Pembrolizumab dose reduction in metastatic NSCLC – an opportunity for improving cost-effectiveness?

There were many new developments, including practice-changing clinical trials, presented at this year's European Society of Medical Oncology (ESMO) Congress in Barcelona. From the vast number of abstracts available in the rapidly evolving field of thoracic oncology, we have selected one abstract that was of particular interest to us: Low-dose versus standard dose pembrolizumab for treatment of advanced-stage non-small cell lung cancer (NSCLC) – Results of the pre-planned interim analysis of the clinical trial NVALT-30.

Progress in the field of oncology over the past few decades has been impressive, with an increase in the number of people potentially cured after cancer treatment and an increase in response rates leading to improved overall survival in the metastatic disease setting. While innovation and scientific progress have been a great benefit for patients and their families, this progress was also accompanied by a significant increase in costs (1). With the expected increase of patients living with cancer as life expectancy rises (2), there is a need to improve cost-effectiveness of oncology therapies and thus make the distribution of drugs more equitable.

The introduction of immunotherapy marked a turning point in the treatment of various tumor entities. Immunotherapy has become part of the standard first-line treatment for advanced or metastatic NSCLC without genomic alterations (3). While immunotherapies targeting programmed cell death-1 (PD-1) and its ligand (PD-L1), administered as monotherapy or in combination with chemotherapy, have improved the clinical outcomes of patients with advanced and metastatic NSCLC, they have also contributed to the increase of treatment costs (4).

The trial DEDICATION-1/NVALT-30 is investigating the impact of dose reduction of the PD-1-targeting immune checkpoint inhibitor pembrolizumab on overall survival in advanced NSCLC (5). The authors compare the standard dose of 400 mg every 6 weeks or 200 mg every 3 weeks with a dose reduction to 200 mg every 6 weeks or 100 to 150 mg every 3 weeks. A strength of this study are the broad inclusion criteria: Patients should have an ECOG score of 0-2, no prior therapy and be scheduled for first-line treatment with pembrolizumab. A total of 750 patients are expected to be enrolled and being randomized in a 1:1 ratio. Stratification factors include treatment modality (pembrolizumab monotherapy vs. chemoimmunotherapy), PD-L1 expression status (<50% vs. ≥50%), smoking status, ECOG performance score (0-1 vs. 2) as well gender.

At ESMO, data from the pre-planned interim analysis after the enrolment of the first 250 patients, including 1-year follow-up were presented. There was no significant difference in 1-year overall survival (57.5% (95% CI: 49.5% - 67.3%) in the standard dose group and 55.0% (95% CI: 47% - 64.4%) in the reduced dose group) or median progression-free survival (6.9 months (95% CI: 6-9.8) in the standard dose group vs. 7.6 months (95% CI: 5.8-11.3) in the reduced dose group). The rate of adverse events was also similar between the two groups, with 8% vs 10% in the standard dose and reduced dose groups, respectively. Based on the data from this interim analysis, with a one-year survival difference of 2.7%, the study has met the pre-specified criterion for continuing inclusion.

Presentation of efficacy data on the primary endpoint (overall survival) from a pre-planned safety interim analysis could raise statistical and ethical concerns as it may jeopardize further patient recruitment. However, in the event that the preliminary results are confirmed in the future, this trial could have far-reaching health economic consequences: In Switzerland, around 155 million CHF was spent on pembrolizumab in 2022, making it the second highest cost of a single drug (6), and a dose-reduction regimen could lead to a significant reduction in healthcare costs and contribute to the need for greater cost-effectiveness in oncology. □

Author: Dr. Jonas Lötscher MD-PhD, University Hospital Basel
Mentor: Prof. Dr. med. Dr. phil. nat. Sacha Rothschild, MD PhD. Kantonsspital Baden

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