HTA85

Company-Led Submissions to the Agency for Care Effectiveness (ACE) in Singapore: What Drives Patient Access?

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Objective

To evaluate factors influencing recommendations for subsidy and listing of new oncology drugs on the Ministry of Health Cancer Drug List (CDL).

To compare the HTA recommendations issued by ACE with those by NICE, CDA and PBAC.

Background

- Before 2021, HTA topics in Singapore have primarily been identified through applications by public healthcare professionals. In 2021, ACE introduced a company-led submission (CLS) process for oncology drugs, enabling pharmaceutical companies to apply for HTA of their drugs.
- The CLS process allows subsidy decisions to be made close to regulatory approval, expediting patient access. This also enables the listing of new oncology drugs on the CDL, whereby listed drugs are claimable from public and private insurance, and patients' medical savings accounts.

Methods

- As of July 2024, 7 appraisals that underwent the CLS process have been published.[1–7] The 7 appraisals were reviewed to identify factors influencing ACE's conclusions regarding clinical need, clinical effectiveness and safety, cost-effectiveness and budget impact, and their impact on the final recommendations.
- Appraisals for the same drug and indication by NICE, CDA and PBAC were reviewed, and the recommendations were compared against those issued by ACE.

Results

Factors Influencing Recommendations for Subsidy and CDL Listing

- 2/7 drugs were recommended for subsidies under the Medication Assistance Fund, and all 7 drugs were listed on the CDL.
- The factors that ACE considers when making subsidy recommendations,[8] as well as the extent to which each factor was deemed to be met for each appraisal, are summarised in **Figure 1**.
  - All technologies were deemed to address a clinical need. However, the extent of clinical benefit of most (6/7) technologies was considered uncertain, mainly due to immature overall survival data, and reliance on uncertain surrogate outcomes. For the remaining technology, data were mature and statistically significant.
  - 5/7 technologies were not deemed cost-effective following ACE's modelling revisions, and budget impact was considered high. The remaining technologies were recommended for subsidy only after price revisions.

Recommendations by ACE Versus International HTA Bodies

- There is no clear alignment in recommendations across HTA bodies (**Figure 2**), suggesting that ACE's recommendation may not necessarily be consistent with those by other HTA bodies.
- The modelling parameters that are deemed suitable by other HTA bodies may also not align with ACE's preferences. For example, ACE tends to prefer a shorter, more conservative time horizon to estimate clinical and cost effectiveness (**Figure 3**).

Conclusion

It appears challenging for new oncology drugs to be considered cost-effective by ACE, which may in part be attributed to immature clinical evidence, and associated conservative modelling assumptions. Price reductions can increase the likelihood of a recommendation. Drugs that are unsuccessful for subsidy listing can still be listed on the CDL, which helps improve patient access through insurance coverage.

The likelihood of success of ACE submissions cannot be inferred by the outcome of appraisals by other HTA bodies. Local companies need to consider ACE's feedback when developing the economic models for submission.

FIGURE 1

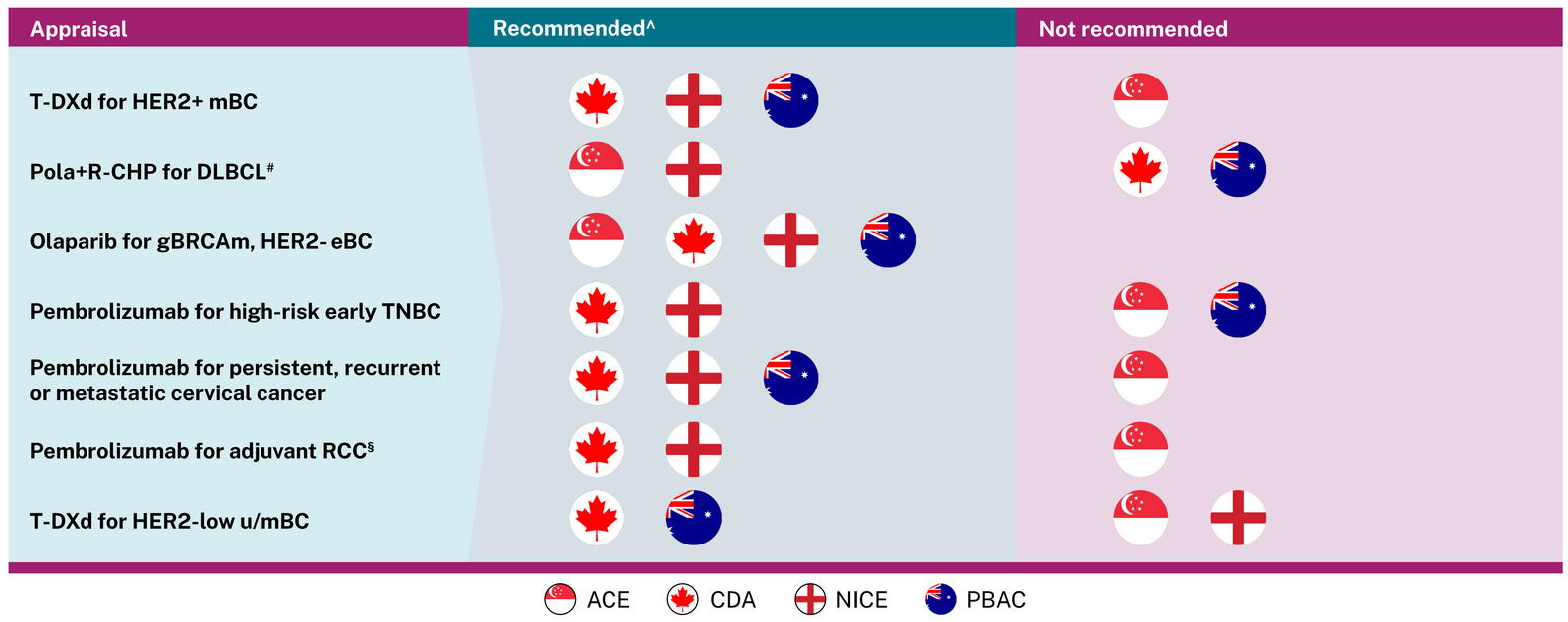
Summary of appraisals evaluated by ACE*

Appraisal	Clinical need	Clinical effectiveness and safety	Cost effectiveness	Budget impact	Subsidy recommendation	CDL listing
T-DXd for HER2+ mBC	✓	?	✗	✗	Negative	✓
Pola+R-CHP for DLBCL (IPI score 3–5)	✓	?	✓^	✓^	Positive^	✓
Olaparib for gBRCAm, HER2- eBC	✓	?	✓^	✓^	Positive^	✓
Pembrolizumab for high-risk early TNBC	✓	?	✗	✗	Negative	✓
Pembrolizumab for persistent, recurrent or metastatic cervical cancer	✓	?	✗	✗	Negative	✓
Pembrolizumab for adjuvant RCC	✓	?	✗	✗	Negative	✓
T-DXd for HER2-low u/mBC	✓	✓	✗	✗	Negative	✓

*Interpretation for each factor is as follows: Clinical need: ACE, clinical experts or patients acknowledged the need for new treatments; Clinical effectiveness and safety: Extent of clinical benefit was uncertain or drug was superior in terms of PFS and OS; Cost effectiveness: Technology represented an unacceptable or acceptable use of healthcare resources; Budget impact: Financial estimates/PVA cap was high or acceptable. ^Factor was not met/recommendation was negative during initial submission, and was met/positive only following a revised proposal.

FIGURE 2

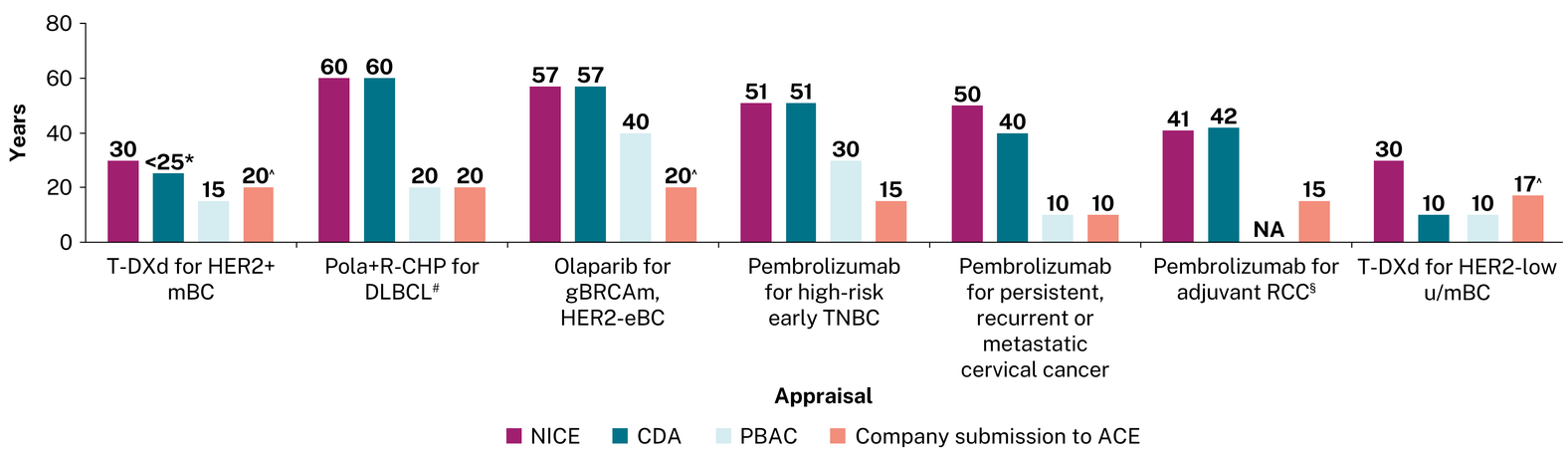
Recommendations by ACE* versus other HTA bodies



*This figure illustrates ACE's subsidy recommendations, rather than CDL listing. ^All recommendations by NICE, PBAC and CDA were contingent on price reduction, or the availability of a managed access/commercial access arrangement. #NICE and CDA evaluated patients with DLBCL IPI score 2–5, while ACE and PBAC evaluated patients with DLBCL IPI score 3–5. §Evaluation ongoing by PBAC.

FIGURE 3

Time horizon of cost-effectiveness models considered/accepted by ACE versus other HTA bodies



*25 years was considered too long by CDA, but the acceptable time horizon was not reported. ^ACE suggested to reduce the time horizon. #NICE and CDA evaluated patients with DLBCL IPI score 2–5, while ACE and PBAC evaluated patients with DLBCL IPI score 3–5. §Evaluation ongoing by PBAC.

Abbreviations: ACE: Agency for Care Effectiveness; **CDA:** Canada's Drug Agency; **CDL:** Cancer Drug List; **CLS:** company-led submission; **DLBCL:** diffuse large B-cell lymphoma; **eBC:** early breast cancer; **gBRCAm:** germline breast cancer gene-mutated; **HER2:** human epidermal growth factor receptor 2; **HTA:** health technology assessment; **IPI:** international prognostic index; **mBC:** metastatic breast cancer; **NA:** not available; **NICE:** National Institute for Health and Care Excellence; **OS:** overall survival; **PBAC:** Pharmaceutical Benefits Advisory Committee; **Pola+R-CHP:** polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone; **PFS:** progression-free survival; **PVA:** price-volume agreement; **RCC:** renal cell carcinoma; **T-DXd:** trastuzumab deruxtecan; **TNBC:** triple negative breast cancer; **u/mBC:** unresectable/metastatic breast cancer.

References: [1]Agency for Care Effectiveness. 2023. Trastuzumab deruxtecan for previously treated HER2-positive metastatic breast cancer; [2]Agency for Care Effectiveness. 2024. Polatuzumab vedotin for previously untreated diffuse large B-cell lymphoma; [3]Agency for Care Effectiveness. 2024. Olaparib for treating germline BRCA-mutated HER2-negative high-risk early breast cancer; [4]Agency for Care Effectiveness. 2024. Pembrolizumab for treating high-risk early-stage triple-negative breast cancer; [5]Agency for Care Effectiveness. 2024. Pembrolizumab for treating persistent, recurrent, or metastatic cervical cancer; [6]Agency for Care Effectiveness. 2024. Pembrolizumab for the adjuvant treatment of renal cell carcinoma; [7]Agency for Care Effectiveness. 2024. Trastuzumab deruxtecan for HER2-low unresectable and/or metastatic breast cancer after at least one prior line of chemotherapy. References 1–7 accessed at: https://www.ace-hta.gov.sg/healthcare-professionals/ace-technology-guidances [Last accessed 30 Jul 24]; [8]Agency for Care Effectiveness. 2024. Procedures and guidelines for company submissions to the Agency for Care Effectiveness for funding consideration. Accessed at: https://www.ace-hta.gov.sg/docs/default-source/company-led-submission/procedures-and-guidelines-for-company-submissions_v1-5_apr2024.pdf [Last accessed 30 Aug 24]. **Acknowledgements:** The authors thank Niki Lim, Costello Medical, for graphic design assistance. We also thank Audrey Ang, Costello Medical for their contributions in the preparation of this poster. **Disclosures:** None.

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