進行扁平上皮NSCLCの予後改善 (Abstract LBA9000)

IMpower131：化学療法にアテゾリズマブによる免疫療法を上乗せすることにより進行扁平上皮肺がんの増殖を遅らせることができる

IMpower131: Adding atezolizumab immunotherapy to chemotherapy slows growth of advanced squamous lung cancer

第III相臨床試験の初回結果によると、進行扁平上皮非小細胞肺がん（NSCLC）患者にとって、化学療法単独による初回治療に比べ、化学療法にアテゾリズマブによるPD-L1標的免疫療法を上乗せする初回治療の方がより有益である-疾患増悪または死亡リスクが化学療法単独に比べ29%低かった（p=0.0001）。この併用療法により無増悪生存の有益性が倍になった：12か月後、がんが悪化していなかったのは、免疫療法と化学療法の併用群で24.7%、化学療法単独群では12% であった。この有益性は、PD-L1発現サブグループすべてにおいて認められた。IMpower131試験のこの結果は、2018 ASCO Annual Meetingで発表された。

Full Text

Initial findings from a randomized phase III clinical trial show that patients with advanced squamous non-small-cell lung cancer (NSCLC) benefit more from initial treatment with PD-L1 targeted immunotherapy atezolizumab and chemotherapy than from chemotherapy alone – 29% had a reduced risk of disease worsening or death compared with those who received chemotherapy alone. At 12 months, cancer had not worsened in twice as many patients who received atezolizumab plus chemotherapy compared to those who only received chemotherapy. This benefit was observed across all PD-L1 expressing sub-groups.

The findings from the IMpower131 trial were presented at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Until now, there have been few treatment advances for squamous non-small-cell lung cancer. Our findings may provide a new potential treatment option for this type of cancer," said lead study author Robert M. Jotte, MD, PhD, Medical Director and Co-Chair, USON Thoracic Committee, Rocky Mountain Cancer Centers in Denver, CO. "We used to think that chemotherapy just knocked down the patient's immune system and that it would be irrational to combine it with immunotherapy, but growing research, including this study, shows that chemotherapy can help trigger the immune response to the tumor, helping the immunotherapy treatment work better."

Squamous NSCLC, which accounts for 25-30% of NSCLCs, is very difficult to treat. Fewer than 15% of people with advanced squamous NSCLC survive a year after diagnosis, and less than 2% survive five years.

Recent studies have also found a benefit of combining immunotherapy with chemotherapy in non-squamous lung cancer. Given those findings, along with the results from this trial, a rapid change in clinical practice is expected, noted Dr. Jotte.

The IMpower131 trial enrolled 1,021 patients with stage IV squamous NSCLC. Tumors were tested for PD-L1 expression, but patients were included in the trial regardless of tumor PD-L1 expression level. Patients with EGFR or ALK gene changes in the tumor received targeted treatments before starting therapy on this trial. The study participants were randomly assigned to one of three treatment groups. Outcomes for only two of the groups, however, are being reported in this presentation:

- Atezolizumab plus chemotherapy (carboplatin and nab-paclitaxel), 343 patients
- Chemotherapy (carboplatin and nab-paclitaxel), 340 patients

Outcome data for the third treatment group, which received atezolizumab with a slightly different chemotherapy regimen (carboplatin and paclitaxel), are not yet available.

In this study, 29% of all patients, regardless of PD-L1 expression, had a reduced risk of disease worsening or death, compared with those who received chemotherapy alone. Importantly, there was a doubling of progression-free survival (PFS) benefit with this combination: at 12 months, cancer had not worsened in 24.7% patients receiving immunotherapy and chemotherapy, compared to 12% of those receiving chemotherapy alone.

Improved progression-free survival was observed in all groups of patients who received immunotherapy and chemotherapy, including those with PD-L1-negative tumors and liver metastases. Overall survival data are not yet mature.

This is the first phase III trial of an immunotherapy-based combined modality treatment to show a significant improvement in progression-free survival in advanced squamous NSCLC, according to the authors. Although the difference between treatment groups is modest, a statistically significant improvement shows that, overall, people with advanced squamous lung cancer can benefit when immunotherapy is added to standard treatment, according to the authors.

Although the rate of severe side effects was higher with the combined modality treatment than with chemotherapy alone (68% vs. 57%), it had a manageable safety profile, consistent with known safety risks of the individual therapies. The most common side effects of atezolizumab included skin rash, colitis, and low thyroid hormone.

At this interim analysis, a statistically significant overall survival (OS) benefit was not observed (median OS was 14 months for atezolizumab plus chemotherapy vs. 13.9 months for chemotherapy alone). Researchers are continuing to follow patients and anticipate a subsequent analysis later this year.

"This is one more example of how immunotherapy is making steady gains against a number of cancers. Immunotherapy has been shown to be effective in other types of lung cancer, and now we're seeing encouraging improvements in advanced squamous lung cancer, which historically has been very difficult to treat," said ASCO Expert David Graham, MD, FASCO.

More research is needed to determine which patients benefit the most from the addition of immunotherapy to standard chemotherapy. The researchers will explore tumor PD-L1 expression and other molecular markers, such as tumor mutational burden (TMB), that may predict whether a patient will benefit from this treatment regimen.

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