

New Drug Combination Could Prevent Head and Neck Cancer in High-risk Patients

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- Preclinical combination of an EGFR inhibitor and a COX-2 inhibitor was effective.
- Advanced oral precancerous lesions were eliminated in three patients.
- Drug combination could be a new strategy to prevent head and neck cancers.

PHILADELPHIA — A new drug combination shows promise in reducing the risk for patients with advanced oral precancerous lesions to develop squamous cell carcinoma of the head and neck. The results of the study, which included preclinical and clinical analyses, were published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research.

“Squamous cell carcinoma of the head and neck (SCCHN) is the most common type of head and neck cancer,” said Dong Moon Shin, M.D., professor of hematology, medical oncology and otolaryngology at Emory University School of Medicine, and director of the Cancer Chemoprevention Program at Winship Cancer Institute at Emory University in Atlanta, Ga. “The survival rate for patients with SCCHN is very poor. An effective prevention approach is desperately needed, especially since we can identify patients who are at extremely high risk: those with advanced oral precancerous lesions.”

Based on prior research suggesting a role for epidermal growth factor receptor (EGFR) and cyclooxygenase-2 (COX-2) in promoting SCCHN, Shin and colleagues believed combining an EGFR inhibitor and a COX-2 inhibitor could provide an effective chemopreventive approach.

They found that the combination of the EGFR inhibitor erlotinib and the COX-2 inhibitor celecoxib was more effective for inhibiting the growth of human SCCHN cell lines compared with either drug alone. In addition, treating mice with the drug combination prior to transplanting them with human SCCHN cells more effectively suppressed cancer cell growth than did pretreating the mice with either drug alone.

Based on these preclinical analyses, Shin and colleagues initiated a phase I chemoprevention trial. Eleven patients with advanced oral precancerous lesions were assigned to treatment with erlotinib and celecoxib. Tissue samples from the patients were obtained and evaluated pathologically at three, six and 12 months after therapy initiation. Biopsies at baseline and follow-up were available for seven patients.

Pathologic examination of the biopsies indicated that three of the seven patients had a complete pathologic response; that is, there was no longer evidence of the precancerous lesions in the follow-up biopsy sample. Among the other patients, two had a partial pathologic response and two had progressive disease.

“Finding that this drug combination caused some advanced premalignant lesions to completely disappear was great news,” said Shin. “Advanced premalignant lesions rarely regress, so our data are proof-of-principle that a combination chemopreventive strategy with molecularly targeted agents is possible.”

Several patients dropped out of the trial because of severe adverse side effects, according to Shin. “Prevention is not achieved through short-term treatment,” he said. “So, we need to investigate the safety and toxicity of this combination further before planning a large-scale trial. We are also looking to combination therapies using less toxic or nontoxic agents, such as natural compounds.”

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