

Phase II trial of efatutazone shows challenge of matching treatment to population

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Work at the University of Colorado Cancer Center led to phase II trial of efatutazone with erlotinib in patients with refractory non-small cell lung cancer. Results are reported today at the American Association for Cancer Research (AACR) Annual Meeting 2014. While efatutazone did not improve the efficacy of erlotinib in this trial, researchers hope lessons from the trial will allow them to make better future use of the drug or other drugs in its class.

"In oncology and especially in <u>lung cancer</u>, everything is personalized. We're exploring different molecular markers that identify which drugs are for the right patient After this phase II trial, we're working to find the right biomarker that could help us discover who is most likely to respond to efatutazone. This trial was done in an unselected population. But if we had the right population with the right marker, we hope that we could find a meaningful effect," says Ana Oton, MD, investigator at the CU Cancer Center, Associate Professor of Medical Oncology at the University of Colorado School of Medicine, and the study's first author.

Efatutazone belongs to a class of drugs known as thiazolidinediones, members of which are currently in use for the treatment of type II diabetes. Drugs in this class influence the expression of cell proteins by binding to the nuclear receptor PPARy. In diabetes, the drugs increase the production of proteins that drive metabolism. In cancer, the drug showed anti-cancer activity in preclinical models of non-small cell lung cancer. A phase I trial the drug alone showed anti-cancer activity in patients with solid malignancies.



The current, multi-center study compared efatutazone with erlotinib versus <u>erlotinib</u> alone in 90 patients previously treated for non-small cell lung cancer. Unfortunately, Oton explains, "In vitro it looked really promising, but in vivo it was not so good."

The majority of the difference between success in the lab and lack of success in patients was due to the side effect of <u>fluid retention</u>.

"Fluid retention in lower extremities is a side effect that can be easily managed," Oton says, "however, if this fluid retention is in the pleural space in patients that have already metastatic lung cancer, it can be very detrimental."

"We're not denying this combination could be useful, but with the knowledge we have we shouldn't do more studies in vivo at this time. We need to determine what patient population will be best served and second, discover how to manage this side-effect" Oton says.

Provided by University of Colorado Denver

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