Switch of breast tumors to HER2-low in recurrence may provide greater therapeutic options

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	Relapse							
	HER2-0		HER2-low		HER2-positive		Total	
Primary tumor	n	%	n	%	n	%	n	%
HER2-0	134	23%	85	15%	13	2%	232	40%
HER2-low	78	14%	109	19%	9	2%	196	34%
HER2-positive	6	1%	23	4%	118	20%	147	26%
Total	217	38%	218	38%	140	24%	575	100%

This table is part of abstract 4MO_PR by Federica Miglietta. Credit: ESMO

The finding that breast tumours can evolve to express low HER2 potentially widens the number of patients who can benefit from new investigational agents, typically novel antibody-drug conjugate therapies, that are currently in clinical trials for HER2-low tumours.

The first study of its kind exploring how breast cancers change from the primary to the recurrent tumour has revealed that nearly 30% of breast cancer patients convert from, or to, human epidermal growth factor receptor (HER)2-low status. Specifically, the study found that 14% of triple-negative breast cancers with HER2-negative expression (also

referred to as HER2-0) in the primary tumour converted to HER2-low expression in the recurrent tumour possibly offering an option to such hard-to-treat tumours.

Traditionally, breast cancers are categorised as: hormone receptor positive (HR+)/HER 2-negative, (also known as luminal-like), HER2-positive, or triple negative (negative for oestrogen receptors, progesterone receptors, and excess HER2 protein). HER2-low refers to HER2-negative tumours with low HER2 biomarker expression. About half of breast cancers classified as HER2-negative show low HER2 expression.

Presenting the findings at this year's ESMO Breast Cancer Virtual Congress is Dr. Federica Miglietta, School of Oncology, University of Padua, Italy. "The results provide a whole new insight on how HER2-low tumours might evolve as a subgroup, possibly challenging the current dichotomy between HER2-positive and HER2-negative breast cancer," she said. "Our findings stress the importance of re-testing HER2 expression on tumour relapse since it might provide the option of new therapeutic opportunities, currently in a trial, and hopefully in the near future, in the clinic." Several clinical trials are ongoing in HER2-low breast cancer.

In total, 29% of recurrent breast cancer biopsies showed conversion either from, or to, HER2-low expression. In primary tumours and relapse tumours, HER2-low expression was seen in 34% and 38% of tumours, respectively. A total of 15% HER2-negative tumours switched to HER2-low tumours, and 14% HER2-low switched to HER2-negative.

The study also confirmed that HER2-low expression was more frequent in HR+/HER2-negative tumours compared to triple negative tumours (47% vs 36% on primary tumour samples, 54% vs 36% on relapse samples). Plus, the switch from HER2-negative to HER2-low in primary

to recurrent tumours was 21% vs 14% in luminal-like and triple negative, respectively.

Commenting on the findings, Professor Aleix Prat, Head Medical Oncology, at the Hospital Clinic of Barcelona, Spain said: "These changes on HER2-low levels are substantial. There could be a biological rationale for this, or a technical one, given that there is currently no standardisation of how to determine levels of the HER2 biomarker in metastatic biopsies, which could be biopsied from skin, liver or bone and give different results."

"We need to work out how the HER2 status determines response to therapies—is it the HER2 status in the primary tumour, or in the metastatic biopsy that is important? Maybe some patients have HER2-low expression in metastatic tumours and now respond when they didn't previously, and this might change again over time and further relapses."

"This all speaks to a much greater need to biopsy metastatic tumours. Importantly, we need to determine who will benefit from treatments for HER2-low, because patients will be asking about this in the clinic soon if trial results are positive," said Prat.

More information: Abstract 4MO_PR 'HER2-low breast cancer: evolution from primary breast cancer to relapse.' will be presented by Federica Miglietta during the Mini Oral Session 2 on Saturday, 8 May, 12:45-14:00 (CEST). Annals of Oncology, Volume 32, Supplement 2, May 2021

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