Prediction of complete pathologic response to veliparib/carboplatin plus standard neoadjuvant therapy in HER2-negative breast cancer: Exploratory protein pathway marker results from the I-SPY 2 TRIAL


George Mason University; University of California, San Francisco; QuantamLeap Healthcare; Mayo Clinic; Berry Consultants, LLC

Abstract

Bayesian Evaluation of total ERBB2 and Cyclin D1 as Biomarkers of
Patient Subset (95% prob. Interval) is Superior of Success
Cutoff Value using reverse phase protein microarray (RPPA) data from pre-treatment LCM purified tumor epithelium.

I-SPY 2 TRIAL – A Prototype for Adaptive Design Trials

I-SPY...The Right Drug, The Right Patient, The Right Time...NOW!

Materials and Methods

Bayesian Evaluation of total ERBB2 and Cyclin D1 as Biomarkers of

Conclusions

- Higher relative measurements of both Cyclin D1 and total ERBB2 expression were identified as negative predictors of response to Veliparib + Carboplatin therapy. Exploratory and retrospective analysis indicated that biomarker stratified and patient populations identified using these two protein markers had substantially increased pCR rates compared to HER2/HER2 status alone, either in expanded “all comers” groups or in the HR- or HER2-positive populations. Verification of this observation in independent study sets is necessary given the small sample sizes analyzed in this study and because no FDR corrections were used in the analysis.

- The observed significance of total ERBB2 expression levels in an HR/HER2-measured HER2- patient populations is intriguing and suggests that more quantitative measurements of HER2 expression than those provided by current technologies provide may improve therapeutic response predictions even in an “off-target” environment.

- Cyclin D1 has a known, lineage-independent role in mediating DNA repair through a direct interaction with RAD51. Decreased expression of Cyclin D1 has been shown to impede homologous recombination-mediated DNA repair mechanisms (Brown et al. Nature 2012 474:233-234). Lower levels of Cyclin D1 may enhance response to PARP inhibition which would be consistent with our observations of lower Cyclin D1 levels being related with response to V/C.

For more information visit visit ispy2.org