SYSTEMATIC REVIEW AND META-ANALYSIS OF THE EFFICACY AND SAFETY OF TARGETED AND IMMUNOTARGETED AGENTS IN THE TREATMENT OF NON-SMALL CELL LUNG CANCER

Rajabova N.Kh.
Tashkent Pharmaceutical Institute, Tashkent city, Republic of Uzbekistan
e-mail: nargiza-rh@mail.ru
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Relevance: non-small cell lung cancer (NSCLC) remains one of the leading causes of cancer-related morbidity and mortality worldwide. The introduction of targeted therapies (EGFR, ALK, ROS1 inhibitors, etc.) and immune checkpoint inhibitors (PD-1/PD-L1) has markedly transformed therapeutic strategies, shifting clinical practice toward a more personalized approach. Despite notable advances, a systematic evaluation of accumulated data is required to determine the optimal sequencing and combination of treatments, as well as to balance clinical efficacy with safety outcomes.

Purpose of the study: to conduct a systematic review and meta-analysis of clinical trials comparing the efficacy and tolerability of targeted therapies and immunotherapeutic agents in NSCLC.

Materials and methods: a literature search was performed in PubMed, Embase, and the Cochrane Library for the period 2015–2024. Eligible studies included randomized clinical trials and meta-analyses reporting overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and adverse event profiles. Pooled estimates were calculated using a random-effects model, and interstudy heterogeneity was assessed with the I^2 statistic.

Results: a total of 36 studies, including over 14,000 patients, were analyzed. In patients with driver mutations, targeted therapies significantly improved PFS (HR = 0.48; 95% CI: 0.41–0.56) and increased ORR up to 65%, markedly outperforming chemotherapy. Immunotherapy with PD-1/PD-L1 inhibitors demonstrated a clinically meaningful OS benefit in patients without EGFR/ALK mutations and with high PD-L1 expression (≥50%) (HR = 0.74; 95% CI: 0.66–0.83). Safety analysis revealed distinct toxicity profiles: targeted therapies were associated with dermatologic and gastrointestinal adverse events, whereas immunotherapy was more frequently linked to immune-related toxicities such as pneumonitis, thyroid dysfunction, and colitis.

Conclusions: This meta-analysis supports the preferential use of targeted therapies in patients with defined molecular alterations and highlights the efficacy of immunotherapy in cohorts with high PD-L1 expression and no driver mutations. Optimal therapeutic strategies should be guided by molecular profiling and biomarker assessment. Combination regimens involving targeted and immunotherapeutic agents represent a promising direction, warranting further multicenter trials and pharmacoeconomic evaluation within national healthcare systems.