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RESEARCH ARTICLE

Reducing the Financial Toxicity of Prolonged Therapy in Advanced/ Metastatic Lung Cancer, Saving Methodology

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ABSTRACT

Introduction: Value of the monoclonal antibodies and targeted therapy have been extensively addressed in advanced/metastatic non-small cell lung cancer (a/d-NSCLC). Costs, however, have largely been overlooked. The monoclonal antibodies (MABs) were approved at 2-year- overall survival. Targeted therapy (TT), approved at 2-3-year-survival, are currently continued as long as efficacious and safe. Drug costs were proportional to duration of therapy (Guirgis, ESMED, 2024). Previous attempts to control the high cost of anticancer drugs including cap-imposed limits have failed. There is a pressing need for cost cutting and saving methodology that is fair, voluntary and equitable for both patients and pharma. Our goals in a/d-NSCLC: A- Demonstrate the unnecessarily high cost of 3rd year MABs. B- Pay in full the 1st- TT 3-year-costs but reduce by 50% the 4th year and throughout the entire course.

Methods: MABs costs were calculated as dose in mg x United States price x number of years and TT as the monthly optimal dose x 12 x duration of use.

Results: The median yearly cost of 5-MABs was $163,640. In view of overall survival outcome, the 2-year $327,2802 cost was justified. However, the 3-year $490,920 cost was unjustified due to lack of further survival improvement.

The annual TT median cost was $229,600, 4- years $918,400 and the 10-years $2,296,000. Treatment of 1,000 patients in the United States by all TT for 4-years would cost $918,400,000 and in Europe 2,000 patients would mount to $1,836,800,000. Costs continue to climb up with every extended year.

Applying a 50% reduction to the 4th year of $229,600, the potential saving was $114,800. The 4-year total payments would be $229,600 x 3 + $114,800 = $803,600, instead of $918,400. The 10-year $2,296,000 cost would drop to $1,492,400.

Conclusion: In a/d-NSCLC, a 3rd year-MABs cost was considered unnecessary due to lack of further survival improvement. A 50% reduction of TT annual costs beginning the 4th-year and throughout the entire course would avoid the heavy financial toxicity of prolonged use.

Introduction

We previously reported the case of 65 yo female who presented in 2014 with advanced/metastatic non-small cell lung cancer (a/d-NSCLC) and anaplastic lymphoma kinase (ALK+). She was successfully treated by the 2nd generation Alectinib 600 mg po bid daily [1]. The approximate 10-year estimated cost was $2,211,100. Targeted Therapy (TT) are approved after 2-3-year-trials. Use is currently continued as long as effective and safe. However, such policy is currently debated. The monoclonal antibodies (MABs) were approved at 2-year overall survival. Costs were proportional to number of purchases and/or duration of use [2]. Previous attempts to control the high cost of anticancer drugs including cap-imposed limits have failed. The high costs of prolonged use of both MABs and TT prompted the present investigation. We purposed to quantify in a/d-NSCLC: 1- The unnecessarily high cost of MABs 3rd year. 2 –Pay in full the 1st 3-years TT costs but reduce by 50% the 4th -year and throughout the entire treatment 3- Quantify the cost savings based on our proposal.

Methods: MABs costs were calculated as dose in mg x posted price x number of years and TT as the monthly optimal dose x 12 x number of years use.

Results

The 5-MABs [3-7] median annual cost was $163,640, (Table 1). The 3rd year costs were unjustified due to lack of further survival improvement.

Osimertinib, approved as neoadjuvant, adjuvant and in metastatic disease [8,9], had an annual $229,600 cost and was the median of 5-TT. Costs increased with every year of further use. At present, proper Identification of genomic marker aberrations is crucial in the proper and order of therapy. The price tag of 2-3-tests of a reliable wide spectrum marker was estimated at $2,000.

The 3-year TT $688,800 costs seemed reasonable in view of the reported value and ought to be fully paid. However, the 4-year $918,400 costs were considered excessive. We reasoned that if 1,000 American patients were treated by TT at $229,600 for 4-years, the cost would mount to $918,400,000. The 10-year cost would be $2,296,000. In Europe, treating 2,000 patients would cost $4,592,000.

A 50% reduction applied only to year 4th year would save $114,800. The 4-year total would be $918,400 - $114,800 = $803,600. The 10-year would drop from $2,296,000 to $1,492,400, resulting in potential $803,600 savings.

Table 1 demonstrates comparison between chemo and various tyrosine kinase inhibitors. Deucravacitinib [10,11] was included to demonstrate its use and cost in non-cancer indication. It has wider application in moderate-severe plaque psoriasis. Osimertinib, Alectinib, Selpercatinib [12] and Repotrectinib [13] are widely used in a/d-NSCLC

Table 1: Costs of MABS

Drug	2-year Costs	3-year Costs
Pembrolizumab	$380,800	$571,200
Durvalumab	$327,280	$490,920
Atezolizumab	$305,340	$458,010
Nivolumab	$404,660	$606,990
Cemiplimab	$295,040	$442,560

With no evidence of overall survival improvement after 2-years, the 3-year- MABs cost was considered unnecessary

Table 2: Cost Comparison of various Tyrosine Kinase Inhibitors and Chemo

Drugs and Doses	**Annual Costs**
Generic Chemo	$1,000
Alectinib [1] 600 bid po	$221,110
Osimertinib 80 mg once daily + chemo [8,9]	$230,600
Deucravacitinib, Tyrosine Kinase 2 (TYK2), 6.0 mg po once daily (non-cancer drug) [10,11]	$82,680
Selpercatinib [12] 120-160 mg bid	$271,164
Repotrectinib (Trident -1 trial) [13] 160 mg bid	Negotiable, varying from $159,984-$364,032

All the above drugs were approved and utilized in the US, Canada, European Nations, and Japan.

The 2-3-year $688,800 TT costs seemed reasonable in view of the reported outcome and ought to be fully paid. However, the 4-year $918,400 costs were considered excessive. We reasoned that if 1,000 American patients were treated by TT at $229,600 for 4-years, the cost would mount to $918,400,000. The 10-year cost would be $2,296,000. In Europe, treating 2,000 patients would cost $4,592,000. The potential cost savings were summarized in Table 3.

Table 3: Proposed Cost 50% Reduction of Targeted Therapy starting on the 4-th Cycle

Costs	**1st to 3rd year**	**4th year**	**4,5,6 total costs**	**4-10 total costs**
Current Annual Costs	$204,000	$204,000	$812,000	$1,428,000
Proposed 50% cost reduction starting the 4th year	$204,000	$102,000	$406,000	$714,000

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Discussion

Development of a new cancer therapy from inception to delivery takes an years of ingenuity, hard work, and strong financial backing. Pharma needs to be compensated for such sacrificial endeavors. At present, value, and cost effectiveness [14-16] of cancer drugs are calculated and documented before or soon after drug efficacy and safety approval. Reports on cancer drug costs are currently scanty and generally labelled excessive. Utilization, if any, is rare by nations and patients with limited resources. Admittedly, costs are negotiable, and the subject is indeed sensitive. Cap-imposed limits have been proposed but received minimal acceptable [17,18]. The painful financial toxicity of oral anti-cancer drugs has been clearly outlined [19,20]. Pharma is unlikely to sponsor cost cancer studies, leaving the academic intuitions to carry out this delicate task.

At present, proper Identification of genomic marker aberrations is crucial in the proper and order of therapy. The estimated at $2,000 price tag of 2-3-tests of a reliable wide spectrum marker was undeniably worthy it.

The 2-year overall survival of MABs have been well-defined in a/d- NSCLC with programmed death ligand 1 (PD-L1) expression at 50% and above [3-7]. Some oncologists and patients continue therapy for a third year. Such cost was considered unnecessary due to lack of further survival improvement.

The terminology of all TT ends in "nibs", and hence referred at times as "NIBs". They belong to the tyrosine kinase inhibitors family. Osimertinib is a prototype and antagonist of epidermal growth factor (EGFR). The drug was originally planned to treat T7M mutations, but presently used to prevent the potential development of such mutations. The U.S. Food and Drug Administration (FDA) has recently approved Osimertinib with platinum-based chemotherapy for patients with a/d-NSCLC and no prior systemic therapy for tumors with *EGFR* exon 19 deletions or exon 21 L858R mutations (FLAURA2): clinical validation through TRIDENT-1 Trial (NCT03093116).

Other TT followed Osimertinib including Alectinib [1], Selpercatinib [13] in RET aberrations with up to 2.0% incidence and Repotrectinib [14] with ROS1 Fusions with 1.0-2.0 %. Many other genomic alterations are presently targetable.

Access to financial assistance programs and their impact on the overall spending on oral anticancer medications has been recently described [21]. For patients and countries with limited resources, TT use at any duration is essentially unaffordable. In the US and Europe, treatment of few thousand patients for 10 years is economically burdensome and could divert finances resources from other health expenditures e.g. vaccines and other essentials.

The Canadian health system demonstrated the rapid rising costs of cancer medicines [22]. The wide difference in Repotrectinib costs from $159,984-$364,032 clearly affirm the variation in cancer drugs prices and the need for negotiation and reduction. The present work takes a step further, focusing on and pointing to the prolonged therapy as the core underlying problem.

In summary, safe, and effective cancer care [23], with affordable cancer drugs are worthy goals to pursue and attain. Previous attempts to control the high costs of anti-cancer drugs have failed. Proper Identification of genomic marker aberrations is crucial for appropriate and successful cost-management. The estimated $2,000 costs for 2-3-tests of a reliable wide spectrum marker were worthy of the price tag. Currently, continued TT costs are too high to sustain. A 50% TT cost reduction at 4-10-year is even-handed and win-win for 1- Patients buying at reduced costs 2- Pharma enjoying wider sales. The cost-reduction approach is simple, direct, voluntary and most of all, not requiring approval of any clinical trial.

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