Amsterdam 70-gene profile (MammaPrint), low risk, even in the HER2 positive subset, identifies a population of women with lower early risk for recurrence despite low response rates to chemotherapy and to HER2 targeted therapy.

P. R. Pollihan1, C. You1, A. DeMichiels2, C. Assal1, J. C. Boughey3, N. Hylton1, E. M. Mangad1, J. Pettermann1, H. S. Rugo4, N. Symmans2, ISPY 2 TRAL Consortium, D. A. Berry5, L. Esserman6

1Georgetown Lombardi Comprehensive Cancer Center, Washington, DC; 2University of California, San Francisco, San Francisco, CA; 3University of Pennsylvania, Philadelphia, PA; 4Mayo Clinic, Scottsdale, AZ; 5University of Texas, MD Anderson Cancer Center, Houston, TX; 6Berry Consultants, LLC, Houston, TX.

Background

It is essential to refine the populations most likely to benefit from targeted chemotherapy combinations. The MINDACT trial showed that molecularly low risk patients, as assessed by the Amsterdam 70-gene profile MammaPrint® (Agenda), did not benefit from chemotherapy. In the ISPY 2 TRAL, MP low risk patients were randomized to hormone therapy alone vs hormone therapy plus letrozole.

Incidence of MP-Low Risk

Of the 1038 enrolled patients by November 2016, 24 patients (2.3%) had molecular low risk disease as defined by MP.

From the 950 patients of the EFS/DRFS cohort, 23 patients had MP low risk (2.4%) and 173 patients were diagnosed with HR+HER2+ breast cancer.

Methods

1038 patients enrolled in ISPY 2 from March 2010 to November 2016 and were available for analysis. All enrolled patients underwent pretreatment biopsies for evaluation of early recurrence risk with MP for risk stratification and with the 80-gene BluePrint® (Agenda) test for intrinsic subtype (primary endpoint of the study is pCR in breast tumors with high node positivity (pt0/is, yp0)). Secondary outcomes included event-free survival (EFS) and distant recurrence free survival (DRFS). Follow-up data was available for 950 patients. Association between pCR and survival outcomes was assessed using the Cox proportional hazard model within the ISPY2 cohort with/without the MP low risk cases; and the EFS and DRFs at 3 and 5 years in the pCR vs non-pCR groups were determined using the Kaplan Meier method.

Outcomes in MP-Low Risk Group

23 eligible for outcome assessment

None achieved pCR

Conclusions

• ISPY2 requires HR+HER2+ to be molecularly high risk
• Only 2.3% of randomized patients have low molecular risk tumors
• 20 Her2+ HR-, 2 Her2+HR+, and 1TNBC
• 11.6% of all HER+ HR+ breast cancer patients enrolled on ISPY2 are MP low

No pCR, only one had a distant recurrence

Outcomes of MP-Low Risk ISPY 2 Patients

Figure 1: Proportion of pCR in the ISPY2 study scheme. Shows low risk overall and in the HR+HER2+ subtype.

Figure 2: Incidence of MP-low risk and overall in the HR+HER2+ subtype.

Figure 3: Summary plot of hormone subgroups and intrinsic subtypes per BluePrint expression.

Figure 4: Bar plot showing outcomes of MP-low risk patients.

The right drug, the right patient, the right time... now.

This presentation is the intellectual property of the author/presenter. Contact them at Paula.R.Pollihan@unet.georgetown.edu for permission to reprint and/or distribute.

ISPY2 trial