# First new drug in years reduces recurrence in high risk HR+ early breast cancer

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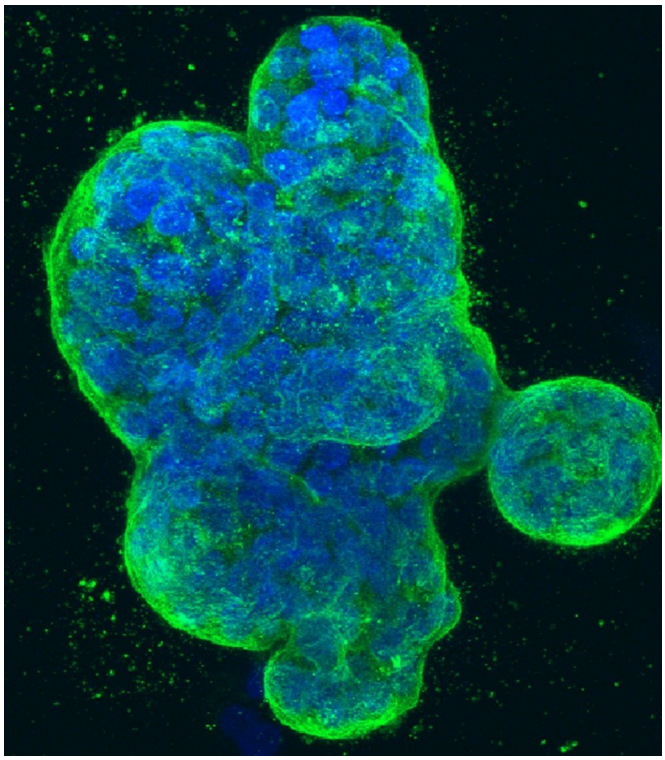

Three-dimensional culture of human breast cancer cells, with DNA stained blue and a protein in the cell surface membrane stained green. Image created in 2014 by Tom Misteli, Ph.D., and Karen Meaburn, Ph.D. at the NIH IRP.

Adding abemaciclib to hormonal therapy reduces the risk of cancer recurrence by 25% in patients with high-risk early hormone receptor positive (HR+) human epidermal growth factor receptor 2 negative (HER2-) breast cancer, according to results from a study at ESMO 2020.

"This is the first time in more than 20 years that we have seen an advance in the adjuvant treatment of this form of breast cancer," said lead author Prof Stephen Johnston, from the Royal Marsden Hospital NHS Foundation Trust, London, UK. He explained that hormone receptor positive breast cancer is the commonest form of breast cancer, affecting 70% of patients, with most being diagnosed with early disease.

"Many of these patients can be cured with currently available treatments: surgery, radiotherapy, chemotherapy and hormone treatment. But about 20% have high-risk disease and will develop a recurrence either locally in the breast or elsewhere in the body over the first ten years of treatment," he explained.

"These patients with high-risk early breast cancer show a degree of resistance to hormone therapy, relapsing early despite everything we currently give them," said Johnston. "CDK4/6 inhibitors, such as abemaciclib, have transformed the way we treat metastatic breast cancer over the last few years, overcoming primary endocrine resistance and improving survival. So it was an obvious step to see whether adding abemaciclib to hormone treatment in patients with high-risk early breast cancer could reduce the risk of their cancer returning."

The international phase 3 monarchE study included 5637 patients with HR+ HER2- early breast cancer with clinical and/or pathological risk factors putting them at high risk for relapse. After completing their primary treatment they were randomised on an open-label basis to abemaciclib (150mg twice daily for two years) plus endocrine therapy or endocrine therapy alone.

"We found a 25% reduction in recurrence of cancer with the first two years when abemaciclib was added to hormone therapy compared to hormone therapy alone," reported Johnston. During this time 11.3% of patients in the control group had a relapse of their cancer compared to 7.8% of those in the abemaciclib group, an absolute difference of 3.5% which translates to a 25.3% reduction in risk. Most of the reductions occured in sites of distant metastases, especially to liver and bone.

"This is the first study to show that adding a CDK4/6 inhibitor to endocrine therapy significantly improves invasive disease free survival in the adjuvant setting," said Giuseppe Curigliano, Associate Professor of Medical Oncology at the University of Milan, Italy, and Chair of the ESMO Guidelines Committee.

"This is a very important trial and the findings will change practice. Once approved for high risk HR+ HER2- early breast cancer the new standard of care for these patients will be to add two years of abemaciclib to endocrine therapy," he suggested.

Curigliano suggested it would have been interesting to have included genetic signature into the assessment of patients at high risk, in addition to number of positive lymph nodes, tumour size, histologic grade and Ki-67 (a marker of proliferation). Johnston said that tissue and plasma samples had been collected from all of the study participants for translational research that will include looking at genomic signatures and response to abemaciclib.

"The safety data are important, particularly the number of patients treated with abemaciclib who had to discontinue or required dose reductions due to side-effects," said Curigliano. A total of 463 (16.6%) of patients discontinued abemaciclib due to adverse events, most commonly diarrhea; 306 of these continued on endocrine therapy. The protocol allowed dose reduction from 150 to 100mg twice daily if required. He noted: "Adherence to treatment will be an important issue to be considered in the real life population of patients when this treatment is approved and used in clinical practice."

Curigliano added, "For the future it will be important to understand if we can potentially spare chemotherapy in this group of patients treated with a CDK4/6 inhibitor. This would need to be investigated in a randomised clinical trial."

**More information:** Abstract LBA5_PR 'Abemaciclib in high risk early breast cancer' will be presented by Stephen Johnston in the Presidential Symposium II on Sunday, 20 September 2020. *Annals of Oncology*, Volume 31 Supplement 4, September 2020.

Stephen R. D. Johnston et al. Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2?, Node-Positive, High-Risk, Early Breast Cancer (monarchE), *Journal of Clinical Oncology* (2020). DOI: 10.1200/JCO.20.02514

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