ASPiRATION Information Sheet for Clinicians

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Background

Tissue-based Comprehensive Genomic Profiling (CGP) may identify potentially targetable genomic alterations in up to 50% of patients with newly diagnosed metastatic non-squamous NSCLC and provide opportunities for these patients to access targeted treatments.

What is ASPiRATION?

The aim of the study is to investigate the clinical impact of upfront CGP in the management of newly diagnosed metastatic non-squamous NSCLC and assess the feasibility of CGP implementation nationally.

ASPiRATION is an observational cohort study, which will screen tumour tissue from 1000 people with newly diagnosed metastatic (de-novo or recurrent) non-squamous NSCLC using CGP. The study is part of a larger research project called The *Molecular Screening and Therapeutics (MoST) Program*, which aims to identify actionable mutations to match patients to targeted treatments.

In ASPiRATION, the expected frequency of actionable mutations with phase II/III data available to guide targeted treatment is 40 – 50%. Targeted treatment recommendations may be ASPiRATION clinical substudies, other clinical trials, or targeted treatments available outside a clinical trial (e.g. available on PBS, compassionate access or self-funded).

Referral

To refer a patient to ASPiRATION, a patients' treating oncologist is asked to:

- Review the eligibility criteria (refer to page 3)
- Complete an **ASPiRATION Referral Form** and provide a copy to most@garvan.org.au or to the study site along with a copy of the histopathology report
- Provide the patient with the **ASPiRATION General Information Sheet**

Histopathology

To be eligible for ASPiRATION, patients require sufficient FFPE tumour material to conduct SoC molecular profiling and concurrent CGP.

- Preferred samples are core biopsies (minimum surface area = 5mm^2, ideal surface area = 25mm^2)
- FNA samples (EBUS or CT guided) may be considered on a case-by case basis, provided there is sufficient tumour cell content within the FFPE / cell block
- Archival biopsies or lung resection specimens may be suitable in some cases
- Pleural effusion samples are not considered sufficient

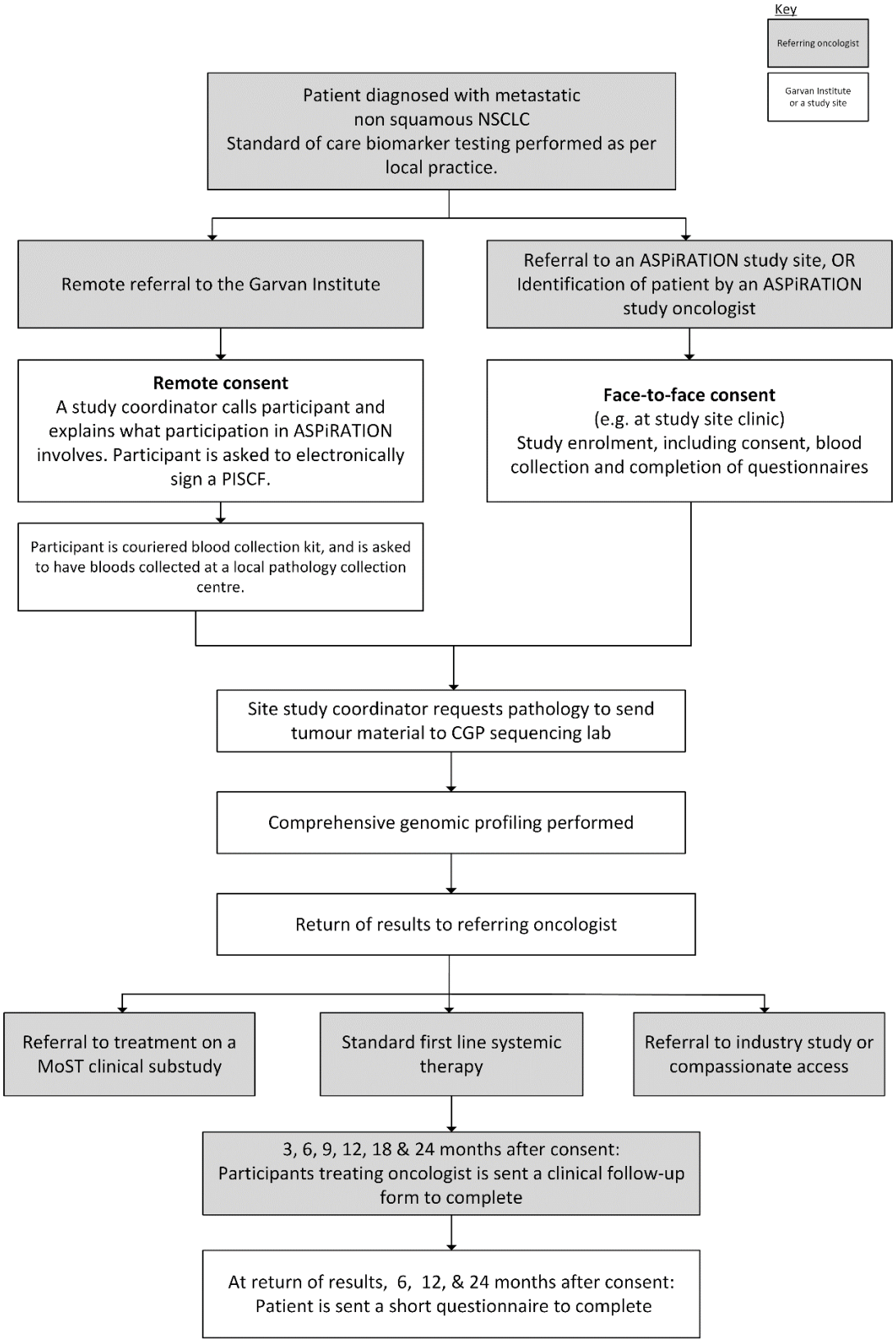
Turnaround times

The target turnaround time of CGP is approximately 3 weeks from the time that a study site receives a patients' signed consent form, however this may not always be possible, and measuring turnaround times is an endpoint of the study. In the case of unexpected delays to CGP results and recommendations, the referring clinician will be notified by email, with a reason for the delay.

What does participation involve for a participant?

Participants can be enrolled in ASPiRATION via a remote consent model (e.g. patients who undergo diagnostic investigation at other centres), or at a study site.

Figure 1: ASPiRATION Flow diagram



Eligibility Criteria

Inclusion Criteria

Patients must fulfil all of the following criteria to be eligible for this study.

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Aged 18 years and older.
Newly diagnosed pathologically confirmed metastatic non-squamous non-small cell lung cancer that have not commenced systemic therapy. *Exception: patients with a typical pattern of disease recurrence following treatment with curative intent may not require a confirmatory repeat biopsy, unless the diagnosis is unclear, such as an isolated pulmonary nodule, in which case repeat biopsy should be considered per standard practice. In exceptional circumstances, patients may be considered eligible without the need for histopathological confirmation of disease recurrence after approval from the ASPiRATION study chair or delegates;* *Mixed or other histologies:* • *Eligible: Mixed adenosquamous where adenocarcinoma is dominant, carcinoma not otherwise specified (NOS) favouring adenocarcinoma or sarcomatoid carcinoma* • *Ineligible: Mixed small cell lung cancer or Large cell neuroendocrine carcinoma*
ECOG performance status 0 or 1.
Sufficient and accessible tissue for molecular screening. • *Preferred samples are core biopsies (minimum surface area = 5mm^2, ideal surface area = 25mm^2)* • *FNA samples (EBUS or CT guided) may be considered on a case-by case basis, provided there is sufficient tumour cell content within the FFPE / cell block.* • *Archival biopsies or lung resection specimens may be suitable in some cases* • *Pleural effusion samples are not considered sufficient*
Willing and able to comply with study requirements, including: • *Willing to provide signed written informed consent to participate in molecular profiling and linkage to Medicare data, and* • *In principle willing to consider participation in a MoST sub-study if found to have an appropriate biomarker.*
Life expectancy of at least 12 weeks.
Inclusion Criteria *(Patients must fulfil all of the following criteria to be eligible for this study).*

Exclusion Criteria

Patients with any one of the following characteristics will not be eligible for this study.

Current enrolment or participation in another clinical study with an unregistered investigational product during the last 12 months. *Current participation in an observational (non-interventional) clinical study or during the follow-up period of an interventional study must first be discussed the study team before study enrolment.*
Previous treatment for metastatic non-squamous NSCLC. • *For patients with symptomatic or bulky disease, where it would be detrimental to delay treatment, systemic therapy may be commenced at the clinician's discretion whilst awaiting CGP results (this is not 'previous' treatment). Patients who have had prior treatment with curable intent are eligible.* • *Up to 2 cycles of systemic treatment may be permitted prior to treatment on an ASPiRATION therapeutic substudy.*
Comorbidities or conditions (e.g. psychiatric) which may contraindicate participation and/or ability to receive any systemic therapy(s).
History of another primary malignancy. • *Note: The following are permitted:* • *Malignancy treated with curative intent and with no known active disease within 2 years before consent to molecular screening and of low potential risk for recurrence* • *Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease* • *Adequately treated carcinoma in situ without evidence of disease*

Eligibility Scenarios

40-year-old male, non-smoker, required decompressive surgery of bone lesion, tissue adenocarcinoma, EGFR/ALK/ROS1 wild type, PD-L1 25%, currently post-operative radiation.	**Eligible***
35-year-old female, non-smoker, metastatic NSCLC diagnosed in November 2020. EGFR/ALK/ROS1 wild type, PD-L1 0%. Cycle 1 IMPower150 administered December 30th. Site submit ASPiRATION referral prior to Cycle 2.	**Not eligible** as patient has commenced systemic therapy prior to consent
50-year-old male, metastatic NSCLC with symptomatic brain metastasis, resected 2 months ago, subsequent WBRT. Stage IIIA NSCLC resected 3 years ago with adjuvant chemotherapy. Has not started systemic treatment for metastatic disease.	**Eligible***
40-year-old male, non-smoker, resected brain lesion - adenocarcinoma, intestinal subtype. PET no GI primary. Radiologically lung cancer (lung lesion, adrenal and bone metastasis). EGFR/ALK/ROS1 wild type. Undergoing RT to resection bed, and has not started systemic treatment.	**Eligible***
60-year-old female, non-smoker. Initially diagnosed in 2017, primary lung resection, stage IIB. Disease reoccurrence in 2020 of metastatic disease, with radiological confirmation of brain metastasis treated with radiation, no pathological confirmation. 2017 lung sample tested for EGFR/ALK/ROS1 wild type.	**Requires review by study Investigators,** as there is no recent histopathology to confirm metastatic disease.

** provided there is adequate tissue and all other inclusion criteria are met and no exclusion criteria.*

FAQ's

Can a patient commence treatment whilst awaiting CGP results?

For patients with symptomatic or bulky disease, where it would be detrimental to delay treatment, systemic therapy may be commenced whilst awaiting CGP results. In this situation, up to 2 cycles of standard of care treatment are allowed prior to commencing an ASPiRATION therapeutic substudy. However, industry studies may not allow prior systemic therapy (refer to the entry criteria for the industry study).

What are possible factors that may cause delays in obtaining CGP results?

- Difficulty contacting patients
- For remote consents, delays in participants returning signed consent (study sites are unable to access tissue without signed consent).
- Delays in pathology labs providing tumour tissue
- Low DNA and/or RNA extraction yield/s (repeat extraction may be required).

Who receives the MTB Report when CGP is complete?

The referring clinician, and any associated health practitioners included on the referral form are sent a copy of the MTB Report. Additionally, a patient is notified by email/phone when CGP is complete. A patient is only provided with a copy of the report if requested.