Response rate high for some patients with metastatic melanoma treated with vemurafenib

March 16 2012

An international team of researchers from the United States and Australia, including researchers at Moffitt Cancer Center in Tampa, Fla., have found that the oral BRAF inhibitor vemurafenib (PLX4032) when tested in a phase II clinical trial offered a high rate of response in patients with previously treated metastatic melanoma and who had the BRAF mutation. More than 50 percent of the patients in the trial had positive, prolonged responses and a median survival of almost 16 months.

The study was published in a recent issue of the New England Journal of Medicine.

According to study co-author Jeffrey S. Weber, M.D., Ph.D., director of the Donald A. Adam Comprehensive Melanoma Research Center at Moffitt, approximately 50 percent of melanomas harbor the activating (V600) mutation threonine protein kinase B-RAF. Unfortunately, treatment options for these patients are "limited."

The BRAF inhibitor vemurafenib had been found effective in phase I and phase III trials. However, to determine the overall response rate in previously treated stage IV melanoma patients, the researchers designed a multi-center, phase II trial with 132 patients with previously treated BRAF V600-mutant metastatic melanoma. The trial was designed by senior academic authors and representatives of the trial sponsor,

Hoffman-La Roche, and was open to adults over the age of 18 with histologically proven stage IV melanoma, progressive disease, and at least one prior systemic treatment.

"Few patients with metastatic melanoma bearing the BRAF V600 mutation have a response to systemic chemotherapies," said Weber. "Additionally, most have a median survival of only six to 10 months. However, this study yielded an overall response rate of 56 percent and a median survival of nearly 16 months."

The 56 percent response rate for this study was higher than the response rates reported on studies with other therapies for a majority of patients, such as the monoclonal antibody impilimumab. Once more, the response for patients in the vemurafenib phase II trial was "rapid," said the study authors, with less than 15 percent of patients having had disease progression at their first evaluation.

"This trial showed that vemurafenib has clinically evident anti-tumor activity in metastatic melanoma, and that response rates are higher than those associated with previously used treatments," concluded Weber.

The authors reported that toxic effects were common, but not severe or life-threatening in most cases. They added that, as with most targeted therapies that block a driver oconogene, cancer cells can develop resistance with continued dosing and the molecular mechanisms of vemurafenib are "under investigation" at Moffitt by Keiran S. Smalley, Ph.D., and at other institutions to answer questions about resistance.

Provided by H. Lee Moffitt Cancer Center & Research Institute