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Cost-Effectiveness of Pembrolizumab in Combination with Chemotherapy in the 1st Line Treatment of Metastatic NSCLC in Taiwan

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INTRODUCTION

- The anti-programmed death receptor-1 (PD-1) immunotherapy Pembrolizumab was previously shown to substantially extend life expectancy when used as monotherapy in metastatic non-small cell lung cancer (NSCLC) in first-line (1L) PD-L1 total proportion score (TPS) ≥50% patients and second-line (2L) PD-L1 TPS ≥ 1% patients, and associated cost-effectiveness analyses have been reported.
- PD(L)1 inhibitors are regarded as new SOC for certain cancer types. PD(L)1 inhibitors have been reimbursed since April 1st, 2019 in Taiwan for the treatment of Melanoma, NSCLC, Head and Neck Squamous Cell Carcinoma, Hodgkin's lymphoma, Urothelial carcinoma, Gastric cancer, Hepatocellular carcinoma.

OBJECTIVE

- To describe the cost-effectiveness of pembrolizumab plus chemotherapy in non-squamous (NSQ) or squamous (SQ) metastatic NSCLC patients, regardless of PD-L1 expression, from Taiwan 3rd party health care payer (National Health Insurance Administration, NHIA) perspective.

METHODS

- Two models were developed utilizing a partitioned survival approach to estimate cost-effectiveness based on interim analyses from the KEYNOTE-189 trial (Nov 2017 data cut-offs)and KEYNOTE-407 trial (Apr 2018 data cut-offs).
  - KEYNOTE-189 trial: pembrolizumab + carboplatin/cisplatin + pemetrexed versus chemotherapy alone in NSQ; KEYNOTE-407 trial: pembrolizumab + carboplatin + paclitaxel versus chemotherapy alone in SQ.
  - Clinical efficacy, treatment utilization, health utility and safety data were derived from the trials and projected over 20 years.
  - For extrapolating survival beyond the trial, a novel Surveillance Epidemiology and End Results (SEER) program population-data approach was applied.
  - Costs (expressed in New Taiwan Dollar, NTD) for drugs and their administration, and non-drug disease management are also incorporated. Resource use and unit costs were from the NHIA perspective.
  - The ICER for the overall population was calculated as a weighted average of the ICERs in the PD-L1<50% and PD-L1≥50% sub-groups to reflect the fact that immunotherapies are available post-discontinuation in the PD-L1≥50% but not in PD-L1<50% sub-groups.
  - A 3% discount rate is applied to costs and outcomes in reporting ICERs.
- Cost-effectiveness is evaluated versus Taiwanese SOC chemotherapy comparators.
  - For NSQ: platinum + pemetrexed/docetaxel/gemcitabine/paclitaxel/vinorelbine;
  - For SQ: carboplatin + paclitaxel utilizing results from a network meta-analysis since nab-paclitaxel is not reimbursed for lung cancer in Taiwan.
- Based on WHO, treatments with cost/QALY less than 3 times of GDP per capita are cost-effective. Taiwan GDP per capita is NTD848,626 and 3 times of which is NTD 2,309,943.

NSCLC, Non small cell lung cancer; SOC, standard of care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; GDP, Gross Domestic Product

RESULTS

- Based on data from the KEYNOTE-189 trial, the cost-effectiveness of Pembrolizumab plus Carboplatin/Cisplatin (Platinum) and Pemetrexed or Platinum + Pemetrexed chemotherapy in metastatic, non-squamous, NSCLC patients is presented in Table 1.
  - Pembrolizumab + Chemotherapy is projected to increase discounted life expectancy by 0.96 years (2.64 years versus 1.67 years), for around a 58% increase in life years.
  - Based on the NHIA net price for Pembrolizumab, Pembrolizumab + Chemotherapy in the comparison against chemotherapy yields a resultant incremental cost/QALY of NTD 1,401,985 and cost/LY of NTD 922,461.

Table 1. Cost-effectiveness of Pembrolizumab + Chemotherapy vs. Chemotherapy in metastatic NSQ NSCLC patients

	Trial Chemotherapy Arm	Pembrolizumab + Chemotherapy strategy	Incremental Pembrolizumab + Chemotherapy strategy vs. Trial Chemotherapy Arm
Life years	1.67	2.64	0.96
time in progression free state (months)	7.59	11.53	3.94
time in progressive state (months)	12.50	20.13	7.63
QALYs	0.96	1.60	0.63
Costs	NTD 1,234,004	NTD 2,124,000	NTD 889,996
ICER			
Cost per LYG			NTD 922,461
Cost per QALY			NTD 1,401,985

- The cost-effectiveness of Pembrolizumab plus Carboplatin/Cisplatin and Pemetrexed r vs. Taiwanese SOC chemotherapy using indirect comparisons in metastatic, non-squamous, NSCLC patients is presented in Table 2.
  - Incremental gains in discounted life expectancy with use of pembrolizumab + chemotherapy versus each comparator ranged from 1.40 versus platinum + docetaxel to 2.18 versus platinum + paclitaxel.
  - Incremental QALYs similarly ranged from 0.92 to 1.43 versus each of these comparators, respectively. ICERs were less than NTD 2,309,943 /QALY versus all comparators.

Table 2. Cost-effectiveness of Pembrolizumab + Chemotherapy vs. Indirect Treatment Comparators in metastatic NSQ NSCLC patients

	Incremental vs. Platinum + Docetaxel	Incremental vs. Platinum + Gemcitabine	Incremental vs. Platinum + Paclitaxel	Incremental vs. Platinum + Vinorelbine
Life years	1.40	2.03	2.18	1.80
Time in PF state (months)	7.89	8.76	11.01	8.86
Time in PD state (months)	8.80	15.58	15.11	12.62
QALYs	0.92	1.33	1.43	1.19
Costs	NTD 1,969,928	NTD 2,118,390	NTD 2,230,471	NTD 2,041,390
ICER				
Cost per LYG	NTD 1,406,540	NTD 1,043,921	NTD 1,024,085	NTD 1,133,760
Cost per QALY	NTD 2,132,484	NTD 1,587,625	NTD 1,559,142	NTD 1,721,939

LYG, life years gained; PF, progression-free; PD, progressive disease

- Based on data from the KEYNOTE-407 trial, the cost-effectiveness of Pembrolizumab plus Carboplatin and Paclitaxel chemotherapy in metastatic, squamous, NSCLC patients is presented in Table 3.
  - Pembrolizumab + Chemotherapy is projected to increase discounted life expectancy by 1.14 years vs. chemotherapy (2.70 years versus 1.56 years).
  - Based on the NHIA net price for Pembrolizumab, Pembrolizumab + Chemotherapy in the comparison against chemotherapy yields a resultant incremental cost/QALY of NTD1,134,614.

Table 3. Cost-effectiveness of Pembrolizumab + Chemotherapy vs. Chemotherapy in metastatic SQ NSCLC patients

	Trial Chemotherapy Arm	Pembrolizumab + Chemotherapy strategy	Incremental Pembrolizumab + Chemotherapy strategy vs. Chemotherapy
Life years	1.56	2.70	1.14
Time in progression free state (months)	9.69	18.06	8.37
Time in progressive state (months)	9.02	14.31	5.29
QALYs	0.92	1.69	0.77
Costs	NTD 594,517	NTD 1,465,571	NTD 871,054
ICER			
Cost per LYG			NTD 764,752
Cost per QALY			NTD 1,134,614

CONCLUSION

- In NSQ patients, comparing with all Taiwanese SOC chemotherapy, pembrolizumab + chemotherapy is projected to increase life expectancy by almost 1 year and the resultant incremental cost/QALY is less than 2 times Taiwan per capita GDP.
- Similarly, in the comparison against chemotherapy for SQ patients, the same resultant incremental cost/QALY is less than 2 times Taiwan per capita GDP for pembrolizumab + chemotherapy regimen.
- Overall, the addition of Pembrolizumab to chemotherapy is projected to extend patient life expectancy. The results suggest Pembrolizumab plus chemotherapy yields an ICER below a 3 times Taiwan per capita GDP ICER threshold of NTD 2,309,943/QALY and is cost-effective compared to SOC chemotherapy for first-line treatment for metastatic NSCLC.

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