OCTANE: Adjuvant liposomal doxorubicin and carboplatin for early-stage triple negative breast cancer

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BACKGROUND

Patients with stage 1 triple negative breast cancer (TNBC) are at high risk of recurrence, given the aggressive nature of the disease. A meta-analysis that reviewed the data for T1a/bN0 TNBC tumors showed that the breast cancer recurrence rate in patients receiving chemotherapy was significantly lower than those who did not receive chemotherapy (OR 0.54, 95% CI 0.37–0.78, P = 0.001).

Other studies have shown the benefit of adjuvant chemotherapy for stage 1 triple negative breast cancers, Given the recurrence free survival and overall survival benefit seen with systemic therapy, guidelines recommend adjuvant chemotherapy for TNBC tumors greater than 0.5 cm in size.

An investigator-initiated study at Rutgers Cancer Institute evaluated the combination of neoadjuvant liposomal doxorubicin and carboplatin for patients with stage II-III TNBC (ClinicalTrials.gov Identifier: NCT02315196). This study showed that the combination achieved pathologic complete response (pCR) similar to standard regimens with good tolerability –reduced risk of febrile neutropenia, alopecia and neuropathy compared to current standard treatment regimens.

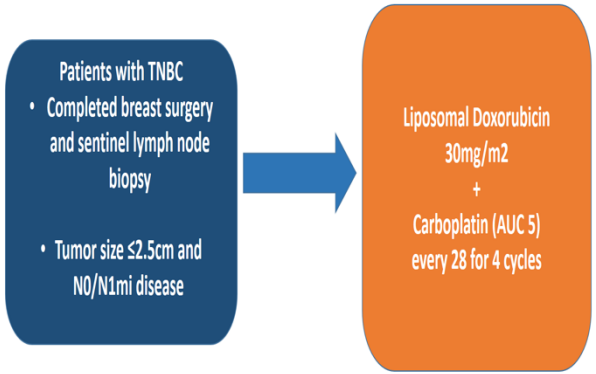
Based on the results of this study, this regimen is being evaluated in the adjuvant setting for patients with Stage I/II TNBC who did not receive neoadjuvant therapy.

TRIAL DESIGN

The study is a phase 2, single-arm study evaluating the combination of liposomal doxorubicin and carboplatin in the adjuvant setting for patients with early-stage TNBC.
Liposomal doxorubicin and carboplatin are administered every 4 weeks for 4 cycles.
Patient will be monitored for disease recurrence.
ctDNA analysis to be done at baseline, Cycle 2, cycle 4, 6months, 12 month, 18 months and 24 months using MRD assay from Haystack Oncology.

ELIGIBILITY CRITERIA

Inclusion Criteria	Exclusion Criteria
Newly diagnosed early-stage TNBC with primary tumor < 2.5cm and nodal disease of N0/N1mi on final surgical pathology	Clinically significant cardiac disease (e.g. congestive heart failure, symptomatic coronary artery disease and cardiac arrhythmias not well controlled with medication) or myocardial infarction within the last 6 months
ER≤20%, PgR≤20%, HER2 0-2+ by IHC or FISH≤2.0	Patients with stage III-IV breast cancer
Age>18year with ECOG performance status of 0 or 1	History of immunodeficiency, interstitial lung disease, active pneumonitis or receiving chronic systemic steroids.
Baseline LVEF > 50%	



STUDY OBJECTIVES

PRIMARY OBJECTIVES	PRIMARY ENDPOINTS
To determine the efficacy of liposomal doxorubicin and carboplatin in the adjuvant setting	To determine 5-year recurrence free survival.
SECONDARY OBJECTIVES	**SECONDARY ENDPONTS**
To characterize the safety and toxicity profile of the study treatment as measured by the adverse events rates.	Rates of AE as measured by CTCAE v.5
EXPLORATORY OBJECTIVES	**EXPLORATORY ENDPOINTS**
Evaluate changes in circulating tumor DNA (ctDNA)	Monitor trends in ctDNA pre and post treatment.

STATISTICAL DESIGN

The primary objective of this study is to evaluate the efficacy of liposomal doxorubicin and carboplatin in the adjuvant setting for patients diagnosed with early-stage TNBC as measured by the 5-year recurrence-free survival (RFS) rate. Recurrence-free survival (RFS) is 92.5% in patients treated with chemotherapy compared with 66.5% for patients treated without chemotherapy.[1] With an accrual period of 2 years and a minimum of 5 years of follow-up, a sample size of 55 will provide approximately 80% power to detect an improvement in the five-year recurrence-free survival (RFS) rate from 66.5% (historical control) to 80.5%, using a two-sided 5% significance level.

ACCRUAL

The study will enroll up to 55 patients at Rutgers Cancer Institute of New Jersey and Robert Wood Johnson Barnabas Health System hospitals.

1. Cancer . 2020 Aug 15:126 Suppl 16:3837-3846.

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