NEW INSIGHTS INTO OPTIMIZING ADJUVANT ENDOCRINE THERAPY

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HISTORY
- TAMOXIFEN
  - 5 Years has been the standard
  - Still favored in many countries due to cost and efficacy
- DURATION OF TREATMENT
  - 5 years has been standard but ATLAS and ATTOM suggest 10 years is superior (?)
- COMPARISON OF AI’S TO TAMOXIFEN
  - 3 AI’s head to head comparisons with improved DFS
  - TAM/AI switch trials have a DFS and OS benefit
  - 2 placebo controlled trials of AI’s after TAM show benefit of 10 years of combined treatment

QUESTION?
HAVE WE MADE PROGRESS?

IES Trial Design
- Tamoxifen
- Exemestane (2-3 years)
- Tamoxifen (2-3 years)
- Post-treatment follow-up

IES Demographics
- ER+ = 85.8%, ER unknown = 11.6%, ER- = 2.6%
- 51.8% patients were node negative
- 32.6% of patients received adjuvant chemotherapy
- Mean age at randomisation = 64.2 years (SD=8.2)

Disease Free Survival - ER+/Unknown
- On treatment: 0.2-5 years HR=0.64 95%CI (0.52, 0.79)
- Post treatment follow-up: 2-3 years HR=0.93 95%CI (0.80, 1.07)
Number of events/at risk

Overall Survival - ER+/Unknown

HR = 0.86 (95% CI: 0.75-0.99); p=0.04

Absolute difference at 5 years = 1.4% (95% CI: 0.1 – 2.5)

Absolute difference at 8 years = 2.4% (95% CI: 0.1 – 4.8)

TEAM Trial: Revised Design 2004

N = 9775 accrued

Postmenopausal receptor-positive women

Diagnosis and adequate primary therapy of early breast cancer

Randomization

Tamoxifen

Exemestane

IES Positive Results

Exemestane

Total of 5 years’ treatment

Co-primary end points

DFS at 2.75 years

DFS at 5 years

TEAM TRIAL PUBLISHED 2011

TEAM TRIAL PUBLISHED

LANCET 377: 321-331, 2011

IES UPDATE

IN PRESS, JCO, 2011
COMPARISON OF 2 AI’S FOR 5 YEARS
- MA27: randomized comparison of anastrozole v. exemestane for 5 years
- Numerous substudies
- Goss et al. SABCS 2011 presented first results: NO difference in DFS
- Some differences could emerge from substudies or side effect profiles
- One additional head to head AI trial results pending: letrozole v. anastrozole

WHAT TO DO TODAY?
- THE FIRST 5 YEARS
  - Initial AI use: no survival advantage
  - TAM/AI switch: modest survival advantage
  - TEAM trial shows no difference in outcome between initial AI or TAM/AI switch (DFS and OS)
- Compliance and bone health
- LONGER TREATMENT
  - Compliance
  - Monitor bone health

Poster # P008-03
Competing Causes of Mortality vs. Breast Cancer Mortality at 5-Years Among 9766 Postmenopausal Women with Hormone Receptor Positive Early Breast Cancer Treated on the TEAM Study of Adjuvant Hormonal Therapy

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SABCS 2010
Patients and Methods

The TEAM (Tamoxifen Exemestane Adjuvant Multinational) trial is now a mature adjuvant endocrine study comparing a switch strategy (Tamoxifen to Exemestane) vs. Exemestane alone for 5 years (Figure 1).

Results

- 9,766 women have been followed for 5.14 years with 67% having at least 5 years of follow-up. 608 (6.2%) have died due to breast cancer and 435 (4.5%) from other causes.
- 5 years OS is 90.5% (95% CI 89.9 – 91.1)

Causes of Death (Table 1)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N (%)</th>
<th>N (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exemestane</td>
<td>393 (76.1)</td>
<td>296 (60.2)</td>
<td>696 (67.4)</td>
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<tr>
<td>Tamoxifen to Exemestane</td>
<td>61 (11.6)</td>
<td>55 (10.7)</td>
<td>116 (11.1)</td>
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<tr>
<td>Endometrial cancer</td>
<td>5 (0.9)</td>
<td>1 (0.2)</td>
<td>6 (0.6)</td>
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<tr>
<td>Cardiac</td>
<td>46 (8.7)</td>
<td>31 (6.2)</td>
<td>77 (7.4)</td>
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<tr>
<td>Thromboembolism</td>
<td>8 (1.5)</td>
<td>4 (0.8)</td>
<td>12 (1.2)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>13 (2.5)</td>
<td>17 (3.3)</td>
<td>30 (2.9)</td>
</tr>
<tr>
<td>CNS cancer</td>
<td>20 (3.8)</td>
<td>14 (2.7)</td>
<td>34 (3.3)</td>
</tr>
<tr>
<td>Vascular</td>
<td>4 (0.8)</td>
<td>3 (0.6)</td>
<td>7 (0.7)</td>
</tr>
<tr>
<td>Other</td>
<td>44 (8.3)</td>
<td>54 (10.5)</td>
<td>98 (9.4)</td>
</tr>
<tr>
<td>Unknown</td>
<td>35 (6.6)</td>
<td>25 (4.8)</td>
<td>60 (5.8)</td>
</tr>
<tr>
<td>Total</td>
<td>527</td>
<td>518</td>
<td>1043</td>
</tr>
</tbody>
</table>

Cumulative Probability of Dying from Breast Cancer or Other Causes

All patients

Cumulative Probability of Dying by Axillary Lymph Node Status

N positive  N negative
Conclusion

- The TEAM trial with mature follow-up had a 90.5% 5-year overall survival with 5.5% probability of death due to breast cancer and 4.0% due to other competing causes of mortality.
- In women with node negative cancer, the odds of dying from other causes were greater than dying from breast cancer (3.7% vs. 2.7%, P=0.011).
- In women with positive nodes, the odds of dying at 5 years from breast cancer remained higher than dying from other causes (8.6% vs. 4.2%, P<0.001).
- The odds of dying by 5 years from other causes increased with patients’ age at diagnosis (Age <60, 1%; Age 60-69, 2.5%; Age ≥70, 9.8%, P<0.0001).
- The vast majority of women with HR+ early breast cancer entered into the TEAM trial survived breast cancer but are at increasing risk of dying from other unrelated causes.

WE HAVE MADE PROGRESS!!!

- FOR ENDOCRINE SENSITIVE BREAST CANCER, TAMOXIFEN REMAINS A POTENT LIFE-SAVING AGENT
- 3 AROMATASE INHIBITORS ARE SUPERIOR TO TAMOXIFEN
- 5 YEARS OF AN AI OR SWITCHING FROM TAM TO AN AI ARE EQUAL
- MOST WOMEN WITH ENDOCRINE SENSITIVE BREAST CANCER SURVIVE THE CANCER
- COMPLIANCE WITH TAKING LONGTERM MEDICATIONS STILL IS A CHALLENGE

THANK YOU