Tailored neoadjuvant epirubicin and cyclophosphamide (EC) and nanoparticle albumin-bound paclitaxel (nab-P) in breast cancer.

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Background: We evaluated the feasibility and the likelihood of achieving high response rates by tailoring neoadjuvant therapy based on individual patient and tumor characteristics. Triple negative (TNBC) and HER2+ pts were treated with chemotherapy. Hormone Receptor (HR)+ HER2- pts were treated based on the Oncotype DX Breast Recurrence Score (RS) result. Methods: Between 4/2013 and 1/2015, 40 pts with stage II (T > 2cm) or III were enrolled: 15 HER2+, 15 TNBC and 10 with HR + HER2- breast cancer with RS ≥25. HR+ HER2-tumors with RS <25 were treated in an exploratory cohort. The primary cohort (n=40) was treated with preoperative epirubicin 90mg/m2 and cyclophosphamide 600mg/m2 Q3 weeks x 4, followed by nab-P (125mg/m2days 1, 8, 15 Q4 weeks) for 12 weeks, with the addition of trastuzumab in HER2+ pts. The primary endpoint was pCR in breast (ypT0/ypTis). A single stage binomial design was planned to discriminate between overall pCR rates of 30 and 50% with a type I error of 6% and 87% power. Secondary endpoints included pCR in breast and lymph nodes (LN), toxicity, PFS, and translational endpoints using pre- and post-chemotherapy MRIs and tissue biomarker analysis. An independent data safety board assessed trialsafety. Clinicaltrials.gov: NCT01830244. Results: Median age was 50 yrs (34 – 76). Clinical stages were T2 (67.5%), T3 (25%), T4 (7.5%), N0 (32.5%), N1 (40%), N2 (22.5%) and N3 (5%). LN involvement was confirmed with biopsy in 20 of 27 pts with N1 – N3. Breast conservation rate was 48% (n=19). Overall pCR rate in the breast was 55% (n=22). pCR rate in subsets is shown below pCR %(n): See table. Grade 3/4 Adverse Events (AEs): febrile neutropenia (8%), neutropenia (18%), sensory neuropathy (5%), deranged transaminases (5%), fatigue (2%), diarrhea (2%), pneumothorax (2%). Common grade 1/2 AEs: alopecia (95%), fatigue (68%), nausea (57%), neutropenia (57%) and neuropathy in (50%). Conclusions: This EC and nab-P regimen resulted in a high rate of pCR, demonstrating that tailored neoadjuvant therapy including patient selection by OncotypeDX is feasible and warrants further investigation. Clinical trial information: NCT01830244

	All (40)	HER2+ (15)	TNBC (15)	HR+ HER2- RS ≥25 (10)
Breast	55 (22)	80 (12)	46 (7)	30 (3)
Breast & LN	48 (19)	80 (12)	40 (6)	10 (1)