Does the HER2 FISH ratio predict pathologic complete response for patients who receive dual anti-HER2 therapy without chemotherapy?

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**Background**
Recent clinical trials have shown that a subgroup of HER2+ breast cancer patients achieves a pathologic complete response (pCR) to neoadjuvant dual HER2-targeted therapy without chemotherapy. Currently there is no optimal strategy to identify the subgroup of patients with oncogene addicted tumors who may benefit from this de-escalation treatment approach. We hypothesized that higher levels of HER2 amplification may be associated with increased rates of response to neoadjuvant dual HER2-targeted therapy.

**Objective**
To assess whether a higher HER2/CEP17 FISH ratio is associated with a pCR in patients receiving neoadjuvant dual anti-HER2 therapy without chemotherapy.

**Methods & Cohort**
Single-center, cross-sectional study of 3 combined trials

- 56 HER2+ breast cancer patients
- HER2/CEP17 FISH ratio ≥2
- Stage II — III
- Received dual anti-HER2 therapy followed by surgery
  - Lapatinib + trastuzumab
  - Pertuzumab + trastuzumab
  - Pertuzumab + trastuzumab emtansine

**Outcome**
- pCR
  - Median HER2/CEP17 FISH ratio
    - 10.3 (IQ range: 8.1 – 13.1)
    - Unadjusted odds ratio*: 2.28 (p=0.04)
    - Multivariate odds ratio**: 1.40 (95% CI: 0.96 – 5.42)
  - no pCR
    - Median HER2/CEP17 FISH ratio
      - 5.9 (IQ range: 3.5 – 12.8)
      - Unadjusted odds ratio*: 5.9 (95% CI: 0.96 – 5.42)
      - Multivariate odds ratio**: 0.60 (95% CI: 0.0 – 32.51)

The HER2/CEP17 FISH ratio predicted pCR among patients receiving neoadjuvant dual anti-HER2 therapy when median HER2 FISH ratio values were compared (10.3 vs 5.9). The upper quartile of HER2 FISH ratio trended more likely to have a pCR compared to the lower quartile (OR 2.28; p=0.06). This association did not persist when adjusted for treatment regimen and estrogen receptor status. While the sample size and power are limited, these results suggest that a high HER2 FISH ratio at baseline core biopsy may be a potential biomarker to select patients for neoadjuvant dual anti-HER2 therapy without chemotherapy.

**Conclusions**

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