Preoperative Endocrine Therapy in ER positive Breast Cancer

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Selection for Preoperative (Neoadjuvant) Therapy

• Patient who will benefit
  – Locally advanced → Operable
  – Large operable tumors
    • Mastectomy → Breast conserving surgery (BCS)
    • BCS → More cosmetic BCS

• Primary therapy: in frail, elderly, and infirm patients
Preoperative endocrine therapy

Clinical Benefits
- Down-staging of tumors
- Knowledge of treatment efficacy

Research Benefits
- Correlation of biomarkers to clinical response
- Sequential access to tumor

Neoadjuvant endocrine therapy without chemotherapy was considered reasonable for postmenopausal patients with strongly receptor-positive disease. If used, such treatment should be considered for a duration of 5–8 months or until maximum tumour response.
Preoperative Chemotherapy Guideline

**PRIMARY TREATMENT**

- **No response after 3-4 cycles or Progressive disease**
  - Partial response, lumpectomy not possible
  - Partial response, lumpectomy possible or Complete response
  - See Lumpectomy Pathway (BINV-12)

- **Preoperative chemotherapy**
  - Endocrine therapy alone may be considered for receptor positive disease in postmenopausal patients
  - Clinical negative axillary lymph node(s), consider sentinel lymph node procedure
  - Clinically positive axillary lymph node(s), consider core biopsy or FNA; or consider sentinel lymph node procedure if FNA or core biopsy negative

**Desires breast preservation**

- Core biopsy of breast tumor, localization of tumor bed for future surgical management
- Clinical negative axillary lymph node(s), consider sentinel lymph node procedure
- Clinical positive axillary lymph node(s), consider core biopsy or FNA; or consider sentinel lymph node procedure if FNA or core biopsy negative

**See Mastectomy Pathway (BINV-12)**
LHRH analogues in premenopausal patients are investigational.

Primary endocrine therapy with aromatase inhibitors should be offered to postmenopausal women if the tumor is expected to be highly endocrine responsive.
### Advantages and disadvantages of preoperative endocrine therapy

<table>
<thead>
<tr>
<th></th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgical</strong></td>
<td>May enable conserving surgery</td>
<td>Delay to definitive surgery might be detrimental in poor responder</td>
</tr>
<tr>
<td><strong>considerations</strong></td>
<td>Gives the option to avoid surgery in elderly patients</td>
<td></td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td><strong>Prognostic</strong></td>
<td>Allows assessment of response to treatment</td>
<td>Accurate baseline pathological staging is not obtained</td>
</tr>
<tr>
<td><strong>considerations</strong></td>
<td>Prognostic value from assessment of PR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Enables assessment of change in proliferative marker</td>
<td></td>
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<td></td>
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<tr>
<td><strong>Comparison</strong></td>
<td>Less toxic, better tolerability</td>
<td>Ineffective in ER/PR(-)</td>
</tr>
<tr>
<td><strong>with</strong></td>
<td>Cheaper</td>
<td>Longer time to response</td>
</tr>
<tr>
<td><strong>neoadjuvant</strong></td>
<td>Good response rate in postmenopausal, ER/PR (+) pts</td>
<td>Lower pCR rate</td>
</tr>
<tr>
<td><strong>chemotherapy</strong></td>
<td></td>
<td>Less effective in premenopause</td>
</tr>
</tbody>
</table>
# Studies on primary use of tamoxifen

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Follow up</th>
<th>Overall survival/Disease-free survival</th>
<th>Time to first locoregional failure</th>
<th>Number or percentage of local progresses or distance metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tan et al.</td>
<td>Tamoxifen</td>
<td>52 months</td>
<td>NS/NS</td>
<td>ND</td>
<td>27 vs 106, ( p &lt; 0.005 )</td>
</tr>
<tr>
<td>Mustacchi et al.</td>
<td>Tamoxifen vs multimodal treatment</td>
<td>80 months</td>
<td>NS/NS</td>
<td>ND</td>
<td>27 vs 106, ( p = 0.0001 )</td>
</tr>
<tr>
<td>Gazet et al.</td>
<td>Tamoxifen vs surgery + adjuvant tamoxifen</td>
<td>80 months</td>
<td>NS/NS</td>
<td>ND</td>
<td>27 vs 106, ( p = 0.0001 )</td>
</tr>
<tr>
<td>Van Dalsen and De Varies</td>
<td>Tamoxifen vs tamoxifen + surgery</td>
<td>41 months</td>
<td>NS/NS</td>
<td>ND</td>
<td>27% vs 6%, ( p &lt; 0.005 )</td>
</tr>
<tr>
<td>Bates et al.</td>
<td>Tamoxifen vs tamoxifen + surgery</td>
<td>34 months</td>
<td>NS/NS</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

NS: Non-significant / ND: not done

New evolution of preoperative endocrine therapy in postmenopausal women with selective aromatase inhibitor
# Trials using letrozole in neoadjuvant treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration of treatment</th>
<th>Treatment</th>
<th>Clinical response</th>
<th>Conservative surgery</th>
<th>Pathological complete response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dixon et al.</td>
<td>3 months</td>
<td>Letrozole 2.5mg vs 10mg</td>
<td>5 CR/7 PR vs 9 PR</td>
<td>ND</td>
<td>8.3% vs 0%</td>
</tr>
<tr>
<td>Miller et al.</td>
<td>3 months</td>
<td>Letrozole 2.5mg or 10mg vs Anastrozole 1mg or 10mg vs Tamoxifen 40mg</td>
<td>88% OR vs 70% OR vs 46% OR $p&lt;0.0001$</td>
<td>ND</td>
<td>0% vs 0% vs 0%</td>
</tr>
<tr>
<td>Eiermann et al. (P024 trial)</td>
<td>4 months</td>
<td>Letrozole 2.5mg vs Tamoxifen 20mg</td>
<td>55% OR vs 36% OR $p&lt;0.001$</td>
<td>45% vs 35% $p=0.022$</td>
<td>ND</td>
</tr>
<tr>
<td>Paepke et al.</td>
<td>4-8 months</td>
<td>Letrozole 2.5mg</td>
<td>57% OR vs 80% OR</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Renshaw et al.</td>
<td>3-12 months</td>
<td>Letrozole 2.5mg</td>
<td>9.5% CR vs 36% CR</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Dixon et al.</td>
<td>3 months</td>
<td>Letrozole 2.5mg</td>
<td>80% OR for Allred 8 74% OR for Allred 6-7</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

CR: complete response/PR: partial response/OR: objective response (CR + PR)/ND: not done

P024 trial design

(N=337)

Patients in the intent-to treat population (n=324)

Patient excludes (n=13)

Letrozole 2.5mg (n=154)

Tamoxifen 20mg (n=170)

4 months

Follow up therapy (Investigator driven)

### Objective Response

<table>
<thead>
<tr>
<th></th>
<th>Letrozole (Femara&lt;sup&gt;®&lt;/sup&gt;)</th>
<th>Tamoxifen</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>55%</td>
<td>36%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>35%</td>
<td>25%</td>
<td>0.042</td>
</tr>
<tr>
<td>Mammography</td>
<td>34%</td>
<td>16%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BCS</td>
<td>45%</td>
<td>35%</td>
<td>0.022</td>
</tr>
</tbody>
</table>

P024: Response rates and ER expression

Total % of cases in each Allred category

<table>
<thead>
<tr>
<th>Allred ER Score</th>
<th>7.0</th>
<th>1.5</th>
<th>1.5</th>
<th>3.0</th>
<th>2.2</th>
<th>7.0</th>
<th>21.4</th>
<th>56.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Response rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Tamoxifen

Letrozole (Femara®)

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with the 7th Biennial Meeting of the Asian Breast Cancer Society
P024 : Response by PgR Allred score

Total % of cases in each Allred category

Logistic regression analysis of “inverse V” model

P024 : Response by HER-1/2

Clinical response to Letrozole vs Tamoxifen in HER1+ and/or HER2+ cases that are also ER+

<table>
<thead>
<tr>
<th>Category</th>
<th>Letrozole</th>
<th>Tamoxifen</th>
<th>Odds Ratio LET vs TAM</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER1/2+</td>
<td>15/17</td>
<td>4/19</td>
<td>28</td>
<td>0.0004</td>
</tr>
<tr>
<td>ER+</td>
<td>(88%)</td>
<td>(21%)</td>
<td>(4.5-177)</td>
<td></td>
</tr>
<tr>
<td>HER1/2-</td>
<td>55/101</td>
<td>42/100</td>
<td>1.7</td>
<td>0.0789</td>
</tr>
<tr>
<td>ER+</td>
<td>(54%)</td>
<td>(42%)</td>
<td>(0.9-2.9)</td>
<td></td>
</tr>
</tbody>
</table>

LET = letrozole; TAM = tamoxifen.

P024: Percentage change in Ki67

- Letrozole (Femara®) is a more effective anti-proliferative agent than Tamoxifen

Post-treatment geometric mean is lower after Letrozole than Tamoxifen, \( P=0.0009 \) by ANCOVA (analysis of covariance of logged values with baseline adjustment).

## Trials using anastrozole in neoadjuvant treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration of treatment</th>
<th>Treatment</th>
<th>Clinical response</th>
<th>Conservative surgery</th>
<th>Pathological complete response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dixon et al.</td>
<td>3 months</td>
<td>Anastrozole 1mg vs 10mg</td>
<td>Median reduction ultrasound: 80.5% vs 69.6%</td>
<td>91.6%</td>
<td>ND</td>
</tr>
<tr>
<td>Milla-Santos et al.</td>
<td>3 months</td>
<td>Anastrozole 1mg</td>
<td>55% CR &amp; 29% PR</td>
<td>0%</td>
<td>12%</td>
</tr>
<tr>
<td>Smith and Dowsett (IMPACT)</td>
<td>3 months</td>
<td>Anastrozole 1mg vs tamoxifen 20mg vs anastrozole + tamoxifen</td>
<td>37% OR vs 36% OR vs 39% OR 46% vs 22% p=0.03</td>
<td>46% vs 22% p=0.03</td>
<td>ND</td>
</tr>
<tr>
<td>Cataliotti et al (PROACT)</td>
<td>3 months</td>
<td>Anastrozole 1mg vs tamoxifen 20mg</td>
<td>39.5% shrinkage &gt; 30% vs 35.4% p=0.29</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

CR: complete response/PR: partial response/OR: objective response (CR + PR)/ND: not node

The IMmediate Preoperative Anastrozole, tamoxifen, or Combination with Tamoxifen (IMPACT) trial design

Baseline assessments including surgeon decision on preference for mastectomy or breast-conserving surgery (BCS)

Random Assignment 1:1:1

Anastrozole 1 mg + placebo for 3 months

Tamoxifen 20 mg + placebo for 3 months

Combination-anastrozole 1 mg + tamoxifen 20 mg for 3 months

3 months' therapy

Actual mastectomy or BCS

Unblinding of study and 5 years' adjuvant anastrozole 1 mg or tamoxifen 20 mg

The PRe-Operative “Arimidex” Compared to Tamoxifen (PROACT) trial design

Postmenopausal women with operable or potentially-operable, locally advanced ER and/or PgR +ve (T2, T3, T4b, NO-2, MO) measurable breast cancer

Double-blind randomization 1:1

Anastrozole (Arimidex™) 1mg + placebo for 3 months

Tamoxifen (Nolvadex™) 20mg + placebo for 3 months

3 months therapy

Response evaluation and surgery

30-day post surgery follow-up

Therapy continued for 5 years or until recurrence, intolerable toxicity or patient refusal

Outcomes from IMPACT and PROACT studies of 3 months preoperative anastrozole or tamoxifen

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>IMPACT (n=330)</th>
<th>PROACT (n=314, Hormonal only)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anastrozole (%)</td>
<td>Tamoxifen (%)</td>
</tr>
<tr>
<td>Ultrasound ORR</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>Clinical ORR</td>
<td>37</td>
<td>36</td>
</tr>
<tr>
<td>Breast-conserving surgery</td>
<td>46</td>
<td>22</td>
</tr>
</tbody>
</table>

* For feasible surgery at 3 months (n=220)
** In hormonal only mastectomy or inoperable baseline (n=262)

Summary of anastrozole studies

• There was significantly higher ORR in favor of anastrozole in those patients initially assessed as requiring mastectomy.

• There was no statistical significant reduction but feasible tumor shrinkage than tamoxifen and actual surgery in those patients whose tumors were thought to require a mastectomy or who were inoperable at initial assessment.
## Trials with exemestane in neoadjuvant setting

<table>
<thead>
<tr>
<th>Study</th>
<th>Included study</th>
<th>Response rate</th>
<th>pCR</th>
<th>Downstaging</th>
<th>BCS-rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miller et al.</td>
<td>Locally advanced</td>
<td>85% reduction of tumor volume</td>
<td>NR</td>
<td>NR</td>
<td>80%</td>
</tr>
<tr>
<td>Krainick et al.</td>
<td>T &lt; 2cm</td>
<td>37%</td>
<td>0</td>
<td>51%</td>
<td>52%</td>
</tr>
<tr>
<td>Tubiana-Hulin et al.</td>
<td>Operable T2-4</td>
<td>76%</td>
<td>18%</td>
<td>45%</td>
<td>45%</td>
</tr>
<tr>
<td>Semiglazov et al.</td>
<td>NR</td>
<td>76%</td>
<td>3%</td>
<td>NR</td>
<td>36%</td>
</tr>
<tr>
<td>Gil et al.</td>
<td>T2-4a-b &gt; 3cm non BCS</td>
<td>45%</td>
<td>2%</td>
<td>NR</td>
<td>38%</td>
</tr>
<tr>
<td>Mustacchi et al.</td>
<td>60%</td>
<td>0</td>
<td>NR</td>
<td>76%</td>
<td></td>
</tr>
<tr>
<td>Mlineritsch et al.</td>
<td>T2-4a-b</td>
<td>34%</td>
<td>3%</td>
<td>45%</td>
<td>76%</td>
</tr>
</tbody>
</table>

pCR: pathologic complete response/BCS: breast conserving surgery/NR: not reported

Summary of exemestane studies

• There was substantial response rate, a valuable downsizing and breast-conserving surgery rate in post-menopausal women with HR-positive tumors.

• The efficacy results on neoadjuvant exemestane are at least closely similar to those of non-steroidal AIs and also taxane/anthracycline combination chemotherapies in HR-positive patients.

### Trial comparing preoperative AIs vs Tamoxifen

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Patients</th>
<th>Results</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>AI</td>
<td>Tam</td>
</tr>
<tr>
<td>p024</td>
<td>Let vs Tam 4 months</td>
<td>337</td>
<td>CR 55%</td>
<td>CR 36%</td>
</tr>
<tr>
<td>IMPACT</td>
<td>Ana vs Tam vs Combine</td>
<td>330</td>
<td>CR 37%</td>
<td>CR 36%</td>
</tr>
<tr>
<td></td>
<td>12 weeks</td>
<td></td>
<td>BCS 44%</td>
<td>BCS 31%</td>
</tr>
<tr>
<td>PROACT</td>
<td>Ana vs Tam 3 months</td>
<td>314</td>
<td>RR 36.2%</td>
<td>RR 26.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCS 43%</td>
<td>BCS 31%</td>
</tr>
<tr>
<td>Exemestane</td>
<td>Exe vs Tam 3 months</td>
<td>151</td>
<td>RR 76%</td>
<td>RR 40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BCS 37%</td>
<td>BCS 20%</td>
</tr>
</tbody>
</table>
ACOSOG Z1031: Randomised Neoadjuvant AI Protocol

ER+ PMW stage II and III (target: 375 pts)

- Exemestane
- Anastrozole
- Letrozole

4 months

Post-surgery management at investigator’s discretion

ACOSOG = American College of Surgeons Oncology Group; AI = aromatase inhibitor; ER = estrogen receptor; PMW = postmenopausal women.
Neoadjuvant use of fulvestrant
Neoadjuvant Endocrine Therapy for Women with Endocrine Sensitive Tumours
Phase II, Randomised Trial

Postmenopausal patients with ER-positive and measurable (>2 cm) stage breast cancer (n=160)

Open Label Randomisation 1:1

Fulvestrant HD

Fulvestrant AD

16 weeks

Surgery

Surgery

Core biopsy at baseline and 4 weeks for correlative studies, surgery performed at 16 weeks

High dose: rationale

- Clinical data have shown that fulvestrant 125 mg is less effective than 250 mg.
- Fulvestrant induces dose-related reductions in estrogen receptor (ER), progesterone receptor (PgR) and Ki67.
- Pharmacokinetic data suggest that higher fulvestrant plasma concentrations may:
  - lead to higher ER downregulation (and thus may improve overall efficacy)
  - reduce time to steady state.
NEWEST – results summary

- NEWEST is the first study to compare the biological and clinical activity of fulvestrant HD and AD regimens.
- At week 4 fulvestrant HD:
  - reduced Ki67 LI to a significantly greater extent (p<0.0001) than AD (primary endpoint)
  - reduced ER levels significantly more (p<0.0003) than AD and reduced PgR expression
- Similar reductions were also observed for HD vs AD at week 16.
- All other efficacy parameters were numerically in favour of the HD regimen.
- Both doses were well tolerated:
  - AEs consistent with known toxicity profile of fulvestrant
  - no adverse effects on bone markers or endometrium

Kuter et al. SABCS newsletter; Issue 1, December 13 2007: 13
Neoadjuvant use of combined therapy
Preoperative bevacizumab combined with letrozole and chemotherapy in locally advanced ER(+) and/or PgR(+) breast cancer

- Antiangiogenic agent bevacizumab showed a synergic effect when combined with chemotherapy and endocrine therapy
- Investigated the bevacizumab in combination with chemotherapy (capecitabine and vinorelbine) and endocrine therapy (letrozole) (+triptorelin in premenopausal women)

Conclusion

➢ Bevacizumab is feasible and active in association with primary chemo-endocrine therapy for ER-positive tumors in terms of proliferation inhibition, clinical response and antiangiogenic activity.

Neoadjuvant **Everolimus** + Letrozole in ER-positive breast cancer

**Postmenopausal women with operable ER-positive breast cancer**
(N = 270)

**Everolimus 10 mg/day + Letrozole 2.5 mg/day**
(n = 138)

**Placebo + Letrozole 2.5 mg/day**
(n = 132)

*Week 16*

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Conclusion of neoadjuvant Everolimus + Letrozole in ER-positive breast cancer

- Everolimus significantly increased the efficacy of letrozole in the treatment of newly diagnosed, ER-positive breast cancer in terms of both clinical and antiproliferative response.

- The safety profile of the combination is acceptable, and toxicity in the everolimus arm was consistent with historical data.

- The benefit/risk assessment calls for additional evaluation of the potential value of the combination.

Celecoxib anti-aromatase neoadjuvant (CANN) trial for locally advanced breast cancer

Randomised, double-blind trial in postmenopausal women with ER(+) &/or PgR(+) invasive breast cancer

Exemestane 25mg daily + celecoxib 400mg twice daily

Exemestane 25mg daily

Letrozole 2.5mg daily

3 months

Surgery and assessment


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Conclusion of CANN trial

- Three anti-aromatase therapies are effective and safe
- Serum levels of CA15.3 dropped more significantly when combined with celecoxib

Neoadjuvant use of premenopausal patients
Rationale for Combination Therapy

Goserelin

Gonadotrophins (FSH + LH)

Estrogens

Ovary

Pituitary gland

LHRH (hypothalamus)

ACTH

Adrenal glands

Androgens

Peripheral conversion (aromatase enzyme)

Estrogens

Aromatase inhibitor

ACTH, adrenocorticotrophic hormone

FSH, follicle-stimulating hormone

LH, luteinising hormone

LHRH, LH-releasing hormone
Summary of preoperative endocrine therapy in premenopause patients

- In interim analysis of results indicate that therapy with AIs, in combination with a GnRH analogue, is safe and effective in pre-menopausal women with locally advanced breast cancer.

- A biological response, in terms of down-regulation of the estrogenic signaling, was observed in all patients.

- The trend to improved response rate observed with longer duration in selected populations of premenopausal patients with endocrine-responsive tumors.

Direct comparison of chemotherapy
Unpublished Pilot Russian Study

ER &/or PgR (+) PMW
T 2-4
(target : 121 pts)

Doxorubicin + Paclitaxel (n=62)

Anastrozole (n=30)

Exemestane (n=29)

3 months

ER = estrogen receptor; PgR = progesterone receptor; PMW = post-menopausal women; T = tumor size; pts = patients.

Proc Am Soc Clin Oncol 2004;22(14s):519
Results

- Clinical and mammographic objective response rates (ORR) were similar for endocrine therapy and chemotherapy, and there was a trend for increasing rates of breast-conserving surgery in favor of endocrine therapy with no significant differences in local recurrence rates.

Proc Am Soc Clin Oncol 2004;22(14s):519
## Neoadjuvant endocrine versus chemotherapy

<table>
<thead>
<tr>
<th></th>
<th>Neoadjuvant Chemotherapy</th>
<th>Neoadjuvant Endocrine Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimen</td>
<td>Anthracycline based</td>
<td>Letrozole</td>
</tr>
<tr>
<td>Median volume decreased</td>
<td>78%</td>
<td>75%</td>
</tr>
<tr>
<td>Responses</td>
<td>85%</td>
<td>88.7%</td>
</tr>
<tr>
<td>pCR</td>
<td>18%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Central scars</td>
<td>4%</td>
<td>58.5%</td>
</tr>
<tr>
<td>Breast-conserving surgery</td>
<td>32%</td>
<td>86.7%</td>
</tr>
</tbody>
</table>

ER+, 31/50 (CTx), All in 53 Letrozole
Conclusion

- Neoadjuvant endocrine therapy was better tolerated than chemotherapy: the most common adverse events reported were hot flushes, fatigue, vaginal spotting, and arthralgia.

- This data confirms that endocrine therapy is a safe alternative to chemotherapy, with similar response rates but less toxicity.

Proc Am Soc Clin Oncol 2004;22(14s):519
Conclusion and Take Home Message
Neoadjuvant hormone therapy is effective at down-staging tumors, particularly large tumors, initially thought to be inoperable or requiring mastectomy.

Aromatase inhibitors are superior to tamoxifen in terms of clinical response.

When compared with neoadjuvant chemotherapy, aromatase inhibitors have similar ORR and rates of local recurrence after down-staging and breast-conserving treatment, but are better tolerated because of their much lower toxicity.
The aromatase inhibitors are clinically and biologically effective in both HER2 positive and negative tumors, whereas HER2 positive tumors show a level of resistance to tamoxifen.

In neoadjuvant studies comparing aromatase inhibitors with tamoxifen, the duration of use has been 3-4 months, by which time any response is usually evident, but optimum duration of treatment has yet to be identified.
Thank You for Your Attention!