dECMT

digital Experimental Cancer Medicine Team

Overview

Digital Experimental Cancer Medicine Team

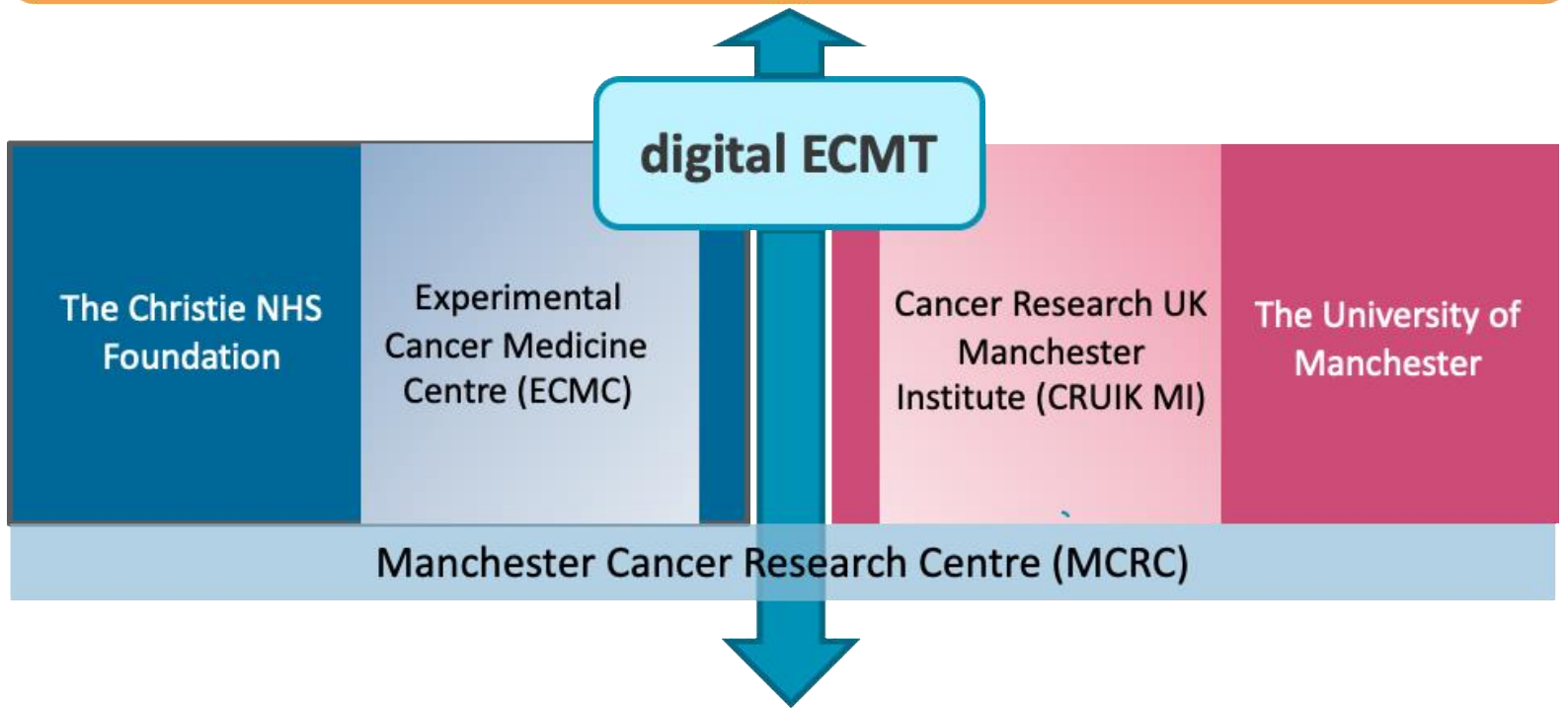
The University of Manchester

CANCER RESEARCH UK | MANCHESTER INSTITUTE

Where we are?

Digital Experimental Cancer Medicine Team

Multidisciplinary team, freedom to operate, focussed on decision Science R&D and and patient benefit



MANCHESTER INSTITUTE
CANCER BIOMARKER CENTRE

We operate at the intersection between patients, science, technology and the clinic.

www.digitalecmt.org

Experimental Cancer Medicine

Digital Experimental Cancer Medicine Team

- Digital methods for supporting clinical trials.
- Personalised treatments.
- Evolving clinical decision-making.

Experimental Cancer Medicine

Digital Experimental Cancer Medicine Team

Phase I	Phase II	Phase III	Phase IV
20-80 participants	**100-300 participants**	**1,000-3,000 participants**	**Thousands of participants**
Up to several months	Up to (2) years	One (1) - Four (4) years	One (1) year +
Studies the safety of medication/treatment	Studies the efficacy	Studies the safety, efficacy and dosing	Studies the long-term effectiveness; cost effectiveness
70% success rate	33% success rate	25-30% success rate	70-90% success rate

https://www.cern-foundation.org/education/clinical-trials/clinical-trial-phases

AI@dECMT

Digital Experimental Cancer Medicine Team

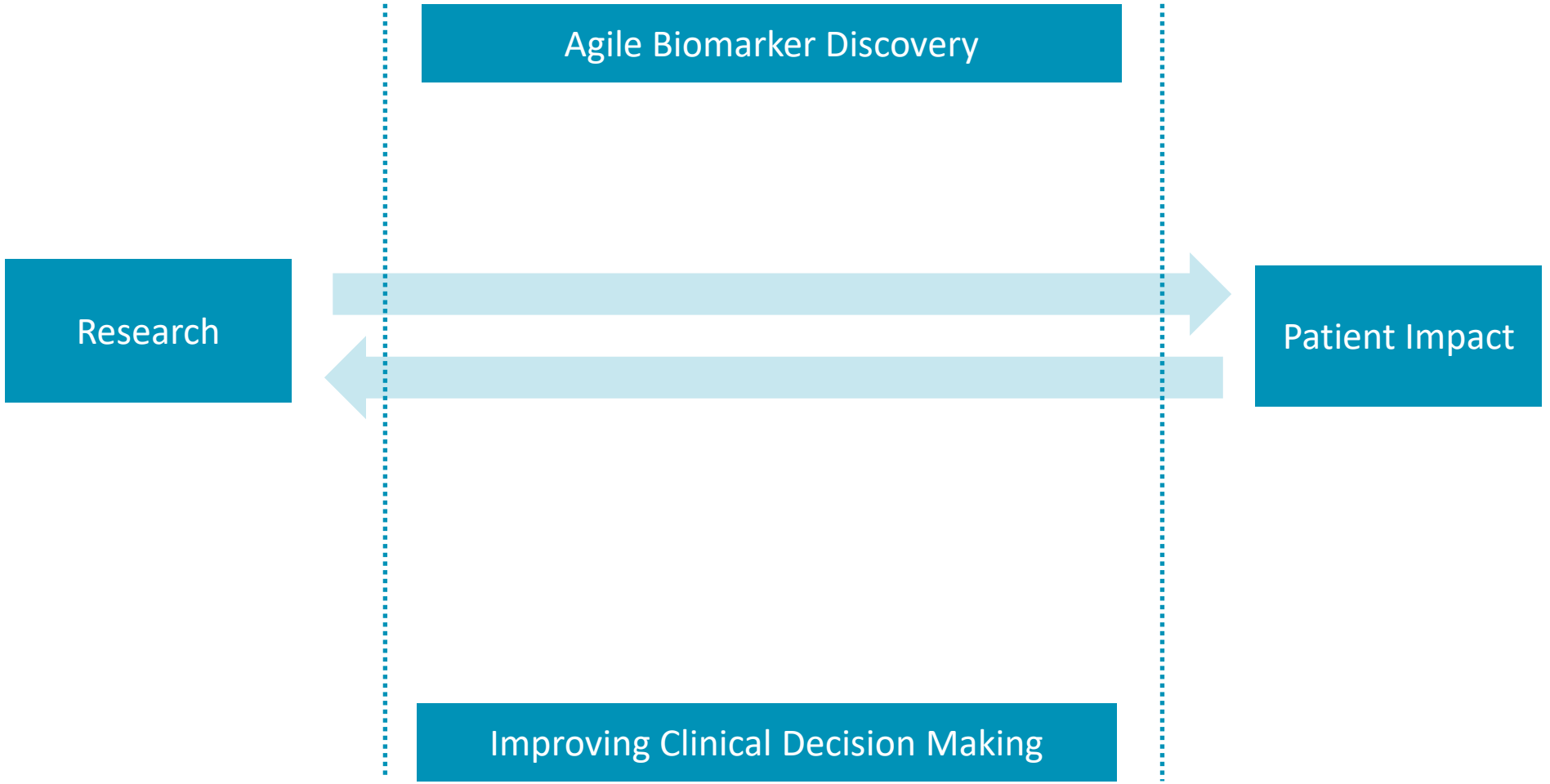
- Agile AI-supported biomarker discovery and clinical validation.
- Measurable impact on patient’s lives.
- AI: Safe, Explainable &Ethical (SEE).
- Technology clinical trials as a first-class citizen.

The Gap

Digital Experimental Cancer Medicine Team

Strategy – Focal Points

Digital Experimental Cancer Medicine Team



Agile Biomarker
Discovery & Validation

Strategy – Focal Points

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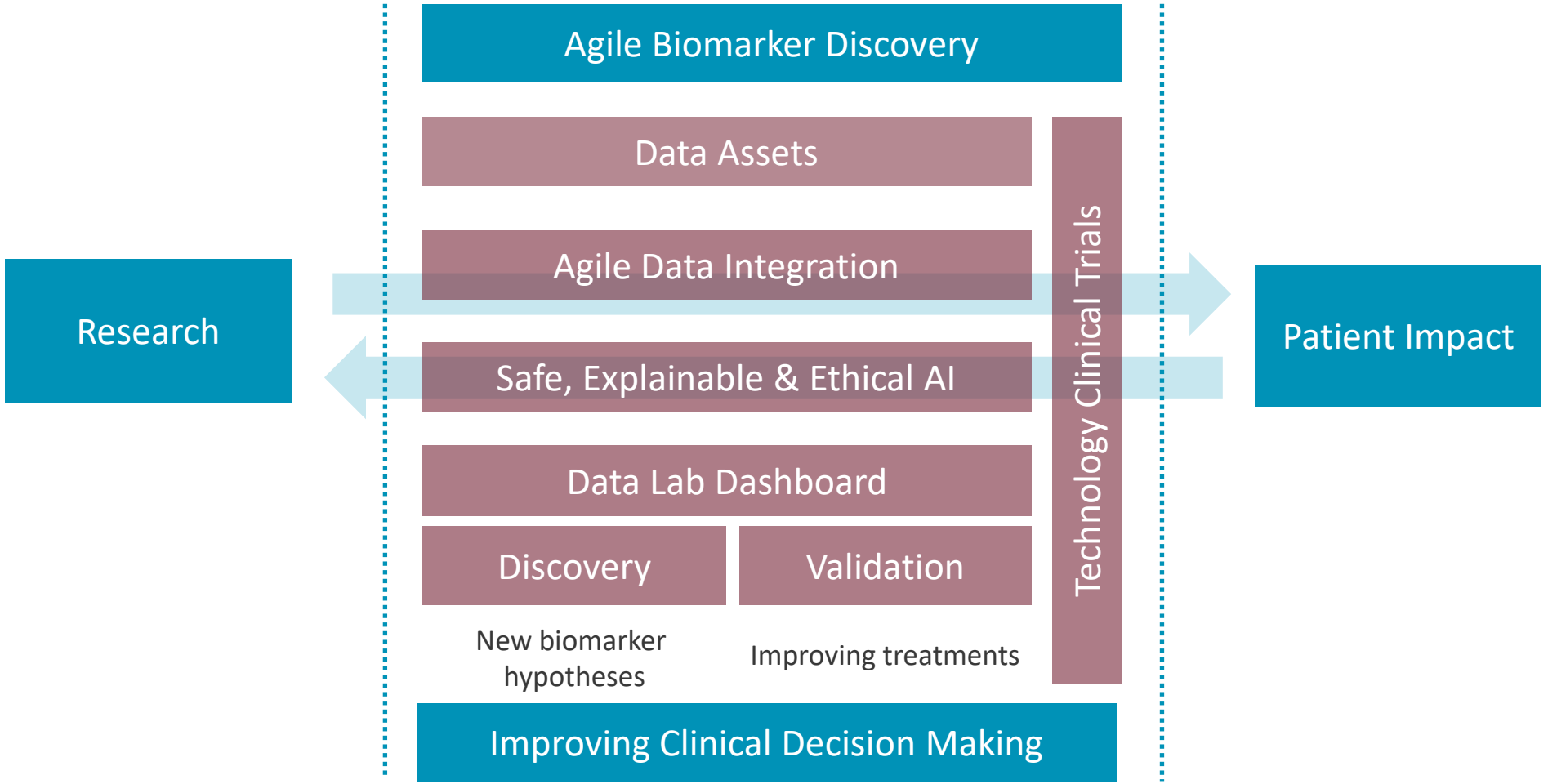
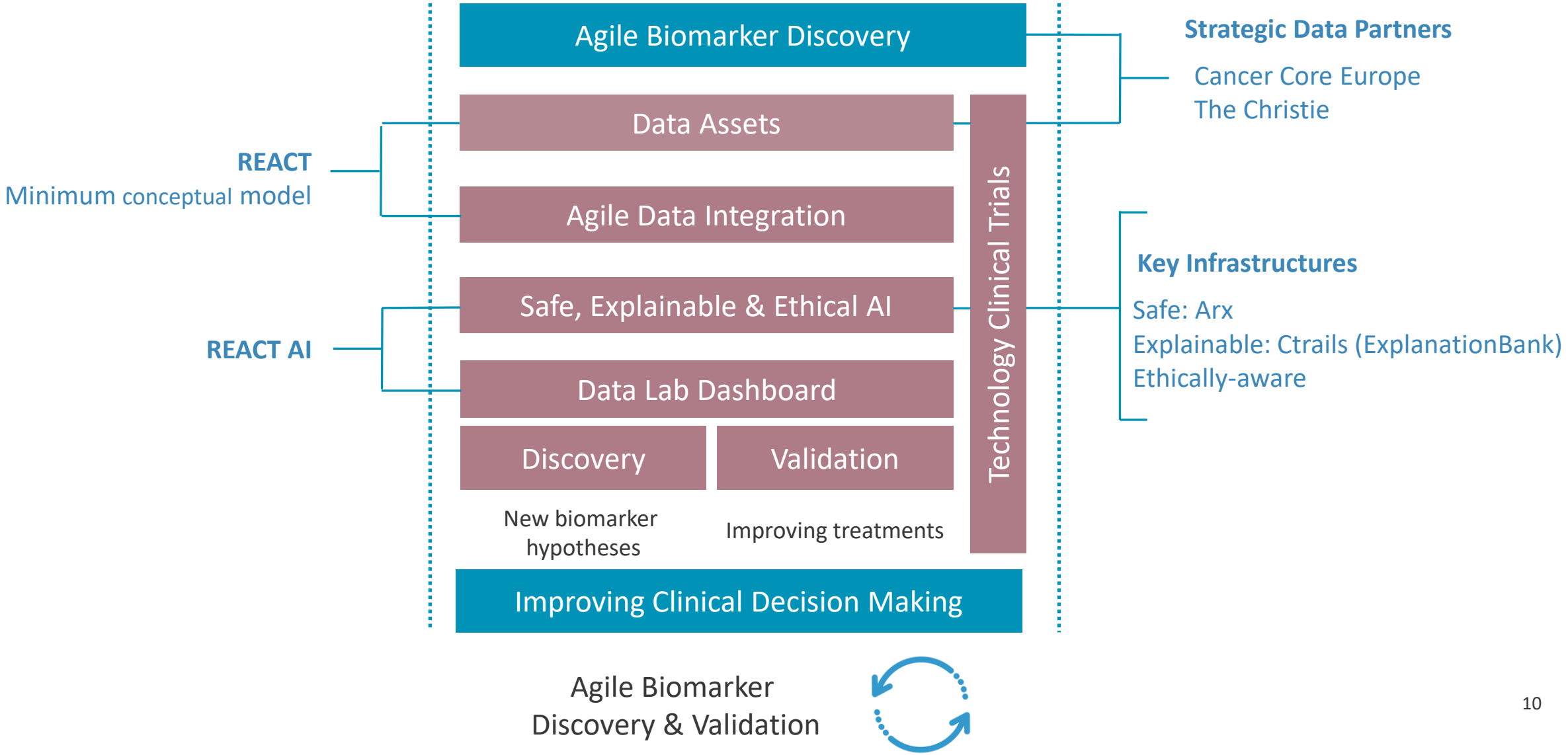


Agile Biomarker Discovery & Validation

Strategy – Focal Points

Digital Experimental Cancer Medicine Team



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Project Portfolio

Portfolio of Digital Tools

Digital Experimental Cancer Medicine Team

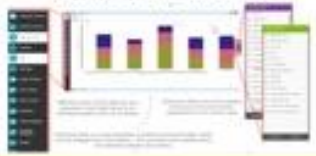
Data interpretation

PROACT

In-trial patient insight about an experimental medicine

REACT

Advanced visualisations for real-time clinical decisions



eTARGET

Virtual molecular tumour board: supports decision making

Data acquisition

IN-HOME (nephro-oncology)

Improve kidney injury detection:

- in-home sampling
- data-driven algorithms

eSOURCE

Digital solution for data acquisition in early phase trials

Treatment tracker

Giving patients back control over their time in hospital

Data science and research

NOTION Study

Early detection of immune toxicity

Ophthalmo-oncology

AI/machine learning enhanced retinal monitoring

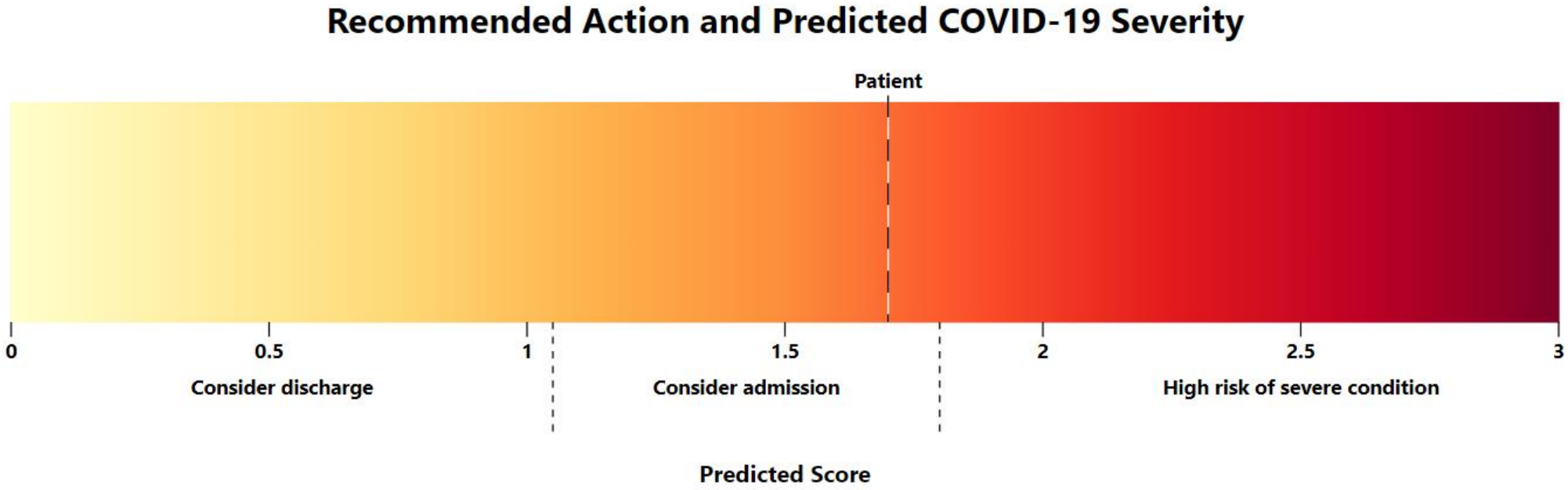
iMATCH

Digital science to develop rapid monitoring capabilities and early-warning systems

Building Data Rich Clinical Trials (CCE-DART)

- **Adaptive treatment decisions** over the course of the trial;
- **Longitudinal analysis of molecular data** collected prospectively and enabling intermediate tumor response assessment and **early treatment response predictive markers**;
- Incorporation of **novel complex multi-layer integrated biomarkers** to better stratify patients based on a systems cancer view perspective;
- **new statistical methodologies facilitating a more precise calculation of sample size as well as seamless designs**;
- infrastructure to collect and share real world data for retrospective/ prospective validation and data mining, with emphasis in supporting **new analytical algorithms (including AI-based models)**;
- **new imaging techniques to assess treatment efficacy** (i.e. beyond RECIST1.1);
- **standardized** procedures for data representation and analysis optimizing the use of modern technological platforms;

COVID-19 Risk in ONcology Evaluation Tool



https://coronet.manchester.ac.uk/

Longitudinal characterisation of haematological and biochemical parameters in cancer patients prior to and during COVID-19 reveals features associated with outcome, ESMO Open, 2021.

Establishment of CORONET; COVID-19 Risk in Oncology Evaluation Tool to identify cancer patients at low versus high risk of severe complications of COVID-19 infection upon presentation to hospital, medRXiv, 2021.

COVID-19 Risk in ONcology Evaluation Tool

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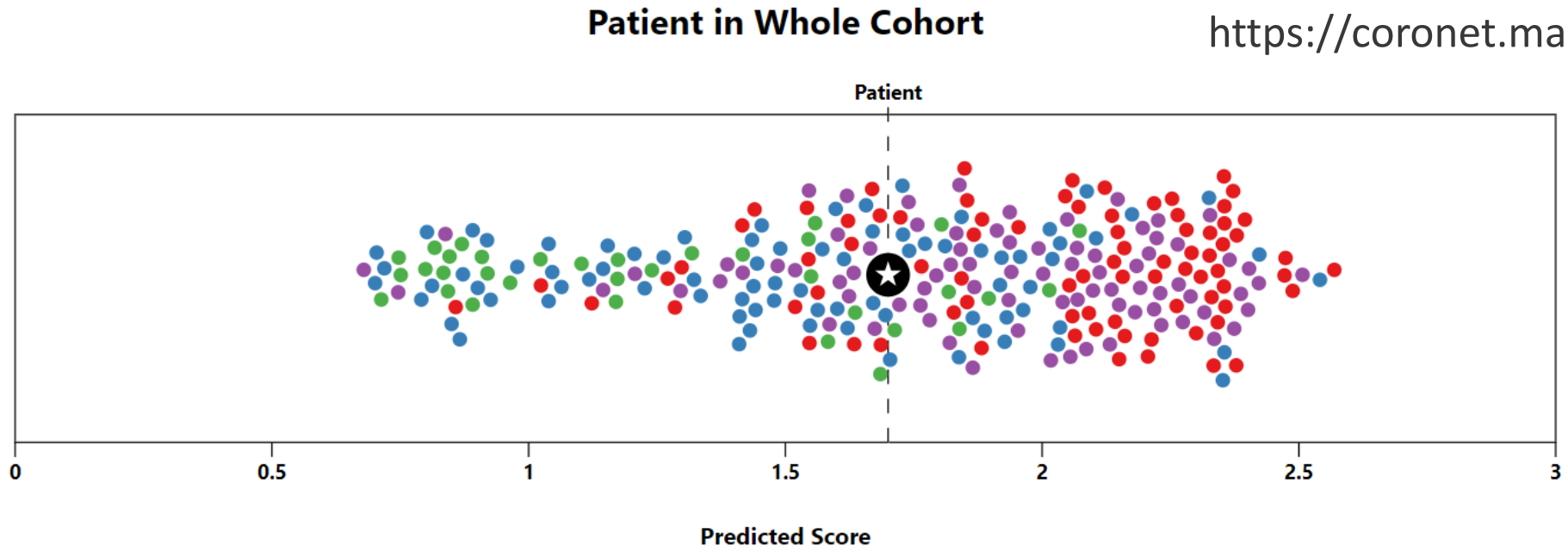

Hide Information

The plot shows all patients used for training of the CORONET model. Each dot represents an individual patient. The colour corresponds to their true outcome. The location on the X-axis is determined by the CORONET score based on the individual's data.

All patients are sorted from left to right according to the predicted CORONET score. The plot allows you to locate your patient in the whole cohort, considering both true outcomes and CORONET recommendations.

COVID-19 Risk in ONcology Evaluation Tool

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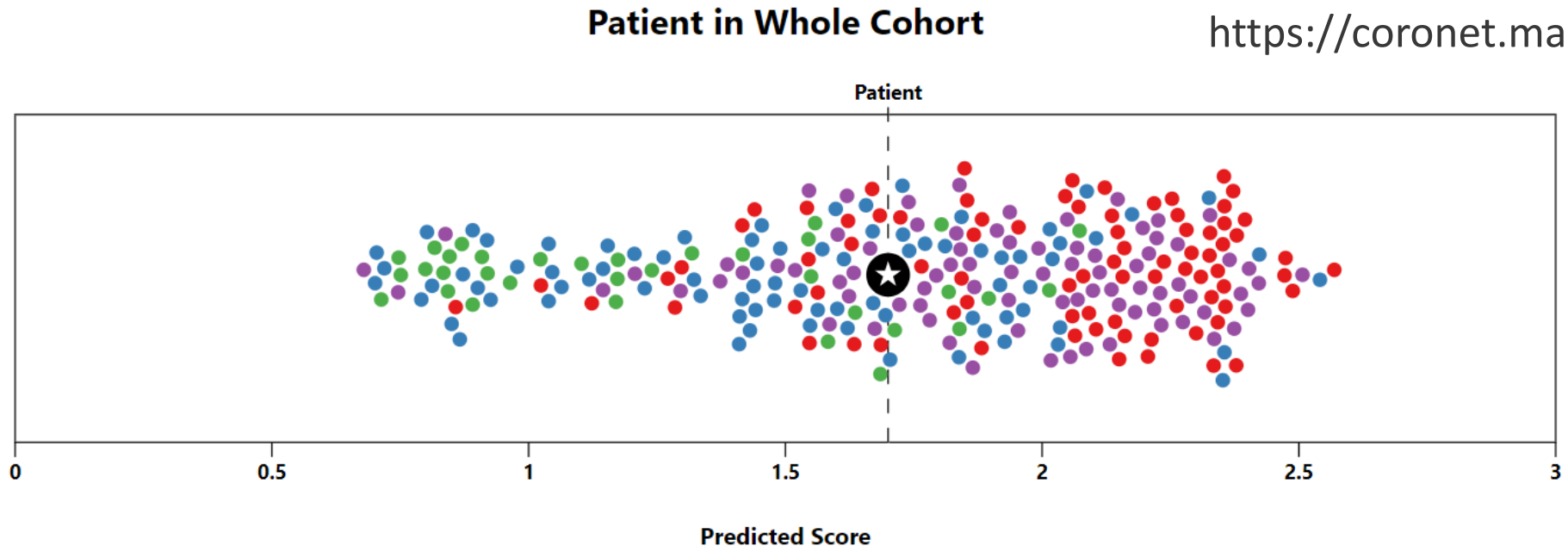

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COVID-19 Risk in ONcology Evaluation Tool

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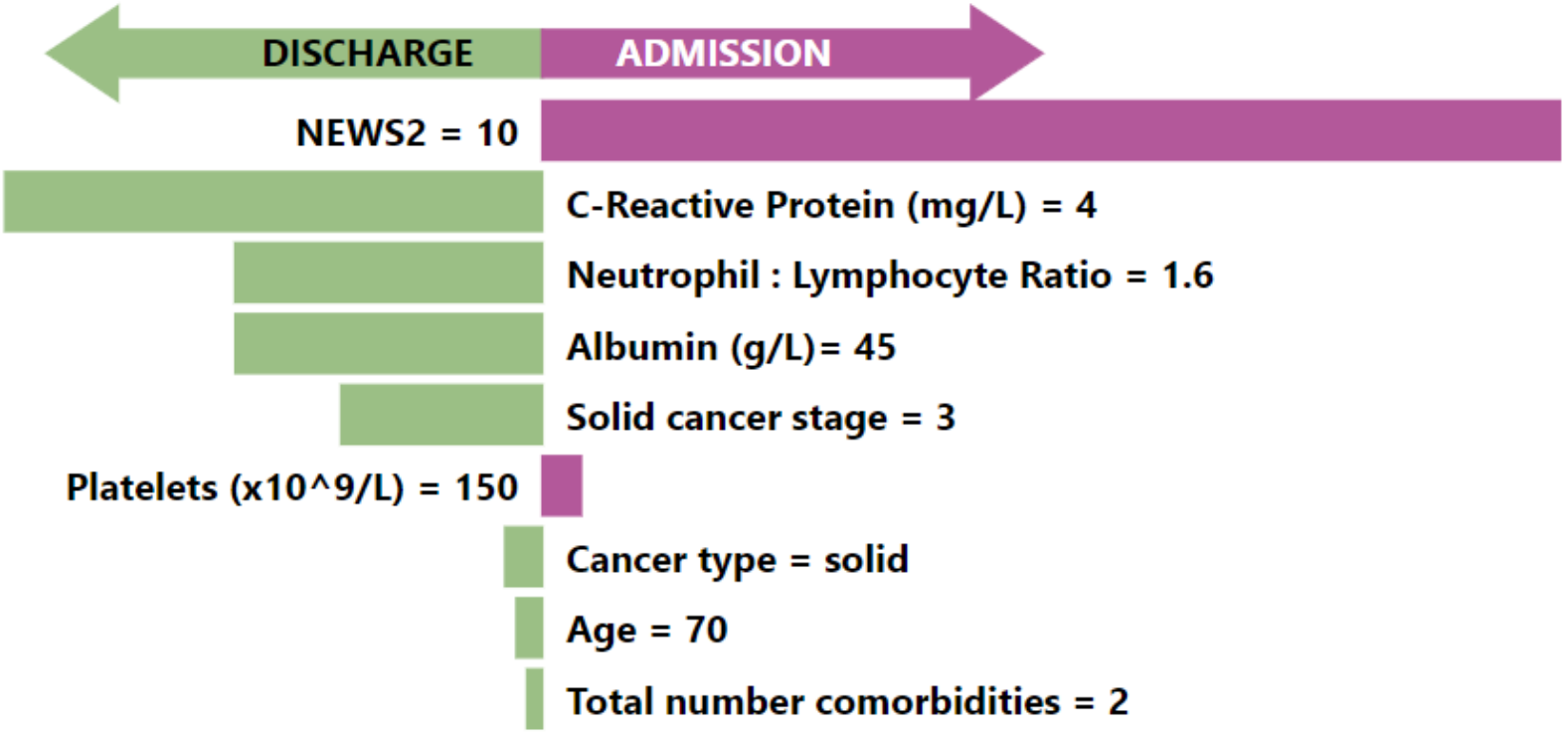
Important Features Contributing to the Model Prediction for Your Patient



The score recommends overall to: consider admission.

https://coronet.manchester.ac.uk/

- Personalised Clinical Trials
- Cytokine Release Syndrome
- Predicting/Detecting Toxicity Effects
  e.g. Acute Kidney Injury
  OCT scans
- SARS-CoV-2/Oncology

Toxicity Monitoring

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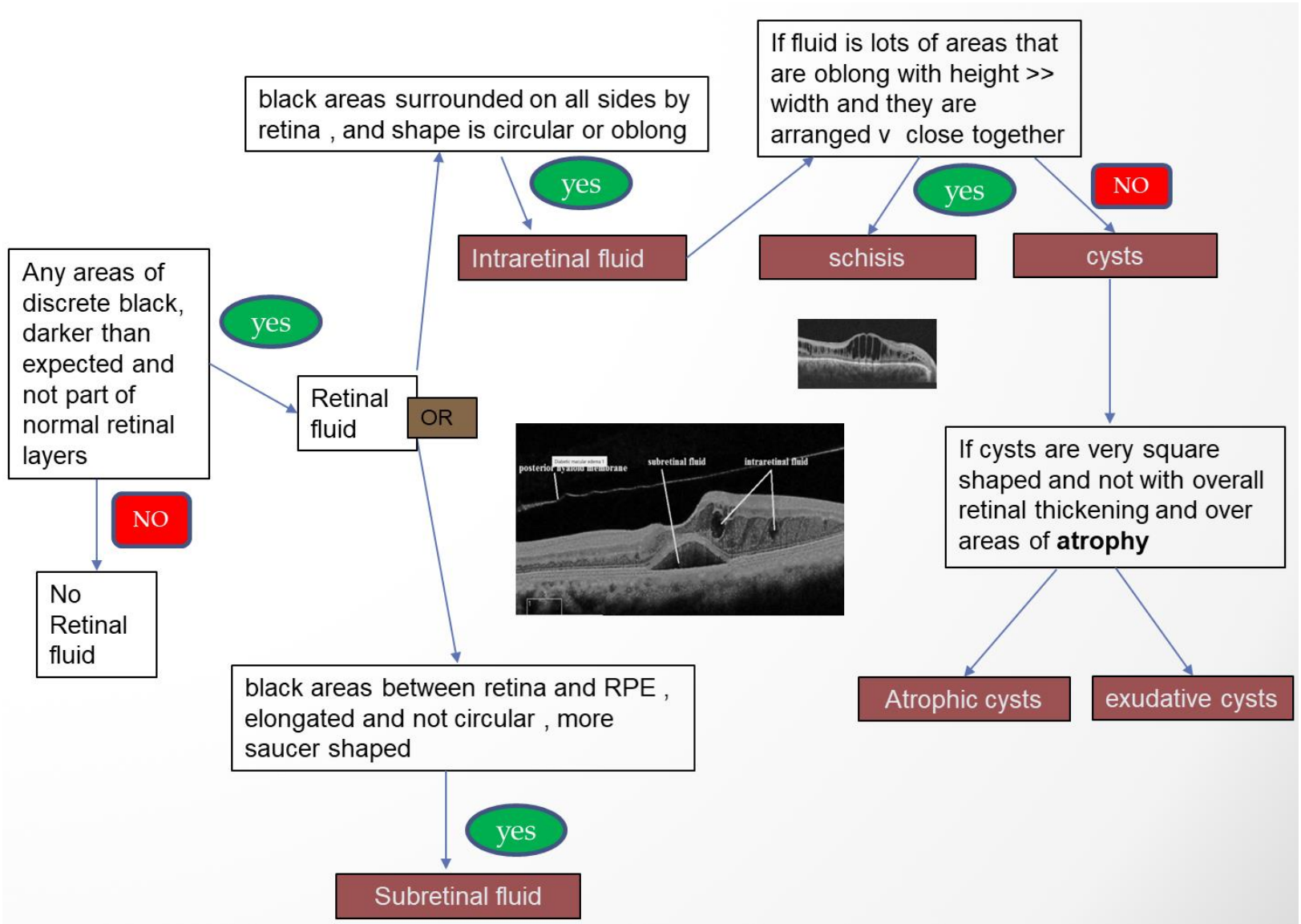

Molecular Tumour Boards (MTBs)

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Explainable & Knowledge-based AI

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Patient with prostate cancer, R130STOP mutation in *PTEN* gene
AI Model recommends clinical trial NCT02975934

because:

- R130STOP causes loss of PTEN function - COSMIC database
- PTEN protein is involved in homologous recombination repair - KEGG pathway
- Loss of PTEN function causes a defect in homologous recombination repair - source
- A defect in homologous recombination repair makes cells sensitive to DNA double strand breaks - source
- Inhibition of the DNA base excision repair pathway blocks DNA single strand break repair - KEGG pathway
- Blockage of DNA single strand break repair leads to creation of DNA double strand breaks - source
- PARP1 is part of the DNA single strand break repair pathway - KEGG pathway

- **-> PARP1 inhibition might be effective in this patient.**

- No PARP inhibitors are approved in the UK for treatment of prostate cancer.
- Rucaparib inhibits PARP1 - NCI thesaurus
- Rucaparib is approved in the UK for treatment of ovarian, fallopian tube and peritoneal cancers - NICE

§ (Rucaparib is well-tolerated)

- NCT02975934 includes rucaparib - AACT
- NCT02975934 is currently recruiting - AACT
- NCT02975934 has open sites in the UK - AACT
- NCT02975934 is enrolling patients with prostate cancer - AACT

Key Message

Digital Experimental Cancer Medicine Team

- Engaged clinical (oncology) partners.
- Access to experts and to data*.