DETERMINE: A pioneering UK precision medicine trial for rare cancers

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DETERMINE is a tumour-agnostic umbrella-basket platform trial evaluating genotype-matched targeted agents outside of their licensed indication in rare adult, teenage and young adult (TYA) & paediatric cancers with actionable genomic alterations

Background

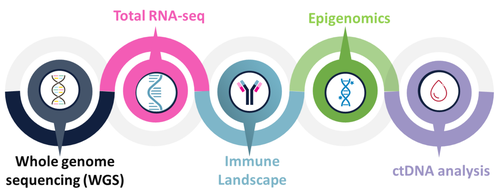
- **Precision medicine** (PM) is transforming outcomes in cancer. Through increased genomic profiling, actionable alterations are being identified in patients that could benefit from targeted therapies licensed in other indications.
- **Platform trials**, including NCI-MATCH[1], TAPUR[2] and DRUP[3] have shown feasibility and promising results of genotype-matched therapy.
- **Rare cancers** account for 22% of cancers overall[4], have limited treatment options and are underrepresented in clinical trials. It remains uncertain whether rare cancer patients with genomic variants known to be responsive to targeted therapy in other settings could benefit.
- **Translational research** is needed to better understand the tumour context on which the genomic driver is inscribed and relevance to response to therapy[5].

Inclusion Criteria

- Children and adults diagnosed with an advanced cancer, an actionable genomic alteration, and a good performance status. Additional treatment specific protocol inclusion and exclusion criteria apply.
- Co-primary outcome measures: objective response (OR) and durable clinical benefit (DCB) (≥24 weeks without disease progression).
- Secondary outcome measures: duration of response, progression-free survival, overall survival, adverse events, quality of life.

Translational Programme

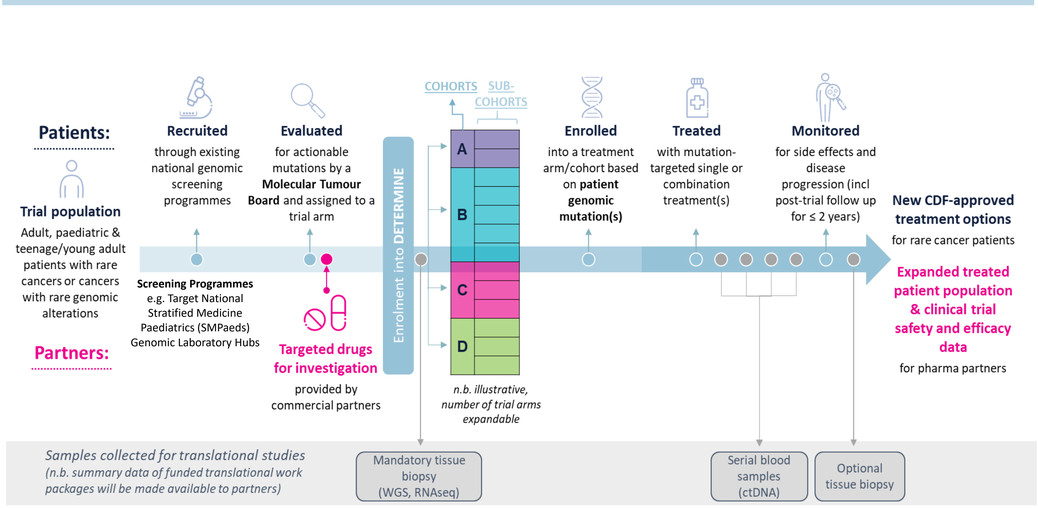
- DETERMINE will analyse the genomic, transcriptomic, immunomic and epigenomic characteristics of different cancers driven by a specific genomic alteration, across different ages and sites of origin.
- **Aims:** To better understand the processes that drive cancer development and their affect on outcome to therapy, identify new targets, and determine if there are biomarkers that can predict how patients will respond.



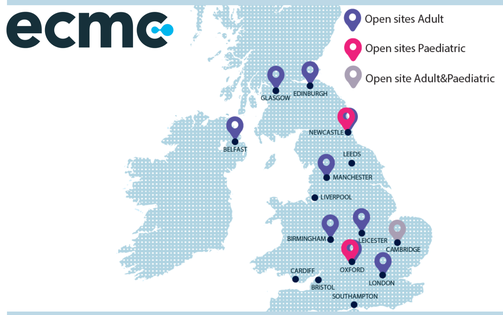
Main Study Objectives

- Assess the efficacy of licensed therapies in unlicensed indications to provide new treatment options for patients with rare cancers
- To gain new insights into the biology of rare cancers through a comprehensive translational research programme
- Transfer promising cohorts to the Cancer drugs Fund (CDF) for reimbursement

Trial Overview

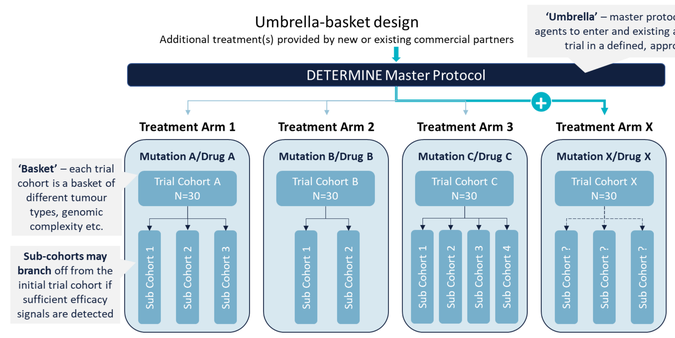


Recruitment Plan



Enrolment Opened: November 2022
Current Enrolment: 10 patients
Current Sites Opened: 12 sites
Number Of Patients Planned: 300-400
Number Of Sites Planned: 20 (Across the Adult and Paediatric Experimental Cancer Medicine Centre network)
Study Duration: 5 years

Statistical design



- Bayesian optimal phase II (BOP2) design based on true OR and DCB rates of > 30% and <10%, respectively, representing clinically relevant activity or not.
- Each treatment arm targets recruitment of 30 evaluable patients with interim analyses at N=10 and then every 5 patients thereafter.
- Decisions regarding expansion or termination of molecular sub-cohorts are based on a Bayesian analysis that generates the predicted probability of success.
- Bayesian approach allows cumulative learning about the drugs activity across multiple sub-cohorts and enhances signal detection in small patient numbers.

Key collaborations

PRIME-ROSE www.prime-rose.eu
DETERMINE joined the PRIMEROSE consortium with 24 other partners across Europe.
- Developing a platform to pool data and increase evidence generation of successful drug cohorts.

NHS England/Cancer Drugs Fund
- Promising cohorts will be submitted to the CDF, who together with the NHS Clinical Policy team, will decide whether a period of data collection is necessary to consider the drug as a routine treatment on the NHS.

Pharmaceutical partners
- Roche Products Ltd UK (Founding partner – funding for infrastructure and five treatment arms) and Novartis Pharmaceuticals UK Ltd (one treatment arm). New partners are being onboarded.

Foster Age Inclusivity Research (FAIR) for Adolescents and Young Adults (AYA) stamp
- Accolade that credits medical research which avoids unnecessary barriers based on age

Public and Patient Involvement

PPI has been embedded in DETERMINE from trial design through to delivery.

To date:
- PPI input from TYA group VoiceUp! for research questions and study rationale.
- Patient representatives involved in reviewing protocol, informed consent documents, website and animation videos.
- Four patient representatives on Trial Steering Committee and will be involved in reviewing and disseminating results.
- Patient experience questionnaires to gather feedback on trial experience.

DETERMINE video for children

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CONTACT INFORMATION

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