Real-World Prevalence, Treatment Patterns, and Economic Impact of EGFR and ALK Targeted Therapies in Non-Small Cell Lung Cancer: A Nationwide Analysis from Greece.

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RWD137

CONCLUSIONS

- **This nationwide analysis highlights the rapid adoption of second and third-generation TKIs for EGFR- and ALK-positive NSCLC in Greece, reflecting evolving clinical practice patterns.**
- **Although the target patient populations are relatively small, the associated eco-nomic burden is considerable.**
- **To ensure long-term sustainability of the Greek healthcare system, policymakers should critically assess the cost-effectiveness of these innovative therapies and align resource allocation with value-based care principles.**

INTRODUCTION & OBJECTIVE

- In Greece, lung cancer poses a substantial clinical and economic burden. It is the leading cause of cancer-related death [1], accounting for significant healthcare resource utilization and costs, including hospitalizations, medications, diagnostic procedures, and indirect societal costs due to lost productivity [2].
- The lack of national evidence limits stakeholders' ability to assess the affordability, sustainability, and value of precision oncology in clinical practice. In particular, the budgetary impact of rapidly evolving tyrosine kinase inhibitors (TKI) therapies remains underexplored in the Greek setting, where cost-containment policies and health technology assessments are becoming increasingly central to reimbursement decisions.
- **The current study aims to address these gaps by presenting a nationwide real-world analysis of EGFR and ALK targeted therapy use among patients with non-small cell lung cancer (NSCLC) in Greece. Specifically, we assess the prescribing prevalence, patterns of treatment uptake and the direct economic impact of these therapies within the context of the Greek National Health System.**

METHODS

- This study was a retrospective observational analysis utilizing anonymized data derived from the nationwide electronic prescription database of Greece, managed by e-Government Center for Social Security Services (IDIKA S.A.)
- Patients with NSCLC who initiated treatment with at least one TKI between January 1, 2020, and December 31, 2022, were included in the analysis. Eligible cases were identified through the nationwide electronic prescription database using International Classification of Diseases, Tenth Revision (ICD-10) diagnostic codes of: C34, C34.0, C34.1, C34.2, C34.3, C34.8 and C34.9.
- These diagnostic entries were cross-referenced with prescriptions for EGFR or ALK-targeted TKIs, identified by their Anatomical Therapeutic Chemical (ATC) classification codes: Gefitinib (L01EB01), Erlotinib (L01EB02), Afatinib (L01EB03), Osimertinib (L01EB04), Dacomitinib (L01EB07), Crizotinib (L01ED01), Ceritinib (L01ED02), Alectinib (L01ED03), Brigatinib (L01ED04), and Lorlatinib (L01ED05).
- Only patients who initiated first-line TKI therapy within the defined study window were included to ensure consistency in treatment initiation. The index date was defined as the date of the first executed prescription for a TKI. Patients remained in the same treatment line until a documented switch to another TKI or a transition to chemotherapy occurred. Hence, the treatment time per patient was defined as the difference between the date of the first and last recorded dispensation of an ALK or EGFR-TKI in the period from 1 January 2020 to 31 December 2022.
- Data extracted from the national prescription database were stratified into two primary cohorts based on molecular subtype: patients receiving EGFR TKIs and those receiving ALK TKIs. For each patient, demographic variables including age and sex were recorded. Prescription patterns were evaluated in terms of the frequency and distribution of specific EGFR and ALK-targeted agents.
- To assess the economic burden associated with EGFR and ALK-targeted therapies, the annual pharmaceutical expenditure for TKIs was calculated based on reimbursed drug unit prices applicable for each calendar year within the study period. Following the payer perspective, the drug cost estimations were derived from the ex-factory prices published in the official price bulletin of the Greek Ministry of Health.
- In addition, the prevalence of patients receiving at least one EGFR or ALK TKI prescription was estimated using population data from the Hellenic Statistical Authority as the denominator. Age and sex-standardized prevalence estimates were calculated separately for each molecular subgroup, and a weighted average prevalence was reported across the full observation period (2020–2022).
- Categorical variables were reported using frequencies (n) and percentages (%), while continuous variables were described using means and standard deviations (SD). Before analysis, continuous variables were assessed for normality using the Shapiro–Wilk test. Statistical significance was defined as a p-value < 0.05. All statistical analyses were conducted using IBM SPSS Version 29.

RESULTS

- According to the nationwide prescription database, a total of 1,188 patients with EGFR-positive and 246 with ALK-positive NSCLC initiated first-line therapy with at least one TKI during the three-year study period. The mean (SD) age of patients in the EGFR-positive cohort was 70.93 years (±11.16), while ALK-positive patients were younger, with a mean age of 64.26 years (±12.6).
- The three-year period prescribing prevalence of EGFR-positive NSCLC was estimated at 10.09 per 100,000 males (95% CI: 9.25–10.92) and 13.99 per 100,000 females (95% CI: 12.89–15.07), yielding an overall prevalence of 11.84 per 100,000 population (95% CI: 11.16–12.51).
- For ALK-positive patients, the corresponding prescribing prevalence was 2.15 per 100,000 in males (95% CI: 1.77–2.54) and 2.81 per 100,000 in females (95% CI: 2.32–3.30), with an overall prevalence of 2.45 per 100,000 (95% CI: 2.14–2.76).
- Among patients with EGFR-mutant NSCLC, there was a clear and progressive shift in treatment patterns over the three-year study period, reflecting the evolving landscape of targeted therapy. Osimertinib, which accounted for 41% of first-line EGFR TKI use in 2020, rose to 45% in 2021 and reached 63% in 2022 (Figure 1), becoming the most commonly prescribed agent across all age groups and both sexes.
- Treatment patterns for ALK-positive NSCLC patients evolved considerably over the study period, reflecting a clear shift toward the adoption of second-generation TKIs. In 2020, crizotinib was the most commonly prescribed agent, accounting for 60% of ALK TKI use, followed by ceritinib at 40% (Figure 2).
- Annual expenditures for EGFR-targeted TKIs remained relatively stable throughout the study period, rising only marginally from €11.49 million in 2020 to €11.88 million in 2022. This budgetary stability conceals a marked shift in the composition of spending: by 2022, osimertinib alone accounted for the vast majority of EGFR-related pharmaceutical expenditures, increasing from €9.32 million in 2020 to €10.73 million. As for the mean cost per patient per year for EGFR TKIs showed only a modest increase, from €28,024 in 2020 to €31,758 in 2022 (Figure 3).
- A similar trend was observed for ALK-targeted therapies. Total annual expenditure remained stable, ranging from €3.45 million in 2020 to €3.30 million in 2022. At the patient level, the mean cost per ALK-positive patient rose from €39,220 in 2020 to €44,609 in 2022 (Figure 4).

Figure 1. Distribution of the EGFR tyrosine kinase inhibitor treatment per year.

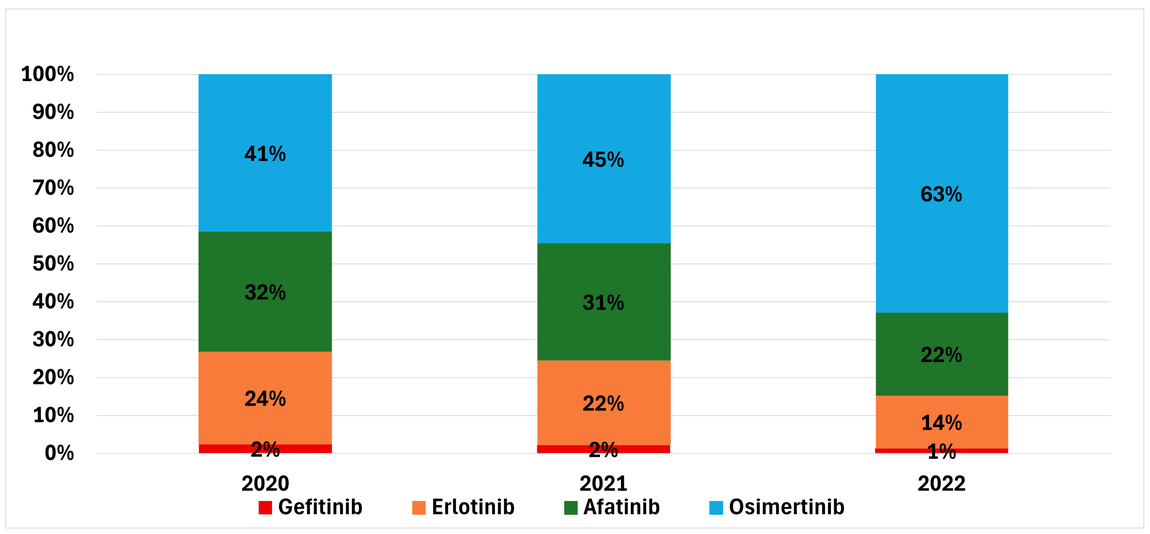


Figure 2. Distribution of the ALK tyrosine kinase inhibitor treatment per year.

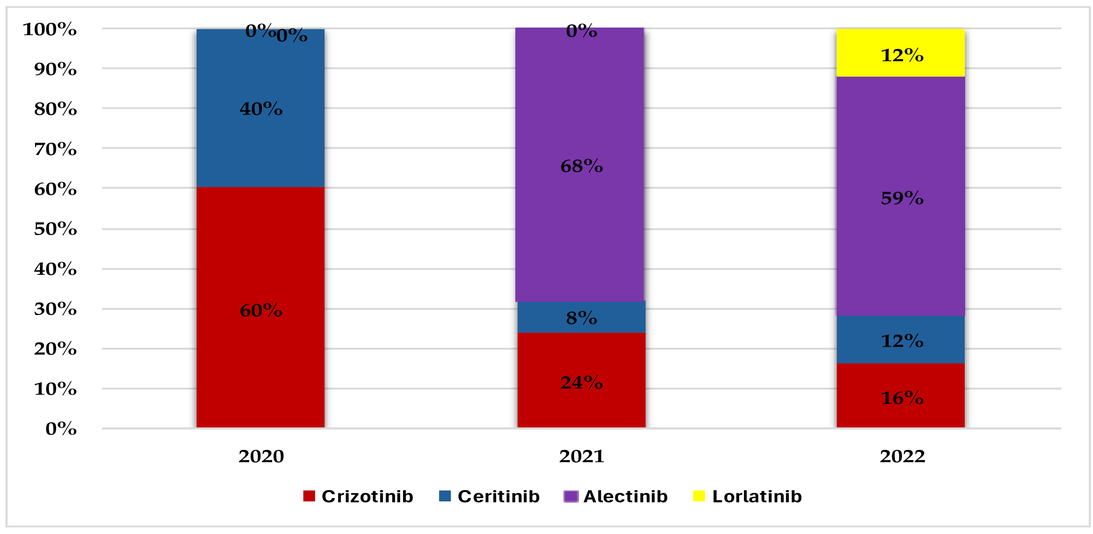


Figure 3. Total and Per-Patient Cost of First-Line EGFR Tyrosine Kinase Inhibitors

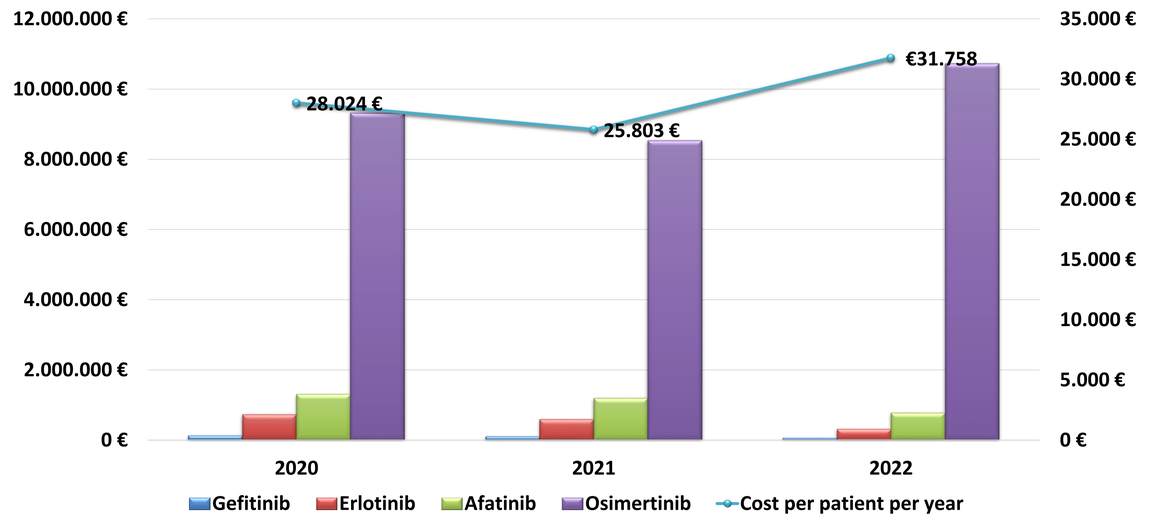
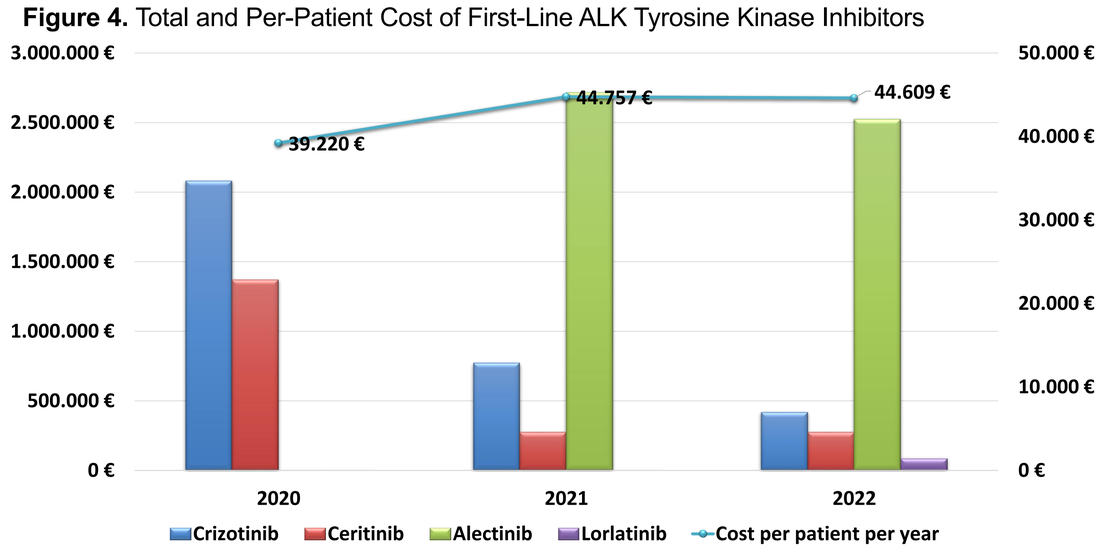


Figure 4. Total and Per-Patient Cost of First-Line ALK Tyrosine Kinase Inhibitors



Disclosures

Anonymized data were utilized in this study following formal authorization by the ad-ministration of IDIKA S.A. and approval by the data protection officer (DPO) of the Hellenic Ministry of Health. Moreover, the institutional review board of the University of the Peloponnese approved the study protocol.

The study was conducted in full compliance with national regulations governing the protection of per-sonal data and adhered to the ethical principles outlined in the declaration of Helsinki and its subsequent amendments.

References

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