A laboratory comparison of the 21-gene assay and PAM50-ROR

M. Alvarado1, C. Prasad2, M. Rothney3, D. Cherbavaz4, A. Sing5, C. Svedman6, C. Markopoulos7

1Helen Diller Comprehensive Cancer Center, University of California, San Francisco, San Francisco, CA, USA
2Pathology, Marin Medical Laboratories, Novato, CA, USA
3Biostatistics, Genomic Health, Inc., Redwood City, CA, USA
4Genomics Laboratory, Genomic Health, Inc., Redwood City, CA, USA
5Medical Affairs, Genomic Health, Inc., Redwood City, CA, USA
6Medical Affairs, Genomic Health International, Geneva, SWITZERLAND
7Department of Surgery, Athens University Medical School, Athens, GREECE

Aim: The 21-gene Recurrence Score® assay is validated in patients (pts) with ER+ early stage invasive breast cancer (EBC) and predicts 10-yr distant recurrence risk and chemotherapy (CT) benefit. The Prosigna® assay (ROR) which uses 46 of the PAM50 genes, was validated in post-menopausal pts with ER+ EBC and is a prognostic assay only. Despite differences in platforms and methods used for development and validation, it is frequently believed that the assay results are interchangeable. We performed a study comparing results from the two assays obtained from the same tumor blocks. The first 40 samples showed a substantial disagreement in how the assays stratify risk.

Methods: 70 sequential BC tumors from Marin Medical Laboratories with sufficient tumor material were selected to be tested with the standard 21-gene assay. Samples were sent to an independent lab where Prosigna ROR and intrinsic subtype was performed with the operators blinded to Recurrence Score results. The first 40 cases were stratified by Recurrence Score (20 low, 10 intermediate and 10 high) Descriptive statistics were used to compare results from the two assays.

Results: Of the 40 initial pts evaluated, 7 were excluded: 3 for low RNA signal in the Prosigna assay and 4 were ER(-) by RT-PCR. Of the 33 remaining cases; 24 ductal, 7 lobular; 27 N(−); 6 N(+). The Spearman rank correlation between Recurrence Score and ROR was 0.40 (95% CI 0.06–0.65). Risk group assignment (low/intermediate/high) between Recurrence Score and ROR was in agreement in 56% (15/27) of N(−). Prosigna classified 19 luminal A, 12 luminal B, 2 HER2 enriched and 0 basal. In both the luminal A and B groups there was a wide range of Recurrence Score results.

Conclusions: Consistent with prior comparisons between the Oncotype DX and other genomic assays, there are substantial differences in the way pts are risk stratified and it cannot be assumed that the assay results are interchangeable. These results suggest that there is only a modest agreement between Recurrence Score results and ROR, with almost half of N(−), ER+ pts classified differently, including ~30% of high ROR pts being classified as low risk by the Recurrence Score with expected minimal if any benefit from chemotherapy. Final data from 70 pts will be presented.

Disclosure: M. Rothney, D. Cherbavaz, and C. Svedman: is an employee of Genomic Health International; C. Markopoulos: has an interest in relation with Genomic Health Inc: Speaker’s Honoraria. All other authors have declared no conflicts of interest.