# Trametinibは進行メラノーマの生存期間を改善する（Abstract # LBA8509）

## METRIC study:新たなMEK阻害薬は進行BRAF-変異メラノーマ患者の生存期間を改善する

## METRIC study:  New MEK inhibitor improves survival for patients with advanced BRAF-mutated melanoma

第48回American Society of Clinical Oncology学会で発表された第3相試験のデータから、経口治験薬が標準的な化学療法と比較し、BRAF変異を有する進行メラノーマ患者の腫瘍増殖を遅延させ生存期間を延長させることが示された。METRICとして知られるこのスタディにおいて、最高1回の化学療法を受けたことのある進行BRAF変異メラノーマ患者をtrametinib（214人）または標準的な化学療法（108人；dacarbazineまたはパクリタキセル）を受ける群に無作為に割り付けた。全体で、trametinib治療を受けた患者の22%が治療に奏効したのに対し化学療法群患者でのそれは8%であった。無増悪生存期間中央値はtrametinib投与群（4.8か月）の方が化学療法群（1.5か月）よりも有意に長かった—増悪リスクは55%低下した。中間全生存期間もまたtrametinib治療群で有意に長く、死亡リスクは46%低下した；6か月後に生存していたのはtrametinib群患者で81%であったのに対し、化学療法群では67%であった。化学療法中に疾患が増悪した患者のほぼ半数（47%）はtrametinib内服を許可されたため、全生存期間に関する有益性はこの“クロスオーバー効果”を考慮するとさらに大であることが最終的に証明されるであろう。

## Full Text

Data from a Phase III study presented at the American Society of Clinical Oncology's 48th Annual Meeting show that the oral investigational drug trametinib delayed tumor growth and extended survival for patients with advanced melanoma who have BRAF mutations, compared with standard chemotherapy. This is the first Phase III trial evaluating a melanoma treatment that inhibits a protein known as MEK ─ part of the MAP kinase-signaling pathway, of which BRAF is also a component.

"This is the first in a new class of targeted drugs that could benefit patients with melanoma who have BRAF mutations. The findings show that targeting the MEK molecular pathway is a viable strategy for treating many people with the disease," said Caroline Robert, M.D., Ph.D., Head of Dermatology at the Institute Gustave Roussy in Paris, France. "Trametinib is likely to become another first-line treatment option for patients with advanced melanoma."

Only one targeted therapy, vemurafenib, is currently approved for advanced melanoma. Vemurafenib targets a protein produced by a mutation in the BRAF gene that fuels melanoma growth, and is present in roughly half of patients with melanoma. MEK lies downstream from BRAF in the same signaling pathway. Since most patients taking vemurafenib eventually develop resistance to the drug and many experience serious side effects, MEK inhibitors could help address a continuing need for new therapies in these patients.

In this study, known as METRIC, patients with advanced BRAF-mutated melanoma who had received up to one prior chemotherapy regimen were randomly assigned to receive trametinib (214 patients) or standard chemotherapy (108 patients; either dacarbazine or paclitaxel). Overall, 22 percent of patients who received trametinib responded to treatment, compared with 8 percent of those who received chemotherapy.

Median progression-free survival was significantly greater in the trametinib group (4.8 months) than the chemotherapy group (1.5 months) – a 55 percent reduction in the risk of progression. Interim overall survival was also longer among the patients treated with trametinib, with a 46 percent reduced risk of death; 81 percent of patients in the trametinib group were alive after six months of follow-up, versus 67 percent in the chemotherapy group. Approximately half (47 percent) of patients whose disease progressed while on chemotherapy were permitted to take trametinib, so the overall survival advantage may ultimately prove to be greater if this "crossover effect" is taken into account, according to the researchers.

Side effects of trametinib were generally manageable. Severe adverse events included skin rash (7 percent of patients), eye problems (less than 1 percent), high blood pressure (12 percent) and reduced heart function (7 percent).

## ASCO2012特集