進行肝臓がんに対する免疫療法 (Abstract LBA101)

早期段階トライアルにおいてnivolumabは進行肝臓がんにおいて非常に有望な作用を示した

Nivolumab shows highly promising activity in advanced liver cancer in early stage trial

第51回American Society of Clinical Oncology年次集会で報告された第I/II相スタディの結果、進行肝臓がんにおいてnivolumabは安全で有効であることが示唆された。スタディ登録患者の75%が過去に全身療法を受け、うち68%が現在の標準治療であるソラフェニブを投与された。Nivolumabは経静脈的に2週ごとに最長2年間投与された。今回のスタディの第I相の結果に基づくと、評価可能な患者42人中8人(19%)において抗PD-1抗体が奏効し、腫瘍縮小が30%を超えた。2人の患者は完全寛解した。持続的な奏効が認められ50%においては12か月以上持続し、ほとんどの患者が治療を継続した。さらに、48%の患者において腫瘍増殖が停止し、その期間は最長で17か月を超えた。12か月後の全生存率は62%であった。NivolumabはB型肝炎またはC型肝炎のウイルス感染が持続していても安全であり、忍容性は良好であった。これらの結果は大規模スタディで検証する必要はあるが、この試験は免疫チェックポイント阻害による免疫療法が肝臓がん治療において役割を果たすであろうことを示す初めてのものである、と筆者らは指摘している。

Full Text

Findings from a phase I/II study reported at the American Society of Clinical Oncology's 51st Annual Meeting suggest that nivolumab is safe and effective in advanced liver cancer. Based on the results of the phase I part of the study, eight (19%) of the 42 evaluable patients responded to the anti-PD-1 antibody with tumor reduction beyond 30%. More importantly, the responses have been durable and surpassed 12 months in four patients. The overall survival rate at 12 months was 62%.

Patients with advanced liver cancer are in particular need of new treatments. There is currently only one FDA-approved systemic treatment for advanced liver cancer, the multi-targeted tyrosine kinase inhibitor, sorafenib. However, just 2% of patients have an objective tumor response (more than 30% shrinkage) to sorafenib, and the average overall survival is 10-11 months.

"We are encouraged to see that nivolumab was safe overall, and the response rate as well as preliminary survival data look quite promising," said lead study author Anthony B. El-Khoueiry, M.D., an associate professor of clinical medicine and phase I program director at the University of Southern California Norris Comprehensive Cancer Center in Los Angeles, CA. "While we have to verify this early signal in larger studies, this is one of the first signs that immunotherapy with immune checkpoint inhibitors will have a role in the treatment of liver cancer."

Liver cancer is the leading cause of cancer death worldwide, accounting for more than 600,000 deaths each year.

Seventy-five percent of the patients enrolled on the study had previously received systemic therapy, including 68% who had received sorafenib. Nivolumab was given intravenously every two weeks for up to two years.

The overall response rate was 19%, with eight patients experiencing objective tumor shrinkage beyond 30%, and two having complete remissions. The responses were durable, with 50% lasting beyond 12 months as most patients continued on treatment. In addition, tumors stabilized in 48% of patients, with the longest case lasting beyond 17 months.

Nivolumab was safe and well tolerated, even in patients with ongoing hepatitis B or C infections. Specifically, there have not been any safety concerns related to flares of hepatitis B infection or worsening viral infection. The majority of the side effects were mild to moderate in nature with abnormal liver enzymes, rash, and elevation of amylase and lipase being the most common; the abnormal liver enzymes and elevated amylase and lipase were not accompanied by any significant clinical symptoms.

Dr. El-Khoueiry remarked that the findings from this early trial open the door to a new class of drugs for patients with liver cancer. "While these results are preliminary and limited to a small number of patients, they remain exciting and provide strong justification for more studies of nivolumab and other immunotherapy approaches for patients with advanced liver cancer," he said.

"PD-1 immunotherapies continue to break new ground in diseases where nothing else seems to work well. The fact that this drug might stop advanced liver cancer in its tracks for months, even a year, is great news for patients," said ASCO Expert Lynn Schuchter, M.D., FASCO. "To understand the full impact of this approach, however, larger trials are needed."

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