P032 Central lab HER2 testing by RT-PCR, IHC and FISH in locally HER2-Neg, ER+ IBC with in situ carcinoma

Poster Abstracts I

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Goals: Our HER2 QA program requires confirmatory testing with IHC and FISH at an outside central lab on all IBC samples with in situ carcinoma (IS) that are HER2-positive (HER2+) by central Oncotype DX (ODX) but are locally IHC/FISH HER2-negative (HER2-Neg), equivocal (EQ), or unknown (UNK). The objective of this QA program is to further assess the quality of HER2 testing by RT-PCR and to identify rare intratumoral differences in HER2 expression between IBC and IS.

Methods: From 12/1/10 to 8/26/14, RT-PCR HER2+ IBC cases with IS which were locally HER2-Neg, EQ, or UNK were sent to a central lab (Vitro Molecular Labs; Miami, FL) for IHC/FISH testing using HER2 SP3 IVD assay and PathVysion, respectively. HER2 status was determined before 10/13 by the 2007 ASCO-CAP guidelines, and after 10/13 by the 2013 revised ASCO-CAP HER2 guidelines. In cases of central IHC/FISH discordances (in <2% of cases), HER2 status was recorded as + if at least 1 method was +. RT-PCR for HER2 used ODX and the pre-defined HER2 cutoffs: + = ?11.5 units, EQ = 10.7–11.4 units, and negative = <10.7 units, where each unit represents a 2-fold change in gene expression.

Results: See the table. 2,454 of 310,525 cases were RT-PCR HER2+. 327 IBC cases with IS that were HER2+ by RT-PCR and locally HER2-Neg, 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 with IS were local HER2-Neg, EQ, or UNK in 212 (66.9%), 26 (8.2%), or 79 (24.9%) cases, respectively. 131 of 212 (61.8%) HER2-Neg cases by local sites were HER2+ by central IHC, FISH, and RT-PCR. 56 of 212 (26.4%) locally HER2-Neg cases were found to have differences between IBC and IS by central IHC/FISH. 22 of 212 (10.4%) of locally HER2-Neg cases were central IHC/FISH HER2-Neg.