Using the 21-gene assay from core needle biopsies to choose neoadjuvant therapy for breast cancer: A multi-center trial

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Neoadjuvant systemic therapy (NST) can facilitate breast conserving surgery (BCS) for large cancers. While hormone receptor positive (HR+) cancers respond to neoadjuvant chemotherapy (NCT), pathologic complete responses (pCR) are unlikely. Neoadjuvant hormonal therapy (NHT) may make BCS possible with less toxicity than NCT. We hypothesized that the Oncotype Dx® 21-gene Recurrence Score (RS), could guide the decision to treat with NHT versus NCT to facilitate BCS. This hypothesis is based on the ability of the RS to identify ER+ patients (pts) likely to benefit from adjuvant CT vs unlikely to benefit, as well as prior studies showing that pts with a low RS have no pCRs when receiving NCT (Yardley, et al 2015).
Methods: This prospective multi-center study enrolled pts with HR+, HER2-negative, invasive breast cancers not suitable for BCS (size ≥ 2 cm). Diagnosis was made by core needle biopsy (bx). Tissue blocks from the bx's were sent to Genomic Health for RS testing. Pts whose tumors had a RS < 11 were to receive NHT; pts with RS >25 tumors were to receive NCT; pts with midrange RS of 11-25 were randomized to NHT or NCT.
The primary objective was the feasibility of randomizing pts with RS values 11-25 between NHT and NCT. The primary endpoint was whether 1/3 or more of randomized pts would refuse assigned treatment. Secondary endpoints included: clinical partial and complete response (cPR, cCR) rates, overall clinical response rates (CR), pCR in the breast, pCR in the breast and nodes and successful BCS. One-sample binomial test was used to compare the observed refusal rate with 1/3, along with its 95% CI. Fisher's exact test, logistic regression (for a binary endpoint), and/or ordinal regression (for an ordinal endpoint) were used to compare the 4 treatment groups for secondary endpoints.
Results: Seven US and Canadian centers enrolled 64 pts; 5 were excluded (1 delay in RS result, 1 lost block, 1 HR testing discrepancy, 2 not eligible). Of 33 pts with RS 11-25, 5 (15%; 95% CI =2.9% - 27.4%) refused assignment to NCT (2 chose NHT and finished the study). This was significantly lower than the 33% target (binomial test, p=0.0292). Results for other endpoints are shown in the Table (according to treatment received); the total number of pts for the analyses is 55; 1 pt had missing data for clinical response.

Results According to Treatment

Treatment Group	RS<11 NHT	RS 11-25 NHT	RS 11-25 NCT	RS>25 NCT	Overall P
N	N=12	N=18	N=11	N=14	
cCR	8.3%	22.2%	36.4%	28.6%	0.0422
cPR	75%	27.8%	36.4%	64.3%	
CR (cCR + cPR)	83.3%	50%	72.7%	92.9%	0.0490
pCR Breast	8.3%	6%	0	21.4%	NS
pCR Breast + Nodes	0	0	0	14.3%	NS
Successful BCS	75%	72.2%	63.6%	57.1%	NS

Conclusions: This pilot showed the feasibility of using the RS to guide NST, with only a 15% refusal rate of randomly assigned treatment. Of greater interest is the finding that pts with a RS <11 had a high CR rate with NHT and that pts with a RS 11-25 who received NHT had a similar rate of BCS success as the pts with RS <11. Conversely, pts with RS>25 treated with NCT had the highest CR (cCR + cPR) and pCR rates. These results demonstrate that conducting a similarly designed larger trial is feasible and suggests that for pts with a low RS, NHT is a potentially effective strategy.

Session: Poster Session 2: Treatment: Neoadjuvant Endocrine Therapy (7:30 AM-9:00 AM)
Date/Time: Thursday, December 8, 2016 - 7:30 am
Room: Hall 1

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