Welcome

ECMC network meeting 2023

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Jointly funded by:

CANCER RESEARCH UK

Little Princess Trust

NIHR | National Institute for Health and Care Research

Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales

CHIEF SCIENTIST OFFICE

HSC Public Health Agency Research and Development

ECMC: A network approach to clinical trial delivery

Sheona Scales

Head of ECMC Programme Office

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The ECMC network

1
pan-age network

4
nations of the UK

29
Experimental Cancer Medicine Centres

~1,000
trials opened*

9,500
patients recruited*

£150m
invested to date

* 2017-22

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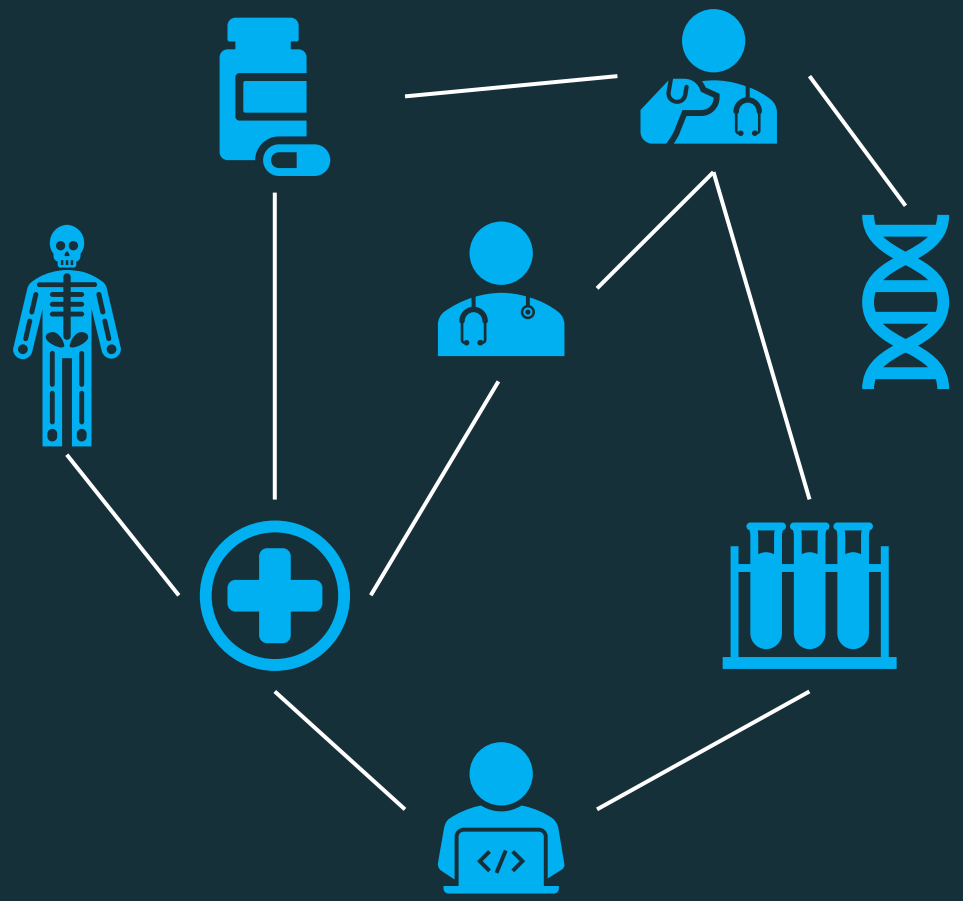
The ECMC Network:

- The ECMC award provides infrastructure support depending on areas of local need

- Most of the funding supports salaries of >200 staff associated with delivery:
  - Translational studies (incl. biomarkers)
  - Biobanking activity
  - Early phase trials



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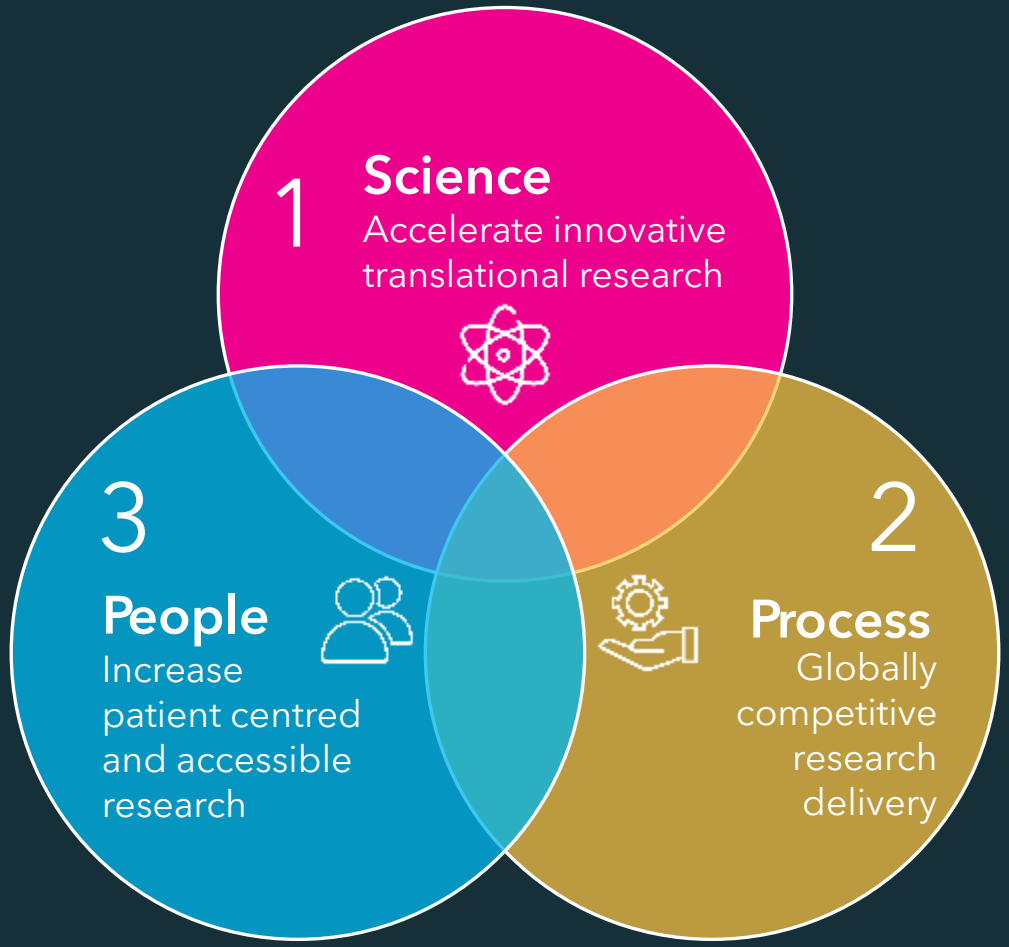
Our Vision

To build a truly collaborative, internationally competitive national network of early phase experimental cancer medicine centres, translating the most promising innovations from the academic and industry sectors into the cancer medicines of tomorrow



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Delivering the ECMC Strategy

The ECMC achieves impact by working in collaboration

Innovative Translational Research

Haematology Network

UKTCPN

Translational Research Forum

Competitive Operational Delivery

Centre Business Lead forum

Clinical trials coordinator group

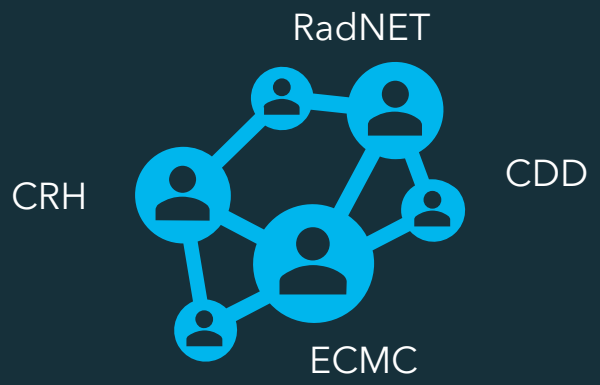
Patient Centred & Accessible Research

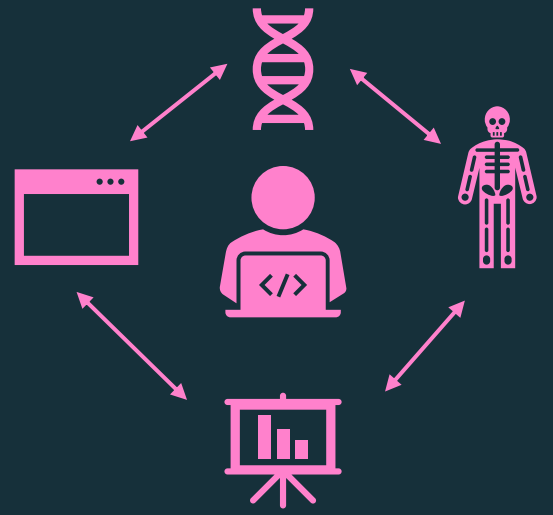
ECMC network PPI Group

Junior Investigator Network group

Research Nurse Network Group

We work collaboratively to improve the early phase trial landscape





Convene

Share best practice

Scale existing initiatives

Create new resources

Low risk & resource

High risk & resource

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Enhancing the regulatory environment:

1. Consensus paper on CID trials: Effective delivery of Complex Innovative Design (CID) cancer trials – A consensus statement
   - Author group included ABPI, MHRA, HRA, NICE, clinical investigators and patient groups

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Enhancing the regulatory environment: Impact

1. Consensus paper on CID trials: Effective delivery of Complex Innovative Design (CID) cancer trials – A consensus statement
   - Author group included ABPI, MHRA, HRA, NICE, clinical investigators and patient groups
   - Over 10k downloads

2. Podcast series: Effective trial planning and design of CID trials
   - Accessed over 1,800 times

3. Follow up paper: Additional consensus recommendations for conducting complex innovative trials of oncology agents: a post-pandemic perspective

4. ECMC resource paper: New regulatory routes for cancer treatment in Britain

Share best practice

ECMC Centre Business Leads Forum

The ECMC Centre Business Leads Forum discuss challenges on the management and delivery of research portfolios and create solutions to get early phase cancer trials set up and recruiting as soon as possible.

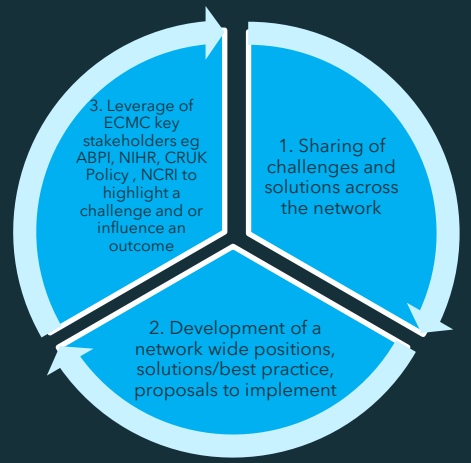
Knowledge Share

Identify Key challenges

Create Solutions

Collaboration space & resource hub

Sounding Board - 'Ask a colleague' at regular coffee catch ups



Action Framework

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Share best practice

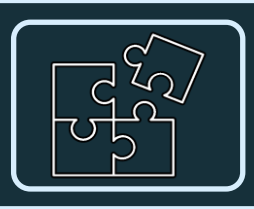
ECMC Centre Business Leads Forum: Impact

Remote Monitoring Guidance

Clinical Trial Restart Guidance

Clinical Trial Coordinator Network

ECMC Network-Level Feasibility Standard



ECMC Network Optimal Study Set up Process

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Scale existing initiatives

Enhancing engagement with industry

Business development strategy for network

- Improving interactions with industry to keep early phase studies in the UK
- Key account management
- Business model for engagement with Clinical Research Organisations

Streamlined network processes

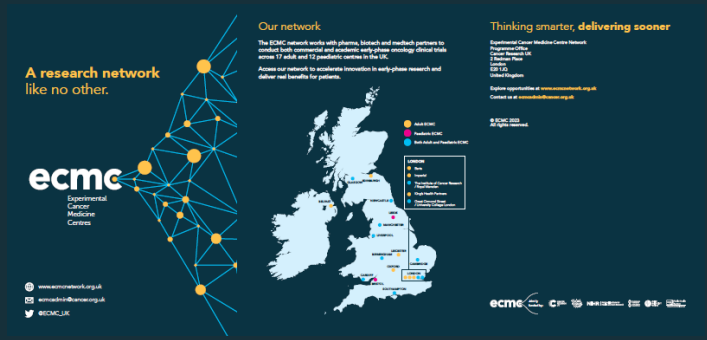
- Single entry point to the network via the Programme Office
- Suite of agreements that streamlined the process for sponsors to engage with the network
- Industry/academic collaboration framework

Specialised resources

- Suite of communications and marketing materials
- Network feasibility standard

Programme Office presence at key international conferences and events

- Engagement with key accounts and new business



Scale existing initiatives

Enhancing engagement with industry: Impact

2017	7 (7)	2020	80 (15)
2018	7 (7)	2021	90 (29)
2019	41 (37)	2022	81 (21)

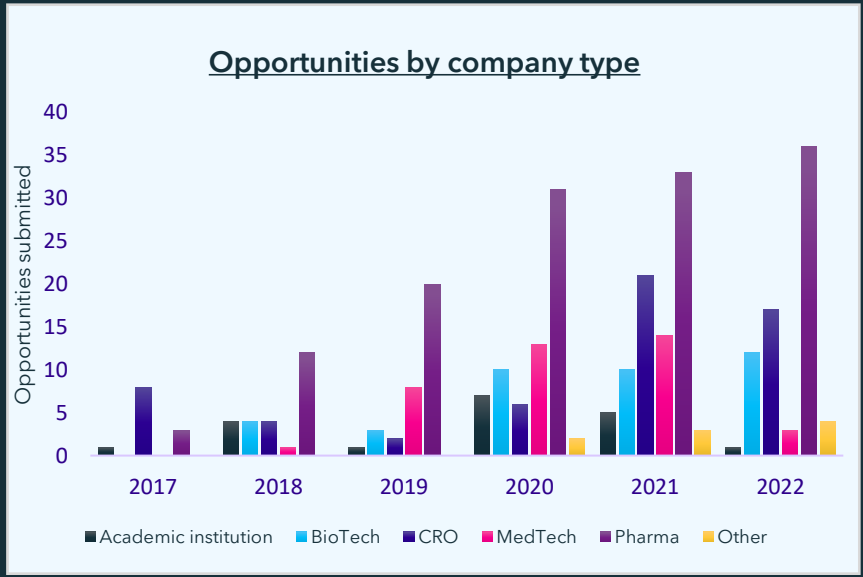
Companies interacted with (new)

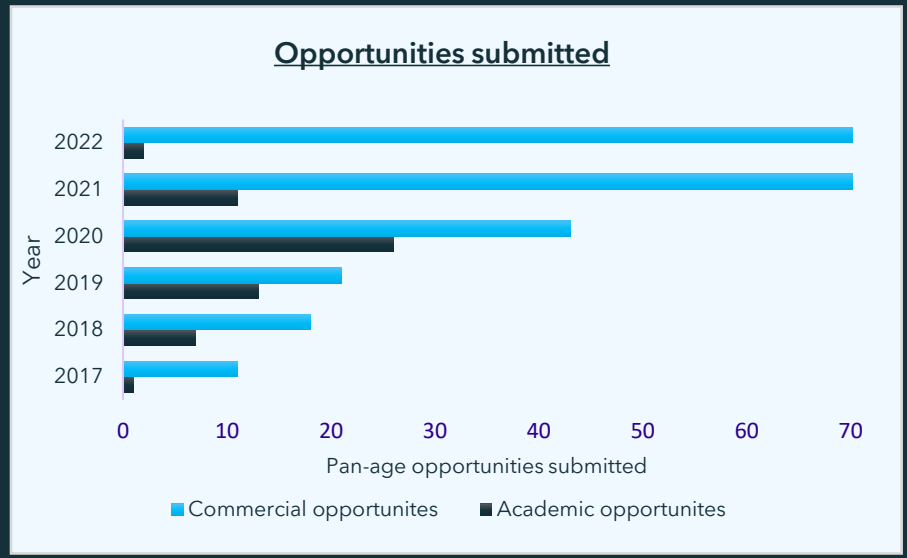
2022
2 Webinars
6 EOIs received

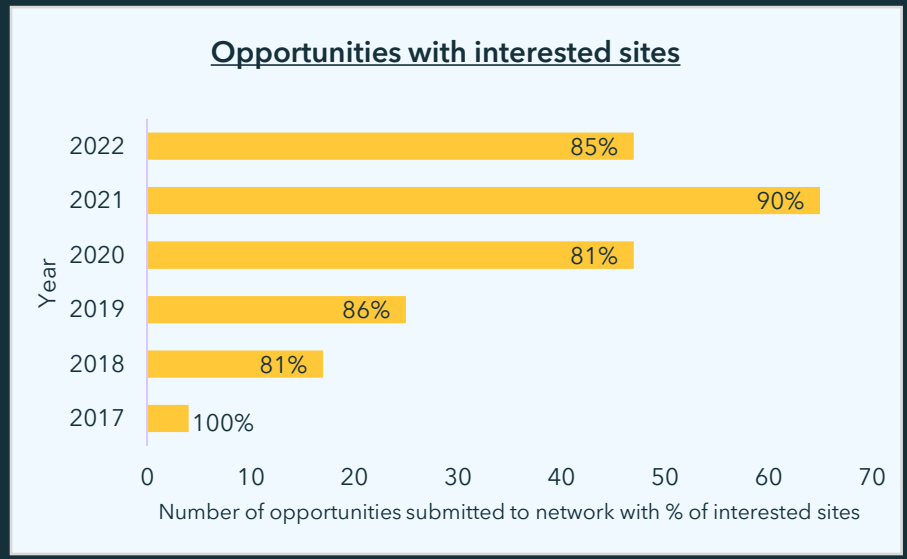
2021
1 Webinars
2 EOIs received

2020
1 Webinars
4 EOIs received

2019
1 Webinars
7 EOIs received







Create new resources

ECTrial Finder- Enabling patient access to experimental therapies

Accurate & up-to-date: monthly trial information updates are submitted directly by the local NHS Location EC Trial Finder coordinator, assuring that the database stays accurate and up-to-date.

Search and filtering functionality: custom designed allowing medical staff to more quickly identify suitable trials (i.e. location, age, markers, treatment type) without scrolling hundreds of options.

Contact details: includes the contact details of the recruiting site, enabling you to quickly contact the site to gather further information and determine whether your patients may be eligible and gauge slot availability.

Over **400 trials** listed in EC Trial Finder that are open to patients

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Create new resources

Experimental Cancer Trial Finder: Impact

Since its initial launch EC Trial Finder has significantly increased the speed, ease and feasibility of trial matching within the ECMC network.

ECTF prototype used in the network by over 200 users since 2019

Evaluation data from pilot:

55% increase in speed and ease of trial matching

77% of users said they had greater knowledge of clinical trials

71% of users had made or received a referral using the information found on ECTF

Phase Two:

- Improve data collection process
- Improve search functionality based on feedback from Phase I
- Create more value via partnerships

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What are we doing next?

- The fourth ECMC Quinquennium began in April 2023
- Within this funding period the network, together with the programme office, will implement the new ECMC strategy and new activity
- To do this we will continue to build our collaborative approach to improve the early phase clinical trial environment.
- Our key focus for the coming months are improving the study set up, improving our translational science approach and developing new approaches to patient referral.

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Convene

Improving the efficiency & set-up of trials

Working in partnership with the Health Research Authority and Clinical Research Recovery, Resilience & Growth board

Work with key clinical trial stakeholders to create transformative change

Create routes that will allow us to compete on set up times internationally

Sustainability and transferability of learnings beyond early phase cancer

Globally Competitive Research Delivery

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Lamise Nasr
Paediatric Network Manager

Caroline-May Huxley
Children and
Young People Manager

This team supports the Programme Office by:
Facilitating paediatric & young adult input into Network activity

Patient Access &
Workforce Lead

Digital Healthcare
Business Development
Manager

Hannah Brown
Project Manager
(workforce)

This team supports the Programme Office by:
Co-ordinating training and development of our workforce
Raising awareness of the Network through our website and external comms
Engaging with patients and embedding PPI in Network activities

Sharan Sandhu
Operations & Deliver Lead

Project Manager

Sheona Scales
Head of Programme
Office

Research Manager

Insights Manager

Amy Wiles
Project Officer

Neil Bhattacharjee
Project Officer

Eleanor Davies
Intern

Catherine Cowell
Translational Research
Lead

Mollie Stebbings
Data Analyst

This team supports the Programme Office by:
Engaging with industry to bring new trials and research collaborations
Shaping the future landscape by engaging with key stakeholders including regulators and developing Network strategy

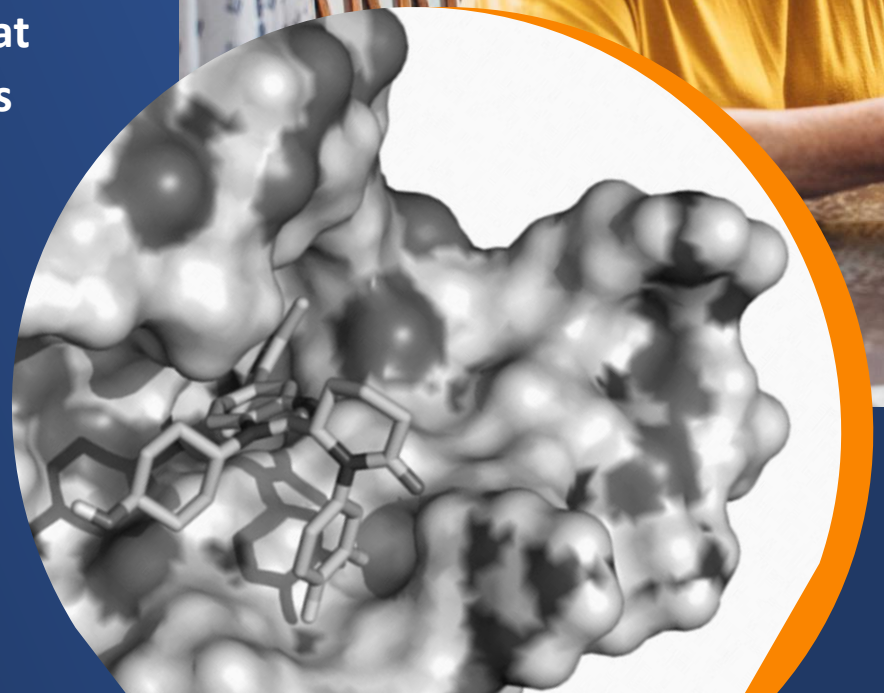
This team supports the Programme Office by:
Creating a innovative digital tool to support trial recruitment and access
Using data to power strategic thinking and collaboration

CellCentric

The p300/CBP inhibitor company

Inobrodib

First-in-class oral small molecule to treat specific cancers



ECMC Network Meeting 2023

24 May 2023

CellCentric and inobrodib (CCS1477)

Karen Clegg, Clinical Operations Director, CellCentric

CellCentric

- Karen Clegg, Clinical Operations Director
- >20 years experience (Parexel, Napp, AZ)
- CellCentric since 2017

- UK based biotechnology company
- Offices in: Cambridge, Manchester and Oxford
- 21 employees

Head office

Cambridge
CellCentric
Chesterford Research Park
Cambridge
CB10 1XL
United Kingdom

Clinical

Manchester
CellCentric
Alderley Park
Alderley Edge
Cheshire
SK10 4TG
United Kingdom

R&D

Oxford
CellCentric
Oxford Science Park
Magdalen Centre
Oxford
OX4 4GA
United Kingdom

Management

- Company founded with pioneer of epigenetics and gene regulation, Azim Surani
- Explored >50 epigenetic-related targets/pathways

Senior Leadership Team

Will West MBA PhD
CEO: P&G Healthcare

Neil Pegg PhD
CSO: Glaxo, PI3Ks (> Genentech)

Andrew Hughes MD
NED: AZ PhI-II Oncology

Tomasz Knurowski MD
CMO: TMC, Simbec-Orion

Debbie Haynes BSc
COO: Genentech, Sarah Cannon

Karen Clegg PhD
Clin Ops Dir: AZ, Kesios

Thea Stanway CA
FD: PWC, WWF

Kris Frese PhD
Dir Cancer Biology: CRUK

Clinical Operations

Clinical Operations Team

Fay Ashby
Senior Clinical Trials Manager

Tracy Woods
Senior Clinical Trials Manager

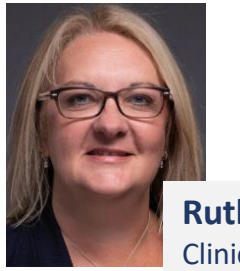
Delyth Carnes
Senior Clinical Trials Manager

Kate Fisher
Clinical Trials Manager

Steven Salomon
Clinical Trials Manager

Carrie Walker
Administrator

Clinical Research Associates



- Belfast
- Cambridge
- UCL

Ruth Tysoe
Clinical Trials Manager/CRA

- The Christie

Laura Johnson
Clinical Trials Manager/CRA

- Birmingham
- Cardiff
- Leicester

Gail Millward
Clinical Research Associate

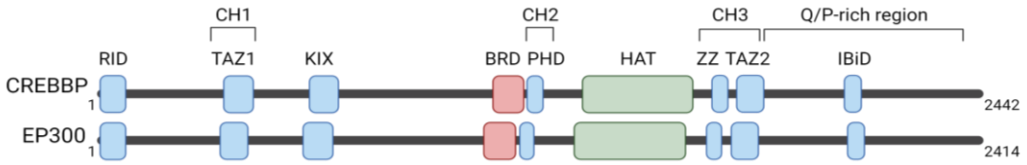
- Edinburgh
- Glasgow
- Newcastle

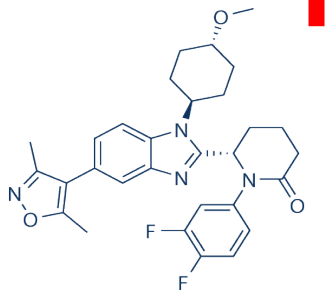
Elaine Gilmore
Clinical Research Associate

- Oxford
- RMH
- Southampton

Oliver Hook
Clinical Research Associate

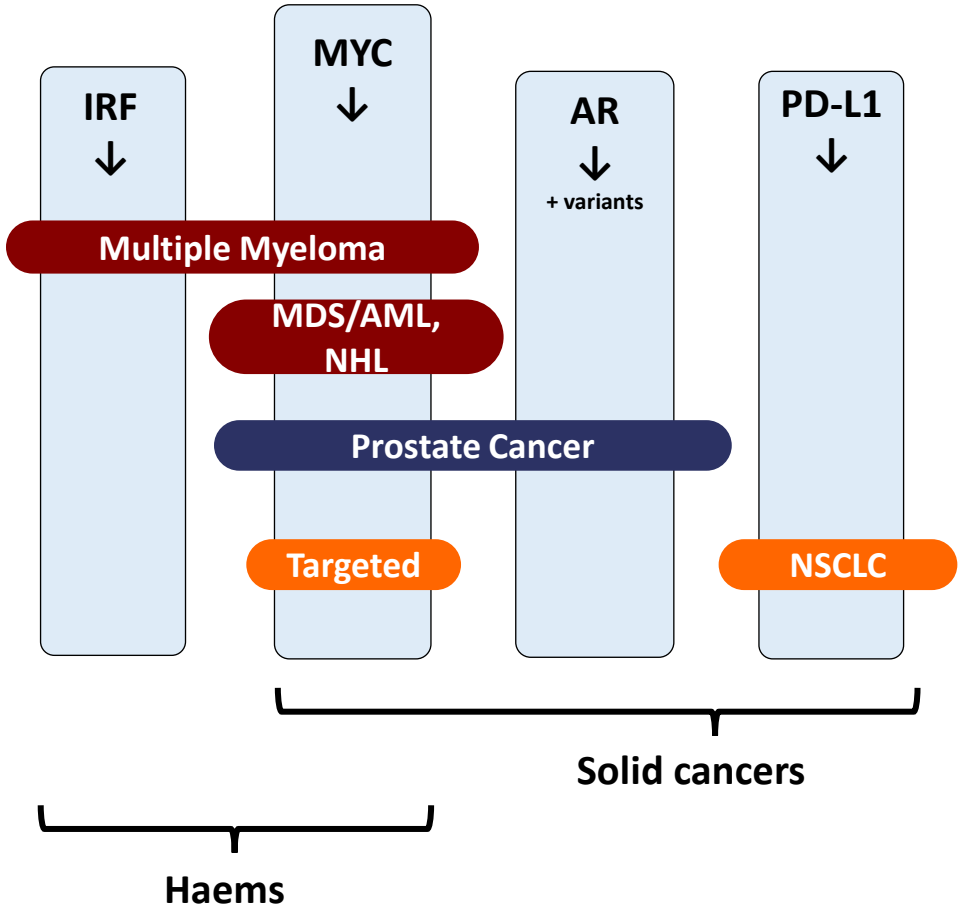
p300/CBP and inobrodib – First in Class





Potent (Kd 1nM) & highly selective (>200-5000 fold) for EP300/CBP versus bromodomains in other proteins e.g. BRD2/3/4

inobrodib (CCS1477)



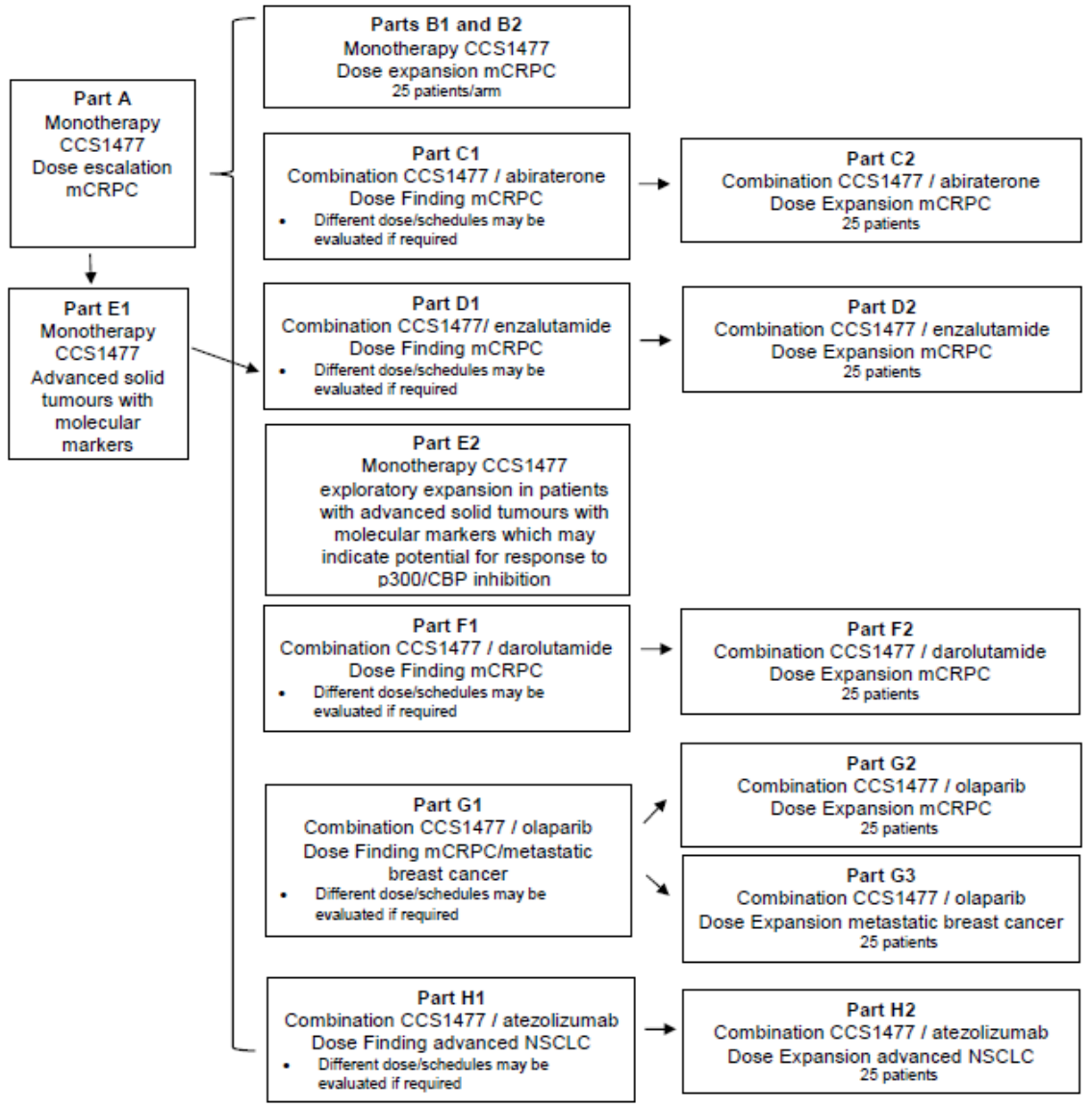
- Inobrodib (CCS1477) is a small molecule inhibitor targeting the p300/CBP bromodomain
- Inobrodib inhibits transcriptional co-activation by p300/CBP
- Impacts key cancer drivers, relevant to multiple tumour types

Clinical Trial - Solids

CCS1477-01

An open-label Phase I/IIa study to evaluate the safety and efficacy of CCS1477 as monotherapy and in combination in patients with advanced solid/metastatic tumours.

Led by Prof. Johann de Bono of the Royal Marsden Hospital/Institute of Cancer Research.



Clinical Trial - Haems

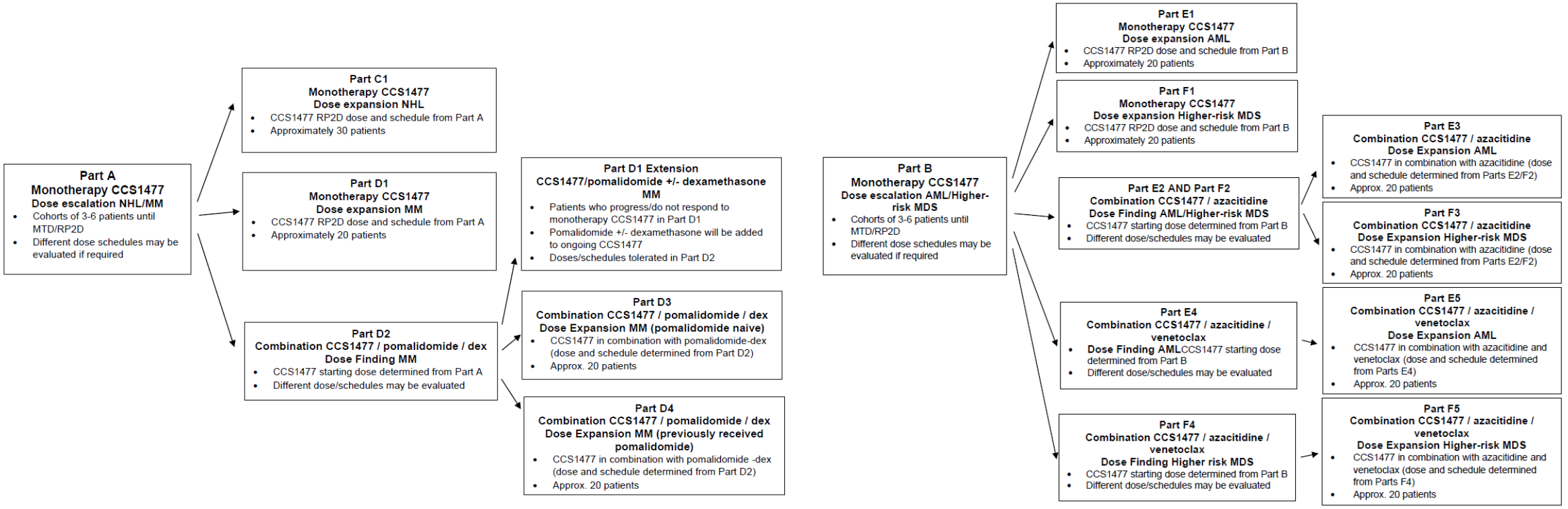
CellCentric

CONFIDENTIAL

CCS1477-02

An open-label Phase I/IIa study to evaluate the safety and efficacy of CCS1477 as monotherapy and in combination in patients with advanced haematological malignancies.

Led by Prof. Tim Somervaille of the Christie Hospital, Manchester.



Clinical Trials - Locations

CellCentric

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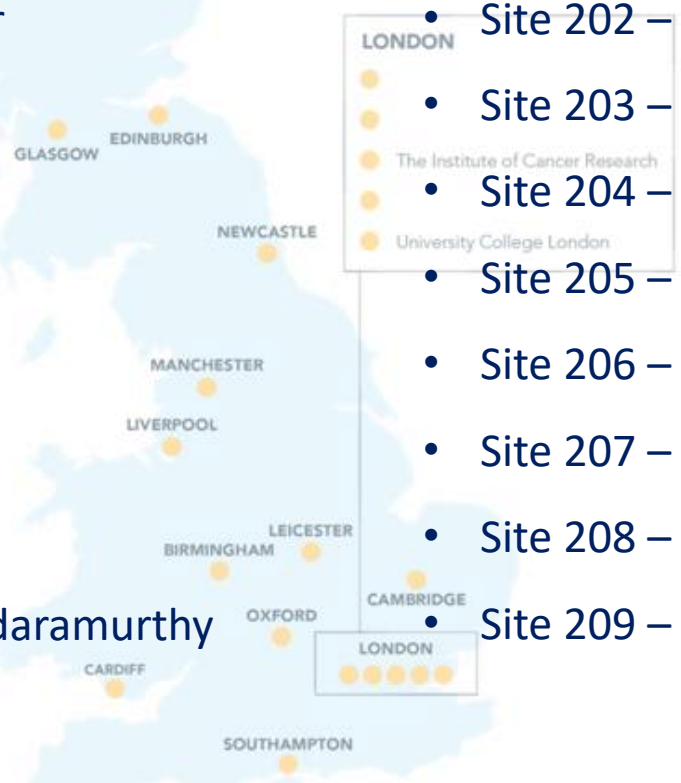
UK Sites

CCS1477-01

- Site 101 – Royal Marsden Hospital, Prof. Johann de Bono
- Site 102 – Newcastle, Prof. Ruth Plummer
- Site 103 – Belfast, Dr Victoria Coyle
- Site 104 – Southampton, Dr Simon Crabb
- Site 105 – Leicester, Dr Harriet Walter
- Site 106 – Christie, Dr Louise Carter
- Site 107 – Glasgow, Prof. Richard Wilson
- Site 108 – Cambridge, Dr Simon Pacey
- Site 109 – Edinburgh, Dr Aravindhan Sundaramurthy
- Site 110 – Birmingham, Dr Daniel Ford



CCS1477-02

- Site 201 – Leicester, Dr Harriet Walter
- Site 202 – Southampton, Prof. Andrew Davies
- Site 203 – The Christie, Dr Emma Searle
- Site 204 – Cardiff, Dr Steven Knapper
- Site 205 – Oxford, Prof. Paresh Vyas
- Site 206 – Glasgow, Prof. Mhairi Copland
- Site 207 – Edinburgh, Dr Victoria Campbell
- Site 208 – Royal Marsden Hospital, Dr Dima El-Sharkawi
- Site 209 – UCL, Dr Jenny O'Nions

ECMC site benefits

Sites

- International KOLs with academic affiliation
- Very experienced, trusted sites - traditional feasibility not required
- Broad scope of capabilities
- Extensive FTIM experience
- Fast set-up times
- Large, broad patient population
- Patient referrals within network

Study Set-up – ECMC expertise

Protocol Design / Review

- Input from Johann de Bono and team - solids and prostate study
- Input from Tim Somervaille and Emma Searle - haematology study

ICFs

- Regulatory team/clinical team at RMH provided templates and reviews

EC/IRAS/MHRA

- Regulatory team at RMH review of IRAS form, co-ordination of Radiation Assurance
- Attendance at EC meetings
- Input/review of amendments
- Input/review of EC/Regulatory responses

eCRF

- Input from Emma Searle and Christie DM/Ops team for design of haematology CRFs

ECMC - Ongoing support during study

Patient recruitment

- Targets met/exceeded
- Patient referrals between centres

Safety Review Committee (SRC)

- Active participation from all PIs/Sub Is and wider team
- Active discussion between PIs
- Dose decision discussions
- Advise on SOC combinations
- Direct engagement with CellCentric CMO

Wider support

- KOLs not directly involved in trials

ECMC - Biomarkers

Molecular profiling

- Availability of patients with molecular profiling – biomarker targeted arms of trial

Biomarker sample preparation/analysis

- Solid tumour biopsies / Bone marrow aspirates
  - Advice on sampling
  - Protocols for taking/prepping samples
  - Preparation, storage, analysis of samples
  - Fast set-up, cost effective
- CTCs – real time analysis

Biomarkers and translational science

- CRUK MI translational research during the study has impacted the design of the trial (opening MLL specific parts), and potential biomarker work

Extended Team

Nurses

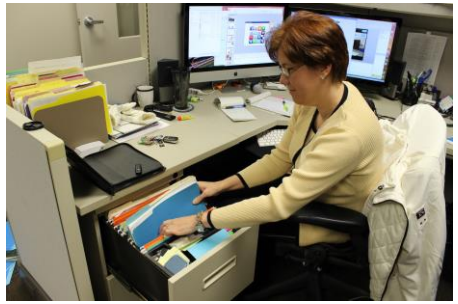
- Expertise in patient management
- Protocol procedures
- Samples

Trial managers

- Co-ordination
- Expertise

Data managers

- Complicated data
- Timely entry



Pharmacists

- Stock management
- Re-labelling
- Provision of combination agents

Lab staff

- Process/shipping samples

R&D/contracts

- Budgets
- Amendments

Site staff

Abigail Downing, Adele Farrugia, Abbie Hassan, Abhijit Pal , Abraham Anoopa, Adam Mead, Adam Sharp, Ahmed Abdulgawad, Aina Maria Rigo Miralles, Aisling Barrett, Alaiza Lidasan, Alan Simms, Alec Paschalis, Alexander Lee , Alexandia Hynes, Alexandria Hynes, Alice Johnson, Alisha Pancholi, Alison Bonner, Alison Ryan, Alistair Greystoke, Amisha Desai, Amit Sud, Ammara Jones, Amy Johnson, Ana Goldrick, Ana Ortega - Franco, Andra Curcean, Andrea Biondo, Andrea Fruzzetti, Andrea Stanton, Andrew Bennie, Andrew Davies, Andrew Peniket, Andria Staniford, Andy Davies, Angela Little, Angelika Turbuch, Aniket Thakerer, Anitra Chhabra, Ann Lloyd, Ann Tivey, Anna Kullenberg, Anna Minchom, Annabel Scott, Annie Rainey, Antoine Italiano, Anuja Satam, Anuta Scridon, Aoife Dervin, Aravindhan Sundaramurthy, Barbara Redmond, Becky Scott, Ben Elliot, Ben Elliot , Ben Elliott, Berni Ebbs, Bhavika Lodia, Brendan Peltier, Brodie Mckirdle, Carina Mundy, Carol Evans, Carol Falcon, Carol Pearce, Carol Spencer, Carolina Haddon, Caroline Miles, Catherine Garnett, Catherine Woods, Celine Le Rest, Celine Pagnat, Ceri Armstrong, Ceri Bygrave, Cesaria Ehibhatiomhan, Charlotte Armstead, Charlotte Gray, Charlotte Pawlyn, Charlotte Randell, Charmaine Gilbert, Chiara Dalla Torre, Chin Neoh, Chris Barron, Christina Guo, Christina Roberts, Christine Pearson, Christoph Oing, Chyrelle Mcallister, Claire Livings, Claire Mcnicol, Claire Pelham, Claire Pettinger, Claire Wheeler, Clara Redondo, Clare Mcnicol, Clemency Stephenson, Courtney Lewis, Crescens Tiu, Cristiana Goncalves, Daisy Underwood, Dan Muller, Daniel Ford, Danielle Campbell, Danielle Rice, David Taussig, David Wan, Dawn Chalk, Debra Mansergh, Diane Law, Dima El-Sharkawi, Dominika Chwialkowska, Dorothy Aitken, Duncan Mcclaren, Edyta Bielecka, Efe Evboumwan, Eimear Nicholl, Eleanor Johnston, Eleanor Pearce, Elena Cojocaru , Elise Harbord, Elise Nash, Elise Seneca, Elizabeth Munden, Ellen Brown, Elliott Phillips, Emily Underwood, Emma Barker, Emma Hanna, Emma Kipps , Emma Nicholson, Emma Norling, Emma Searle, Eve Broadley, Fariha Rahman, Fatin Sammour, Faye Cruz, Faye Lowe, Fiona Greaves, Fiona Mcqueen, Francesca Hogan, Francesco Forconi, Gabriela Andrusca, Gary Middleton, Gemma Cutting, Gemma Fowler, Gemma Wickert, George Bakirtzis, George Pettitt, Georgia Pateman, Gillian Foden, Giovanni Perra, Grace Morgan, Hamal Sharma, Hannah Martin, Harriet Walter, Hashim Kabash, Heather Parry, Helder Ramos, Helen Ashcroft, Helen Hughes, Helen Porteous, Helena Rangert, Holly Bond, Holly Inman, Huben Hubenov, Ioannis Charalampidis , Ioannis Karydis, Iram Babarrashid, Irene Moreno, Isabel Farrar, Isla Currie, Ismail Mohammed, Jack Broadfoot, Jack Taylor-Stuart, James Masters, Jane Denyer, Jane Halliwell, Jane Robertson, Jane Rogan, Jane Thomas, Janet Prentice, Janlyn Falconer, Jeffrey Yachnin, Jennalyn Michalakoudis, Jennifer Baxter, Jenny Hartley, Jenny O'Nions, Jessica Hallett, Jessica Wong, Jim Cavet, Joanna Searle, Joanne Todd, Johann De Bono, John Barwood, Jonathan Lau, Jonathan Martin, Joo Ern Ang, Judith Kok, Julia Lai-Kwon, Julia Walker, Julie - 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Beyond the day to day trials

Conferences

- Face to face meetings at conferences
- Presentation of data at conferences
  - de Bono – posters
  - Somervaille – oral presentation
  - Searle – EHA / ASH

Papers

- de Bono Lab (ICR)
- Somervaille Lab (Christie)

Patient Engagement

- Working with our sites to improve patient engagement and share patient experiences
- The Christie Haematology team helped facilitate discussions with a lovely patient on a different study, highlighting the most important factors of treatment to her.
- This was shared in our podcast; which also included talking to top Haematology experts

9 min PLAY

The Christie – Highlighting the Patient Experience

CellCentric

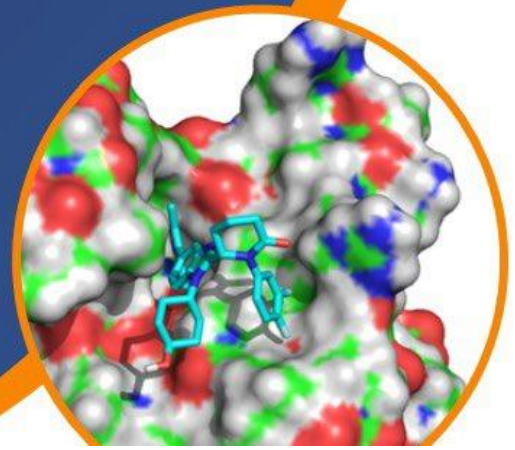
CONFIDENTIAL

CellCentric

Making a difference to patients

Inobrodib

first-in-class p300/CBP inhibitor to treat cancer



Daily Express Wednesday, January 18, 2023 23

Cancer was killing me but I'm better than ever thanks to wonder pill

'I didn't think I'd ever see a grandchild' ...Chris with little Tommy, who is now 18 months. Right, enjoying life with husband Steve

EXCLUSIVE
By **Chris Riches**

CANCER patient Chris Rennie lovingly holds a grandson she never thought she would see, thanks to a UK-developed wonder drug.

Doctors once gave Chris just months to live. But her disease has now shrunk by more than half and she is in "partial remission".

In 2017, the ex-primary school teacher was diagnosed with myeloma, an incurable blood cancer that develops from bone marrow cells.

She endured nine gruelling chemotherapy treatments over five years and a failed stem cell transplant before being referred to The Christie NHS Foundation Trust in Manchester last year.

There, the mother of two and grandmother of three joined the first phase of a clinical trial for CellCentric's drug, inobrodib.

Overjoyed Chris, 63, from Meols, Merseyside, and her husband Steve, 65, are now preparing for the birth of their fourth grandchild in April.

Chris said yesterday: "I feel better than I've felt in years. The drug has exceeded my wildest dreams after the years of treatments that were awful and exhausting.

"I simply take two tablets in the morning and another two at night. Every four weeks I return to The Christie for blood tests.

"A blood test this morning showed no change, meaning no more cancer growth, which is amazing."

She added: "When they told me myeloma was incurable and basically terminal, I didn't think I'd ever see a grandchild. Now I spend so much time with them.

"It's joyous. I do something enjoyable every day and I also make sure I walk 10,000 steps. Life is definitely for living."

Twenty-six patients with relapsed/refractory multiple myeloma have been treated solely with inobrodib.

Six out of seven had a reduced clinical marker – used to determine the cancer's presence. Three out of six patients remain on treatment after more than eight months. Crucially, inobrodib could be effective for other blood cancers such as lymphoma and acute myeloid leukaemia.

Professor Tim Somervaille, who is leading the inobrodib trial across Europe, said: "We've seen some remarkable responses, with an improvement for some patients within days.

"This is an early phase trial so there's a lot more work to do. But the data we have so far is very encouraging and could help many thousands of people in the future."

Around 3,100 people die from myeloma in the UK every year. It is the country's 17th most common cause of cancer death.

Cancer Research UK funded the laboratory pre-clinical work at the Cancer Research UK Manchester Institute.

COMMENT

TIM SOMERVAILLE
Consultant haematologist

CHRIS Rennie's case is absolutely indicative of the potential of inobrodib.

We naturally need to be cautious as it is in its early days. But in some of the early phase patients we are seeing some really striking results.

This new drug came about thanks to the past two or three decades of careful, patient science study trying to understand how cancer cells work by whole teams of people and Cancer Research UK.

It has the potential in some patients to stop the cancer cells in their tracks from growing, while at the same time sparing the normal cells.

It will not be a revolutionary treatment for everyone and for all cancers. However, it is showing itself to be a really exciting medical development by a proud British company, CellCentric, and a real UK success story.

Expertise

Locations

Flexibility

Enthusiasm

Network

Commitment

Relationships

Collaboration

Meet the CellCentric Team

Thank you to everyone involved!

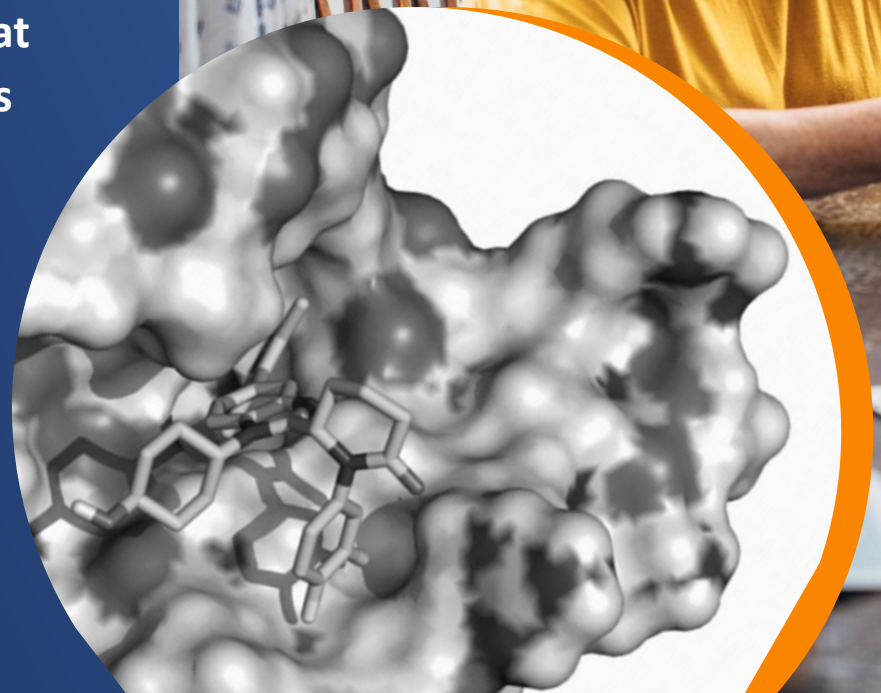
Any Questions?

CellCentric

The p300/CBP inhibitor company

Inobrodib

First-in-class oral small molecule to treat specific cancers



May 2023

The DETERMINE Trial

(Determining Extended Therapeutic indications for Existing drugs in Rare Molecularly-defined Indications using a National Evaluation platform trial)

DETERMINE

Founding partners:

cruk.org/determine

MANCHESTER 1824 The University of Manchester

CANCER RESEARCH UK | CENTRE FOR DRUG DEVELOPMENT

UNIVERSITY OF BIRMINGHAM

The ROYAL MARSDEN NHS Foundation Trust

Aims of DETERMINE

DETERMINE is an umbrella, basket platform trial evaluating genotype-matched targeted agents outside of their licensed indication in **rare* adult, TYA and paediatric cancers** with actionable genomic alterations

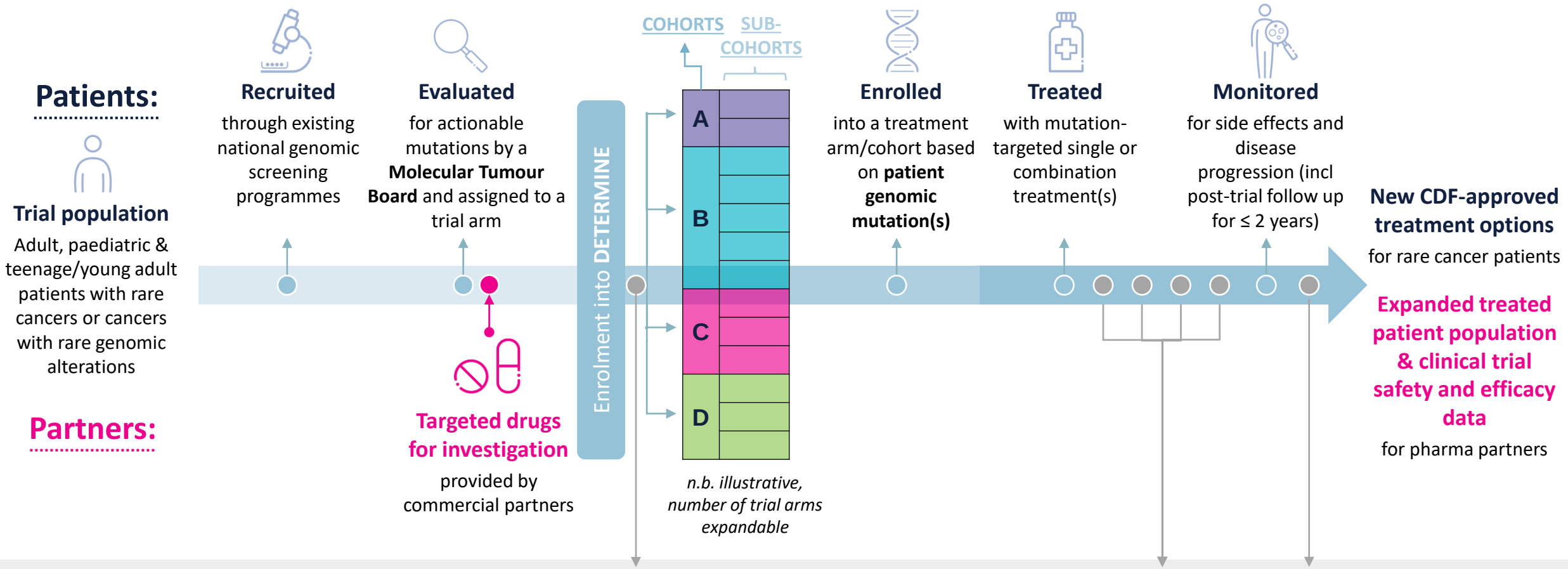
Aims

1. Translate positive findings to the NHS (**Cancer Drugs Fund**) to provide new treatment options for patients with rare malignancies

2. Build a rich translational package to better understand the molecular (genomic, transcriptomic and immune) context behind response to targeted therapies

* Defined as <6 in 100,000/year (RARECARENet. RARECARE - Surveillance of Rare Cancers in Europe, International rare cancers initiative. Lancet Oncol 2013; 14: 109–110)

Trial overview



DETERMINE

Patient recruitment

Given the costly nature and high attrition rates of pre-screening programmes, DETERMINE will recruit patients through **existing national screening programmes**

NHS Genomic Medicine Service	TARGET National study	SMPaeds study	Other screening programs
• 7 genomic hub labs • Aiming to offer sequencing as part of standard of care for all cancer patients	• 18 adult-recruiting centres • ~6k advanced solid cancer patients to be recruited across 5 years	• 20 paediatric-recruiting centres • Routine analysis of biopsies from all children with solid tumours who relapse in the UK	• Existing screening programmes e.g., IMAGINE in Scotland • Also includes commercial trials that have screening programmes embedded

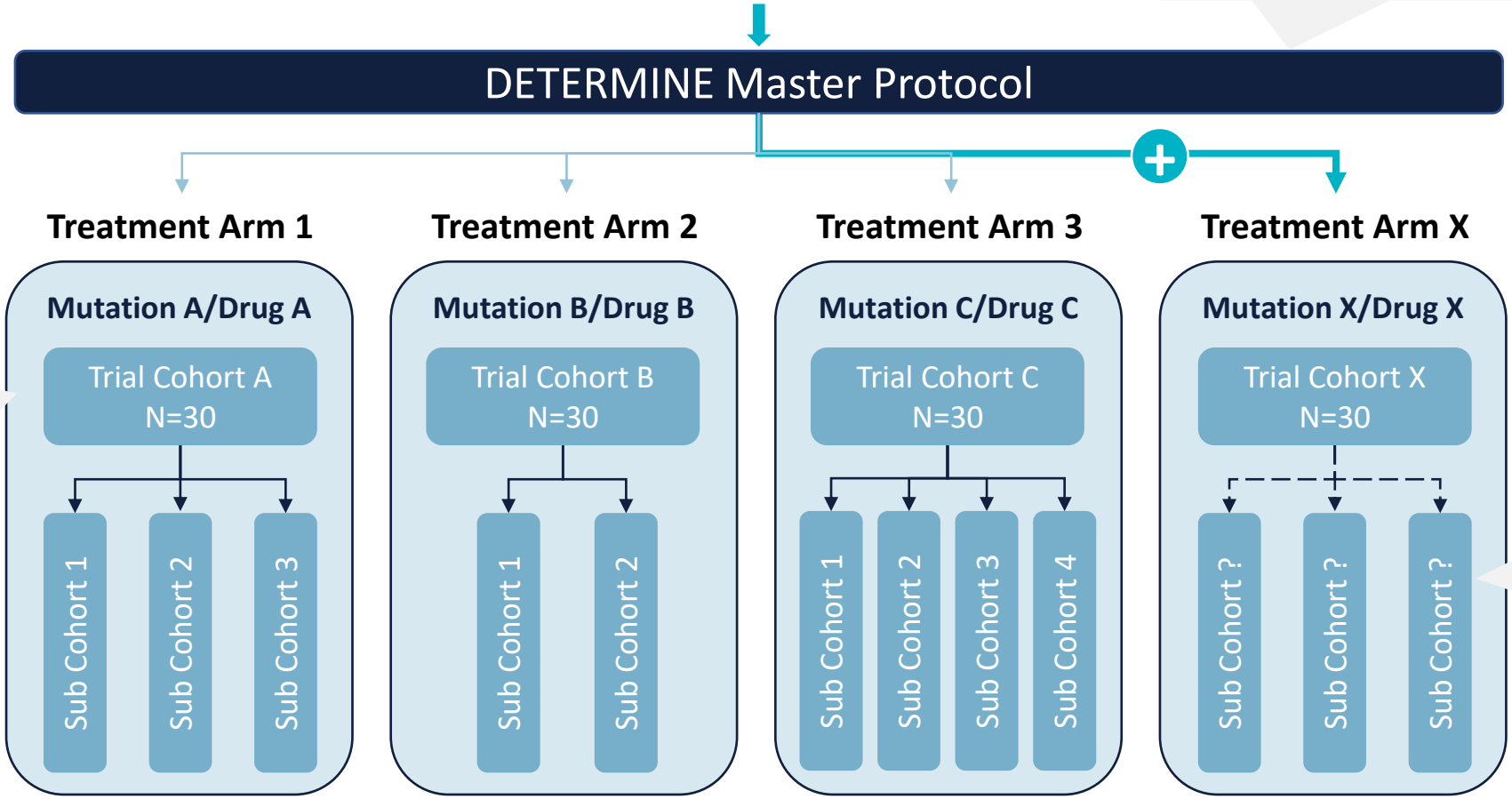
- ✓ **Use of multiple national screening programmes that incorporate screening as part of routine / standard care**
- ✓ **Proven recruitment success from other umbrella trials using similar approaches** e.g. over 5 years, the TAPUR trial (U.S.) recruited 3581 patients and the DRUP trial (Netherlands) recruited 950 participants - both without use of a pre-screening programme

DETERMINE

Umbrella-basket design

'Umbrella' – master protocol allowing new agents to enter and existing agents to leave the trial in a defined, approved process

Additional treatment(s) provided by new or existing commercial partners



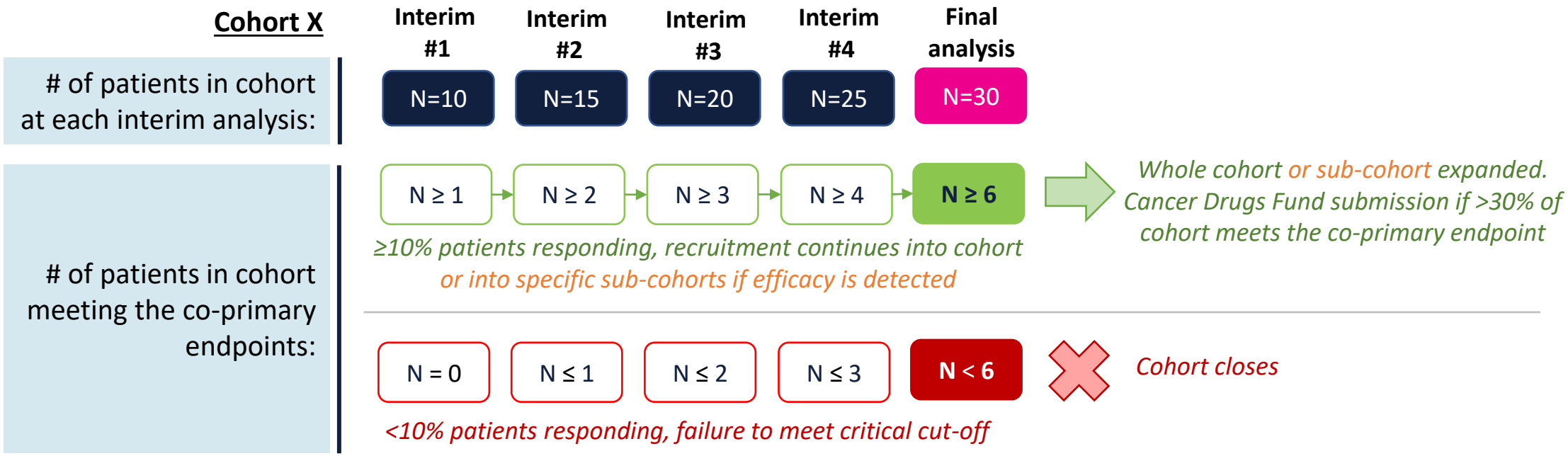
'Basket' – each trial cohort is a basket of different tumour types, genomic complexity etc.

Sub-cohorts may branch off from the initial trial cohort if sufficient efficacy signals are detected

DETERMINE

Statistical design: Bayesian-adaptive approach

- Decision making is based on the number of patients observed to meet the co-primary endpoints: **Objective Response and Durable Clinical Benefit (DCB)***
- **Critical cut-off**: arm closure if **<10%** patients meet the co-primary endpoints

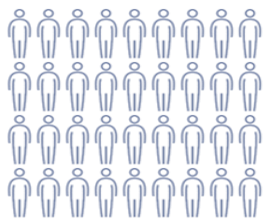


* Objective Response (OR), defined as the occurrence of a confirmed complete response (CR) or partial response (PR) as the best overall response according to Response Evaluation Criteria in Solid Tumours (RECIST). Durable clinical benefit is defined as the absence of disease progression for at least 24 weeks from the start of trial treatment, measured according to RECIST 1.1

Bespoke route to approval

DETERMINE will generate an alternative, more efficient route to indication expansion for rare cancers, enabling pharma partners to avoid the high costs of traditional, single-arm trials

TRADITIONAL PATHWAY



Large 'N' required due to trial design and diverse patient cohorts

Phase II single-arm RCT — **N = ~25-100**

Phase III single-arm RCT — **N = ~100s-1,000s**

NICE submission

- **Approval** — Safety and efficacy data satisfies NICE criteria
- **CDF approval** — Initial data promising, **more data needed**
- **Rejection** — Safety or efficacy data fails to meet criteria

≤ 2 years

NICE re-evaluation

- **Approval**
- **Rejection**

DETERMINE PATHWAY

***Less data required** due Bayesian approach and precise patient stratification*

DETERMINE trial arm — **N = ~30**

DCB rate <10% → **Recruitment stops, trial arm closed**

DCB rate >30%

CDF approval
Initial data promising, **real world data collected**

NICE submission

- **Approval**
- **Rejection**

DETERMINE

Translational studies

In addition to generating clinical trial data for CDF submissions, patient sample collection allows for a range of potential translational studies that can help improve understanding of biological mechanisms behind response

Whole genome & transcriptome sequencing	Tissue biopsies collected can facilitate study of tumour genomic complexity and better understanding of the influence of co-mutations and multi-omic parameters on patient response and resistance
ctDNA analysis	Serial blood samples taken during the course of treatment can enable monitoring of disease evolution and novel resistance mechanisms to targeted agents
Immune landscape	Tissue biopsies also allow study of the immune microenvironment and spatial immune heterogeneity, with potential for predictive biomarker identification

DETERMINE

Data pooling with equivalent trials in the EU through the PRIME-ROSE* consortium

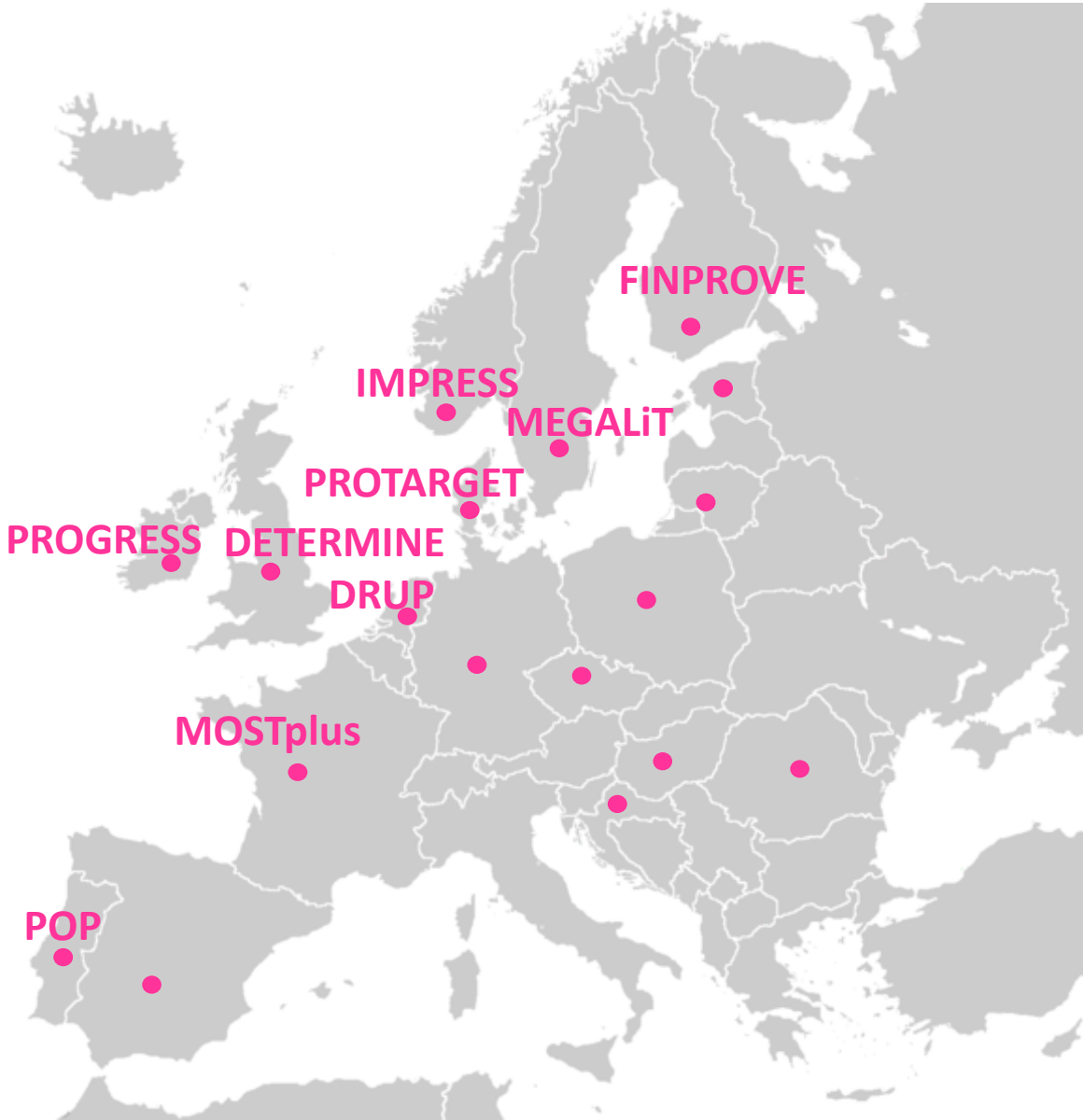
- The consortium consists of altogether **24 partners**, including **nine beneficiaries** and **fifteen associated partners** (including University of Manchester and Cancer Research UK representing the UK)

Lead applicant – Oslo University Hospital (NO)

- A key objective of the consortium is to **develop a shared data platform to:**

✓ Enable data sharing between institutions

✓ Aggregate data and evidence for overlapping cohorts to support review by regulatory agencies and payors



PCM4EU
Personalised Cancer Medicine for all EU Citizens

HORIZON EUROPE

* PRecisIon Cancer MEdicine RepurpOsing SystEm Using Pragmatic Clinical Trials.

DETERMINE – a collaborative effort

The DETERMINE team is comprised of multiple experienced clinicians and researchers that will be working closely with CRUK and its various partner organisations

Key individuals

Dr Krebs
CI/Clinical lead
MANCHESTER 1824
The University of Manchester

Dr Marshall
Paediatric lead
The ROYAL MARSDEN
NHS Foundation Trust

Prof Middleton
Translational lead
UNIVERSITY OF BIRMINGHAM

Prof Billingham
Stats lead
UNIVERSITY OF BIRMINGHAM

Dr Chaturvedi
Pathologist lead
The Christie NHS
NHS Foundation Trust

Miss Gath & Mr Burchill
Patient representatives
voice science for patient advocates
Vision On Information, Confidence & Engagement

Key organisations

Sponsor and Commercial
CANCER RESEARCH UK | CENTRE FOR DRUG DEVELOPMENT

Trial delivery
ecmc

Co-Investigators / Collaborators
- Clinical trial experience
- Translational research (ctDNA, genomics)

Pharma partners
Roche
NOVARTIS

CDF
NHS England

DETERMINE

Centre for Drug Development (CDD)

Based at CRUK's headquarters, we are a multidisciplinary team of over 100 scientists, physicians and operational specialists with expertise across regulatory driven drug development

Translational & Medical Sciences

Quality, Regulatory, PV & Medical Writing

Study, Project & Portfolio Management

CENTRE FOR DRUG DEVELOPMENT

Clinical Operations & Data Management

Drug Supply & Manufacturing

Business Development & Legal

DETERMINE

CDD experience & track record

Extensive clinical development experience and proven track record of delivering early phase trials

160
early-phase trials delivered with novel cancer drugs

14
agents under active development in our current portfolio

6
agents registered as medicines

including:

Zytiga® (abiraterone acetate)

Rubraca® (rucaparib) tablets

Temodal® temozolomide

MORE THAN 60
agents taken in to first-in-human clinical trials

100%
success rate with regulatory applications to the Medicines & Healthcare products Regulatory Agency

14
first-in-class agents clinically investigated

29

collaborations under the Clinical Development Partnerships (CDP) initiative

DETERMINE

DETERMINE Eligibility Criteria

Drugs entering DETERMINE must:

- **Target a genomic aberration** which is a) specified on the approved licence and b) detectable by genetic screening

- **Be licensed for use* in at least one indication in a major market** (e.g., MHRA approval in UK, FDA approval in U.S., EMA approval in EU)

  n.b. the drug does not have to be licensed in the UK / have MHRA approval specifically

- **Have an established (or the potential to establish) a UK-compliant drug supply mechanism in UK/EU** (this can be clinical trial supply or commercial stock)

  n.b. associated documentation will also be required to support a CTA submission in the UK

* Drugs that are close to being licensed (i.e., in late phase three trials and/or have submitted for NDA/BLA approval) may also be eligible, please contact us for further details

DETERMINE

Existing commercial partners

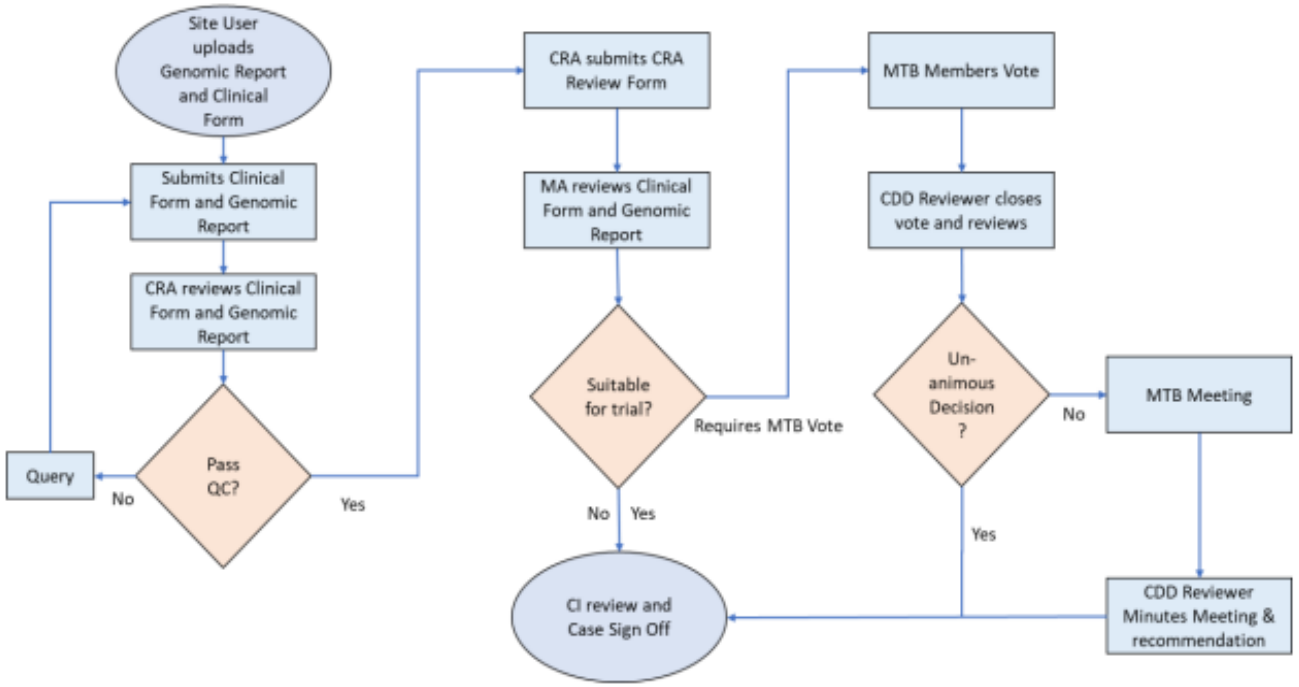
Partner	Drug	Mechanism of action	Treatment arm / Trial cohort
Roche	Alectinib (Alcensa)	ALK inhibitor (TKI)	Adult, Teenage/Young Adults and Paediatric patients with ALK (RET) gene fusion positive solid tumours
	Atezolizumab (Tecentriq)	PD-L1 inhibitor	Adult, Teenage/Young adults and Paediatric patients with solid tumours with high tumour mutational burden (TMB) and microsatellite instability-high (MSI-high) or proven constitutional mismatch repair deficiency (CMMRD) disposition
	Entrectinib (Rozlytrek)	ROS1/ALK/TRK inhibitor (TKI)	Adult, Teenage/Young Adult and Paediatric patients with NTRK or ROS1 gene fusion positive solid tumours
	Trastuzumab / Pertuzumab combo	HER2 inhibitor	Adult, Teenage/Young adults and Paediatric patients with solid tumours with HER2 amplification or mutations
	Vemurafenib / Cobimetinib combo	MEK/BRAF inhibitors (TKI)	Adult patients (aged ≥16 years) with solid tumours with BRAF V600 mutations
NOVARTIS	*(Confidential for the time-being)*		

We are continuing to engage multiple pharma companies to access desired medicines

DETERMINE

Patient selection

- The Medidata Adjudicate platform will be the primary method of decision making for patient cases



Molecular Tumour Board (MTB)

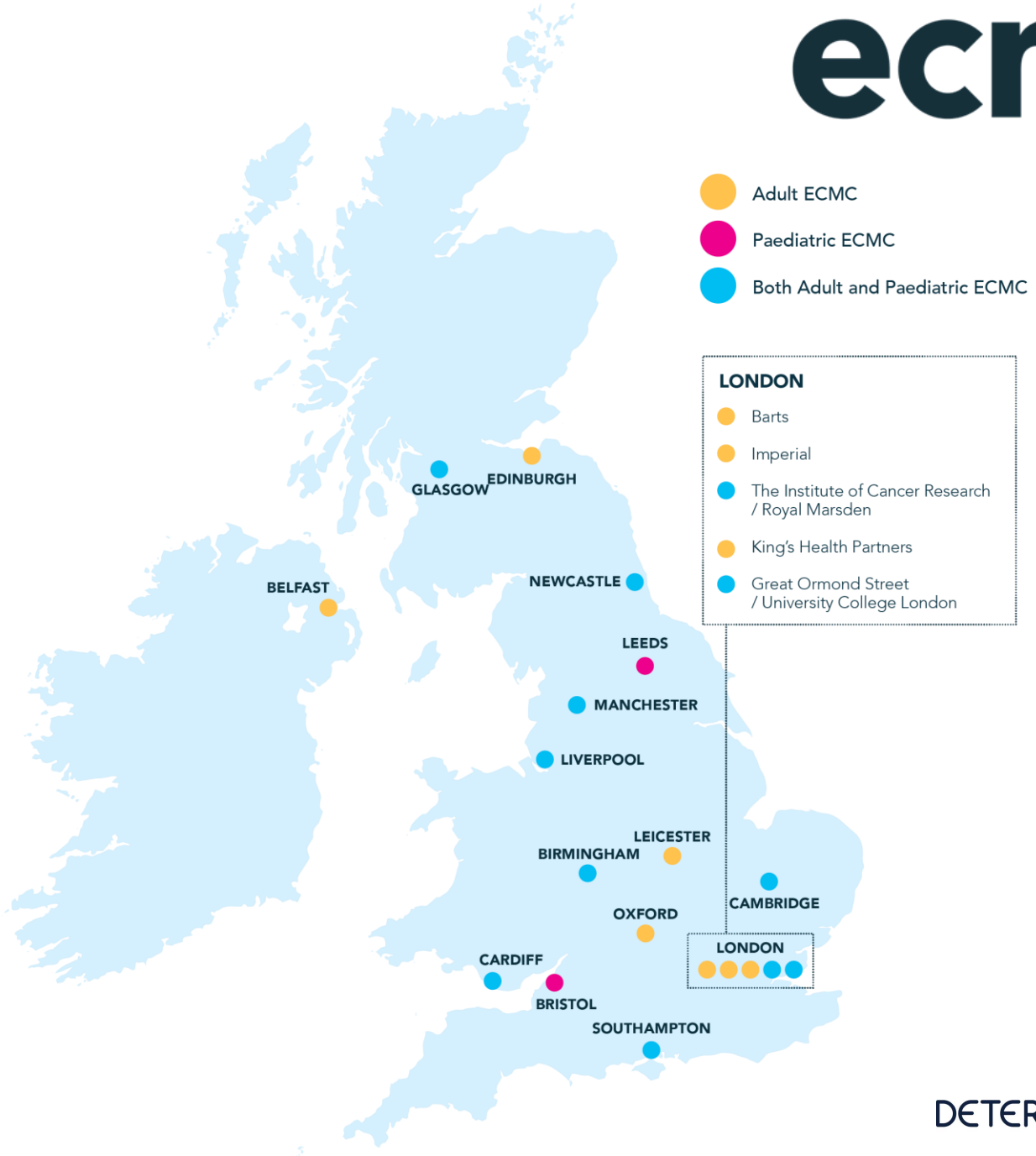
- Assess and advise on the selection of appropriate matches between actionable genetic alterations in genomically-profiled patients and treatment arms.
- The MTB consists of representatives with expertise in adult/paediatric/teenage and young adult (TYA) oncology and clinical genetics.
- They will base their recommendations on a pre-defined list of matching drugs (available at the time of enrolment) and known genetic alterations.
- MTB recommendation within five (5) working days after receipt of a valid genomic report from the treating investigator

DETERMINE

Trial Delivery

Opening date: November 2022
Current Enrolment: 5 patients
Current Sites Opened: 5 sites
Recruitment target: 650

Number Of Sites Planned: 23 across both the adult and paediatric Experimental Cancer Medicine Centre network (ECMC)
Study Duration: 5 years



Join us across the network!

- **CDD is seeking to appoint Treatment Arm Investigator Leads to join the Project Team and work with the Chief Investigator (Dr Matthew Krebs) to lead the precision medicine DETERMINE trial.**

- ✓ **TA01 Alectinib**
- ✓ **TA03 Entrectinib**
- ✓ **TA04 Trastuzumab/Pertuzumab**
- ✓ **TA05 Vemurafenib/Cobimetinib**
- ○ **TA02 Atezolizumab**

- Take the lead on one of the DETERMINE treatment arms and work closely with the CI, CDD Medical Advisor and wider project team to manage the trial and in particular optimising patient recruitment.
- We are reaching out to motivated Clinicians who may be interested and/or have experience with rare tumour types and are willing to provide oversight to the allocated treatment arm.

DETERMINE

Patient and Public Engagement

DETERMINE has continuous wide-ranging patient and public engagement and involvement from initial trial design through to delivery

- Research questions and rationale – Received input from TYA group *VoiceUp!.*
- Protocol and Informed Consent Documents (ICDs)
- Study website cruk.org/determine and short animation videos
- DETERMINE Trial Steering Committee
- Dissemination of results
- Patient experience questionnaires

DETERMINE video for adults

Thank you

DETERMINE

Founding partners:

cruk.org/determine

MANCHESTER 1824 The University of Manchester

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