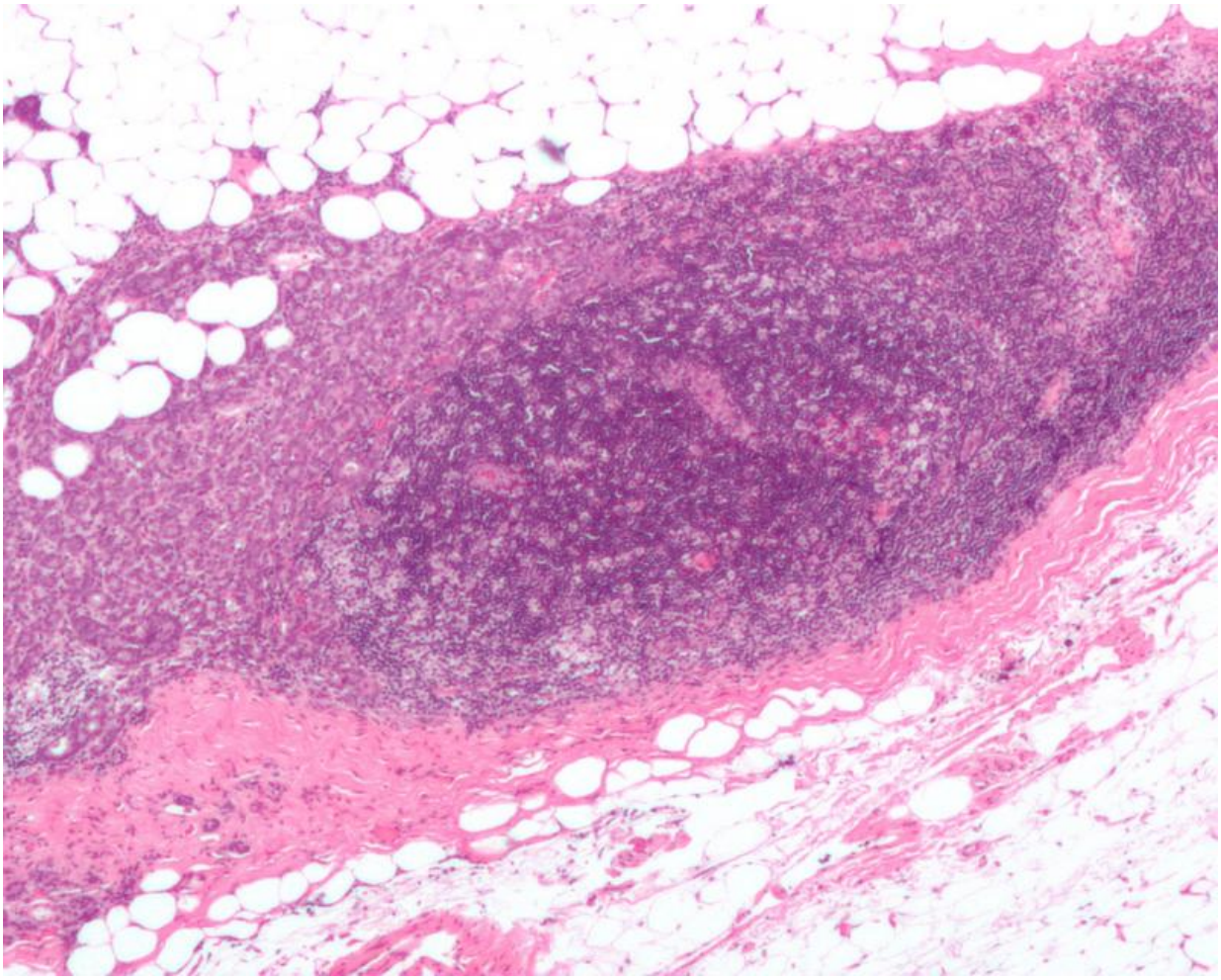
Asian women with endocrine-resistant breast cancer benefit from combination therapy

December 18 2015



Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumour beyond the lymph node. Credit: Nephron/Wikipedia

Data collected in Japanese and Korean patients included in the global PALOMA3 trial provides evidence that combining palbociclib with fulvestrant is an effective strategy to overcome endocrine resistance in women with hormone receptor positive (HR+), HER2 negative (HER2-) advanced breast cancer. The analysis of efficacy and safety of the combined therapy in an Asian population was presented at the first ESMO Asia 2015 Congress in Singapore, and results are in line with those reported in all patients (both Asian and non-Asian) earlier this year.

Endocrine resistance is a major clinical issue that makes advanced breast cancer more difficult to treat. Hormone therapy is generally well tolerated and an easy-to-administer option for breast cancer, with demonstrated benefits in patients whose tumours express hormone receptors (HR), particularly the HR+/HER2- subgroup. The ideal option for patients is to be on one endocrine therapy after another, as long as the disease responds or remains unchanged. "However, unavoidably, resistance develops in almost all advanced patients a median ten months after the first-line hormonal agent is administered, and a much shorter median time after the second- or third-line hormonal agents, eventually driving patients to switch to the more toxic chemotherapy," one of the study authors, Dr. Jungsil Ro, Center for Breast Cancer at the National Cancer Center, Goyang, Korea, said.

Palbociclib is an orally active selective inhibitor of the CDK 4/6 growth signal that blocks cell proliferation and cellular division. It has high activity in HR+ breast cancer cell lines and is synergistic in combination with different endocrine therapies.

The PALOMA3 trial assessed the safety and efficacy of the combination of palbociclib and fulvestrant in premenopausal and postmenopausal women with HR+/HER2- advanced breast cancer that progressed during prior endocrine therapy. By March 2015, 105 Asian patients in Korea

and Japan were randomised, 74 to receive palbociclib plus fulvestrant and 31 to placebo plus fulvestrant. "For postmenopausal women, the study definitely showed positive results —-progression-free survival more than doubled. Patients suffered from more adverse events in the palbociclib arm, specifically haematologic toxicity, which was easily manageable. "For premenopausal women, the outcome looks as promising as in postmenopausal women, although the numbers are quite small for definitive conclusions," Ro said.

The analysis containing Asian patients nicely confirms that combining palbociclib with fulvestrant is a promising therapeutic approach. "Although median progression-free survival in Asian patients was not reached for the drug combination, it is a reasonable therapeutic option in this population," ESMO spokesperson, Dr. Fabrice André, Institut de Cancérologie Gustave Roussy, Villejuif, France, said. "Palbociclib shows clinical activity with modest toxicity. Although the difference in toxicity profile between Asian and non-Asian populations is really interesting, no clear explanation could be made from this study because of the existing differences reported in non-Asian and Asian patients."

To support the superiority of this drug combination over the hormonal agent alone, a longer follow-up for the overall survival result is needed, Ro said. "So far, we do not have predictive biomarkers to select patients for palbociclib in addition to fulvestrant other than the subtype itself, HR+/HER2- breast cancer. We also need to see that other results from the first-line hormone therapy with palbociclib clinical trial verify the efficacy of the drug, but a longer time is needed to have these results."

Commenting on the results, ESMO spokesperson Dr. Evandro de Azambuja, medical director of the Br.E.A.S.T. Data Centre, Jules Bordet Institute in Brussels, Belgium, not involved in the study, said: "Targeting CDK4/6 represents a further promising option to address endocrine resistance. Other mechanisms of resistance to endocrine

therapy include the activation of tyrosine kinase signalling, the up-regulation of the PI3 kinase mammalian target of rapamycin (mTOR) signalling and, lastly, the mutation of ESR1." On the basis of the impressive results from the phase II PALOMA-2 trial, the combination of palbociclib plus endocrine therapy has been approved by U.S. Food and Drug Administration (FDA). "These results should help in the registration of the combinated therapy in Asian countries too," he said.

More information: Abstract 53O_PR, Efficacy and safety of palbociclib plus fulvestrant in Asian women with hormone receptor-positive (HR+)/human epidermal growth factor-2 negative (HER2-) metastatic breast cancer (MBC) that progressed on prior endocrine therapy (ET) cslide.ctimeetingtech.com/libr … rowse/itinerary/5225

Provided by European Society for Medical Oncology