Evaluation of patrimonial/parcitallex/trastuzumab over early standard patcicallex/trastuzumab in stage II, high-risk HER2 positive breast cancer: Results from the neoadjuvant I-SPY 2 TRIAL


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Induction therapy is a monoclonal antibody against HER2. Patrimonial, in combination with parciallex and trastuzumab (PTH), was evaluated for efficacy in the neoadjuvant I-SPY 2 TRIAL in patients with early-stage, high-risk HER2-positive breast cancer.

The control arm was 16 weeks of paclitaxel in combination with trastuzumab (TH) followed by doxorubicin and cyclophosphamide (AC) q3w for 3 cycles and surgery. In the PTH arm, patrimonial was given (q4w × 4 cycles (18mg/kg loading dose followed by 9mg/kg/dose) concurrent with paclitaxel and TH was given (q4w × 4 cycles × 12 weeks) followed by AC q3w.

Methods

Women with tumors ≥2.5 cm were eligible for screening. MP low/HER2 tumors were ineligible. Longitudinal MRI volume reduction from baseline (3 cycles after start of therapy, prior to AC, and prior to surgery) were used to predict pCR for individual patients until their pCR data becomes available. A novel adjusted Bayesian model adjusts for time trends in use to estimate probabilities and assess graduation. Analysis was modified intention-to-treat. Subjects who switched to non-poetic therapy count as non-pCR. Subjects on experimental therapy at time of arm closure are considered non-evaluable. PTH was open to HER2+ patients and was eligible for evaluation in 3 of 10 predefined signatures: all HER2+, HR-HER2+, and HR+HER2+

RESULTS

PTH did not meet criteria for graduation and was stopped at the recommendation of the Safety Working Group and DSMB based on a safety event (Grade 3 bilateral sensorineural hearing loss) observed in one participant.

The participant who developed Grade 3 sensorineural hearing loss 6 days after the 2nd PTH treatment did not receive her after treatment was stopped, and also reported G1 vaginal pain, vulvitis, and vaginal inflammation.

CONCLUSIONS

The I-SPY 2 study aims to assess the probability that investigational regimens will be successful in a phase III neoadjuvant trial. PTH was stopped due to safety concerns, although there was activity in the HR-HER2+ signature. This is the first report of Grade 3 hearing loss associated with patrimonial/parcitallex/trastuzumab.

ACKNOWLEDGEMENTS:

With support from Quantum Leap Healthcare Collaborative, FHI 360 (Grant 28XS197 P00151), Safeway, an Albertsons Company, William K. Bowes, Jr. Foundation, Breast Cancer Research Foundation, UCB, Genentech, and Breast Cancer Research Foundation, OpenChina, Forneola, Illumina, CCS Associates, Berry Consultants, Breast Cancer Research Foundation, American Society of Clinical Oncology, Alliance for Clinical Research Excellence, National Comprehensive Cancer Network, and Breast Cancer Research Foundation. The Association for Clinical Research Excellence (ACRE), American Society of Clinical Oncology, Breast Cancer Research Foundation, American Society of Clinical Oncology, and Alliance for Clinical Research Excellence (ACRE) provided grant support for the I-SPY 2 TRIAL. I-SPY 2 TRIAL data is used at the discretion of the investigators. All investigators and staff are informed about the receipt of these grants.

Disclosure: Investigational agent provided and funding for the I-SPY 2 TRIAL provided by Duke Oncology.