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Study finds ribociclib improves progression-free survival for women with metastatic breast cancer

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In a randomized, Phase III trial led by researchers at The University of Texas MD Anderson Cancer Center, ribociclib, in combination with the aromatase inhibitor letrozole, dramatically improved progression-free survival (PFS) of post-menopausal women with hormone receptor-positive metastatic breast cancer, compared to the hormone therapy alone.

The study found a 44 percent improvement in PFS with ribociclib, a CDK4/6 inhibitor, and letrozole as a front line therapy. Gabriel Hortobagyi, M.D., professor of Breast Medical Oncology, presented the findings at ESMO 2016 Congress, and is the corresponding author of the *New England Journal of Medicine* paper.

According to the American Cancer Society, 246,660 women will be diagnosed with breast cancer in 2016, and 40,450 women will die from the disease. More than two-thirds of all breast cancers are hormone dependent, says Hortobagyi.

"These findings have the potential to impact tens of thousands of women each year," says Hortobagyi, the study's principal investigator. "At some point, all breast cancers become resistant to endocrine therapy, so reversing, preventing or delaying that resistance is a major unmet need in this population.

"Women with metastatic disease will be on some therapy for the rest of their lives, and it's paramount that we delay the progression of their disease for as long as possible," continues Hortobagyi.

The international double-blind study, MONALEESA-2, enrolled 668 post-menopausal women with advanced breast cancer at 223 trial sites in 29 countries. They were randomized to receive either ribociclib and letrozole, or letrozole and placebo. None had been previously treated for their advanced disease.

The study's primary endpoint was PFS; secondary endpoints included overall survival, overall response rate (ORR) and safety. The median follow up of patients was 15.3 months.

The median PFS was not reached in the study arm at data cut-off, compared to 14.7 months in the placebo arm. In those with measurable disease who received ribociclib, the ORR was 52.7 percent, compared to 37.1 percent in those who received letrozole alone.

Serious adverse events occurred in less than five percent of patients overall, but side effects were higher in the ribociclib arm, including neutropenia (59 percent vs, 1 percent) and leukopenia (21 percent vs. 1 percent). Most could be managed through dose interruption and reduction, says Hortobagyi. The discontinuation rate of the investigative drug was 7.5 percent, compared to 2.1 percent in the placebo cohort.

These findings could represent a paradigm shift in the future medical management of this patient population.

"When I started my career at MD Anderson in the 1970s, the median survival for women with metastatic breast cancer was just under two years. Now, with this discovery and other advances in the field, we can increasingly treat this as a chronic disease," says Hortobagyi. "Also,

because we are able to delay or avoid chemotherapy, the quality of these women's lives has improved dramatically."

As follow-up, adjuvant trials with ribociclib are now being designed, says Hortobagyi. Ribociclib will also be studied in younger, pre-menopausal women with breast cancer.

Ribociclib is developed by Novartis, who also sponsored the trial. The drug received Breakthrough Therapy Designation by the Food and Drug Administration in August 2016.

Regarding relevant disclosures, Hortobagyi receives research support from Novartis and has served as a consultant.

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