治療によりメラノーマの進行が半減する (Abstract LBA1)

進行メラノーマにおいて初回のニボルマブベースの治療は疾患進行までの時間を2倍以上にする

Initial nivolumab-based treatment more than doubles time to disease progression in advanced melanoma

未治療の進行メラノーマ患者におけるニボルマブ単独またはイピリムマブとの併用による初回治療は、イピリムマブ単独治療よりも有効性が高い、と第51回American Society of Clinical Oncology年次集会で発表された。第III相スタディでは、945人の患者をイピリムマブ、ニボルマブ、またはこれら2剤の併用にランダムに割り付けた。少なくとも9か月の追跡期間後に、疾患進行までの平均期間はニボルマブ単独群においてイピリムマブ群の倍であり(8.9か月対2.2か月)、この有益性はイピリムマブとニボルマブを併用することでさらに増大した(11.5か月)。奏効率もまた、併用療法群(57.6%)およびニボルマブ単独群(43.7%)において、イピリムマブ群(19%)よりも実質的に高かった。腫瘍量の平均軽減率は併用療法群で51.9%であり、ニボルマブ単独群で34.5%であった。対照的に、イピリムマブ単独投与患者では腫瘍量が5.9%増大した。予想通り、重篤な薬剤性副作用の発現率は併用群(55%)において最も高く、この群の36%の患者が治療を中止しなければならなかった。先行研究では、免疫療法を早期に中止した多くの患者が依然として経過が良好であることが示されている、と筆者らは述べている。

Full Text

A randomized phase III trial indicates that initial therapy with nivolumab alone or in combination with ipilimumab is significantly more effective than ipilimumab alone in patients with previously untreated advanced melanoma according to researchers at the American Society of Clinical Oncology's 51st Annual Meeting.

Nivolumab alone more than doubled the average time to disease progression, compared to ipilimumab (8.9 months vs. 2.2 months), and the benefit was even greater when ipilimumab and nivolumab were combined (11.5 months). The response rates were also substantially higher in patients receiving the combination therapy (57.6%) and nivolumab (43.7%) alone, as compared to ipilimumab (19%).

"We're very encouraged that the initial observations about the efficacy of this combination held up in this large phase III trial," said lead study author Jedd Wolchok, MD, PhD, Chief of Melanoma and Immunotherapeutics Service at Memorial Sloan Kettering Cancer Center in New York, NY. "Our study also suggests that patients with a specific tumor marker appear to benefit the most from the combination treatment, whereas other patients may do just as well with nivolumab alone. This will help doctors provide important insight for patients on which treatment is right for them."

Nivolumab and ipilimumab are monoclonal antibodies that block two different immune checkpoints – PD-1 and CTLA-4, respectively. Both treatments, commonly referred to as checkpoint inhibitors, essentially boost the immune system's ability to fight cancer.

Prior research has shown that immune checkpoint inhibitors can improve survival for patients with melanoma and lung cancer.

This study randomly assigned 945 patients with previously untreated, advanced melanoma to receive ipilimumab, nivolumab, or the combination of the two. After a follow-up period of at least nine months, the median progression-free survival was 2.2 months for ipilimumab, 8.9 months for nivolumab, and 11.5 months for the combination. The differences between the combination and ipilimumab groups, and nivolumab and ipilimumab groups were statistically significant (both comparisons p=0.001).

The response rates for the combination, nivolumab, and ipilimumab groups were 57.6%, 43.7%, and 19%, respectively. The average reductions in tumor burden were 51.9% with the combination and 34.5% with nivolumab alone. In contrast, patients who received ipilimumab alone experienced a 5.9% increase in tumor burden.

As expected, the rate of serious drug-related side effects was the highest in the combination group (55%), and 36% of patients in this group had to stop the therapy due to side effects. Dr. Wolchok remarked that prior studies have shown that many patients who stop immunotherapy early still continue to do well.

This prolonged benefit is explained by the fact that immunotherapy works by activating the immune system rather than targeting the tumor directly. It is not yet clear how long patients need to be treated to fully activate the immune system, and the minimal duration of therapy probably varies from patient to patient.

Quality of life data were collected on the study, and the analysis of those results will be reported at a later time.

The PD-1 protein on immune cells attaches to another protein called PD-L1, which is sometimes found on the surface of some tumor cells. Prior research suggested that patients who had detectable PD-L1 levels in their tumor (PD-L1-positive tumors) typically had better responses to PD-1 therapy.

In this study, nivolumab alone seemed to be as effective against PD-L1-positive tumors as the combination of nivolumab and ipilimumab. For patients with PD-L1-negative tumors, however, the combination treatment was significantly more beneficial than nivolumab alone.

"Immunotherapy drugs have already revolutionized melanoma treatment, and now we're seeing how they might be even more powerful when they're combined," noted ASCO Expert Steven O'Day, MD. "But the results also warrant caution – the nivolumab and ipilimumab combination used in this study came with greater side effects, which might offset its benefits for some patients. Physicians and patients will need to weigh these considerations carefully."

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