Background

AURKA is a key regulator of the mitotic spindle, G2/M checkpoint and epithelial-mesenchymal transition1. AURKA is amplified and/or overexpressed in breast cancer and is associated with therapy resistance and worse survival2,3.

A randomized phase II trial in hormone receptor (HR)-positive, HER2-negative and triple negative (TN) metastatic breast cancer patients showed that addition of Axitinib to weekly Paclitaxel significantly improved progression-free survival (PFS) compared with Paclitaxel alone4.

Here, pretreatment archival tissues from this clinical trial were analyzed for biomarkers associated with clinical benefit from Axitinib.

Methods

- **Cohort**
  - Women with metastatic HR+ or TN breast cancer enrolled on NCT02187991

- **Retrospective Biomarker Analysis**
  - Pretreatment FFPE Tumor Biopsies
    - Tumor Whole Transcriptome Sequencing
    - Tumor Whole Exome Sequencing
  - Compare molecular features in tumors by treatment arm and response group

- **Histology**
  - Hematoxylin and eosin
  - Immunohistochemistry

- **Biomarker Analysis**
  - MYC (clone MYC41S; Cell Signaling Technology, Danvers, MA), PIK3CA (clone 3A2C7; Cell Signaling Technology), CCND1 (clone FJ7; Cell Signaling Technology), CCNE1 (clone N21/1; Cell Signaling Technology), AR (clone D-19; Cell Signaling Technology), ER (clone 6F11; Cell Signaling Technology), PR (clone 1E2; Cell Signaling Technology), ERBB2 (clone 2H3; Cell Signaling Technology), and HER2 (clone SP28; Cell Signaling Technology)

- **RNA-Seq**
  - Exome and RNA-Seq libraries
  - For 68 patients with RNA-seq data available (n = 17 Axitinib + Paclitaxel, 17 Paclitaxel alone, 34 HER2-negative tumors)

- **Enrichment Analysis**
  - Gene Set Enrichment Analysis (GSEA) of the 50 Cancer Hallmark Gene Sets from the Human Molecular Signature Database by kall and response

Results

**While Genomic Alterations Were Not Significantly Associated with Response to Axitinib + Paclitaxel**

**Conclusions:**

Patients whose breast cancers had increased MYC expression and high MYC activation derived greater clinical benefit from Axitinib + Paclitaxel than from Paclitaxel alone.

**EMT signaling did not preclude prolonged response (≥12 months PFS) to Axitinib + Paclitaxel.**

**References**


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