LORELEI: Taselisib boosts breast tumor shrinkage

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Adding taselisib to letrozole before surgery significantly improved outcomes for patients with early breast cancer that was both estrogen receptor positive and HER2-negative (ER+/HER2-) according to results of the LORELEI trial, presented at the ESMO 2017 Congress in Madrid.

"We were able to detect a reduction in tumor size after only 16 weeks of treatment, compared to patients who received letrozole plus placebo," said study investigator Dr. Cristina Saura, from Vall d'Hebron University Hospital in Barcelona, Spain. "Any decrease in tumor measurements is something positive for patients because this means the drug has had activity against their tumor in a short period of time."

LORELEI is the first randomized study to demonstrate a significant increase in objective response rate (ORR) upon treatment with a PI3K selective inhibitor in this population of patients, noted the authors of the study, which was conducted in 85 sites across the world.

Taselisib is an alpha specific PI3K inhibitor which blocks a signalling pathway known as PIK3 that promotes cancer growth.

"The alpha-specific story is important, because other PI3K inhibitors have had only a small effect, and the benefit-risk ratio was less favourable," noted Prof. Sibylle Loibl, Chair of the German Breast Group, who was not involved in the study but provided comment for ESMO. "In general it is believed that alpha specific inhibitors will be

more efficacious and less toxic than others".

LORELEI included 334 postmenopausal patients with ER+/HER2-, stage I-III, operable early breast cancer.

All of them had tissue analysed for PIK3CA mutant cancer cells, and were randomised to receive letrozole plus either a placebo (n=168) or taselisib (n=166) for 16 weeks in order to shrink their tumour before surgery.

The study had two co-primary endpoints: one was ORR which was assessed by measuring the tumour size with magnetic resonance imaging; the second was the pathologic complete response (pCR) rate, which is a measure of the presence of cancer cells at the site after the tumour is surgically removed.

The study showed that ORR was better in patients who received taselisib compared to placebo (50% versus 39.3%, odds ratio [OR] 1.55, 95% CI 1.00-2.38, P=0.049), but there was no significant difference between the groups for pCR.

Among the 152 patients who had PIK3CA mutant cancer cells detected at baseline, taselisib worked particularly well, with 56.2% showing an ORR compared to 38% of patients who received placebo (odds ratio [OR] 2.03, 95%CI 1.06-3.88, p = 0.033).

"For me, the main message is that even though all patients seems to derive some benefit from taselisib, those who had this mutation seemed to derive more benefit," said Saura.

Discontinuation and reduced dosing of taselisib occurred in 10.8% and 11.4% of patients, respectively. The most common serious (grade 3 and 4) adverse events associated with the drug included gastrointestinal

disorders (7.8%), infections (4.8%), skin / subcutaneous tissue disorders (4.8%), vascular disorders (3.6%), and metabolism and nutrition disorders (3.6%) including hyperglycemia (1.2%).

Although there was one sudden death in the taselisib-treated group, the study investigators considered it unrelated to the drug.

Loibl concluded that "these are the first data indicating that the addition of an alpha specific PI3K inhibitor might work in addition to an endocrine therapy in HER2-/Hr+ breast cancer. More data from LORELEI as well as data from the Phase III studies in metastatic breast cancer need to be awaited for evaluating the role of PIK3 Kinase inhibitors in breast cancer."

More information: Abstract LBA10_PR 'Primary results of LORELEI: a phase II randomized, double-blind study of neoadjuvant letrozole (LET) plus taselisib versus LET plus placebo (PLA) in postmenopausal patients (pts) with ER+/HER2-negative early breast cancer (EBC)' will be presented by Dr. Saura during Proffered Paper Session 'Breast cancer, early stage' on Friday, 8 September 2017, 14:00 to 15:30 (CEST) in Pamplona Auditorium.

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