Cost-effectiveness and budget impact of pembrolizumab monotherapy as a first-line treatment for metastatic non-small cell lung cancer patients with PD-L1 \geq 50% in Thailand

Background

• Lung cancer is among the top 2 most-common cancers and leading causes of cancer death in Thailand¹, and the majority of lung cancers are Non-Small Cell Lung Cancers (NSCLC)² • Pembrolizumab is one of the standard first-line treatments for metastatic NSCLC patients without oncogenic driver alterations with high PD-L1 expression. Pembrolizumab monotherapy demonstrated significant improvement in the survival and health-related quality of life in these patients, as compared to platinum-based chemotherapy.^{4,5} However, the cost of pembrolizumab is much higher than that of chemotherapy. Therefore, an economic evaluation study in Thailand is required to support the decision-making process on whether pembrolizumab should be enlisted in the National List of Essential Medicines (NLEM)

Objective

• This study aimed to assess the cost-effectiveness and budget impact of pembrolizumab as first-line monotherapy for metastatic NSCLC patients without oncogenic driver alterations who have a PD-L1 tumour proportional score \geq 50%, in Thailand

Methods

- Partitioned survival analysis was used to assess the incremental cost-effectiveness ratio (ICER) of pembrolizumab compared with standard chemotherapy (carboplatin + paclitaxel and carboplatin + gemcitabine). The main clinical efficacy and safety data were derived from the KEYNOTE 024 trial, with July 10, 2017, cut-off date⁴
- Since the initial development of the present analysis, additional follow-up data⁶ and associated modeling from the KN-024 trial has become available. Though not incorporated here, the hazard ratio for overall survival in KN-024 in the final protocol-specific OS analysis (0.63)⁴ reflected in the present modeling was virtually identical to that with longer 5-year follow-up $(0.62)^6$
- The payer perspective was used with a 20-year time horizon. Pembrolizumab cost was based on the local list price. All other cost-related data were retrieved from publications and expert opinions, with a discount rate of 3% for costs and QALYs
- The budget impact model was constructed to calculate 5-year budget impact and reflected the patient population, treatment-related costs, and market share assumptions for each available treatment in Thailand

CEA model overview

Table 1: First-line treatment for metastatic non-small cell lung cancer patients with PD-L1 ≥50%, pembrolizumab versus comparators

Target population	Comparator	Interv
First-line treatment for metastatic non-small cell lung cancer patients with PD-L1 ≥50%	Carboplatin AUC 5 day 1 Q3W for 4-6 cycles + Gemcitabine 1000 mg/m ² days 1 and 8 or Carboplatin AUC 5 day 1 Q3W for 4-6 cycles + Paclitaxel 200 mg/m ² Q3W	Pembrolizur Q3

Partitioned survival modeling⁴: using PFS and OS data from KM graph from KN024³

• Model parameters and clinical data inputs were estimated from KN024 patient - level data for Time on Treatment, Progression free survival & Overall survival. The median follow-up available from KN024 as of the July 10, 2017, data cut-off was 25.2 months (range, 20.4-33.7)

Figure 1. Model structure of evaluation of pembrolizumab in metastatic NSCLC, no mutation, **PD-L1 ≥50%**



References

- 1. Globocan Thailand factsheets, 2022. (https://gco.iarc.who.int/media/globocan/factsheets/
- populations/764-thailand-fact-sheet.pdf)
- 2. Narongwit Nakwan and Kittipong Kumsuk. "Survival Analysis of Lung Cancer: A 10-Year Real-Life Experience in a Non-University-Based Hospital in Thailand (2012-2021)." Asian Pacific Journal of Cancer Prevention, Vol. 24 (9), 3021-3027. doi:10.31557/APJCP.2023.24.9.3021 3. Woods, Bethan Sarah, et al. "NICE DSU technical support document 19:: partitioned survival
- analysis for decision modelling in health care: a critical review." (2017).

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Treatment cost after disease progression. Calculate based on (1) subsequent therapy distribution data (assuming Pembrolizumab is unavailable for either arm as a subsequent therapy) (2) median price from DMSIC. (3) duration (in days) of post-discontinuation regimens from KN024.

	Pembrolizumab arm	Standard of Care arm
Post discontinuation treatment costs (THB)	16,757	12,189

4. Reck, Martin et al. "Updated Analysis of KEYNOTE-024: Pembrolizumab Versus Platinum-Based Chemotherapy for Advanced Non-Small-Cell Lung Cancer With PD-L1 Tumor Proportion Score of 50% or Greater." Journal of clinical oncology : official journal of the American Society of Clinical Oncology vol. 37,7 (2019): 537-546. doi:10.1200/JCO.18.00149 5. Brahmer et al., Health-related quality-of-life results for pembrolizumab versus chemotherapy in advanced, PD-L1-positive NSCLC (KEYNOTE-024): a multicentre, international, randomised, open-label phase 3 trial, *Lancet Oncol* (2017): 18: 1600–09 6. Reck, M, et al. Five-Year Outcomes With Pembrolizumab Versus Chemotherapy for Metastatic Non–Small-Cell Lung Cancer With PD-L1 Tumor Proportion Score ≥ 50%. Journal of Clinical Oncology, 2021. 39(21): p. 2339-2349.

Disclosures

Doungporn Leelavanich, Wannapa Krairojananan, and Ruttanun Chamnanroeng are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ USA and shareholders in Merck & Co., Inc., Rahway, NJ, USA.

Table 3. Disease management costs

Progression-free disease management costs											
Category	Unit cost (THB 2009)	Inflated unit cost (THB 2022)	Weekly HCRU in 1L therapy	Cost per category in 1 week (THB 2022)	Category	Unit cost (THB 2009)	Inflated unit cost (THB 2022)	HCRU in 2L therapy (Pivotal study)	HCRU in 3L therapy (Pivotal study)	Cost per category in 1-week 2L (THB 2022)	Cost per category in 1-week 3L (THB 2022)
Hospital admission charges	2,123	2,322	0.02	46.43	Hospital						
Emergency visit charges	945	1033	0.01	10.33	admission	2,123.00	2,321.52	0.02	_	46.43	0.00
Hospital outpatient charges	283	309	0.19	58.80	charges for 2L						
Medical specialist charges	306	335	0.24	80.31	admission	2,123.00	2,321.52	_	0.06	0.00	139.29
CT scan charges ^a	20,000	-	0.08	1,666.67	charges for 3L						
Total	1,862.54			Emergency visit charges	945.00	1,033.37	0.01	0.03	10.33	31.00	
Abbreviation: CT, computed tomography. ^a Note: CT scan charges are based on expert opinion.				Hospital outpatient charges	283.00	309.46	0.21	0.43	64.99	133.07	
Weekly healthcare resource utilization (HCRU) were extracted from HK CEA KN024 study, which use these data from real world evidence study below:				Medical specialist charges	306.00	334.61	0.26	0.59	87.00	197.42	
Lee, D.H., Isobe, H., Wirtz, H. et al. Health care resource use among patients with advanced non-small cell lung cancer: the PlvOTAL retrospective observational study. BMC Health Serv Res 18, 147 (2018). https://doi.org/10.1186/ s12913-018-2946-8.			CT scan charges	20,000.00	-	0.08	0.08	1,667.67	1,667.67		
Unit cost of each resource category: from HITAP costing menu and expert opinion.			Total					1,875.42	2,167.45		
			Total in average					2,02	1.43		

 Table 4. Adverse event management costs

Only all-cause adverse events (AEs) of Grade 3+ reported in $\geq 5\%$ of patients were included in the model. The total average cost per patient for managing adverse events was calculated by multiplying the incidence of each AE and their corresponding management costs. The total average cost per patient for managing adverse events was THB 676.58 for pembrolizumab and THB 6,502.92 for SoC.

Adverse event	% of Pa	tients			
type	Pembro SoC		Cost per event	Re	
Anemia	4.5%	23.3%	THB 6,265	Permsuwan, U., Thongp	
Neutropenia	0.0%	18.0%	THB 4,496	B. (2020). Cost-utility an plus cisplatin in non-sma Thailand. Value in Healt	
Pneumonia	1.9%	7.3%	THB 8,770	Reechaipichitkul, Wipa e	
Thrombocytopenia	0.0%	12.0%	THB 29,436	Teawtrakul, Nattiya, et a immune thrombocytoper patients: The analysis of databases 2010." J Med (2012): S217-23.	
Pneumonitis	2.6%	0.7%	THB 8,770	Reechaipichitkul, Wipa e	

	SoC	Pembrolizumab	Incremental Pembrolizumab vs. SoC	
Life years	1.66	3.09	1.42	
expected time in progression free state (months)	7.08	15.02	7.94	
expected time in progressive state (months)	12.89	22.03	9.13	
QALYs	1.24	2.38	1.14	
Costs	THB 253,062	THB 3,579,301	THB 3,326,239	
drug acquisition cost	THB 41,556	THB 3,221,430	THB 3,179,874	
pre-medication cost	THB 369	THB 0	-THB 369	
drug administration cost	THB 4,847	THB 8,252	THB 3,405	
disease management cost	THB 170,711	THB 315,357	THB 144,646	
post-discontinuation therapy cost	THB 13,161	THB 18,390	THB 5,229	
terminal care cost	THB 15,914	THB 15,195	-THB 719	
AE cost	THB 6,503	THB 677	-THB 5,826	
ICER				
Cost per LYG			THB 2,336,815	
Cost per QALY			THB 2,921,493	

Results

• Pembrolizumab use resulted in 1.42 life years and 1.14 quality-adjusted life years (QALYs) gained versus chemotherapy, with discounting, at an additional cost of THB 3,326,239. The ICER of pembrolizumab, compared with standard chemotherapy, was THB 2,921,493/QALY which was higher than a currently accepted willingness-to-pay threshold in Thailand at 1.2GNI. Pembrolizumab had lower adverse event management costs than those of chemotherapies. If pembrolizumab was enlisted into the NLEM for this indication, it would increase the 5-year annual budget by THB 1.3 billion Thai Baht with an estimated 1,350-1,361 new patients treated per year.

Key assumptions

1. The number of doses for platinum-based doublet chemotherapy is based on the median number of doses reported in the identified publications. Using average doses is ideal but usually is not reported. 2. The model uses the same number of doses for a specific treatment

across lines of therapy due to a lack of detailed available information.

EE63

*Contributed equally; **Corresponding authors

Progressive disease management costs

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prasert, S., & Sirichanchuen, nalysis of first-line pemetrexed nall cell lung cancer in th Regional Issues, 21, 9-16.

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Table 5. Other costs

Other cost	Cost	Reference
IV Administration cost per time	THB 503	Permsuwan, U., Thongprasert, S., & Sirichanchuen, B. (2020). Cost-utility analysis of first-line pemetrexed plus
Terminal care cost per month	THB 5,376	cisplatin in non-small cell lung cancer in Thailand. Value in Health Regional Issues, 21, 9-16

CEA Results

- The CEA analysis results indicate a difference of THB 3,326,719 in the total average per-patient direct cost of treatment with pembrolizumab (THB 3,579,301) versus SoC (THB 253,062) over a 20-year time horizon.
- The cost breakdown by treatment arm indicates that the higher cost in the pembrolizumab arm was mainly driven by the drug acquisition cost along with disease management costs associated with enhanced survival among pembrolizumab patients

Conclusions

• At the list price, pembrolizumab was not cost-effective as first-line monotherapy for metastatic NSCLC patients with high PD-L1 expression in the Thailand healthcare context. Considering the significant clinical benefits of Pembrolizumab in increasing lifeyears and QALYs as first-line treatment for metastatic NSCLC patients with PD-L1 ≥50% collaboration between the policymaker and the drug company is needed to find a potential solution which can both consider applying a higher ICER threshold for innovative medicines and/or exploring an alternative health financing solution e.g., Manage Entry Agreement to improve access to this treatment for Thai patients

3. The model excludes pre-medication costs, but pre-medication prices are very low compared to those for primary regimens. Thus, the impact on the budget can be omitted without substantively affecting results.

Most chemotherapy drugs are generic and manufactured by multiple companies. The price varies significantly from manufacturer to manufacturer and the model uses the average price to reflect reasonable estimations.

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