ICED study

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- Dr Angela George – Consultant medical oncologist and clinical lead for genetics, CI
- Royal Marsden Hospital, London, UK

ICED study

- Inherited cancers – early diagnosis study
- Liquid biopsy screening for early diagnosis of cancers in patients with cancer-predisposition syndromes
- Application of circulating tumour DNA in early cancer detection for patients with cancer predisposition-syndromes

High-risk populations

- Li Fraumeni (TP53)
  - 90% lifetime risk of cancer, many different types
  - Currently no funded screening except breast MRI
- Lynch (MMR genes)
  - CRC, endometrial, brain, GU cancers
  - GI screening – colonoscopy
  - CAPP2/CAPP3 trial – aspirin
- Other syndromes : PTEN, CDH1, APC, STK11
  - Screening depending on cancer predisposition
  - Risk reducing surgery (CDH1, APC)

ICED cohorts

- Cohort 1: Li Fraumeni cohort
- Cohort 2: Gastrointestinal cohort (Lynch, Peutz Jeghers, PTEN, CHD1, APC)
- 40-50 patients in each cohort

Inclusion/ exclusion criteria

- Germline mutation carrier
- Adults with capacity to consent
- No history of malignancy other than non-melanomatous skin cancer or cervical carcinoma in situ (CIS) in the 5 years prior to the study enrolment
- Risk reducing mastectomy –not an exclusion criteria for Li Fraumeni

Liquid biopsies

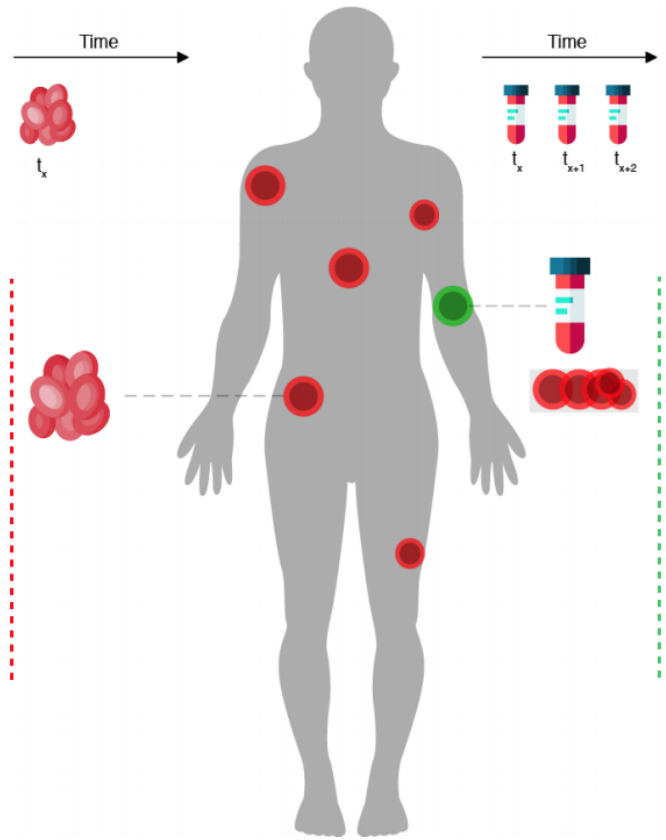
- Our aim is to develop a liquid biopsy (Blood and/or urine biomarker) test that can detect cancer early
- Circulating tumour DNA (ctDNA)
  - tumoral cell fragment floating in the blood stream/urine
  - some cancers shed these ctDNA earlier, some don't (breast, prostate)
  - addition to current available screening or for those cancers with no screening

Blood and urine biomarker (liquid biopsy)

- Aims of the study
  - Assess the use of ctDNA in high-risk patients
  - Correlate detection of tumour in ctDNA with scan results/histopathology
  - Identify groups of patient who would benefit from screening with ctDNA

Tissue Biopsy

- Invasive
- Painful/infections
- Not always feasible (metastatic sites)



Liquid Biopsy

- Minimally invasive
- Minimally painful
- Possible to collect serial samples
  - Tracking of clonal evolution (over time)
  - Early identification of resistance mechanisms
  - Monitoring treatment response
- Early detection of cancer
- Detection of recurrence
- Quantification of MRD

Study protocol/ methods

- Blood and urine sample every 6 months, during a period of 12 months (up to 3X)
- Symptom questionnaire
- Patients would have their own ongoing surveillance care as per their current medical team
- Clinical information (such as scan results/biopsy results) to correlate with the biomarker study

Symptom questionnaire

- To collect clinical information about new symptoms
- If relevant, refer to treating team/GP for further investigations

1. Have you noticed any <u>new symptom</u> in the past 6 months (such as *nausea*, *vomiting*, *diarrhoea*, *constipation*, *fatigue*, *loss of appetite*, *cough, headache, continuous fever or other*), which were not present before taking part in this study?

   Yes / No *(circle the answer that applies to you)*

2. If yes, can you explain <u>which symptom</u> did you experience? (Please write here the symptoms you have or had).

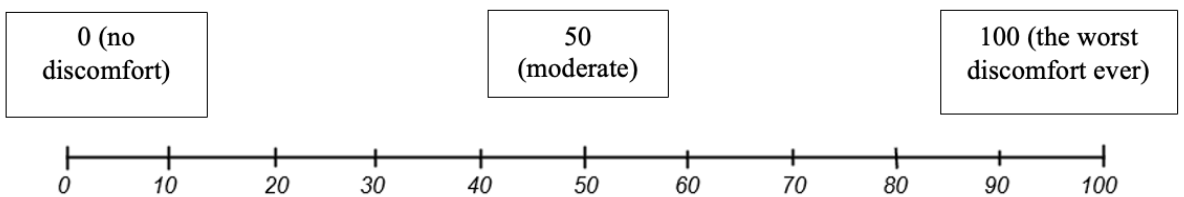
   _____

   If you have more than one symptom, you can request a new questionnaire to detail each one at a time.

3. If yes, <u>how severe</u> (at its worst) is the discomfort given by the new symptom, on a scale from 0 to 100 (where 0 is no discomfort and 100 is the most severe discomfort experienced so far).

   Mark an X on the scale or write your number here to indicate how bad your symptom can be at its worst:

   _____



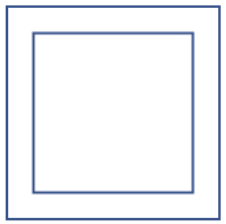
4. On average, <u>how long</u> does this new symptom last?
   - ○ comes a few minutes or a few times per day
   - ○ can last a whole day or a few days at once
   - ○ continuously or hasn't stopped since it started
   - ○ improving or has resolved with medication
   - ○ other:

     _____

5. We would like to know how good or bad your health is TODAY.
   This scale is numbered 0 to 100.
   100 means the <u>best</u> health you can image and
   0 means the <u>worst</u> health you can imagine.

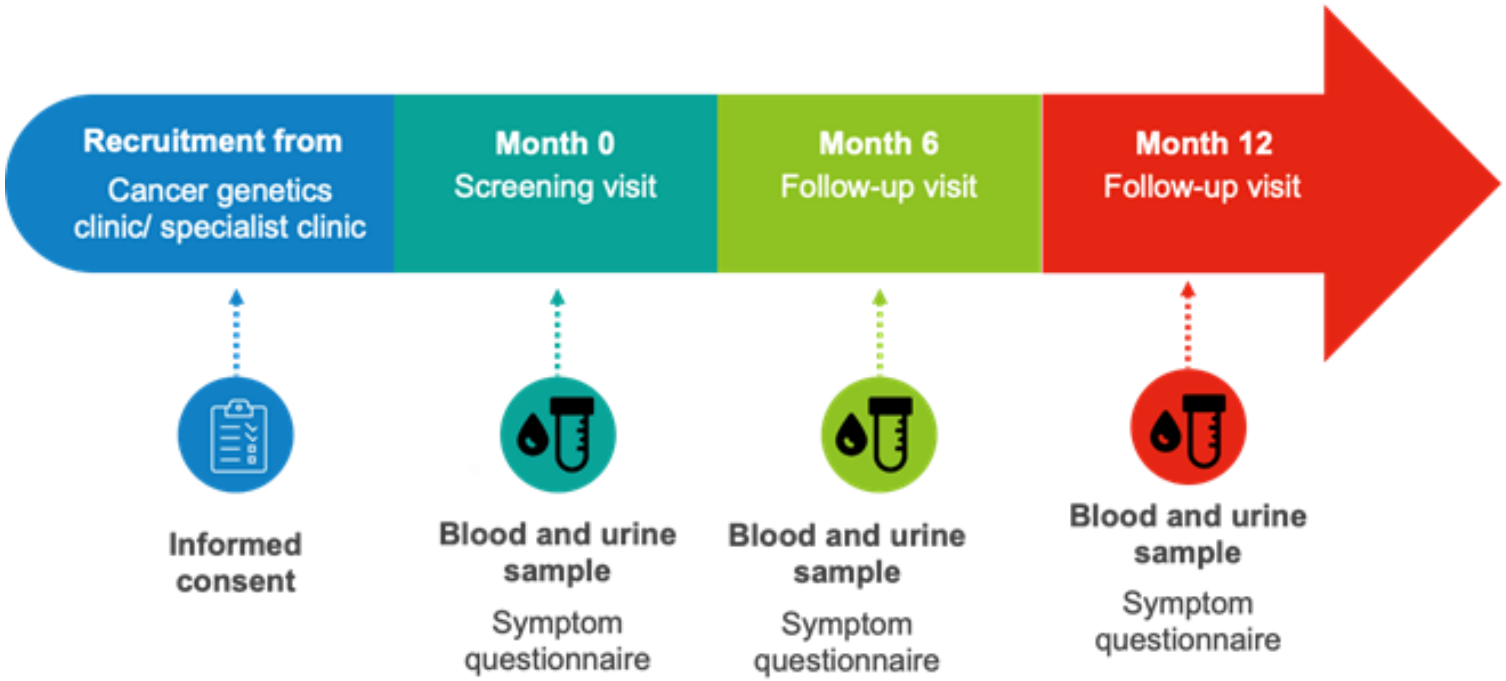
   Mark an X on the scale to indicate how your health is TODAY.

   Now, please write the number you marked in the box below.



Trial participation - patient timeline

Radiological and clinical surveillance as per local guideline



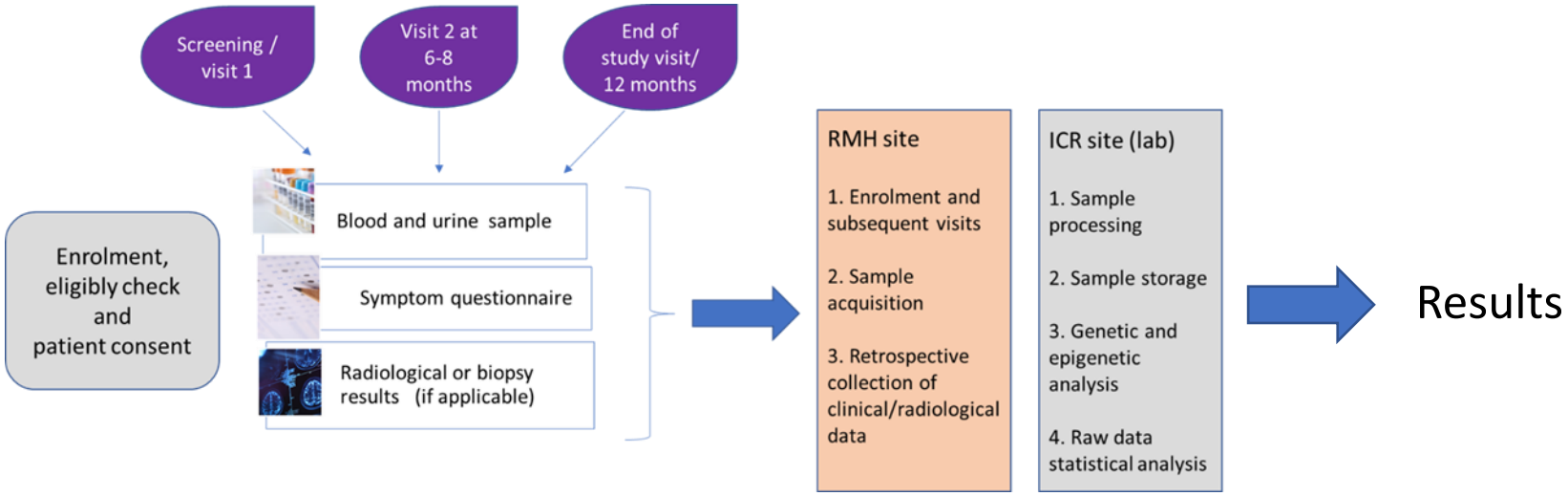
Sample processing

ctDNA analysis

Methylated DNA analysis

Laboratory analysis

- In the Institute of Cancer Research (ICR)- Sutton site of RMH
- Blood and urine samples will be frozen, then analyzed in batches
- If patients have any biopsies during their trial participation, tissue will be requested for analysis



ICED study team

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- Dr Richard Lee, Early diagnosis and detection Consultant
- Prof Ros Eeles, Consultant Oncogenetics
- Research nurse
- Study manager
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