Policy Brief

Executive Summary:

Lung cancer accounts for 5.9% and 11.7% of all cancer cases, and 8.1% and 18% of cancer deaths in India and the world respectively (1). Nearly 70% of patients with lung cancer in India present with locally advanced and metastatic disease with adenocarcinoma being the predominant histology (2).

Targeted therapies, such as crizotinib and ceritinib (both standard and low dose), have shown promising results in treating non-small cell lung cancer (NSCLC) with specific oncogenic drivers like Anaplastic Lymphoma Kinase (ALK) and c-ros (ROS1) oncogene etc. This study aims to assess the cost-effectiveness of these therapies for patients with NSCLC in India. The chemotherapy regimen incurs the lowest costs and health benefits for patients with ALK- and ROS1-positive NSCLC in India.

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Image source: Internet

Crizotinib incurs an incremental cost of ₹936,459 ($11,420 USD) and ₹917,184 ($11,185 USD) per QALY gained as compared with chemotherapy for patients with ALK- and ROS1-positive NSCLC, respectively. Similarly, ceritinib incurs a lower incremental cost of ₹931,928 ($11,365 USD) per QALY gained as compared with the chemotherapy treatment arm. At the current prices of the drugs, none of the treatment options are cost-effective at the WTP threshold of one-time per capita GDP of India.

Policy Recommendations:

- Crizotinib and ceritinib offer higher health gains as compared with chemotherapy; however, the high additional health gain is not cost-effective in the Indian context.

- Nearly 92% and 81% reduction in the price of ceritinib and crizotinib, respectively, is required to make it a cost-effective treatment option for ALK- and ROS1-positive NSCLC.

- The price reduction is required to justify the value for inclusion of these drugs in India's publicly financed health insurance scheme for treatment of patients with locally advanced/metastatic ALK- and ROS1-positive NSCLC, respectively.

Background and Gap in Literature

With the development of precision oncology, the determination of targetable oncogenic drivers in non–small cell lung cancer (NSCLC) such as epidermal growth factor receptor (EGFR) mutations or the anaplastic lymphoma kinase (ALK) and c-ros oncogene (ROS1) rearrangements has become important. The prevalence of EGFR mutations and ALK rearrangements is approximately 30% and 10%, respectively. Similarly, the prevalence of ROS1 rearrangement is reported between 2.82% and 4.1% (3-5). ALK inhibitors like crizotinib, ceritinib, and lorlatinib have shown promise in treating patients with ALK-positive advanced/metastatic NSCLC (6-8). However, treatment options for ROS1-positive disease are limited, and crizotinib is a promising ALK inhibitor for ROS1-positive NSCLC. Molecular testing and the targeted drugs are expensive and inaccessible to the majority of patients in low- and middle-income countries (LMICs) (9). Targeted drugs like crizotinib and ceritinib can cost nearly ₹40,000-₹50,000 a month in the Indian setting. In the absence of targeted therapy, treatment of patients with ALK and ROS1-positive advanced/metastatic NSCLC is typically limited to cytotoxic chemotherapy regimens. In view of the above, economic evaluation becomes necessary to guide decision-makers about treatment choice, resource allocation. Therefore, the cost-effectiveness analysis has an important role, especially in the low-middle income countries such as India, in helping the physicians and payers in choosing appropriate therapy which represents value for money.

Aims and Objective

The study aimed to understand the cost-effectiveness of targeted therapies (crizotinib and ceritinib) as compared with pemetrexed-based chemotherapy in patients with newly diagnosed advanced/metastatic non–small cell lung cancer (NSCLC) and harboring either anaplastic lymphoma kinase (ALK) or ROS1 gene rearrangement.
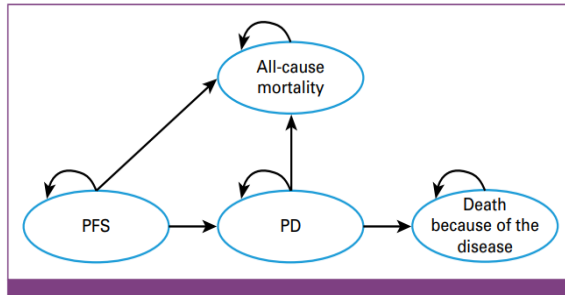
Treatment arms:

1. Crizotinib: 250 mg bottle (60 capsules)

2. Certinib 150 mg bottle (150 capsules)

3. Injection Pemetrexed 500 mg/m2 plus Carboplatin AUC 5

Methods and Approach

We undertook this cost-effectiveness analysis (CEA) using a societal perspective, which accounted for both health system and patients' costs. Lifetime costs and consequences were estimated for three treatment arms: crizotinib, ceritinib, and chemotherapy for patients with ALK- and ROS1-positive NSCLC. Incremental cost per quality-adjusted life-year (QALY) gained with crizotinib and ceritinib was compared to chemotherapy and assessed using a willingness-to-pay threshold of one-time per capita gross domestic product in India. Our methodological principles are consistent with the Indian reference case for conducting economic evaluations used by the agency for Health Technology Assessment in India (HTAIn).

The analysis was performed under the following components:

1. **Markov model** was developed in Microsoft Excel to estimate the lifetime costs and consequences (in terms of Quality Adjusted Life-years (QALYs)* and Life-years). The model consisted of three mutually exclusive health states: Progression-free survival (PFS), Progressive disease (PD) and death. A monthly cycle length based on the treatment schedule of drugs in various treatment arms was considered (Figure 1).
2. Reimbursement rates were used to estimate the treatment cost in each health state.
3. In order to obtain the Out-of-Pocket Expenditure (OOPE) incurred on out-patient consultations, the primary data was analysed as a part **CADCQoL database** (10).
4. Transition probabilities and effectiveness parameters were obtained from the pivotal clinical trials and systematic reviews (8,11).
5. The Quality of Life (QoL) scores were estimated from the published studies (10,12).

Figure 1: Markov model to determine the most cost-effective treatment option for NSCLC. NSCLC, non-small cell lung cancer; PFS: Progression-Free State; PD: Progressive Disease

*Quality Adjusted Life-years:

- QALY is a generic measure of health and is used to compare the health gains across different diseases and hence provide a uniform platform to compare effectiveness across all the different areas of healthcare.
- EQ5D is the most utilised tool worldwide to measure QoL.

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Results:

- Crizotinib incurs an incremental cost of ₹936,459 and ₹917,184 per QALY gained as compared with chemotherapy for patients with ALK- and ROS1-positive NSCLC, respectively.
- Similarly, ceritinib incurs a lower incremental cost of ₹931,928 per QALY gained as compared with the chemotherapy treatment arm.
- At the current prices of the drugs, none of the treatment options are cost-effective at the WTP threshold of one-time per capita GDP of India.
- Nearly 92% and 81% reduction in the price of ceritinib and crizotinib is required to make it a cost-effective treatment option for ALK- and ROS1-positive NSCLC, respectively

Cancer Type	Treatment sequence	Total lifetime cost in ₹ (95% CI)	Total QALYs (95% CI)	ICER, ₹/QALY	Interpretation	
For ALK-positive Lung cancer patients	Chemotherapy (Pemetrexed + Carboplatin)	332,456 (258,460 to 708,667)	1.20 (0.89 –2.56)	-	-	-
	Crizotinib vs Chemotherapy	1,284,100 (844,810 – 1,853,764)	2.21 (1.71 – 2.85)	936,459 [(-1,392,571) – (4,316,470)]	Cost-ineffective	81% reduction in the market price of Crizotinib (from ₹ 42,000 to ₹ 7,980 per bottle of 60 capsules)
	Ceritinib vs Chemotherapy	2,337,779 (1,198,141 – 3,192,849)	3.35 (2.16 – 4.11)	931,928 [566,109 – 2,108,514)]	Cost-ineffective	92% reduction in the market price of the drug (from ₹ 42,000 to ₹ 3,360 per month)
For ROS1-positive Lung cancer patients	Chemotherapy (Pemetrexed + Carboplatin)	323,011 (266,807 – 387,416)	1.16 (0.91 – 1.47)	-	-	-
	Crizotinib	1,763,541 (1,144,802 – 2,618,855)	2.73 (2.02 – 3.67)	917,184 (561,231 – 1,477,696)	Cost-ineffective	81% reduction in the market price of Crizotinib (from ₹ 42,000 to ₹ 7,980 per bottle of 60 capsules)

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