Endocrine Therapy in Premenopausal Breast Cancer

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Texas Oncology, PA
US Oncology

Ovarian Ablation or Suppression vs. Not in ER + or ER UK Breast cancer

Recurrence

Breast Cancer Mortality

15-year gain 4.3% (SE 1.9) Logrank 2p=0.00001

15-year gain 3.2% (SE 2.0) Logrank 2p=0.004

Lancet. 2005;365:1687
Tamoxifen Efficacy Does Not Differ Significantly According to Patient Age

**Table 1.** Five Years of Tamoxifen in ER-Positive or ER-Unknown Breast Cancer by Age: Early Breast Cancer Trialists’ Collaborative Group Overview Analysis

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Breast Cancer Recurrence Rate</th>
<th>Breast Cancer Death Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk Ratio</td>
<td>SE</td>
</tr>
<tr>
<td>For all age groups</td>
<td>0.59</td>
<td>0.03</td>
</tr>
<tr>
<td>&lt; 40</td>
<td>0.56</td>
<td>0.10</td>
</tr>
<tr>
<td>40-49</td>
<td>0.71</td>
<td>0.07</td>
</tr>
<tr>
<td>50-59</td>
<td>0.66</td>
<td>0.05</td>
</tr>
<tr>
<td>60-69</td>
<td>0.55</td>
<td>0.05</td>
</tr>
<tr>
<td>≥ 70</td>
<td>0.49</td>
<td>0.12</td>
</tr>
</tbody>
</table>

NOTE. Reproduced with permission. Abbreviation: ER, estrogen receptor.

OA/OS in Premenopausal ESBC Patients

- Does OA/OS add to standard tamoxifen in premenopausal ER+ ESBC pts?
Overall Survival  HR+ Premenopausal First-Line MBC Pts

Overall Logrank test: p = 0.0114

<table>
<thead>
<tr>
<th></th>
<th>O</th>
<th>N</th>
<th>Number of patients at risk</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>54</td>
<td></td>
<td>29</td>
<td>LHRH-A</td>
</tr>
<tr>
<td>35</td>
<td>53</td>
<td></td>
<td>39</td>
<td>LHRH-A+TAM</td>
</tr>
<tr>
<td>44</td>
<td>54</td>
<td></td>
<td>34</td>
<td>TAM</td>
</tr>
</tbody>
</table>
INT 0142 Tam vs Tam + OFS  
Premenopausal, N0 HR+  
n = 345, did not meet accrual goal of 1684

<table>
<thead>
<tr>
<th></th>
<th>Tam(%)</th>
<th>Tam + OA(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DFS</td>
<td>87.8</td>
<td>90.3</td>
</tr>
<tr>
<td>OS</td>
<td>95</td>
<td>97</td>
</tr>
</tbody>
</table>

RR = DFS .88 and OS .65 with trend favoring OFS

Chemoendocrine Therapy for Premenopausal Women
E5188 INT 0101

Premenopausal
Receptor-positive
Node-positive
n=1503

< 35 10%
35-39 19%
>39 71%

CAF
CAF -- Goserelin (Z) X 5 y
CAF -- Goserelin (Z) + Tamoxifen (T) X 5 y

Disease-Free Survival for Women Under 40 Years
E5188 INT 0101

Disease-Free Survival (Years)

Probability

9 yr DFS

CAF 48%
CAFZ 55%
CAFZT 64%
Disease-Free Survival for Women 40 Years or Over

Proportion

Disease-Free Survival (Years)

Probability

9 yr DFS

CAF 61%
CAFZ 62%
CAFZT 69%
Meta-analysis of LHRH agonists as adjuvant treatment in premenopausal patients with ER + breast cancer

- 11,906 women in 16 trials
  - Median follow-up 6.8 years
  - 9,022 HR positive
- As only adjuvant treatment no benefit (338 pts)
- Addition of LHRH agonists to tamoxifen, chemotherapy, or both reduced recurrence by 12.7% and death after recurrence by 15.1% (relative reduction)
- Similar efficacy to chemotherapy
- No trials of LHRH agonist versus chemotherapy with tamoxifen in both arms

Chemotherapy (± tam) ± LHRH (n=3307)

**RECURRENT DEATH AFTER RECURRENCE**

- HR=0.85, 95% CI = [0.73-0.99], P=0.04
- Chemotherapy ± tamoxifen
- LHRH addition
- 13.1% vs. 11.3%
- 1.8% reduction

- Lancet. 2007;369:1714
### Summary of LHRH Agonists Meta-analysis: Relative Changes

<table>
<thead>
<tr>
<th>COMPARISON</th>
<th>Recurrence (%)</th>
<th>Death after recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil ± LHRH (n=338)</td>
<td>-28.4%</td>
<td>-17.8%</td>
</tr>
<tr>
<td></td>
<td>0.08</td>
<td>0.49</td>
</tr>
<tr>
<td>Chemo vs. LHRH (n=3184)</td>
<td>+3.9%</td>
<td>-6.7%</td>
</tr>
<tr>
<td></td>
<td>0.52</td>
<td>0.40</td>
</tr>
<tr>
<td>Chemo vs. LHRH + tam (n=1577)</td>
<td>-10.1%</td>
<td>-11.1%</td>
</tr>
<tr>
<td></td>
<td>0.25</td>
<td>0.37</td>
</tr>
<tr>
<td>Tam ± LHRH (n=1013)</td>
<td>-14.5%</td>
<td>-15.9%</td>
</tr>
<tr>
<td></td>
<td>0.20</td>
<td>0.33</td>
</tr>
<tr>
<td>Chemo (± tam) ± LHRH (n=3307)</td>
<td>-12.2%</td>
<td>-15.0%</td>
</tr>
<tr>
<td></td>
<td>0.04</td>
<td>0.04</td>
</tr>
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</table>

Lancet. 2007;369:1714
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
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<tr>
<td>C + LHRH vs C</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt; 40 years old</td>
<td>714</td>
<td>–24.7</td>
<td>–39.5 to –6.2</td>
<td>.01</td>
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<tr>
<td>&gt; 40 years old</td>
<td>1,662</td>
<td>–5.1</td>
<td>–20.1 to 12.7</td>
<td>.55</td>
</tr>
<tr>
<td>(C ± T) + LHRH vs (C ± T)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt; 40 years old</td>
<td>795</td>
<td>–25.2</td>
<td>–39.4 to –7.7</td>
<td>.01</td>
</tr>
<tr>
<td>&gt; 40 years old</td>
<td>1,946</td>
<td>–3.9</td>
<td>–18.1 to 12.9</td>
<td>.63</td>
</tr>
</tbody>
</table>

LHRH agonists + chemotherapy +/- tamoxifen: Recurrence risk by age

- ≤ 35 years  HR 0.66
- 35-39 years  HR 0.77
- 40-44 years  HR 0.96
- 45-49 years  HR 1.03
- ≥ 50 years  HR 0.85

Significant interaction for recurrence of age for addition of LHRH agonist to chemotherapy with or without tamoxifen (p=0.046)
Conclusions of LHRH agonist Meta-Analysis

• Effective in premenopausal women with HR+ breast cancer
• Tamoxifen treatment not optimal in some studies
• Similar to CMF
• Small additional benefit when used with chemotherapy with or without tamoxifen especially in women ≤ 40
Amenorrhea and Prognosis

• Evaluation of 10 trials to assess benefit of drug-induced amenorrhea

• 9/10 trials had increased relapse free survival when amenorrhea achieved, hazard ratio 0.56

• Drug-induced amenorrhea associated with a 44% reduction in relapse.
## CIA: Taxane Based

<table>
<thead>
<tr>
<th>Study</th>
<th>N pt</th>
<th>Regimen</th>
<th>Design</th>
<th>CIA%</th>
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<tbody>
<tr>
<td>Martin 2005</td>
<td>823</td>
<td>TAC, FAC</td>
<td>P</td>
<td>62</td>
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<tr>
<td>Ibrahim 2003</td>
<td>88</td>
<td>FAC x4c, FAC x4c-&gt;Paclitaxel x4c</td>
<td>R</td>
<td>69</td>
</tr>
<tr>
<td>Stone 2000</td>
<td>81</td>
<td>AC, AC-&gt;Paclitaxel</td>
<td>R</td>
<td>43</td>
</tr>
<tr>
<td>Alton 2004</td>
<td>64</td>
<td>AC, AC-&gt;taxane</td>
<td>P</td>
<td>71</td>
</tr>
<tr>
<td>Davis 2005</td>
<td>159</td>
<td>AC or CAF, AC or CAF -&gt;taxane</td>
<td>R</td>
<td>29</td>
</tr>
</tbody>
</table>
NSABP B-30

Node Positive

Stratification
# Nodes, RT, Surgery, Tamoxifen

AC x 4 → T x 4
AT x 4
TAC x 4

T = docetaxel
Tam x 5 yrs for all pts ER+ and/or PR +
NSABP B-30: Landmark Analysis
OS and DFS According to Amenorrhea

HR in ER+: 0.52 (p=0.002)  
HR in ER+: 0.51 (p <0.001)

NSAPB B 30 MHS: Duration of Amenorrhea by Age

NSAPB B 30 MHS: Amenorrhea in pts ≤ 40

Proportion of Patients Amenorrheic

Duration of Amenorrhea (Months)

P < .001

NSAPB B 30 MHS: Amenorrhea in pts > 40

P < .001

Duration of Amenorrhea (Months)

NSAPB B 30 MHS: With or without tamoxifen

Conclusions for NSABP B30 MHS

- 90% amenorrhea for ≥ 3 months
- 79% amenorrhea for ≥ 6 months
- Only 5% no change at all
- Amenorrhea increases with age and tamoxifen use
- There are no associations between amenorrhea and QOL indices

Ganz, et al and Swain. J Clin Oncol. 2011;29;1110
IBCSG. J Natl Cancer Inst 2003;95:1833

International Breast Cancer Study Group
Trial VIII Node Neg  5yr DFS

ER-Positive

CMF → G

CMF

G

5-yr DFS Percent

0 20 40 60 80 100

Goserelin

CMF

CMF → Goserelin

Median Age

38 39 40 42 43 44 45 46 47 48 49 51
IBCSG Trial VIII: Premenopausal Node negative

< 39 yrs

≥ 40 yrs

Bernhard J et al. JCO 2007;25:263
ABCSD-12 Trial Design

- Accrual 1999-2006
- 1,803 premenopausal breast cancer patients
- Endocrine-responsive (ER and/or PR positive)
- Stage I&II, <10 positive nodes
- No chemotherapy except neoadjuvant
- Treatment duration: 3 years

75% T1 and 30% node +
Secondary End Points: ANA vs. TAM

Relapse-Free Survival

Overall Survival

Patients at risk

TAM 900 834 719 553 411 243 129 50
ANA 903 844 725 540 411 255 139 51

# ABCSG-12 Trial of Endocrine Therapy With or Without Zoledronic Acid

<table>
<thead>
<tr>
<th></th>
<th>Tamoxifen (n = 900)</th>
<th>Anastrozole (n = 903)</th>
<th>HR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease-Free Survival</td>
<td>65 events</td>
<td>72 events</td>
<td>1.096</td>
<td>.593</td>
</tr>
<tr>
<td>Recurrence-Free Survival</td>
<td>64 events</td>
<td>72 events</td>
<td>1.116</td>
<td>.529</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>15 events</td>
<td>27 events</td>
<td><strong>1.791</strong></td>
<td>.065</td>
</tr>
</tbody>
</table>

Goserelin Plus Anastrozole in Premenopausal, Receptor Positive, Metastatic Breast Cancer

Within 6 months, 3 of 32 women had premenopausal estradiol levels

\[\text{Abstract 1030}\]

\[\text{Abstract 1030}\]

\[\text{\textsuperscript{1}}\text{ Carlson RW, Schurman CM, Rivera E. Proc ASCO:Abst 1030,2006}\]
Enrollment Completed!!

**SOFT**
(any C/no C)
Accrual target 3,000

-ER+ /PgR+
-Localized disease to breast and nodes, fully resected
-Estradiol in premenopausal range

**TEXT**
(any C/no C)
Accrual target 3,000

**R**

- Tamoxifen 5 years
- OAS + tamoxifen 5 years
- OAS + exemestane 5 years

- LHRH + tamoxifen 5 years
  Triptorelin commenced at start of treatment
- LHRH + exemestane 5 years
  Triptorelin commenced at start of treatment
### ADJUVANT ENDOCRINE THERAPY

- **Postmenopausal**: Complete 5 y tamoxifen\(^2\) (category 1) or aromatase inhibitor to complete 5 y (category 1) or longer (category 2B)\(^3,4\)
  - **Complete 5 y tamoxifen\(^2\) (category 1)** → Aromatase inhibitor for 5 y (category 1)\(^3\)
  - **Postmenopausal** → Aromatase inhibitor for 5 y (category 1)\(^3\)
- **Premenopausal**: Tamoxifen\(^2\) for 2-3 y (category 1) ± ovarian suppression or ablation (category 2B)
  - **Tamoxifen\(^2\) for 2-3 y** → Aromatase inhibitor for 5 y (category 1)\(^3\)
  - **Tamoxifen\(^2\) to 4.5-6 y** → Aromatase inhibitor for 5 y (category 1)\(^3\)
- **Women with contra-indication to aromatase inhibitors, who decline aromatase inhibitors or who are intolerant of the aromatase inhibitors, tamoxifen\(^2\) for 5 y (category 1)**

1. NCCN Guidelines™ Version 2.2011
2. Breast Cancer Table of Contents
3. Staging, Discussion
NCCN v.2.2011

• Magnitude of benefit from surgical or radiation ovarian ablation is similar to that which is achieved by CMF alone
• Early evidence suggest benefits of ovarian suppression (LHRH agonist) similar to ovarian ablation
• Combination of endocrine treatment may be superior to suppression alone
• Benefit of ovarian suppression/ablation is unclear in women who have received chemotherapy
St. Gallen’s International Expert Consensus Panel

• Selection of endocrine therapy in premenopausal women with endocrine responsive tumors
  – Tamoxifen ± ovarian suppression (preference for tamoxifen alone)

• For patients with contraindications to tamoxifen:
  – Ovarian suppression ± aromatase inhibitor (suggested to be reasonable)

Cochrane Meta-analysis for LHRH agonists

• 14 trials identified: Updated 2/19/2009
• Support clinical benefit
  – LHRH similar to CMF
  – LHRH + chemo + tam better than chemo alone
• Recommend comparison with 3rd generation chemotherapy and tamoxifen
• Continue current trials

Goel et al Cochrane Database Syst Rev. CD004562
Cancer Care Ontario
Evidence-based recommendation

Adjuvant Ovarian Ablation in the Treatment of Premenopausal Women with Early Stage Breast Cancer

July 6, 2010

ASCO has endorsed recommendations
Cancer Care Ontario

• EBCTCG: OA vs no systemic therapy
  – HR 0.72 for recurrence and HR 0.71 for mortality
• EBCTCG: No benefit in adding OA to chemo
• Meta-analysis of 6 trials found no difference between OA and CMF
• Cuzick meta-analysis found no significant benefit for LHRH addition to tamoxifen or tamoxifen and chemo (individual trials); meta-analysis overall was positive for improved RFS/OS with LHRH agonist

http://www.cancercare.on.ca
For premenopausal women with early stage invasive breast cancer: OA should not be routinely added to systemic therapy with chemotherapy, tamoxifen, or the combination of tamoxifen and chemotherapy.

OA alone is not recommended as an alternative to any other form of systemic therapy, except in the specific case of patients who are candidates for other forms of systemic therapy but who for some reason will not receive any other systemic therapy.

http://www.cancercare.on.ca
Ovarian Function Suppression in Premenopausal Women

- Available data suggest that amenorrhea benefits premenopausal HR+ EBC patients in addition to tamoxifen.

- Uncertain whether addition of LHRH agonist or oophorectomy adds to tamoxifen in women who have had adjuvant chemotherapy. May be some benefit in women under 40.

- Do premenopausal ER+ pts need long duration Endocrine Therapy as in MA-17 Tamoxifen then AI?
Substantial Recurrences after 5 years of Tamoxifen Premenopausal vs Postmenopausal

≈ 5 years tamoxifen vs. Not
RECURRENT
Pre/Peri, ER+

≈ 5 years tamoxifen vs. Not
RECURRENT
Post, ER+

35% @ 15 yr

18% @ 5 y

15–y gain 9.5% (SE 1.8)
Logrank 2p < 0.00001

15–y gain 14.8% (SE 1.5)
Logrank 2p < 0.00001

Extended TAM? No clear benefit - yet?

- **B-14:**
  - 1o: ER+ Tam 5y v Nil ➔ positive
  - 2o: N=1152 DFS @ 5 yr ➔ Tam 5 v Nil
  - Placebo better

- **ATLAS (Adj Tam Longer Against Shorter) Peto**
  SABCS 2007: quality & compliance issues but DFS improved with longer than 5 yrs Tam

- **aTTom (Adj Tam To Offer More?)** N=6938 ER+/unk: Tam 5 v 10y; mF/U 4.2 y; improved DFS but P=NS; OS same; ↑ uterus ca (76 v 35)

Cianfrocca M. Clin Breast Ca 2008; 8:493
Rimawi ME, Osborne CK. *Diseases of the Breast* 4th ed.
EBCCTG Metaanalysis Longer vs Shorter Tamoxifen

To be updated SABCS, 2012

**RECURRENTE**
ER+ / ER unknown

<table>
<thead>
<tr>
<th>Years 0 – 4</th>
<th>Years 5 – 9</th>
<th>Year 10+</th>
</tr>
</thead>
<tbody>
<tr>
<td>'Longer'</td>
<td>3.03 (643 / 21196)</td>
<td>2.42 (95 / 3919)</td>
</tr>
<tr>
<td>'Shorter'</td>
<td>3.45 (710 / 20585)</td>
<td>3.03 (114 / 3767)</td>
</tr>
<tr>
<td>Rate ratio, from (O–E) / V</td>
<td>0.88 SE 0.05</td>
<td>0.78 SE 0.12</td>
</tr>
<tr>
<td></td>
<td>-0.12 / 326.8</td>
<td>-12.6 / 50.7</td>
</tr>
</tbody>
</table>
Premenopausal Breast Cancer

2006 EBCTCG
OA vs NOT and OS vs NOT
No Tamoxifen
Mixed ER Status
OS vs OA Cross-Trial Comparisons
Ovarian ablation/suppression vs not Women under 50 at randomisation Breast cancer mortality - Follow-up

<table>
<thead>
<tr>
<th>Category</th>
<th>Deaths/Women</th>
<th>Deaths/Women</th>
<th>Deaths/Women</th>
<th>Adjusted</th>
<th>Logrank</th>
<th>Variance of O-E</th>
<th>Ratio of annual death rate Abl/Suppr. vs Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Allocated</td>
<td>Abl/Suppr.</td>
<td>control</td>
<td>O-E</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>(a) ovarian ablation in the absence of chemotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years 0–9</td>
<td>250/673 (37:1%)</td>
<td>265/622 (43:1%)</td>
<td>-25:5</td>
<td>93:8</td>
<td></td>
<td>0.76 (SE 0.09)</td>
<td></td>
</tr>
<tr>
<td>Years 10–19</td>
<td>42/3359 (1:3%)</td>
<td>67/2851 (2:9%)</td>
<td>-17:4</td>
<td>20:5</td>
<td></td>
<td>0.43 (SE 0.15)</td>
<td></td>
</tr>
<tr>
<td>Years 20+</td>
<td>15/1846 (1:0%)</td>
<td>13/1372 (0:9%)</td>
<td>-2:4</td>
<td>5:9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) subtotal</td>
<td>311/5578 (5:3%)</td>
<td>348/4645 (7:6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.68 (SE 0.08) 2p = 0.00003</td>
</tr>
<tr>
<td>Test for trend: $\chi^2 = 2:8; 2p = 0.09$</td>
<td></td>
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<tr>
<td>(b) LHRH inhibitor in the absence of chemotherapy</td>
<td></td>
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<tr>
<td>Years 0–9</td>
<td>98/540 (1:8%)</td>
<td>119/531 (2:2%)</td>
<td>-6:7</td>
<td>48:2</td>
<td></td>
<td>0.87 (SE 0.13)</td>
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<td>Years 10–19</td>
<td>8/593 (1:3%)</td>
<td>8/513 (1:2%)</td>
<td>0:3</td>
<td>3:4</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Years 20+ (no data)</td>
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<td></td>
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<td></td>
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<tr>
<td>(b) subtotal</td>
<td>104/1433 (7:3%)</td>
<td>125/1364 (9:2%)</td>
<td>-6:4</td>
<td>51:6</td>
<td></td>
<td>0.88 (SE 0.13) 2p &gt; 0.1; NS</td>
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<tr>
<td>Test for trend: $\chi^2 = 0:2; 2p &gt; 0:1; NS$</td>
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<tr>
<td>(c) ovarian ablation in the presence of chemotherapy</td>
<td></td>
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</tr>
<tr>
<td>Years 0–9</td>
<td>851/1802 (30:6%)</td>
<td>568/1785 (31:8%)</td>
<td>-12:1</td>
<td>262:5</td>
<td></td>
<td>0.95 (SE 0.06)</td>
<td></td>
</tr>
<tr>
<td>Years 10–19</td>
<td>77/5270 (3:4%)</td>
<td>69/5276 (2:8%)</td>
<td>8:9</td>
<td>31:9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years 20+</td>
<td>5/176 (1:9%)</td>
<td>3/165 (1:6%)</td>
<td>-2:5</td>
<td>1:9</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(c) subtotal</td>
<td>630/4248 (14:9%)</td>
<td>634/4229 (15:0%)</td>
<td>-5:7</td>
<td>295:0</td>
<td></td>
<td>0:98 (SE 0.06) 2p &gt; 0:1; NS</td>
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<tr>
<td>Test for trend: $\chi^2 = 0:6; 2p &gt; 0:1; NS$</td>
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<tr>
<td>(d) LHRH inhibitor in the presence of chemotherapy</td>
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<tr>
<td>Years 0–9</td>
<td>542/2652 (20:4%)</td>
<td>620/2780 (22:3%)</td>
<td>-30:9</td>
<td>271:7</td>
<td></td>
<td>0.90 (SE 0.06)</td>
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<tr>
<td>Years 10–19</td>
<td>34/1220 (2:8%)</td>
<td>29/1129 (2:6%)</td>
<td>1:2</td>
<td>15:0</td>
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<tr>
<td>Years 20+ (no data)</td>
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<tr>
<td>(d) subtotal</td>
<td>576/3872 (14:9%)</td>
<td>648/3909 (16:6%)</td>
<td>-29:8</td>
<td>286:7</td>
<td></td>
<td>0.90 (SE 0.06) 2p = 0.09</td>
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<tr>
<td>Test for trend: $\chi^2 = 0:5; 2p &gt; 0:1; NS$</td>
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- 95% or ~95% confidence intervals
Extended Adjuvant Endocrine Therapy in Premenopausal Early Stage Breast Cancer

An analysis of younger women from NCIC CTG MA17


Participating Collaborative Groups
NCIC CTG, ECOG, SWOG, CALGB, NCCTG, BIG

Premenopausal Women had a Greater Benefit

Pre-menopausal
Abs Diff in 4 year DFS=10.1%
HR=0.25
P<0.0001

Post-menopausal
Abs Diff in 4 year DFS=3.3%
HR=0.69
P=0.0008

Premenopausal Women did better than Postmenopausal
HR=0.39, p=0.02
Conclusions

1. **ER+ Premenopausal Breast Cancer Patients** benefit significantly from Extended AI therapy after they become menopausal.

2. The benefit was similar in women who delayed endocrine therapy up to 6 years after tamoxifen.

Medical Oncologists: Methods to Assess Menopause

- Prior bilateral oophorectomy
- Age ≥ 60 years

- Age < 60 and amenorrheic for 12 or more months in the absence of chemotherapy, tamoxifen, toremifene (or raloxifene), OFS, AND FSH and estradiol in the postmenopausal range

- If taking tamoxifen or toremifene and age < 60, then FSH and estradiol in the postmenopausal range (Be careful!!)

NCCN guidelines v.1.2012
Peri-menopause: highly variable process:

- Daily concentrations of urinary gonadotrophins vary significantly
- Single time point test E2, FSH, LH not reliable

Amir E. The Breast (2010), doi:10.1016/j.breast.2010.06.003
Endocrine Therapy for Premenopausal HR+ EBC Patients: Summary

- Endocrine therapy of utmost importance in HR+ premenopausal EBC

- Premenopausal HR+ pts appear to benefit from amenorrhea in addition to tamoxifen - US/Canada guidelines don’t recommend ovarian suppression

- Prolonged endocrine therapy with AI following tamoxifen of benefit in N- and N+ patients who have become postmenopausal