PD-1標的抗体はメラノーマ患者の生存率を上昇させる（Abstract: LBA9500）

PD-1標的免疫療法MK-3475は転移性メラノーマに対し持続性で高い活性作用を有する

PD-1 targeting immunotherapy MK-3475 has high and long-lasting activity against metastatic melanoma

第50回American Society of Clinical Oncology学会で発表された大規模第I相研究の新たな結果から、PD-1標的抗体MK-3475は転移性メラノーマ患者において高率に長期の奏効性を有することが示された。スタディには、ipilimumabによる前治療歴のある患者221人およびipilimumabによる前治療歴のない患者190人が組み入れられた。全ての患者が皮膚、肺、または他の主要臓器に拡散した進行メラノーマを有していた。3つの異なる用量のMK-3475単剤使用が計画された。Ipilimumabによる前治療歴のない患者の40%およびipilimumabによる前治療歴で増悪を認めた28%の患者を含む、全体で34%の患者に奏効が認められた。奏効は持続性であり、解析の時点で88%の患者において持続していた。全ての用量および患者サブグループにわたって活性が認められ、ipilimumab前治療歴の有無、パフォーマンスステータス、LDH値、*BRAF*変異の有無、病期、および前治療の数やタイプとは関係がなかった。推定1年生存率は69%であり、全生存期間中央値には到達しなかった。推定1年生存率はipilimumabによる前治療歴のない患者で74%であり、ipilimumabによる前治療歴のある患者では65%であった。

Full Text

New findings from a large phase I study of 411 patients with advanced melanoma show that the PD-1 targeting antibody MK-3475 yields long-term responses in a high percentage of patients. In the study, the one-year overall survival was 69 percent across all patient subgroups, and responses were ongoing in 88 percent of patients at analysis, after ent options.

"This is probably the biggest phase I trial ever conducted in oncology. We were excited to see that MK-3475 was effective in previously untreated patients as well as in those who had multiple prior therapies, including ipilimumab," said lead study author Antoni Ribas, M.D., Ph.D., a professor of medicine at the David Geffen School of Medicine at the University of California in Los Angeles, CA. "These are early data, but they tell us we are on to something really important."

The study enrolled 221 patients with prior ipilimumab treatment and 190 patients who had not previously received ipilimumab. All patients had advanced melanoma that had spread to the skin, lungs, or other major organs. Three different MK-3475 dose schedules as a single agent were tested.

Overall, 34 percent of patients experienced tumor response, as assessed by Independent Review, including 40 percent of patients not previously treated with ipilimumab and 28 percent of patients whose disease progressed on prior ipilimumab. Responses were durable with 88 percent ongoing at the time of analysis. Activity was observed across all dose levels and patient subgroups, irrespective of prior ipilimumab therapy, performance status, LDH levels, *BRAF* mutation status, tumor stage, and number and type of prior therapies. The estimated one-year survival rate was 69 percent, and median overall survival duration was not reached. The estimated one-year survival rate was 74 percent in patients not previously treated with ipilimumab and 65 percent in patients who received prior ipilimumab therapy. Overall, eight percent of patients experienced serious treatment-related side effects, but only four percent discontinued treatment due to a drug-related side effect.

Ongoing randomized controlled studies are assessing the efficacy and safety of MK-3475 in advanced melanoma patients not previously treated with ipilimumab and those who progressed on or after ipilimumab. Studies in an adjuvant setting are planned.

An expanded access program for MK-3475 is now available for eligible patients with advanced melanoma who have been previously treated with ipilimumab and, if indicated, a *BRAF* inhibitor.

"This large phase I clinical trial demonstrates continued excitement for anti PD-1 therapy. We're seeing that MK-3475 results in long-lasting clinical responses in the majority of patients, and impressive overall survival with low toxicity," said Steven O'Day, M.D., ASCO Expert. "Importantly, it's effective regardless of prior ipilimumab treatment. Anti PD-1 as a single agent is a major breakthrough and improves on the initial success of ipilimumab in metastatic melanoma."

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