Abstract GS6-03
Symptoms and health-related quality of life on endocrine therapy alone (E) versus chemoendocrine therapy (CT+E): TAILORx patient-reported outcomes results


Background: Rationale for TAILORx Patient-Reported Outcomes (PROs)

- TAILORx design: endocrine therapy +/- chemotherapy
  - novel opportunity to evaluate effects of CT
  - common and distressing symptoms, including cognitive impairment, fatigue and endocrine symptoms
- Data on the unique contribution of chemotherapy
  - acute and long-term symptoms
  - improve understanding of mechanisms, inform clinical decision-making and inform expectations
Methods: PRO Objectives

**Primary PRO Objective:**
- Compare changes in patient-reported cognitive impairment between CT+E and E alone from baseline to 3 months

**Secondary Objectives:**
- Compare cognitive impairment change scores between CT+E and E alone at 6, 12, 24 and 36 months
- Compare key symptoms and health-related quality of life acutely and long-term
  - Fatigue
  - Endocrine symptoms
- Examine differences by treatment arm based on menopausal status

### Methods: Patient-Reported Outcomes Measures

<table>
<thead>
<tr>
<th>Domain</th>
<th>PRO</th>
<th># Items</th>
<th>Range</th>
<th>Sample Item</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome:</strong></td>
<td><strong>Functional Assessment of Cancer Therapy (FACT) – Cognitive Function</strong></td>
<td>20</td>
<td>0-80</td>
<td>Trouble concentrating, Thinking has been slow, Work harder than usual to keep track</td>
</tr>
<tr>
<td><strong>Secondary outcomes:</strong></td>
<td><strong>FACT – Fatigue</strong></td>
<td>13</td>
<td>0-52</td>
<td>Fatigue, Trouble finishing things</td>
</tr>
<tr>
<td></td>
<td><strong>FACT – Endocrine symptoms</strong></td>
<td>19</td>
<td>0-76</td>
<td>Hot flashes/hot flushes, Night sweats, Vaginal dryness</td>
</tr>
<tr>
<td></td>
<td><strong>FACT – General</strong></td>
<td>27</td>
<td>0-108</td>
<td>Feel ill, Content with the quality of life</td>
</tr>
</tbody>
</table>

- Items rated on 5-point Likert scale based on past 7 days

PROs: Baseline, 3 m, 6 m, 12 m, 24 m, 36 m

FACT-G: x x x

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Methods: Primary Endpoint and Statistical Considerations

- **Primary end point**
  - FACT-Cog Perceived Cognitive Impairment scale change scores from baseline to 3 months
  - Change score > 0.3 SD defined a priori as clinically meaningful (assuming 15.0 SD = > 4.5 points)
  - Per protocol population (treatment received)

- **Statistical considerations and sample size**
  - 90% power to detect 0.3 SD (4.5-point) difference in mean change scores from baseline to 3 months between CT+E versus E alone (2-sided 5% level test)
  - Planned subset analysis for pre- and postmenopausal groups
    - 90% power to detect differences corresponding to 0.38 and 0.49 SDs

- **Accrual goal = 1000**
  - 640 randomized (RS 11-25)
  - 235 per arm/470 treated per protocol (CT+E and E alone)

### TAILORx Methods: Treatment Assignment & Randomization

**Accrual: April 2006 – October 2010**  
**PRO Substudy: Jan – October, 2010**  
**PRO N = 1,043**

1. **Preregister – Oncotype DX RS**
   - Register (N=10,273)

2. **Randomize**
   - **ARM A: Low RS 0-10**
     - ASSIGN Endocrine Therapy
   - **ARM B: Experimental Arm**
     - Endocrine Therapy  
     - **PRO N = 236**
   - **ARM C: Standard Arm**
     - Chemo + E  
     - **PRO N = 218**
   - **ARM D: High RS 26-100**
     - ASSIGN Chemo + E
   - **Mid-Range RS 11-25**
     - **Stratification Factors: Menopausal Status, Planned Chemotherapy, Planned Radiation, and RS 11-15, 16-20, 21-25**

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## Results: Patient Characteristics and Treatment

<table>
<thead>
<tr>
<th></th>
<th>Arm B</th>
<th>Arm C</th>
<th>Chemo+E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>236</td>
<td>218</td>
<td></td>
</tr>
<tr>
<td>Median Age (range)</td>
<td>56 (32, 75)</td>
<td>55 (35, 75)</td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>31%</td>
<td>36%</td>
<td>36%</td>
</tr>
<tr>
<td>Initial Endocrine Therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>36%</td>
<td>38%</td>
<td></td>
</tr>
<tr>
<td>AI</td>
<td>58%</td>
<td>57%</td>
<td></td>
</tr>
<tr>
<td>OFS +/- Other</td>
<td>3%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Other or None</td>
<td>2%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TC</td>
<td>--</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>Anthracycline +/- taxane</td>
<td>--</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>CMF</td>
<td>--</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>Baseline PRO mean scores (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-Cog PCI</td>
<td>68.0 (12.5)</td>
<td>69.8 (12.4)</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>39.8 (10.3)</td>
<td>42.4 (9.2)</td>
<td></td>
</tr>
<tr>
<td>Endocrine Symptoms</td>
<td>64.6 (9.0)</td>
<td>65.6 (8.3)</td>
<td></td>
</tr>
<tr>
<td>FACT-General</td>
<td>89.3 (14.2)</td>
<td>90.3 (12.2)</td>
<td></td>
</tr>
</tbody>
</table>

- PRO substudy sample generally comparable to TAILORx trial on demographic and clinical characteristics
- Proportion of patients age > 65 higher in E arm (19%) versus C+E (11%), \( p = 0.05 \)

## Results: Primary Outcome

### Change in Cognitive Impairment Baseline to 3 months

**Per protocol analysis**

- Difference between CT+E and E change scores statistically significant:
  - 3 months: -3.82, \( p < 0.001 \)
  - 6 months: -2.62, \( p < 0.05 \)
- CT+E: change from baseline > 0.3 SD (observed SD = 12.5, > 3.75 CMID)
- Similar pattern of results with intent to treat analysis

**Intent to treat analysis**

Wagner et al. ASCO 2012
Results: Secondary Objective
Change in Cognitive Impairment by Menopausal Status

- Menopausal status by treatment interactions were non-significant

- Premenopausal: difference between CT+E and E change scores
  - 3 months, -4.75, p = 0.01

- Postmenopausal: difference between CT+E and E change scores
  - 3 months, -3.34, p < 0.01
  - 6 months, -3.69, p < 0.01
  - 12 months, -3.39, p < 0.05
  - 24 months, -3.26, p = 0.05

Results: Secondary Objective
Fatigue, Endocrine Symptoms and HRQL

- Difference between CT+E and E change scores statistically significant at 3 months
  - Fatigue: -5.32, p < 0.00000001
  - Endocrine symptoms: -1.62, p < 0.05

- Fatigue: Menopausal status by treatment interaction non-significant
Results: Secondary Objective
Change in Endocrine Symptoms by Menopausal Status

- Menopausal status by treatment interactions were significant
  - 24 months (p=0.02); 36 months (p=0.02)
- Difference between CT+E and E increases over time for postmenopausal patients

• Premenopausal women had greater increases in endocrine symptoms than postmenopausal women at all follow-up time points

Summary of Results

- First comparison of symptoms among breast cancer patients randomized to chemoendocrine therapy or endocrine therapy alone
- Patient-reported outcomes precisely capture patients’ experiences with treatment and underscore the value of RS-guided treatment
- Chemotherapy associated with greater cognitive impairment, fatigue, and endocrine symptoms acutely (3-6 months) during treatment
- Cognitive impairment and fatigue comparable between treatment arms at follow-up and persist in both groups
  - Gradual increase in cognitive impairment among E alone converges with CT+E at follow-up
  - Fatigue improves among CT+E to converge with E alone at follow-up
- Premenopausal women had more long-term endocrine symptoms
- Long-term health-related quality of life comparable
Conclusions

- Women with breast cancer receiving chemotherapy will experience acute symptoms, however long-term symptom profile and HRQL is generally comparable to endocrine therapy alone.
- Although both groups experience lingering symptoms, scores appear to stabilize at 12 months and beyond.
- Patient-reported data on extent and duration of symptoms associated with chemotherapy can inform clinician and patient decision-making and expectations for long-term well-being.