Medical Oncology Updates in Breast Cancer -2018-2019

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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?
TAILORRx

- 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
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
• 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.
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</th>
<th>Ribociclib</th>
<th>Abemaciclib and NSAI</th>
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<tr>
<td><strong>Trial PALOMA -2</strong>&lt;br&gt;Letrozole and placebo vs Letrozole and Palbo</td>
<td><strong>Trial MONALEESA-2</strong>&lt;br&gt;Ribo + letrozole vs letrozole + placebo</td>
<td><strong>MONARCH -3</strong></td>
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<td>Median PFS 24.8 mo versus 14.5 mo</td>
<td>Median PFS 14. mo vs 22.5 mo&lt;br&gt; ORR 52.7% vs 37.1%</td>
<td>Median PFS 14.7 mo versus not reached</td>
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<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