新たな免疫療法は多くの進行がんにおいて有効である（Abstract＃3000）

進行したメラノーマ、肺、腎、大腸および胃がんに対する抗PD-L1抗体薬の抗がん作用は有望である

Anti-PD-L1 drug shows promising anti-cancer effects in advanced melanoma, lung, kidney, colorectal and stomach cancers

第49回ASCO年次集会で発表されるPD-L1標的抗体MPDL3280Aの第I相試験の結果、進行メラノーマおよび非小細胞肺がん、腎細胞がん、大腸がんおよび胃がんの患者の21%における腫瘍が縮小したことが分かった。全体で140人中29人（21%）の患者において腫瘍が有意に縮小し、また治療奏効数が最も高かったのは肺がんおよびメラノーマの患者であった。3～15か月の治療に参加中の29人中26人において、治療は現在も奏効を維持している。この新薬は安全であり効果は持続性で、ほぼ全てが奏効を維持している。何人かの患者では治療開始後数日以内に腫瘍の縮小を認めた。重要なことに、多くの患者が酸素吸入を必要としなくなったり疼痛コントロールのための麻薬性鎮痛薬の必要が減ったりという、がんに関連した症状の改善を報告した。このスタディはさらに広範囲の固形がんおよび血液がんに範囲を拡大し、現在275人を超える患者が組み入れられている。これらの早期データは有望であるが、この結果を確認するには無作為化試験が必要である。

Full Text

A phase I expansion study of the investigational drug MPDL3280A – an engineered PD-L1 targeted antibody – shows impressive tumor shrinkage rates in patients with several different cancers – including lung, melanoma, kidney, colorectal and gastric cancers – that had progressed despite several prior treatments. The research will be presented on June 3 at ASCO's 49th Annual Meeting.

The new drug was safe and produced durable responses, with nearly all responses still ongoing. Several patients experienced tumor shrinkage within days of starting treatment. Importantly, many patients reported improvement in their cancer-related symptoms, such as no longer requiring oxygen supplementation or decreased need for narcotics to control pain.

PD-L1 is a protein frequently overexpressed on the surface of cancer cells that acts as a disguise, allowing cancer cells to hide from the immune system. When MPDL3280A attaches to the PD-L1 protein, the cancer can no longer hide from the patient's immune system, allowing the body's T-cells to fight the cancer. MPDL3280A was specifically engineered for enhanced safety and efficacy compared to earlier PD-L1 or PD-1 targeted agents.

"We are impressed with the frequency and duration of the responses in these patients with very difficult-to-treat tumors. So far, almost none of the patients that have had tumor shrinkage have progressed," said Roy S. Herbst, M.D., Ph.D., Ensign professor of medicine at Yale Cancer Center and Chief of Medical Oncology at Smilow Cancer Hospital at Yale-New Haven. "This drug is part of an exciting new generation of drugs that unlock the power of the immune system to attack the cancer."

Efficacy was evaluated in 140 patients with locally advanced or metastatic solid tumors whose disease had progressed despite prior therapies. Tumor shrinkage was observed in patients with non-small cell lung cancer, melanoma, renal cell carcinoma, colorectal cancer, and gastric cancer.

Overall, 29 out of 140 (21 percent) patients experienced significant tumor shrinkage and the highest number of therapy responses occurred in patients with lung cancer and melanoma. Therapy responses are still ongoing, with 26 out of 29 responders continuing to respond (time on study of responders 3-15+ months).

It is not yet clear how PD-L1 expression affects response to MPDL3280A. Using an investigational diagnostic test, researchers analyzed archived tumor tissue from 103 patients and found that tumor shrinkage occurred in 36 percent of patients with PD-L1 positive tumors and, surprisingly, also in 13 percent of patients with PD-L1 negative tumors. The diagnostic test for PD-L1 is still evolving, so currently a negative result on the PD-L1 test could simply mean that tumors have less PD-L1 than the test currently detects.

This study has been expanded to include a larger range of solid tumors and blood cancers, with more than 275 patients currently enrolled. While these early data are encouraging, a randomized trial is needed to confirm the findings. A number of phase II and phase III studies are already planned to confirm the drug's anti-cancer activity and further validate the utility of the PD-L1 diagnostic test. Researchers are also looking at ways it could be combined with other anti-cancer therapies to further boost responses over current standard treatments.

ASCO Perspective: "The fact that this drug was active in such a variety of tumors suggests that PD-L1 is part of a universally or generally important immune mechanism. Over the next few years, drugs that target and help activate and direct the immune system will likely take on a growing role in patient care, and it's particularly exciting to see strong effects in patients whose cancer has progressed despite all other standard therapies," said ASCO President-Elect Clifford A. Hudis, MD.

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Dr. Herbst is the recipient of a 1997 Conquer Cancer Foundation of ASCO Young Investigator Award and 1999 Career Development Award.

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