

## ペンブロリズマブは初回肺がん治療に有効 (Abstract LBA4)

**KEYNOTE-042:** ペンブロリズマブは進行肺がんの治療として化学療法よりもよりベネフィットが得られる

**KEYNOTE-042:** Pembrolizumab provides more benefit than chemotherapy alone as initial treatment for advanced lung cancers

大規模ランダム化第III相KEYNOTE-042試験の結果、最も一般的なタイプの肺がん患者の大多数に対し、ペンブロリズマブによる免疫療法は化学療法（現在の標準治療）に比べより有効な初回治療であることが示された。と2018 ASCO Annual Meetingで取り上げられた。PD-L1が1%以上発現している進行非小細胞肺がん患者で、ペンブロリズマブによる免疫療法で初回治療を施行された者は、化学療法を施行された者に比べ、生存期間中央値が4〜8か月長かった。さらに、重篤な副作用の発現は、化学療法群に比べペンブロリズマブ群で少なかった（18% vs. 41%）。

### Full Text

A large, randomized phase III trial shows that the immunotherapy pembrolizumab is a more effective initial treatment than chemotherapy (the current standard of care) for the majority of patients with the most common type of lung cancer. People with advanced non-small-cell lung cancer (NSCLC) with a PD-L1 expression of 1% or more who were first treated with immunotherapy pembrolizumab lived a median of 4-8 months longer than those who received chemotherapy. In addition, severe side effects occurred in fewer patients receiving pembrolizumab than chemotherapy (18% vs. 41%).

According to the authors, this study (KEYNOTE-042) is the largest clinical trial of pembrolizumab as a standalone therapy. The findings are presented in ASCO's Plenary Session, which features four studies deemed to have the greatest potential impact on patient care, out of the more than 5,800 abstracts featured as part of the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

"A large number of patients with lung cancer now have a new treatment option with better efficacy and fewer side effects than standard chemotherapy," said lead study author Gilberto Lopes, MD, MBA, a medical oncologist at the Sylvester Comprehensive Cancer Center, University of Miami Health System in Florida. "Our study shows that pembrolizumab provides more benefit than chemotherapy for two-thirds of all people with the most common type of lung cancer."

PD-L1 is a biomarker commonly used to predict response to immune checkpoint inhibitors, including pembrolizumab. Generally, tumors with more PD-L1 (high expression) respond better to these treatments, but in some studies, these immunotherapies were effective even against tumors with little or no detectable PD-L1. In prior trials of second-line therapy for NSCLC, pembrolizumab was effective in treating tumors with PD-L1 expression of at least 1%.

Researchers randomly assigned 1,274 people with locally advanced or metastatic NSCLC to receive chemotherapy (paclitaxel plus carboplatin or pemetrexed plus carboplatin) or pembrolizumab. Both squamous and non-squamous cancers were included, but not cancers with genetic changes that can be treated with targeted therapies (EGFR and ALK inhibitors).

For the analysis, researchers explored treatment benefits in three patient groups according to tumor PD-L1 expression score: at least 50% (599 patients), at least 20% (818 patients), and at least 1% (1,274 patients). Equal numbers of patients in each PD-L1 expression group received pembrolizumab and chemotherapy.

The median follow-up time was 12.8 months. Compared to those receiving standard chemotherapy, patients who received pembrolizumab had a longer median overall survival, regardless of PD-L1 expression in the tumor. The benefit of pembrolizumab was greater when the level of PD-L1 expression was higher:

- PD-L1 50% or more: 20 months with pembrolizumab vs. 12.2 months with chemotherapy
- PD-L1 20% or more: 17.7 months with pembrolizumab vs. 13 months with chemotherapy
- PD-L1 1% or more: 16.7 months with pembrolizumab vs. 12.1 months with chemotherapy

"Immunotherapy with pembrolizumab alone benefits a much larger number of patients than we had previously thought. This is yet another promising result with immunotherapy in lung cancer that brings new momentum to the treatment of this notoriously difficult disease," said ASCO Expert John Heymach, MD, PhD.

More research is needed to define patient groups who benefit from pembrolizumab. The three broad groupings by PD-L1 expression in the current analysis do not allow researchers to predict the benefit from pembrolizumab for patients with a specific PD-L1 expression level. Additionally, it is not yet clear whether pembrolizumab combined with chemotherapy is better than pembrolizumab alone in patients who express PD-L1, as there have not been head-to-head comparison trials of the two approaches.

Ongoing research is also exploring use of adjuvant pembrolizumab and combinations of immunotherapy with bevacizumab-containing combination regimens as part of initial therapy for NSCLC.

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