S3-09
Patient-reported endocrine symptoms, sexual functioning and quality of life (QoL) in the IBCSG SOFT trial: Adjuvant treatment with tamoxifen (T) alone versus tamoxifen plus ovarian function suppression (OFS) in premenopausal women with hormone receptor-po

Dr. Ribi: Nothing to disclose.
Dr. Luo: Nothing to disclose.
Dr. Bernhard: Nothing to disclose.
Dr. Francis: Nothing to disclose.
Dr. Bellet: Nothing to disclose.
Dr. Burstein: Nothing to disclose.
Dr. Pavesi: Nothing to disclose.
Dr. Parmar: Nothing to disclose.
Dr. Tondini: Nothing to disclose.
Dr. Visini: Nothing to disclose.
Dr. Torres: Nothing to disclose.

Dr. Karlsson: Nothing to disclose.
Dr. Spazzapan: Nothing to disclose.
Dr. Aveila: Nothing to disclose.
Dr. Ruhstaller: Nothing to disclose.
Dr. Regan: Nothing to disclose.
Dr. Coates: Nothing to disclose.
Dr. Geller: Nothing to disclose.
Dr. Fleming: Nothing to disclose.
Patient-reported endocrine symptoms, sexual functioning and quality of life (QoL) in the IBCSG SOFT trial

Karin Ribi
for SOFT Investigators,
International Breast Cancer Study Group,
Breast International Group,
and North American Breast Cancer Group

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Alan S. Coates
Richard D. Gelber
Gini F. Fleming

SOFT

- Trial coordinated by

- Collaboration of

- Financial support/drug supply: Pfizer, Ipsen, US NCI
Background

- SOFT efficacy results show that Tamoxifen (T)+Ovarian Function Suppression (OFS) provides improved disease control compared with T for the cohort of patients who received prior chemotherapy.

- In premenopausal women with breast cancer receiving adjuvant endocrine therapy with OFS little is known about
  - Patient-reported endocrine symptoms
  - Sexual function
  - Quality of life

1. ZIPP trial
2. TEXT / SOFT trials
3. E-3193 trial
SOFT QoL Assessment

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)

\[ \rightarrow \text{Tamoxifen x 5y (n=1018)} \]
\[ \rightarrow \text{Tamoxifen+OFS x 5y (n=1015)} \]
\[ \rightarrow \text{Exemestane+OFS x 5y (n=1014)} \]

Median follow-up 67 months
OFS=ovarian function suppression

Treatment month

\[ \begin{align*}
0 & \quad 6 & \quad 12 & \quad 18 & \quad 24 & \quad 36 & \quad 48 & \quad 60 \\
\uparrow & \quad \uparrow & \quad \uparrow & \quad \uparrow & \quad \uparrow & \quad \uparrow & \quad \uparrow & \quad \uparrow \\
\end{align*} \]

QoL assessment time points

*According to locally-determined E2 level in premenopausal range

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SOFT QoL Eligibility

- SOFT eligibility criteria
- Completed baseline forms
  - prior to randomization (IBCSG centers), OR
  - prior to initiation of protocol therapy (all other centers)
- Exclusion:
  - cognitive or physical impairment interfering with form completion
  - inability to read any of the 26 languages available on the QoL forms

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SOFT QoL Measures

- Symptom indicators
- Global QoL indicators
  - Physical well-being
  - Mood
  - Coping effort
  - Treatment burden
- All indicators in linear analogue self-assessment (LASA/VAS) format (score range: 0 to 100)
- Higher numbers reflecting better condition
- Clinically significant change: at least +/- 8 points

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SOFT QoL Hypotheses

- Patients receiving T+OFS compared to those with T alone will report
  - more hot flushes
  - greater loss of sexual interest
  - more vaginal dryness
  - being more troubled by weight gain
  - more sleep problems
  - less vaginal discharge
- Patients receiving T+OFS will report no differences in global QoL indicators, but higher treatment burden compared to those with T alone

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SOFT QoL Analysis

- ITT analysis
- Differences in QoL changes between treatments tested overall and by chemotherapy cohort at:
  - short-term (6 months)
  - mid-term (24 months)
  - long-term (60 months) post-randomization
- Mixed-effects linear modeling for repeated measures including chemo cohort, treatment, time point, and interactions
- Adjusted for baseline patient/disease characteristics

Patient Population

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## Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>No Chemo (N=772)</th>
<th>Prior Chemo (N=950)</th>
<th>Overall (N=1722)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>46</td>
<td>40</td>
<td>43</td>
</tr>
<tr>
<td>BMI (median)</td>
<td>24</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>Surgery to random. (median)</td>
<td>1.8 mo</td>
<td>8.1 mo</td>
<td>3.6 mo</td>
</tr>
<tr>
<td>Taking tamoxifen at baseline</td>
<td>6%</td>
<td>45%</td>
<td>27%</td>
</tr>
<tr>
<td>Node positive</td>
<td>9%</td>
<td>57%</td>
<td>35%</td>
</tr>
<tr>
<td>Tumor size &gt; 2 cm</td>
<td>14%</td>
<td>46%</td>
<td>32%</td>
</tr>
<tr>
<td>HER2 positive</td>
<td>5%</td>
<td>19%</td>
<td>13%</td>
</tr>
</tbody>
</table>

## Baseline QoL Scores

<table>
<thead>
<tr>
<th>Type of indicator</th>
<th>QoL indicator*</th>
<th>No Chemo</th>
<th>Prior Chemo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>S.D.</td>
</tr>
<tr>
<td>Vasomotor</td>
<td>Hot flushes</td>
<td>90</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Sweats</td>
<td>86</td>
<td>20</td>
</tr>
<tr>
<td>Gynecological/Sexual problems</td>
<td>Vaginal discharge</td>
<td>88</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Vaginal dryness</td>
<td>91</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Vaginal itching/irritation</td>
<td>92</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Loss of sexual interest</td>
<td>79</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Difficulties becoming aroused</td>
<td>84</td>
<td>22</td>
</tr>
<tr>
<td>Musculoskeletal/Neurology pain</td>
<td>Bone or Joint pains</td>
<td>83</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Headaches</td>
<td>82</td>
<td>23</td>
</tr>
</tbody>
</table>

*Higher scores indicate a better condition

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Baseline QoL Scores (cont.)

<table>
<thead>
<tr>
<th>Type of indicator</th>
<th>QoL indicator*</th>
<th>No Chemo</th>
<th>Prior Chemo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>S.D.</td>
</tr>
<tr>
<td>Constitutional/</td>
<td>Sleep disturbance</td>
<td>71</td>
<td>27</td>
</tr>
<tr>
<td>Psychological</td>
<td>Troubled by weight gain</td>
<td>84</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Being irritable</td>
<td>75</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Feeling dizzy</td>
<td>90</td>
<td>17</td>
</tr>
<tr>
<td>Global indicators</td>
<td>Physical well-being</td>
<td>76</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Mood</td>
<td>72</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Coping effort</td>
<td>68</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Treatment burden</td>
<td>78</td>
<td>24</td>
</tr>
</tbody>
</table>

*Higher scores indicate a better condition

San Antonio Breast Cancer Symposium, December 9-13, 2014

Treatment Effect: Hot Flushes

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Treatment Effect: Symptoms
T+OFS vs. T

<table>
<thead>
<tr>
<th></th>
<th>T+OFS</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 mos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 mos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60 mos</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Hot flushes
- Sweats
- Vaginal discharge
- Vaginal dryness
- Vaginal itching/irritation
- Loss of sexual interest
- Recanal difficulties

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

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Treatment Effect: Symptoms

E+OFS

<table>
<thead>
<tr>
<th>Symptom</th>
<th>6 mos</th>
<th>24 mos</th>
<th>50 mos</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot flushes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweats</td>
<td></td>
<td></td>
<td></td>
</tr>
<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>
<td></td>
<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)

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Treatment Effect: Symptoms (cont.)

![Graph showing change in symptoms over time.]

- Bone or joint pain
- Headaches
- Sleep disturbance
- Weight gain
- Being irritable
- Feeling dizzy

Change of QoL Score from Baseline (Mean with 95% CI)

(±8 is the minimal clinically meaningful change of QoL scores)

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Treatment Effect: Global QoL

T+OFS vs. T

![Graph showing change in QoL over time.]

- Physical wellbeing
- Mood
- Coping effort
- Treatment burden

Change of QoL Score from Baseline (Mean with 95% CI)

(±8 is the minimal clinically meaningful change of QoL scores)

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# Treatment Effect: Global QoL

**E+OFS**

<table>
<thead>
<tr>
<th></th>
<th>T+OFS</th>
<th>T</th>
<th>E+OFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 mos</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 mos</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60 mos</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Change of QoL Score from Baseline (Mean with 95% CI)**

<table>
<thead>
<tr>
<th></th>
<th>Worsening</th>
<th>Improving</th>
<th>Worsening</th>
<th>Improving</th>
<th>Worsening</th>
<th>Improving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical wellbeing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coping effort</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment burden</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

± 8 is the minimal clinically meaningful change of QoL scores.

---

**Treatment Effect: by Cohort**

Changes from baseline to month 6 for selected indicators

<table>
<thead>
<tr>
<th></th>
<th>T+OFS</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot flushes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweats</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of sexual interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone or joint pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coping effort</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment burden</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>No Chemo Cohort</th>
<th>Prior Chemo Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(mean diff = -32)</td>
<td>(mean diff = -26)</td>
</tr>
<tr>
<td></td>
<td>(mean diff = -15)</td>
<td>(mean diff = -6)</td>
</tr>
</tbody>
</table>

± 8 is the minimal clinically meaningful change of QoL scores.

---

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Treatment Effect: by Cohort

Changes from baseline to month 6 for selected indicators

<table>
<thead>
<tr>
<th>Indicator</th>
<th>T+OFS</th>
<th>T</th>
<th>E+OFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot flushes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweats</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of sexual interest</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Sleep disturbance</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Coping effort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment burden</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Conclusions

- 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.

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Conclusions

- 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.