Cost-Effectiveness of Zolbetuximab Plus Chemotherapy as First-Line Treatment for Advanced Gastric or Gastroesophageal Adenocarcinoma in Taiwan

EE836

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Background

- Zolbetuximab, the first monoclonal antibody targeting Claudin 18.2, was approved for advanced gastric or gastroesophageal junction adenocarcinoma (G/GEJ) by Japan's Ministry of Health, Labour and Welfare (MHLW) based on the GLOW and SPOTLIGHT trials.
- The value of add-on zolbetuximab to chemotherapy (either mFOLFOX or CAPOX) has been a subject of debate due to its high treatment cost with limited treatment benefits.
- There is currently no cost-effectiveness analysis (CEA) comparing zolebetuximab with chemotherapy (mFOLFOX or CAPOX) versus chemotherapy alone from the perspective of Taiwan's National Health Insurance Administration (NHIA)

Objective

- To evaluate the cost-effectiveness of adding zolbetuximab to chemotherapy (CAPOX or mFOLFOX) versus chemotherapy alone from Taiwan NHIA's perspective.
- To conduct price reduction scenarios and provide value-based pricing for National Health Insurance (NHI) reimbursement if the results are not cost-effective.

Methods

- The analytical framework and parameters of this decision model are listed below:

Table 1. Analytical framework and model inputs of base case

Population	Patients with CLDN18.2-positive, HER2-negative, untreated locally advanced unresectable or metastatic G/GEJ cancer
Intervention	A combination of zolbetuximab and chemotherapy
Comparator	Chemotherapy alone (1: CAPOX, 2: mFOLFOX)
Cost	Zolbetuximab cost (NT$11,990 per 100 mg per m^2), medication cost of chemotherapy, adverse events cost, and nonmedication cost estimated from NHIRD data
Outcome	Total cost, Quality-adjusted life-years (QALYs)
CEA outcome	Incremental cost-effectiveness ratio (ICER) and incremental net monetary benefit (INMB)
Study design	3-state partitioned survival model: progression-free (PF), post-progression (PP), and death
Perspective	NHIA, Taiwan
Time horizon	10 years
Discount rate	3% per year to costs and outcomes
Willingness-to-pay	3 times the GDP per capita in 2023 (NT$3,023,055)
Sensitivity analysis	■ Deterministic sensitivity analysis (DSA) ■ Probabilistic sensitivity analysis (PSA) ■ Value of information analysis
Scenario analysis	■ Considering life-years as effectiveness ■ Gradual price reduction of zolbetuximab ■ Extending time on treatment ■ Applying an NHI conversion factor to non-medication costs ■ Different adverse events incurred duration and time horizon
Parameter source	■ The efficacy data and time on treatment were derived from the GLOW and SPOTLIGHT trials. ■ Zolbetuximab cost were from Japan MHLW. ■ The utility data were derived from previous literature.

Base-case results

- Adding zolbetuximab to CAPOX gained 0.38 QALYs at an incremental cost of NT$1,109,392, with a cost-effective ICER of NT$2,940,727 per QALY. In contrast, adding zolbetuximab to mFOLFOX gained 0.42 QALYs at NT$1,705,641, with a non-cost-effective ICER of NT$4,024,348 per QALY.

Table 2. Base-case results

	Outcomes				Incremental changes	
Treatment strategy	Zolbetuximab +CAPOX	Comparator 1 CAPOX	Zolbetuximab +mFOLFOX	Comparator 2 mFOLFOX	Zolbetuximab +CAPOX vs. CAPOX	Zolbetuximab +mFOLFOX vs. mFOLFOX
Cost(NT$)	2,726,402	1,617,011	4,549,107	2,843,466	1,109,392	1,705,641
QALY	1.28	0.90	1.68	1.26	0.38	0.42
ICER					2,940,727	4,024,348
INMB					31,058	-424,379
EVPI/person					179,309	96,744

Scenario analysis results

- A 50% discount on zolbetuximab yielded a positive INMB of NT$35,893, making it cost-effective compared to mFOLFOX.
- Extending the treatment duration of zolbetuximab led to a doubling of its ICERs compared to both comparators, rendering it cost-ineffective.
- Adding zolbetuximab to CAPOX was not cost-effective in scenarios with AEs incurred every cycle and a 5-year time horizon.

Table 3 Scenario analysis results

	Zolbetuximab+CAPOX vs. CAPOX							Zolbetuximab+mFOLFOX vs. mFOLFOX						
	Base-case analysis		Probabilistic sensitivity analysis					Base-case analysis		Probabilistic sensitivity analysis				
Scenario	ICER (NT$/QALY)	INMB (NT$)	Probability of being cost-effective	EVPI/person	INMB (NT$) Average	lower bound	upper bound	ICER (NT$/QALY)	INMB (NT$)	Probability of being cost-effective	EVPI/person	INMB (NT$) Average	lower bound	upper bound
1. Base-case (NT$ 11,990/100 mg/m^2)	2,940,727	31,058	55.7%	179,309	34,727	4,192	65,262	4,024,348	-424,379	26.7%	96,744	-430,741	-472,537	-388,944
2. Life-year as effectiveness	2,495,213	234,683	99.7%	41	235,946	229,469	242,423	3,432,618	-203,508	7.4%	3,273	-202,452	-211,142	-193,762
3. 50% price of zolbetuximab (NTD 5,995/100 mg/m^2)	2,051,105	366,669	77.7%	65,854	350,861	322,025	379,697	2,938,369	35,893	56.6%	236,810	55,685	14,390	96,981
4. Drug discontinuation to RCT follow-up	6,402,627	-1,274,946	1.1%	1,633	-1,254,384	-1,288,415	-1,220,354	8,210,392	-2,198,552	0.4%	1,308	-2,228,672	-2,277,918	-2,179,427
5. No drug discontinuation	7,485,221	-1,683,355	0.0%	0	-1,688,282	-1,722,254	-1,654,311	9,994,161	-2,954,567	0.0%	0	-2,937,322	-2,987,105	-2,887,540
6. Applying a conversion factor to nonmedication costs	2,825,488	74,532	59.5%	145,626	91,572	62,543	120,600	3,840,852	-346,607	32.5%	135,011	-338,799	-382,121	-295,477
7. AE incurred every cycle during drug prescription	2,989,555	12,441	51.7%	187,676	8,784	-21,133	38,700	4,118,552	-454,115	25.9%	104,039	-411,079	-452,075	-370,083
8. AE incurred every cycle	3,317,370	-99,197	40.5%	128,888	-112,536	-140,930	-84,142	5,014,231	-685,624	16.2%	50,879	-696,011	-739,343	-652,679
9. Time horizon: 5 years	3,327,956	-88,281	44.2%	133,426	-79,524	-106,207	-52,841	4,799,008	-542,050	22.1%	67,097	-513,741	-552,434	-475,048
10. Time horizon: 15 years	2,852,932	68,938	60.4%	150,314	86,318	56,812	115,825	3,816,600	-375,437	29.6%	115,327	-373,373	-415,742	-331,005

Sensitivity analysis results

- The DSA showed (Fig. 1) that the utility of PF and PP states, the treatment duration of zolbetuximab, and the cost of zolbetuximab, were the most influential factors of uncertainty in both comparator analyses.

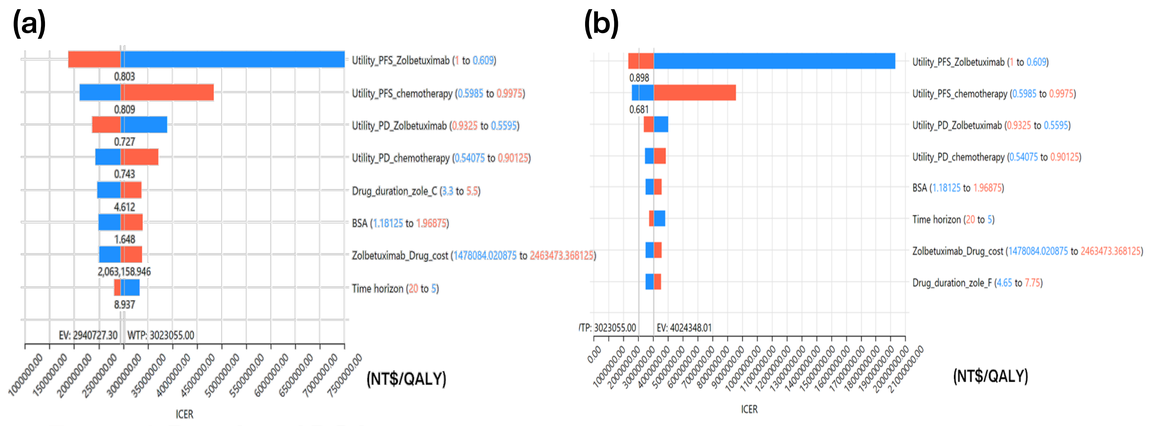

Figure 1. Results of DSA:
(a) Zolbetuximab+CAPOX vs. CAPOX, (b) Zolbetuximab+mFOLFOX vs. mFOLFOX

- Zolbetuximab yielded higher effectiveness at higher costs (Fig. 2).

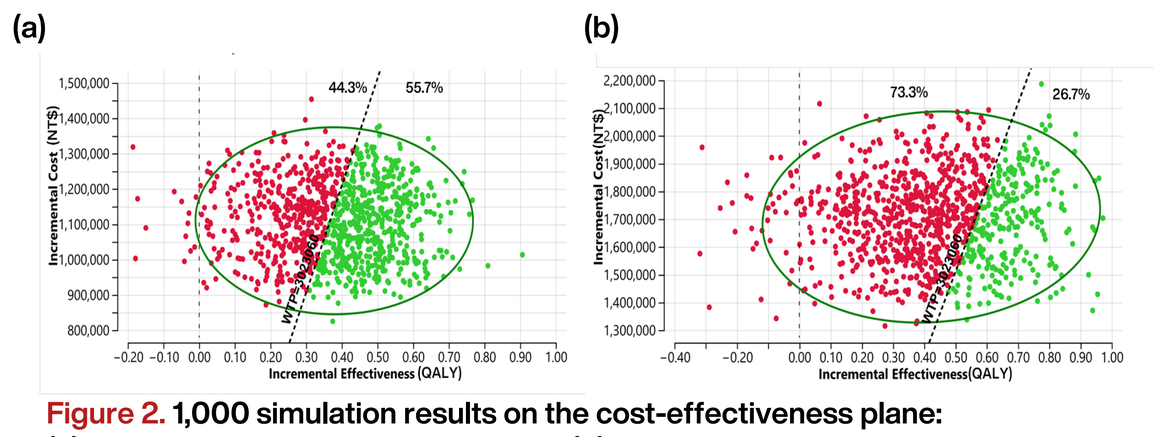

Figure 2. 1,000 simulation results on the cost-effectiveness plane:
(a) Zolbetuximab+CAPOX vs. CAPOX, (b) Zolbetuximab+mFOLFOX vs. mFOLFOX

- Zolbetuximab demonstrated a 55.7% or 26.7% probability of achieving cost-effectiveness when adding zolbetuximab to CAPOX or mFOLFOX (Fig. 3).

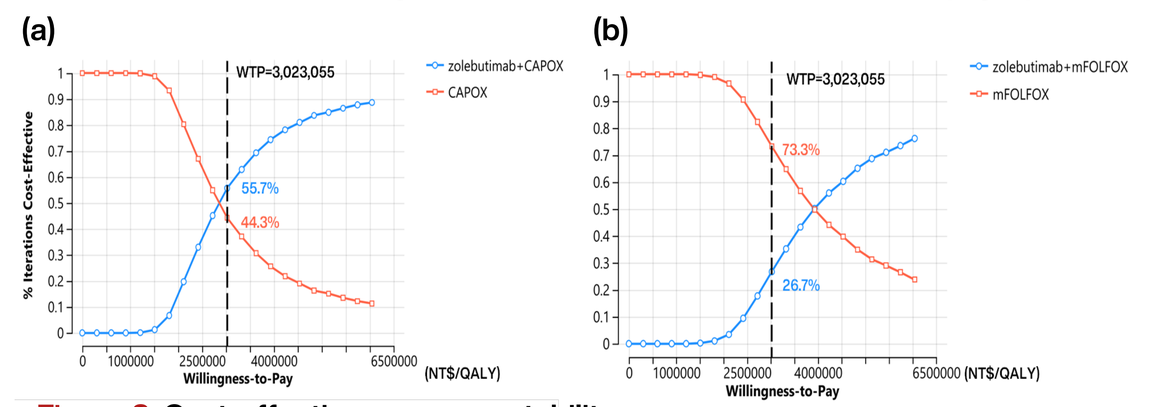

Figure 3. Cost-effectiveness acceptability curve:
(a) Zolbetuximab+CAPOX vs. CAPOX, (b) Zolbetuximab+mFOLFOX vs. mFOLFOX

Conclusions

- Adding zolbetuximab was cost-effective compared with CAPOX alone for advanced G/GEJ with CLDN18.2-positive and HER2-negative from Taiwan NHIA's perspective.
- Zolbetuximab requires a 50% price reduction (NT$5,995/100mg/$m^2$) to become cost-effective when compared with using mFOLFOX alone.

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