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

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**METHODS**

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**Data**

- EML4-ALK fusion frequency in non-squamous NSCLC
- ALK IHC sensitivity and specificity
- Transition probabilities: Crizotinib, pemetrexed
- Erlotinib

**Source**

- Canadian – ALK (C-ALK) pathology study
- Systematic review, unpublished results, expert opinion
- PROFILE 1007 (Shaw et al., 2013)
- CCO Administrative data

**Costs**

- Ontario cost data, previous studies

**Health state utilities**

- Nafees et al., 2008

**Assumptions**

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

**RESULTS**

**Strategy**

- Docetaxel
- Pemetrexed
- Test + Treat
- Crizotinib in known ALK

**Cost (CAD)**

- $19,388
- $33,226
- $35,707
- $119,459

**ΔCost (CAD)**

- $13,838
- $2,481
- $86,233

**ΔQALYs**

- 0.539
- 0.547
- 0.804

**ΔQALYs**

- 0.110
- 0.007
- 0.265

**ICER**

- $125,812
- $333,595
- $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 with 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

**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.

**REFERENCES**


**BACKGROUND**

- Management of non-small cell lung cancer (NSCLC) has developed with molecular agents targeted to treat genomic aberrations 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.
- 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.

**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**

- Decision tree for genomic testing with EML4-ALK fusion testing.
- Tissue adequate 90%
- Accept IHC test 95%
- Tissue inadequate 10%
- Re-biopsy 15%
- No Re-biopsy 85%
- IHC Test not accepted 5%
- No 90%
- Yes 10%

**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.