NRAS mElanoma and MEK inhibitOr

NEMO: A PHASE 3 TRIAL OF BINIMETINIB (MEK162) VERSUS DACARBAZINE IN PATIENTS WITH ADVANCED NRAS-MUTANT MELANOMA WHO ARE UNTREATED OR HAVE PROGRESSED AFTER ANY NUMBER OF IMMUNOTHERAPY REGIMENS


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Background: Melanoma tumors often harbor mutations in the mitogen-activated protein kinase-signaling pathway family members BRAF or NRAS. NRAS mutations, observed in about 20% of patients with melanoma, are associated with higher tumor proliferation and poorer prognosis. A large retrospective analysis (n = 677) demonstrated that NRAS mutations are independently predictive of poor survival in patients with cutaneous melanoma (Jakob et al., 2011). With no approved targeted therapies for melanoma patients with NRAS-mutant tumors, treatments are currently limited to chemotherapy and/or immunotherapy. Binimetinib (MEK162), a potent and selective inhibitor of MEK1/2, has demonstrated promising phase 2 clinical activity in this patient subset. Here we describe the “NRAS mElanoma and MEK inhibitOr” (NEMO) trial, an ongoing phase 3 study designed to compare the efficacy of binimetinib vs dacarbazine in patients with metastatic NRAS-mutant melanoma (NCT01763164).

Trial design: NEMO is a 2:1-arm, open-label, 2:1 randomized trial of binimetinib vs dacarbazine. Eligible patients must have advanced unresectable or metastatic cutaneous melanoma or melanoma of unknown primary origin with a documented NRAS Q61 mutation (by central molecular screening) that was previously untreated or has progressed after any number of immunotherapy regimens. Patients are stratified by stage, performance status, and prior immunotherapy. The primary endpoint of the study is progression-free survival, and secondary endpoints include overall survival, overall response, disease control rate, safety, and quality of life. Binimetinib is administered orally at 45 mg twice daily and dacarbazine is dosed intravenously at 1000 mg/m2 once every 3 weeks. This phase 3 trial is designed to enroll 393 patients and is currently recruiting patients at more than 150 centers worldwide. This abstract was accepted and previously presented at the 2014 ASCO Annual Meeting Chicago, June 2014 Abstract ID 7022.

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