This Evidence-to-Decision (EtD) framework addresses **durvalumab + chemotherapy** for **biliary tract cancer irrespective of PD-L1 expression**.

# QUESTION

| **Should immune checkpoint inhibitors vs. alternative regimens be used for adult biliary tract cancer?** | |
|---|---|
| **POPULATION:** | adult biliary tract cancer (BTC) irrespective of PD-L1 expression |
| **INTERVENTION:** | immune checkpoint inhibitors (ICIs) |
| **COMPARISON:** | alternative regimens |
| **MAIN OUTCOMES:** | overall survival; progression-free survival; health-related quality of life; adverse events (CTCAE ≥ 3) |
| **SETTING:** | treatment in the palliative 1st line setting |
| **BACKGROUND:** | application includes one ICI-based treatment for adult BTC irrespective of PD-L1 expression:<br>• durvalumab + chemotherapy (ESMO-MCBS non-curative score = 4) |

# SUMMARY OF JUDGEMENTS

| | JUDGEMENT | | | | | | |
|---|---|---|---|---|---|---|---|
| **PROBLEM** | No | Probably no | Probably yes | **Yes** | | Varies | Don't know |
| **DESIRABLE EFFECTS** | Trivial | **Small** | Moderate | Large | | Varies | Don't know |
| **REDUCTION IN UNDESIRABLE EFFECTS** | Increased harms and toxicity | **No/Trivial** | Small | Moderate | Large | Varies | Don't know |
| **CERTAINTY OF EVIDENCE** | Very low | Low | **Moderate** | High | | | No included studies |
| **VALUES** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability | | | |
| **BALANCE OF EFFECTS** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **RESOURCES REQUIRED** | **Large costs** | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | Varies | Don't know |
| **COST EFFECTIVENESS** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | **Varies** | No included studies |
| **EQUITY** | **Reduced** | Probably reduced | Probably no impact | Probably increased | Increased | Varies | Don't know |
| **ACCEPTABILITY** | No | Probably no | Probably yes | Yes | | **Varies** | Don't know |
| **FEASIBILITY** | No | Probably no | Probably yes | Yes | | **Varies** | Don't know |
| **AVAILABILITY** | Not available in most settings | **Probably not available in most settings** | Probably available in most settings | Available in most settings | | Varies | Don't know |

# ASSESSMENT

## Problem
Is the problem a priority?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|
| ○ No<br>○ Probably no<br>○ Probably yes<br>○ **Yes**<br>○ Varies<br>○ Don't know | An application addressing ICIs for the treatment of 12 adult cancer entities in the palliative 1st line setting has been submitted for consideration by the Expert Committee. This EtD framework focuses on BTC (irrespective of PD-L1 expression), for which one ICI-based treatment is proposed: durvalumab + chemotherapy.<br><br>In 2019, the global age-standardized prevalence of gallbladder and biliary tract cancers was estimated at 3.2 (95% uncertainty interval (UI): 2.7 to 3.5) per $10^5$ population. They were associated with 72,441 deaths (95% UI: 144,899 to 188,615) and 3,621,473 (95% UI: 3,102,423 to 3,969,071) disability-adjusted life years (DALYs) worldwide (1). The standard of care includes chemotherapy, which is associated with a reduced quality of life in treated patients because of its cytotoxic effects. |

## Desirable Effects
How substantial are the desirable anticipated effects?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|
| ○ Trivial or no<br>○ **Small**<br>○ Moderate<br>○ Large<br>○ Varies<br>○ Don't know | The application provides evidence addressing desirable effects from one randomized trial for durvalumab (TOPAZ-1) (2, 3).<br><br>**Biliary tract cancer irrespective of PD-L1 expression**<br><br>**Durvalumab-based treatment regimen compared to SoC for BTC**<br><br>**Patient or population:** BTC, irrespective of PD-L1 expression<br>**Intervention:** Durvalumab-based treatment regimen (durvalumab + cisplatin/gemcitabine)<br>**Comparison:** SoC (cisplatin + gemcitabine) |

| Outcomes | Anticipated absolute effects* (95% CI) | | Relative effect (95% CI) | № of participants (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|---|
| | **Risk with SoC** | **Risk with Durvalumab-based treatment regimens** | | | | |
| | **At 1 year** | | | | | |
| Overall survival (OS)<br>follow-up: median 22.9 months[a] | 47 per 100[b] | **56 per 100**<br>(50 to 61) | **HR 0.76**<br>(0.64 to 0.91)<br>[death] | 685<br>(1 RCT)[c] | ⊕⊕⊕◯<br>Moderate[d,e,f] | Durvalumab-based treatment regimens likely increases overall survival. |
| | **At 1.5 years** | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | 24 per 100 | **34 per 100** (27 to 40) | | | | |
| | The median overall survival was **11.3** months | The median survival was **3.6 months more** (1.1 more to 6.4 more)[g] | | | | |
| Progression-free survival (PFS) follow-up: median 16.4 months | **At 1 year** | | **HR 0.75** (0.63 to 0.89) [disease progression or death] | 685 (1 RCT) | ⊕⊕⊕◯ Moderate[d,e] | Durvalumab-based treatment regimens likely increases progression-free survival. |
| | 6 per 100[h] | **12 per 100** (8 to 17) | | | | |
| Global Health Score/Quality of Life (GHS/QoL) assessed with: EORTC-QLQ C30 Scale from: 0 to 100 follow-up: median 9.9 months from baseline | The mean global Health Score/Quality of Life was **0.35** change score from baseline | MD **0.88 change score from baseline more** (1.8 fewer to 3.65 more) | - | 646 (1 RCT) | ⊕⊕⊕◯ Moderate[d,i] | Durvalumab-based treatment regimens likely results in little to no difference in global Health Score/Quality of Life. |

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**CI:** confidence interval; **HR:** hazard ratio; **MD:** mean difference; **RR:** risk ratio

**GRADE Working Group grades of evidence**
**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.
**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

## *Explanations*

a. Weight-adjusted median follow-up across treatment arms
b. 12-month survival rate in control arm extracted from Kaplan-Meier curve; 18-month overall survival rate directly reported in publication
c. TOPAZ-1 (NCT03875235)
d. Inconsistency not applicable (single trial only); publication bias not applicable due to prespecified selection process
e. Downgraded for imprecision (confidence interval crosses defined appreciable effect at 0.75; single study only)
f. Only 7% of trial participants in the control arm subsequently received immunotherapy therefore we did not downgrade for imprecision
g. The corresponding difference in median survival time was calculated using the directly reported median survival point estimate from the relevant trial publication and the pooled HR and CIs (assuming proportional hazards throughout the trial follow-up period)
h. 12-months progression-free survival rate (6%) in control arm extracted from survival plot reported in publication with shorter follow-up, because long term follow-up publication did not report progression-free survival data
i. Downgraded for risk of attrition bias (considerable proportion of participants without QoL assessments)

## Magnitude of effect judgements:

| Domain | Judgement per critical outcome | Judgement across desirable critical outcomes |
|---|---|---|

| ICIs | Overall survival | Health-related quality of life | Overall |
|---|---|---|---|
| Durvalumab-based treatment regimen | Small | Trivial to no | Small |

**Additional considerations:**

In 2019, the Expert Committee recommended adoption of a threshold for benefit of at least 4-6 months overall survival gain and without detriment to quality of life for cancer medicines or regimens to be considered as candidates for inclusion on the WHO EML (4). Based on this recommendation, the following decision rules were considered in judging the magnitude of effects:

- The outcomes overall survival and health-related quality of life were considered of critical importance to patients with BTC – more weight was placed on them in the decision-making process when compared to progression-free survival and adverse events.
- ICIs demonstrating a median overall survival benefit greater than the recommended WHO threshold (i.e. > 4-6 months) would be considered to have a large benefit.
- ICIs demonstrating a median overall survival benefit within the range of the recommended WHO threshold (i.e. between 4 and 6 months) would be considered to have a moderate benefit.
- ICIs demonstrating a median overall survival benefit smaller than the recommended WHO threshold (i.e. < 4-6 months) would be considered to have a small benefit.

The median overall survival was 3.6 months more in people treated with durvalumab-based treatment regimens and the ESMO-MCBS Scorecard reported a score of 4. Therefore, the magnitude of effect for overall survival, based on the point estimate, WHO benefit threshold and ESMO-MCBS Scorecard, was judged as small.

In terms of health-related quality of life, durvalumab-based treatment regimens probably result in trivial to no difference.

The overall judgement related to the magnitude of desirable effects cannot be lower than the highest rating across critical outcomes. Therefore, the overall magnitude of desirable effects was judged as small for the durvalumab-based treatment regimen.

## Undesirable Effects

How substantial is the **reduction** in the undesirable anticipated effects?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|

| | |
|---|---|
| ○ Increased harms and toxicity<br><br>Magnitude of reduction in harms and toxicity:<br><br>○ **Trivial or no**<br>○ Small<br>○ Moderate<br>○ Large<br>○ Varies<br><br>○ Don't know | The application provides evidence addressing undesirable effects from one randomized trial for durvalumab (TOPAZ-1) (2, 3).<br><br>**Biliary tract cancer irrespective of PD-L1 expression**<br><br>**Durvalumab-based treatment regimen compared to SoC for BTC**<br><br>**Patient or population:** BTC<br>**Intervention:** Durvalumab-based treatment regimen (durvalumab + cisplatin/gemcitabine)<br>**Comparison:** SoC (cisplatin + gemcitabine) |

| Outcomes | Anticipated absolute effects* (95% CI) | | Relative effect (95% CI) | № of participants (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|---|
| | **Risk with SoC** | **Risk with Durvalumab-based treatment regimens** | | | | |
| Adverse events (CTCAE ≥ 3) irrespective of treatment attribution[a] | 79 per 100 | **78 per 100** (72 to 84) | **RR 0.98** (0.91 to 1.06) | 680 [b] (1 RCT) | ⨁⨁⨁⨁ High | Durvalumab-based treatment regimens result in little to no difference in adverse events (CTCAE ≥ 3) irrespective of treatment attribution. |

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**CI:** confidence interval; **HR:** hazard ratio; **MD:** mean difference; **RR:** risk ratio

**GRADE Working Group grades of evidence**
**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.
**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

***Explanations***

a. Safety data from safety analysis set; number of any adverse events of maximum grade 3 and 4 added to number of adverse events leading to death
b. TOPAZ-1 (NCT03875235)

**Additional considerations:**

High certainty evidence showed that durvalumab-based treatment regimens result in trivial to no difference in adverse events when compared to standard of care (RR 0.98, 95% CI 0.91 to 1.06).

## Certainty of evidence

What is the overall certainty of the evidence of effects?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|

| | |
|---|---|
| ○ Very low<br>○ Low<br>○ **Moderate**<br>○ High<br>○ No included studies | |

| Domain | Judgement per critical outcome | | | Judgement across critical outcomes |
|---|---|---|---|---|
| **ICIs** | **Overall survival** | **Health-related quality of life** | **Adverse events** | **Overall** |
| Durvalumab-based treatment regimen | Moderate | Moderate | High | Moderate |

**Additional considerations:**

Across the critical outcomes, the lowest certainty of evidence rating was moderate for the durvalumab-based treatment regimen.

## Values

Is there important uncertainty about or variability in how much people value the main outcomes?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|
| ○ Important uncertainty or variability<br>○ Possibly important uncertainty or variability<br>○ **Probably no important uncertainty or variability**<br>○ No important uncertainty or variability | A systematic review of qualitative research identified 17 studies published between 2017 and 2022 that addressed the experience of patients considering or using checkpoint inhibitors in cancer (5). Overall, patients viewed ICIs positively when compared to other anti-cancer treatments, noting newfound hope, fewer or more manageable treatment-related side effects, and among those experiencing treatment success, improved quality of life when compared to chemotherapy and radiation therapy. In some cases, patients were uncertain about response durability long term and checkpoint inhibitor-specific adverse events. Patient concerns around checkpoint inhibitors may be mitigated, at least in part, by positive patient-practitioner relationships and support from other patients with lived checkpoint inhibitor experience by way of community groups. Further, fatigue is a common checkpoint inhibitor-specific adverse event. Implementing supportive care programs can help patients undergoing checkpoint inhibitor treatment cope with fatigue and maximize their quality of life.<br><br>It was noted that most studies included in this systematic review omitted patients that discontinued checkpoint inhibitor treatment due to serious adverse events or failed to respond to checkpoint inhibitor treatment limiting our understanding of patient experiences with checkpoint inhibitors in this regard. |

| Importance of uncertainty and variability of how people value outcomes | | |
|---|---|---|
| **ICIs** | **Net balance** | **Judgement** |
| Durvalumab-based treatment regimen | Small net desirable | Probably no important uncertainty or variability |

**Additional considerations:**

A judgement was made that how much people value the main outcomes, including overall survival, lies on a spectrum, and depends on the magnitude of benefit and harm from treatment. In a situation with trivial benefit and large harm, it was inferred that most people would not choose to pursue treatment if available. In a situation with large benefit and trivial harm, it was inferred that all or almost all people would choose to pursue treatment if available.

For the durvalumab-based treatment regimen, considering the small net benefit based on the point estimate (3.6 months), trivial to no reduction in harms when compared to standard of care, trivial to no difference in health-related quality of life when compared to standard of care and the ESMO-MCBS Scorecard, it was

| | |
|---|---|
| | judged that people would probably have no important uncertainty or variability in how much they value the main outcomes, particularly preferring avoiding premature death. |

## Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

**JUDGEMENT**

- ○ Favors the comparison
- ○ Probably favors the comparison
- ○ Does not favor either the intervention or the comparison
- ○ **Probably favors the interventio n**
- ○ Favors the intervention
- ○ Varies
- ○ Don't know

**RESEARCH EVIDENCE**

| ICIs | Net balance | Values | Certainty of evidence | Balance of effects |
|---|---|---|---|---|
| Durvalumab-based treatment regimen | Small net desirable | Probably no important uncertainty or variability | Moderate | Probably favors the intervention |

**Additional considerations:**

A judgement based on the net balance between desirable and undesirable effects, patient values and the certainty of evidence was made that the balance of effects probably favors the durvalumab-based treatment regimen. However, from a public health perspective, a small net benefit may not be enough for the Expert Committee to recommend as an essential medicine.

## Resources required

How large are the resource requirements?

**JUDGEMENT**

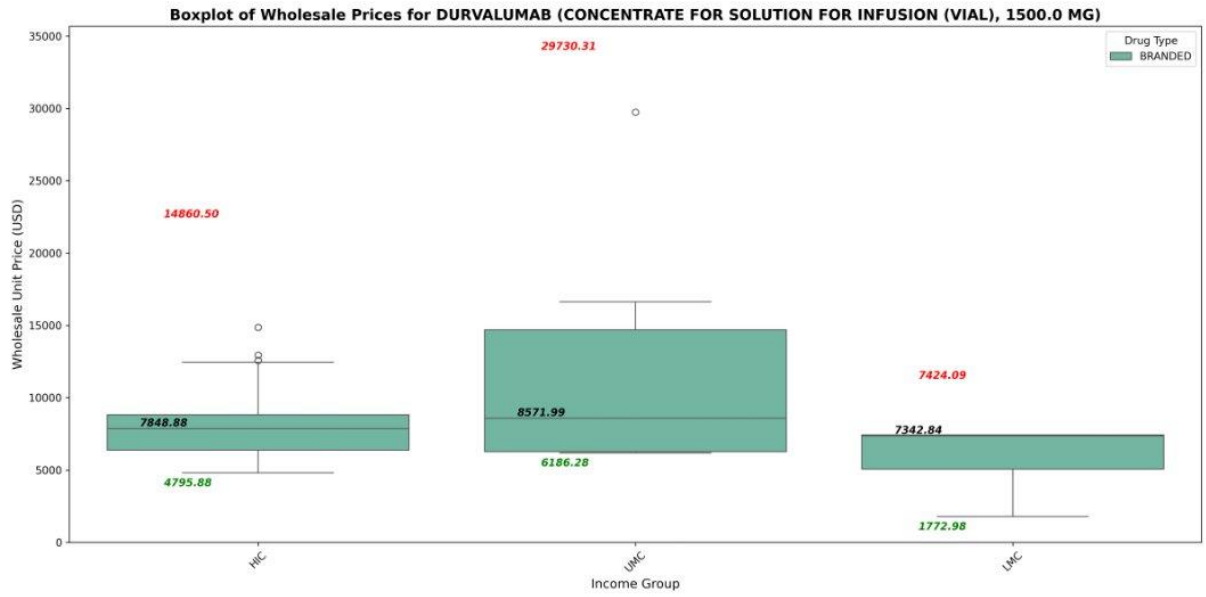
- ○ **Large costs**
- ○ Moderate costs
- ○ Negligible costs and savings
- ○ Moderate

**RESEARCH EVIDENCE**

**Median wholesale unit price (USD) for durvalumab (concentrate for solution for infusion, 1500 mg vial) across World Bank income levels:**

| Income level | Median | IQR | Sample size based on number of countries |
|---|---|---|---|
| HIC | 7848.88 | 6364.79 to 8808.71 | 36 |
| UMIC | 8571.99 | 6266.52 to 14678.40 | 9 |
| LMIC | 7342.84 | 5054.37 to 7424.09 | 3 |

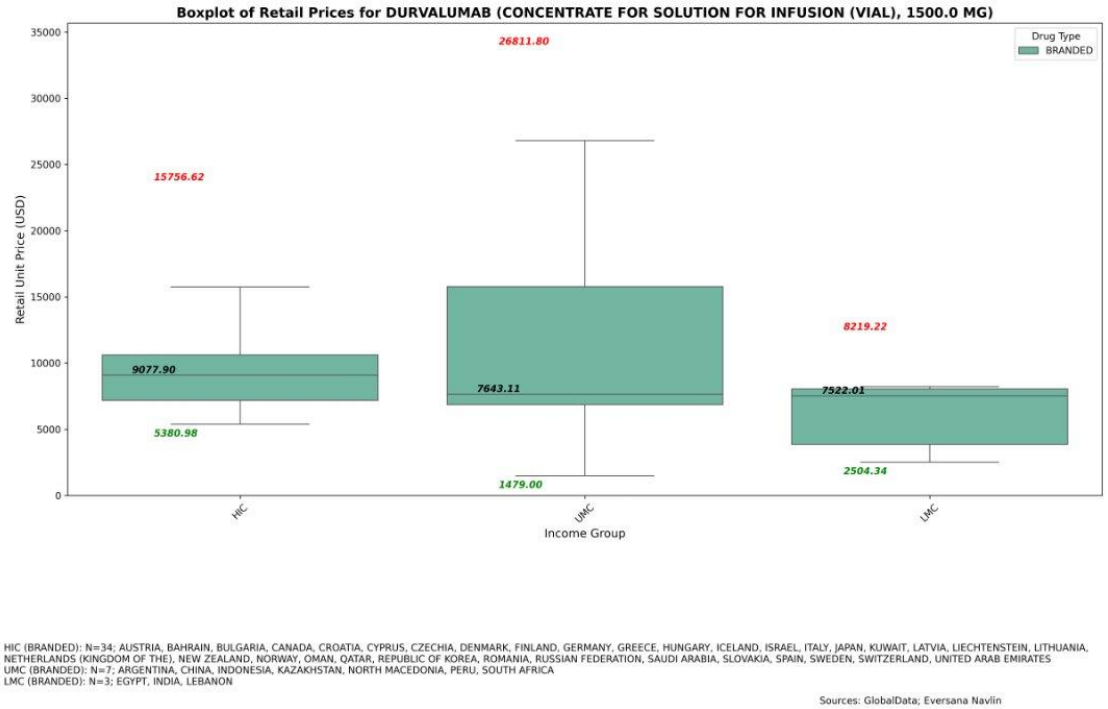
savings
○ Large savings
○ Varies
○ Don't know




Source: author derived calculation based on most recent available wholesale prices (as of November 2024) extracted from GlobalData Price Intelligenc (POLI) and Eversana NAVLIN Price & Access datasets. Latest publicly available country-specific prices may be accessed via sources listed here, where available: https://www.who.int/teams/health-product-and-policy-standards/medicines-selection-ip-and-affordability/affordability-pricing/med-price-info-source

**Median retail unit price (USD) for durvalumab (concentrate for solution for infusion, 1500 mg vial) across World Bank income levels:**

| Income level | Median | IQR | Sample size based on number of countries |
|---|---|---|---|
| HIC | 9077.90 | 7179.67 to 10624.14 | 34 |
| UMIC | 7643.11 | 6855.05 to 15764.25 | 7 |
| LMIC | 7522.01 | 3857.16 to 8044.91 | 3 |




Source: author derived calculation based on most recent available retail prices (as of November 2024) extracted from GlobalData Price Intelligenc (POLI) and Eversana NAVLIN Price & Access datasets. Latest publicly available country-specific prices may be accessed via sources listed here, where available: https://www.who.int/teams/health-product-and-policy-standards/medicines-selection-ip-and-affordability/affordability-pricing/med-price-info-source

**Additional considerations:**

Direct evidence addressing the unit price for durvalumab was available.

Relative to other EML medicines, the costs of durvalumab at the current unit pricing are large across World Bank income levels. There was more variation in prices for upper middle-income countries (UMICs) compared to high-income and lower middle-income countries (LMICs), which can be in part attributed to pricing dynamics at the country level. These small sample sizes reduce our confidence in the estimates, especially for UMICs and LMICs for which data from less than 10 countries was available for each. Further, there were no data available for low-income countries.

## Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|

| | |
|---|---|
| ○ Favors the comparison<br>○ Probably favors the comparison<br>○ Does not favor either the intervention or the comparison<br>○ Probably favors the intervention<br>○ Favors the intervention<br>○ **Varies**<br>○ No included studies | Evidence addressing cost-effectiveness of adding durvalumab to chemotherapy as first-line treatment for advanced biliary tract cancer was available from select countries, including China (UMIC) and the United States (HIC) (6). In these UMIC and HIC settings, the ICER exceeded WTP thresholds.<br><br>**Country** \| **Income level** \| **WTP threshold** \| **ICER** \| **Cost-effective?**<br>United States \| HIC \| USD 150,000 / QALY \| USD 381,864.39 / QALY \| No<br>China \| UMIC \| USD 38,334 / QALY \| USD 367,608.51 / QALY \| No<br><br>Empirical evidence estimating cost-effective thresholds based on health expenditures per capita and life expectancy at birth was available for 174 countries (7). As of 2019, the following cost-effectiveness thresholds in USD per QALY were estimated for each country income level. The authors noted that their empirically derived thresholds were lower than those used in many countries. If used, they may result in more conservative health decision-making.<br><br>**Income level** \| **Range** \| **Median** \| **IQR** \| **Sample size based on number of countries** \| **Cost-effective?**<br>HIC \| $5480–$95958 \| $18,218 \| $10229–$43175 \| 54 \| No<br>UMIC \| $1108–$10638 \| $4,355 \| $2886–$5301 \| 48 \| No<br>LMIC \| $190–$3249 \| $745 \| $451–$1389 \| 49 \| No<br>LIC \| $87–$320 \| $163 \| $131–$229 \| 23 \| No<br><br>To help achieve cost-effective use of ICIs across World Bank income settings without compromising efficacy and safety, alternative dosing strategies have been proposed (8). They include electronic rounding, hybrid dosing, lower dose selection, interval extension and shortening of treatment duration. The scientific basis for these alternative dosing strategies is growing and is based on evidence from both clinical trials and pharmacokinetic studies.<br><br>**Additional considerations:**<br><br>In the absence of a *de novo* cost-effectiveness model that considers diverse income settings and alternative dosing strategies, a judgement on the cost-effectiveness was made based on select examples and empirically derived cost-effective thresholds.<br><br>While the checkpoint inhibitor under consideration for biliary tract cancer irrespective of PD-L1 expression has small net desirable effects, at the current price, it is likely not cost-effective in most settings, particularly in LMICs and LICs, and when diagnostic requirements are considered. Very high WTP thresholds would be required to demonstrate cost-effectiveness.<br><br>Clinically proven alternative dosing strategies may be an important step in helping achieve cost-effective use of this checkpoint inhibitor in more settings. |

## Equity

What would be the impact on health equity?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|

| | |
|---|---|
| ○ **Reduced**<br>○ Probably reduced<br>○ Probably no impact<br>○ Probably increased<br>○ Increased<br>○ Varies<br>○ Don't know | **Additional considerations:**<br><br>Despite checkpoint inhibitors being accessible in many HICs, the WHO EML is a global list and the impact on LMICs and LICs was considered.<br><br>Because the ICI under consideration offers small net desirable benefits but is not accessible to patients globally because of its prohibitively high price, a judgement was made that health equity would be reduced. On the other hand, if price decreased substantially, access in disadvantaged populations would improve and health equity would increase. |

## Acceptability

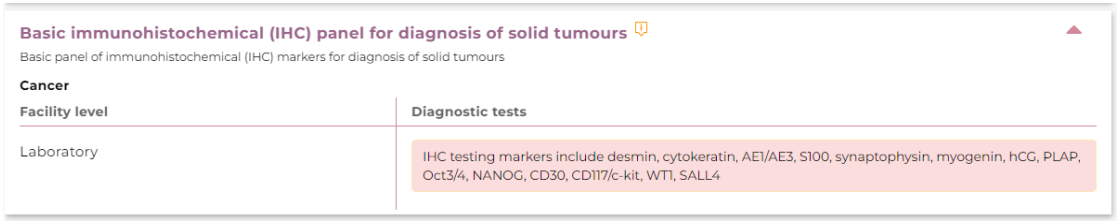
Is the intervention acceptable to key stakeholders?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|
| ○ No<br>○ Probably no<br>○ Probably yes<br>○ Yes<br>○ **Varies**<br>○ Don't know | A systematic review of qualitative research identified 17 studies published between 2017 and 2022 that addressed the experience of patients considering or using checkpoint inhibitors in cancer (5). Overall, patients viewed ICIs positively when compared to other anti-cancer treatments, noting newfound hope, fewer or more manageable treatment-related side effects, and among those experiencing treatment success, improved quality of life when compared to chemotherapy and radiation therapy. Of note, hope is key for cancer patient acceptance of further treatment and is associated with improved symptom burden and quality of life and decreased psychological distress.<br><br>**Additional considerations:**<br><br>Empiric evidence from the patient perspective provides support for the acceptability of ICIs.<br><br>Durvalumab-based treatment regimens are likely not acceptable to most health decision makers and health systems, especially those in LMICs and LICs, due to cost. The large costs associated with this checkpoint inhibitor when compared to other anti-cancer treatments risks diverting resources from health budgets at the expense of other essential medicines. |

## Feasibility

Is the intervention feasible to implement?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|
| ○ No<br>○ Probably no<br>○ Probably yes<br>○ Yes | Diagnostic requirements – immunohistochemistry companion tests – to identify patients with the indication approved for treatment. Lack of standardized biomarker testing may lead to the overuse or misuse of the immune checkpoint inhibitor.<br><br>The WHO Essential Diagnostics List includes a basic panel for immunohistochemical (IHC) markers for diagnosis of solid tumors, but the panel does not include IHC testing markers for PDL1 (9). |

| | |
|---|---|
| ○ **Varies**<br>○ Don't know |  <br><br>Additional considerations for healthcare-worker training, resources for the management of side-effects and monitoring capabilities.<br>**Additional considerations:**<br>The interventions are already implemented in many high-income settings. Beyond the large cost, another barrier to implementation is the need for diagnostic companion tests. |

## Availability

What is the regulatory status, market availability and on-the-ground availability/access of the medicine to patients?

| JUDGEMENT | RESEARCH EVIDENCE |
|---|---|
| ○ Not available in most settings<br>○ **Probably not available in most settings**<br>○ Probably available in most settings<br>○ Available in most settings<br>○ Varies<br>○ Don't know | Pembrolizumab is approved for use in 85 countries worldwide – mainly high-income countries including Canada, the United States, European Union member countries and Japan (10). The landscape is similar for other ICIs, including durvalumab.<br>Data on the availability, out-of-pocket costs, and accessibility of pembrolizumab for melanoma, non-small cell lung cancer, colorectal cancer and renal cell carcinoma were available from the 2023 update to the ESMO Global Consortium Study (11). In HICs, pembrolizumab for melanoma was "almost always available to patients at no cost or on a subsidized basis". In LMICs and LICs, when available, however, pembrolizumab was "generally provided only at full cost as an out-of-pocket expenditure for patients". Although pembrolizumab for melanoma was almost always actually available in HICs (accessibility with a valid prescription), there was important variation in the actual availability across UMICs, LMICs and LICs. Outside of HICs, pembrolizumab for non-small cell lung cancer, colorectal cancer and renal cell carcinoma was more commonly provided as an out-of-pocket expenditure for patients than not – often at full cost to the patient. These data provide indirect evidence regarding the extent of durvalumab availability across World Bank income settings.<br>**Additional considerations:**<br>Durvalumab is approved for use in many countries; however, on-the-ground access outside of HICs is limited. |

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