

Technology Guidance

Osimertinib

for maintenance treatment of locally advanced, unresectable EGFR mutation-positive non-small-cell lung cancer during or following chemoradiation therapy

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended osimertinib for inclusion on the MOH List of Subsidised Drugs for maintenance treatment of locally advanced, unresectable epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutation-positive non-small-cell lung cancer during or following chemoradiation therapy. The decision was based on the uncertain extent of clinical effectiveness, unfavourable cost effectiveness compared with active surveillance, and the unacceptable price-volume agreement proposed by the company.

Clinical indication, subsidy class and MediShield Life claims eligibility for osimertinib are provided in the Annex.

Technology Evaluation

- 1.1. At the July 2026 meeting, the MOH Drug Advisory Committee (“the Committee”) considered the technology evaluation of osimertinib for maintenance treatment of locally advanced (stage III), unresectable epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutation-positive non-small-cell lung cancer (“unresectable stage III EGFR mutation-positive NSCLC”) during or following chemoradiation therapy (CRT). The evaluation considered the company’s evidence submission by AstraZeneca for osimertinib (Tagrisso), and a review conducted by one of ACE’s evidence review centres.
- 1.2. Expert opinion from clinicians at healthcare institutions, the MOH Cancer Drug Subcommittee, and patient experts from local patient and voluntary organisations helped ACE ascertain the clinical value of osimertinib.
- 1.3. The evidence was used to inform the Committee’s deliberations around four core decision-making criteria:
 - Clinical need of patients and nature of the condition;
 - Clinical effectiveness and safety of the technology;
 - Cost effectiveness (value for money) – the incremental benefit and cost of the technology compared to existing alternatives; and
 - Estimated annual technology cost and the number of patients likely to benefit from the technology.
- 1.4. Additional factors, including social and value judgments, may also inform the Committee’s funding considerations.

Clinical need

- 2.1. In Singapore, approximately 46 patients with unresectable stage III EGFR mutation-positive NSCLC are expected to remain progression-free following CRT each year. The current standard of care for these patients is active surveillance, as durvalumab, although funded as maintenance treatment for unselected NSCLC, has limited effectiveness in the EGFR mutation-positive subgroup. The Committee considered the submission’s nominated comparator, active surveillance, to be appropriate.
- 2.2. Local clinicians held differing views on the clinical value of osimertinib maintenance therapy, with some considering the demonstrated progression-free survival (PFS) benefit to be clinically meaningful, while there was also a view that more mature data were required to establish its clinical value.

- 2.3. The Committee considered three testimonials from local patients describing their lived experiences with lung cancer and the treatments they have received. The Committee noted that the condition had a significant negative impact on patients' emotional wellbeing, and that symptoms impacted their ability to carry out daily activities, including work. All three patients were willing to accept manageable side effects from a new treatment if it effectively reduced disease progression. They also considered that any new treatment should allow them to continue daily activities, be more affordable, and prolong their lifespan.

Clinical effectiveness and safety

- 3.1. The Committee reviewed the clinical evidence from an ongoing Phase III, double-blind, randomised controlled trial (LAURA), which compared osimertinib with placebo (active surveillance) in patients with unresectable stage III EGFR mutation-positive NSCLC without disease progression during or following platinum-based chemoradiation therapy. Patients in the placebo arm could cross over to receive osimertinib upon disease progression.
- 3.2. At the primary analysis (median follow-up of 22.0 months in the osimertinib arm and 5.6 months in the placebo arm), osimertinib demonstrated a statistically significant improvement in PFS versus placebo (39.1 versus 5.6 months; hazard ratio [HR] 0.16; 95% confidence interval [CI] 0.10 to 0.24, $p < 0.001$) and was associated with a reduced risk of central nervous system progression or death (CNS PFS, HR 0.17; 95% CI 0.09 to 0.32, nominal $p < 0.001$).
- 3.3. At the updated overall survival (OS) analysis (median follow-up of 39.4 months in the osimertinib arm and 35.2 months in the placebo arm), OS data remained immature, with no statistically significant difference observed between treatment arms (HR 0.67; 95% CI 0.40 to 1.14, $p = 0.140$). The Committee further noted that the PFS-OS surrogate relationship in this setting remained uncertain. While the submission attributed the lack of OS benefit to crossover in the placebo arm, the Committee considered the extent of crossover was reflective of local clinical practice and may therefore better represent the Singapore setting.
- 3.4. The Committee also considered that the magnitude of the PFS benefit may have been overestimated. Median PFS in the active surveillance arm of LAURA (5.6 months) was notably shorter than real-world estimates from KINDLE-Asia (11.5 to 13.2 months). This may in part reflect differences in staging practices, as 48% of patients did not undergo positron emission tomography (PET) staging at baseline. As PET staging is standard practice in Singapore, the treatment effect observed may therefore overestimate the benefit expected in local practice.
- 3.5. Regarding safety, a higher proportion of patients in the osimertinib arm experienced grade ≥ 3 treatment-emergent adverse events (TEAEs), serious TEAEs and TEAEs leading to dose modifications compared with the placebo arm.

- 3.6. The submission described osimertinib as superior in clinical effectiveness compared with active surveillance, with a tolerable safety profile. Based on the submitted evidence, the Committee considered the claim of superiority in systemic and CNS PFS to be reasonable but remained uncertain whether the observed PFS improvements would translate into a clinically meaningful long-term OS benefit. In terms of safety, the Committee considered osimertinib to be inferior to active surveillance.

Cost effectiveness

- 4.1. The Committee considered the results of the submission's cost-utility analysis that compared osimertinib with active surveillance as maintenance treatment of unresectable stage III EGFR mutation-positive NSCLC, based on the LAURA trial. Key components of the base-case economic evaluation provided in the submission are summarised in Table 2.

Table 2: Key components of the company-submitted base-case economic evaluation

Component	Description															
Type of analysis	Cost-utility analysis															
Population	Patients with unresectable stage III EGFR mutation-positive NSCLC															
Outcomes	Total and incremental costs; total and incremental LY; total and incremental QALYs; ICER															
Perspective	Singapore healthcare system															
Type of model	Semi-Markov state-transition model															
Time horizon	15 years in the model base case															
Health states	Progression-free; progressed disease; dead															
Cycle length	30 days															
Extrapolation methods used to generate results	Time-to-event outcomes from the LAURA trial (DCO1) were extrapolated independently for osimertinib arm and active surveillance arm using standard parametric models. Parametric functions were fitted to time-to-event data to derive transition probabilities in the model; transition probabilities from progression-free to progressed disease were informed by TTP, progressed disease to dead were informed by PPS, and progression-free to dead were informed by the difference between TTP and PFS. Parametric models fitted to each treatment arm based on goodness of fit, visual fit and feedback from clinicians. Treatment waning was not applied in the base case. Extrapolation for PFS was aligned with TTP to prevent variations arising from difference in curve selection, given that transition probability of PF to dead was derived from the difference of TTP and PFS curves. <table><tr><th></th><th>Osimertinib</th><th>Active surveillance</th></tr><tr><td>TTP</td><td>Log-normal</td><td>Generalised gamma</td></tr><tr><td>PFS</td><td>Log-normal</td><td>Generalised gamma</td></tr><tr><td>PPS</td><td>Log-logistic</td><td>Weibull</td></tr><tr><td>TTD</td><td>Log-normal</td><td>N/A</td></tr></table>		Osimertinib	Active surveillance	TTP	Log-normal	Generalised gamma	PFS	Log-normal	Generalised gamma	PPS	Log-logistic	Weibull	TTD	Log-normal	N/A
	Osimertinib	Active surveillance														
TTP	Log-normal	Generalised gamma														
PFS	Log-normal	Generalised gamma														
PPS	Log-logistic	Weibull														
TTD	Log-normal	N/A														
Health-related quality of life	- Utilities for the PF health state (0.824) were based on UK utility of general population - Utilities for the PD health state (0.725) were based on an average of PF and PD utility values informed by NICE's appraisal of osimertinib for untreated EGFR mutation-positive advanced NSCLC.															

Component	Description
Types of healthcare resources included	• Drug acquisition and drug administration costs • Disease management costs • Subsequent treatment costs • AE management costs • Terminal care costs

Abbreviations: AE, adverse event; DCO, data cut-off; EGFR, epidermal growth factor receptor; ICER, incremental cost-effectiveness ratio; LY, life year; N/A, not applicable; NICE, National Institute for Health and Care Excellence; NSCLC, non-small cell lung cancer; OS, overall survival; PD, progressed disease; PF, progression-free; PFS, progression-free survival; PPS, post-progression survival; QALY, quality-adjusted life year; TTD, time to treatment discontinuation; TTP, time to progression; UK, United Kingdom.

4.2. The base-case incremental cost-effectiveness ratio (ICER) in the submission was between SG\$105,000 and SG\$135,000 per quality-adjusted life year (QALY) gained. However, the Committee considered the ICER to be highly uncertain and likely underestimated, in view of the following:

- The choice of extrapolations in the submission resulted in poor visual fit between modelled and observed OS Kaplan-Meier (KM) curves, increasing uncertainty in the estimated long-term OS benefit of osimertinib, particularly given the immature OS data from the LAURA trial. The model was also highly sensitive to the choice of post-progression survival extrapolation.
- The submission did not apply treatment waning across the 15-year time horizon for the osimertinib arm, which may have overestimated the long-term treatment effect given the uncertainty in whether the observed benefits would be sustained.
- The subsequent treatment costs in the active surveillance arm in the submission were uncertain. The assumed duration of subsequent osimertinib treatment was not reported in the cited publication and therefore could not be substantiated.

4.3. The Committee considered the respecified base case, which accounted for several uncertainties in the company's model. Key changes to the economic model included selecting time-to-progression (TTP) and PPS curves to better align with the observed OS KM curve, applying treatment waning to the TTP of the osimertinib arm, and adjusting the duration of subsequent osimertinib treatment in the active surveillance arm. These changes substantially increased the ICER to between SG\$135,000 and SG\$165,000 per QALY gained.

4.4. The Committee noted that based on one-way sensitivity analysis and scenario analyses of the respecified base case, the key model drivers were health utilities for PF and PD health states, the time horizon, and choice of survival extrapolation curves. When these parameters were varied within their uncertainty ranges, the ICERs remained unfavourably high.

- 4.5. Overall, the Committee considered that osimertinib did not represent a cost-effective use of healthcare resources for maintenance treatment of unresectable stage III EGFR mutation-positive NSCLC at the price proposed by the company.

Estimated annual technology cost

- 5.1. Using an epidemiological approach, the submission estimated that the annual cost impact to the public healthcare system would increase from between SG\$1 million and SG\$3 million in the first year, to between SG\$5 million and SG\$10 million in the fifth year of listing osimertinib on the MOH List of Subsidised Drugs for maintenance treatment of unresectable stage III EGFR mutation-positive NSCLC.
- 5.2. The Committee considered that the submission estimates were high and uncertain due to an overestimation of eligible patients with EGFR mutation-positive NSCLC and treatment duration. Based on the respecified budget impact model, the annual cost impact to the public healthcare system was estimated to be less than SG\$1 million in the first year, and between SG\$1 million and SG\$3 million in the fifth year of listing. The Committee also considered that the submission's price-volume agreement (PVA) caps were unacceptably high and inadequate to provide budget certainty.

Recommendations

- 6.1. Based on available evidence, the Committee recommended not listing osimertinib on the MOH List of Subsidised Drugs for maintenance treatment of locally advanced, unresectable EGFR exon 19 deletion or exon 21 L858R substitution mutation-positive NSCLC during or following chemoradiation therapy. The decision was based on the uncertain extent of clinical effectiveness, unfavourable cost effectiveness compared with active surveillance and the unacceptable PVA proposed by the company.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Company-proposed clinical indication	Subsidy class	Eligible for MediShield Life claims
Osimertinib 40 mg and 80 mg tablets	For patients with locally advanced, unresectable (stage III) non-small-cell lung cancer whose tumours have EGFR exon 19 deletions or exon 21 L858R substitution mutations and whose disease has not progressed during or following platinum-based chemoradiation therapy.	Not recommended for subsidy	No

Abbreviation: EGFR, epidermal growth factor receptor.

 Agency for Care Effectiveness - ACE  Agency for Care Effectiveness (ACE)

About the Agency

The Agency for Care Effectiveness (ACE) was established by the Ministry of Health (Singapore) to drive better decision-making in healthcare through health technology assessment (HTA), clinical guidelines, and education.

As the national HTA agency, ACE conducts evaluations to inform government funding decisions for treatments, diagnostic tests and vaccines, and produces guidance for public hospitals and institutions in Singapore.

The guidance is not, and should not be regarded as, a substitute for professional or medical advice. Please seek the advice of a qualified healthcare professional about any medical condition. The responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

Find out more about ACE at <https://www.ace-hta.gov.sg/about-us/>

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