Incorporating Real Option Value in the Economic Evaluation of Osimertinib for Advanced EGFR-Mutated Non-small Cell Lung Cancer

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Kwame Adjei[1]; Vakaramoko Diaby[2]; Meng Li[3]; Fatimah Sherbeny[1]; Sandra Suther[1]; Askal Ali[1]

[1]Florida A&M University; College of Pharmacy and Pharmaceutical Sciences; [2]Ostuka Pharmaceuticals; [3]Tufts Medical Center; Center for the Evaluation of Value and Risk in Health

Background

- Cost effectiveness analysis (CEAs) have gained importance in healthcare resource allocation, but do not fully capture value when treatment landscapes evolve rapidly.[1,2]
- Longer survival creates added value by allowing patients to access future treatment advances – this is the concept of real option value (ROV).[3]
- Although ROV is increasingly recognized, its use remains limited for epidermal growth factor receptor - tyrosine kinase inhibitors in advanced non-small cell lung cancer (NSCLC).[4]
- Osimertinib improves progression-free survival and overall survival versus earlier generation EGFR-TKIs in NSCLC.[5]
- Prior CEAs report greater quality-adjusted life years (QALYs) with osimertinib, but incremental cost effectiveness ratio (ICERs) often exceed willingness-to-pay (WTP) thresholds.

Objective

- To assess the impact of ROV of first-line osimertinib compared with first-generation EGFR-TKIs in advanced NSCLC.

Methods

- A three-state Markov model was developed with progression-free survival (PFS), progressed disease (PD), and death.
- The model compared osimertinib versus standard EGFR-TKIs (erlotinib/gefitinib).
- Two scenarios were evaluated: a conventional cost-effectiveness analysis and ROV-adjusted analysis.
- The model used a starting age of 64 years old, 1-month cycle, a lifetime horizon, a U.S. health system perspective, and 3% annual discounting.
- In the ROV scenario, the SEER-Medicare mortality trend was applied to the PD → death transition.
- Outcomes included costs, life-years (LYs), quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs).
- Uncertainty was assessed using one-way sensitivity analysis, and probabilistic sensitivity analysis (10,000 iterations).
- All costs were adjusted to 2024 US dollars using consumer price index (CPI-U).

Table 1. Key model inputs and data sources

Input domain	Key inputs	Base-case values / approach	Distribution	Source
Clinical efficacy	PFS and OS for osimertinib and standard EGFR-TKIs	Derived from fitted survival curves	Parametric survival models	FLAURA phase 3 trial
ROV survival trend	Lung cancer mortality trend on later-line treatment	HR = 0.810; 95% CI: 0.800–0.819	Analysis	SEER-Medicare trend analysis
Drug costs	Osimertinib, erlotinib, gefitinib, cisplatin + pemetrexed	Osimertinib: $19,171/month; erlotinib: $9,466/month; gefitinib: $8,724/month; cisplatin + pemetrexed: $1,136/ cycle	Gamma	Drug costs were based on average wholesale prices from RED BOOK
Other medical costs	EGFR testing, physician fees, monitoring, supportive care, administration, end-of-life care	Direct medical costs included by health state and treatment pathway	Gamma	Center for Medicare & Medicaid Services / published literature
Utilities	PFS and PD utilities by treatment	PFS: 0.803 osimertinib; 0.784 standard EGFR-TKIs. PD: 0.712 osimertinib; 0.699 standard EGFR-TKIs	Beta	NICE evidence report

Abbreviations: CEA, cost-effectiveness analysis; CEAC, cost-effectiveness acceptability curve; CI, confidence interval; EGFR, epidermal growth factor receptor; EGFR-TKI, epidermal growth factor receptor–tyrosine kinase inhibitor; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; LY, life-year; NSCLC, non-small cell lung cancer; OS, overall survival; PD, progressed disease; PD-1, programmed cell death protein 1; PFS, progression-free survival; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life-year; ROV, real option value; SEER, Surveillance, Epidemiology, and End Results; WTP, willingness-to-pay.

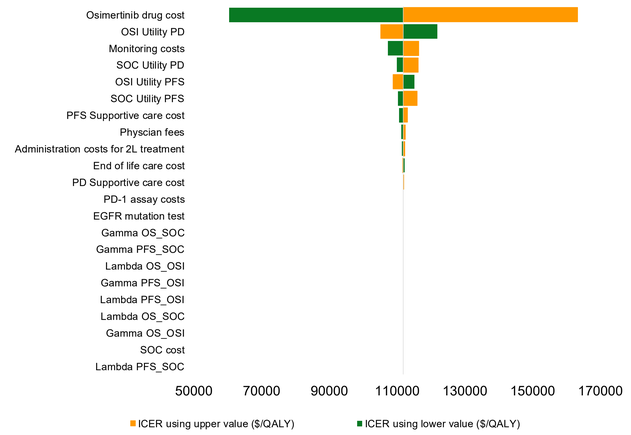
Results

Table 2. Base-case cost effectiveness results for osimertinib vs. standard EGFR-TKIs under conventional and ROV scenarios

Outcome	Conventional: Osimertinib	Conventional: Standard EGFR-TKIs	Conventional: Incremental	ROV: Osimertinib	ROV: Standard EGFR-TKIs	ROV: Incremental
LYs	5.6750	3.7480	1.9270	6.5216	3.8524	2.6692
QALYs	4.3450	2.8251	1.5199	4.9460	2.8983	2.0477
Costs	$910,300.12	$670,520.17	$239,779.95	$927,559.07	$698,332.27	$229,226.80
ICER ($/QALY)	—	—	$157,761	—	—	$111,942

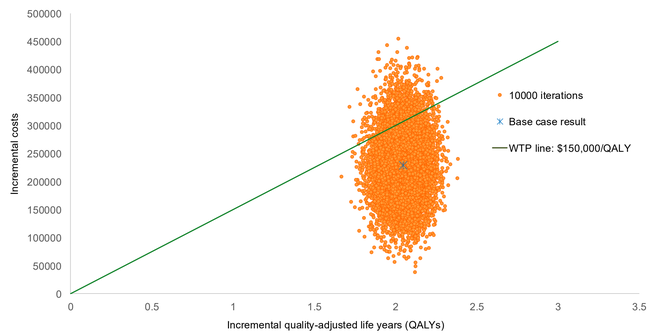
- Osimertinib accrued higher LYs and QALYs than standard EGFR-TKIs in both scenarios.
- Adding ROV increased incremental QALYs by 35% and reduced incremental costs by 4%.
- After incorporating ROV, the conventional ICER decreased by 29%, from $157,761/QALY to $111,942/QALY.

Figure 2. One-way sensitivity analysis of the ICER for osimertinib versus standard EGFR-TKIs in the ROV scenario



- The ROV-adjusted ICER was most sensitive to osimertinib drug cost, same as the conventional scenario. Value estimates remain most influenced by treatment cost and post-progression quality-of-life assumptions.

Figure 3. Probabilistic sensitivity analysis plane for osimertinib vs. standard EGFR-TKIs in the ROV scenario



- PSA showed that osimertinib remained economically favorable in majority of the simulations at $150,000/QALY.

Figure 4. Cost-effectiveness acceptability curve for osimertinib vs. standard EGFR-TKIs in the ROV scenario

- At $150,000/QALY, osimertinib had an estimated 89% probability of being cost-effective in the ROV scenario, compared with 43% in the conventional scenario.
- At $100,000/QALY, the probability was 31% in the ROV scenario versus 6% in the conventional scenario, highlighting sensitivity to the selected WTP threshold.
- The CEAC supports the PSA plane indicating how probability of cost-effectiveness changes across WTP thresholds.

Discussion

- ROV captures value from survival-enabled access to future therapies beyond immediate trial-based benefits.
- Incorporating ROV increased incremental QALYs and reduced the modeled ICER from $157,761/QALY to $111,942/QALY, moving osimertinib below the $150,000/QALY benchmark.
- The lower ICER was driven primarily by larger incremental QALY gains, with a modest reduction in incremental costs.
- Dynamic value elements are particularly relevant in oncology, where rapid innovation and survival extension can affect future treatment pathways.
- The threshold shift highlights a limitation of fixed WTP benchmarks: value estimates may differ when dynamic value elements are included, which can influence how therapies are interpreted for coverage and access decisions.
- Findings align with broader efforts to move beyond conventional ICER-based assessment by incorporating additional value elements, as seen in generalized CEA and distribution-sensitive value approaches.

Limitations

- ROV estimates rely on projected future innovation; future therapeutic breakthroughs, survival gains, and treatment pathways cannot be directly observed.
- The SEER-Medicare trend approach assumes historical survival improvements continue, although future gains may accelerate, slow, or plateau.
- Adverse event costs and disutilities were excluded; only Grade 3/4 events occurring in ≥5% of either treatment arm were considered, and the only qualifying event was skin rash with standard EGFR-TKIs.
- SEER-Medicare reflects an older population; findings may not fully generalize to younger patients with different treatment patterns, comorbidities, or healthcare use.

Conclusion

- Incorporating ROV increased incremental QALYs from 1.53 to 2.05 and reduced the modeled ICER from $157,761/QALY to $111,942/QALY.
- At a $150,000/QALY benchmark, the ROV-adjusted CEA estimated a more favorable value profile for osimertinib versus standard EGFR-TKIs.
- There is a need for value assessment frameworks to reflect how survival today may shape treatment opportunities tomorrow.

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