Monitoring response to neoadjuvant therapy using a combination of circulating tumor dna and circulating tumor cells: a prospective study in patients with inflammatory breast cancer

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Abstract

Background: Inflammatory breast cancer (IBC) is an aggressive form of breast cancer with high disease burden and poor prognosis.

Objective: To determine whether serial circulating tumor DNA (ctDNA) and circulating tumor cell (CTC) measurements are associated with pathologic complete response (pCR) among IBC patients receiving neoadjuvant systemic therapy (NST).

Methods: This was a prospective study of IBC patients receiving NST prior to surgical resection. Serial plasma samples were collected at baseline and regular intervals throughout treatment course (range: every 3 weeks – 3 months). ctDNA was quantified using a tumor-informed ctDNA assay (Signatera) and reported as mean tumor molecules per milliliter (MTM/ml). CTCs were enumerated using CellSearch with the presence of ≥ 1 considered positive.

Results: In total, 33 IBC patients underwent 84 ctDNA and 26 CTC timepoint assessments. Median age was 46 years (IQR 38.0-64.0) and 51.5% (17) had BMI ≥ 30 kg/m2. 45.5% had clinical stage III (10 IIIB, 5 IIIC) disease while 54.5% (18) had stage IV disease. Receptor subtype consisted of 33.3% (11) triple negative, 30.3% (10) HR+/HER2-, 21.2% (7) HR+/HER2+, and 15.2% (5) HR-/HER2+. Of the 20 patients with baseline ctDNA samples, ctDNA positivity rate was 100% with median 16.6 MTM/ml (IQR 3.5-65.8). 13 patients had corresponding baseline CTC assessments (median 1, IQR 0-2). Baseline ctDNA and CTC status were concordant in 61.5% (8/13). Among 17 patients with baseline and neoadjuvant ctDNA assessments, nine cleared their ctDNA during neoadjuvant therapy. Of the nine patients with ctDNA clearance, four have undergone surgery and two achieved pCR. Of the eight patients with residual ctDNA, two have undergone surgery and one achieved pCR. Ten patients are currently pending surgery and pathologic assessment. Additional correlation of ctDNA and CTC measurements with pCR and residual cancer burden will be presented at the meeting.

Conclusion: A multi-analyte biomarker assessment in the neoadjuvant setting might help predict pCR in patients with IBC. Early identification of patients unlikely to achieve pCR could be used to guide alternate treatment selection during neoadjuvant therapy.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.