Breast Cancer in Young Adults: Treatment Considerations and Supportive Care Options

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NCCN.org – For Clinicians  |  NCCN.org/patients – For Patients
Young women have higher risk of recurrence

Kim HJ et al, unpublished
Breast cancer can be difficult for a person of any age…
Life is harder for young women with breast cancer
The mix of breast cancer subtypes is different in young women:
data from the Young Women’s Breast Cancer Study (YWS)

Table 2. Subtype by age group

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Total (n=1136)</th>
<th>≤ 30 yrs (n=144)</th>
<th>31-35 yrs (n=314)</th>
<th>36-40 yrs (n=678)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal A-like</td>
<td>377 (33%)</td>
<td>48 (33%)</td>
<td>99 (32%)</td>
<td>230 (34%)</td>
</tr>
<tr>
<td>Luminal B-like</td>
<td>477 (42%)</td>
<td>59 (41%)</td>
<td>137 (44%)</td>
<td>281 (41%)</td>
</tr>
<tr>
<td>*ER/PR+, HER2-, grade 3</td>
<td>245 (22%)</td>
<td>27 (19%)</td>
<td>68 (22%)</td>
<td>150 (22%)</td>
</tr>
<tr>
<td>*ER/PR+, HER2+</td>
<td>232 (20%)</td>
<td>32 (22%)</td>
<td>69 (22%)</td>
<td>131 (19%)</td>
</tr>
<tr>
<td>HER2 Enriched</td>
<td>95 (8%)</td>
<td>13 (9%)</td>
<td>34 (11%)</td>
<td>48 (7%)</td>
</tr>
<tr>
<td>Triple Negative</td>
<td>187 (16%)</td>
<td>24 (17%)</td>
<td>44 (14%)</td>
<td>119 (18%)</td>
</tr>
</tbody>
</table>
Cancer Specific Survival in SEER 2010-2015:*  
Focus on HER2+

HER2+, ER/PR -  
HER2+, ER/PR +

*unadjusted analysis

Kim HJ et al, unpublished
Age and Breast Cancer Mortality* by Subtype in NCCN: Focus on HER2+

*adjusted analysis

Partridge et al, JCO 2016
Age Neither Prognostic Nor Predictive for Early Recurrence in the HERA Trial

STEPP Analyses According to Age

These data suggest that treatment principles should be similar regardless of age in women with HER2+ disease
Cancer Specific Survival in SEER 2010-2015:*
Focus on Triple Negative (TNBC) and ER+/HER2-

TNBC

ER/PR +, HER2-

*unadjusted analysis

Kim HJ et al, unpublished
Age and Breast Cancer Mortality* by Subtype in NCCN: Disparity Greatest in Luminal A

Hazard Ratio

*adjusted analysis

Partridge et al, JCO 2016
TAILORx Results: Association between Continuous RS 11-25 and 9-Year Distant Recurrence Rate by Treatment Arms Stratified by Age (\(<=50 \text{ vs. }>50 \text{ Years})

RS modeled with a natural spline with 2 degrees of freedom, adjusted for tumor size and grade.

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### TailorX: Effect of Age & Menopausal Status on Chemo Benefit

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of Patients</th>
<th>No. of Events</th>
<th>Hazard Ratio for Recurrence, Second Primary Cancer, or Death (95% CI)</th>
<th>No. of Distant Recurrences</th>
<th>Hazard Ratio for Distant Recurrence (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤40 Yr of age</td>
<td>203</td>
<td>35</td>
<td></td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>41–45 Yr of age</td>
<td>441</td>
<td>51</td>
<td></td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>46–50 Yr of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before menopause</td>
<td>630</td>
<td>69</td>
<td></td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>After menopause</td>
<td>141</td>
<td>15</td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>51–55 Yr of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before menopause</td>
<td>287</td>
<td>34</td>
<td></td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>After menopause</td>
<td>472</td>
<td>54</td>
<td></td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>56–60 Yr of age</td>
<td>826</td>
<td>94</td>
<td></td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>61–65 Yr of age</td>
<td>710</td>
<td>109</td>
<td></td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>&gt;65 Yr of age</td>
<td>628</td>
<td>117</td>
<td></td>
<td>31</td>
<td></td>
</tr>
</tbody>
</table>

Sparano et al, NEJM 2019
**RxPONDER - Role of Chemotherapy in N1-3, Oncotype ≤ 25**
San Antonio Breast Cancer Symposium®, December 8-11, 2020

**IDFS Stratified by Menopausal Status**

**Postmenopausal**
- ET 5-year IDFS 91.9%
- CET 5-year IDFS 91.6%
- No Statistically Significant IDFS Difference

**Premenopausal**
- ET 5-year IDFS 94.2%
- CET 5-year IDFS 99.0%
- 5-year IDFS Absolute Difference 5.2%

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>CET (N=1,675; 147 events)</th>
<th>ET (N=1,675; 158 events)</th>
<th>Adjusted HR = 0.97; 95% CI 0.78-1.22; p=0.82</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number at risk</td>
<td>CET (N=834; 51 events)</td>
<td>ET (N=831; 91 events)</td>
<td>Adjusted HR = 0.54; 95% CI 0.38-0.76; p=0.0004</td>
</tr>
</tbody>
</table>

**Absolute Difference in Distant Recurrence as 1st site:**
- 0.3% (2.3% CET vs. 2.6% ET) for Postmenopausal
- 2.9% (3.1% CET vs. 6.0% ET) for Premenopausal

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Landmarked Exploratory Analysis for IDFS in Premenopausal Women on Endocrine Therapy arm:
Ovarian Function Suppression (n=126) vs. no Ovarian Function Suppression (n=647) at 6 months: HR 0.73 (95% CI: 0.39-1.37), p=0.33
Oncotype is prognostic in N0 and N1 in the YWS

Poovu et al, JCO 2020
Oncotype seems predictive in N0, RS 11-25 by receipt of chemotherapy in the YWS (N=195)

<table>
<thead>
<tr>
<th></th>
<th>Chemo received</th>
<th>No chemo received</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>109</td>
<td>86</td>
</tr>
<tr>
<td>Events</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>6-Yr DRF (95% CI)</td>
<td>96.7 (89.9-98.9)</td>
<td>97.3 (89.4-99.3)</td>
</tr>
</tbody>
</table>

Log rank P=0.247
Benefits of Ovarian Function Suppression in Women Age <35

Saha et al, JCO 2017
Discontinuation Rates Higher in Younger Women

Saha et al, JCO 2017
SOFT/TEXT-Cost of Progress

- Adherence:
  - SOFT: 15% stopped OFS by 2 years, 22% by 3 years

- Provider reported:
  - Depression symptoms: reported in ~ 50% in all groups
    - 4% severe, 5% increase with OFS
  - Marked increase in menopausal symptoms, insomnia, osteoporosis

- Patient reported:
  - Exemestane+OFS more bone or joint pain, vaginal dryness, loss of sexual interest and difficulties becoming aroused
  - Tamoxifen+OFS were significantly more affected by hot flushes, sweats and vaginal discharge
  - Similar global QOL
  - Endocrine differences are less pronounced after 2 years
  - Endocrine toxicity change less in women with prior chemotherapy

Hot Flash Therapies in Midlife Women and Breast Cancer Patients

1. Environmental, lifestyle
2. OTC/complementary/behavioral
   - OTC (vitamin E, omega-3, black cohosh, soy) → ineffective
   - Acupuncture → mixed
   - Hypnosis, group CBT → effective
   - Paced respiration, exercise, yoga → ineffective
     - Yoga and exercise improve QOL; yoga improves sleep
3. Pharmacological—non-hormonal
   - SSRI/SNRI → effective
   - Gabapentin/pregabalin → effective
   - Clonidine → mixed
   - Oxybutynin → effective
4. Pharmacological—hormonal- non-estrogenic
   - Progestins → effective
5. Procedural
   - Stellate ganglion blockade → effective (preliminary)

Oxybutynin Reduces Hot Flashes

• 150 women enrolled, mean age was 57 years; 65% on tam or AI

• Randomized to 2.5 mg bid, 5mg bid or placebo

• Both oxybutynin doses lead to:
  ▪ greater reductions in the weekly HF score P < .005
  ▪ HF frequency P < .003
  ▪ improvement in most HF-related daily interference scale measures and in overall quality of life
  ▪ more side effects (most grade 1 or 2): dry mouth, difficulty urinating, and abdominal pain
  ▪ No differences in study discontinuation because of adverse effects
  ▪ 5mg bid a little more effective numerically

Leon-Ferre et al. JNCI Cancer Spectrum 2019
Mean Hot Flash Score Percent Reduction

Randomized Trials

Not superior to placebo:
- Soy
- Flaxseed
- Black Cohosh
- Mg oxide
- Vitamin E

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Non-hormonal Options for Genitourinary Dysfunction in Breast Cancer Survivors

• Dyspareunia- Non-hormonal water-based products
  • Lubricants
  • Moisturizers
  • Topical liquid lidocaine
  • Laser therapy

• Atrophy/Stenosis/Pelvic floor weakness
  • Vaginal dilation
  • Kegel exercises
  • Pelvic PT

• SNRI therapy for hot flashes led to improved libido

• Psychotherapy, sex therapy; couples counseling

Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsive Breast Cancer

IBCSG 48-14 / BIG 8-13
ALLIANCE # A221405

THE POSITIVE TRIAL

INTERNATIONAL STUDY CHAIR: O. PAGANI
NA STUDY CHAIR: A. PARTRIDGE
The POSITIVE Trial

- Prospective study to evaluate safety and pregnancy outcomes of interrupting ET (available data suggests safety of pregnancy after breast cancer treatment)

- Enroll 500 women, <42, premenopausal, have completed between 18-30 months of ET

- Study participants come off ET for up to 2 years for a pregnancy attempt, pregnancy, breast feeding, restart hormonal therapy

- Outcomes: disease, reproductive, psychosocial
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Accrual complete as of December 2019
Conclusions

• Breast cancer in young women requires special consideration of treatment issues, in particular how the newest data apply to the very young and taking care not to overtreat young women just because they are young

• These patients have important and unique supportive care that can be addressed clinically today and with novel research, better in the future
Who We Are
An alliance of leading cancer centers devoted to patient care, research, and education

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To improve and facilitate quality, effective, efficient, and accessible cancer care so patients can live better lives

Our Vision
To define and advance high-quality, high-value, patient-centered cancer care globally

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