

EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY MADRID, SPAIN, 26–30 SEPTEMBER

Adding cediranib to chemotherapy improves outcomes in patients with advanced cervical cancer

Adding the experimental vascular endothelial growth factor (VEGF) receptor tyrosine kinase inhibitor cediranib to standard chemotherapy improves progression-free survival in patients with metastatic or recurrent cervical cancer, according to results from a phase II trial.

Around 70% of women treated for cervical cancer are cured with either surgery or chemoradiotherapy but those with recurrent or secondary cancer currently have a very poor outlook – survival is generally less than 1 year.

The phase II CIRCCa trial randomized 69 women with relapsed or metastatic cervical cancer to conventional chemo-

therapy with carboplatin plus paclitaxel with either cediranib or placebo. Patients treated with cediranib showed greater tumour shrinkage (66%) than those given placebo (42%). They also showed a modest but statistically significant improvement in median progression-free survival (35 *vs* 20 weeks) but no difference in median overall survival. Side effects, particularly raised blood pressure and diarrhoea, were increased in patients taking cediranib and were treated with standard medication.

One month into treatment, VEGF receptor 2 levels in blood were more likely to be reduced in women treated with cediranib (median change in

log₁₀ VEGFR-2 from baseline 0.036 *vs* 0.067).

Targeting the tumour blood supply seems to be a promising way to increase the effectiveness of chemotherapy in cervical cancer, suggested lead research-

**Professor Paul Symonds,
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er Professor Paul Symonds, from the Department of Cancer Studies and Molecular Medicine at the University of Leicester, UK. ‘Cervical cancers with a well-developed blood supply can have a particularly bad outcome. Cediranib blocks the cell surface receptor VEGF, which stimulates the growth of new blood vessels to feed the growth of tumours.’

He added: ‘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.’

Commenting on the study, Dr Andres Poveda, Head of the Gynecological Oncology Clinic at Fundación Instituto Valenciano de Oncología, Valencia, Spain, noted that the CIRCCa study is the second recent trial to show the benefit of adding an antiangiogenic drug to chemotherapy in cervical cancer. The first study, which used bevacizumab, showed a survival benefit of 4 months. ‘The FDA recently approved the use of bevacizumab as it completely changed clinical practice,’ he said. ‘We are now waiting for phase III results to confirm the favourable predictions of this treatment with cediranib.’

Susan Mayor

Symonds P, Grouley C, Davidson S et al (2014) CIRCCa: A randomised double blind phase II trial of carboplatin-paclitaxel plus cediranib versus carboplatin-paclitaxel plus placebo in metastatic/recurrent cervical cancer. (CRUK Grant Ref: C1256/A11416). Abstract LBA25_PR

Abiraterone acetate increases survival in chemotherapy-naïve metastatic prostate cancer

Data from the final analysis of the phase 3 study COU-AA-302 show that abiraterone acetate (Zytiga) plus low dose prednisolone significantly prolongs overall survival with a median life extension of 4.4 months.

The study involved men with metastatic castration-resistant prostate cancer who have not previously been treated with chemotherapy (median overall survival 34.7 *vs* 30.3 months with placebo plus prednisolone; hazard ratio=0.81, 95% confidence interval=0.70–0.93, *P*=0.0033), after a median follow-up of more than 4 years (Ryan et al, 2014).

The final analysis is the first to demonstrate a statistically significant improvement in overall survival in this study. This is particularly noteworthy as men in both treatment arms received other subsequent therapy, including 44% of men in the placebo plus prednisolone arm who subsequently received abiraterone plus prednisolone. The treatment effect with abiraterone was more pronounced when adjusting for 44% of prednisolone patients who crossed over to abiraterone (hazard ratio = 0.74).

Dr Alison Birtle, Consultant Clinical Oncologist at the Rosemere Cancer Centre,

Royal Preston Hospital, said: ‘This study has ... now shown that treatment with abiraterone can also add more than 4 months additional survival in these patients. The availability of a treatment option that can both maintain quality of life and also increase survival is a very welcome development.’

Ryan CJ, Smith MR, Fizazi K et al (2014) Final overall survival (OS) analysis of COU-AA-302, a randomized phase 3 study of abiraterone acetate (AA) in metastatic castration-resistant prostate cancer (mCRPC) patients (pts) without prior chemotherapy. Abstract 753O. www.webges.com/cslide/library/esmo/browse/search/pBC#9B9k02Lm (accessed 31 October 2014)

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Chemotherapy and radiotherapy during pregnancy have no ill effects on offspring

Children exposed to chemotherapy or radiotherapy while in the womb suffer no long-term ill effects on neurocognitive or cardiac development, show results from studies reported at ESMO.

Oncologists can be hesitant to give chemotherapy to treat cancer in women who are pregnant because of lack of knowledge about the impact on the unborn child. To find out more, researchers studied 38 children prenatally exposed to

chemotherapy who were listed on the International Network for Cancer, Infertility and Pregnancy Registry (Amant et al, 2014a). They were matched with 38 control children and measures of mental development and cardiac health assessed.

Results showed no difference between the two groups of children at a median age of almost 2 years. Neurocognitive development, measured by the Mental Development Index,

was in the normal range for both groups, as were cardiac dimensions and functioning.

‘When chemotherapy is administered after the first trimester of pregnancy, we cannot discern any problems in the children,’ said lead author Dr Frédéric Amant, Professor of Medicine, from University Hospitals Leuven in Belgium. ‘Fear about the risks of chemotherapy administration should not be a reason to terminate a pregnancy, delay cancer treat-



Dr Frédéric Amant, Professor of Medicine, University Hospitals Leuven, Belgium

ment for the mother, or to deliver a baby prematurely.’

A second study of 16 children and 10 adults listed on the registry (Amant et al, 2014b) gave similarly reassuring results on the exposure to radiotherapy in utero. This first long-term follow-up study of prenatal medical radiation treatment showed that neuropsychological, behavioural and general health outcomes were within normal ranges for those exposed to radiotherapy. One child had a severe cognitive delay but had been exposed to a relatively low dose of radiotherapy and the problem was attributed to other pregnancy-related complications.

Susan Mayor

Amant F, Vandenbroucke T, Verheecke M et al (2014a) 268PD_PR Cancer during pregnancy: A case-control analysis of mental development and cardiac functioning of 38 children prenatally exposed to chemotherapy. www.webges.com/cslide/library/esmo/browse/itinerary/478/2014-09-27#9fad (accessed 29 October 2014)

Amant F, Vandenbroucke T, Verheecke M et al (2014b) LBA49_PR - Long-term neuropsychological and cardiac follow-up of children and adults who were antenatal exposed to radiotherapy. www.webges.com/cslide/library/esmo/browse/itinerary/478/2014-09-27#9fad (accessed 29 October 2014)

Pertuzumab plus trastuzumab increases survival in patients with HER2-positive breast cancer

Adding pertuzumab to trastuzumab and chemotherapy increases overall survival by 16 months in women with HER2-positive metastatic breast cancer, according to final results from the CLEOPATRA trial (Swain et al, 2014).

The phase III trial randomized 808 patients with HER-2 positive metastatic breast cancer to trastuzumab and docetaxel plus pertuzumab or placebo. Results showed significantly longer median overall survival in patients treated with the pertuzumab combination (56.5 months) than those treated without (40.8 months).

‘The median overall survival of 56.5 months is unprecedented in metastatic breast cancer. This confirms a regimen of pertuzumab plus trastuzumab and chemotherapy as the first-line standard of care for these

patients,’ said lead author Dr Sandra Swain, from the Medstar Washington Hospital Center, Washington, USA. She added: ‘Many of us work all our careers in cancer research to present data like this.’

Pertuzumab and trastuzumab both target the HER2 receptor, but pertuzumab prevents the HER2 receptors from pairing with other HER receptors, while trastuzumab activates the body’s immune system and suppresses HER2 signalling to target and destroy a tumour.

Commenting on the study, Dr Giuseppe Curigliano, Director of the Division of Experimental Therapeutics in Milan, Italy, said: ‘The CLEOPATRA trial changes clinical practice. We now have a new standard of care for patients with metastatic HER2-positive breast cancer.’

He noted that similar efficacy results have been reported in the neoadjuvant setting. The NeoSphere trial found that dual targeting with pertuzumab and trastuzumab plus chemotherapy significantly improved the percentage of patients with early HER2-positive breast cancer who had a pathological complete response. The potential of dual targeting in the adjuvant setting is being investigated in the ongoing APHINITY trial, which is comparing dual targeting with pertuzumab and trastuzumab *vs* trastuzumab alone.

Susan Mayor

Swain S, Kim S, Cortes J et al (2014) Final overall survival (OS) analysis from the CLEOPATRA study of first-line (1L) pertuzumab (Ptz), trastuzumab (T), and docetaxel (D) in patients (pts) with HER2-positive metastatic breast cancer (MBC). Abstract 350O_PR