Medical and Clinical Research: Open Access

Research Article

The Unsustainable Costs of Prolonged Targeted Therapy in Lung Cancer, Saving Methodology

Helmy M Guirgis*

University of California, Irvine, California, USA.

Corresponding Author Information

Helmy M Guirgis

University of California, Irvine, California, USA.

Received: April 01, 2024; **Accepted:** May 08, 2024; **Published:** May 15, 2024

Citation: Sung Yi, Khazaei H, Khazaei D, Junejo N, Etesami F. The Unsustainable Costs of Prolonged Targeted Therapy in Lung Cancer, Saving Methodology. Med Clin Res Open Access. 2024; 5(1):1-3.

ABSTRACT

Background: Anticancer drug costs were reported proportional to number of purchases and/or duration of use. The monoclonal antibodies (MABs) were approved at 2-years and targeted therapy (TT) at 3. The value of MABs and TT have been extensively addressed and confirmed, but costs have rarely been dissected. After careful accounting of prolonged TT high costs, saving methodology is being presented in advanced/metastatic non- squamous cell lung carcinoma (a/d-NSCLC).

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

Results: The median yearly cost of MABs, approved at 2-year overall survival, was $163,640 with an optional 3rd year totaling $490,920. The annual TT median cost was $229,600, 4- years $918,400 and10-years $2,296,000. Costs counting starts the 1st-year and saving on 4. We reasoned that if 1,000-2000 American patients were treated by all TT for 4-years, cost would mount to $918,400,000 - $1,836,800,000. In Europe with a larger population number, the cost would be higher. TT is essentially unaffordable for patients and counties with limited resources.

Conclusion: In a/d-NSCLC, the use of a 3rd year-MABs is questionable due to lack of extended survival. A 50% reduction of TT annual costs beginning the 4th-year, would circumvent and attenuate the unsustainable economic burden of prolonged use.

KEYWORDS

Cancer, Monoclonal antibodies.

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 10-year cost was $2,211,100. Targeted Therapy (TT) was mostly approved after 3-year-trials. Use is currently continued as long as effective and safe. Costs were proportional to number of purchases and/or duration of use [2]. The monoclonal antibodies (MABs) were approved at 2-years trials [3-7]. The high costs of prolonged use prompted the present investigation. Cost TT counting was based on 50% reduction starting the 4th -year and continued till end of treatment.

Methods

MABs costs were calculated as dose in mg x pric1 x number of cycles or years and TT as the monthly optimal dose x 12 x duration of use.

Results

The MABs [3-7] median annual cost was $163,640. The 3rd year costs seemed unjustified due to lack of extended survival. 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 would be fully paid. However, the 4-year $918,400 costs were considered excessive. We reasoned that if 1,000-2000 American patients were treated by TT at $229,600 for 4-years, the cost would mount to $918,400,000 - $1,836,800,000. In Europe with a larger population number, the cost would be higher.

If a 50% reduction is applied only to year 4, the saving is $114,800. The 4-year total would be $918,400 - $114,800: $803,600. The 10-year would drop from $2,296,000 to $1,148,000, resulting in significant 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 probably has wider application in moderate-severe plaque psoriasis than Osimertinib, Alectinib [12], Selpercatinib [13] and Repotrectinib [14], currently used in a/d-NSCLC.

Table 1: Cost Comparison of various Tyrosine Kinase Inhibitors and Chemo.

Drugs and Doses	Annual Costs
Deucravacitinib, Tyrosine Kinase 2 (TYK2), 6.0 mg po once daily (non-cancer drug) [10,11]	$82,680
Generic Chemo	$1,000
Osimertinib 80 mg once daily + chemo [8,9]	$230,600
Alectinib [12] 600 bid po	$221,110
Selpercatinib [13] 120-160 mg bid	$271,164
Repotrectinib (Trident -1 trial) [14] 160 mg bid	$159,984-$364,032

In comparison, the median annual cost of MABs was $163,640.

Discussion

Development of a new cancer therapy from inception to delivery and marketing takes an estimated 10 years of ingenuity, hard work, and strong financial backing. Pharma needs to be compensated for such endeavors. At present, value, and cost effectiveness [15-17] of cancer drugs are published at or 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 [18,19]. The painful financial toxicity of oral anti-cancer drugs has been clearly outlined [20,21]. Pharma is unlikely to sponsor cost cancer studies, leaving the academic intuitions to carry out this delicate task.

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 might be unnecessary due to lack of further survival.

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 [12], 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 [22]. For patients and countries with limited resources, TT use at any duration is unthinkable. In the US and Europe, treatment of few thousand patients for 10 years is economically burdensome, potentially diverting finances from other health expenditures e.g. vaccines and other essentials.

The Canadian health system demonstrated the rapid rising costs of cancer medicines [23]. 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 pointing to the prolonged therapy as the core serious problem. Costs count from the 1st-year, in contrast to savings starting the 4th and multiply annually thereafter.

In summary, safe, and effective cancer care [24] with affordable cancer drugs are worthy goals to pursue and attain. Currently, the 10-year TT cost is unsustainable. A 50% TT cost reduction at 4-10-year is even-handed and beneficial to patients buying at lower costs and pharma having wider sales. The cost-reduction approach doesnot require not any clinical trial.

References

1. Guirgis H. Cost matters. journal of Cancer & Oncology (OAJCO). 2023; 7: 1-2.
2. Guirgis HM. Costs of Target Therapy and Proportionality to Number of Purchases: Propose Using Maintenance Dose and Limited Duration. ESMED. 2024; 12: 1-5.
3. Garon EB, Rizvi NA, Hui R, Natasha Leighl, Ani S Balmanoukian, et al. Pembrolizumab for the treatment of non-small cell lung cancer. N Engl J Med. 2015; 372: 2018-2028.
4. Reck M, Rodriguez-Abreu D, Robinson AG, Rina Hui, Tibor Csőszi, et al. Pembrolizumab versus chemotherapy for PD-L1-positive non-small-cell lung cancer. N Engl J Med. 2016; 375: 1823-1833.
5. Herbst RS, Baas P, Kim D-W, Enriqueta Felip, José L Pérez-Gracia, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-postive, advanced non-small-cell lung cancer (KEYNOTE -010): A randomised controlled trial. Lancet. 2016; 387: 1540-1550.
6. Herbst RS, Gluseppe G, de Marinis F, Niels Reinmuth, Alain Vergnenegre, et al. Atezolizumab for First-Line Treatment of PD-L1–Selected Patients with NSCLC. N Engl J Med. 2020; 383: 1328-1339.
7. Sezer A, Kilickap S, Gümüş M, Igor Bondarenko, Mustafa Özgüroğlu, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. Lancet. 2021; 397: 592-604.
8. Herbest RS, Wu Yi-long, John T, Christian Grohe, Margarita Majem, et al. Adjuvant Osimertinib for Resected EGFR-Mutated Stage IB-IIIA Non–Small-Cell Lung Cancer: Updated Results from the Phase III Randomized ADAURA Trial. J Clin Oncol. 2023; 41: 1830-1840.
9. Lv C, Fang W, Wu N, Wenjie Jiao, Shidong Xu, et al. Osimertinib as Neoadjuvant Therapy for EGFR-Mutant Resectable Stage II-IIIB Lung Adenocarcinoma. Lung Cancer. 2023; 178: 151-156.
10. Chimalakonda A, Burke J, Cheng L, Ian Catlett, Michael Tagen, et al. Selectivity profile of the tyrosine kinase 2 inhibitor deucravacitinib compared with janus kinase 1/2/3 inhibitors. Dermatol Ther (Heidelb). 2021; 11:1763-1776.
11. Armstrong AW, Mehta MD, Schupp CW, George C Gondo, Stacie J Bell, et al. Psoriasis prevalence in adults in the United States. JAMA Dermatol. 2021; 157: 940-946.
12. Vavala T, Novello S. Alectinib in the treatment of ALK-positive non-small cell lung cancer: an update on its properties, efficacy, safety and place in therapy. Ther Adv Med Oncol. 2018; 10: 1758835918789364.
13. Drilon A, Oxnard GR, Daniel SW, Daniel S W Tan, Herbert H F Loong, et al. Efficacy of Selpercatinib in RET Fusion–Positive Non–Small-Cell Lung Cancer. N Engl J Med. 2020; 383: 813-824.
14. Drilon A, Camidge DR, Lin JJ, Sang-We Kim, Benjamin J Solomon, et al. Repotrectinib in ROS1 Fusion–Positive Non–Small-Cell Lung Cancer. N Engl J Med. 2024; 390:118-131.
15. Schnipper LE, Davidson NE, Wollins DS, Courtney Tyne, Douglas W Blayney, et al. American Society of Clinical Oncology statement: A framework to assess the value of cancer treatment options. J Clin Oncol. 2015; 33: 2563-2577.
16. Cherny NI, Sullivan R, Dafni U, et al. A standardized, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies. The European Society for Medical Oncology: magnitude of clinical benefit scale (ESM-MCBS). Ann oncl. 2015; 26: 1547-1573.
17. Siegel JE, Weinstein MC, Russell LB, M R Gold. Panel on cost-effectiveness in health and medicine. Recommendations for reporting cost effectiveness analyses. JAMA. 1996; 276: 1339-1341.
18. Guirgis, HM. Costs of extended immune check point inhibitors treatment in advanced/metastatic lung cancer: Bundling of cost proposal. ASCO. 2020; 39: 21034.
19. Kline RK. Bundled Payment Models in Oncology: Learning to Think in New Ways. JCO Oncol Pract. 2021; 17: 169-172.
20. Li M, Liao K, Pan I-Wen, Ya-Chen Tina Shih. Growing Financial burden from high cost targeted oral anticancer medicines among Medicare beneficiaries with cancer. JCO oncol pract. 2002; 18: 1739-1749.
21. Peppercorn J. The impact of financial toxicity on cancer care. Clin Adv Hematol Oncol. 2023; 21: 520-523.
22. Ragavan MV, Swartz S, Clark M, Mimi Lo, Arjun Gupta, et al. Access to financial assistance programs and their impact on overall spending on oral anticancer medications at an integrated specialty pharmacy. JCO Oncol Pract. 2024; 20: 291-299.
23. The lancet Oncology. Safe and effective cancer care: how long must we wait?. Lancet Oncol. 2024; 25: 265.
24. Del Paggio JC, Naipaul R, Gavura S, Rebecca E Mercer, Rachel Koven, et al. Cost and value of cancer medicines in a single-payer public health system in Ontario, Canada: a cross-sectional study. Lancet Oncol. 2024; 25: 431-438.