Abstract P1-14-03: The evaluation of trebananib plus standard neoadjuvant therapy in high-risk breast cancer: Results from the I-SPY 2 TRIAL

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Background: I-SPY 2 is a multicenter phase 2 trial using response-adaptive randomization within biomarker subtypes to evaluate a series of novel agents when added to standard neoadjuvant therapy for women with high-risk stage II/III breast cancer. The primary endpoint is pathologic complete response (pCR). The goal is to identify/graduate regimens with ≥85% Bayesian predictive probability of success (statistical significance) in a 300-patient phase 3 neoadjuvant trial defined by hormone-receptor (HR), HER2 status & MammaPrint (MP). Regimens may also leave the trial for futility (< 10% probability of success) or following accrual of maximum sample size (10%< probability of success <85%). We report the results for trebananib, an angiopoietin-1/2-neutralizing peptibody that inhibits interaction with the Tie2 receptor.

Methods: Women with tumors ≥2.5cm were eligible for screening. MP low/HR+/HER2- tumors were ineligible for randomization. Serial MRI scans (baseline, 2 during treatment and pre-surgery) were used in a longitudinal model to improve the efficiency of adaptive randomization. Participants are categorized into 8 subtypes based on: HR status, HER2 status and MP High 1 (MP1) or High 2 (MP2). MP1 and MP2 are determined by a predefined median cut-point of I-SPY 1 participants who fit the eligibility criteria for I-SPY 2. Trebananib was initially assigned to HER2- patients only; once safety data with trastuzumab (H) were obtained, it was also assigned to HER2+ patients. Analysis was intent to treat -- patients who switched to non-protocol therapy were designated non-pCRs.

Results: Trebananib +/-H did not meet the criteria for graduation in any of the 10 signatures tested. When the maximum sample size was reached, accrual ceased. We report probabilities of trebananib +/-H being superior to control and Bayesian predictive probabilities of success in a 1:1 randomized neoadjuvant phase 3 trial for the 10 biomarker signatures, using the final pCR data from all patients.

Signature	Estimated pCR Rate (95% probability interval)		Probability Trebananib Is Superior to Control	Predictive Probability of Success in Phase 3
	Trebananib (n=134)	Control (n=133)		
ALL	0.259(0.16 -0.36)	0.158(0.09-0.23)	0.986	0.564
HR+	0.157(0.05-0.26)	0.115(0.03-0.20)	0.805	0.281
HR-	0.378(0.22-0.53)	0.207(0.11-0.31)	0.991	0.784
HER2+	0.279(0.07-0.49)	0.17(0.04-0.30)	0.879	0.553
HER2-	0.254(0.15-0.36)	0.155(0.08-0.23)	0.981	0.555
MP2	0.342 (0.19-0.49)	0.177(0.07-0.28)	0.991	0.786
HR-/HER2-	0.368 (0.21-0.53)	0.201(0.10-0.30)	0.988	0.771
HR-/HER2+	0.444(0.15-0.74)	0.244(0.07-0.42)	0.926	0.739
HR+/HER2+	0.201(0.01-0.39)	0.135(0.01-0.26)	0.775	0.41
HR+/HER2-	0.143(0.04-0.24)	0.11(0.03-0.19)	0.758	0.248