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Spread of nasopharyngeal carcinoma is reduced by bevacizumab, according to phase 2 trial results

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The trial conducted by the Radiation Therapy Oncology Group (RTOG) shows the feasibility to deliver bevacizumab to the current chemoradiation standard without any apparent increased adverse side effects.

Combining the widely used anti-cancer drug bevacizumab with standard chemoradiation therapy is safe and could prolong survival in patients with advanced nasopharyngeal carcinoma, according to a new phase 2 trial published Online First in today's The Lancet Oncology. The results indicate that bevacizumab might be more effective at preventing the spread of nasopharyngeal carcinoma to other parts of the body, the most common cause of death in patients with advanced disease.

RTOG 0615 Principal Investigator Nancy Lee, MD (Memorial Sloan-Kettering Cancer Center, New York) and colleagues report the new combination treatment resulted in over 90% of patients surviving 2 years with no distant metastases and 75% of patients without the disease getting worse.

Interestingly, treatment with bevacizumab increased the overall likelihood of patients surviving 2 years or more compared with findings from previous studies of chemoradiation alone. At 2 years, an "unexpectedly high" number (91%) of patients were still alive.

"[The trial]…resulted in a 2-year distant metastases-free survival rate of about 90%, which seems to be an improvement compared with the expected figure of 70□□%. These outcomes are certainly promising and give new hope to patients with nasopharyneal carcinoma, explains Joseph Wee from the National Cancer Center and Duke-NUS Graduate Medical School, Singapore in an accompanying comment.

The introduction of intensity-modulated radiotherapy (IMRT) resulted in local tumor control rates of greater than 90% for patients with nasopharyneal carcinoma. However, the disease has the highest rate of metastases among head and neck cancers and within 4 to 5 years spreads to distant organs or lymph nodes in around 30% of patients.

Bevacizumab is a monoclonal antibody that blocks vascular endothelial growth factor (VEGF-A) which is associated with poor prognosis in head and neck cancers and is overexpressed in around two-thirds of patients with nasopharyneal carcinoma. Bevacizumab has been shown to reduce the rate of distant metastasis and improve disease-free survival in many types of advanced cancer including breast cancer, colorectal cancer, renal cell cancer, and non-small cell lung cancer.

The study included 46 previously untreated patients with locoregionally advanced nasopharyneal carcinoma from 19 RTOG member centres in North America and Hong Kong. Bevacizumab was added to the concurrent and adjuvant phases of chemotherapy with cisplatin and fluorouracil.

The bevacizumab regimen was well-tolerated with no grade 3 to 4 bleeding or grade 5 adverse events, but 9 (20%) patients experienced grade 1 to 2 bleeding. The most common grade 3 or higher adverse events were blood or bone marrow related complications (36%) and acute mucositis (painful inflammation of mucous membranes in mouth; 77%).

The authors say: "The addition of bevacizumab to chemoradiation for nasopharyneal carcinoma is feasible in that it causes no major compromise in the delivery of standard chemoradiation…and might delay the progression of subclinical disease."

They add: "Although the addition of bevacizumab did not seem to result in any unusual grade 3?? events, toxicity was still substantial and compliance to protocol treatment was not ideal…So further research is needed to identify those at risk of distant metastasis and hence those who might benefit most from additional bevacizumab."

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