6.05 DURVALUMAB

Solution concentrate for I.V. infusion 120 mg in 2.4 mL

Solution concentrate for I.V. infusion 500 mg in 10 mL

Imfinzi®

Astrazeneca Pty Ltd

1 Purpose of submission

1.1 The Category 2 submission requested Section 100 (Efficient Funding of Chemotherapy Program) PBS listing of durvalumab for the perioperative treatment (i.e. before and after surgery) of adult patients with gastric cancer (GC) or gastroesophageal junction cancer (GOJC) who are eligible for neoadjuvant FLOT (fluorouracil, leucovorin, oxaliplatin, docetaxel) chemotherapy (i.e. eligible for FLOT chemotherapy given prior to surgery).

1.2 Listing was requested on the basis of a cost-effectiveness analysis versus standard of care (SOC) FLOT regimen alone.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Patients with resectable gastric or GOJ adenocarcinoma and eligible for neoadjuvant FLOT
Intervention	Neoadjuvant: Durvalumab (1,500 mg IV Q4W) + FLOT for 2 cycles Adjuvant: Durvalumab (1,500 mg IV Q4W) + FLOT for 2 cycles followed by durvalumab monotherapy (1,500 mg Q4W) for 10 cycles
Comparator	SOC – neoadjuvant-adjuvant FLOT regimen (FLOT4)
Outcomes	EFS; OS; pCR; Surgery rate; R0 resection rate; MFS; DSS; HRQoL; Safety
Clinical claim	Durvalumab + FLOT is superior in terms of efficacy and has an inferior but manageable safety profile compared with FLOT alone for the treatment of patients with gastric or GOJ adenocarcinoma

Source: Table 1-1 p 29 of the submission

DSS = disease-specific survival; EFS = event-free survival; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; GOJ = gastroesophageal junction; HRQoL = health-related quality of life; IV = intravenous; MFS = metastasis-free survival; OS = overall survival; pCR = pathological complete response; Q4W = every 4 weeks; SOC = standard of care.

2 Background

Registration status

2.1 Durvalumab for the treatment of G/GOJ adenocarcinoma was submitted to the TGA on 7 July 2025 with the proposed indication under priority review. The Delegate's Overview was received prior to ESC consideration of durvalumab. The Australian TGA PI for durvalumab includes the following indication:

"IMFINZI in combination with FLOT chemotherapy as neoadjuvant and adjuvant treatment, followed by adjuvant IMFINZI monotherapy, is indicated for the treatment of adults with resectable gastric or gastroesophageal junction adenocarcinoma".

3 Requested listing

Medicinal product	DPMA, published (effective)		Max. Amount	№. of Rpts
	Public hospital	Private hospital		
Initial treatment				
Durvalumab 500 mg/10 mL; 10 mL vial	$10,853.55 [$[redacted] with SPA]	$11,049.89 [$[redacted] with SPA]	1,500 mg	1
Durvalumab 120 mg/2.4 mL; 10 mL vial	$10,853.55 [$[redacted] with SPA]	$11,049.89 [$[redacted] with SPA]		
Continuing treatment				
Durvalumab 500 mg/10 mL; 10 mL vial	$10,853.55 [$[redacted] with SPA]	$11,049.89 [$[redacted] with SPA]	1,500 mg	11
Durvalumab 120 mg/2.4 mL; 10 mL vial	$10,853.55 [$[redacted] with SPA]	$11,049.89 [$[redacted] with SPA]		
Available brands				
IMFINZI®, durvalumab 500 mg/10 mL, 10 mL vial for IV infusion/durvalumab 120 mg/2.4 mL, 10 mL vial for IV infusion				

Source: Tables 1-9 and 1-10 of the submission
DPMA = dispensed price for maximum amount; IV = intravenous; Rpts = repeats; SPA = special pricing arrangement.

Category/Program: Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals	
Prescriber Type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Restriction Summary / Treatment of Concept:	Authority Required (telephone/online PBS Authorities system)
PBS Indication:	Resectable gastric and gastroesophageal junction adenocarcinoma
Treatment phase	Neoadjuvant phase
Population criteria	Patient must be initiating treatment with this drug for this condition OR Patient must be transitioning from existing non-PBS to PBS subsidised supply of this drug
Clinical criteria:	The condition must be resectable AND The treatment must be for the purpose of neoadjuvant use in a patient preparing for surgery AND Patient must have a WHO performance status no greater than 1 AND The treatment must be initiated in combination with neoadjuvant FLOT AND The condition must be untreated with systemic therapy
Treatment criteria	Patient must not be undergoing PBS subsidised treatment where this prescription extends treatment beyond whichever comes first: (i) 2 cycles from treatment initiation, irrespective of whether initial treatment was PBS subsidised/non-PBS subsidised, (ii) disease progression/recurrence despite treatment with this drug, (iii) unacceptable toxicity; annotate any remaining repeat prescriptions with the word 'cancelled' where this occurs Patient must be undergoing treatment with a dosing regimen as set out in the drug's Therapeutic Goods Administration (TGA) approved Product Information.
Administrative advice	The prescribing dose of durvalumab is 1,500 mg administered every 4 weeks is equivalent to one cycle. No increase in the maximum amount or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

Source: Table 1-11 p43 of the submission
FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; PBS = Pharmaceutical Benefits Scheme; TGA = Therapeutic Goods Administration; WHO = World Health Organization.

Category/Program: Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals	
Prescriber Type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
Restriction Summary / Treatment of Concept:	Authority Required (telephone/online PBS Authorities system)
PBS Indication:	Resectable gastric and gastroesophageal junction adenocarcinoma
Treatment phase	Adjuvant phase
Population criteria	Patient must have previously received PBS subsidised neoadjuvant treatment with this drug for this condition OR Patient must be both: (i) transitioning from existing non-PBS to PBS subsidised supply of this drug, (ii) treated with combined therapy with durvalumab and FLOT as neoadjuvant treatment for this condition
Clinical criteria:	The treatment must be for the purposes of adjuvant use following complete surgical resection AND The treatment must be initiated in combination with adjuvant FLOT for up to 2 cycles unless intolerant to FLOT requiring permanent discontinuation. AND The treatment must be as monotherapy for up to an additional 10 cycles after completing the first 2 cycles. AND Patient must have previously received PBS subsidised neoadjuvant treatment with this drug for this condition. AND Patient must not have developed disease progression while being treated with this drug for this condition
Treatment criteria	Patient must be undergoing treatment that does not occur beyond the following, whichever comes first: (i) the first instance of disease progression/recurrence, (ii) maximum of 12 cycles for this condition from the first administered dose following surgery, (iii) unacceptable toxicity; annotate any remaining repeat prescriptions with the word 'cancelled' where this occurs Patient must be undergoing treatment with a dosing regimen as set out in the drug's Therapeutic Goods Administration (TGA) approved Product Information
Administrative advice	The prescribing dose of durvalumab is 1,500 mg administered every 4 weeks for up to a maximum of 12 cycles (including 2 cycles of durvalumab + FLOT and 10 additional cycles of durvalumab monotherapy) No increase in the maximum amount or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

Source: Table 1-12 p 43-44 of the submission
FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; PBS = Pharmaceutical Benefits Scheme; TGA = Therapeutic Goods Administration.

3.1 The requested effective price presented in the submission was AEMP $[redacted] per 500 mg vial.

3.2 The proposed restrictions were generally aligned with the clinical evidence presented in the submission and with the Therapeutic Goods Administration (TGA) draft product information (PI). The ESC noted that staging classification was not included in the indication or as a clinical criterion. The submission and Pre-Sub-Committee Response (PSCR) claimed that there is variability and uncertainty in staging classification in

clinical practice and that the restrictions capture the intended population as only patients with Stage II or higher resectable disease receive FLOT. The ESC noted that interpreting scans for staging can be challenging, but considered that it would be reasonable to require confirmation that the patient has Stage II or higher disease prior to prescribing. The ESC also noted that patients included in the MATTERHORN trial had histologically documented G/GOJ adenocarcinoma of Stage II or higher (T3-4 N0–3 M0 or T0–4 N1–3 M0) and considered that it would be appropriate to include staging criteria in the restrictions to ensure consistency with the trial. The pre-PBAC response maintained it is not necessary to specify staging in the clinical criteria of the restriction, however the PBAC agreed with the ESC that it would be appropriate for the restriction to include staging criteria, consistent with the trial.

3.3 The PBAC agreed with the ESC that the treatment criteria "Patient must be undergoing treatment with a dosing regimen as set out in the drug's Therapeutic Goods Administration (TGA) approved Product Information" was unnecessary and could be removed.

3.4 The submission noted that the sponsor anticipates that durvalumab will be provided via an Early Access Program for patients with resectable G/GOJ adenocarcinoma following registration. The initial and continuing treatment restrictions were worded to allow grandfathered patients from the planned patient access program to transition to PBS subsidised therapy. The PBAC considered this was appropriate.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 In Australia, the number of diagnosed cases of GC and GOJC is estimated to be 2,740 in 2025. Of these, 38.8% were GOJ cancer and 61.2% were GC. The incidence of GC and GOJC is disproportionately higher in people aged 60 years and older. The burden of disease is higher among males (63%) than females (37%).

4.2 GC and GOJC are clinically classified as early or advanced stage to guide treatment, and are further subtyped histologically. Real-world Australian data indicate that a substantial proportion of G/GOJ cancer patients are diagnosed with advanced stage disease, with approximately 60% diagnosed at stage III or IV. [1,2] Adenocarcinoma represents 93.2% of GC. In GOJC, adenocarcinoma is also the predominant histology.

[1] Abbas et al. (2021). Patterns of care and outcomes for gastric and gastro-oesophageal junction cancer in an Australian population. ANZ J Surg. Dec;91(12):2675-2682.
[2] Arnold et al. (2022). International variation in oesophageal and gastric cancer survival 2012-2014: differences by histological subtype and stage at diagnosis (an ICBP SURVMARK-2 population-based study). Gut. Aug;71(8):1532-1543.

4.3 Optimal management in resectable disease includes complete resection with adequate lymphadenectomy. Given the high risk of recurrence with surgery alone, chemotherapy should also be administered preoperatively (neoadjuvant), postoperatively (adjuvant), or both (perioperative). Perioperative chemotherapy is the SOC for resectable GC and GOJC. Current guidelines recommend neoadjuvant FLOT as the preferred regimen for both gastric and oesophageal cancers, including GOJC.

4.4 The most common reasons for FLOT ineligibility are poor performance status/frailty (Eastern Cooperative Oncology Group [ECOG] ≥ 2), serious pre-medical conditions and hypersensitivity or grade ≥ 3 toxicity to oxaliplatin/docetaxel. These patients would be eligible for chemoradiation therapy, such as the Chemoradiotherapy for Oesophageal Cancer followed by Surgery Study (CROSS) regimen and subsequent adjuvant nivolumab.[3] The proposed PBS population is considered distinct from patients treated with chemoradiation followed by nivolumab. Nivolumab is currently PBS-listed for use as an adjuvant treatment for patients with stage II or III oesophageal cancer or GOJC who receive neoadjuvant chemoradiation.

4.5 PBS-listed treatments for metastatic G/GOJ cancers are: nivolumab, tiselizumab, trifluridine + tipiracil, and trastuzumab (HER2 positive only).

4.6 Durvalumab is an anti-programmed cell death ligand-1 (PD-L1) human monoclonal antibody and is indicated as add-on to FLOT therapy for the neoadjuvant and adjuvant treatment of G/GOJ adenocarcinoma.

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Comparator

5.1 The submission nominated perioperative FLOT alone, the current SOC, as the comparator. FLOT consists of fluorouracil, leucovorin, oxaliplatin and docetaxel. The choice of comparator is appropriate.

5.2 At the time of ESC advice the current PBS listed immunotherapies had a 'once in a lifetime' restriction, and patients with disease progression or recurrence after perioperative durvalumab would not be eligible for subsequent IO-based treatment. This was considered in the economic analysis and financial estimates. At the time of PBAC consideration the PBS listing for nivolumab and ipilimumab had been broadened to expand access to include the treatment of advanced and metastatic cancers, without exclusion of re-treatment. The PBAC noted that patients would be able to

[3] Obermannová et al. (2025). ESMO Clinical Practice Guideline interim update on the treatment of locally advanced oesophageal and oesophagogastric junction adenocarcinoma and metastatic squamous-cell carcinoma. ESMO Open. Feb;10(2):104134.

access nivolumab following treatment with durvalumab or as an alternative to perioperative durvalumab in the advanced setting.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer inputs

6.2 The PBAC noted and welcomed the input from Rare Cancers Australia, which included statements from patients. The input described the impact of GC/GOJC on eating and appetite, the burden of surgical treatments and ongoing monitoring, the significant cost barrier to accessing durvalumab, the benefit of infusion (reducing the need for daily medication management), the potential for reduced pain and enhancement of surgical outcomes.

Clinical trials

6.3 The submission was based on one head-to-head trial comparing D + FLOT to placebo (Pbo) + FLOT (n = 948) (MATTERHORN).

6.4 Details of the MATTERHORN trial presented in the submission are provided in Table 2.

Table 2: MATTERHORN trial and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
MATTERHORN NCT04592913	MATTERHORN CSR - DCO2: 20 December 2024	MATTERHORN second interim analysis Clinical Study Report (CSR)
	Clinical Study Protocol (CSP) v3: March 2024	MATTERHORN clinical study protocol (CSP)
	Publication	Yelena Y et al (2025) Perioperative Durvalumab in Gastric and Gastroesophageal Junction Cancer N Engl J Med 2025;393:217-230
	Final OS analysis abstract	MATTERHORN Final OS analysis Tabernero et al. (2025). Final overall survival and the association of pathological outcomes with event-free survival in MATTERHORN: a randomised, Phase 3 study of durvalumab plus 5-fluorouracil, leucovorin, oxaliplatin and docetaxel in resectable gastric/gastroesophageal junction adenocarcinoma. ESMO Congress, Berlin, 17-21 October 2025.

Source: Table 2-3, p51 of the submission.
CSP = clinical study protocol; CSR = clinical study report; DCO = data cut-off; OS = overall survival.

6.5 The key features of the MATTERHORN direct randomised controlled trial (RCT) are summarised in Table 3.

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
D + FLOT vs Pbo + FLOT						
MATTERHORN	948	R, DB, MC Median f/u: for OS: 38.6-39.6 months	Some concern [a]	Patients with resectable G/GOJ adenocarcinoma that is eligible for neoadjuvant FLOT therapy	Primary: EFS Key secondary: OS, pCR Other secondary: MFS, DFS, HRQoL	Yes

Source: p53, Table 2-7 p59, Table 2-15 p73 of the submission.
D = durvalumab; DB = double blind; DFS = disease-free survival; EFS = event-free survival; f/u = follow-up; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; G/GOJ = gastric/gastroesophageal junction; HRQoL = health-related quality of life; MC = multicentre; MFS = metastasis-free survival; OS = overall survival; pCR = pathological complete response; R = randomised
[a] Risk of bias (RoB) was conducted using ROB2 during the evaluation as no formal assessment was presented in the submission.

6.6 Patient disposition indicated that the proportions entering the neoadjuvant, surgical and adjuvant phases of therapy were balanced across treatment arms. However, approximately 25% of patients in each arm did not proceed to adjuvant therapy, representing more than 100 patients per treatment arm. As demographic and prognostic characteristics of those who did and did not receive adjuvant therapy were not reported, it is uncertain whether prognostic factors were similar between those who received adjuvant treatment versus those who did not. Nevertheless, the study was double-blinded at the decision-point, which may have mitigated any risk of bias. The ESC noted that the proportion of patients in each arm that did not proceed to adjuvant therapy was consistent with clinical experience and was also substantially less that in the FLOT4 trial, in which around half of all patients did not continue to adjuvant therapy[4]. As such, the ESC considered that the risk of bias from this issue was small.

Comparative effectiveness

6.7 The MATTERHORN trial included 948 patients (D + FLOT: n = 474; Pbo + FLOT: n = 474) with stage II or higher resectable G/GOJ adenocarcinoma and an ECOG performance status (PS) of 0 or 1. Patients were to be medically fit for treatment with neoadjuvant FLOT prior to radical surgery and should have known PD-L1 status prior to randomisation. The majority of patients had tumour area positivity (TAP) score ≥ 1% for PD-L1 expression (90.0%).

6.8 The primary outcome was event-free survival (EFS), and key secondary outcomes were overall survival (OS) and pathological complete response (pCR). Other secondary outcomes included disease-free survival (DFS), metastasis-free survival (MFS) and rate

[4] Al-Batran SE, Homann N, Pauligk C, et al. Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adeno-carcinoma (FLOT4): a randomised, phase 2/3 trial. Lancet. 2019;393:1948-1957

of surgery. Efficacy outcomes (with the exception of DFS) were assessed in the full analysis set (FAS), defined as all randomised patients. DFS was assessed in the R0 resected analysis set (the FAS population who had margin-negative resection based on local pathology assessments) and is defined as having no evidence of disease at the post-surgery adjuvant baseline scan. Safety outcomes were assessed in the safety analysis set defined as all randomised patients who received at least one dose of study drug based on the treatment they received.

6.9 The survival outcomes from the MATTERHORN trial indicate that the addition of durvalumab to FLOT therapy resulted in statistically significant improvements in EFS, OS, DFS and MFS (Table 4; Figure 1). For the primary efficacy outcome, the median EFS was not reached for D + FLOT versus 32.82 months for Pbo + FLOT. Treatment with D + FLOT demonstrated improved EFS compared with Pbo + FLOT (hazard ratio [HR] 0.71; 95% confidence interval [CI]: 0.58, 0.86; $p < 0.001$).

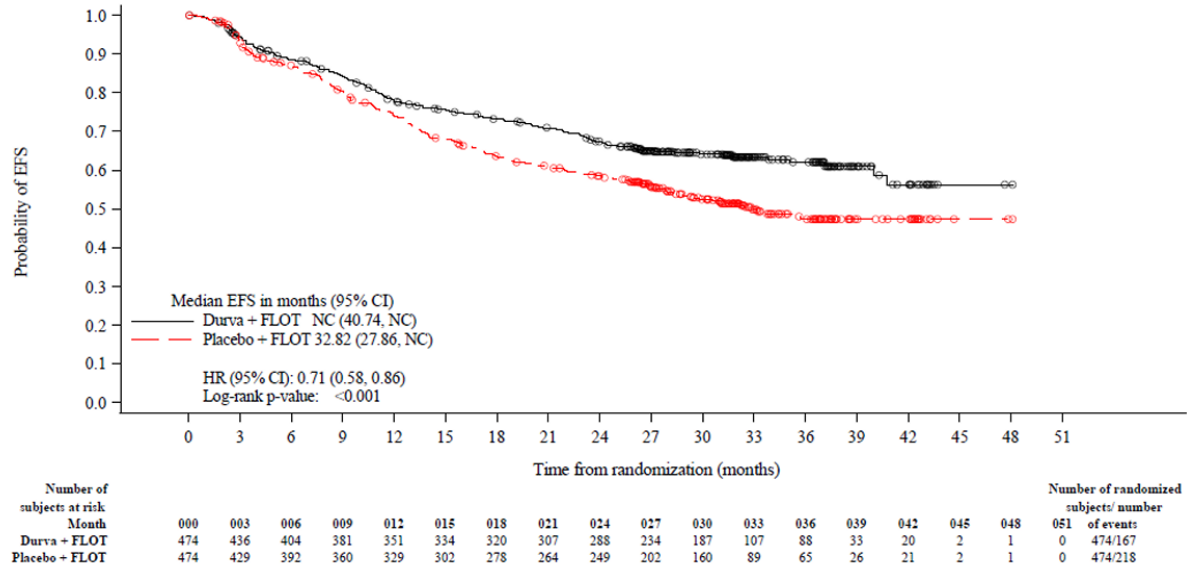
6.10 EFS by subgroup analysis consistently demonstrated favourable outcomes for D + FLOT compared with Pbo + FLOT, with hazard ratios between 0.61 and 0.85.

Table 4: Summary of survival outcomes in the MATTERHORN trial

Outcome [a]	D + FLOT n = 474	Pbo + FLOT n = 474	HR (95% CI), p-value
Primary outcome: EFS			
Number of events, n (%)	167 (35.2)	218 (46.0)	**0.71 (0.58, 0.86); p<0.001**
Median EFS (95% CI), months	NC (40.74, NC)	32.82 (27.86, NC)	
Key secondary outcome: OS			
At DCO2			
Number of events, n (%)	145 (30.6)	176 (37.1)	0.78 (0.62, 0.97); p=0.025 [b]
Median OS (95% CI), months	NC (NC, NC)	47.21 (45.08, NC)	
At FA			
Number of events, n (%)	NR	NR	**0.78 (0.63, 0.96); p=0.021**
Median OS (95% CI), months	NC (NC, NC)	NC (NC, NC)	
Secondary outcome: MFS			
Number of events, n (%)	171 (36.1)	224 (47.3)	**0.72 (0.59, 0.88)**
Median MFS (95% CI), months	NC (39.46, NC)	32.79 (27.04, 42.58)	
Secondary outcome: DFS (in R0 resected analysis set)			
Number of events, n (%)	90/339 (26.5)	119/323 (36.8)	**0.70 (0.53, 0.93); p=0.012**
Median DFS (95% CI), months	NC (NC, NC)	39.75 (38.67, NC)	

Source: Table 2-18, p78, Table 2-19 p80, Table 2-23 p85 and Table 2-24 p87 of the submission.
CI = confidence interval; D = durvalumab; DCO = data cut-off; DFS = disease-free survival; EFS = event-free survival; FA = final analysis; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR = hazard ratio; MFS = metastasis-free survival; NC = not calculable; NR = not reported; OS = overall survival; Pbo = placebo.
[a] Outcomes reported at DCO2 unless otherwise specified.
[b] A p-value < 0.0001 was required to declare statistical significance at DCO2.
Bolded results indicate statistically significant differences between treatment arms.

Figure 1 Kaplan-Meier Plot of EFS (FAS, DCO2)



Source: Figure 2-4 p79 of the submission.
CI = confidence interval; DCO = data cut-off; EFS = event-free survival; FAS = full analysis set; FLOT = 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; HR = hazard ratio; KM = Kaplan-Meier; NC = not calculable; Pbo = placebo.

At DCO2, the median OS was not reached for D + FLOT and was 47.21 months for Pbo + FLOT. Treatment with D + FLOT demonstrated improved OS over Pbo + FLOT (HR 0.78; 95% CI: 0.62, 0.97; p = 0.025). This did not reach statistical significance based on the prespecified threshold for statistical significance at DCO2 ($p < 0.0001$) (Table 4;

6.11 Figure 2).

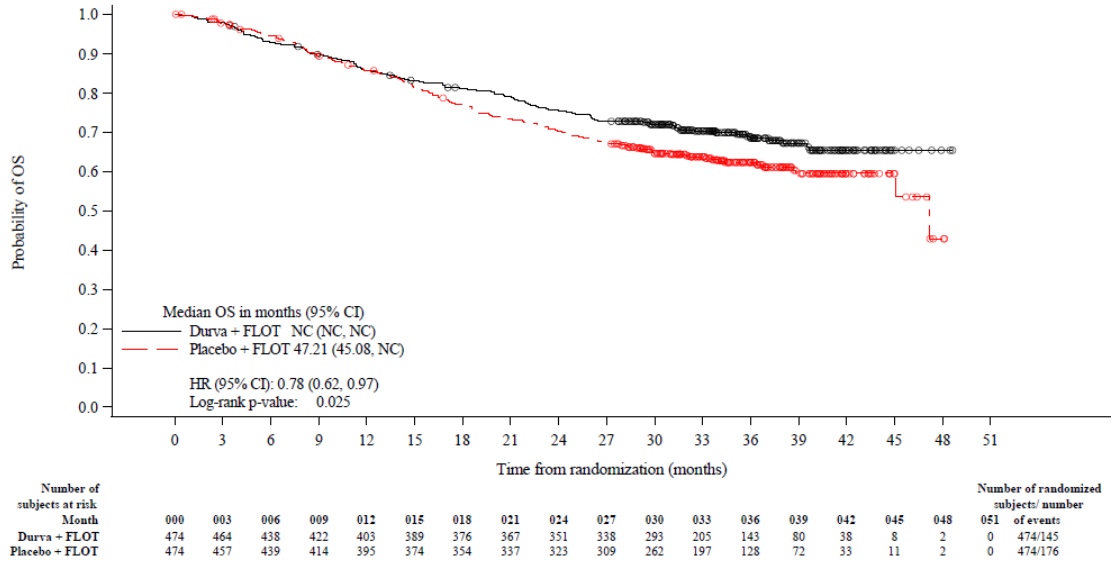
At the final analysis for OS, the median OS was not reached for both treatment arms. Treatment with D + FLOT demonstrated improved OS over Pbo + FLOT, demonstrating a statistically significant improvement in OS (HR 0.78; 95% CI: 0.63, 0.96; p = 0.021) (Table 4;

6.12 Figure 2).

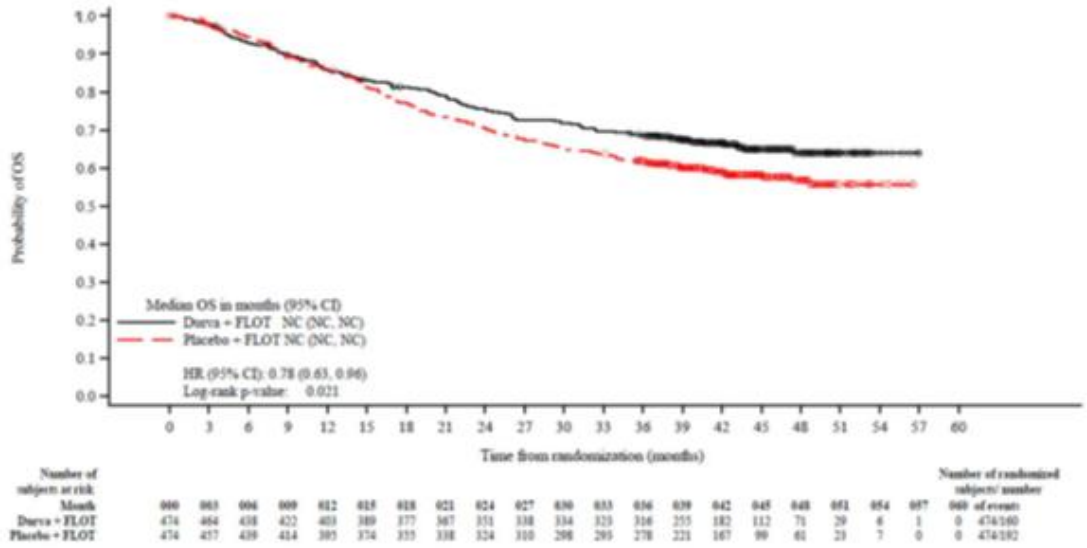
6.13 The use of subsequent IO in MATTERHORN differed from Australian clinical practice. The evaluation considered that the higher proportion of patients on D + FLOT (3.4% vs 0%), and the lower proportion of patients on Pbo + FLOT (9.5% vs estimated [redacted]%) who received subsequent IO compared with Australian clinical practice may affect the magnitude of treatment benefit for OS. The ESC considered that, given the modest efficacy of immunotherapy in metastatic disease, the impact on OS outcomes for the placebo arm from low use of subsequent immunotherapy is likely to be minimal. The ESC also considered that use of immunotherapy as subsequent therapy in the D + FLOT arm is unlikely to have had any impact on survival outcomes as there were very few patients who received it and retreatment is even less effective where patients have progression on prior immunotherapy.

Figure 2 Kaplan-Meier Plot of OS (FAS) at DCO2 and FA

DCO2



FA



Source: Figure 2-5 p80, Figure 2-6 p 81 of the submission.
CI = confidence interval; DCO = data cut-off; Durva = durvalumab; FA = final analysis; FAS = full analysis set; FLOT = 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; HR = hazard ratio; KM = Kaplan-Meier; NC = not calculable; OS = overall survival.
Source: ESMO Congress 2025 p7.
CI = confidence interval; ECOG = Eastern Cooperative Oncology Group; FA = final analysis; FAS = full analysis set; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; GEJ = gastroesophageal junction; HR = hazard ratio; OS = overall survival; PD-L1 = programmed cell death ligand-1; PS = performance status; TAP = tumour area positivity.

6.14 Treatment with D + FLOT led to statistically significant improvements in MFS (HR 0.72; 95% CI: 0.59, 0.88) and DFS (HR 0.70; 95% CI: 0.53, 0.93) compared with Pbo + FLOT (Table 5).

6.15 A statistically significantly higher proportion of patients on D + FLOT (19.2%) achieved pCR by central review compared with Pbo + FLOT (7.2%) (OR 3.08; 95% CI: 2.03, 4.67; p<0.001) (Table 5). pCR by investigator assessments supported those by central review (OR 2.95; 95% CI: 2.00, 4.35; p<0.001).

6.16 The addition of durvalumab to FLOT therapy did not affect the proportion of patients who proceeded to surgery (D + FLOT: 86.9%; Pbo + FLOT: 84.4%) (OR 1.23; 95% CI: 0.85, 1.77) (Table 5).

Table 5: Summary of categorical efficacy outcomes in the MATTERHORN trial

Outcome	D + FLOT n = 474	Pbo + FLOT n = 474	Absolute difference, %	Odds ratio (95% CI)
Key secondary outcome: pCR				
Proportion of patients with response (central review), n (%)	91 (19.2)	34 (7.2)	12	**3.08 (2.03, 4.67); p<0.001**
Proportion of patients with response (investigator assessment), n (%)	103 (21.7)	41 (8.6)	13	**2.95 (2.00, 4.35); p<0.001**
Secondary outcome: Surgery rate				
Proportion of patients who completed surgery, n (%)	412 (86.9)	400 (84.4)	3	1.23 (0.85, 1.77)

Source: Table 2-20 p82, Table 2-21 p83, Table 2-22 p84 and Table 2-24 p87 of the submission.
CI = confidence interval; D = durvalumab; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; pCR = pathological complete response.
Bolded results indicate statistically significant differences between treatment arms.

6.17 Patient reported outcomes were assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, Core 30 items (EORTC QLQ-C30), Quality of Life Questionnaire-Stomach 22-item module (QLQ-STO22) + Item Library 38, 2-item disease-specific measure (IL38) questionnaires. A 10-point change from baseline was prespecified as clinically meaningful.

6.18 No clinically meaningful differences were detected between D + FLOT and Pbo + FLOT for any EORTC QLQ-C30 or QLQ-STO22 symptom or functional scale at any timepoint during treatment or follow-up.

6.19 For global health status/quality of life (EORTC QLQ-C30), both arms experienced meaningful deterioration (≥ 10 points) at times, especially around treatment cycles 4 and 5, which coincided with surgery and chemotherapy. Physical functioning, role functioning, fatigue, and appetite loss showed similar temporary declines. There was improvement after treatment, with no ongoing deterioration and no differences between arms.

6.20 The EORTC QLQ-STO22 + IL38 instruments showed similar patterns. Eating restrictions, dry mouth, taste changes, hair loss, body image, and weight loss worsened during chemotherapy cycles but improved after stopping. Taste and hair loss were the only symptoms with sustained deterioration during treatment, but levels returned toward baseline in follow-up. Anxiety, which was the most impaired

symptom at baseline, improved from Cycle 10 onwards in both treatment arms, with no apparent differences between treatment arms.

6.21 Overall, there were no significant differences in the time to deterioration between the D + FLOT and Pbo + FLOT arms in patient reported outcomes. The exception was emotional function (EORTC QLQ-C30), where patients receiving D + FLOT (29.70 months; 95% CI: 23.36, 36.01) had a longer median time to deterioration than those on Pbo + FLOT (23.89 months; 95% CI: 18.73, 27.93) (HR 0.82; 95% CI: 0.68, 0.99). This corresponds to an approximately 6-month median difference and a statistically significant 18% lower hazard of emotional-function deterioration with D + FLOT.

Comparative harms

6.22 A summary of the safety outcomes is presented in Table 6.

6.23 At DCO2, the median duration of exposure for the overall study was 12.68 months (range 0.3-13.4 months) for the D + FLOT arm and 12.48 months (range 0.4-13.2 months) for Pbo + FLOT (MATTERHORN CSR Table 35, p 174).

6.24 Adverse events (AEs), Serious adverse events (SAEs) and discontinuation due to AEs reported in the MATTERHORN trial were numerically higher with D + FLOT than Pbo + FLOT for the overall study period. Any AEs possibly related to study drug were higher for durvalumab than placebo (relative risk [RR] 1.14; 95% CI: 1.02, 1.28). AEs of grade 3 or 4, treatment-emergent AEs leading to death, SAEs and AEs leading to dose modification were not different between the treatment arms. AEs leading to discontinuation of study drug (RR 1.31; 95% CI: 1.06, 1.63) and those related to study drug (RR 1.31; 95% CI: 1.05, 1.70) were higher for D + FLOT than Pbo + FLOT.

6.25 Immune-mediated AEs (imAEs) were higher for D + FLOT than Pbo + FLOT (RR 3.19; 95% CI: 2.22, 4.59), as were infusion reactions (RR 1.67; 95% CI: 1.25, 2.25). The higher incidence in imAEs was mainly driven by endocrine events; hypothyroid events (8.2% vs 1.5%), hyperthyroid events (1.5% vs 0), adrenal insufficiency (1.5% vs 0.2%), and diabetes mellitus (0.8% vs 0).

Table 6: Safety outcomes for the overall study

Category	D + FLOT (N = 475)	Pbo + FLOT (N = 469)	RD (95% CI) a	RR (95% CI) a
Any AE	471 (99.2%)	463 (98.7%)	0.00 (-0.01, 0.02)	1.00 (0.99, 1.02)
possibly related to durvalumab/pbo	282 (59.4%)	244 (52.0%)	0.07 (0.01, 0.14)	1.14 (1.02, 1.28)
possibly related to any FLOT (at least 1 drug)	450 (94.7%)	438 (93.4%)	0.01 (-0.02, 0.04)	1.01 (0.98, 1.05)
Any AE of maximum CTCAE Grade 3 or 4	340 (71.6%)	334 (71.2%)	0.00 (-0.05, 0.06)	1.01 (0.93, 1.09)
possibly related to durvalumab/pbo [b]	67 (14.1%)	58 (12.4%)	0.02 (-0.03, 0.06)	1.14 (0.82, 1.58)
possibly related to any FLOT (at least 1 drug) [b]	272 (57.3%)	268 (57.1%)	0.00 (-0.06, 0.06)	1.00 (0.90, 1.12)
Treatment-emergent AEs with an outcome of death	23 (4.8%)	20 (4.3%)	0.01 (-0.02, 0.03)	1.14 (0.63, 2.04)
SAEs	229 (48.2%)	207 (44.1%)	0.04 (-0.02, 0.10)	1.09 (0.95, 1.25)
possibly related to durvalumab/pbo	40 (8.4%)	25 (5.3%)	0.03 (-0.00, 0.06)	1.58 (0.97, 2.56)
possibly related to any FLOT (at least 1 drug)	81 (17.1%)	72 (15.4%)	0.02 (-0.03, 0.06)	1.11 (0.83, 1.49)
AEs leading to discontinuation of study drug	142 (29.9%)	107 (22.8%)	0.07 (0.01, 0.13)	1.31 (1.06, 1.63)
AEs leading to discontinuation of any study drug, possibly related to any study drug	122 (25.7%)	90 (19.2%)	0.06 (0.01, 0.12)	1.34 (1.05, 1.70)
imAEs and infusion reaction AEs				
imAEs	110 (23.2%)	34 (7.2%)	0.16 (0.11, 0.20)	3.19 (2.22, 4.59)
infusion reaction AEs	100 (21.1%)	59 (12.6%)	0.08 (0.04, 0.13)	1.67 (1.25, 2.25)

Source: Table 2-27 pp91-92 of the submission.
AE = adverse event; CI = confidence interval; CTCAE = common terminology criteria for adverse event; D = durvalumab; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; imAE = immune-mediated adverse event; Pbo = placebo; RD = risk difference; RR = relative risk; SAE = serious adverse event.
[a] Calculated using RevMan for the purpose of this Commentary.
[b] Patients with any Grade 5 AE are not included.

Benefits/harms

6.26 A summary of the comparative benefits and harms for D + FLOT versus Pbo + FLOT is presented in Table 7.

Table 7: Summary of comparative benefits and harms for D + FLOT and Pbo + FLOT

Benefits				
	D + FLOT (N = 474)	**Pbo + FLOT (N = 474)**	**Absolute difference, % [a]**	**HR (95% CI)**
EFS (DCO2: median duration follow-up 25.82-26.79 months)				
Number of events, n (%)	167 (35.2)	218 (46.0)		**0.71 (0.58, 0.86); p<0.001**
Median EFS, months (95% CI)	NC (40.74, NC)	32.82 (27.86, NC)		
EFS rate at 12 months, % (95% CI)	78.18 (74.11, 81.70)	74.01 (69.71, 77.70)	4.2	-
EFS rate at 24 months, % (95% CI)	67.44 (62.71, 71.77)	58.54 (53.03, 63.64)	8.9	-
EFS rate at 36 months, % (95% CI)	61.99 (56.95, 66.61)	46.61 (41.20, 52.49)	15.4	-
OS (FA: median duration follow-up 42.9-43.0 months)				
Number of events, n (%)	160 (33.8)	192 (40.5)		**0.78 (0.63, 0.96); p=0.021**

Median OS, months (95% CI)	NC (NC, NC)	NC (NC, NC)		
OS rate at 18 months, %	81.1	77.1	4.0	-
OS rate at 24 months, %	75.5	70.4	5.1	-
OS rate at 36 months, %	68.6	61.9	6.7	-
pCR (DCO2)				
	D + FLOT (N = 474)	**Pbo + FLOT (N = 474)**	**Absolute difference, % (95% CI) [a]**	**OR (95% CI)**
Number of events, n (%)	103 (21.7)	41 (8.6)	13 (7, 21)	**2.95 (2.00, 4.35); p<0.001**

Harms (DCO2)						
	D + F LOT (N = 475)	**Pbo + FLOT (N = 469)**	**RR (95% CI) [a]**	**Event rate/100 patients**		**Absolute difference, % (95% CI) [a]**
				D + FLOT	**Pbo + FLOT**	
Any AE, n	471	463	1.00 (0.99, 1.02)	99.2	98.7	0 (-1, 2)
Any grade 3 or 4 AE, n	340	334	1.01 (0.93, 1.09)	71.6	71.2	0 (-5, 6)
SAE, n	229	207	1.09 (0.95, 1.25)	48.2	44.1	4 (-2, 10)
AEs leading to drug discontinuation, n	142	107	1.31 (1.06, 1.63)	29.9	22.8	7 (1, 13)
imAEs, n	110	34	3.19 (2.22, 4.59)	23.2	7.2	16 (11, 20)
Infusion reaction AEs, n	100	59	1.67 (1.25, 2.25)	21.1	12.6	8 (4, 13)

Source: Table 2-27 pp91-92 of the submission; ESMO Congress 2025 p6.
AE = adverse event; CI = confidence interval; D = durvalumab; DCO = data cut-off; EFS = event-free survival; FA = final analysis; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR = hazard ratio; imAE = immune-mediated adverse event; NC = not calculable; OS = overall survival; Pbo = placebo; pCR = pathological complete response; SAE = serious adverse event; RR = relative risk; OR = odds ratio.
[a] Values calculated during evaluation.
Bolded results indicate statistically significant differences between treatment arms.

6.27 On the basis of direct evidence presented by the submission, for every 100 patients treated with D + FLOT in comparison with Pbo + FLOT over a median follow-up of approximately 26 months:

- Approximately 9 additional patients will remain free of progression, recurrence or death at 24 months.
- Approximately 13 additional patients will demonstrate no remaining cancer cells in tissue samples removed during surgery or biopsy (pathological complete response).
- Approximately 4 additional patients will experience an SAE, 7 additional patients will discontinue treatment due to AEs, 16 additional patients will experience side effects caused by the immune system's response to treatment (imAEs), and 8 additional patients will experience infusion reaction AEs.

6.28 On the basis of direct evidence presented by the submission, for every 100 patients treated with D + FLOT in comparison with Pbo + FLOT over a median follow-up of approximately 43 months:

- Approximately 7 additional patients will remain alive at 36 months.

Clinical claim

6.29 The submission described D + FLOT as superior in terms of effectiveness compared to Pbo + FLOT. The evaluation considered this claim was adequately supported but the magnitude of the effect is unclear, the key issue being the difference in the use of subsequent IO compared with Australian clinical practice. The ESC agreed with the evaluation that the claim of superior effectiveness compared to Pbo + FLOT was adequately supported but considered that the difference in subsequent immunotherapies compared with Australian clinical practice is unlikely to have a substantial impact on OS outcomes (see also paragraph 6.13). The ESC noted that the EFS benefit was small, but clinically significant and resulted in a statistically significant OS benefit based on relatively mature OS data (in an early disease setting).

6.30 The submission described D + FLOT as inferior in terms of safety compared to Pbo + FLOT. The ESC agreed with the evaluation that this claim was adequately supported.

6.31 The PBAC considered that the claim of superior comparative effectiveness was reasonable.

6.32 The PBAC considered that the claim of inferior comparative safety was reasonable.

Economic analysis

6.33 The submission presented a stepped economic evaluation of perioperative D + FLOT compared with FLOT only for the treatment of resectable stage II-IVA GC/GOJC, over a 25-year time horizon. The modelled evaluation presented a cost-utility approach, consistent with the clinical claims that D + FLOT is superior to FLOT only in terms of both OS and EFS, with inferior safety. A semi-Markov model was utilised to estimate the incremental cost per quality-adjusted life year (QALY) gained.

6.34 Table 8 summarises the key components of economic evaluation.

Table 8: Summary of model structure, key inputs and rationale

Component	Summary
Treatments	Perioperative D + FLOT vs FLOT
Time horizon	25 years in the model base case versus 48 months median follow up in MATTERHORN trial
Outcomes	EF years gained, LYs gained, QALYs gained
Methods used to generate results	Semi-Markov model
Health states	EF, RD, death
Cycle length	Monthly
Allocation to health states	Derived from the primary analysis of patient-level data from the MATTERHORN trial
Extrapolation method	Parametric models independently fitted to TFR, time to death as first event and time from first recurrence or progression to death data for each treatment arm. Generalised gamma, lognormal and exponential models were selected in the base case for TFR, time to death as first event and post-recurrence survival, respectively. The same parametric models were selected for each arm. Selection primarily based on goodness of fit (AIC). The fitted models were used to predict outcomes both during the trial follow-up period and to extrapolate outcomes beyond 48 months. Patients remaining EF beyond 10 years were assumed to be "cured".
Health related quality of life	MATTERHORN trial-based EF: 0.840 RD: 0.785

Source: Table 3-1, p113 of the submission.
AIC = Akaike Information Criterion; D = durvalumab; EF = event-free; EFS = event-free survival; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; LY = life year; OS = overall survival; QALY = quality-adjusted life year; RD = recurred disease; TFR = time to first recurrence.

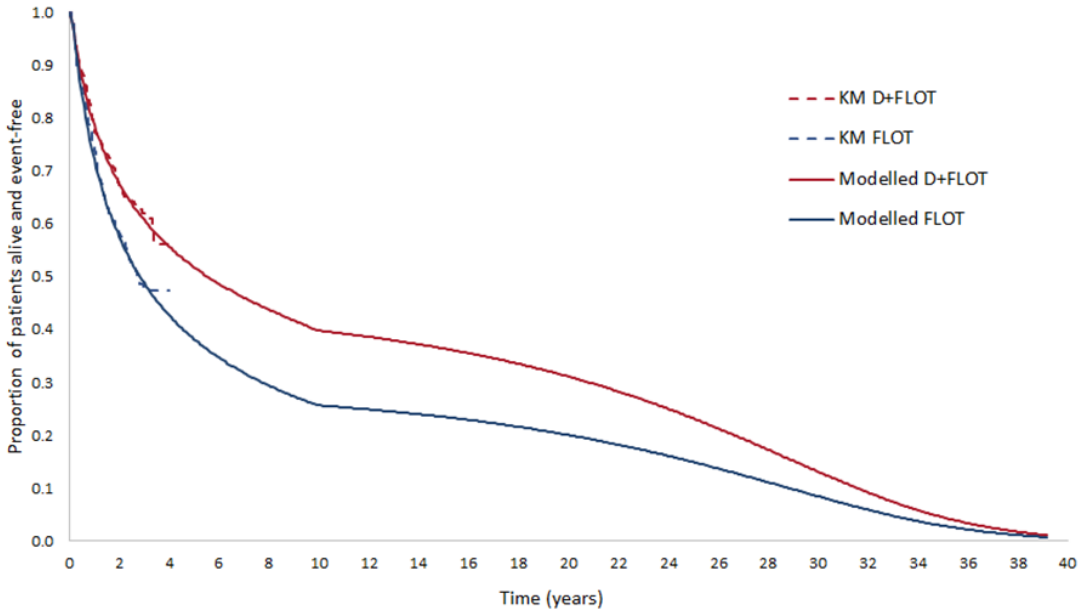
6.35 Parametric models were fitted to patient-level time to event data from the MATTERHORN trial. These survival models were used to predict outcomes both during the trial follow-up period and to extrapolate outcomes up to a 25-year time horizon. Data from DCO2 were utilised in the model fitting, which included data up to 48 months follow-up. The submission's use of modelled data, both during the trial follow-up and extrapolation periods, does not align with the PBAC Guideline (Subsection 3A.4.3) recommendation to use time-to-event data in preference to be modelled data up to the point at which the observed data become unreliable. The ESC agreed with the evaluation that it would be preferable to use KM data for the model as per the PBAC guidelines, but noted that it was unlikely to have a substantial impact on the ICER.

6.36 There was no strong evidence against the proportional hazards assumption, suggesting sensitivity analyses using dependently modelled survival curves could have been presented.

6.37 Parametric models were fitted to time-to-first recurrence (TFR), time to death as first event and post-recurrence survival (PRS) data. Generalised gamma, lognormal and exponential models were selected in the base case for TFR, time to death as first event and PRS, respectively, with selection primarily based on goodness of fit (Akaike Information Criterion [AIC]). The TFR and time to death as first event transition

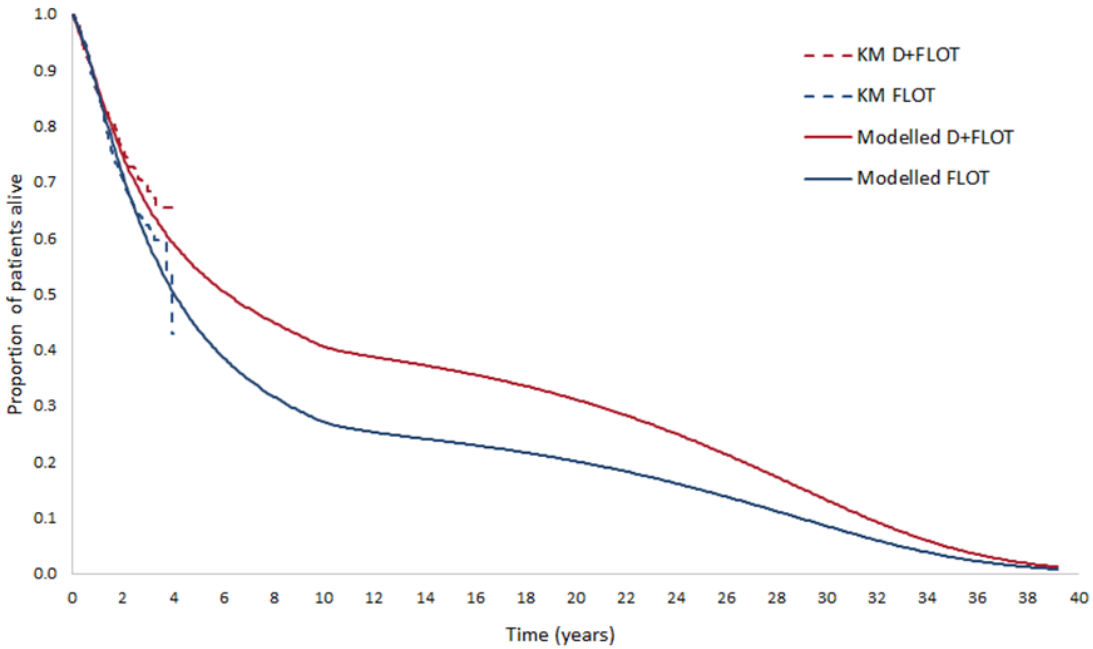
probabilities combined provided the EFS curve (Figure 3). Modelled OS is shown in Figure 4.

Figure 3 Extrapolated event-free survival incorporating cure at 10 years



Source: Figure 3-6, p128 of the submission.
D = durvalumab; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; KM = Kaplan-Meier.

Figure 4 Extrapolated overall survival incorporating cure at 10 years



Source: Figure 3-9, p133 of the submission.
D = durvalumab; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; KM = Kaplan-Meier.

6.38 The ICER was generally not sensitive to the choice of various extrapolation functions. However, selection of the Generalised Gamma function for time to death as the first event in both arms (which provided the second best fit for the D + FLOT arm according to AIC) reduced the ICER by [redacted]% ($25,000 to < $35,000 per QALY). Use of a Log-logistic function to model PRS in both arms (which provided the best fit for the FLOT arm according to AIC) increased the ICER by [redacted]% ($35,000 to < $45,000/QALY).

6.39 The model applied a 25-year time horizon for the base case analysis, with patients entering the model at a mean age of 60.8 years based on MATTERHORN trial. The PSCR argued that it was reasonable to apply a 25 year (lifetime) horizon in this setting, where a proportion of patients are expected to be cured. The PSCR also noted that the time horizon is consistent with other perioperative/adjuvant oncology models (olaparib, pertuzumab in early breast cancer). The ESC considered that the time horizons applied in submissions for breast cancer treatments were not relevant to the GC/GOJC population as patients were not comparable. The ESC and PBAC advice on the nivolumab submission (stage II or III or GOJC patients who have received CRT prior to surgery) was that the 25-year time horizon be reduced to 15–20 years due to long term surgical and clinical risks for this patient population (paragraphs 6.33 and 7.10, nivolumab Public Summary Document [PSD], July 2022 PBAC meeting). The PSCR and Pre-PBAC response argued that comparison with this population was not appropriate as they have a poorer prognosis than the population proposed for perioperative durvalumab and no OS benefit was demonstrated for nivolumab in this population. The ESC considered that the time horizon of 25 years was too long given the starting age and underlying morbidity of the GC/GOJC population. The ESC considered that a time horizon of 15 years would be reasonable and up to 20 years may also be acceptable in the context of more conservative assumptions for other model inputs. The Pre-PBAC response maintained that the 25-year time horizon used in the base case was clinically plausible in a perioperative, curative intent setting, but also stated that a time horizon no shorter than 20 years was reasonable, representing a conservative approach while still capturing expected long-term benefits.

6.40 There is a sustained separation of the modelled EFS and OS curves over the full 25-year period, with application of a cure assumption at 10 years (equivalent transition probabilities for recurrence and death as first event applied beyond this point) and more favourable post-recurrence survival in the FLOT arm. This implies long-term gains are driven by the accumulation of benefit during the first 10 years. While observed data support separation up to 4 years, the continued benefit between 4 and 10 years is assumed.

6.41 The submission assumes that patients remaining in the EF state at 10 years are effectively “cured”, with no further risk of recurrence and mortality equal to general population. The expert advisory board consulted by the sponsor suggested that clinical cure is assumed if a patient remains EF for 5 years. While the submission suggested

the 10-year cure point is 'conservative' this is not reflected in the sensitivity analysis results, as the ICER increases when the cure point is reduced to 5 years or increased to 15 years. This is because the difference in EFS in the extrapolated curves is greatest at around 10 years. Expert advice received during the evaluation supported the assumption of cure beyond 10-years, but noted that recurrences after 5 years are rare, and those beyond 7 years exceedingly unlikely. The ESC agreed with the evaluation that the inclusion of a cure fraction was reasonable. The ESC also agreed that recurrences after 5 years are rare and noted that in clinical practice patients would typically be considered cured after 5 years of EFS. The ESC considered that the most appropriate cure point was 5 years. The pre-PBAC response referred to longer term EFS data from Al Batran (2019) and Hoeppner (2025) demonstrating that a small number of recurrences occur past the 5-year time point. On this basis the sponsor considered a 7-year cure timepoint to better capture the small proportion of later recurrences. The pre-PBAC response also argued that the time horizon and cure time point should be considered jointly to ensure consistency.

6.42 The submission identified that use of subsequent IO post FLOT may be higher in the Australian context than in the control arm of the MATTERHORN trial. Post-recurrence subsequent IO (nivolumab) use in the model for the FLOT arm was increased from 29.4% (MATTERHORN trial data) to [redacted]% (AstraZeneca Australian Gastric Advisory Board input) (assuming 90% of patients who progress will receive subsequent therapy). This assumption was operationalised through a reduction in the death rate in the RD health state in the FLOT arm, as well as increased subsequent therapy costs in the FLOT arm. An HR of 0.87 was applied to the instantaneous hazard of death from the RD heath state in the FLOT arm, derived by applying the HR for nivolumab + chemotherapy versus chemotherapy in patients with advanced or metastatic GC, GOJC or oesophageal adenocarcinoma (OAC) reported in the Checkmate 649 trial (HR = 0.80; paragraph 6.15, nivolumab, PSD, November 2021 PBAC Meeting) for the proportion of modelled IO-recipients not captured in the MATTERHORN trial estimates. The assumed cost per course of subsequent IO was $[redacted] per patient, based on a treatment course comprising 12.37 doses and an assumed [redacted]% rebate on the published price.

6.43 The evaluation and the ESC considered it reasonable to expect that in clinical practice subsequent nivolumab use would be high in the comparator arm; expert advice received during the evaluation validated the [redacted]% assumption as appropriate to the Australian context. The ESC noted that, although a substantial impact on OS from subsequent immunotherapy is not expected, there was uncertainty associated with the adjustment applied in the model. A sensitivity analysis removing the adjustment [i.e. using the trial-informed 29.4% of IO use] increased the ICER by [redacted]% [$$35,000 to < $45,000 per QALY]).

6.44 In the model, it is assumed that 0% of patients who progress on D + FLOT would receive subsequent IO, given the current once-per-lifetime restrictions. However, in

the MATTERHORN trial, 14.7% of patients in the D + FLOT arm who received subsequent therapy received IO (3.4% of D + FLOT patients overall). This suggests survival benefits in the D + FLOT arm may be slightly overestimated relative to the Australian context, although the impact on the ICER is minimal (<1% variation).

6.45 Health state utility values were derived from MATTERHORN trial data for the EF and RD health states, pooled across treatment arms. No meaningful differences between arms for any symptom or scale of the EORTC QLQ-C30 were observed at any timepoint in the MATTERHORN trial, and regression analysis conducted by the sponsor showed no statistically significant differences in pre-progression or post-progression utility scores across arms. Overall, the approach to pool data across treatment arms seems broadly reasonable, especially considering treatment-related disutility were presumably captured through application of arm-specific AE disutilities. However, the utility decrement due to AEs is lower in the D + FLOT arm of the model, which does not align with the inferiority safety claim. Based on this observation, the QALY benefits for D + FLOT may be overstated.

6.46 While D + FLOT was associated with higher rates of imAEs, infusion reactions, AEs possibly related to durvalumab/placebo, study drug-related AEs and AEs leading to treatment discontinuation relative to FLOT, the overall incidence AEs of grade 3 or 4—including those possibly related to durvalumab/placebo—did not differ across treatment arms. The model only captured AEs of grade ≥3 occurring in ≥5% of patients in either treatment arm (neutropenia, neutrophil count decreased, diarrhoea, and white blood cell count decreased). The proportion of patients with imAEs was higher in the D + FLOT arm (23.2%) compared to the Pbo + FLOT arm (7.2%). Most imAEs were grade 1–2 events and were therefore not captured in the economic model. However, the PSCR noted that the ICER is not sensitive to the QALY decrements associated with AEs.

6.47 Based on the sensitivity analyses conducted in the submission and during the evaluation, the key model drivers were the time horizon, the incorporation of cure assumption, and the adjustment to the proportion of IO use as subsequent therapy. The key drivers of the model are summarised in Table 9.

Table 9: Key drivers of the model

Description	Method/Value	Impact Base case: $[redacted][1]/QALY gained
Time horizon	A 25-year time horizon was used in the base case and alternate time horizons (5, 10, 15, 20 and 30 years) tested in the sensitivity analyses.	Moderate-high, potential to favour D + FLOT. Use of a 20-year time horizon increased the ICER to $[redacted][1]/QALY gained.
Proportion IO use in FLOT arm	Post-recurrence subsequent IO (nivolumab) for the FLOT arm was adjusted from 29.4% to [redacted]% in the base case.	Moderate-high, favour D + FLOT. Exclusion of adjustment (i.e. use of trial-informed 29.4% IO use) increased the ICER by [redacted]% ($[redacted][1]/QALY).
Extrapolation	The Lognormal parametric function was applied for the time to death as first event and Exponential function for the post-recurrence survival for the base case for both arms.	Direction of impact is unclear. Use of Generalised Gamma function for time to event as a first event reduced the ICER by [redacted]% ($[redacted][2]/QALY). Use of Log-logistic function for post-recurrence survival increased the ICER by [redacted]% ($[redacted][1]/QALY).
Cure assumption	The model incorporated a 10-year 'cure' timepoint; beyond 10 years patients remaining EF are assumed to be effectively 'cured' (i.e. no longer at risk of recurrence and with a risk of death equal to that of the general population).	Moderate, favours D + FLOT. Exclusion of the cure assumption increased the ICER by [redacted]% ($[redacted][1]/QALY) and using earlier cure timepoints of 5 and 7 years, increased the ICER by [redacted]% ($[redacted][1]/QALY) and [redacted]% ($[redacted][1]/QALY), respectively.

Source: Table 3-37, p158 of the submission.
D = durvalumab; EF = event free; ESC = Economics Sub-Committee; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; ICER = incremental cost-effectiveness ratio; IO = immunotherapy; PBAC = Pharmaceutical Benefits Advisory Committee; PSD = public summary document; QALY = quality-adjusted life-years.
The redacted values correspond to the following ranges:
[1] *$35,000 to < $45,000*
[2] *$25,000 to < $35,000*

6.48 The results of stepped economic evaluation are summarised in Table 10.

Table 10: Results of the stepped economic evaluation

Step and component	D + FLOT	FLOT	Increment
Step 1: trial-based costs and outcomes over 48 months (cost per event-free year gained)			
Costs	$[redacted]	$7,589	$[redacted]
Event-free years gained	2.85	2.52	0.33
Incremental cost/extra event-free year gained			$[redacted] [1]
Step 2: time horizon extended to 25 years (cost per LYG)			
Costs	$[redacted]	$53,994	$[redacted]
LYG	7.32	5.86	1.46
Incremental cost/extra LYG gained			$[redacted] [2]
Step 4: Transform LYs into QALYs over 25-year time horizon (cost per QALY)			
Costs	$[redacted]	$53,994	$[redacted]
QALY	6.14	4.89	1.24
Incremental cost/extra QALY gained (base case)			$[redacted] [3]

Source: Table 3-35, p155 of the submission.

D = durvalumab; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; LYG = life years gained; QALY = quality adjusted life-years.

The redacted values correspond to the following ranges:

[1] *$155,000 to < $255,000*

[2] *$25,000 to < $35,000*

[3] *$35,000 to < $45,000*

6.49 Over the 25-year time horizon, treatment with D + FLOT was associated with an undiscounted incremental LYG of 2.63 relative to FLOT.

6.50 The model captured costs of subsequent therapies, applied as a once-off cost upon recurrence or progression. Due to the confidential special pricing arrangements (SPAs) that exist for nivolumab, the sponsor estimated the effective price of nivolumab (assumed [redacted]% of the published price would be rebated under the SPA).

6.51 The results of key univariate/multivariate sensitivity analyses are summarised in Table 11.

Table 11: Sensitivity analyses

Analyses	Incremental cost	Incremental QALY	ICER	% change to ICER
Base case	**$[redacted]**	**1.24**	**$[redacted][1]**	**NA**
Time horizon (base case 25 years)				
15 years	$[redacted]	0.88	$[redacted][2]	[redacted]%
20 years	$[redacted]	1.10	$[redacted][1]	[redacted]%
Discount rate (base case: 5%)				
0% costs and outcomes	$[redacted]	2.23	$[redacted][3]	–[redacted]%
3.5% costs and outcomes	$[redacted]	1.46	$[redacted][4]	–[redacted]%
Cure assumption (base case applied at 10 years)				
Applied at 7 years	$[redacted]	1.22	$[redacted][1]	[redacted]%
Applied at 5 years	$[redacted]	1.17	$[redacted][1]	[redacted]%
Not applied	$[redacted]	1.12	$[redacted][1]	[redacted]%
Proportion receiving subsequent IO in the FLOT arm (base case [redacted]%)				
Trial-based proportion (29.4%)	$[redacted]	1.30	$[redacted][1]	[redacted]%
Time to death as first event parametric function (base case Lognormal for both arms)				
Generalised Gamma for both arms	$[redacted]	1.41	$[redacted][4]	–[redacted]%
Post-recurrence survival parametric function (base case Exponential for both arms)				
Gamma for both arms	$[redacted]	1.24	$[redacted][1]	[redacted]%
Loglogistic for both arms	$[redacted]	1.10	$[redacted][1]	[redacted]%
Multivariate analyses				
20-year time horizon and cure assumed at 7 years	$[redacted]	1.09	$[redacted][1]	[redacted]%
20-year time horizon and cure assumed at 5 years	$[redacted]	1.04	$[redacted][1]	[redacted]%
15-year time horizon and cure assumed at 5 years	$[redacted]	0.84	$[redacted][5]	[redacted]%

Source: Table 3-37, p158 of the submission.

EF = event-free; ICER = incremental cost-effectiveness ratio; MRU = medical resource use; NA = not applicable; QALY = quality adjusted life years; TFR = time to first recurrence.

The redacted values correspond to the following ranges:

[1] *$35,000 to < $45,000*

[2] *$45,000 to < $55,000*

[3] *$15,000 to < $25,000*

[4] *$25,000 to < $35,000*

[5] *$55,000 to < $75,000*

Drug cost/patient/course

6.52 A comparison of durvalumab use between the trial setting, the economic model and the financial estimates model is presented in Table 12. The same treatment regimen was used for each analysis: durvalumab 1,500 mg every 4 weeks for a maximum duration of 14 cycles (4 cycles administered with FLOT [2 as neoadjuvant and 2 as adjuvant], and 10 cycles administered as monotherapy in the adjuvant setting). The

mean treatment duration of durvalumab in the economic model was directly sourced from the MATTERHORN trial.

6.53 The mean total duration of exposure to durvalumab in the MATTERHORN trial was 9.36 months (8.87 months after subtracting dose delays). The economic model estimated treatment costs based on the proportion of the D + FLOT arm of the MATTERHORN trial receiving treatment each cycle.

Table 12: Drug cost per patient for per course for durvalumab

	Trial dose and duration	Economic model	Financial estimates
Mean dose	1,500 mg Q4W		
Mean duration of treatment (months)	9.36 (total)/ 8.87 (actual)[a]	NR[b]	8.90[c]
Requested effective EMP	–	$[redacted] per 500 mg vial	$[redacted] per 500 mg vial
Cost per cycle (28 days)	–	$[redacted] (with FLOT) [d] $[redacted] (without FLOT)[e]	$[redacted][d]
Mean number of cycles per course	2.0 (neoadjuvant), n=475 10.1 (adjuvant), n= 361 (76%) Total: 9.68	NR[b]	9.68
Cost/patient/course	–	$[redacted][f]	$[redacted][g]

Source: MATTERHORN CSR, Table 14.3.1.1.1 and Table 14.3.1.2.1; Attachment 10 (Economic Evaluation) of the submission
DPMA = dispensed price for maximum amount; EMP = ex-manufacturer price; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; NR = not reported; Q4W = every 4 weeks

[a] Actual overall treatment duration reflects total exposure minus total duration of dose delays.

[b] Durvalumab usage derived based on proportion of cohort receiving treatment each cycle. Aligns with utilisation in the MATTERHORN trial, for which mean of 2.0 and 10.1 treatment cycles were reported during the neoadjuvant and adjuvant phases, respectively.

[c] Estimated as (9.676 [mean number of cycles] × 28 days [cycle length]) / 30.4375

[d] Based on public and private hospital markups effective from 1 July 2025, the effective DPMA is $[redacted] in public hospitals and $[redacted] in private hospitals per 1,500 mg. Weighted by public and private utilisation rates, the DPMA per 1,500 mg (including mark ups) was calculated as $[redacted].

[e] Based on relative dose intensity of 96.2% during durvalumab monotherapy phase

[f] Undiscounted disaggregated cost from the economic model –durvalumab acquisition cost (neoadjuvant and adjuvant phases).

[g] Calculated as 9.676 (mean number of cycles) × $[redacted] (cost per cycle)

Estimated PBS usage & financial implications

6.54 This submission was not considered by DUSC.

The submission took an epidemiological approach and assumed [redacted]% market uptake among eligible GC/GOJC patients. The annual number of treated patients was estimated based on incident patient numbers, plus < 500 grandfathered patients in year 1. Key inputs relied on in the financial analyses are presented in

6.55 Table 13.

Table 13: Key inputs for financial estimates

Data	Value applied and source	Comment
Incident patients	Yr 1: 2,833; Yr 2: 2,892; Yr 3: 2,954; Yr 4: 3,011; Yr 5: 3,076; Yr 6: 3,141 AIHW. Long-term incidence projections for stomach cancers (ICD-10 16.0).	Captures all stomach (gastric) cancers classified under ICD-10 code C16.0. The C16.0 (cardia subsite) subcode has previously been accepted as representative of the GOJC population (Table 14, nivolumab PSD, July 2022 PBAC meeting); therefore, the C16 data used is likely representative of all gastric and GOJ cases.
Proportion of G/GOJC eligible for D + FLOT	Yr 1−6: 41% Multiplicative of the following inputs: • proportion of G/GOJ of adenocarcinoma histology (93.2%)[5] • proportion of G/GOJ adenocarcinoma patients receiving surgery (50.0%)[6] • proportion of surgically treated patients who receive perioperative FLOT ([redacted]%) (expert opinion) • Adjusted for patients who initiate FLOT but do not progress to surgery (110.0%)	The evaluation noted that some of these estimates were uncertain (see paragraph 6.58).
Uptake rate	Yr 1−6: [redacted]% Expert opinion	The evaluation considered it was reasonable to consider a high uptake rate once listed on the PBS; however, assuming an immediate uptake rate of [redacted]%, including in Year 1 of listing, may be optimistic. The pre-PBAC response noted that adoption is expected to be strong given there is already high awareness and clinician endorsement for the MATTERHORN regimen by the international ESMO and NCCN guidelines and that there will be a patient access program prior to listing on the PBS
Grandfathered patients	Yr 1: [redacted][1] Assumed	The sponsor is planning to commence a patient access program, through which they assume ~[redacted][1] patients will transition to PBS-funded treatment in year 1 of listing. While the inclusion of grandfathered patients is appropriate, the financial estimates appear to account for the full treatment course for grandfathered patients, overestimating the number of PBS-subsidised cycles.
Durvalumab (effective DPMA)	$[redacted] (public hospitals) $[redacted] (private hospitals)	

[5]Arnold, M, Morgan, E, Bardot, A, Rutherford, MJ, Ferlay, J, Little, A, Møller, B, Bucher, O, De, P, Woods, RR, Saint-Jacques, N, Gavin, AT, Engholm, G, Achiam, MP, Porter, G, Walsh, PM, Vernon, S, Kozie, S, Ramanakumar, AV, Lynch, C, Harrison, S, Merrett, N, O'Connell, DL, Mala, T, Elwood, M, Zalcberg, J, Huws, DW, Ransom, D, Bray, F & Soerjomataram, I 2022, 'International variation in oesophageal and gastric cancer survival 2012–2014: differences by histological subtype and stage at diagnosis (an ICBP SURVMARK-2 population-based study)', Gut, vol. 71, no. 8, pp. 1532-43.

[6] Abbas, MN, Bright, T, Price, T, Karapetis, C, Thompson, S, Connell, C, Watson, D, Barnes, M, Bull, J, Singhal, N & Roy, A 2021, 'Patterns of care and outcomes for gastric and gastro-oesophageal junction cancer in an Australian population', *ANZ J Surg*, vol. 91, no. 12, pp. 2675-82.

Data	Value applied and source	Comment
Subsequent nivolumab (assumed effective DPMA)	$[redacted] (public hospitals), 13121N $[redacted] (private hospitals), 13117J Based on published AEMP (360mg) of $4,734.79 and assumed SPA rebating [redacted]% of the published price. [a]	An assumed effective price for subsequent nivolumab was applied. The modelled reduction in nivolumab utilisation may not be fully realised given that patients may access nivolumab under the broad listing.

Source: Table 4-1 −Table 16, section 4.1, 4.2, 4.3 pp160-174 of the submission.
AIHW= Australian Institute of Health and Welfare; CIC = committee-in-confidence; D = durvalumab; DPMA = dispensed price for maximum amount; FLOT = 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; FOLFIRI = folinic acid, 5-fluorouracil, and irinotecan; G/GOJA(C) = gastric/gastro-oesophageal junction adenocarcinoma (carcinoma); ICD = International Classification of Diseases; MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme; PSD = public summary document; SPA = special pricing arrangement; Yr = year.
[a] A total of 12.37 cycles of 360 mg Q3W nivolumab was used in the economic modelling. However, the dosing schedule and cycle number was adjusted to 18.55 cycles of 240 mg Q2W nivolumab in the financial model to align with the frequency of dosing with FOLFIRI in this setting.
The redacted values correspond to the following ranges:
[1] < 500

6.56 The estimated use and financial implications to the PBS/RPBS presented in the submission are provided in Table 14.

Table 14: Estimated use and financial implications (based on proposed effective price)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of incident patients initiating durvalumab	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Number of grandfathered patients	[redacted][2]	0	0	0	0	0
Number of scripts dispensed	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Estimated financial implications of durvalumab						
Cost to PBS/RPBS less copayments	$[redacted][4]	$[redacted][4]	$[redacted][4]	$[redacted][4]	$[redacted][5]	$[redacted][5]
Estimated financial implications for nivolumab						
Cost to PBS/RPBS less copayments[a]	−$[redacted][6]	−$[redacted][6]	−$[redacted][6]	−$[redacted][6]	−$[redacted][6]	−$[redacted][6]
Estimated financial implications for FOLFIRI						
Cost to PBS/RPBS less copayments	−$[redacted][6]	−$[redacted][6]	−$[redacted][6]	−$[redacted][6]	−$[redacted][6]	−$[redacted][6]
Total cost offsets	**−$[redacted][6]**	**−$[redacted][6]**	**−$[redacted][6]**	**−$[redacted][6]**	**−$[redacted][6]**	**−$[redacted][6]**
Net financial implications						
Net cost to PBS/RPBS	$[redacted][4]	$[redacted][7]	$[redacted][7]	$[redacted][7]	$[redacted][7]	$[redacted][7]
Net cost to MBS	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]
Net cost to health budget	$[redacted][4]	$[redacted][7]	$[redacted][7]	$[redacted][7]	$[redacted][7]	$[redacted][7]

Source: Table 4-10, Table 4-11, Table 4-17, Table 4-18, Table 4-19, pp161-176 of the submission.
FOLFIRI = folinic acid, 5-fluorouracil, and irinotecan; MBS = Medicare Benefits Scheme; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.
a estimates assume [redacted]% rebate to the published price for nivolumab
The redacted values correspond to the following ranges:
[1] *500 to < 5,000*
[2] *< 500*
[3] *10,000 to < 20,000*
[4] *$60 million to < $70 million*
[5] *$70 million to < $80 million*
[6] *net cost saving*
[7] *$50 million to < $60 million*
[8] *$0 to < $10 million*

6.57 The total cost to the PBS/RPBS of listing durvalumab was estimated to be $70 million to < $80 million in Year 6, and a total of $400 million to < $500 million in the first 6 years of listing.

6.58 Several uncertainties were identified during the evaluation, including a high uptake rate for the first year of listing, the proportion of patients receiving surgery, the proportion of patients who received prior FLOT and the proportion of GC/GOJC patients eligible for D + FLOT. The estimates were most sensitive to the proportion of GC/GOJC patients eligible for D + FLOT, which relied on several sources and assumptions. The PBAC considered that these assumptions were somewhat uncertain but appeared to be reasonable overall.

Quality Use of Medicines

6.59 The sponsor noted that they intend to work collaboratively with healthcare professionals to ensure that durvalumab is used appropriately and in line with the available clinical evidence and the TGA restriction. Furthermore, the sponsor also indicated that several international post-marketing surveillance studies for durvalumab are planned internationally, though no further details on these studies were provided.

Financial Management – Risk Sharing Arrangements

6.60 No risk sharing arrangement (RSA) was proposed in the submission. There do not appear to be any major risks in terms of the patient population, dose escalation or use beyond disease progression to be managed through an RSA. However, RSAs are in place for other immunotherapies for gastro-oesophageal cancers in the advanced or metastatic setting which could be impacted by the proposed listing. Both the cost-effectiveness and financial estimates presented rely on modelling a reduction in use of subsequent IO. The pre-PBAC response maintained that an RSA was not proposed as the requested listing is tightly aligned to the clinically appropriate population and expected use.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC recommended the listing of durvalumab for the perioperative treatment of gastric cancer or gastroesophageal junction cancer (GC/GOJC) in patients who are eligible for neoadjuvant FLOT (fluorouracil, leucovorin, oxaliplatin, docetaxel) chemotherapy, on the basis that it should be available only under special arrangements under Section 100 (Efficient Funding of Chemotherapy Program). The PBAC is satisfied that the addition of perioperative durvalumab to FLOT improves event free survival (EFS) and overall survival (OS) in patients with GC/GOJC, compared with FLOT alone. The PBAC considered that durvalumab would be considered acceptably cost-effective with some revision to model inputs and a price reduction that resulted in an acceptable incremental cost-effectiveness ratio (ICER). The PBAC considered that the financial estimates were reasonable, with minor revisions.

7.2 The PBAC considered that the proposed clinical place for durvalumab was well-defined, supported by the clinical evidence, and consistent with local and international guidelines.

7.3 The PBAC noted that the submission assumed that nivolumab would not be available as later line therapy in patients with progressive disease after treatment with durvalumab, however the broad listing for nivolumab/ipilimumab in the advanced and

metastatic setting would allow for subsequent nivolumab. The PBAC also noted that there may be some patients with advanced GC/GOJC who would be eligible for nivolumab under the broad nivolumab/ipilimumab listing, though the likely extent of perioperative use of nivolumab is unclear.

7.4 The submission nominated perioperative FLOT alone, the current SOC, as the comparator. The PBAC considered that FLOT alone was the appropriate primary comparator.

7.5 The submission was based on one large head-to-head trial comparing D + FLOT to Pbo + FLOT (MATTERHORN). The primary outcome in MATTERHORN was EFS, and key secondary outcomes were OS and pCR. The PBAC considered that the patient population included in MATTERHORN is likely to be similar to the PBS population under the proposed restrictions. The circumstances of use are also likely to be similar, with the exception of subsequent immunotherapy in MATTERHORN, which differed from Australian clinical practice. The PBAC considered that the lower proportion of patients on Pbo + FLOT who received subsequent IO compared with Australian clinical practice (29.4% vs estimated [redacted]%) may affect the magnitude of treatment benefit for OS, however the impact is likely to be small, given the modest efficacy of immunotherapy in metastatic disease.

7.6 The PBAC noted that the addition of durvalumab to FLOT therapy resulted in statistically significant improvements in EFS, OS, and pCR. Treatment with D + FLOT demonstrated improved EFS compared with Pbo + FLOT (hazard ratio [HR] 0.71; 95% confidence interval [CI]: 0.58, 0.86; p<0.001) and a statistically significant improvement in OS compared with Pbo + FLOT (HR 0.78; 95% CI: 0.63, 0.96; p = 0.021). A statistically significantly higher proportion of patients on D + FLOT (19.2%) achieved pCR by central review compared with Pbo + FLOT (7.2%) (OR 3.08; 95% CI: 2.03, 4.67; p<0.001). The PBAC considered that the clinical claim of superior efficacy was supported, noting that the EFS benefit was small, but clinically significant and resulted in a statistically significant OS benefit based on relatively mature OS data (in an early disease setting).

7.7 The PBAC noted that AEs, SAEs and discontinuation due to AEs reported in the MATTERHORN trial were numerically higher with D + FLOT than Pbo + FLOT. Immune-mediated AEs were higher for D + FLOT than Pbo + FLOT (RR 3.19; 95% CI: 2.22, 4.59), as were infusion reactions (RR 1.67; 95% CI: 1.25, 2.25). The PBAC considered that the claim of inferior comparative safety was reasonable and supported by the clinical data.

7.8 The PBAC noted that the submission presented a cost-utility analysis comparing D + FLOT with FLOT alone, using a Semi-Markov model with a 25 year horizon. The PBAC agreed with the ESC that the time horizon of 25 years was too long given the starting age and underlying morbidity of the GC/GOJC population and considered that a time

horizon of up to 20 years would be acceptable in the context of more conservative assumptions for other model inputs. The PBAC noted that the model assumed that patients remaining in the event-free state at 10 years are effectively cured, with no further risk of recurrence and mortality equal to the general population. The PBAC considered that the application of a cure assumption was reasonable. However, the PBAC noted that the chosen time point of 10 years was not conservative and considered that it was not well-supported as recurrences after 5 years are rare. The PBAC considered that the longer term EFS data from Al Batran (2019) and Hoeppner (2025) referred to in the pre-PBAC response were consistent with the application of a cure point at 5 years. The PBAC considered that a revised model including a time horizon of 20 years and cure assumed at 5 years would be appropriate, which increased the ICER from $35,000 to < $45,000/QALY in the base case to $35,000 to < $45,000/QALY.

7.9 The PBAC noted that the ICER was relatively robust for most of the sensitivity analyses applied, but that there are other considerations that may increase the ICER, including uncertainty in the adjustment for subsequent immunotherapy in the FLOT only arm of the model. The PBAC considered that durvalumab would be acceptably cost-effective with an ICER of no more than $25,000 to < $35,000 per QALY, with changes to the economic model as described in paragraph 7.8. The PBAC considered this was consistent with the ICERs accepted in the perioperative setting, and would be appropriate in the context of the uncertainties outlined above and the changing landscape with respect to PBS listings for immunotherapy. The PBAC noted that the cost-effective price for durvalumab would also need to account for the effective price of nivolumab as later line treatment.

7.10 The submission took an epidemiological approach to estimate the financial impact of the proposed durvalumab listing. The PBAC considered that the approach to the financial estimates was reasonable. The PBAC considered that the main areas of uncertainty were the uptake and the proportion of GC/GOJC patients eligible for D + FLOT. The PBAC considered it was reasonable to assume high uptake ([redacted]% from year 1 onwards) as there is high awareness and acceptance of the clinical place for durvalumab in guidelines. The PBAC considered that the assumptions and sources informing the proportion of GC/GOJC patients eligible for D + FLOT were somewhat uncertain but appeared to be reasonable overall. The PBAC considered that the financial estimates would need to reduce the duration of treatment for grandfathered patients and apply the cost-effective price for durvalumab, which would reduce the total cost to Government for durvalumab.

7.11 The PBAC considered that the population for the proposed listing was well-defined and use outside the clinically appropriate population unlikely. In addition, the duration of treatment was limited in the restrictions.

7.12 The PBAC advised that durvalumab is not suitable for prescribing by nurse practitioners.

7.13 The PBAC considered that the proposed authority level (telephone/online) was consistent with other similar medicines in this setting and would be appropriate to capture the maximum total number of cycles under the listing. The PBAC considered that the number of repeats for the adjuvant phase listing should be reduced to 5 to allow approximately 6 months of treatment per prescription, with the intention that two prescriptions fulfil the total 12 cycles needed for adjuvant treatment. The PBAC considered that the restrictions were generally consistent with the clinical evidence and TGA indication for durvalumab. However, the PBAC considered that, for clarity, the restrictions should also include staging criteria, limiting treatment to patients with stage II or higher disease, consistent with the MATTERHORN trial.

7.14 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically the PBAC found that in the circumstances of its recommendation for durvalumab:

a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy, over alternative therapies as the overall survival benefit is expected to be small;

b) The treatment is not expected to address a high and urgent unmet clinical need as alternative effective treatments are available as standard care (FLOT);

c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed

7.15 The PBAC noted that this submission is not eligible for an Independent Review as it is a positive recommendation.

Outcome:
Recommended

8 Recommended listing

8.1 Add new listing:

Neoadjuvant treatment

MEDICINAL PRODUCT Form	PBS item code	Max. Amount	№.of Rpts
DURVALUMAB Injection	{NEW (Public)} {NEW (Private)}	1500mg	1
Available brands			
Imfinzi 500 mg/10 mL injection, 10 mL vial			
Imfinzi 120 mg/2.4 mL injection, 2.4 mL vial			
Restriction Summary [new1]/ Treatment of Concept: [new1A]			
Concept ID (for internal Dept. use)	**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals		
	Prescriber type: ☒Medical Practitioners		
	Restriction type: ☒Authority Required (Telephone/Online PBS Authorities System)		
Prescribing rule level	**Administrative Advice:** The recommended dose of durvalumab in the neoadjuvant phase is 1500 mg administered every 4 weeks, for up to 2 cycles.		
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.		
	Administrative Advice: No increase in the maximum amount or number of units may be authorised.		
	Administrative Advice: No increase in the maximum number of repeats may be authorised.		
	Administrative Advice: Special Pricing Arrangements apply.		
	Episodicity: [Blank]		
	Severity: [Blank]		
	Condition: Resectable gastric and gastroesophageal junction adenocarcinoma		
	Indication: Resectable gastric and gastroesophageal junction adenocarcinoma		
	Treatment Phase: Neoadjuvant treatment		
	Clinical criteria		
	Patient must be initiating treatment with this drug for this condition; OR		
	Patient must be transitioning from existing non-PBS to PBS subsidised supply of this drug		
	AND		
	Clinical criteria:		
	The condition must be Stage II or higher		
	AND		
	Clinical criteria:		
	The condition must be resectable		
	AND		
	Clinical criteria:		
	The treatment must be for the purpose of neoadjuvant use in a patient preparing for surgery		
	AND		
	Clinical criteria:		
	Patient must have a WHO performance status no greater than 1		
	AND		
	Clinical criteria:		
	The treatment must be initiated in combination with neoadjuvant FLOT		
	AND		
	Clinical criteria:		

	The condition must be untreated with systemic therapy for this condition
	AND
	Treatment criteria:
	Patient must not be undergoing PBS subsidised treatment where this prescription extends treatment beyond whichever comes first: (i) 2 cycles of neoadjuvant treatment from treatment initiation, irrespective of whether initial treatment was PBS subsidised/non-PBS subsidised, (ii) disease progression/recurrence despite treatment with this drug, (iii) unacceptable toxicity; annotate any remaining repeat prescriptions with the word 'cancelled' where this occurs
	Prescriber Instruction: Where 'FLOT' is referenced in this restriction, it refers to the combination therapy of fluorouracil (5-FU) + leucovorin (folinic acid) + oxaliplatin + docetaxel.

Adjuvant treatment

MEDICINAL PRODUCT **Form**	**PBS item code**	**Max. Amount**	**№.of Rpts**
DURVALUMAB Injection	{NEW (Public)} {NEW (Private)}	1500mg	5
Available brands			
Imfinzi 500 mg/10 mL injection, 10 mL vial			
Imfinzi 120 mg/2.4 mL injection, 2.4 mL vial			
Restriction Summary [new2]/ Treatment of Concept: [new2A]			

Concept ID (for internal Dept. use)		**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals
		Prescriber type: ☒Medical Practitioners
		Restriction type: ☒Authority Required (Telephone/Online PBS Authorities System)
Prescribing rule level		**Administrative Advice:** The recommended dose of durvalumab in the adjuvant setting is 1500 mg administered every 4 weeks for up to a maximum of 12 cycles (including 2 cycles of adjuvant durvalumab + FLOT and 10 additional cycles of durvalumab monotherapy)
		Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
		Administrative Advice: No increase in the maximum amount or number of units may be authorised.
		Administrative Advice: No increase in the maximum number of repeats may be authorised.
		Administrative Advice: Special Pricing Arrangements apply.
		Episodicity: [Blank]
		Severity: [Blank]
		Condition: Resected gastric and gastroesophageal junction adenocarcinoma
		Indication: Resected gastric and gastroesophageal junction adenocarcinoma
		Treatment Phase: Adjuvant treatment
		Clinical criteria
		Patient must have previously received PBS subsidised neoadjuvant treatment with this drug for this condition; OR
		Patient must be both: (i) transitioning from existing non-PBS to PBS subsidised supply of this drug, (ii) treated with combined therapy with durvalumab and FLOT as neoadjuvant treatment for this condition
		AND
		Clinical criteria:

	The treatment must be for the purposes of adjuvant use following complete surgical resection
	AND
	Clinical criteria:
	The treatment must be/have been initiated in combination with adjuvant FLOT for up to 2 cycles unless intolerant to FLOT requiring permanent discontinuation
	AND
	Clinical criteria:
	The treatment must be sole PBS-subsidised systemic anti-cancer therapy from cycles 3-12 of adjuvant treatment
	AND
	Clinical criteria:
	Patient must not have developed disease progression while being treated with this drug for this condition
	AND
	Treatment criteria:
	Patient must be undergoing treatment that does not occur beyond the following, whichever comes first: (i) the first instance of disease progression/recurrence, (ii) maximum of 12 cycles of adjuvant treatment for this condition from the first administered dose following surgery, (iii) unacceptable toxicity; annotate any remaining repeat prescriptions with the word 'cancelled' where this occurs
	Prescriber Instruction: Where 'FLOT' is referenced in this restriction, it refers to the combination therapy of fluorouracil (5-FU) + leucovorin (folinic acid) + oxaliplatin + docetaxel.

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor had no comment.