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

Diane Ling MD
UPMC Hillman Cancer Center
Department of Radiation Oncology, Pittsburgh, PA, USA

Frontiers of Radiosurgery Conference, Milan, Italy
October 24, 2019

Disclosure and Co-authors

Disclosure

- No conflict of interest exists.

Co-authors

- Diane C. Ling MD, Hayeon Kim PhD, John A. Vargo MD, Sushil Beriwal MD MBA, Kenneth J. Smith MD MS

Background

- 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.
- Ongoing phase III trials are investigating potential survival benefit of SBRT
  - Potential to effect a paradigm shift in treatment of oligometastatic disease

Background

- Contemporaneously, the emergence of targeted therapy based on individualized molecular tumor profiling has transformed the expected response and survival for stage IV NSCLC.

- Subset of patients with EGFR or ALK mutations achieve prolonged progression-free survival, in some cases many years, with targeted therapy.

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Background

- However, both SBRT and targeted therapy come at an increased monetary cost compared to conventional systemic chemotherapy.

- The value of incorporating SBRT into management for different molecular subgroups of stage IV NSCLC remains unclear.

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Purpose

- We aimed to evaluate the cost-effectiveness of routinely adding SBRT to upfront therapy in different mutational subgroups of stage IV NSCLC.

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Methods

- Markov state transition model constructed to perform cost-effectiveness analysis comparing SBRT + maintenance therapy with maintenance therapy alone for oligometastatic NSCLC.
- 3 hypothetical cohorts analyzed:
  - EGFR or ALK mutation-positive
  - PDL-1 positive
  - Mutation-negative/PDL-1 negative
- Clinical parameters were obtained from clinical trial data, and cost data were based on 2018 U.S. Medicare reimbursement.

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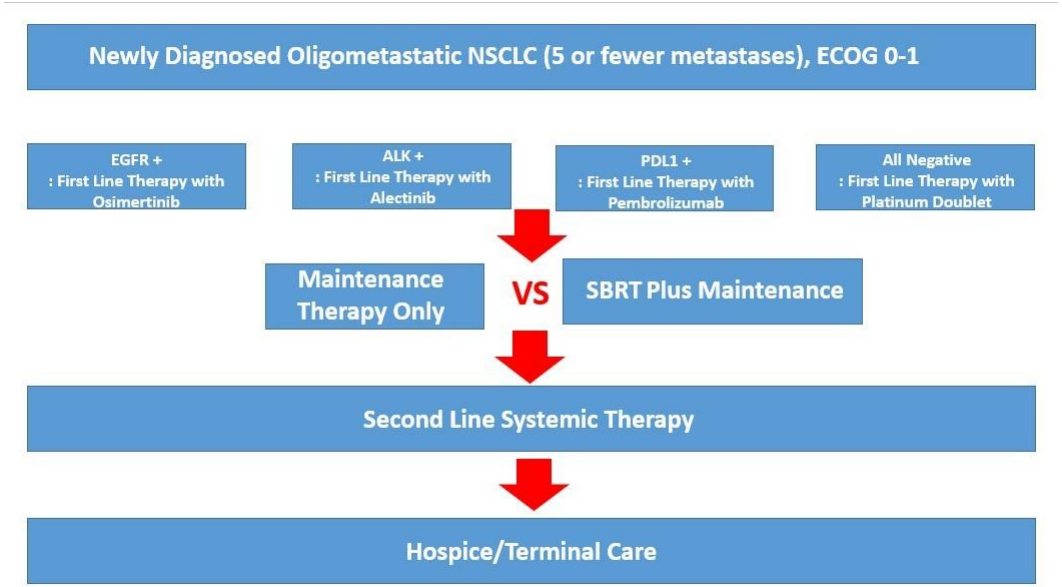
Methods

- In the model, all patients were initially treated with first-line systemic therapy according to their mutational/PDL-1 expression status.
- After first-line therapy, cohorts entered the model and received either SBRT + maintenance therapy or maintenance therapy alone.
- **Following SBRT, patients received maintenance therapy until disease progression.**

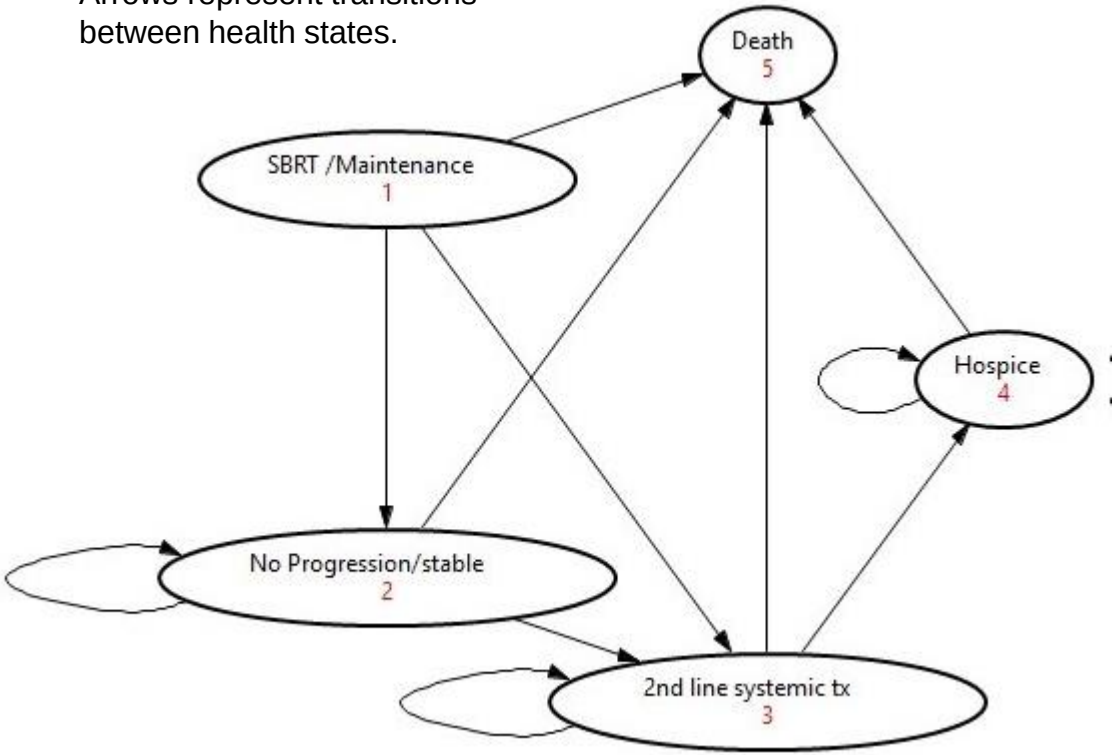


Methods

Markov Model

- Model health states were: treatment, no disease progression, second-line systemic therapy, hospice (terminal care), and death.
- Markov cycle length = 1 month.
- With a lifetime time horizon, the model cycled until the entire cohort had died.

Arrows represent transitions between health states.



Methods

- We assumed a progression-free survival gain of 7 months for SBRT group compared to maintenance alone group.
  - Estimated by taking the average of the PFS differences reported in 3 recent phase II trials comparing SBRT/local consolidative therapy to maintenance therapy or observation only
- No difference in overall survival with the addition of SBRT was assumed.

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Methods

- Strategies compared using incremental cost-effectiveness ratio (ICER)
  - Ratio of cost to effectiveness
  - Effectiveness measured in quality-adjusted life years (QALYs)
- Cost-effectiveness evaluated using willingness-to-pay (WTP) threshold of $100,000 per QALY gained

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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.
- ICER was :
  - $564,186/QALY gained for the EGFR or ALK positive cohort
  - $299,248/QALY gained for the PDL-1 positive cohort
  - $128,424/QALY gained for the mutation-negative cohort (nearly cost-effective).

Results

One-way sensitivity analyses

- In one-way sensitivity analyses, results were most sensitive to **maintenance therapy drug costs.**
- Results were also sensitive to variation in: utility of hospice/terminal care, median survival, and median progression-free survival.

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Results

One way sensitivity analysis:

EGFR or ALK positive cohort

- If cost for maintenance osimertinib and alectinib therapy was lowered by ≥20%, the ICER for SBRT plus maintenance therapy would be <$100,000/QALY gained.
- If maintenance tx cost was cheaper by ≥26%, SBRT + maintenance became a dominant (more effective, less costly) strategy.

Results

One way sensitivity analysis:

PDL1-positive cohort

- If the cost of pembrolizumab was lowered by ≥35%, SBRT + maintenance became a dominant strategy.

Mutation-negative cohort

- If the cost of maintenance therapy was reduced by ≥25%, ICER would be <$50,000/QALY gained, which is a commonly cited benchmark for a “good buy.”

Conclusions

- Adding SBRT to maintenance therapy is not a cost-effective strategy for oligometastatic NSCLC compared with maintenance therapy alone when equivalent survival is assumed, as the progression-free survival benefit of SBRT is overshadowed by additional cost of further maintenance drug.

- 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.

THANK YOU

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