

Combining MEK and PI3K inhibitors appears encouraging in a safety study with early signs of anti-tumor activity

April 2 2011

The combination of two compounds that inhibit two of the most frequently mutated cancer pathways is showing promise in an ongoing Phase I trial, according to data presented at the AACR 102nd Annual Meeting 2011, held here April 2-6.

The research, presented by Johanna Bendell, M.D., tests a combination of GDC-0973, which inhibits MEK1/2 and GDC-0941, which inhibits PI3K. Bendell, director of Gastrointestinal Oncology Research and associate director of the drug development unit at the Sarah Cannon Research Institute in Nashville, said the RAS/RAF/MEK and PI3K pathways are altered in most tumors.

"Combining agents that block multiple pathways in tumor cells is likely the future of targeted therapy in cancer medicine. Blocking two pathways that interact with each other has the potential to have more anti-cancer activity than blocking either pathway alone," says Bendell.

The researchers enrolled 27 patients who received the combination of different doses of GDC-0973 and GDC-0941 on a daily 21 day on/7 day off schedule. The most common side effects seen were diarrhea, fatigue, rash, nausea, vomiting, decreased appetite and taste changes. Most of these side effects were mild.

Several patients have demonstrated decreases in tumor size, including

two patients with melanoma, one with [prostate cancer](#), two with non-small cell lung cancer. One patient with [lung cancer](#) and two patients with [melanoma](#) had stable disease over six months. The study is ongoing.

"We are very encouraged by this early data. We are able to give these agents together safely and we are seeing early signs of anti-cancer activity," said Bendell.

Provided by American Association for Cancer Research

Citation: Combining MEK and PI3K inhibitors appears encouraging in a safety study with early signs of anti-tumor activity (2011, April 2) retrieved 27 April 2024 from <https://medicalxpress.com/news/2011-04-combining-mek-pi3k-inhibitors-safety.html>

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