Adding cediranib to chemotherapy improves progression-free survival for metastatic or recurrent cervical cancer

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For patients with cervical cancer that has recurred after treatment or has spread elsewhere in the body, adding the experimental drug cediranib to standard chemotherapy improves tumour shrinkage and adds a modest improvement in progression-free survival, researchers report at the ESMO 2014 Congress in Madrid.

In Europe, about 70% of patients with cervical cancer are cured by either surgery or chemo-radiotherapy. Those patients with recurrent or secondary cancer have a very poor outlook. Only about 20-30% have tumour shrinkage after conventional chemotherapy and survival is usually less than one year.

In the phase II CIRCCa trial, researchers compared two groups of patients with relapsed or metastatic cervical cancer given conventional chemotherapy with carboplatin and paclitaxel plus either cediranib (34 patients) or an identical looking placebo tablet (35 patients).

"Cervical cancers with a well-developed blood supply can have a particularly bad outcome. The experimental drug cediranib blocks the cell surface receptor VEGF, which stimulates the growth of new blood vessels to feed the growth of tumours," explains study researcher Dr Paul Symonds, of the Department Cancer Studies & Molecular Medicine at the University of Leicester, UK.

In the study, patients who received cediranib in addition to chemotherapy had greater tumour shrinkage than those treated by chemotherapy plus placebo (66% versus 42%). There was also a modest but statistically significant increase in median progression-free survival (35 versus 30 weeks). There was no statistically significant difference in median overall survival.

One month into treatment, VEGF receptor 2 levels in blood were more likely to be reduced in cediranib group (median change in log10 VEGFR-2 from baseline 0.036 versus 0.067).

Side-effects, particularly raised blood pressure and diarrhoea were increased in patients taking cediranib and were treated with standard medication.

Targeting the tumour blood supply seems to be a promising way to increase the effectiveness of chemotherapy in cervical cancer, Symonds says. "Recurrent or metastatic cervix cancer is really difficult to treat with a low response rate and poor survival. This study has opened up a new avenue of investigation for a difficult-to-treat cancer."

The researchers are now conducting an individual patient analysis to correlate response to chemotherapy with the fall in VEGFR receptor levels in the blood. They are also looking at other tumour biomarkers that may have been reduced by cediranib.

Commenting on the study, Dr Andres Poveda, Head of the Gynecological Oncology Clinic at Fundación Instituto Valenciano de Oncología, Valencia, Spain, who was not involved in the research, said the CIRCCa study is the second recent trial to show the benefit of adding an antiangiogenic drug to chemotherapy in cervical cancer.

"The impact on progression-free survival is important, and other trial

objectives were reached, such as response rate," Poveda said.

Poveda also noted that recent years have been positive for the treatment of cervical cancer. "For two decades, advances in treatment for patients with advanced cervical cancer had been slow and scarce," he said. "Between 1989 and 2009, modifications of chemotherapy regimens resulted in an increased survival rate of just four months. Then the first study to include an antiangiogenic drug, bevacizumab, obtained spectacular results, offering a survival benefit of four months in one study—which is the equivalent to that obtained over the previous 20 years."

"The FDA recently approved the use of bevacizumab as it completely changed clinical practice," Poveda added. "We are now waiting for phase III results to confirm the favorable predictions of this treatment with cediranib."

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