
<th>PART B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process feasibility 20 patients</td>
<td>Decision making feasibility 80 patients</td>
<td>Profiling based trial selection 250 patients</td>
</tr>
<tr>
<td>- Result in 28 days</td>
<td>- Eligible for Phase I trials</td>
<td>- Eligible for Phase I trials</td>
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<tr>
<td>- Establish clinical reporting</td>
<td>- Results in 14 days</td>
<td>- Targeted gene panel</td>
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<tr>
<td>- Establish MTB</td>
<td>- Functionalise MTB</td>
<td>- Results in 14 days</td>
</tr>
<tr>
<td>3-6 months</td>
<td>12-18 months</td>
<td>2-3 years</td>
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**Objectives:**
- Establish a mechanism to offer personalised medicine to patients with advanced solid cancer based on tumour molecular characteristics and/or blood borne biomarkers e.g. ctDNA.

**Outcomes:**
- Number and range of molecular aberrations detected in blood/tumour, number of patients successfully stratified to a trial, response rate, progression-free and overall survival rates, set-up of pre-clinical models to explore cancer biology.

**TRANSLATIONAL RESEARCH**
- Protocol allows for creation of a PDX model to better understand tumour biology and undertake avatar drug testing, if profiling reveals molecular aberrations of uncertain clinical significance or potential novel targets.
- Serial ctDNA analysis to monitor for tumour response and emerging resistance mechanisms.

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