

Technology Guidance

Durvalumab

for treating resectable gastric or gastroesophageal junction adenocarcinoma

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended durvalumab for inclusion on the MOH List of Subsidised Drugs, when used in combination with fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) chemotherapy as neoadjuvant and adjuvant treatment, followed by adjuvant durvalumab monotherapy, for resectable gastric or gastroesophageal junction adenocarcinoma. The Committee considered that the company's proposal, including the price-volume agreement, was not acceptable.

Clinical indication, subsidy class and MediShield Life claims eligibility for durvalumab 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 durvalumab for treating resectable gastric or gastroesophageal junction (GEJ) adenocarcinoma, used in combination with fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) chemotherapy as neoadjuvant and adjuvant treatment, followed by adjuvant durvalumab monotherapy. The evaluation considered the company’s evidence submission by AstraZeneca for durvalumab (Imfinzi), and a review conducted by one of ACE’s evidence review centres.
- 1.2. Expert opinion from clinicians at public healthcare institutions and the MOH Cancer Drug Subcommittee helped ACE ascertain the clinical value of durvalumab. Local patient and voluntary organisations were also invited to provide their lived experiences to inform the evaluation; however, no submissions were received.
- 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 220 patients are diagnosed with resectable gastric or GEJ adenocarcinoma each year. Surgical resection is the primary treatment, with chemotherapy given before and/or after surgery to improve cure rates. The Committee acknowledged the clinical need for more effective treatments as the risk of disease recurrence remains high despite this multimodal approach.
- 2.2. In local practice, FLOT is the preferred chemotherapy regimen in patients with good performance status and high disease burden. As durvalumab (a programmed cell death ligand 1 [PD-L1] inhibitor) is expected to be added to FLOT in eligible patients, the Committee considered FLOT to be the appropriate comparator for this submission.

Clinical effectiveness and safety

- 3.1. The Committee reviewed the clinical evidence from a Phase III, double-blind, randomised controlled trial (MATTERHORN) that compared peri-operative durvalumab plus FLOT versus peri-operative placebo plus FLOT in 948 patients with stage II to IVA resectable gastric or GEJ adenocarcinoma.
- 3.2. The Committee noted that the primary endpoint was event-free survival (EFS), assessed by blinded independent central review. At the final EFS analysis, durvalumab was associated with improved EFS compared with placebo (hazard ratio [HR] 0.71; 95% confidence interval [CI] 0.58 to 0.86), with median EFS not reached with durvalumab compared with 32.8 months with placebo. At a median follow-up of 43 months, durvalumab was also associated with improved overall survival (OS) compared with placebo (HR 0.78; 95% CI 0.63 to 0.96), with median OS not reached in either arm. The OS data remained immature and the durability of the observed OS benefit was uncertain.
- 3.3. The Committee also noted that the rate of subsequent immunotherapy use in local practice was likely higher than that observed in the placebo arm of the trial. Hence, the trial may have overestimated the incremental benefit of durvalumab in the local setting.
- 3.4. Regarding safety, a higher proportion of patients treated with peri-operative durvalumab plus FLOT experienced treatment-emergent adverse events (TEAEs) leading to treatment discontinuation and immune-mediated TEAEs, compared to those who received peri-operative placebo plus FLOT.
- 3.5. The submission described durvalumab plus FLOT as superior in clinical effectiveness and comparable in safety compared with FLOT alone. The Committee considered that the claim of superior effectiveness was supported, although the magnitude of OS benefit from durvalumab was uncertain and likely overestimated. In terms of safety, the Committee considered a claim of inferior safety was more appropriate for durvalumab plus FLOT versus FLOT alone, based on the trial evidence.

Cost effectiveness

- 4.1. The Committee considered the submission's cost-utility analysis comparing durvalumab plus FLOT versus FLOT alone based on the MATTERHORN trial. Key components of the base-case economic evaluation provided in the submission are summarised in Table 1.

Table 1: Key components of the company-submitted base-case economic evaluation

Component	Description
Type of analysis	Cost-utility analysis
Population	Patients with resectable gastric or GEJ adenocarcinoma
Outcomes	Total and incremental direct medical costs; total and incremental LY gained; 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, based on a median follow-up of 31.6 months (durvalumab plus FLOT) and 31.4 months (FLOT) in the MATTERHORN trial
Health states	Event-free; recurred disease; death
Cycle length	One month
Transition probabilities	Transition probabilities from event-free to recurred disease, event-free to death, and recurred disease to death were derived from independent parametric extrapolations of the corresponding time-to-event outcomes from the MATTERHORN trial. The selection of parametric survival distributions was based on statistical and visual fit. - Event-free to recurred disease: Estimated from TFR, with a generalised gamma distribution selected for both treatment arms. - Event-free to death: Estimated from time-to-death as the first EFS event, with a Gompertz distribution selected for both treatment arms. - Recurred disease to death: Estimated from post-recurrence survival, with a log-logistic distribution selected for both treatment arms. In both treatment arms, the model assumed that patients who remained event-free at 5 years were cured, such that they were no longer at risk of recurrence and experienced a mortality risk slightly higher than that of the general population, based on a SMR of 1.1.
Health-related quality of life	Event-free health state utility was based on the UK general population utility value for the starting age of 65 years, and recurred disease health state utility was sourced from a previous related evaluation by NICE. - Event-free: 0.824 - Recurred disease: 0.747 Age-adjustment of utility values was applied multiplicatively to the event-free and recurred disease health state utilities at each cycle to account for utility decrement associated with ageing. Total AE-related utility decrement in each arm: - Durvalumab plus FLOT: -0.00418 - FLOT: -0.00450
Types of healthcare resources included	- Drug and drug administration costs - Disease management costs - Subsequent treatment costs - AE management costs - Terminal care costs

Abbreviations: AE, adverse event; EFS, event-free survival; EQ-5D, EuroQol 5-Dimension; FLOT, fluorouracil, leucovorin, oxaliplatin and docetaxel; GEJ, gastroesophageal junction; ICER, incremental cost-effectiveness ratio; LY, life year; NICE, National Institute for Health and Care Excellence; QALY, quality-adjusted life year; SMR, standardised mortality ratio; TFR, time-to-first recurrence.

- 4.2. The submission's base-case incremental cost-effectiveness ratio (ICER) was between SG\$15,000 and SG\$45,000 per QALY gained. However, the Committee considered the ICER to be uncertain and likely underestimated, due to the following:
- The submission's chosen extrapolation functions for time-to-first recurrence and time-to-death were optimistic compared to the observed data and did not account for potential waning of treatment effect over time. This led to an overestimation of the incremental benefits of durvalumab over the 15-year time horizon.
 - The submission assumed a 100% cure rate at Year 5 in both arms, after which patients in the event-free health state were assumed to be no longer at risk of disease recurrence.
 - The submission applied different drug costs and healthcare resource utilisation inputs arising from alternative data sources and assumptions, which favoured the durvalumab plus FLOT arm.
- 4.3. The Committee considered the respecified base case, incorporating revised time-to-death extrapolation, treatment waning at 4 years, a 90% cure rate at 5 years, and adjusted costs, which increased the ICER to between SG\$15,000 and SG\$45,000 per QALY gained. In a multivariate scenario analysis applying more conservative assumptions, including no cure benefit and an alternative time-to-first recurrence extrapolation, the ICER increased to between SG\$45,000 and SG\$75,000 per QALY gained. The Committee noted that the ICER remained sensitive to assumptions regarding long-term treatment benefit and extrapolation.

Estimated annual technology cost

- 5.1. Using an epidemiological approach, the submission estimated that the annual cost impact to the public healthcare system would be between SG\$5 million and SG\$10 million over the first five years of listing durvalumab on the MOH List of Subsidised Drugs for treating resectable gastric or GEJ adenocarcinoma.
- 5.2. The Committee considered that the submission's financial estimates were high and uncertain, due to an overestimation of eligible patients for peri-operative treatment, treatment duration, and uptake rate for durvalumab in local clinical practice. Based on the respecified budget impact model, the annual cost impact to the public healthcare system was estimated to be between SG\$1 million and SG\$3 million over the first five years of listing durvalumab. 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 durvalumab, used in combination with FLOT chemotherapy as neoadjuvant and adjuvant treatment, followed by adjuvant durvalumab monotherapy, on the MOH List of Subsidised Drugs for treating resectable gastric or GEJ adenocarcinoma. The Committee considered that the company's proposal, including the PVA, was not acceptable.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Company-proposed clinical indication	Subsidy class	Eligible for MediShield Life claims
Durvalumab 120 mg/2.4 mL and 500 mg/10 mL concentrate for solution for infusion	Durvalumab in combination with fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) chemotherapy as neoadjuvant and adjuvant treatment, followed by adjuvant durvalumab monotherapy, for the treatment of resectable gastric or gastroesophageal junction adenocarcinoma.	Not recommended for subsidy	No

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