MSAC Application 1811

Testing for MET overexpression & amplification in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) to determine eligibility for treatment with PBS subsidised savolitinib in combination with osimertinib

PICO Set

Population

Describe the population in which the proposed health technology is intended to be used:

The population proposed comprises patients with locally advanced (Stage IIIB/C) or metastatic (Stage IV) non-small cell lung cancer (NSCLC), who have progressed on or after treatment with osimertinib.

The biomarker is MET protein overexpression determined by immunohistochemistry (IHC) and/or MET gene amplification determined by fluorescence in situ hybridisation (FISH) which is present in approximately 34% of patients progressing post osimertinib (de Marinis et al., 2025). The MET overexpression and/or amplification tests would comprise additional tests for these patients. Patients would be required to undergo a biopsy to retrieve a tumour tissue sample at the point of progression on or after osimertinib treatment. The primary objective of this application is to request two new MBS items for these technologies to determine the MET status of locally advanced or metatstatic NSCLC patients who have progressed on or after treatment with osimertinib.

Test Comparator:

Specify any characteristics of patients with, or suspected of having, the medical condition, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian healthcare system in the lead up to being considered eligible for the technology:

Lung cancer is the fifth most commonly diagnosed cancer in Australia and the most common cause of cancer-related death, accounting for 17.0% of cancer-related deaths (AIHW, 2024). NSCLC is the most common type, representing approximately 85% of all diagnoses (Cancer Council Australia, 2022). In Australia, EGFR mutations account for 12% to 36% of NSCLC and confer sensitivity to EGFR-TKIs (Kim et al., 2020; Peters, Bowden, Carpenter, Lewis, & Solomon, 2014; Yang et al., 2024)

For patients with locally advanced (Stage IIIB/C) or metastatic (Stage IV) NSCLC who are not amenable to curative surgery or radiotherapy, and whose tumours harbour EGFR mutations, the first-line (1L) standard-of-care (SoC) is osimertinib monotherapy. Despite the strong performance of osimertinib monotherapy, progression is still frequent due to the emergence of resistance pathways, with an approximate median time to progression of 19 months in 1L EGFRm NSCLC (Soria et al., 2018).

Alterations to the mesenchymal-epithelial transition (MET) gene have been identified as the most frequent resistance mechanism to osimertinib treatment (Leonetti et al. 2019), occurring in approximately 34% of patients (Ahn et al. 2022). MET encodes a tyrosine kinase receptor which is activated by hepatocyte growth factor (HGF) and is found primarily in epithelial cells (Trusolino et al. 2010). Downstream MET signalling activates RAS-MAPK, PI3K/AKT, and STAT3 pathways and leads to cell migration, invasion, proliferation and cell survival (Coleman et al. 2021, Comoglio et al. 2018). MET overexpression or amplification has been recognised as a pivotal EGFR-treatment resistance mechanism because it bypasses EGFR inhibition through the activation of these downstream pathways (Gomatou et al. 2023). In clinical settings, MET alterations can be assessed using IHC to determine overexpression, by FISH to determine amplification of the MET gene, or by NGS to detect exon 14 skipping mutations and amplifications (Feldt SL and Bestvina CM 2023). In SAFFRON, patients were selected based on IHC overexpression (IHC 3+ in ≥90% of tumour cells) using the Roche CONFIRM anti-Total c-MET (SP44) Rabbit Monoclonal Primary Antibody or

FISH amplification (≥10 MET gene copies) using the Abbott Vysis MET Spectrum Red FISH probe kit. Notably, NGS is not currently considered an appropriate technology to detect MET resistance for two reasons. Firstly, exon 14 skipping mutations occur de novo in lung adenocarcinomas and have yet to be reported as a resistance mechanism to osimertinib (Gomatou et al. 2023). Secondly, FISH amplification is determined by the ratio of MET to chromosome 7 centromere (CEP7) copies to distinguish between polysomy and true amplification (Coleman et al. 2021). NGS assays are therefore not recommended as they may not control for CEP7 to comparably evaluate gene copy number gain to FISH (Piper-Vallillo et al. 2020).

Currently no targeted treatments are available for MET-driven resistance in post-osimertinib patients. Patients who progress post osimertinib are not routinely tested for MET amplification/overexpression; instead, they usually receive platinum-based doublet chemotherapy. As such, there remains a significant unmet clinical need for effective treatments for patients with NSCLC who have progressed on osimertinib

Clinical trial results (de Marinis et al., 2025) show that savolitinib plus osimertinib when used in patients who have progressed on osimertinib, results in a clinically meaningful improvement in response rates and progression-free survival.

Provide a rationale for the specifics of the eligible population:

Non-Small Cell Lung Cancer (NSCLC) with EGFR mutations who are initially treated with the EGFR-targeted medicine Tagrisso (osimertinib) are a specific subtype of lung cancer patients. Despite the strong performance of osimertinib monotherapy, progression is still frequent due to the emergence of resistance pathways.

AstraZeneca is planning to seek PBS listing for the combination of savolitinib and osimertinib to treat adult patients with locally advanced or metastatic NSCLC who have progressed on or after osimertinib treatment, with MET overexpression and/or amplification as the mechanism of resistance. Savolitinib is a highly specific inhibitor of the MET tyrosine kinase receptor. Results from the Phase II SAVANNAH trial demonstrate that osimertinib resistance due to MET overexpression and/or amplification can be overcome by the concomitant use of savolitinib and osimertinib, leading to clinically meaningful and statistically significant improvements in progression-free survival.

For the purposes of this MSAC application, changes to MET can be detected in two ways. Firstly, an IHC stain can be applied to tumour cells that enables anatomical pathologists to visualise the concentration of the MET receptor on the tumour cell wall. Changes can also be detected using FISH, which binds a fluorescent marker to the MET gene, allowing pathologists to count the number of copies present in each cell.

Screening data from the Phase II SAVANNAH study suggests the anticipated positivity rate of MET overexpression or amplification is 34% (see Figure 1). In this study, 29% were IHC-positive, whilst 20% were FISH-positive, with the discordance indicated in Figure 1. Due to the difference in cost between the two services, the most efficient use of healthcare resources would be to first test all eligible patients with IHC. The remaining 71% of IHC-negative patients would then be tested with FISH.

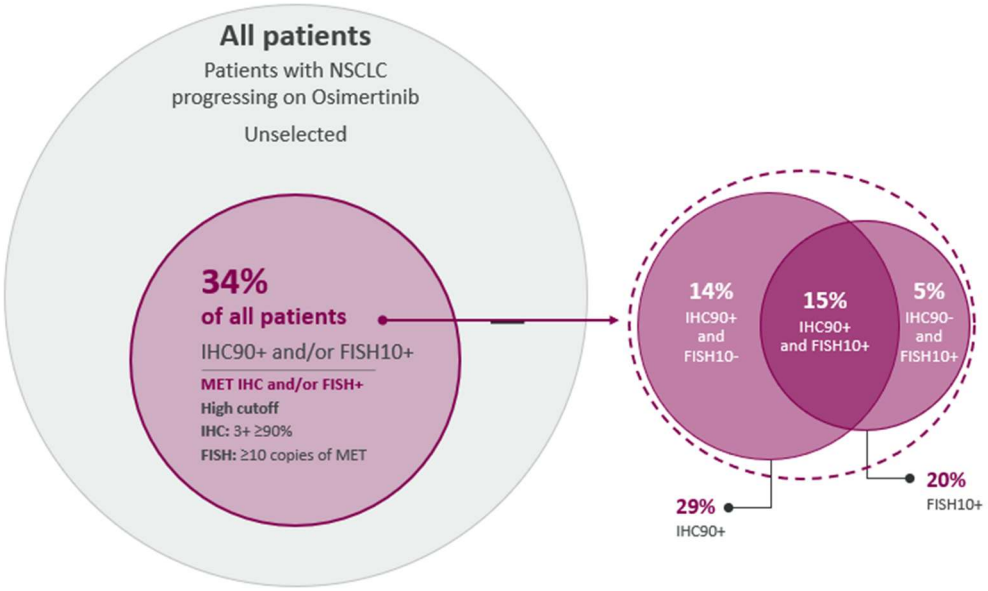


Figure 1: The Phase II SAVANNAH trial determined the prevalence of MET overexpression or amplification would be 34% when applying the SAFFRON IHC and FISH cut-offs. Of note, prevalence appeared similar between lines of therapy and regions (Ahn et al. 2022).

IHC and FISH can identify MET changes in NSCLC patients and influence their course of treatment but currently these tests are not routinely performed. There are targeted therapies specifically designed to treat cancers with EGFR mutations which have developed MET resistance. Such treatment will provide a more personalised and more effective treatment approach than current standard treatments.

Are there any prerequisite tests?

No

Are the prerequisite tests MBS funded?

No

Provide details to fund the prerequisite tests:

Testing for MET resistance post osimertinib is not routinely performed as there are no currently available MET-targeted therapies

Intervention

Name of the proposed health technology:

MET immunohistochemistry (IHC) and/or MET fluorescence in situ hybridisation (FISH) for all patients with prior osimertinib treatment followed by targeted therapy for those with MET overexpression/amplification

Describe the key components and clinical steps involved in delivering the proposed health technology:

Biopsy practice at disease progression is variable across Australian clinical centres treating EGFR-mutated NSCLC. Although there has been a shift away from biopsying in this setting due to the upfront treatment of osimertinib removing EGFR T790M resistance mutations as a target, KOL advice is that biopsy is still being used to determine small-cell lung cancer (SCLC) transformation. As a result, expert clinical opinion indicates that around 25% of patients currently undergo biopsy in the progressed setting.

The standard-of-care treatment for these patients has been to offer platinum-based doublet chemotherapy as the next line of therapy.

With the proposed availability of the savolitinib plus osimertinib combination on the PBS, this clinical pathway will change. After progression on osimertinib, patients will undergo a biopsy to obtain tumour tissue for IHC and/or FISH testing to evaluate for MET amplification or overexpression. If a MET-driven resistance mechanism is confirmed, eligible patients can then be considered for treatment with the combination of savolitinib and osimertinib, as supported by clinical evidence.

Identify how the proposed technology achieves the intended patient outcomes:

In patients diagnosed with non-small cell lung cancer (NSCLC) who are positive for the EGFR mutation following a tissue biopsy, osimertinib is the currently preferred first-line therapy. While osimertinib is highly effective in achieving a high response rate and prolonged disease control, resistance to the treatment inevitably develops. Among the most common mechanisms of acquired resistance is MET overexpression or amplification, occurring in approximately 34% of cases (Ahn et al., 2022).

Currently, MET overexpression and amplification are not considered actionable genetic mutations due to a lack of targeted therapies available on the PBS. As a result, these patients typically transition to platinum-based chemotherapy as their next line of therapy.

Identification of resistance mechanisms to guide subsequent treatment is recommended in treatment guidelines (Bazhenova et al., 2024; Hendriks et al., 2023). However, there are currently no approved, chemotherapy-free, biomarker-selected treatment options specifically indicated to treat MET overexpression and/or amplification-driven resistance for patients with EGFR-mutated NSCLC following progression on first-line osimertinib. As such, following progression on osimertinib, if an appropriate clinical trial is not available, patients typically transition to platinum-based chemotherapy as their next line of therapy. Among patients with tumour MET-driven resistance mechanisms, there remains an unmet need for a treatment approach that inhibits the activity of both EGFR mutation and MET overexpression and/or amplification that can be administered orally and is also chemotherapy-free, to avoid the toxicity associated with chemotherapy and overcome lack of efficacy caused by resistance to previous treatments.

AstraZeneca is planning to seek PBS listing for the combination of savolitinib and osimertinib to treat adult patients with locally advanced or metastatic NSCLC who have progressed on or after osimertinib treatment, with MET overexpression and/or amplification as the mechanism of resistance. Savolitinib is a highly specific inhibitor of the MET tyrosine kinase receptor. Results from the Phase II SAVANNAH trial demonstrate that osimertinib resistance in EGFR-mutated NSCLC with MET overexpression and/or amplification can be overcome by the concomitant use of savolitinib and osimertinib, leading to clinically meaningful and statistically significant improvements in progression-free survival. It is anticipated the Phase III SAFFRON trial will confirm this earlier study, results of which will underpin this application and the PBAC co-dependent application.

The PBS listing criteria for the savolitinib and osimertinib combination would require patients to show evidence of MET overexpression and/or amplification, verified through IHC and/or FISH testing. Therefore, MBS items xxx and xxx is proposed to include MET overexpression and/or amplification.

Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?

No

Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:

Similar MBS Items for IHC (Items 72814, 72848) and FISH (Items 73341, 73344, 73430) have generic descriptors not specific to a trademark. It is anticipated that laboratories will develop in-house IVD solutions that meet the NPAAC Companion Diagnostic standards, and that manufacturers, including the clinical trial manufacturers, may register their IVDs on the ARTG.

Are there any proposed limitations on the provision of the proposed health technology delivered to the patient:

The tissue biopsy will be the primary limitation on the provision of the proposed technology.

Provide details and explain:

The introduction of savolitinib in combination with osimertinib is expected to lead to an increase in the number of biopsies to determine MET status. Approximately 90% of patients will be fit enough to undergo a tissue biopsy, with approximately 10% experiencing rapid clinical deterioration, refractory disease, severe competing illness or biopsy refusal (Chouaid et al. 2014, Al-Kateb et al. 2015, Magios et al. 2021). KOLs estimate that, with the availability of a new approved targeted treatment on osimertinib progression, biopsy rates could increase to approximately 90% among progressed patients. This reflects the expectation that nearly all patients with sufficient tissue at progression, aside from those who are unfit or who refuse, would be tested. Furthermore, if a targeted and well-tolerated treatment is available, it is anticipated that even more patients would be willing to undergo biopsy, potentially reducing the rate of patient refusal.

If applicable, advise which health professionals will be needed to provide the proposed health technology:

A registered anatomical pathologist is responsible for conducting the detection, diagnosis and reporting of the pathology result to help guide and determine treatment.

If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:

N/A

If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:

A registered anatomical pathologist is responsible for conducting the detection, diagnosis and reporting of the pathology results which guide and determine treatment. A specialist (e.g. throracic surgeon, interventional radiologist) collects the specimen and a test request form (e.g. medical oncologist, thoracic surgeon) for IHC and FISH testing of MET alterations.

Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?

No

Indicate the proposed setting(s) in which the proposed health technology will be delivered:

MET testing is conducted by an accredited anatomical pathology laboratory

Is the proposed health technology intended to be entirely rendered inside Australia?

Yes

Provide additional details on the proposed health technology to be rendered outside of Australia:

N/A

Comparator

Nominate the appropriate comparator(s) for the proposed medical service (i.e., how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian healthcare system). This includes identifying healthcare resources that are needed to be delivered at the same time as the comparator service:

The proposed comparator is no testing and the standard platinum-based doublet chemotherapy.

List any existing MBS item numbers that are relevant for the nominated comparators:

Whilst no MBS items are relevant for the nominated comparator, note that the same technology on the MBS has been approved for the proposed medical services, see IHC MBS items: 72814, 72848

For FISH, see MBS items: 73341, 73344, 73430

Provide a rationale for why this is a comparator:

Currently, patients who progress on or after treatment with osimertinib are not tested for MET amplification/overexpression; instead, they usually receive platinum-based doublet chemotherapy. The proposed intervention is expected to replace this clinical management with testing for MET amplification/overexpression, and if positive, treating with savolitinib plus osimertinib. Therefore, the proposed comparator is no testing and the standard platinum-based doublet chemotherapy.

Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator?

Partial (in some cases, the proposed technology will replace the use of the comparator, but not all)

Outline and explain the extent to which the current comparator is expected to be substituted:

When MET overexpression and/or amplification are taken into account, approximately 34% of patients with progression on osimertinib will have evidence of MET-driven resistance. These patients will become eligible for treatment with the savolitinib plus osimertinib combination. Conversely, the remaining 66% of patients, who test negative for MET resistance, will continue to receive platinum-based chemotherapy, which represents the current standard comparator treatment.

In practice, this means that while the introduction of the savolitinib plus osimertinib combination will provide a new treatment pathway for a specific biomarker-defined subgroup (about one-third of patients), platinum-based chemotherapy will remain the

primary treatment option for the majority (two-thirds) of patients who do not exhibit MET alterations. Thus, the extent to which the current comparator will be substituted is proportional to the incidence of MET-positive resistance among patients progressing on osimertinib, with a limited but meaningful shift in treatment allocation toward the new combination therapy.

Outcomes

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

Health benefits

Outcome description – include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Treatment with savolitinib plus osimertinib, in patients who have progressed on osimertinib and are confirmed to have MET-driven resistance, provides significantly improved outcomes compared to standard platinum-based chemotherapy. In the phase II SAVANNAH study, the investigator-assessed confirmed objective response rate (ORR) was 56.3% (95% CI: 44.7%–67.3%), with a median duration of response of 7.1 months (95% CI: 5.6–9.6 months) and a median progression-free survival (PFS) of 7.4 months (95% CI: 5.5–7.6). These findings were corroborated by blinded independent central review, which reported a confirmed ORR of 55.0% (95% CI: 43.5%–66.2%), a median duration of response of 9.9 months (95% CI: 6.0–13.7), and a median PFS of 7.5 months (95% CI: 6.4–11.3). These results highlight the clinical benefit of the combination in this biomarker-selected patient population.

Proposed MBS items

How is the technology/service funded at present? (e.g., research funding; State-based funding; self-funded by patients; no funding or payments)

No funding

Provide at least one proposed item with their descriptor and associated costs, for each Population/Intervention:

Table 1 Proposed MBS item for IHC

MBS item number (where used as a template for the proposed item)	TBC
Category number	6-Pathology Services
Category description	P5 – Tissue Pathology
Proposed item descriptor	Immunohistochemical examination of biopsy material by immunoperoxidase or other labelled antibody techniques using the mesenchymal-epithelial transition (*MET*) antibody of tumour material from a patient diagnosed with recurrent epidermal growth factor receptor (*EGFR*)-mutated non-small cell lung cancer to determine if requirements for access to savolitinib in combination with osimertinib as listed under the Pharmaceutical Benefits Scheme (PBS) are fulfilled.
Proposed MBS fee	$74.50
Indicate the overall cost per patient of providing the proposed health technology	TBC
Please specify any anticipated out of pocket expenses	No gap
Provide any further details and explain	N/A

Table 2 Proposed MBS item for FISH

MBS item number	TBC
Category	6 – Pathology Services
Group	P7 – Genetics
Proposed item descriptor	Fluorescence in situ hybridisation (FISH) test of tumour tissue from a patient diagnosed with recurrent epidermal growth factor receptor (*EGFR*)-mutated non-small cell lung cancer, and with documented evidence of mesenchyma-epithelial transition (*MET*) expression by immunohistochemical (IHC) examination giving a staining intensity score of 2+ or less, requested by a specialist or consultant physician, to determine if requirements relating to *MET* gene amplification status for access to savolitinib in combination with osimertinib as listed under the Pharmaceutical Benefits Scheme (PBS) are fulfilled.
Proposed MBS fee	$400.00
Indicate the overall cost per patient of providing the proposed health technology	TBC
Please specify any anticipated out of pocket expenses	No gap
Provide any further details and explain	N/A

Algorithms

PREPARATION FOR USING THE HEALTH TECHNOLOGY

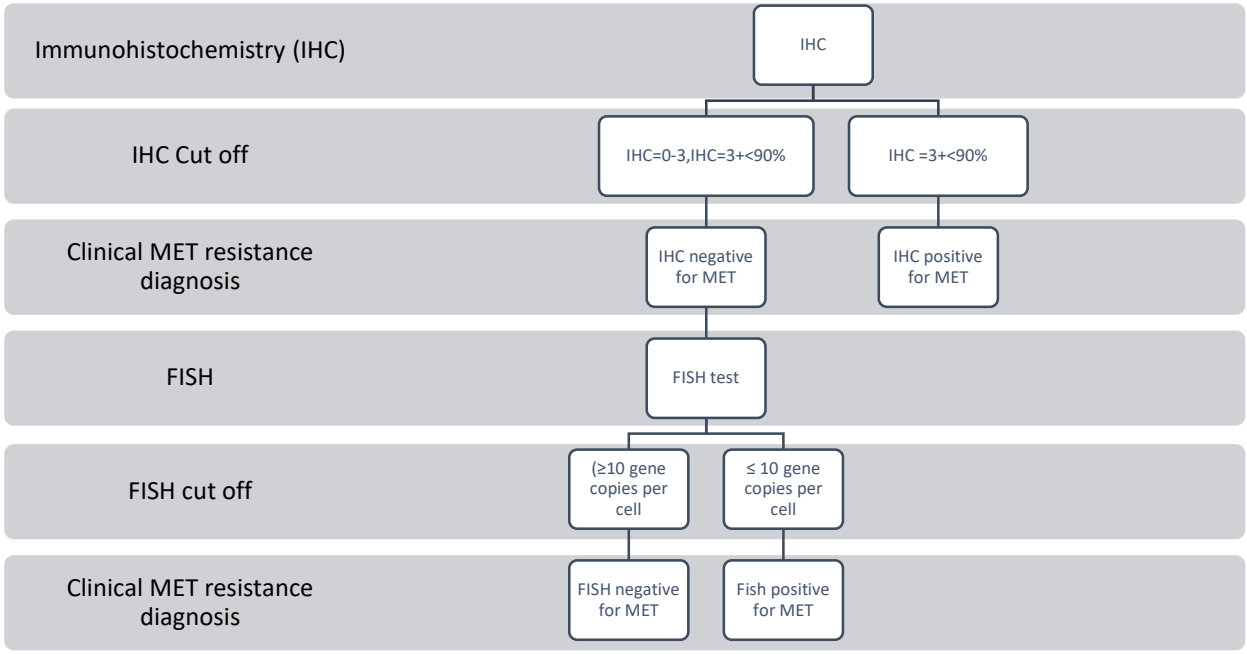
Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:

Australian patients are currently not tested for MET alterations following progression after osimertinib treatment.

Pathologists in Australia will assess MET status in NSCLC patients using validated scoring criteria. For immunohistochemistry (IHC), scores range from 0 to 3+, with MET negativity defined as IHC 0–2+ or IHC 3+ in less than 90% of tumour cells, and MET positivity defined as IHC 3+ in 90% or more of tumour cells. For fluorescence in situ hybridisation (FISH), MET negativity is defined as fewer than 10 MET gene copies, while MET positivity is defined as 10 or more MET gene copies per cell.

In the SAFFRON study, patient selection for MET-driven resistance was based on these criteria: IHC overexpression (IHC 3+ in at least 90% of tumour cells) was detected using the Roche CONFIRM anti-Total c-MET (SP44) Rabbit Monoclonal Primary Antibody, and MET amplification (≥10 gene copies per cell) was detected using the Abbott Vysis MET SpectrumRed FISH probe kit.

Figure 1 MET resistance (overexpression/amplification) testing system



Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?

Yes

Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:

The clinical management of a majority of patients will change as a result of the proposed health technology due to the need to collect a new tissue biopsy at progression to perform the MET overexpression and/or amplification testing. KOLs estimate that approximately 25% of patients are currently being biopsied in this setting to determine small-cell lung cancer (SCLC) transformation.

USE OF THE HEALTH TECHNOLOGY

Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:

A tissue biopsy is required to perform MET testing. With the availability of MET-targeted therapies beyond first-line, it is expected that there will be an increase in the extent of biopsying to support MET testing.

Explain what other healthcare resources are used in conjunction with the comparator health technology:

Currently, re-biopsy for MET resistance (overexpression/amplification) is not routinely performed after progression on osimertinib because there are no MET targeted therapies available for use in this setting.

Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:

There will be an increase in resource use of radiology (interventional radiologists) and surgery (thoracic surgeons) to collect a new biopsy at progression, as well as an increase of pathology resources to process the new specimen including histopathological assessment, and to perform the MET IHC and FISH testing compared to the comparator health technology.

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:

Figure 2 Clinical management algorithm without the proposed health technology

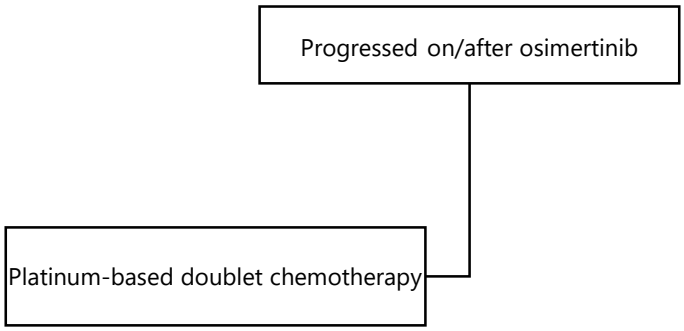
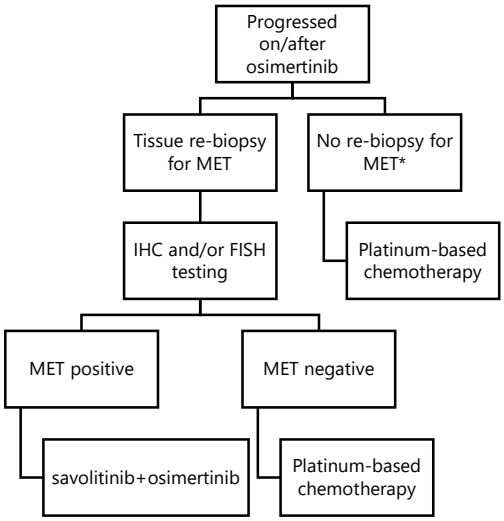


Figure 3 Clinical management algorithm with proposed health technology



*some patients receive re-biopsy for determining other resistance mechanisms such as small cell transformation

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?

Superior

Please state what the overall claim is, and provide a rationale:

The overall clinical claim is that proposed codependent technologies (testing for MET overexpression/amplification and treatment with osimertinib plus savolitinib) are superior in terms of clinical effectiveness, patient safety and quality of life versus the main comparator (no testing and treatment with platinum-based doublet chemotherapy).

Data from the SAVANNAH (Phase II) study demonstrate that the combination of savolitinib plus osimertinib yields a high, clinically meaningful, and durable response in patients with EGFR-mutated advanced NSCLC and MET IHC3+ and/or FISH10+ status who have experienced disease progression on first-line osimertinib. According to investigator assessment, the objective response rate (ORR) was 56.3% (55.0% by BICR), with a median duration of response (DoR) of 7.1 months (9.9 months by BICR) and a median progression-free survival (PFS) of 7.4 months (7.5 months by BICR).

Further comparative evidence will be provided by SAFFRON, a confirmatory Phase III study evaluating the efficacy and safety of savolitinib (300 mg b.i.d.) in combination with osimertinib (80 mg o.d.) versus platinum-based chemotherapy in patients with EGFR-mutated, MET-overexpressed, and/or amplified advanced NSCLC following progression on first- or second-line osimertinib.

These findings highlight the clinical importance of MET testing and reporting in routine practice to optimise treatment access and improve patient outcomes.

Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?

In patients with osimertinib resistance due to MET alterations, the combination of savolitinib and osimertinib could offer a more durable and effective treatment option compared to chemotherapy. Data from the SAVANNAH (Phase II) study demonstrate that the combination of savolitinib plus osimertinib yields a high, clinically meaningful, and durable response in patients with EGFR-mutated advanced NSCLC and MET IHC3+ and/or FISH10+ status who have experienced disease progression on first-line osimertinib. According to investigator assessment, the objective response rate (ORR) was 56.3% (55.0% by BICR), with a median duration of response (DoR) of 7.1 months (9.9 months by BICR) and a median progression-free survival (PFS) of 7.4 months (7.5 months by BICR).

Identify how the proposed technology achieves the intended patient outcomes:

The proposed technology aims to confirm MET resistance in patients who progress after osimertinib treatment. Upon confirmation of MET resistance, MET-targeted therapy, Savolitinib plus osimertinib can be used as the subsequent treatment in place of standard platinum-based chemotherapy, offering patients improved progression-free survival.

For some people, compared with the comparator(s), does the test information result in:

A change in clinical management? Yes

A change in health outcome? Yes

Other benefits? No

In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator?

More costly

Provide a brief rationale for the claim:

The listing of savolitinib plus osimertinib combination on the PBS will slightly impact the utilisation of biopsy, IHC and FISH procedures for MET testing.

Summary of Evidence

Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At 'Application Form lodgement',

<table>
<tr><th></th><th>Type of study design*</th><th>Title of journal article or research project</th><th>Short description of research</th><th>Website link to journal article or research</th><th>Date of publication</th></tr>
<tr><td>1</td><td>Global, Phase 2 study investigating the efficacy and safety of savolitinib plus osimertinib in patients with EGFR-mutated, MET-overexpressed, and/or amplified advanced NSCLC with progression following osimertinib treatment.</td><td>de Marinis F et al.,Savolitinib plus osimertinib in EGFR-mutated advanced NSCLC with MET overexpression and/or amplification following disease progression on osimertinib: primary results from the phase II SAVANNAH study ClinicalTrials.gov ID NCT03778229</td><td>Patients had EGFR-mutated, advanced NSCLC with MET overexpression and/or amplification. The primary endpoint was investigator-assessed objective response rate (ORR) in patients with progression on first-line osimertinib and MET immunohistochemistry (IHC)3+/≥90% (3+ intensity in ≥90% of tumour cells) and/or FISH10+ (≥10 MET gene copies). The primary efficacy population (n=80) consisted of patients who received 300 mg twice daily plus osimertinib 80 mg once daily.
Key results are shown below:
<table><tr><th>Endpoint</th><th>Investigator-assessed</th><th>BICR assessed</th></tr><tr><td>Confirmed ORR (95% CI)</td><td>56.3 (44.7 to 67.3)</td><td>55 (43.5 to 66.2)</td></tr><tr><td>median duration of response (95% CI)</td><td>7.1 (5.6-9.6)</td><td>9.9 (60-13.7)</td></tr><tr><td>median Progression-free survival (95% CI)</td><td>7.4 (5.5-7.6)</td><td>7.5 (6.4-11.3)</td></tr></table></td><td>https://clinicaltrials.gov/study/NCT03778229
https://pubmed.ncbi.nlm.nih.gov/40461383/</td><td>2025 May 22</td></tr>
</table>

Identify yet-to-be-published research that may have results available in the near future (that could be relevant to your application).

	Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
1.	Phase 3, randomised, open-label trial of savolitinib in combination with osimertinib vs platinum-doublet chemotherapy	Ongoing SAFFRON trial – (data yet to read out): Savolitinib plus osimertinib vs platinum-based doublet chemotherapy in participants with non-small cell lung cancer who have progressed on osimertinib treatment	Locally advanced or metastatic NSCLC patients with EGFR-mutations who have progressed on 1L or 2L osimertinib as the most recent treatment. Patients treated with osimertinib in adjuvant setting can be included if progression occurred <6 months after the last dose. Patients must have centrally-confirmed MET overexpression and/or amplification (IHC 3+ in ≥90% of tumour cells) and/or FISH10+ (≥10 MET gene copies). The study plans to randomize a total of 324 patients 1:1 to receive savolitinib 300mg BID plus osimertinib 80mg QD or pemetrexed plus cisplatin/carboplatin (Q3W x 4 cycles, followed by pemetrexed Q3W). The primary endpoint is PFS per BICR in MET positive IHC and/or FISH (ITT). Secondary endpoints include OS, ORR and DoR in ITT and CDx subgroups (IHC90+, FISH10+), PRO, safety, PK.	https://clinicaltrials.gov/study/NCT05261399	TBC

2.	Randomized, phase 3, open-label study in patients with EGFR-mutated, MET-amplified advanced NSCLC post progression on first-line EGFR-TKI compared to platinum-doublet chemotherapy (China only)	Study on Savolitinib combined with Osimertinib in Treatment of Advanced NSCLC with MET Amplification (SACHI) - initial results presented at ASCO2025	The ITT population EGFRm and METamp advanced NSCLC patients consisted of two subgroups: 1. patients progressing on 1st/2nd generation EGFR-TKIs with MET copy number of ≥5 or MET/CEP ≥2, 2. patients progressing on 3rd-generation EGFR-TKIs with MET copy number ≥10 Patients were randomized 1:1 to receive savolitinib 600mg (body weight ≥50kg) or 400mg (body weight ≤50kg) plus osimertinib 80mg QD (n=106) OR platinum + pemetrexed 4-6 cycles then pemetrexed maintenance (n=105) until progressive disease or intolerable toxicity. The primary endpoint, PFS, by investigator (INV) per RECIST 1.1, was hierarchically tested first in patients who received prior 1st/2nd-gen EGFR-TKIs and then in the ITT population (including patients post progression on 3rd gen EGFR-TKIs). Secondary endpoints included PFS by Independent Research Committee (IRC), ORR, Disease Control Rate (DCR), Duration of Response (DoR), Overall Survival, Safety. mPFS by INV was significantly longer with savo + osi in both the 1st/2nd-gen EGFR-TKI group (9.8 vs 5.4 months, HR 0.34, p<0.0001) and the ITT set (8.2 vs 4.5 months, HR 0.34, p<0.0001).	https://clinicaltrials.gov/study/NCT05015608 https://ascopubs.org/doi/10.1200/JCO.2025.43.17_suppl.LBA8505	TBD

			In patients previously who progressed on 3rd-gen EGFR-TKIs, the mPFS was significantly longer with savo + osi compared to chemo (6.9 vs 3.0 months, HR 0.32, p<0.0001). Treatment-related adverse events occurred in 56.6% vs 57.3% of patients with savo + osi vs chemo. Conclusion: Savo + osi significantly improved PFS vs chemo and the combination was safe and well-tolerated.		

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