Cost-Effectiveness of Second-Line Treatment for Advanced Endometrial Carcinoma in Taiwan: Lenvatinib Plus Pembrolizumab Versus Doxorubicin

Szu-Ting Chiang[1,4], Chen-Han Chueh[1], Pei-Kuan Ho[1], Yu-Wen Wen[3], Ming-Neng Shiu[1], Jin-Hwang Liu[1, 2], Wai-Hou Li[1, 2], Yi-Wen Tsai[1]

[1]National Yang Ming Chiao Tung University, Taipei, Taiwan, [2]Cheng Hsin General Hospital, Taipei, Taiwan, [3]Chang Gung University, Taoyuan, Taiwan, [4]National Taiwan University Hospital , Taipei, Taiwan

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Introduction

Background

- The European Society for Medical Oncology (ESMO) recommends the combination of lenvatinib and pembrolizumab (LP) as a second-line therapy for advanced endometrial carcinoma (EC) patients, irrespective of their microsatellite status.
- However, Taiwan's National Health Insurance (NHI) has not covered LP for this indication, and current economic evaluations have yielded inconsistent results.

Objective

- To evaluate the cost-effectiveness of the LP regimen as a 2nd-line treatment for advanced or recurrent EC under the context of Taiwan's NHI.
- To propose a reference price for addressing reimbursement concerns.

Methods

Study design

- **Perspective:** National Health Insurance Administration, Ministry of Health and Welfare, Taiwan.
- **Target population:** adult women with advanced EC who experienced disease progression after platinum-containing chemotherapy (ChT).
- **Intervention:**
  Lenvatinib + pembrolizumab (LP) regimen (NT$152,194 per 3-week).
- **Comparator:**
  Taiwan's conventional ChT with doxorubicin (NT$6,778 per 3-week).

Cost-effectiveness model

Decision-analytical model	partitioned survival model
Disease model	• progression-free state (PFS) • progressed disease (PD) • death
Time horizon	20 years
Cycle length	3 weeks
Discount rate	3%
Willingness-to-pay (λ)	3 times the GDP per capita in 2022 (NT$2,925,582)
Extrapolation	hybrid method

Cost-effectiveness analysis estimators

- **Incremental cost-effectiveness ratio (ICER) =** $\frac{C_2-C_1}{E_2-E_1}=\frac{\Delta C}{\Delta E}$
- **Net monetary benefit (NMB) =** $\lambda \times \Delta E - \Delta C$
- **Expected value of perfect information (EVPI)**

  $EVPI = E_\theta \max_j NB(j,\theta) - \max_j E_\theta NB(j,\theta)$

Sensitivity analysis

- **Deterministic sensitivity analysis (DSA):** 95% confidence interval (CI) or $\pm$ 25% of the base value.
- **Probabilistic sensitivity analysis (PSA):** 1,000 times Monte Carlo simulation with respective to parameters' probability distributions.
- **Scenario analysis:**
  - Time horizon: 5 years and increase every ten years from 20, 30, 40 to 50 years.
  - Gradual 10% reduction on the drug cost of LP.

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Welcome to contact us

Szu-Ting Chiang
E-mail: tina59801@gmail.com
Phone: +886928541593

Results

1. Base case

The LP regimen is not cost-effective in comparison with ChT at WTP of NT$2,925,582.

Table 1. Cost-effectiveness outcomes in the base-case analysis in 20 years

	Cost		Life-years		QALY		ICER	NMB
Strategy	Cost	Incr. cost*	LYs	Incr. LYs*	QALY	Incr. QALY*		
ChT	1,274,021	-	1.74	-	1.37	-	-	-
LP regimen	4,388,613	3,114,593	2.88	1.13	2.29	0.92	3,399,709	-423,058

* Incr. cost/LYs/QALY: incremental cost/life-years/quality-adjusted life-years.

2. DSA result

Major factors cause uncertainty are

- Time horizon
- Cost of pembrolizumab
- Cost of lenvatinib

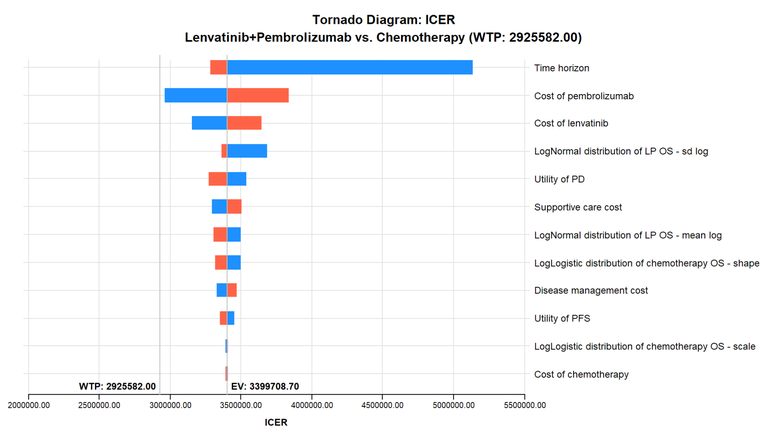

Figure 1. Tornado diagram from one-way sensitivity analysis.

3. PSA result

The probability of LP being cost-effective is only 0.3%, when compared to conventional chemotherapy.

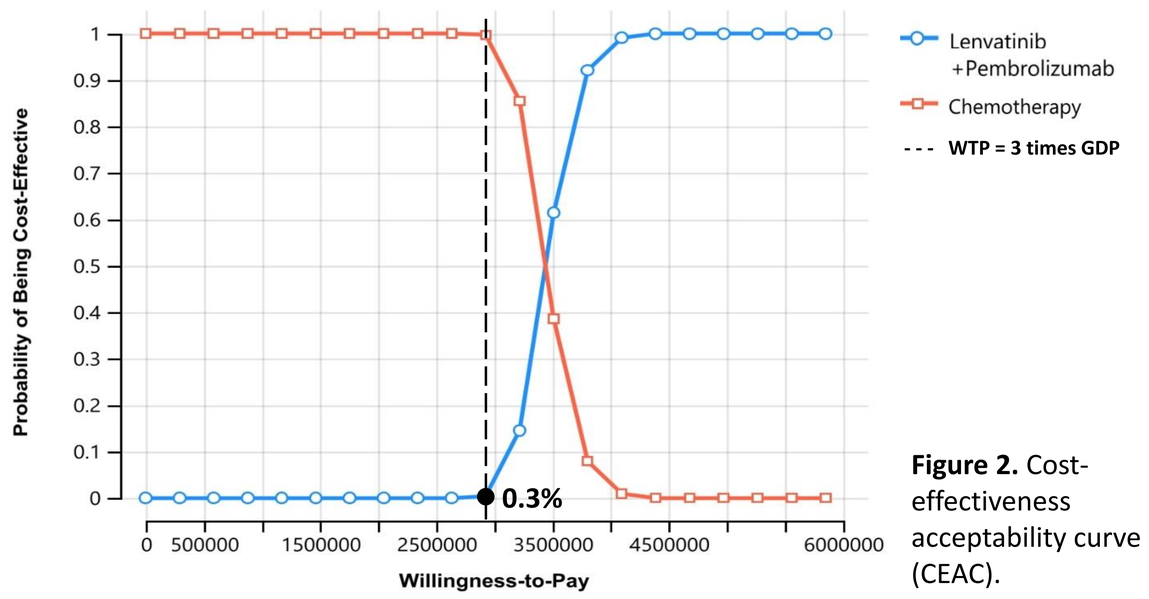

Figure 2. Cost-effectiveness acceptability curve (CEAC).

4. Scenario analysis

The new regimen would become cost-effective if the cost LP reduced by 20% or more.

Table 2. Main economic outcomes of each scenario

Scenario	ICER	NMB	Probability of cost-effectiveness*	EVPI*
Base case	3,399,709	-423,058	0.30%	32
Life years	**2,744,156**	**191,315**	**88.6%**	**8,716**
Time horizon				
5 years	5,136,994	-1,121,089	0.0%	0
30 years	3,315,319	-378,304	2.0%	1,095
40 years	3,290,572	-362,376	3.4%	2,482
50 years	3,282,268	-337,749	3.6%	3,526
LP price				
90%	3,125,790	-172,111	12.5%	7,712
80%	**2,851,871**	**78,836**	**57.9%**	**48.64.86**
70%	**2,577,952**	**329,782**	**96.4%**	**1,432**

* Probability sensitivity analysis results

Conclusion

From the Taiwanese NHI payer's perspective, when the WTP threshold set at 3 times Taiwan's GDP in 2022, the 2nd-line therapy LP regimen is not cost-effective in comparison to the current chemotherapy for advanced EC patients, unless the price of LP is reduced more than 20%.