VIEWPOINTS

ASCO 2023: Recent Progress in Lung Cancer Therapy

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Keywords: Viewpoints, Lung, Cancer, ASCO, ASCO 2023

https://doi.org/10.36000/hbT.OH.2023.16.112

healthbook TIMES Oncology Hematology

Vol. 16, Issue 2, 2023

Osimertinib improves OS in *EGFR*-mutated NSCLC: Bright future for lung cancer therapy

Ample evidence shows that patients with stage IV lung cancer harboring certain genetic alterations, such as an *EGFR* mutation, achieved improved overall survival (OS) when treated with oral targeted therapies.[1] For the first time in the lung cancer setting, an OS advantage with oral targeted therapy against *EGFR*-mutant non-small cell lung cancer (NSCLC) has now been reported for patients who have undergone surgical resection. This was demonstrated in ADAURA, a randomized, double-blind, phase III trial evaluating the EGFR tyrosine kinase inhibitor (TKI), osimertinib, in patients with early-stage NSCLC positive for exon 19 deletion or *EGFR* L858R mutation (ex19del/L858R). In the primary analysis, osimertinib demonstrated significant and clinically meaningful disease-free survival (DFS) improvement versus placebo.[2] However, at this point, it was not clear whether the DFS data transform into an OS advantage. At ASCO 2023, Dr Roy S. Herbst presented the final OS data from ADAURA which showed that osimertinib also significantly prolonged OS versus placebo in this patient population.[3] The 5-year OS rates for osimertinib were 85% versus 73% for placebo in patients with stage II–IIIA disease (HR: 0.49 [95% CI: 0.33–0.73]; p=0.0004), and 88% versus 78% with placebo in the overall population (HR: 0.49 [95% CI: 0.34–0.70]). These data set the stage for precision medicine in early-stage lung cancer and suggest that this approach could be applied not only to *EGFR*-mutated tumors but also to disease subsets harboring mutations in other genes, such as *ALK*, *RET* or *ROS*.

Perioperative therapy with pembrolizumab improves EFS in NSCLC

Over the last three years, significant progress has been made in the application of neoadjuvant and adjuvant (chemo)immunotherapy in lung cancer. Data from the AEGEAN trial have previously shown a 32% reduction in the risk of disease recurrence or progression in NSCLC patients treated with durvalumab before and after surgery.[4] At the ASCO 2023 meeting, the results were presented from KEYNOTE-671, a large, randomized, phase III trial that assessed the use of pembrolizumab in patients with early-

stage NSCLC.[5] In this study, patients received 4 cycles of cisplatin-based chemotherapy plus pembrolizumab or placebo, followed by surgery and pembrolizumab or placebo for up to 13 cycles. Pembrolizumab-containing therapy achieved significantly longer event-free survival (EFS) versus placebo (HR 0.58 [95% CI: 0.46–0.72]; p<0.00001). Interim results further showed a trend toward improved OS with this treatment regimen at a median follow-up of 25.2 months (HR: 0.73 [95% CI: 0.54–0.99]), although the significance boundary was not met at this time point (p=0.02124). Overall, these findings support the application of immunotherapy in the early-stage NSCLC setting.

Immunotherapy duration in NSCLC: When to stop?

It has been historically established in several clinical trials that patients with stage IV NSCLC who did not have disease progression undergo two years of immunotherapy.[6] However, in clinical practice, many patients continue to receive immunotherapy indefinitely, which has financial and toxicity implications. The study conducted at Penn Medicine's Abramson Cancer Center used the nationwide Flatiron Health electronic health record (EHR)-derived de-identified database to investigate whether prolongation of immunotherapy provides survival benefit in advanced-stage NSCLC.[7] Notably, this analysis showed that only about 1 in 5 patients treated with front-line immunotherapy stopped the treatment after two years rather than continuing it. Results further indicated no significant difference in OS between the fixed duration and indefinite duration groups (HR: 1.26 [95% CI: 0.77–2.08]). These data provide physicians and patients with the confidence to discontinue immunotherapy for advanced-stage NSCLC after two years.

Conflict of interest

The author reports receiving institutional research funding from AstraZeneca, Genentech, Incyte, Macrogenics, Medimmune, and Merck Sharp & Dohme, and receiving consultation fees from Genentech, Lilly, Celgene Merck, AstraZeneca, Blueprint Genetics, Shionogi, Daiichi Sankyo/ Astra Zeneca, Regeneron/ Sanofi, Eisai, BeiGene, Turning Point, Pfizer, Janssen, Boehringer Ingelheim.

Funding

The author has declared that no financial support was received from any organization for the submitted work.

Author Contributions

The author created and approved the final manuscript.

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