SABCS15: Promising phase 1 results lead to phase 2 for ONT-380 in HER2+ breast cancer

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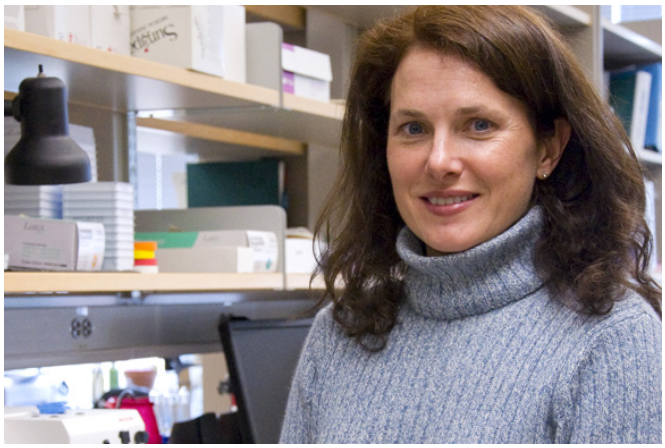

Virginia Borges, M.D., M.M.Sc. and colleagues present phase 1b results showing promise of ONT-380 against HER2+ breast cancer, especially against brain metastases associated with disease. Credit: University of Colorado Cancer Center

Results of an ongoing phase 1b clinical trial presented today at the 2015 San Antonio Breast Cancer Symposium show promise of the experimental anti-cancer agent ONT-380 against metastatic HER2+ breast cancer, especially against brain metastases commonly associated with progression of the disease. Of 33 evaluable patients with metastatic HER2+ breast cancer (with and without brain metastases), 19 (58 percent) showed clinical benefit, with 16 achieving at least "stable disease" (i.e. no tumor progression while on trial), of which 11 patients experienced "partial response" (i.e. tumor shrinkage of more than 30 percent). Of 8 patients with brain metastases, 5 achieved at least stable disease, with 2 partial responses and one complete response in which existing brain metastases were undetectable after treatment.

"When you look at the clinical benefit for women previously treated, we've had patients with controlled brain lesions for over six months or a year, which is pretty unheard of," says Virginia Borges, MD, MMSc, director of the Breast Cancer Research Program and Young Women's Breast Cancer Translational Program at the University of Colorado Cancer Center and one of the study's co-principal investigators.

"And they're able to get this benefit by taking a pill that has essentially no side effects for most women," she says.

Results of this ongoing phase I clinical trial (NCT01983501) support the initiation of a phase II clinical trial (NCT02614794), which Borges hopes will start accruing patients by the end of January 2016.

In about 25 percent of the 1-in-8 women who will develop breast cancer during their lifetimes, the HER2 gene creates an abnormal amount of HER2 protein, which acts as a "receptor" for human epidermal growth factor. The presence of more HER2 receptors allows a cell to trap more growth-promoting hormones, which tells the cell to grow in an out-of-control, cancerous way.

ONT-380, invented by Array Biopharma in Boulder, CO and now being developed by Oncothyreon in Seattle, WA, is a small molecule inhibitor of the HER2 growth factor receptor. The drug works by targeting the HER2 "tyrosine kinase" - a link in the chain of communication that allows HER2 receptors to signal the growth of the cell. The fact that it is a small molecule means the drug is able to pass through the blood-brain barrier to act against brain metastases of the disease. HER2+ breast cancer is more likely to affect younger women and also more likely than other breast cancers to metastasize specifically to the brain.

"I don't want to downplay this drug's potential to provide overall control of HER2+ breast cancer, but it's a real game-changer for its specific ability to

control brain metastases. What distinguishes ONT-380 from other players in the field is that you get both," Borges says.

Side-effects were generally mild and included nausea, fatigue, diarrhea, vomiting, thrombocytopenia, AST/ALT elevation, headache, decreased appetite, epistaxis, constipation, and hypokalemia.

"If ONT-380 continues its current trajectory, we hope it could present a real option for controlling brain metastases in HER2+ breast cancer," Borges says.

Provided by University of Colorado Denver