

Cost-Effectiveness Analysis of Upfront SBRT for Oligometastatic Stage IV Non-Small Cell Lung Cancer Based on Mutational Status

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Abstract

Objective(s): Current National Comprehensive Cancer Network guidelines support systemic therapy based on mutational status in stage IV non-small cell lung cancer (NSCLC), with stereotactic body radiation therapy (SBRT) reserved for oligoprogression. However, a clear progression-free survival benefit for SBRT in the oligometastatic setting has been demonstrated through several phase II trials, and an overall survival benefit has been suggested. While clinical trials studying the impact on survival of adding SBRT to targeted therapies continue to accrue, we aimed to evaluate the cost-effectiveness of routinely adding SBRT to upfront therapy in different mutational subgroups of stage IV NSCLC.

Methods: A Markov state transition model was constructed to perform a cost-effectiveness analysis comparing SBRT plus maintenance therapy with maintenance therapy alone for oligometastatic NSCLC. Three hypothetical cohorts were analyzed: EGFR or ALK mutation-positive, PDL-1 positive, and mutation-negative/PDL-1 negative. Clinical parameters were obtained from clinical trial data, and cost data were based on 2018 U.S. Medicare reimbursement. In the model, all patients were initially treated with first-line systemic therapy according to their mutational/PDL-1 expression status (osimertinib for EGFR-positive patients, alectinib for ALK-positive patients, pembrolizumab for PDL-1 expressing patients, and platinum-based systemic therapy for mutation-negative patients). After first-line therapy, cohorts entered the model and received either SBRT plus maintenance therapy or maintenance therapy alone. Following SBRT, patients received maintenance therapy until disease progression. To account for uncertainty, one-way sensitivity analyses were performed. Strategies were compared using the incremental cost-effectiveness ratio (ICER) with effectiveness in quality-adjusted life years (QALYs), and evaluated with a willingness-to-pay (WTP) threshold of \$100,000 per QALY gained.

Results: Base case analysis showed that SBRT plus maintenance therapy was not cost-effective at a WTP threshold of \$100,000/QALY gained, assuming equal survival between the two treatments, for any cohort. The ICER was \$564,186/QALY gained for the EGFR or ALK positive cohort and \$299,248/QALY gained for the PDL-1 positive cohort. For the mutation-negative cohort, SBRT was nearly cost-effective, at \$128,424/QALY gained. In one-way sensitivity

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analyses, results were most sensitive to maintenance therapy drug costs. If cost for maintenance osimertinib & alectinib therapy was lowered by $\geq 20\%$, the ICER for SBRT plus maintenance therapy would be $< \$100,000/\text{QALY}$ gained for the EGFR or ALK positive cohort. If the cost of maintenance osimertinib and alectinib was cheaper by $\geq 26\%$, SBRT plus maintenance became a dominant (cost-saving) strategy. Likewise, if the cost of pembrolizumab was lowered by $\geq 35\%$, SBRT plus maintenance became a dominant strategy for PDL1-positive patients. For the mutation-negative cohort, if the cost of maintenance therapy was reduced by 25% or more, ICER would be $< \$50,000/\text{QALY}$ gained, which is a commonly cited benchmark for a "good buy."

Conclusion(s): Adding SBRT to maintenance therapy is not a cost-effective strategy for oligometastatic NSCLC compared with maintenance therapy alone. SBRT would be cost-effective if the cost of maintenance therapy could be lowered, or if future studies confirm larger improvements in survival or progression-free survival with the addition of SBRT.