**Presentation title:** Quantitative digital PCR measurement of ERBB2 copy number is predictive of outcome in early breast cancer patients treated with adjuvant trastuzumab

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**Abstract (250-300 words):**

HER2/ERBB2 evaluation is necessary for treatment decision-making in breast cancer, however current dynamic range is limited and considerable variability exists between antibodies, probes, and evaluators. Copy number evaluation by digital PCR (dPCR) has advantages as an alternative or complementary method for ERBB2/HER2 diagnostics. In this study, we developed a single-reaction multiplex droplet dPCR assay for determination of ERBB2 DNA copy number (CN) in reference to two control regions, CEP17 and a copy-number-stable region of chr. 2p13.1, validated CN estimations to clinical in situ hybridization (ISH) HER2 status, and investigated the association of ddPCR-quantified ERBB2 CN with clinical outcomes. 909 primary breast cancer tissues were evaluated for ERBB2 CN. The area under the curve for concordance to HER2 status was 0.93 and 0.96 for ERBB2 CN using either CEP17 or 2p13.1 as reference, respectively. The accuracy of ddPCR ERBB2 CN assay was 93.7% and 94.1% compared to HER2 ISH in the training group and validation group. Positive and negative predictive value for classic HER2 amplification and non-amplification group based on ddPCR was 97.2% and 94.8% respectively. A biological "ultrahigh" ERBB2 ddPCR CN group had significantly worse survival within patients treated with trastuzumab for both recurrence-free survival (hazard ratio, HR: 3.3; 95% CI 1.1 to 9.6; P = 0.031) and overall survival (HR: 3.6; 95% CI 1.1 to 12.6; P = 0.041). Using RNA-seq gene expression as surrogate, in a cohort of 682 patients receiving trastuzumab, the ultrahigh-ERBB2 mRNA group had significantly worse survival. Multiplex ddPCR is useful for ERBB2 CN estimation and ultrahigh ERBB2 may be a predictive factor for long-term survival after trastuzumab treatment.

**Biography**

Hina Dalal (Heena Saini) is a dedicated researcher specializing in the convergence of bioinformatics, genomics, and data-driven methodologies. With a comprehensive understanding of NGS data set analysis methods, Hina is currently navigating the realms of cancer genomics and diagnostics during her PhD studies at Lund University's Division of Oncology. Previously, she in 2012 completed a Masters in Stem Cell Bioinformatics at the MRC Centre for Regenerative Medicine, University of

Edinburgh. She is adept in multiple programming languages and machine learning approaches to analyze high-dimensional datasets, and is also proficient in wet-lab molecular biology methods and techniques. Her passion lies in harnessing data in a multidisciplinary setting to identify actionable healthcare insights, ensuring improved patient outcomes and well-being.