Immunotherapy prolongs survival in recurrent, persistent or metastatic cervical cancer

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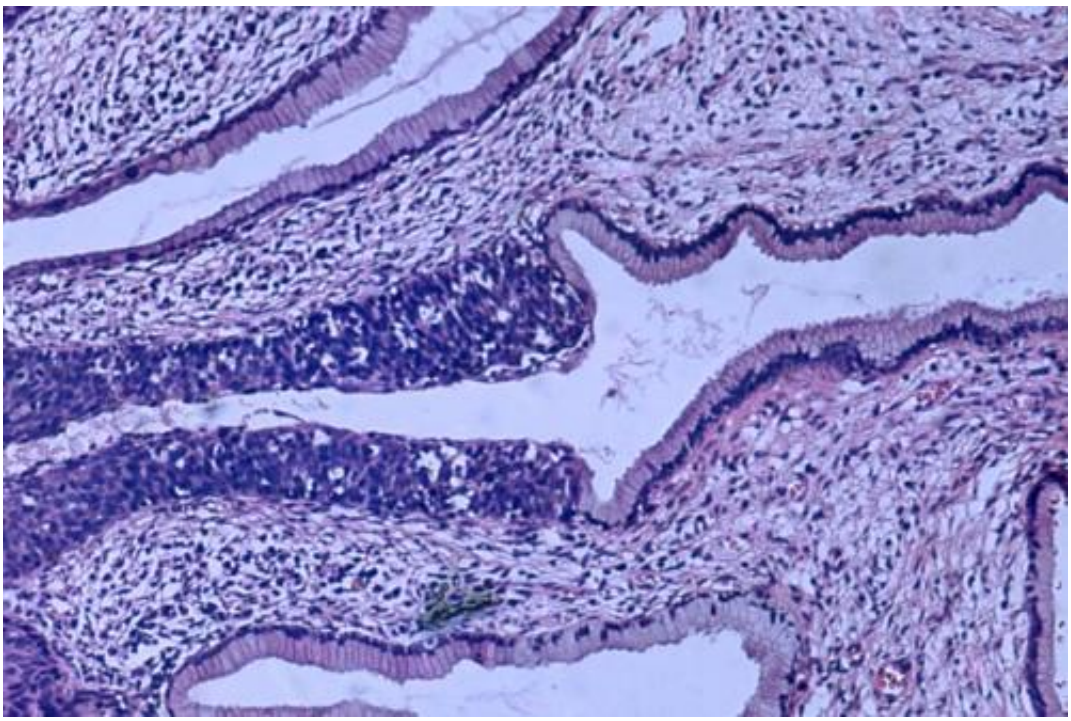

High grade dysplasia (carcinoma in situ) in the uterine cervix. The abnormal epithelium is extending into a mucus gland to the left of centre. This disease can progress to invasive cancer (squamous cell carcinoma) of the cervix. Credit: Haymanj/public domain

The addition of immunotherapy to standard first-line treatment extends survival by eight months for patients with recurrent, persistent or

metastatic cervical cancer, according to late breaking results from the KEYNOTE-826 study presented at the ESMO Congress 2021.

Cervical cancer is a global problem, with more than 600,000 new cases and approximately 340,000 deaths in 2020. In women aged 15 to 44 years, it is the second most frequent cancer and the second cause of cancer death.

Commenting on today's results, Dr. Antonio González-Martín, Cancer Centre Director, Clínica Universidad de Navarra, Madrid, Spain said: "Patients with persistent, recurrent or metastatic cervical cancer have suffered historically from a dismal prognosis with an overall survival no longer than 12 months. The KEYNOTE-826 study is a new milestone, demonstrating a very relevant increment in the overall survival of patients with this condition and, for the first time, showing that incorporating immunotherapy into front line treatment can change the natural history of the disease."

The trial randomly allocated 617 women to immunotherapy (pembrolizumab) or placebo. Both groups also received chemotherapy (paclitaxel plus the doctor's choice of cisplatin or carboplatin) and they could be given bevacizumab at the discretion of their doctor. Adding pembrolizumab reduced the risk of death by 33% and lowered the likelihood of disease progression or death by 35%. The most common side-effects were anemia (30.3% in the pembrolizumab group versus 26.9% in the placebo group) and low concentration of white blood cells (12.4% versus 9.7%, respectively).

Study author Prof. Nicoletta Colombo, Director of the Gynaecology Programme, European Institute of Oncology, Milan, Italy said: "Previous studies showed that adding anti-angiogenesis therapy with bevacizumab to chemotherapy prolonged survival by 3.7 months over chemotherapy alone. KEYNOTE-826 was the first study to explore the addition of

PD-1 inhibition to chemotherapy with or without bevacizumab, and benefits in survival and disease progression were observed regardless of expression of PD-L1, a protein related to immunomodulation. Side-effects with the new combination therapy were manageable and the observed adverse events were as expected based on previous data on the individual drugs."

Colombo noted that the benefit of the novel combination therapy was seen in those who received bevacizumab and in those who did not receive bevacizumab. But she added: "The study was not designed to statistically compare outcomes between these subgroups since bevacizumab treatment was not randomized but was left to the physician's discretion. Some common complications of recurrent/persistent or metastatic cervical cancer are contraindications for the use of this drug. In this study, 63% of patients received bevacizumab. The trial indicates that bevacizumab should be used with pembrolizumab when it is safe. For patients who cannot use bevacizumab, adding pembrolizumab to chemotherapy alone still has clinically meaningful benefit."

"This is a practice-changing study," highlighted González-Martín. "The data are so solid in terms of increment in overall survival that this combination should be considered the new standard of care for women with persistent, recurrent or metastatic cervical cancer. The backbone systemic therapy used with the immunotherapy (paclitaxel with cisplatin or carboplatin, with or without bevacizumab) reflects the standard treatment options in the real world, making the results easy adaptable. One potential limitation will be how to adopt this innovation in resource-limited healthcare systems."

While the findings could help many patients, González-Martín pointed out that: "One of the greatest challenges is to select the correct population for a new therapy, or at least the patients likely to obtain the

most benefit. PD-L1 may be a potential biomarker, but other biomarkers are needed."

Colombo and González-Martín agreed that the next step for researchers is to evaluate the impact of immunotherapy in patients with earlier stages of cervical cancer. Ongoing trials adding immunotherapy to standard chemoradiotherapy in women with locally advanced cervical cancer include the CALLA study and the KEYNOTE-A18/ENGOT-cx11/GOG-3047 study.

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