

Abstract #1421

Title: HER2 Concordance between Central Laboratory Immunohistochemistry, FISH and Quantitative RT-PCR in Intergroup Trial E2197

Authors: FL Baehner, R Gray, B Childs, T Maddala, S Rowley, S Shak, NE Davidson, GW Sledge, LJ Goldstein, JA Sparano, S Badve. UCSF, San Francisco, CA; ECOG, Indianapolis, IN; Sanofi-aventis, Bridgewater, NJ; Genomic Health, Redwood City, CA

Background: Laboratory assessment of HER2 is of marked clinical importance. Accurate quantification remains problematic within and between laboratories. Here we report central laboratory HER2 results comparing IHC, FISH and quantitative RT-PCR using Oncotype DX in patients enrolled in a large adjuvant breast cancer trial.

Design: 755 patients with 0 to 3 positive lymph nodes from Intergroup study E2197 were studied. Central IHC for HER2 was performed using duplicate 1.0 mm microarrays (HercepTest™; Dako). Percent positive cells and staining intensity (0-3+) was assessed, where IHC positive cases exhibited 3+ staining in >30% cells, IHC equivocal cases exhibited 3+ staining in <30% cells or 2+ staining, and IHC negative cases exhibited 0 or 1+ staining. For HER2 measurement by FISH, analysis for amplification ratio is in progress by a central laboratory with positive >2.2, equivocal 1.8 to 2.2, and negative < 1.8. Quantitative RT-PCR for HER2 used Oncotype DX and pre-defined cutoffs: positive ≥ 11.5 units, equivocal >10.7 - <11.5 units, and negative ≤ 10.7 units (each unit represents a 2-fold change in expression). Concordance analysis excluded the equivocal range from both assays according to ASCO/CAP Guidelines (Wolff et al, 2006).

Results: HER2 expression by IHC and by RT-PCR is shown in the Table below. Of the 134 cases positive by IHC, 27 (20%) cases were negative by RT-PCR. 175 cases were equivocal by IHC (165 of these were HER2 negative by RT-PCR). 26 cases were equivocal by RT-PCR (3 of these were HER2 negative by IHC). The overall concordance for HER2 status by central IHC and central RT-PCR was 95% (95% CI, 92%, 96%). FISH hybridizations are complete, analyses are in progress and results will be presented at meeting.

| HER2 Concordance: RT-PCR & IHC | | | | |
|--------------------------------|--------------|-----------------------|--------------|--------------|
| HER2 | Central IHC+ | Central IHC equivocal | Central IHC- | Total RT-PCR |
| RT-PCR+ | 94 | 0 | 4 | 98 |
| RT-PCR equivocal | 13 | 10 | 3 | 26 |
| RT-PCR- | 27 | 165 | 439 | 631 |
| Total IHC | 134 | 175 | 446 | 755 |

Conclusions: There is a high degree of overall concordance between central IHC and central RT-PCR positive and negative HER2 cases. Assessment of HER2 status by RT-PCR using Oncotype DX is an alternative to IHC.

Category: Breast

Tuesday, March 10, 2009 11:45 AM

Platform Session: Section B, Tuesday Morning

