Adjuvant Endocrine Therapy in Breast Cancer: 2015 Update

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Magee Womens Cancer Program
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Questions in Adjuvant Endocrine Therapy: Focus on Premenopausal Women

• What is the optimal duration of adjuvant endocrine therapy?
• What is the optimal treatment for premenopausal women?
• What is next in endocrine therapy?
ON THE TREATMENT OF INOPERABLE CASES OF CARCINOMA OF THE MAMMA: SUGGESTIONS FOR A NEW METHOD OF TREATMENT, WITH ILLUSTRATIVE CASES.¹

BY GEORGE THOMAS BEATSON, M.D. EDIN., SURGEON TO THE GLASGOW CANCER HOSPITAL; ASSISTANT SURGEON, GLASGOW WESTERN INFIRMARY; AND EXAMINER IN SURGERY TO THE UNIVERSITY OF EDINBURGH.

I have no doubt it has fallen to the lot of nearly every medical man to have been consulted from time to time by patients suffering from carcinoma so widely spread or so situated that it has been quite apparent that nothing in the way of operative measures could be recommended. Such cases naturally excite our sympathy, but they also bring home to us the fact that once a case of cancer has passed beyond the reach of the knife or of the cautery, it...
## Current Guidelines for Adjuvant Endocrine Therapy

<table>
<thead>
<tr>
<th>Status</th>
<th>St Gallen 2013</th>
<th>ASCO 2014</th>
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<tbody>
<tr>
<td><strong>Premenopausal</strong></td>
<td>Tam X 5 yr</td>
<td>Tam X 5-10 yr</td>
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<tr>
<td><strong>Postmenopausal</strong></td>
<td>Tam X ≥ 5 yr OR AI X 5 y OR Switch AI to Tam OR Switch Tam to AI</td>
<td>AI X 5 yr OR Tam X 5-10 yr OR Tam X 5 yr to AI X 5 yr</td>
</tr>
</tbody>
</table>
Some Questions about Duration of Adjuvant Endocrine Therapy

- How did we get to 5 years of adjuvant tamoxifen?
- What is the evidence for longer duration?
- What do we know about duration of aromatase inhibitors?
- How can we select for candidates for shorter or longer therapy today?
5 Years of Tamoxifen versus No Tamoxifen

RECURRENTCE

Breast Cancer Mortality

Recurrence Yrs 0-4 Yrs 5-9 Yrs 9-14
Reduction 47% 31% 4%
p < 0.0001 p < 0.0001 p = 0.7

Breast cancer mortality Yrs 0-4 Yrs 5-9 Yrs 9-14
Reduction 29% 33% 34%
p < 0.0001 p < 0.0001 p < 0.0001

EBCTCG, Lancet, 2011
Randomized Trials of 10 vs 5 Years of Adjuvant Tamoxifen

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patient Number</th>
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<tbody>
<tr>
<td>ECOG, Scottish, NSABP B-14</td>
<td>1588</td>
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<tr>
<td>ATLAS</td>
<td>11646</td>
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<tr>
<td>aTTom</td>
<td>6953</td>
</tr>
<tr>
<td>Total</td>
<td>20187</td>
</tr>
</tbody>
</table>

ATLAS, Lancet, 2013
aTTom, ASCO, 2013
ATLAS: 6846 Women, ER+, 10 years vs. 5 years

RECURRENTNESS

- Years 5–9: RR 0.90 (0.79–1.02)
- Years 10+: RR 0.75 (0.62–0.90)
- All years: logrank p = 0.002

BREAST CANCER MORTALITY

- Years 5–9: RR 0.97 (0.79–1.18)
- Years 10+: RR 0.71 (0.58–0.88)
- All years: logrank p = 0.01

ATLAS, Lancet, 2013
ATLAS--All Subsets Benefit

No Impact of:

- Age
- Nodal status
- Tumor size
- Previous tamoxifen duration
- Extent of surgery
- Previous TAH
- Menopausal status
- Geography

ATLAS, Lancet, 2013
aTTom: 6953 women, 10 years vs. 5 years RECURRENCE

580 vs 672 recurrences  
RR=0.85 (95%CI 0.76-0.95)  
p=0.003

Gray, ASCO 2013
aTTom: 10 vs 5 Years of Adjuvant Tamoxifen OVERALL SURVIVAL

<table>
<thead>
<tr>
<th></th>
<th>No. Patients</th>
<th>No. Events Obs.</th>
<th>Exp.</th>
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<tbody>
<tr>
<td>5 years</td>
<td>3485</td>
<td>939</td>
<td>912.2</td>
</tr>
<tr>
<td>10 years</td>
<td>3468</td>
<td>885</td>
<td>911.8</td>
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</tbody>
</table>

885 vs 939 deaths

RR=0.94 (95%CI 0.86-1.03; p=0.2)

At risk:

<table>
<thead>
<tr>
<th></th>
<th>5 years</th>
<th>10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 years</td>
<td>3485</td>
<td>3468</td>
</tr>
<tr>
<td>6</td>
<td>3451</td>
<td>3440</td>
</tr>
<tr>
<td>7</td>
<td>3391</td>
<td>3370</td>
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<tr>
<td>8</td>
<td>3319</td>
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<td>9</td>
<td>3231</td>
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<td>10</td>
<td>3142</td>
<td>3112</td>
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<td>11</td>
<td>3053</td>
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<td>17</td>
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<td>19</td>
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<tr>
<td>20</td>
<td>303</td>
<td>294</td>
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Gray, ASCO 2013
Combined Outcomes in ATLAS and aTTom

<table>
<thead>
<tr>
<th></th>
<th>Breast Cancer Mortality</th>
<th>Overall Survival</th>
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<tbody>
<tr>
<td>Years 5-9</td>
<td>0.97 (0.84-1.15)</td>
<td>0.99 (0.89-1.10)</td>
</tr>
<tr>
<td>Years 10+</td>
<td>0.75 (0.65-0.86)*</td>
<td>0.84 (0.77-0.93)*</td>
</tr>
<tr>
<td>All years</td>
<td>0.85 (0.77-0.94)*</td>
<td>0.91 (0.84-0.97)*</td>
</tr>
</tbody>
</table>

* P < 0.05 favoring 10 years

Gray et al, ASCO, 2013
ASCO Guidelines 2014 update:

◆ If women are pre- or perimenopausal and have received 5 years of adjuvant tamoxifen, they should be offered 10 years total duration of tamoxifen.

◆ If women are postmenopausal and have received 5 years of adjuvant tamoxifen, they should be offered the choice of continuing tamoxifen or switching to an aromatase inhibitor for 10 years total adjuvant endocrine therapy

Some Questions about Duration of Adjuvant Endocrine Therapy

• How did we get to 5 years of adjuvant tamoxifen?
• What is the evidence for longer duration?
• What do we know about duration of aromatase inhibitors?
• How can we select for candidates for shorter or longer therapy today?
### Summary of Reported Adjuvant AI Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Time Since Random Assignment</th>
<th>Adjuvant Treatment</th>
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</thead>
<tbody>
<tr>
<td><strong>Primary Adjuvant</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATAC</td>
<td>-6 -4 -2 -1 0 2 3 4 5</td>
<td>TAM, ANA, TAM + ANA</td>
</tr>
<tr>
<td>BC 1-5yr</td>
<td>60-month strategy</td>
<td>TAM</td>
</tr>
<tr>
<td></td>
<td>Median follow-up 75 mos</td>
<td>TAM (3 yrs), TAM (3 yrs)</td>
</tr>
<tr>
<td></td>
<td>Postmenopausal, HR (+)</td>
<td>TAM (2 yrs), LET (3 yrs)</td>
</tr>
<tr>
<td>ABCSG-12</td>
<td>36 month strategy</td>
<td>TAM + GOS</td>
</tr>
<tr>
<td></td>
<td>Median follow-up 47.8 mos</td>
<td>TAM + GOS + ZOL</td>
</tr>
<tr>
<td></td>
<td>Premenopausal, ER and/or PR (+)</td>
<td>ANA + GOS + ZOL</td>
</tr>
<tr>
<td><strong>Sequencing</strong></td>
<td></td>
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<tr>
<td>ABCSG-40</td>
<td>Primary random assignment</td>
<td>TAM</td>
</tr>
<tr>
<td></td>
<td>60-month strategy</td>
<td>TAM (2 yrs), ANA (3 yrs)</td>
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<tr>
<td></td>
<td>Median follow-up 72 mos</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Postmenopausal, ER (+) or PR (+), no chemo</td>
<td></td>
</tr>
<tr>
<td>TAM</td>
<td>Randomly assigned to 3.3 yrs tx (5 yrs total)</td>
<td>TAM (2-3 yrs)</td>
</tr>
<tr>
<td></td>
<td>Median follow-up 64 mos</td>
<td>TAM</td>
</tr>
<tr>
<td></td>
<td>Postmenopausal, HR (+)</td>
<td>ANA</td>
</tr>
<tr>
<td>TEAM</td>
<td>Primary random assignment</td>
<td>TAM (2½ yrs), EXE (2½ yrs)</td>
</tr>
<tr>
<td></td>
<td>69 month strategy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Follow-up 61 mos</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Postmenopausal, ER and/or PR (+)</td>
<td>EXE</td>
</tr>
<tr>
<td>IRS</td>
<td>Randomly assigned to 3.3 yrs tx (5 yrs total)</td>
<td>TAM (2-3 yrs)</td>
</tr>
<tr>
<td></td>
<td>Median follow-up 55.7 mos</td>
<td>TAM</td>
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<tr>
<td></td>
<td>Postmenopausal, ER (+) or unknown</td>
<td>EXE</td>
</tr>
<tr>
<td>NSABP B-39</td>
<td>Randomly assigned to 1-4 yrs tx (5 yrs total)</td>
<td>TAM (1-4 yrs)</td>
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<tr>
<td></td>
<td>Median follow-up 42 mos</td>
<td>TAM</td>
</tr>
<tr>
<td></td>
<td>Postmenopausal</td>
<td>ANA</td>
</tr>
<tr>
<td>ARNO 91</td>
<td>Randomly assigned to 3 yrs tx (5 yrs total)</td>
<td>TAM (2 yrs)</td>
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<td></td>
<td>Median follow-up 30.1 mos</td>
<td>TAM</td>
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<tr>
<td></td>
<td>Postmenopausal, hormone responsive</td>
<td>ANA</td>
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<tr>
<td><strong>Extended Adjuvant</strong></td>
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<tr>
<td>MA 17m</td>
<td>5 yrs of TAM, randomly assigned to 80 mos of tx</td>
<td>TAM</td>
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<tr>
<td></td>
<td>Median follow-up 84 mos</td>
<td>LET</td>
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<tr>
<td>ABCSG-64</td>
<td>6 years of TAM, randomly assigned to 36 mos of tx</td>
<td>TAM + PLACEBO</td>
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<td>Median follow-up 92.3 mos</td>
<td>ANA</td>
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<tr>
<td>NSABP B-32</td>
<td>6 yrs of TAM, randomly assigned to 80 mos of tx</td>
<td>TAM</td>
</tr>
<tr>
<td></td>
<td>Postmenopausal, HR (+)</td>
<td>EXE</td>
</tr>
</tbody>
</table>

**Absolute Gain in DFS at 3-6 Years:**

- **Primary**: 2-4%
- **Switch (sequencing)**: 3-5%
- **Extended**: 6%

Burstein et al, J Clin Oncol, 2010
Benefit of Extended Adjuvant Letrozole in MA-17

Notable benefit for women who were premenopausal at time of diagnosis and became postmenopausal during tamoxifen.

Lack of Benefit from Extended AI in Obese Women in ABCSG6a

Figure 2. (A) DFS: Anastrozole vs Control, normal weight patients and (B) OS: Anastrozole vs Control, normal weight patients.

Figure 3. (A) DFS: Anastrozole vs Control, overweight + obese patients and (B) OS: Anastrozole vs Control, overweight + obese patients.
What We Are Waiting For.....

- Little information about > 5 years of AI
- Ongoing trials include:

<table>
<thead>
<tr>
<th>MA17R</th>
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<tbody>
<tr>
<td>NSABP B42</td>
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<tr>
<td>IDEAL</td>
</tr>
<tr>
<td>ABCSG-16</td>
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Some Questions about Duration of Adjuvant Endocrine Therapy

• How did we get to 5 years of adjuvant tamoxifen?
• What is the evidence for longer duration?
• What do we know about duration of aromatase inhibitors?
• How can we select for candidates for shorter or longer therapy today?
Some Potential Factors to Support Use of Extended Adjuvant Endocrine Therapy

• Higher stage at diagnosis
• Limited or absent toxicity
• Absence of life-threatening co-morbidities
• Younger age
• Patient preference
• Biomarkers for late recurrence?
## Potential Molecular Tests for Late Recurrence

<table>
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<tr>
<th>Test</th>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>Clinical Treatment Score</td>
<td>CTS</td>
<td>T, N, grade, age, treatment</td>
</tr>
<tr>
<td>Immunohistochemical Score 4</td>
<td>IHC4</td>
<td>IHC for ER, PR, Ki67, HER-2</td>
</tr>
<tr>
<td>Oncotype Dx</td>
<td>RS</td>
<td>21 gene assay</td>
</tr>
<tr>
<td>Prosigna Risk of Recurrence</td>
<td>ROR</td>
<td>PAM50</td>
</tr>
<tr>
<td>Breast Cancer Index</td>
<td>BCI</td>
<td>HOXB13/IL17BR</td>
</tr>
<tr>
<td>EndoPredict</td>
<td>EPClin</td>
<td>12 gene assay</td>
</tr>
</tbody>
</table>

Adapted from Sestak et al, J Clin Oncol, 2014
Use of BCI to Predict Early and Late Recurrence

BCI includes:
- HOXB13:IL17 BR (H/I) and
- Molecular Grade Index

Low BCI associated with high DRFS at 0-5 yr and >5 yr

Zhang et al, Clin Cancer Res, 2013
PAM50 Risk of Recurrence Score for Late Distant Recurrence

N=2137 women from TransATAC & ABCSG 8 trials who were recurrence-free 5 yrs after diagnosis

Sestak et al, J Clin Oncol, 2014
Optimal Duration of Endocrine Therapy

- Evidence supports > 5 yrs of tamoxifen or extended adjuvant therapy of tamoxifen to AI
- Waiting for results of > 5 yrs of AI
- Multiple molecular tests under study that may predict late relapse but not known if they predict benefit for extended therapy
Questions in Endocrine Therapy

• What is the optimal duration of endocrine therapy?
• What is the optimal treatment for premenopausal women?
• What is next in endocrine therapy?
Key Questions about Adjuvant Endocrine Therapy in Premenopausal Women

• What is the role of ovarian function suppression (OFS) for women receiving tamoxifen? SOFT and E3193

• What is the role of aromatase inhibitors (AI) for women treated with OFS? SOFT, TEXT and ABCSG 12

• What is the role of chemotherapy in women receiving combined endocrine therapy? PERCHE
Premenopausal HR+ Early Breast Cancer

- Adjuvant tamoxifen for ≥ 5 years is recommended
- The value of ovarian function suppression or ablation (OFS) for women who receive tamoxifen (T) is uncertain
  - Historical studies do not answer this question...
- Women who develop chemotherapy-induced ovarian suppression (amenorrhea) have a reduced risk of relapse
- Likelihood of chemotherapy-induced amenorrhea correlated with older age; less likely in women < 35 years age
Questions in Premenopausal Hormone-Receptor Positive Early Breast Cancer

• What is the value of adding OFS to adjuvant tamoxifen in premenopausal women?

• What is role of adjuvant therapy with the aromatase inhibitor (AI) exemestane + OFS in premenopausal women?
SOFT: SUPPRESSION of OVARIAN FUNCTION TRIAL
Premenopausal ER+ve and/or PR+ve Breast Cancer

3047 Patients Randomized in ITT, Dec 2003 - Jan 2011

Primary Analysis (n= 2033)

Two Patient Cohorts

No Chemotherapy (47%)
Premenopausal, within 12 weeks of surgery
(Median time since surgery = 1.8 months)

Prior Chemotherapy (53%)
Premenopausal* after completing chemotherapy;
Randomization within 8 months of completion
(Median time since surgery = 8.0 months)

→ Tamoxifen x 5y (n=1018)

→ Tamoxifen+OFS x 5y (n=1015)

→ Exemestane+OFS x 5y (n=1014)

Median follow-up 5.6 years
OFS=ovarian function suppression

*According to locally-determined E₂ level in premenopausal range
Primary analysis in overall population not significant ($p=0.10$)

Multivariable Cox model HR=0.78 (95% CI 0.62-0.98) $p=0.03$

SOFT Secondary Objectives

T+OFS v T: 19% relative reduction in recurrence, $p=0.09$
E+OFS v T: 36% relative reduction in recurrence with 5-yr BCFI >90%

No chemotherapy cohort selected for low risk features:
90% ≥ age 40yr, 91% node negative, 85% tumor ≤ 2cm, 41% grade 1

SOFT—Outcomes for Women < 35 yr

- 350 patients (11.5%) under age 35
- 94% received chemotherapy in this age group

TEXT and SOFT Joint Analysis

Enrolled: Nov03-Apr11

**TAMOXIFEN AND EXEMESTANE TRIAL (N=2672)**

- Premenopausal
- ≤12 wk after surgery
- Planned OFS
- ± Planned chemo

- Tamoxifen+OFS x 5y
- Exemestane+OFS x 5y

**SUPPRESSION OF OVARIAN FUNCTION TRIAL (N=3066)**

- Premenopausal
- ≤12 wk after surgery
- No chemo

- Tamoxifen x 5y
- TAMOXIFEN+OFS x 5y
- Exemestane+OFS x 5y

**SOFT**

- Remain premenopausal
- ≤ 8 mo after chemo

- Tamoxifen+OFS x 5y
- Exemestane+OFS x 5y

**Joint Analysis (N=4690)**

- Tamoxifen+OFS x 5y
- Exemestane+OFS x 5y

Enrolled: Nov03-Apr11

Median follow-up 5.7yr

OFS=ovarian function suppression
## Primary Analysis: Patient Characteristics Similar to SOFT analysis

<table>
<thead>
<tr>
<th></th>
<th>No chemo 47% (n=949)</th>
<th>Prior Chemo 53% (n=1084)</th>
<th>Overall (n=2033)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age</td>
<td>46 y</td>
<td>40 y</td>
<td>43 y</td>
</tr>
<tr>
<td>Lymph Node +ve</td>
<td>9%</td>
<td>57%</td>
<td>35%</td>
</tr>
<tr>
<td>Tumor &gt; 2 cm</td>
<td>14%</td>
<td>47%</td>
<td>32%</td>
</tr>
<tr>
<td>Grade 1</td>
<td>41%</td>
<td>14%</td>
<td>27%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>7%</td>
<td>35%</td>
<td>22%</td>
</tr>
<tr>
<td>HER2+ve</td>
<td>4%</td>
<td>18%</td>
<td>12%</td>
</tr>
<tr>
<td>Median time since surgery</td>
<td>1.8 mo</td>
<td>8.0 mo</td>
<td>3.2 mo</td>
</tr>
</tbody>
</table>
Exemestane+OFS Improved DFS

Difference 3.8% at 5 years

5.7 years median follow-up

### Joint Analysis of TEXT and SOFT

**Exemestane + OFS vs Tamoxifen + OFS**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>DFS</td>
<td>0.72 (0.60-0.85)</td>
<td>0.0002</td>
</tr>
<tr>
<td>BCFI</td>
<td>0.66 (0.55-0.80)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DDFI</td>
<td>0.78 (0.62-0.97)</td>
<td>0.02</td>
</tr>
<tr>
<td>OS</td>
<td>1.14 (0.86-1.51)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

**Median Follow-up of 5.7 years**

Premenopausal No Chemotherapy: Excellent Outcomes

Cohort selected for low risk clinicopathologic features
90% ≥ age 40yr, 91% node negative, 85% tumor ≤ 2cm, 41% grade 1
Premenopausal after Prior Chemotherapy

T+OFS v T: Absolute improvement in 5-yr BCFI of 4.5%
E+OFS v T: Absolute improvement in 5-yr BCFI of 7.7% and 5-yr DRFI of 4.2%
All women < 35 years of age:
Greatest improvement with E+ OFS

350 patients (11.5%) under age 35
94% received chemotherapy in this age group
Treatment Effect: Symptoms

E+OFS

<table>
<thead>
<tr>
<th>Symptom</th>
<th>T+OFS</th>
<th>T</th>
<th>E+OFS</th>
</tr>
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<tbody>
<tr>
<td>Hot flushes</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sweats</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Vaginal discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal dryness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal itching/irritation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of sexual interest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arousal difficulties</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Change of QoL Score from Baseline (Mean with 95% CI)
(±8 is the minimal clinically meaningful change of QoL scores)

Ribi, SABCS, 2014
Quality of Life

- Overall, patients receiving T+OFS experienced worse endocrine symptoms and sexual functioning than those receiving T alone.
- Most differences in symptoms between treatments were seen during the first 2 years of treatment, no longer apparent at 5 years.
- Global QoL did not differ between T+OFS and T alone.
- E+OFS vs. T+OFS showed differential effects on endocrine symptoms burden, but not on global QoL indicators.
Quality of Life

• Less improvement in coping and greater treatment burden were seen with T+OFS vs. T in patients with no prior chemotherapy.

• For patients who received prior chemotherapy, differences in endocrine symptoms between T+OFS and T were less pronounced.

• The cohort of women receiving prior chemotherapy benefited most from OFS in terms of disease control.
Optimal Endocrine Therapy for Premenopausal Hormone-Responsive Breast Cancer ABCSG12

- Accrual 1999-2006
- 1,803 premenopausal breast cancer patients
- Endocrine-responsive (ER and/or PR positive)
- Stage I&II, <10 positive nodes
- Neoadjuvant chemo only
- Treatment duration: 3 years

Median age 45 yrs
T1 tumor 75%
N0 66%
Grade 1/2 75%
Preop chemo 5%

Surgery (+RT) → Goserelin 3.6 mg q28d → Randomize 1:1:1:1 →
- Tamoxifen 20 mg/d
- Tamoxifen 20 mg/d + Zoledronic acid 4 mg q6m
- Anastrozole 1 mg/d
- Anastrozole 1 mg/d + Zoledronic acid 4 mg q6m

Median follow-up=94 mo

Gnant et al, Ann Oncol, 2014
Final Analysis of ABCSG 12

Gnant et al, Ann Oncol, 2014
Why the different results with ABCSG and SOFT/TEXT?

- Different AIs
- Different LHRH agonists
- Duration of endocrine therapy
- Different patient characteristics
- Use of and timing of chemotherapy
- Size and statistical power
Adjuvant Endocrine Therapy for Premenopausal Women

• Several evidence-based choices now available:
  - Tamoxifen X 5-10 yr
  - Tamoxifen X 5 yr to AI X 5 yr (MA-17)
  - OFS + Tamoxifen
  - OFS + AI

• **Low risk:** Tam alone for 5 (or 10) years

• **High risk (chemo, node +, young):** Consider use of OFS+Tam or OFS+AI Optimal duration of OFS-based therapy uncertain

• **Long term follow-up for toxicity & benefit critical**
Questions in Endocrine Therapy

• What is the optimal duration of endocrine therapy?
• What is the optimal treatment for premenopausal women?
• What is next in endocrine therapy?
Challenges in Optimal Endocrine Therapy

- Predictive markers beyond ER, PR
- Understanding pathways of resistance
- Optimizing host environment—BMI?
- Monitoring long term benefit & toxicity
- Compliance of patient (and doctor)
- Dissemination of endocrine prevention strategies for high risk women
Mutations of ESR1 in Metastatic Breast Cancer But Rarely in Primary Breast Cancer

Oesterreich and Davidson, Nature Genetics, 2013
Some Potential Strategies to Overcome Endocrine Resistance in Breast Cancer

• Everolimus
• Other PI3K/mTOR inhibitors
• Epigenetic modifiers—eg HDAC inhibitor like entinostat
• CDK4/6 inhibition—palbociclib
• FGFR inhibitors
• Use of SERDs
• Biomarker-driven use of serial endocrine agents?
Thank you!

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  – Adrian Lee, PhD
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