

Study combines lapatinib with cetuximab to overcome resistance in EGFR-driven tumors

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Targeted therapies have been studied for years, but recent laboratory research is providing robust clues about drugs that might work better in combination, particularly in treating cancers that have become resistant to therapy. That kind of information is behind a novel clinical trial at Georgetown Lombardi Comprehensive Cancer Center that combines cetuximab and lapatinib. Findings from this phase I study will be presented at the American Society of Clinical Oncology annual meeting in Chicago, June 1st through 5th.

Cetuximab works by blocking the [epidermal growth factor receptor](#) (EGFR) found on the outside of a cell. In cancers such as colon, head and neck, and lung, when cetuximab stops EGFR signaling, the machinery inside the cell doesn't get the signal to grow, in turn causing it to die. However, cancer cells can become resistant to cetuximab when the EGFR receptor combines with a related receptor HER2 (ErbB2) -- which cetuximab can't block. Once again, the cell gets the signal to grow. Lapatinib however blocks HER2 and EGFR from the inside of cancer cells.

"[Cancer cells](#) are good at developing ways around our treatments, including new targeted therapies such as cetuximab." says John Deeken, M.D., a medical oncologist at Georgetown Lombardi Comprehensive Cancer Center. "By combining different targeted therapies, we hope to be able to overcome such [resistance](#) and turn off the cancer cell signal to grow."

Deeken, an expert in how cells [metabolize](#) or process drugs, took the information learned from these recent pre-clinical studies and designed a novel clinical trial - combining cetuximab, which blocks EGFR, with lapatinib which works inside the cell and shuts down [HER2](#). GlaxoSmithKline provided lapatinib for the study and additional financial support for the study.

Cetuximab, marketed as Erbitux, has been

approved by the U.S. Food and Drug Administration (FDA) for the treatment of metastatic colorectal cancer and head and neck cancer. Lapatinib, marketed as Tykerb, is FDA-approved for the treatment of some types of breast cancer.

Sixteen patients whose tumors are driven by EGFR were enrolled in the study and received the established dose of [cetuximab](#) (intravenously once a week). Lapatinib, a drug taken orally on a daily basis, was given in escalating doses. Twelve of thirteen patients were evaluable for toxicities (side effects). The most common side effects of the combination were rash and diarrhea, both of which can be managed with supportive medications and care.

"While this study isn't designed to evaluate whether or not this combination of drugs works, we have seen some positive signs of clinical activity," Deeken says.

Of nine patients evaluable for response (completed at least two cycles of treatment), two had a partial response (more than 30 percent tumor shrinkage), and two had prolonged stable disease of 2 cycles or more, for a clinical benefit rate of 44 percent.

Phase II studies to test this combination in colon as well as head and neck cancer patients are under development, Deeken says.

Provided by Georgetown University Medical Center

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