Cost-effectiveness analysis of a new second-line treatment for advanced intrahepatic cholangiocarcinoma:
biomarker-driven targeted therapy with pemigatinib versus chemotherapy with 5-FU

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Background

- The National Comprehensive Cancer Network recommends second-line treatment of pemigatinib for patients with advanced intrahepatic cholangiocarcinoma (ICC) with fibroblast growth factor receptor 2 (*FGFR2*) fusions/rearrangements and a combination of oxaliplatin, folinic acid, and fluorouracil (modified FOLFOX, mFOLFOX) for those without *FGFR2* alterations.
- However, these regimens are not yet covered by Taiwan's National Health Insurance (NHI), and there is currently no cost-effectiveness analysis (CEA) evidence for the NHI reimbursement scheme to reference.

Objectives

- This CEA evaluates the cost-effectiveness of the pemigatinib/mFOLFOX regimen as the second-line treatment for advanced ICC based on *FGFR2* status in comparison with the regimen of fluorouracil (5-FU) chemotherapy and provides a CEA-based reference price for pemigatinib.

Methods

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

Table 1. Analytical framework

Population	Advanced ICC patients who failed first-line therapy
Intervention	Patients with *FGFR2* fusions/rearrangements use pemigatinib and those without *FGFR2* alterations use mFOLFOX
Comparator	5-FU
Cost	Genetic testing fee, direct medication cost, and nonmedication cost (Self-paying items are not included.)
Outcome	Life-years (LYs) and quality-adjusted life-years (QALYs)
Study design	3-state partitioned survival model (progression-free, progressed disease, and death)
Perspective	National Health Insurance Administration, Taiwan
Time horizon	5 years
Discount rate	3% per year to costs and outcomes
Willingness-to-pay	3 times the GDP in 2021 (NT$2,889,684)
Scenario analysis	■ Gradual price reduction of pemigatinib ■ Alternative survival models ■ Applying an NHI payment conversion factor to nonmedication costs ■ Consideration of LYs as effectiveness ■ Adverse events (AEs) incurred every cycle during the first six months and entire time horizon
Sensitivity analysis	■ Deterministic sensitivity analysis (DSA) ■ Probabilistic sensitivity analysis (PSA) ■ Value of information analysis (VOI)
Parameter source	■ The effectiveness data are derived from the FIGHT-202, ABC-06, and NIFTY trials. ■ The cost data are derived from market price and NHI claim database. ■ The utility data are derived from previous literature.

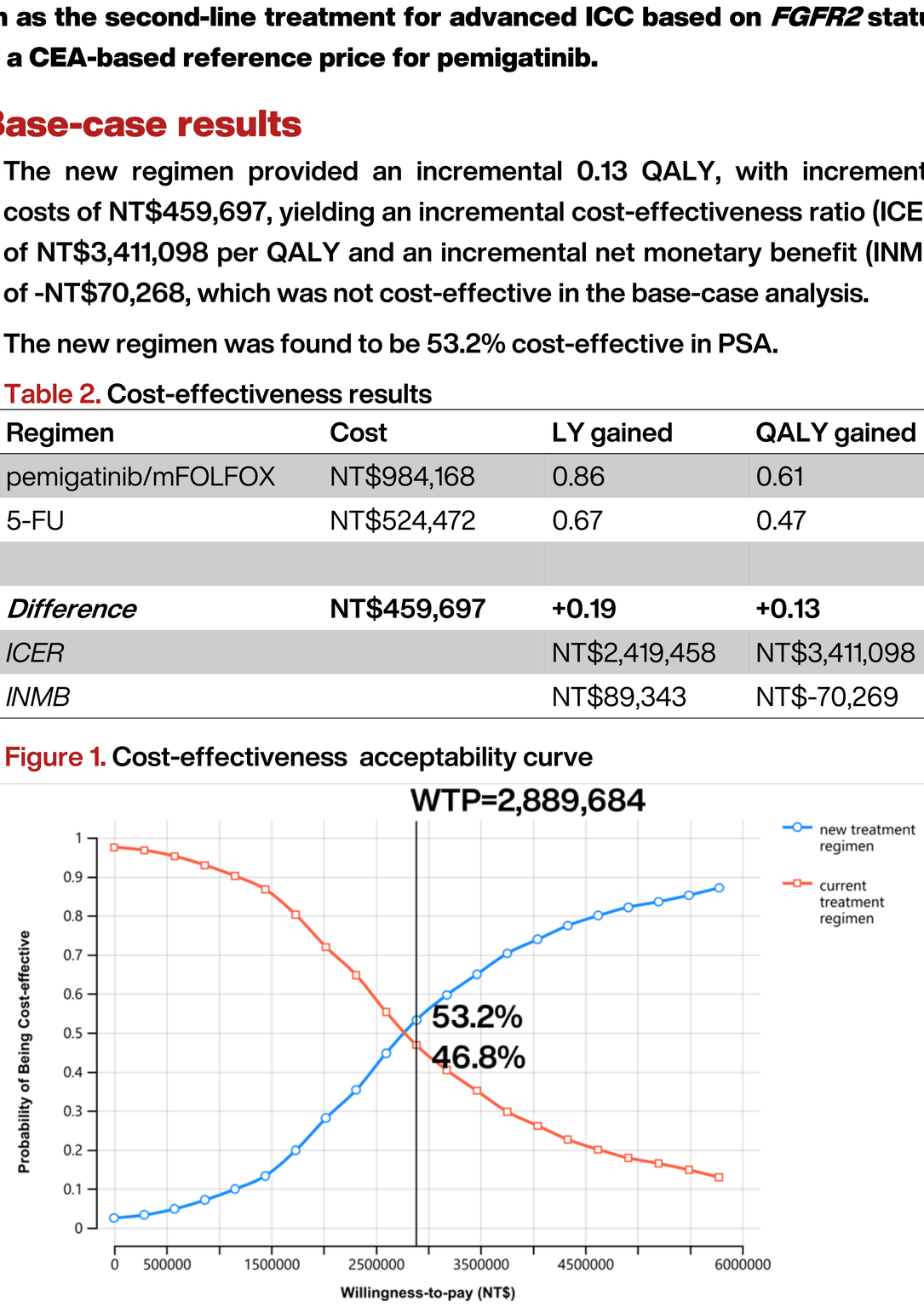
Base-case results

- The new regimen provided an incremental 0.13 QALY, with incremental costs of NT$459,697, yielding an incremental cost-effectiveness ratio (ICER) of NT$3,411,098 per QALY and an incremental net monetary benefit (INMB) of -NT$70,268, which was not cost-effective in the base-case analysis.
- The new regimen was found to be 53.2% cost-effective in PSA.

Table 2. Cost-effectiveness results

Regimen	Cost	LY gained	QALY gained
pemigatinib/mFOLFOX	NT$984,168	0.86	0.61
5-FU	NT$524,472	0.67	0.47
Difference	**NT$459,697**	**+0.19**	**+0.13**
ICER		NT$2,419,458	NT$3,411,098
INMB		NT$89,343	NT$-70,269

Figure 1. Cost-effectiveness acceptability curve

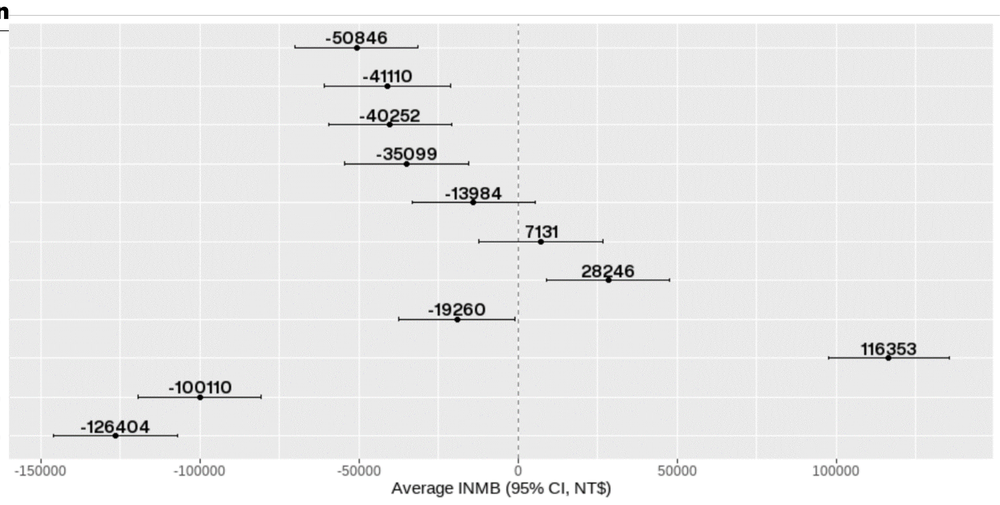


Scenario analysis results

- The INMB was positive when the price of pemigatinib was reduced by 40% or more.
- The new regimen gained similar probabilities of being cost-effective under the scenario of reducing 20% price of pemigatinib, using log-logistic distributions for all survival curves, and applying a conversion factor to nonmedical costs.
- When assuming AEs incurred every cycle during the first six months and the entire time horizon, the probability of the new regimen being cost-effective was dramatically reduced.

Figure 2. Scenario analysis results

	Base-case analysis		Probabilistic sensitivity analysis	
Scenario	**ICER**	**INMB**	**Probability of being cost-effective**	**EVPI/person**
Base-case	3,411,098	-70,268	53.2%	80,695
Log-logistic distributions for all survival curves	3,301,843	-59,096	55.1%	88,891
90% price of pemigatinib	3,252,339	-48,873	54.9%	86,023
80% price of pemigatinib	3,093,579	-27,478	56.3%	89,564
70% price of pemigatinib	2,934,819	-6,083	59.3%	101,355
60% price of pemigatinib	2,776,060	15,313	62.6%	106,768
50% price of pemigatinib	2,617,300	36,708	66.0%	99,050
Applying a conversion factor to nonmedication	3,250,940	-48,686	56.5%	83,188
Life-year as effectiveness	2,383,559	97,612	76.4%	71,951
AE incurred every cycle during first six months	3,918,044	-120,656	41.0%	57,405
AE incurred every cycle	4,256,393	-147,607	36.3%	47,445



Conclusions

- **Although the new second-line genetic-based and biomarker-driven regimen of pemigatanib/mFOLFOX is not cost-effective for patients with advanced ICC in the base-case analysis, it is highly likely to be cost-effective in the case of a 40% price reduction on pemigatinib.**

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