ESMO PRECEPTORSHIP ON BREAST CANCER

Special Issues in Treatment of Young Women with Breast Cancer

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DISCLOSURES

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Honoraria: AstraZeneca, Novartis
Overseas Lectures (travel): Pfizer, Ipsen
Young Women with Breast Cancer

Overview of Issues

• General
• Pathobiology
• Prognosis
• Genetic considerations
• Loco-regional therapy considerations
• Adjuvant systemic therapy considerations
• Reproductive issues
• Menopause and treatment related issues
• Psycho-social issues
• Lifestyle optimization
Young Women with Breast Cancer

Definitions

• Young women < 40 years age at diagnosis

• Very young women < 35 years age at diagnosis

• Higher percentage diagnosed at young age in Asia, compared to western countries
Special Issues in Treatment of Young Women with Breast Cancer

• Due to increased complexity of management, young women benefit from management in a specialized/dedicated Breast Clinic

• Care of young patients should be discussed by multidisciplinary team before any treatment decisions
Special Issues in Treatment of Young Women with Breast Cancer

Multidisciplinary team members:
- Breast Surgeon, Breast Nurse
- Medical Oncologist, Radiation Oncologist,
- Radiologist, Pathologist, Plastic Surgeon

Plus Access to:
- Genetics expertise
- Fertility specialist
- Psycho-social health professionals
- Sexual health/Menopause expertise
Special Issues in Treatment of Young Women with Breast Cancer

- Pathobiology
  - Stage at presentation
  - Histopathology
  - Phenotype
Pathobiology of Breast Cancer in Young Women

Adverse histopathologic features more common:

• Symptomatic/higher stage disease at presentation
• Triple negative tumours (ER-ve, PR-ve, and HER2-negative)
• HER2-positive tumours
• PR-negative tumours
• High grade tumours
• High Ki67 (proliferation biomarker)
• p53 mutations
• EGFR overexpression
• Extensive intraduct component (EIC)
Breast cancer is the leading cause of cancer-related deaths in young women.
Young Women with Breast Cancer

Prognosis

• Young women have increased risks of local and distant recurrence due to a higher proportion of aggressive tumours

However

• Even with luminal A-like tumours (ER+ve, PR high, HER2-negative, Ki67 low or low risk genomic assay), young women ≤ 40 yrs had a significantly higher risk of breast cancer death than older women

Partridge et al, J Clin Oncol 2016
Outcomes from Premenopausal Adjuvant Chemotherapy Trials with no Hormonal Rx

Goldhirsch A et al. JNCI Monogr 2001;30:44-51
Premenopausal HR+ Early Breast Cancer

• Chemotherapy can have both direct cytotoxic effects and indirect endocrine effect in HR+ breast cancer

• Women who develop chemotherapy-induced ovarian suppression (amenorrhea) have a reduced risk of relapse

• Chemotherapy-induced amenorrhea is correlated with older premenopausal age - less likely in women < 35 yrs

• Very young women with HR+ tumours may miss out on endocrine effect of chemotherapy
IBCSG 13: Premenopausal Node+ve: ER+ subgroup
Adj Chemo $\rightarrow$ Tamoxifen: Better DFS if amenorrhea

IBCSG, J Clin Oncol 2006
Prognosis: Very Young Premenopausal

5-yr Breast Cancer-Free Interval by age in SOFT-TEXT trials if assigned to oral Endocrine Therapy plus Ovarian Function Suppression (OFS)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Women &lt; 35 years</th>
<th>Women &gt; 35 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal A-like</td>
<td>83.6%</td>
<td>96.2%</td>
</tr>
<tr>
<td>Luminal B-like</td>
<td>79.2%</td>
<td>86.4%</td>
</tr>
</tbody>
</table>

Luminal A-like: ER+ve, HER2-negative, PR > 20%, Ki67 < 20%
Luminal B-like: ER+ve, HER2-negative, PR < 20% and/or Ki67 > 20%

Saha et al, J Clin Oncol 2017
Special Issues in Treatment of Young Women with Breast Cancer

• Genetic considerations
  – Genetic counselling/testing (see also BRCA Module)
  – BRCA mutation carriers (see also BRCA Module)

• Loco-regional therapy considerations
  – Imaging considerations
  – Surgical considerations
  – Radiotherapy considerations
Loco-regional therapy considerations in Young Women with Breast Cancer

• Genetic counselling should be offered before Rx as results of genetic testing may change decisions

• MRI may be added to diagnostic imaging when
  – predisposing gene mutation
  – high risk due to prior chest radiation (ie. Hodgkins)
  – very dense breast tissue
Loco-regional therapy considerations in Young Women with Breast Cancer

• Breast conserving surgery (BCS) and sentinel node biopsy are valid options in young women with breast cancer, as in older women.

• BCS mandates whole breast radiation + boost (avoid Partial Breast Irradiation in young women)

• EORTC randomized trial showed reduction in local recurrence in women ≤ 40 yrs from 24% to 10% at 10 yrs with addition of a 16 Gy boost to WBRT
EORTC Trial: Ipsilateral Breast Cancer Recurrence in women < 40 yrs with BCS and WBRT +/- Boost

Bartelink et al, J Clin Oncol 2007
Surgical considerations in Young Women with Breast Cancer

• Young women are at increased risk for local recurrence but there is no evidence that mastectomy provides better survival than BCS.

• Attention should be paid to margins with regard to DCIS in young women to minimize the risk of local recurrence.
### Table 3. Overall 5-Year Local, Regional, and Distant Recurrence Rates Over Time in Patients With Breast Cancer Age < 35 Years Treated Between 2003 and 2008 (n = 1,000)

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of Patients</th>
<th>Local Recurrence, No. (%)</th>
<th>Regional Recurrence, No. (%)</th>
<th>Distant Metastases, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>1,000</td>
<td>31 (3.5)</td>
<td>33 (3.7)</td>
<td>131 (13.9)</td>
</tr>
<tr>
<td>2003</td>
<td>213</td>
<td>8 (4.2)</td>
<td>11 (6.1)</td>
<td>36 (17.8)</td>
</tr>
<tr>
<td>2004</td>
<td>212</td>
<td>10 (5.6)</td>
<td>10 (5.1)</td>
<td>38 (19.2)</td>
</tr>
<tr>
<td>2005</td>
<td>182</td>
<td>3 (2.0)</td>
<td>5 (3.1)</td>
<td>25 (14.6)</td>
</tr>
<tr>
<td>2006</td>
<td>170</td>
<td>5 (3.2)</td>
<td>2 (1.2)</td>
<td>13 (8.2)</td>
</tr>
<tr>
<td>2007†</td>
<td>117</td>
<td>2 (2.1)</td>
<td>1 (0.9)</td>
<td>9 (8.1)</td>
</tr>
<tr>
<td>2008†</td>
<td>106</td>
<td>3 (3.2)</td>
<td>4 (4.4)</td>
<td>10 (10.0)</td>
</tr>
</tbody>
</table>

NOTE. Rates represent Kaplan-Meier estimates.
*Local recurrence (ipsilateral in-breast recurrence and new primary).
†P < .05 for trend in recurrence risk over time using linear regression analyses.
‡Only 43 of 92 hospitals were included in the years 2007 and 2008.

Aalders et al, J Clin Oncol 2016
Loco-regional therapy considerations in Young Women with Breast Cancer

• Cosmetic outcomes of surgery and impact of the type of surgery on sexuality may be of even greater importance to young women

• Options for reconstruction should be discussed in cases when mastectomy will be performed
Loco-regional therapy considerations in Young Women with Breast Cancer

• Young women more likely to have high grade tumours

• Neoadjuvant chemotherapy in high grade tumours in young women allows:
  – Timely start of systemic therapy
  – Time for genetic testing results
  – Time to plan reconstruction if mastectomy
Surgical considerations in Young Women with Breast Cancer

• There is no evidence that performing a contralateral mastectomy improves overall survival for young women with unilateral disease, if they are not a high-risk gene carrier.

• Offer psycho-social assessment/support, particularly when patient is considering contralateral risk-reducing mastectomy.
Radiation therapy considerations in Young Women with Breast Cancer

• Modern RT techniques to optimize treatment and minimize toxicity

• Late effects of radiation: heart, lungs, second malignancy etc. need to be considered. Smokers have increased late effects.

• Smokers who undergo radiation to conserved breast have significant increased risk for developing ipsilateral lung cancer → refer for cessation program

Taylor et al, J Clin Oncol 2017
Radiation therapy considerations in Young Women with Breast Cancer

• **MA.20** Regional Nodal Irradiation (RNI) trial: tested addition of RNI to whole breast RT in N+ or high risk N- tumours

• Adding RNI $\rightarrow$ Improved disease-free survival (DFS) and distant disease-free survival (DDFS), with stronger effect in ER-negative tumours which are more common in young patients

Special Issues in Treatment of Young Women with Breast Cancer

• **Adjuvant Systemic Therapy Considerations**
  – Gene-expression assays
  – Chemotherapy
  – Adjuvant Endocrine therapy - Tamoxifen
  – Role Ovarian Suppression (see Lecture Module 7)
  – Adjuvant HER2-targeted therapy
  – Adherence with adjuvant endocrine therapy
Premenopausal ER+ Breast Cancer
Multigene Assays in Young Women

• Gene-expression assays may be used to help clarify role of chemotherapy but limited outcome data for very young women with a Low Risk assay score and Rx adjuvant tamoxifen alone

• TAILORx trial RS 0-10 cohort (n=1,629) had 58 (<4%) women < 40 y and some received ovarian suppression in addition to tamoxifen


• MINDACT trial (n=6,693) had 122 women < 35 y, including 44 women with genomic low risk

Premenopausal ER+ Breast Cancer Multigene Assays in Young Women

• Most assays were validated in postmenopausal women (or rendered postmenopausal by CMF) and so recurrence estimates may not be well calibrated for young premenopausal patients

• Results from TAILORx trial for RS 11-25 showed a significant interaction between benefit from chemotherapy and age (≤ 50 years)

Sparano et al, N Engl J Med 2018
Chemotherapy considerations in Young Women with Breast Cancer

- No regimens that are specific to young women

- Women < 35 years with ER+ tumours are more likely to be offered chemotherapy due to insufficient data on outcomes in very young age group with endocrine therapy alone

- Addition of platinum to a standard anthracycline-cyclophosphamide-taxane regimen for TNBC has not been shown to improve DFS but does ↑ pCR rate (CALGB 40603, BrighTNess) – may be considered for high risk TNBC neoadjuvant Rx (regardless of gBRCA status)

Sikov et al, J Clin Oncol 2016
Loibl et al, Lancet Oncol 2018
Premenopausal women with hormone receptor-positive (HR+) breast cancer should be recommended to receive adjuvant endocrine therapy.

Guidelines define HR+ if > 1% cells positive for ER or PR.

Patients with > 10% tumor cells ER+ are considered to derive benefit from adjuvant endocrine therapy.

Patients with borderline ER+ (1-9% cells positive) derive less certain benefit (NB. they were not eligible for SOFT and TEXT).
Adjuvant Endocrine Therapy
Premenopausal ER+ Breast Cancer

• Reduces local recurrence (so increases likelihood of retaining conserved breast)

• Reduces regional recurrence (undissected axilla is now more common after sentinel node biopsy)

• Reduces distant metastases and so improves overall survival

• Reduces risk of new contralateral breast cancer (NB relevant if predominantly DCIS with very small invasive component)
### Adjuvant Tamoxifen in ER+ or unknown Effective in Young Premenopausal Women

#### Recurrence / Woman-years

<table>
<thead>
<tr>
<th>Category</th>
<th>Event/ Woman-years</th>
<th>Tamoxifen events</th>
<th>Ratio of annual event rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Allocated Logrank</td>
<td>Tamoxifen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Variance centred</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>O-E</td>
<td>O-E</td>
</tr>
<tr>
<td>(a) Dose of tamoxifen ($\chi^2_0 = 6.0$; $p &gt; 0.1$; NS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 mg/day</td>
<td>841/309</td>
<td>896</td>
<td>1199/275998</td>
</tr>
<tr>
<td>(5.7%)</td>
<td>(4.4%)</td>
<td>(9.1%)</td>
<td>(5.9%)</td>
</tr>
<tr>
<td>50–40 mg/day</td>
<td>577/116079</td>
<td>-164-7</td>
<td>291-4</td>
</tr>
<tr>
<td>(5.9%)</td>
<td>(5.9%)</td>
<td>(5.9%)</td>
<td>(5.9%)</td>
</tr>
<tr>
<td>(b) Presence or absence of cytotoxic ($\chi^2_0 = 0.0$; $p &gt; 0.1$; NS)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Chem with Tam vs Chem alone</td>
<td>22239264</td>
<td>27176799</td>
<td>-54-5</td>
</tr>
<tr>
<td>(5.7%)</td>
<td>(9.1%)</td>
<td>(9.1%)</td>
<td>(9.1%)</td>
</tr>
<tr>
<td>Chem then Tam vs Chem alone</td>
<td>242926</td>
<td>3197622</td>
<td>-161-6</td>
</tr>
<tr>
<td>(2.9%)</td>
<td>(4.2%)</td>
<td>(4.2%)</td>
<td>(4.2%)</td>
</tr>
<tr>
<td>Tam alone vs Nil (no adjuvant)</td>
<td>94737495</td>
<td>135230387</td>
<td>-214-1</td>
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<tr>
<td>(7.7%)</td>
<td>(4.4%)</td>
<td>(7.7%)</td>
<td>(4.4%)</td>
</tr>
<tr>
<td>(c) Entry age (trend $\chi^2_0 = 6.0$; $p = 0.05$)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Age &lt; 40</td>
<td>11333231</td>
<td>17705853</td>
<td>-36-8</td>
</tr>
<tr>
<td>(5.7%)</td>
<td>(9.7%)</td>
<td>(9.7%)</td>
<td>(9.7%)</td>
</tr>
<tr>
<td>40–49</td>
<td>27531061</td>
<td>26169770</td>
<td>-49-0</td>
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<td>(2.9%)</td>
<td>(4.0%)</td>
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<tr>
<td>50–59</td>
<td>45634694</td>
<td>57631114</td>
<td>-94-5</td>
</tr>
<tr>
<td>(2.1%)</td>
<td>(4.4%)</td>
<td>(4.4%)</td>
<td>(4.4%)</td>
</tr>
<tr>
<td>60–69</td>
<td>40810669</td>
<td>72414546</td>
<td>-162-0</td>
</tr>
<tr>
<td>(2.9%)</td>
<td>(5.0%)</td>
<td>(5.0%)</td>
<td>(5.0%)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>7021050</td>
<td>1071887</td>
<td>-25-0</td>
</tr>
<tr>
<td>(2.3%)</td>
<td>(5.7%)</td>
<td>(5.7%)</td>
<td>(5.7%)</td>
</tr>
</tbody>
</table>
Adjuvant Tamoxifen in ER+ Breast Cancer
Effective in Premenopausal age group

EBCTCG Lancet 2011
Adjuvant Tamoxifen for Premenopausal ER+ Breast Cancer

• Tamoxifen 5 years reduced 15-year breast cancer mortality by ~ 1/3 in women < 45 y

• Women < 45 y allocated 5 years tamoxifen - contralateral breast cancer risk halved over 15 years (abs difference 2.9%)

• Safety of adjuvant tamoxifen for 5 years more favourable in younger women

• Among women < 45 years at trial entry – no deaths from uterine cancer or pulmonary embolism

EBCTCG, Lancet 2011
EBCTCG: ER+ve Distant Recurrence in years 5-20 by Age after 5 years adjuvant endocrine therapy

Pan et al, ASCO 2016 abstract # 505
ATLAS Trial: ER+ve after 5 years tamoxifen
Continue to 10 years vs Stop at 5 years

Recurrence

BC-Mortality

Davies et al, Lancet 2013
ATLAS Trial: 10 vs 5 years Tamoxifen
Recurrence by menopausal status at entry

![Table and Figure]

Davies et al, Lancet 2013
ATLAS Trial: ER+ve after 5 years tamoxifen

- Continuing for a total of 10 years significantly reduced breast cancer recurrence (after year 7) and breast cancer specific mortality (after year 10)

- Absolute benefit ~ 4% for recurrence and ~ 3% for BC-specific mortality

- Overall survival significantly improved (p=0.01)

Davies et al, Lancet 2013
Adjuvant Systemic Therapy Considerations in Young Women with HER2+ Breast Cancer

• Young women have increased frequency of HER2+ve tumours compared to older women

• Efficacy of adjuvant trastuzumab HER2-targeted therapy is independent of age
Adjuvant Systemic Therapy Considerations in Young Women with HER2+ Breast Cancer

- ALTTO HER2+ve trial retrospective analysis: better survival in premenopausal HR+ve (but not HR-ve) if treatment related amenorrhoea
  
  Lambertini et al, J Natl Cancer Inst 2019

- SOFT Trial: addition of Ovarian Function Suppression (OFS) to tamoxifen beneficial in HER2+ve subgroup

  Francis et al. N Engl J Med 2018
(non) Adherence with Adjuvant Endocrine Therapy

• Numerous studies reported that adherence to adjuvant endocrine therapy is worse in young women

• Reasons likely multifactorial but this requires attention when seeing young patients for follow-up of early breast cancer in clinic
Special Issues in Treatment of Young Women with Breast Cancer

• Reproductive issues
  – Fertility preservation
  – Contraception
  – Pregnancy (see other Lecture Module)
Fertility Considerations in Premenopausal Breast Cancer

• If child-bearing not complete, offer fertility consultation before start systemic therapy (if cryopreservation of oocytes or embryos would be a consideration for the patient)

• Consider fertility consultation even if chemotherapy not planned (ie. before endocrine therapy).

• Age is a risk factor for reduced fertility - reduction in fertility during 5-10 years of endocrine Rx
Options for Fertility Preservation
Premenopausal Breast Cancer Patients

Main methods
• Embryo cryopreservation
• Oocyte cryopreservation
• GnRH agonists

Other method
• Ovarian tissue cryopreservation and subsequent transplantation – has resulted in some births
Fertility Considerations in Premenopausal Breast Cancer

• If future pregnancy desired and chemotherapy planned, consider starting GnRHa ≥1 week prior and continue during chemotherapy

• Randomized POEMS trial in ER-negative breast cancer reassuring re safety of this approach re cancer outcomes

• Analysis of cancer outcomes in women < 40 y with ER+ve cancers in TEXT trial vs. SOFT trial also support concurrent GnRHa and chemotherapy as a safe option.


Moore et al, J Natl Cancer Inst 2018

Regan et al, Ann Oncol 2017
Meta-analysis of GnRHa during chemo in breast cancer for preservation of ovarian function/fertility

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Events/pts</th>
<th>Control Events/pts</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td>51/363</td>
<td>111/350</td>
<td>0.38</td>
<td>0.26 to 0.57</td>
</tr>
<tr>
<td><strong>Age distribution, y</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 40</td>
<td>21/254</td>
<td>58/235</td>
<td>0.28</td>
<td>0.16 to 0.49</td>
</tr>
<tr>
<td>≥ 41</td>
<td>30/109</td>
<td>53/124</td>
<td>0.52</td>
<td>0.29 to 0.92</td>
</tr>
<tr>
<td><strong>Estrogen receptor status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>30/174</td>
<td>52/167</td>
<td>0.40</td>
<td>0.27 to 0.79</td>
</tr>
<tr>
<td>Negative</td>
<td>20/187</td>
<td>58/190</td>
<td>0.31</td>
<td>0.17 to 0.56</td>
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<tr>
<td><strong>Type of chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anthracycline only</td>
<td>32/160</td>
<td>56/170</td>
<td>0.51</td>
<td>0.30 to 0.87</td>
</tr>
<tr>
<td>Anthracycline plus taxane</td>
<td>17/188</td>
<td>49/174</td>
<td>0.26</td>
<td>0.14 to 0.48</td>
</tr>
<tr>
<td>Non-anthracycline</td>
<td>0/4</td>
<td>1/8</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration of chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 4 months</td>
<td>12/102</td>
<td>31/102</td>
<td>0.34</td>
<td>0.16 to 0.73</td>
</tr>
<tr>
<td>&gt; 4 months</td>
<td>16/164</td>
<td>34/144</td>
<td>0.35</td>
<td>0.18 to 0.68</td>
</tr>
</tbody>
</table>

Lambertini et al, J Clin Oncl 2018
Meta-analysis of GnRHa during chemo in breast cancer – post Rx pregnancies

Lambertini et al, J Clin Oncol 2018
Is it safe to use OFS with GnRH agonist during adjuvant chemotherapy in Premenopausal ER+ve Breast cancer?
OFS Timing in TEXT and SOFT

Protocol treatment was for 5 years from randomization

**TEXT**

- All women started GnRH agonist triptorelin (IM q28d)
- Triptorelin started **concurrently** with chemotherapy, if chemotherapy was given
- Permanent ovarian ablation allowed after 6 months

**SOFT**

- Choice of initial OFS method (triptorelin or permanent ablation) for women assigned OFS. If chemotherapy was given, OFS was **started after** chemotherapy.
Timing of OFS and Chemotherapy
Concurrent in TEXT - Sequential in SOFT

Non-randomized comparison
Patients Rx GnRHa HR+ve HER2-ve

Regan et al, Ann Oncol 2017
Timing of OFS and Adjuvant Chemotherapy in Premenopausal ER+ve Breast Cancer

• If child-bearing not complete, recommend commence OFS with GnRH agonist ≥ 1 week prior to adjuvant chemotherapy with aim of improving future pregnancy prospects

• If child-bearing completed, adjuvant OFS can be started either sequential after or concurrent with chemotherapy

Regan et al, Ann Oncol 2017
Contraception in Young Women after early Breast cancer

- Women should be advised to avoid pregnancy during chemotherapy, adjuvant endocrine therapy, and for 7 months after trastuzumab (long half-life).

- After chemotherapy induced amenorrhea, a woman can become pregnant before menses recommence.

- Tamoxifen was first used to improve fertility.

- Avoid all hormonal contraception including levonorgestrel IUD (Mirena).
Special Issues in Treatment of Young Women with Breast Cancer

• Menopause and treatment-related issues
  – Sexuality
  – Vasomotor symptoms
  – Sleep disturbance
  – Bone Health
  – Metabolic Health (BP, glucose, cholesterol etc)
  – Musculoskeletal complaints
  – Assessing menopausal status
Assessing Menopausal Status

• Tamoxifen reduces FSH and LH levels making biochemical determination of menopause more difficult while women continue to take tamoxifen
  (ie. postmenopausal women on tamoxifen may have premenopausal levels of FSH/LH)
Risk of Reversal of Chemotherapy-Induced Menopause when commence an AI

- Prospective study by Guerrero et al (Ann Oncol 2012)

- Women (n=53) with chemotherapy induced amenorrhea > 2 years and postmenopausal E2 on adjuvant tamoxifen → switched to AI (exemestane)

- Median age 48 (range 41-55 y)
- Median duration amenorrhea 2.5 years (range 2- 4.5 y)
- 75% had prior anthracycline + taxane chemotherapy
Risk of Reversal of Chemotherapy Induced Menopause when commence an AI

• ~ 30% had ovarian function recovery after switch to AI
• In women < 48 yrs - 50% ovarian recovery on AI
• In women > 50 yrs - 12% ovarian recovery on AI
• Age at commencement of AI associated with risk
• Similar results other studies
• Cannot guarantee efficacy of AI in women with chemotherapy-induced amenorrhea without concurrent OFS (GnRH or oophorectomy)
Special Issues in Treatment of Young Women with Breast Cancer

• **Psycho-social issues**
  – Relationships
  – Distress/Depression
  – Non-adherence to systemic therapy
  – Professional - Financial

• **Lifestyle optimization**
  – Weight, diet
  – Exercise
  – Smoking, Alcohol
Special Issues in Treatment of Young Women with Breast Cancer

**Lifestyle optimization:** Weight, diet

- Patients often experience treatment associated weight gain

- Weight gain after diagnosis of breast cancer is associated with increased risk of recurrence

- Young patients have many years ahead to develop 2\textsuperscript{nd} malignancies associated with high BMI (contralateral breast, endometrium, etc)
Special Issues in Treatment of Young Women with Breast Cancer

Exercise Recommendations

• Engage in regular physical activity
  – avoid inactivity and return to normal daily activities as soon as possible after diagnosis
  – Aim to exercise at least 150 minutes/week
  – Include strength training exercises at least twice per week

• Exercise and strength training may reduce fatigue and musculoskeletal complaints
Lifestyle Optimization in Young Women with Breast Cancer

• For a woman aged 50 who has smoked since adolescence and does not stop, by undergoing breast radiation for cancer, her risk of death from lung cancer by age 80 years is increased from 9.4% to 13.8%

• If the same woman quits smoking at time of radiation, the absolute increase in lung cancer mortality from breast XRT of 4.4% declines to 1.3%

Taylor et al, J Clin Oncol 2017
Special Issues in Treatment of Young Women with Breast Cancer

To achieve optimal outcomes in young women require members of multidisciplinary team to:
(1) communicate well
(2) plan and coordinate management together
(3) understand special issues for this age group
(4) understand the patient’s preferences
ESO-ESMO 3rd International Consensus Guidelines for Breast Cancer in Young Women

Original article

ESO-ESMO 3rd international consensus guidelines for breast cancer in young women (BCY3)

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