Medical Oncology Updates in Breast Cancer -2018-2019

Debra Brandt, D.O.
Smilow Cancer Center
Torrington, Ct
Financial Disclosure

• none
Adjuvant treatment

• Define adjuvant/ neoadjuvant
• Oncotype-how to decide about hormone/chemotherapy
• TAILOR-Rx
Case Study

• You have 2 patients both are 48 yo female with a 1.5 cm LN negative ER+ (100%), PR+ (90%) and Her-2 negative.

• Oncotype is 18

• Oncotype is 24

• What adjuvant therapy would you offer?
TAILORx

• Registered 6711 patients with Oncotype RS- 11-25- stratified by menopause, planned chemo, planned radiation

• Key eligibility- Node negative, ER + Her-2 neg- T1c- T2 (high risk T1b)

• Statistical design to look for NON-INFERIORITY

• Looked a groups 11-5, 16-20, 21-25

• Randomized to ET alone or ET + chemo

• RS=25- 16.1% distant recurrence at 10 years
Eligibility

• Women with invasive breast cancer
• Age 18-75 years
• Node-negative
• ER and/or PR-positive in local lab (before ASCO-CAP guidelines)
• HER2-negative in local lab
• Tumor size - 1.1–5.0 cm (or 0.6-1.0 cm and int-high grade)
• Willing to have chemotherapy treatment assigned or randomized based on RS assay results
• Assay Selected: 21-Gene Assay (Recurrence Score)

• Two prospective validation studies in ER+, node-neg BCA

• Prognostic (B14 study - tamoxifen): low recurrence with ET if RS low

• Predictive (B20 study – tam +/- CMF): large chemo benefit if RS high

• Uncertain chemo benefit for mid-range RS

Target Population: HR+, HER2-neg, node-neg BCA

• 50% of all breast cancers in U.S.

• Adjuvant chemo recommended, but benefit small • Most are overtreated

Yale
Tailor Rx Summary

• RS 11-25  ET was non-inferior to chemo
• RS 0-10  Distant recurrence rates low (2-3%)
• RS 26-100 Significantly higher event rates, driven by more recurrence despite adjuvant chemo and ET

• Other observations
• Age-RS-chemo-treatment interaction
• Some chemo benefit in women 50 or younger with RS 15-25
• Greatest impact on distant recurrence with RS 21-25
TAILOR Rx
RS 11-25

• Absolutely no difference with or without chemo
  (? Add picture)

• SUBGROUP ANALYSIS (50 or younger)

• **SCORE 16-20**
  • 5 year (0.8%-improvement with chemo)
    9 year (1.6% -improvement with chemo)

**SCORE 21-25**
5 year (3.2 % -improvement with chemo)
9 year (6.5%- improvement with chemo)
ADJUVANT POST NEOADJUVANT

- CREATE-X
- KATHERINE
Case Study

- 42 yo female with large palpable breast tumor - Mammogram – 3.5 cm, with enlarged axillary LN, patients are BRCA, ATM and PALB negative
- US confirms above
- Biopsy of both LN and mass confirm invasive ductal cancer – Nuclear grade 3
- ER- Her -2 negative
- Both patients receive dd AC-T and have a clinical response and go for surgery-
- Pathology reveals Residual mass in breast of 7 mm and 4 mm in LN
- What would you do next?
CREATE-X

• s/p neoadjuvant chemotherapy (her-2 negative) ER+ and ER-

• Pathology post chemo shows residual disease

• Randomized to standard tx vs Capecitabine- given after radiation for 6 cycles

• DFS increased in all but particularly in ER-negative

• median follow-up of 7.3 years,
  • 5-year DFS- 79.6% on Xeloda and 76.8% observation

• In subgroup analyses, among the 248 patients with ER-negative, those assigned to receive adjuvant capecitabine were 49% less likely to experience a disease event and 52% less likely to die compared with those assigned to observation.
• Capecitabine group had a significant 30% reduced risk for recurrence, second cancer, or death compared with those in the control group, with 5-year disease-free survival (DFS) rates of 74.1% and 67.6%, respectively.

• Overall survival (OS) was also significantly better in the capecitabine group than in the control group, with 89.2% versus 83.6% of patients alive at 5 years, and a hazard ratio (HR) for death of 0.59.

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Case Study

• 48 yo female presents with 5 cm mass and bulky axillary LN Confirmed on Mammo and US- Pathology – ER+/HER-2 3+

• No evidence of metastatic cancer on staging
• She receives TCHP with excellent response
• She undergoes lumpectomy and SLN biopsy with residual disease of 1 cm in breast only
• What would you do next?
Katherine Trial

• s/p neoadjuvant Herceptin based chemo
• Residual disease at surgery
• Adjuvant T-DM1 was associated with improved invasive disease-free survival vs trastuzumab.
• Invasive disease-free survival at 3 years was 88.3% vs 77.0%.
Metastatic Breast - Estrogen +
CDK4/6 inhibitors

• As we know there are many mechanisms of resistance to hormone therapy
• CDK4/6 controls cell cycle progression from G1 – S phase by regulating the activity of Rb
• 3 drugs approve- Palbociclib, Ribociclib, Abemaciclib
• All almost double improve PFS in first line setting
<table>
<thead>
<tr>
<th>Palbociclib - Trial PALOMA -2 Letrozole and placebo vs Letrozole and Palbo</th>
<th>Ribociclib Trial MONALEESA-2 Ribo + letrozole vs letrozole + placebo</th>
<th>Abemaciclib and NSAI MONARCH -3</th>
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<tbody>
<tr>
<td>Median PFS 24.8 mo versus 14.5 mo</td>
<td>Median PFS 14.0 mo vs 22.5 mo ORR 52.7% vs 37.1%</td>
<td>Median PFS 14.7 mo versus not reached</td>
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<tr>
<td>Neutropenia, mouth sores, anemia, nausea, fatigue, diarrhea, alopecia</td>
<td>Mucositis, increase in QTcF, LFTs abn, nausea</td>
<td>Diarrhea, nausea and neutropenia</td>
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<td>Only 1 approved as single agent</td>
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Metastatic Triple Negative

- Impassion 130 trial (phase III)-
- atezolizumab and nab-paclitaxel improved PFS in ITT and PDL-1 + subgroups
  - PDL+: PFS advantage of 2.5 months

- OS 1st interim analysis median f/u 12.9 mo
- PDL1+ 9.5 month improvement
- Results independent of BRCA mutation
How to use?

• First line with AI or Faslodex?
• Clinical trials ongoing looking at adjuvant
Thank you