PATIENT-REPORTED OUTCOME (PRO) RESULTS, NRG ONCOLOGY/NSABP B-35: A CLINICAL TRIAL OF ANASTROZOLE (A) VS TAMOXIFEN (TAM) IN POSTMENOPAUSAL PATIENTS WITH DCIS UNDERGOING LUMPECTOMY PLUS RADIOTherAPY

Speaker: Patricia A Ganz

S6-03
Patient-reported outcome (PRO) results, NRG Oncology/NSABP B-35: A clinical trial of anastrozole (A) vs tamoxifen (tam) in postmenopausal patients with DCIS undergoing lumpectomy plus radiotherapy

Dr. Ganz: Nothing to Disclose.

Patient-Reported Outcome Results
NRG Oncology/NSABP B-35:
A Clinical Trial of Anastrozole vs. Tamoxifen in Postmenopausal Patients with DCIS Undergoing Lumpectomy Plus Radiotherapy


Abstract # S6-04
Declarations of Potential COIs

- **Mary E. Cianfrocca**: Honoraria and Consulting/Advisory Role with Roche, and Research Funding from Abbvie, Novartis.
- **Howard M. Gross**: Employment with Dayton Physicians.
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- **All other authors declare no other potential conflicts of interest.**

NRG Oncology/NSABP B-35 Schema

Postmenopausal Women
DCIS Treated by Lumpectomy
ER-Positive or PgR-Positive

**STRATIFICATION**
Age (<60 vs. ≥60)

**RANDOMIZATION**

- Tamoxifen (20 mg/day) and placebo for 5 years + Breast Radiation Therapy
- Anastrozole (1 mg/day) and placebo for 5 years + Breast Radiation Therapy
B-35: Primary Aim
Compare: Anastrozole vs. Tamoxifen

- Breast Cancer-Free Interval (BCFI)
  - Time to any breast cancer event
    - Local
    - Regional
    - Distant
    - Breast second primary (Inv or DCIS)

B-35: Secondary Aims

- Disease-free survival (DFS)
- Overall survival (OS)
- Quality of Life and Symptoms
- Invasive breast cancer
- Ipsilateral cancer recurrence (Inv and DCIS)
- Contralateral breast cancer (Inv and DCIS)
- Non-breast second primary cancer
- Osteoporotic fractures
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**B-35: Breast Cancer-Free Interval**

<table>
<thead>
<tr>
<th>At Risk by Year</th>
<th>Treatment</th>
<th># of Events</th>
<th>10 yrs</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tamoxifen</td>
<td>1538 1241</td>
<td>114</td>
<td>89.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anastrozole</td>
<td>1539 1261</td>
<td>84</td>
<td>93.5</td>
<td>0.03</td>
</tr>
</tbody>
</table>

**Time Since Randomization (months)**

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**B-35: BCFI by Age Group**

- < 60 years
  - Tamoxifen 722: 88.2%
  - Anastrozole 731: 92.2%
  - HR: 0.95, P-value: 0.77

- ≥ 60 years
  - Tamoxifen 722: 94.0%
  - Anastrozole 731: 90.2%
  - HR: 0.94, P-value: 0.04

**Qualitative Treatment by Age Interaction**

P=0.04
QOL and Sx Hypotheses

- Primary
  - No difference in QOL between the two treatments
  - Patients receiving Anastrozole would have higher rates of hot flashes
- Secondary
  - Greater vaginal dryness and pain with intercourse with Anastrozole
  - Poorer sexual functioning with A compared to T

PRO Instruments

- SF-12 Mental and Physical Component Scales
- SF-36 Vitality Scale
- BCPT symptom checklist scales
- CES-D short form for depressive symptoms
- MOS Sexual Problems Scale
Methods

- Data analyzed with intention to treat principle
- PROs for two arms were compared using a mixed model for repeated measures analysis with adjustment for baseline scores, time point and age category
- Patients with protocol events were censored
- Only data through 60 months reported here
Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Tamoxifen</th>
<th>Anastrozole</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>278</td>
<td>46.3%</td>
<td>282</td>
</tr>
<tr>
<td>60+</td>
<td>323</td>
<td>53.7%</td>
<td>310</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>529</td>
<td>88.0%</td>
<td>516</td>
</tr>
<tr>
<td>Black</td>
<td>47</td>
<td>7.8%</td>
<td>55</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>2</td>
<td>0.3%</td>
<td>2</td>
</tr>
<tr>
<td>Asian</td>
<td>16</td>
<td>2.7%</td>
<td>12</td>
</tr>
<tr>
<td>Native American/Alaskan</td>
<td>0</td>
<td>0.0%</td>
<td>1</td>
</tr>
<tr>
<td>Multi-racial</td>
<td>4</td>
<td>0.7%</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>0.5%</td>
<td>5</td>
</tr>
</tbody>
</table>

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SF-12 Component Scores

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SF-12 Physical component score

SF-12 Mental component score

p = 0.20

p = 0.38

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Vitality and Depressive Symptoms

SF-36 Vitality score

10-item CES-D

Mean score

Mean score

p = 0.86

p = 0.46

0 6 12 18 24 30 36 42 48 54 60

0 6 12 18 24 30 36 42 48 54 60

Months

Months

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Percent Reporting at Least Slightly Bothersome Symptoms

Hot flashes

Vaginal Dryness

Joint pain

A at 6 mo

T at 6 mo

A at baseline

T baseline

A baseline
**Severity of Vasomotor Symptoms and Musculoskeletal Pain**

Vasomotor symptoms

- **Mean score**
  - Tamoxifen
  - Anastrozole

- **p = 0.0105**

- **Months**
  - 0 6 12 18 24 36 42 48 54 60

Musculoskeletal pain

- **Mean score**
  - Tamoxifen
  - Anastrozole

- **p = 0.0006**

- **Months**
  - 0 6 12 18 24 36 48 54 60

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**Severity of Vaginal and Bladder Control Problems**

Vaginal symptoms

- **Mean score**
  - Tamoxifen
  - Anastrozole

- **p = 0.03534**

- **Months**
  - 0 6 12 18 24 36 42 48 54 60

Bladder control

- **Mean score**
  - Tamoxifen
  - Anastrozole

- **p = 0.0002**

- **Months**
  - 0 6 12 18 24 36 48 54 60
Mean Sexual Functioning Score by Treatment Group and Time Point

- Tamoxifen
- Anastrozole

P = 0.56

Severity of Cognitive and Weight Control Problems

- Cognitive symptoms
- Weight problems

Cognitive symptoms: P = 0.72

Weight problems: P = 0.48
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**Vasomotor Symptoms and Weight Problems by Age**

- **Vasomotor symptoms by age**
  - Mean score
  - Months
  - Tamoxifen <60
  - Tamoxifen ≥60
  - Anastrozole <60
  - Anastrozole ≥60
  - p = 0.0006

- **Weight problems by age**
  - Mean score
  - Months
  - Tamoxifen <60
  - Tamoxifen ≥60
  - Anastrozole <60
  - Anastrozole ≥60
  - p = 0.0001

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**Vaginal Symptoms and Gynecologic Symptoms by Age**

- **Vaginal symptoms by age**
  - Mean score
  - Months
  - Tamoxifen <60
  - Tamoxifen ≥60
  - Anastrozole <60
  - Anastrozole ≥60
  - p < 0.0001

- **Gynecologic symptoms by age**
  - Mean score
  - Months
  - Tamoxifen <60
  - Tamoxifen ≥60
  - Anastrozole <60
  - Anastrozole ≥60
  - p = 0.0140

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Summary

- Both Anastrozole and Tamoxifen were well-tolerated with no significant differences in physical or mental health-related QOL

- There was no increase in severity of fatigue, depressive symptoms, cognitive problems, or weight gain with either therapy

Summary

- Tamoxifen increased the severity of vasomotor symptoms, bladder control and gynecological symptoms compared to Anastrozole
- Anastrozole increased the severity of musculoskeletal and vaginal symptoms compared to Tamoxifen
- Patients <60 yrs had significantly worse vasomotor and vaginal symptoms, as well as weight gain and gynecological symptoms
Conclusions

- Both A and T are well-tolerated in patients with DCIS, with greater severity of some symptoms in women <60 years
- Symptom profiles differ in the expected directions
- With information on PROs as well as BCFL, patients and their physicians can now make personalized decisions about which of these two effective agents to select

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The NSABP B-35 trial treatment outcome results, as well as the patient-reported outcomes from the trial, were published online yesterday at the Lancet

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