[264] Central Lab HER2 Testing By RT-PCR, IHC, & FISH for Quality Assurance (QA) in Locally HER2-Negative (HER2(-)), ER-Positive Invasive Breast Carcinoma (IBC) With Adjacent In Situ Carcinoma (IS)

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Background: Our HER2 QA program requires confirmatory testing w/ IHC & FISH at an outside central lab on all IBC samples w/ IS that are HER2-positive (HER2(+)) by central Oncotype DX (ODX) but are locally IHC/FISH HER2(-), equivocal (EQ), or unknown (UNK). The objective of this QA program is to further assess the quality of HER2 testing by RT-PCR & to identify rare intratumoral differences in HER2 expression between IBC & IS.
Design: From 12/1/10 - 8/26/14, RT-PCR HER2(+) IBC cases w/ IS which were locally HER2(-), EQ, or UNK were sent to a central lab (Vitro Molecular Labs; Miami, FL) for IHC/FISH testing using HER2 SP3 IVD assay & PathVysion, respectively. HER2 status was determined before 10/13 by the 2007 ASCO-CAP guidelines & after 10/13 by the 2013 revised ASCO-CAP HER2 guidelines. In cases of central IHC/FISH discordances (<2% of cases), HER2 status was recorded as (+) if at least 1 method was (+). RT-PCR for HER2 used ODX & the pre-defined HER2 cutoffs: (+) ≥11.5 units, EQ = 10.7 to 11.4 units, & (-) <10.7 units – each unit represents a 2-fold change in gene expression.
Results: 2,454 of 310,525 cases were RT-PCR HER2(+). 327 IBC cases w/ IS that were HER2(+) by RT-PCR & locally HER2(-), EQ, or UNK were sent for central lab IHC/FISH. 10 cases were excluded for inconclusive IHC/FISH due to preanalytic compromise. 317 IBC cases w/ IS were local HER2(-), EQ, or UNK in 212 (66.9%), 26 (8.2%), or 79 (24.9%) cases, respectively. 131 of 212 (61.8%) HER2(-) cases by local sites were HER2(+) by central IHC, FISH, & RT-PCR. 56 of 212 (26.4%) locally HER2(-) cases were found to have differences between IBC & IS by central IHC/FISH. 22 of 212 (10.4%) of locally HER2(-) cases were central IHC/FISH HER2(-)

	Local HER2(-) EQ or UNK N=317	**Local HER2(-) N=212**
RT-PCR concordant w/central IHC/FISH	**211 (66.6%)**	**131 (61.8%)**
RT-PCR+ vs central EQ	**7 (2.2%)**	**3 (1.4%)**
RT-PCR discordant w/central IHC/FISH	**99 (31.2%)**	**78 (36.8%)**
RT-PCR+ vs Central(-)	30 (9.5%)	22 (10.4%)
RT-PCR+ vs Central IBC(-)/IS+	69 (21.8%)	56 (26.4%)

Conclusions: RT-PCR testing has clinical utility in identifying pts who may be HER2(+) by central FISH/IHC & therefore candidates for HER2 targeted therapy. The QA program identifies rare cases where IS is HER2(+) & IBC is HER2(-).
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