Breast Cancer in Young Women: Understanding Differences to Improve Outcomes

Ann Partridge, MD, MPH
December 5, 2019
Young women have higher risk of recurrence and mortality from breast cancer

Kim HJ et al, unpublished

5 year survival
94%
93%
88%

5% difference at 5 years

<40 years of age at diagnosis

Cancer Specific Survival in SEER - 2010-2015*

*unadjusted analysis

Kim HJ et al, unpublished
Breast cancer can be difficult for a person of any age... Life can be harder for young women with breast cancer
Helping Ourselves, Helping Others: The Young Women’s Breast Cancer Study (YWS)

• Prospective cohort enrolled from 2006-2016
  – Women age ≤40 at diagnosis of breast cancer
  – Identified through pathology record review (or clinic lists)
  – Academic and community sites in Massachusetts, Colorado, MN, Canada
  – Separate but related cohorts in Europe, Saudi Arabia, Mexico

• Outcomes
  – Established to explore biological, medical and psychosocial issues in young women with breast cancer

• Accrual and Methods
  – 1302 participants enrolled (of 2162 identified; 60% participation)
  – Median age at diagnosis: 37 years, range 17-40
  – Surveys: every 6 months x 3 years, annually thereafter x 20 years+
  – Medical record review serially
  – Central pathology review, tumor and blood banked at 3 timepoints

PI: A. Partridge
Co-PI: S. Rosenberg
YWS Research Outcomes:

• Annotated, long-term follow-up data on 1302 young women with breast cancer

• Associated biospecimens on vast majority (serial bloods and tumor)

• 20 Manuscripts published to date (first pub 2012)
Prospective Study of Fertility Concerns and Preservation Strategies in Young Women with Breast Cancer

Table 2. Fertility Concerns, Decision Making, and Strategies

<table>
<thead>
<tr>
<th>Concern, Decision, or Strategy</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before breast cancer diagnosis, wished to have biologic children in future</td>
<td>230</td>
<td>37</td>
</tr>
<tr>
<td>At time of survey, wished to have biologic children in future</td>
<td>160</td>
<td>26</td>
</tr>
<tr>
<td>Felt pressured by partner to have children, somewhat or a lot</td>
<td>31</td>
<td>5</td>
</tr>
<tr>
<td>Felt pressured by family to have children, somewhat or a lot</td>
<td>33</td>
<td>5</td>
</tr>
<tr>
<td>If wanted more children, concerned about:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caring for them if cancer recurred</td>
<td>27</td>
<td>4</td>
</tr>
<tr>
<td>Children having increased risk of developing cancer</td>
<td>70</td>
<td>11</td>
</tr>
<tr>
<td>If did not want more children, concerned about:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caring for them if cancer recurred</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>Children having increased risk of developing cancer</td>
<td>33</td>
<td>5</td>
</tr>
<tr>
<td>Pregnancy would increase risk of recurrence</td>
<td>59</td>
<td>9</td>
</tr>
<tr>
<td>At time of decision making about treatment, concerned about fertility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>301</td>
<td>49</td>
</tr>
<tr>
<td>A little</td>
<td>83</td>
<td>13</td>
</tr>
<tr>
<td>Somewhat</td>
<td>88</td>
<td>14</td>
</tr>
<tr>
<td>Very</td>
<td>148</td>
<td>24</td>
</tr>
</tbody>
</table>

- 68% discussed fertility before treatment
- Only 10% took special steps to preserve fertility

38% somewhat or very concerned

Ruddy et al, JCO 2014
Total cohort, n=1076

Interested, n=387 (36%)
- Attempted, n=138 (36%)
- No attempt, n=249 (64%)

Not interested, n=689 (64%)
- Attempted, n=8 (1%)
- No attempt, n=681 (99%)

Poorvu et al, ASCO 2017
Cumulative Pregnancy Interest, Attempts and Pregnancies at 5 Years

Total cohort, n=1076

- Interested, n=387 (36%)
  - Attempted, n=138 (36%)
    - Pregnant, n=94 (68%)
    - Not pregnant, n=44 (32%)
  - Not pregnant, n=249 (64%)
    - Not pregnant, n=236 (95%)
- Not interested, n=689 (64%)
  - Attempted, n=8 (1%)
    - Pregnant, n=1 (13%)
  - Not pregnant, n=681 (99%)
    - Not pregnant, n=672 (99%)

Poorvu et al, ASCO 2017
Early Pregnancy Outcomes

- Median follow-up 5 years
- 173 pregnancies among 117 women
- Majority with hx ER- disease

- Live births, 108, 61%
- Miscarriages, 44, 25%
- Abortion, 7, 4%
- TBD, 15, 9%
- Stillbirths, 2, 1%
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: Endocrine therapy (ET) interruption for pregnancy in breast cancer patients

• Prospective study to evaluate safety and pregnancy outcomes of interrupting ET

• Enroll 500 women <42, premenopausal, 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

Accrual complete as of December 31st
Younger Women are More Likely to be Non-Adherent with Endocrine Therapy

Hershman et al, JCO 2010
Why Are Young Women Less Adherent?

• Non-adherence (including non-initiation, non-persistence) among young women associated with:
  • Non-white race, lower education and lower income
  • Receipt of radiation
  • Experience of, fear of side effects
  • Feeling less informed about endocrine therapy
  • Fertility concerns
  • Negative emotions about endocrine therapy

Llarena et al, JNCI 2015; Rosenberg et al, SABCS 2016; Walker et al, J Adolesc and Young Adult Oncol, 2016; Poorvu et al, SABCS 2017
Breast Cancer Subtypes by Age in CCR

- HER2+ 28% in <40

- even more TNBC in young African American women

- more luminal B than A, more basal type in young women

Keegan et al, BCR 2012; Carey et al, JAMA 2006; Sweeney et al, Cancer Epi Bio Prev 2014
# Breast cancer subtypes in the YWS

## Table 2. Subtype by age group

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Total (n=1136)</th>
<th>( \leq 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>
Breast cancer subtypes in young women by BRCA status

Figure 1. Distribution of molecular phenotypes among BRCA1+ and BRCA2+ women

Figure 2. Distribution of molecular phenotypes among women with no BRCA mutation or not tested
Oncotype in the YWS in N0 and N1 (N=463)

Node negative (N0)

Log rank P= 0.006

Risk Group N Events 6-Yr DRF (95% CI) Chemo Use
RS <18 127 124 114 97.5 (96.1-99.4) 28.3%
RS 18-30 125 120 111 96.9 (95.7-98.1) 44.1%
RS >31 48 47 39 85.1 (72.9-92.1) 91.7%

RS <18 54 50 48 85.9 (72.6-93.3) 39.1%
RS 18-30 69 66 58 87.3 (76.0-93.5) 97.1%
RS >31 40 34 26 63.3 (45.1-76.2) 97.5%

1-3 positive nodes (N1)

Log rank P=0.004

Risk Group N Events 6-Yr DRF (95% CI) Chemo Use
RS <11 33 32 28 94.4 (66.6-99.2) 21.2%
RS 11-25 195 198 175 96.9 (92.7-98.7) 44.1%
RS >26 72 70 61 85.1 (72.9-92.1) 91.7%

RS <11 14 14 14 92.3 (56.6-98.5) 39.1%
RS 11-25 69 67 57 85.2 (75.3-91.4) 97.0%
RS >26 61 61 54 71.3 (57.3-81.5) 96.7%

Log rank P<0.001

Log rank P<0.010
Oncotype in N0, RS 11-25 by receipt of chemotherapy (N=195)

Log rank P=0.247

- Chemo received: 109, Events: 6, 6-Yr DRF (95% CI): 96.7 (89.9-98.9)
- No chemo: 86, Events: 2, 6-Yr DRF (95% CI): 97.3 (89.4-99.3)

Poorvu et al, JCO in press
Young, Empowered and Strong (YES): The Young Women’s Breast Cancer Study 2
YES: from Observation to Intervention

- Surgical Decision Aid
- SYMPTOM and CONCERN Management and Informational Support
- Mindfulness Intervention
- POSITIVE Trial
- Endocrine Therapy Adherence Intervention
- EMBRACE: Advanced Disease Support and Navigation

Enrollment → Diagnosis → Treatment → Long-term Survivorship
Conclusions

• There are a number of issues that are unique to young women or accentuated by being young at the diagnosis of breast cancer

• Addressing behavioral issues and psychosocial concerns is likely to improve not only QoL and survivorship, but survival

• Improved understanding and improvement of tailored care of this vulnerable population is critical to improving outcomes
Young and Strong Staff
Craig Snow
Rachel Gaither
Sonja Derai
Greg Kirkner
Liz Riley
Sylvia Ilahuku
Kathryn Rigby

Numerous additional local, national and international collaborators

• All of the patients who have participated in this work
• Patient advocates who have helped
• Funders whose support is critical