SUPER-NEXT - COMPLETE WHOLE GENOME SEQUENCING FOR CANCER OF UNKNOWN PRIMARY

A prospective cohort study of patients with Cancer of Unknown Primary (CUP) to create a national knowledgebase and to improve treatment through understanding molecular biology, clinical characteristics, quality of life and psychosocial characteristics of CUP.

The information resource is a national cohort of CUP patients with associated biospecimens, clinical, quality of life, health economic and psychosocial data. The work also aims to determine the frequency of clinically actionable mutations in CUP tumour samples and evaluate the impact of performing molecular diagnostic tests. SUPER-NEXT is recruiting participants at 16 metro and rural sites across Australia; please see below for a full list of participating sites.

COMPLETE MOLECULAR TESTING FOR CUP PARTICIPANTS

As part of the SUPER-NEXT team's larger body of work, we currently offer participants two molecular tests; the targeted gene sequencing panel (Illumina TSO500) test, and the whole genome and transcriptome sequencing test. Both test reports are prepared simultaneously at the Peter MacCallum Cancer Centre (PMCC) and University of Melbourne Centre for Cancer Research (UMCCR) and results are fed back to clinicians within 4-6 weeks from receipt of a suitable tissue sample at Peter Mac.

Illumina TSO500 targeted gene sequencing

The TSO500 panel from our industry partner Illumina contains a custom set of genes or gene regions that are implicated as drivers in a range of cancer types. Some of these gene variants detected by this test may be targeted in clinical trials which are currently recruiting. This test can also provide information on whether the genome is unstable (microsatellite instability) and quantify the mutations present across the genome (tumour mutation burden), both of which are biomarkers of potential response to immune-based therapies.

Whole genome/transcriptome (WGTS) sequencing & CUP Prediction Algorithm (CUPPA)

WGTS analyses all of the genome, including both germline and somatic genes and non-coding regions and also measures their complete expression profile. Therefore, WGTS provides a deeper understanding of the genomic and gene expression landscape and reveals extra details not covered by targeted sequencing. WGTS data can reveal mutational and gene expression signatures which indicate tissue of origin of cancer and response to therapy. In addition, WGTS data can be harnessed so that unknown primary cancers can be matched to tumours of known origin using the CUP Prediction Algorithm (CUPPA) test, which matches the unknown origin DNA/RNA to DNA/RNA of known origin in a large WGTS reference set.

**Please note that the largest barrier to conducting molecular testing is the limited tissue remaining in samples following extensive CUP diagnostic workup. Ideally, we prefer to receive core biopsies or excisional specimens rather than cytology specimens and better efficacy is achieved with fresh tissue over formalin fixed, paraffin embedded (FFPE). It is not routine to re-biopsy patients as part of the study. However, should additional sample material be acquired, it is encouraged to collect and analyse the new tissue, over archived material, if this would be clinically appropriate.*

INCLUSION CRITERIA

1. Patient is considered to have a Cancer of Unknown Primary (CUP)* and has had:
   - Preliminary diagnostic work-up (including a detailed clinical assessment, CT of the chest, abdomen & pelvis)
   - Pathological review of tumour tissue
   - Gender appropriate diagnostic tests (e.g. Mammogram, PSA)
2. Can provide written informed consent

EXCLUSION CRITERIA

1. Under 18 years of age
2. ECOG ≥3
3. Uncontrolled medical or psychological conditions

* May have differential diagnosis, but no confirmed primary

STUDY REQUIREMENTS

For Patients:

- Provide 35mL blood sample at time of consent (for germline testing and cell-free nucleic acids)
- Consent to access patient archival diagnostic pathology specimen
- Consent to access Medicare/PBS data (optional)
- Consent to access medical records
- Consent to complete questionnaires at baseline and 3 months

For Clinicians:

Treating clinicians will also be asked to complete a short questionnaire around baseline, with a follow-up when any molecular results are released, to help ascertain the clinical significance of molecular results.

MORE INFORMATION

Please contact your local study coordinator or the SUPER-NEXT project team if you have any questions or would like to refer a patient to the study.

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