The Cancer Molecular Screening and Therapeutics (MoST) Program

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PROGRAM SUMMARY

The Molecular Screening and Therapeutics (MoST) program evaluates a new approach for testing the activity of drugs for the treatment of advanced cancer, with the overall goal of accelerating the clinical development of novel treatments. Up to 1000 patients with advanced cancer and unmet clinical need will be recruited over four years.
The two key components to the MoST program are:

- a molecular screening platform to identify clinically actionable variants; and
- multiple clinical substudies evaluating the activity of novel targeted treatments.

TARGET POPULATION

Patients with advanced solid cancer and no further standard treatment options. The program is open to patients with advanced cancer of any histologic type, with a particular focus on rare/neglected cancers.
It is the intention to screen patients whilst they are receiving the last line of standard therapy. Patients should in principle be willing to take part in a MoST substudy if found eligible.
Study entry criteria are outlined on p.2.

MOLECULAR SCREENING

The primary objective is to identify clinically actionable biomarkers in tumour tissue to be used to guide treatment.
Molecular screening is performed using a 393-gene panel and other molecular assays.
Possible treatment options identified through molecular screening are a MoST clinical substudy, other clinical trial, off-label treatment.

MoST clinical substudies recruiting patients:

- CDK4/6 inhibitor (Palbociclib) for patients with defects in the Rb pathway
- Immune checkpoint inhibitor combination (Durvalumab+Tremelimumab) for patients with no actionable mutations

REFERRAL PROCESS

To refer a patient please:

- Address referral letter to A/Prof Anthony Joshua and Dr Subotheni Thavaneswaran, The Kinghorn Cancer Centre, 370 Victoria Street, Darlinghurst NSW 2010; include your provider number and practice address
- Complete Enrolment Form and Data collection Form
- Include pathology report
- Send referral documents to most@garvan.org.au or fax to +61 2 9355 5872

ELIGIBILITY CRITERIA – MOLECULAR SCREENING

Inclusion criteria:

1. Aged 18 years and older
2. Pathologically confirmed advanced and/or metastatic solid cancer of any histologic type or an earlier diagnosis of a poor prognosis cancer
3. Sufficient and accessible tissue for molecular screening
4. Received and failed all standard anticancer therapy (where standard therapy exists) or have documented unsuitability for any further standard anticancer therapy – with the exception of current therapy patient is receiving (see note 1)
5. ECOG performance status 0, 1 or 2
6. Willing and potentially able to comply with study requirements

Exclusion criteria:

1. Suitable for standard therapy or accepted standard care, if the patient has not been previously treated
2. History of another malignancy within 2 years prior to registration unless adequately treated and determined free of progressive and metastatic disease for at least 6 months (see note 2)
3. For non central nervous system (CNS) cancers, patients with symptomatic CNS involvement of his/her cancer, unless the subject has stable neurological function without evidence of CNS progression within 12 weeks prior to study entry and does not require ongoing treatment with enzyme-inducing anticonvulsants or steroids
4. Comorbidities or conditions which may contraindicate participation, compromise assessment of key outcomes or limit ability to comply with protocol
5. Pregnancy, lactation, or inadequate contraception (see note 3)

Notes:

1. Failure is defined as either progression of disease (clinical or radiological) or intolerance to standard therapy resulting in the discontinuation of the therapy. Documented unsuitability for further standard therapy includes known hypersensitivity, organ dysfunction or other patient factors that would make therapy unsuitable.
2. Patients with a past history of adequately treated carcinoma-in-situ, basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or superficial transitional cell carcinoma of the bladder are eligible.
3. Women must be post-menopausal, infertile, or willing to use a reliable means of contraception. Lactating women must be willing to stop breastfeeding before enrolment onto a substudy. Men must have been surgically sterilised or willing to use a barrier method of contraception.