Disclosures

Can Oncotype DX® testing be omitted in invasive breast cancer patients with clinicopathologic factors predicting very high pre-test probability of a concordant result?

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We do not have relevant financial relationships with commercial interests that pertain to the content of our presentation

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BACKGROUND

- Oncotype DX® (ODX) is a 21-gene assay utilized to guide adjuvant chemotherapy recommendations in estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, early invasive breast cancer[1]
- The cost of ODX testing averages $3800-4000 per assay[2]
- Testing reaps the least value amidst either very low or very high pre-test probability, whereas the greatest value is among those with intermediate pre-test probability[3]

OBJECTIVE

- **To determine if clinicopathologic factors could identify patients at the extremes of 'very low' and/or 'very high' pre-test probability of high ODX recurrence scores that align with systemic chemotherapy recommendations**

METHODS

- Retrospective review of all invasive breast cancer patients who underwent ODX testing from 2008-2018 at a single institution
- Patients were categorized into low, intermediate & high pre-test probability groups based on clinicopathologic factors
- Individual factors & patients with 'all low' risk or 'all high' risk factors were analyzed to determine if ODX testing would change TAILOR-x recommendations

Table 1: Low vs. High-risk Clinicopathologic Factors

Clinicopathologic Factors	Low Risk	High Risk
Grade	Low	High
Lymphovascular invasion	Absent	Present
Total proliferation score	S-phase fraction < 10 Ki67 < 10 DNA proliferative index < 1.0	S-phase fraction ≥ 10 Ki67 ≥ 20 DNA proliferative index ≥ 1.0
Estrogen receptor status	≥ 20%	≤ 10%
Progesterone receptor status	≥ 20%	≤ 10%
HER2 status	Negative	Positive

RESULTS

- **All LOW risk factors n=50 (23.3%)**
- **All HIGH risk factors n=16 (7.4%)**
- **MIXED LOW & HIGH risk factors n=149 (69.3%)**
- **ODX assay results**
  Low-risk: 113 (52.6%)
  Intermediate-risk: 74(34.4%)
  High-risk: 28 (13.0%)
- **TAILOR-x based recommendations**
  Chemotherapy: 59 (27.4%)
  No chemo: 156 (72.6%)
- **Tumor grade, proliferative indices & progesterone receptor (PR) status were significantly predictive of ODX score groups & TAILOR-x recommendations**

Table 2. Clinical and Tumor Characteristics (n=215)

Median tumor size (range)	13 mm (10-20mm)
Lymph node status	
N0	167 (77.7%)
N0 (i+) isolated tumor cells	15 (7.0%)
N1Mi (micrometastases)	18 (8.4%)
N1 (1-3 axillary nodes)	11 (5.1%)
Histology	
Invasive ductal carcinoma	192 (89.3%)
Invasive lobular carcinoma	19 (8.8%)
Infiltrating tubulolobular carcinoma	1 (0.5%)
IDC & ILC combined	2 (0.9%)
Nuclear grade	
Low	64 (29.9%)
Intermediate	119 (55.6%)
High	31 (14.5%)
Lymphovascular invasion	4 (1.9%)
Proliferative total	
Low	107 (62.9%)
Intermediate	16 (9.4%)
High	47 (27.7%)
PR positive	162 (75.3%)

Table 3: Multivariable Odds Ratio Analysis of Clinicopathologic Factors, ODX Score & TAILOR-x Recommendations

	Low ODX recurrence score	TAILOR-x – Chemotherapy NOT Recommended	TAILOR-x – Chemotherapy Recommended
Age	1.03 (1.0-1.1, p=0.2)	**1.2 (1.1-1.3, p<0.0001)**	**0.9 (0.8-0.9, p<0.0001)**
High tumor grade	**0.5 (0.2-0.9, p=0.02)**	**0.2 (0.1-0.6, p=0.002)**	**4.5 (1.7-11.9, p=0.002)**
Lymphovascular Invasion present	1.1 (0.1-13.9, p=0.9)	2.7 (0.2-34.8, p=0.5)	NA
High proliferative indices	**0.5 (0.3-0.8, p=0.007)**	**0.5 (0.3-0.9, p=0.02)**	**2.0 (1.1-3.7, p=0.02)**
PR status 0-10%	**0.4 (0.2-0.6, p=0.0003)**	**1.03 (1.02-1.05, p<0.0001)**	**2.7 (1.5-4.9, p=0.001)**

RESULTS

- Of 50 patients with 'all low' risk factors, 45 did not require chemotherapy per TAILOR-x recommendations
  - 5 patients had intermediate ODX results & TAILOR-x recommendation for chemotherapy (all age ≤50 years)
- Patients with 'all low' risk factors are significantly more likely to have a low ODX recurrence score **(OR 2.9, 1.5-5.9, p=0.002)** & recommendation for no adjuvant chemotherapy per TAILOR-x **(OR 4.4, 1.6-11.7, p=0.002)**
- Of 16 patients with 'all high' risk factors, all 16 were high ODX score with TAILOR-x recommendation for chemotherapy
- Patients with 'all high' risk factors are significantly more likely to have a high ODX recurrence score & TAILOR-x recommendation for chemotherapy **(p<0.0001)**

DISCUSSION

- Cancer care is increasingly costly, requiring value-driven decisions
- ODX testing appears to have low value among patients with 'all high' risk factors and those ≥50 years with 'all low' risk factors
- ODX findings did not change chemotherapy recommendations in those with high tumor grade, high proliferative indices, and PR status ≤10%
- Among those ≥50 years, chemotherapy recommendations were also not changed by ODX findings with low grade, low proliferative indices, and PR status ≥20%

CONCLUSIONS

- In this study, ODX was non-contributary to a subset of patients with 'very low' or 'very high' pre-test probability of high ODX recurrence scores based on standard clinicopathologic factors
- Greatest value for ODX testing is likely among the intermediate group of mixed-risk clinicopathologic factors
- This suggests that tumor grade, proliferative indices, & PR status can be utilized to identify a cohort at 'very low' or 'very high' pre-test probability that may not benefit from ODX testing

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