The Cost-effectiveness of Second-line Crizotinib in EML4-ALK Rearranged Advanced Non-Small Cell Lung Cancer

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BACKGROUND

- Management of non-small cell lung cancer (NSCLC) has developed with molecular agents targeted to treat genomic abberations driving tumor growth.
- Diagnostic testing has cost implications.
- Chromosomal rearrangements of anaplastic lymphoma kinase (ALK) are predictive for response to crizotinib, a first-in-class, oral ALK inhibitor.[1]
- Crizotinib is associated with higher response rate, progression-free survival and improved quality of life compared with docetaxel or pemetrexed as second-line chemotherapy for advanced NSCLC following platinum-based chemotherapy.[2]

OBJECTIVES

To assess the cost-effectiveness of EML4-ALK fusion testing and second line therapy with crizotinib for patients with advanced NSCLC in Ontario.

METHODS

Figure 1. Decision tree for genomic testing

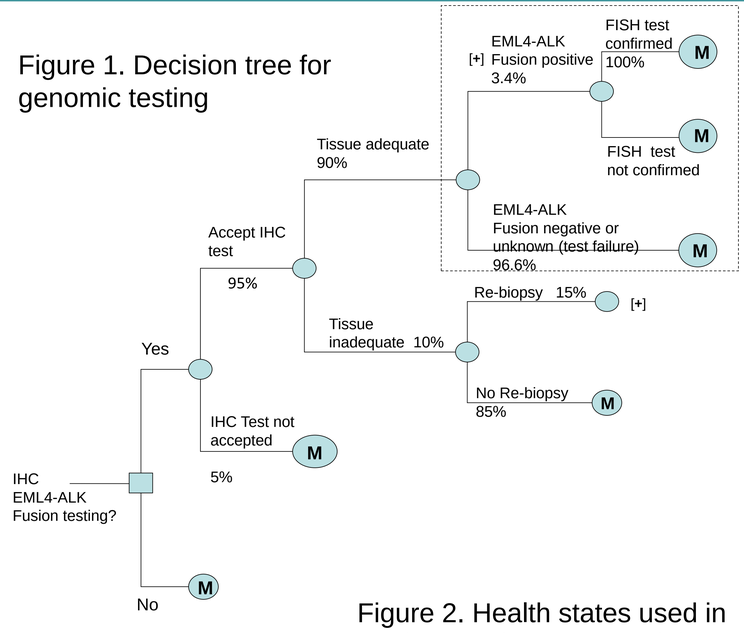
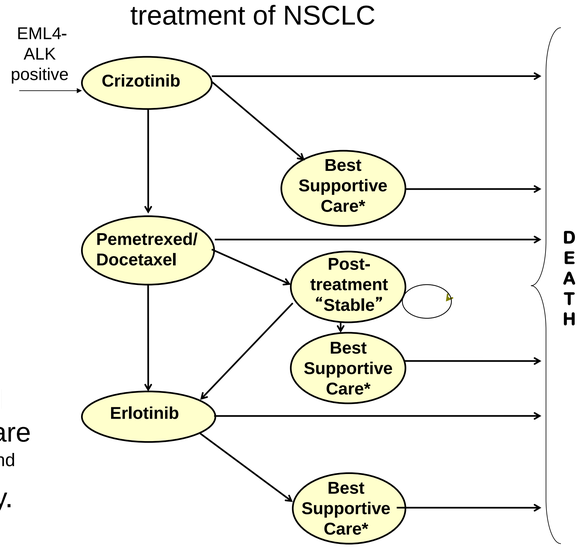


Figure 2. Health states used in Markov model for second-line treatment of NSCLC



Perspective:

Ministry of Health

Patient population:

Ontario patients diagnosed with advanced non-squamous NSCLC who have received prior platinum-based chemotherapy, and are suitable for further 2nd line systemic therapy.

Comparators:

Current strategy: No EML4-ALK fusion testing; standard treatment with 2nd line pemetrexed/docetaxel and 3rd line erlotinib.

New strategy: EML4-ALK fusion testing with crizotinib in EML4-ALK positive patients, followed by pemetrexed and erlotinib as 3rd and 4th line therapies.

METHODS

Data	Source
EML4-ALK fusion frequency in non-squamous NSCLC	Canadian – ALK (C-ALK) pathology study[3]
ALK IHC sensitivity and specificity	Systematic review, unpublished results, expert opinion[4-6]
Transition probabilities: Crizotinib, pemetrexed	PROFILE 1007 (Shaw et al., 2013)[2]
Erlotinib	CCO Administrative data
Costs	Ontario cost data, previous studies[7,8]
Health state utilities	Nafees et al., 2008[9]

Assumptions

- Progression rate from each type of chemotherapy was the same between treatment arms, regardless of line in which it was used;
- ALK IHC testing is 95% sensitive and 100% specific.

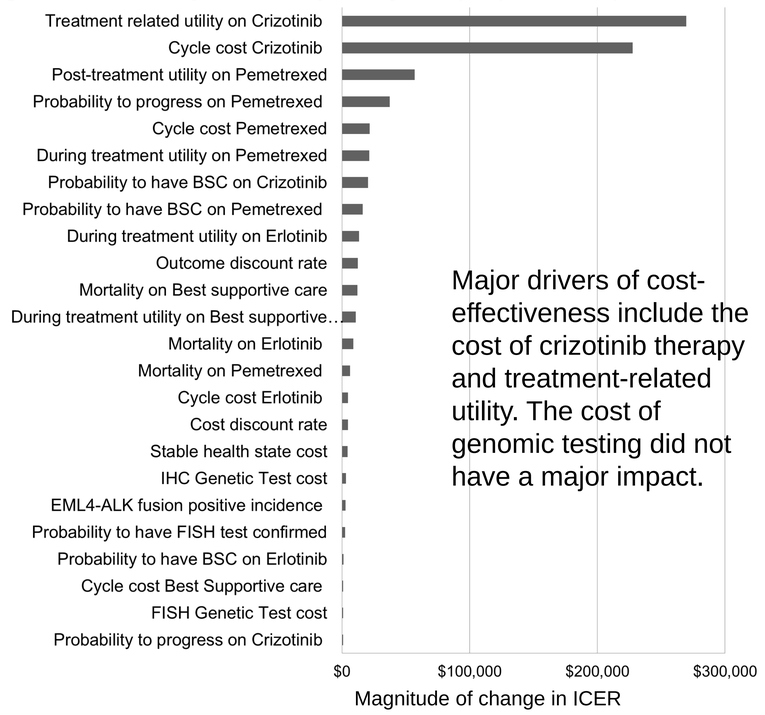
RESULTS

Strategy	Cost (CAD)	ΔCost (CAD)	QALYs	ΔQALYs	ICER*
Docetaxel	$19,388		0.429		
Pemetrexed	$33,226	$13,838	0.539	0.110	$125,812
Test + Treat	$35,707	$2,481	0.547	0.007	$333,595
Crizotinib in known ALK	$119,459	$86,233	0.804	0.265	$325,572

*ICERs for both new strategies are compared to pemetrexed

- "Test + Treat" refers to strategy of ALK testing for all advanced non-squamous NSCLC patients and treatment with crizotinib for ALK+ patients and standard chemotherapy for rest of cohort
- "Crizotinib in known ALK+" refers to the cost of crizotinib treatment compared to standard chemotherapy in patients with known ALK+ NSCLC, without testing costs

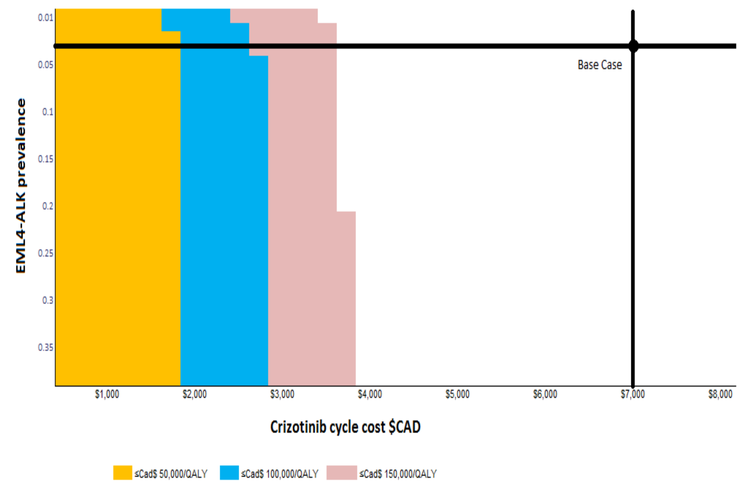
Figure 3. One-way sensitivity analyses (SA) for multiple variables



Major drivers of cost-effectiveness include the cost of crizotinib therapy and treatment-related utility. The cost of genomic testing did not have a major impact.

RESULTS

Figure 4. Two-way SA for EML4-ALK prevalence and cost of crizotinib



Limitations

- Our analysis was based on data from clinical and population based studies, and expert opinion as required, including transitions from 2nd line to subsequent therapy.
- Utility scores were derived from the literature.[7]
- Survival data in the control arm from the Profile 1007 study was compromised by patient crossover to crizotinib. Thus assumptions made post-progression in the model do not reflect long-term trial survival as well. Efforts to address this are ongoing.

CONCLUSION

EML4–ALK genomic testing in advanced non-squamous NSCLC patients with second-line crizotinib for EML4-ALK positive patients yielded an ICER of $333,595.

While this is not cost-effective, variation in drug cost and patient preference for therapy may have a major impact on cost-effectiveness. The cost of testing was not a major driver of cost-effectiveness in this analysis.

REFFERENCES

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