Residual cancer burden (RCB) is a secondary response endpoint in the I-SPY 2 TRIAL that is measured and reported by the pathologists at each treatment site phase 2 trial in high risk stage I1/II1 breast cancer (BC) using adaptive randomization to evaluate novel treatment agents added to standard neoadjuvant chemotherapy (NAC) within subsets of breast cancer.

Residual Cancer Burden (RCB)

RCB Index: Continuous measure of extent of residual disease based on:

- Cellularity of fraction of invasive cancer
- Primary tumor bed dimensions
- Number of positive lymph nodes (N)

RCB Index

Continuous measure of extent of residual disease based on:

- Primary tumor bed dimensions (G)
- Cellularity of fraction of invasive cancer (G)
- Size of largest metastasis (G)
- Number of positive lymph nodes (N)

Local site pathologists reported RCB in case report forms.

- We assessed the prognostic (EFS) index (continuous) and RCB classes using Cox proportional hazard modeling in all patients and in subtypes defined by hormone receptor (HR) and HER2 status.

- We compared the distributions of RCB index in the six first regimens that graduated, versus matching controls, using the Wilcoxon rank sum test.

Methods

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Figure 2: Concept diagram showing primary analyses, including:

A. Overall survival
B. Kaplan Meier curves of EFS by RCB Class within subtype
C. Frequency of RCB classes

Association Between RCB and EFS

RCB and EFS Within Subtypes

- Although the distribution of RCB index differs between subtypes, RCB is prognostic within each subtype

Figure 4: RCB and EFS Within Subtypes. (A) RCB index distribution within subtypes. (B) Forest plot showing hazard ratio associated with 1 unit increase of RCB index (relative to pCR) estimated using smoothing splines. (C) Prognostic gradient of increasing RCB index differs by subtype.

Comparison of RCB Index

Graduated vs Control Rx

In those with residual disease (excluding pCR), there was a trend for decreased RCB index with graduating treatments, relative to control therapy, in HR-HER2+ (p = 0.08), but not in HER2- (p = 0.43) or HR-HER2-cancers (p = 0.94).

Conclusions

RCB was independently validated by local site pathologists as a prognostic surrogate in all subtypes of breast cancer.