Current Issues in Breast Cancer Survivors: What to Expect in Your Primary Care Practice

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www.MSKCC.org
• None of the presenters report relevant conflicts of interest
Background

- >15 million cancer survivors in the US
- Anticipated shortage of oncologists
- Traditional model of follow-up not sustainable
- New strategies for long-term follow-up care of survivors needed

Early stage breast cancer patients have equivalent outcomes when followed by PCPs or oncologists

Treatment Summary and Care Plan

1. Diagnosis and treatment history
2. Persistent treatment effects
3. Cancer related ongoing medications
4. Relevant family history (and results of genetic testing if done)
5. Most recent breast imaging
6. Surveillance recommendations (no tumor markers)
7. Screening recommendations
8. Health promotion recommendations
9. How to contact MSK
Transition of Care

Risk-based approach to PCP transitions

<table>
<thead>
<tr>
<th>Risk of Recurrence</th>
<th>Risk of Late Effects</th>
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<td>Low/Low</td>
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Transition of Care: Eligibility

• Time since diagnosis
  – DCIS 5 years
  – T1-2/Triple-/Node- > 5 years
  – T1-2/ER+/Node- 10 years
  – Any stage >20 years

• Absence of disease

• Absence of significant long-term effects

• >75 years of age
Late medical effects of treatment depend on the types of therapy . . .

and the toxicities of each therapy
Clinical Breast and Chest Wall Exam in Survivors
Breast and/or Chest Wall Changes

- Initial surgeries
  - Breast conservation vs total mastectomy
  - Sentinel node vs full axillary node dissection
- Reconstruction
  - Implants: silicone or saline
  - Mammoplasty
  - Tissue reconstruction
    - TRAM, DIEP
- Adjuvant Radiation
  - Skin changes including thickening and pigmentation
RIPPLING
UPPPER CHEST CONCAVITY
UPPER CHEST CONCAVITY
UPPER CHEST CONCAVITY
Breast Pain and Other Sensations
Sensation Changes After Breast Surgery

- Result of surgery rather than cancer itself
- Injury or resection of nerves during surgery
  - 2nd intercostal nerve (intercostal brachial nerve)
    - Responsible for many sensory disturbances
    - Supplies axilla and upper arm
    - Frequently sacrificed to gain wide access to axilla contents
    - Even when preserved, routinely stretched or injured
  - Other cutaneous sensory nerves

Sensation Changes after Breast Surgery

- Occur in 15-40% of all patients with SLND or ALND
- Most Prevalent Sensations at 5 Years
  - Tender
  - Sore
  - Pull
  - Ache
  - Painful
  - Numb
  - Twinge
  - Tight

Adjuvant Hormonal Therapy for ER+ Breast Cancer
Adjuvant Tamoxifen

• 5 yrs- reduces recurrence and mortality- old standard
• Longer followup revealed 50% recurrences occur >5 yrs
• Extended Tamoxifen improves outcomes:
  – ATLAS N=12,894 and aTTOM N=6,953
  – ATLAS: RCT 5 vs. 10 years tamoxifen therapy (ER+ pts)
    • 10 years tamoxifen reduced mortality
      – Breast cancer mortality: 9.7% vs 11.6% (NNT 53)
      – Overall mortality: 18.6% vs 21.1% (NNT 40)
  • Greater effect after 10 years

EBCTCG 2011 Lancet 387(9793);771-84
Gray et al (2013) aTTOM J Clin Onc 31(suppl abstr 5)
Extended Tamoxifen: potential harms

- Endometrial cancer - absolute increase 1.6%
  - Higher risk age > 55 years (2.6% increase)
  - Low associated mortality
  - Risk is outweighed by lower breast cancer mortality
  - Do not screen for endometrial thickening with TVUS unless symptomatic
    - Post menopausal bleeding
    - Change in baseline for premenopausal women
- Thromboembolic events
  - Increase in PE
  - No increase in stroke

Guideline: ASCO Practice Update 2014

• Previous Recommendations
  – Premenopausal: 5 years of tamoxifen
  – Postmenopausal: 5 years aromatase inhibitor (AI) or tamoxifen followed by an AI in sequence

• New Recommendations: 10 total years hormonal rx
  – Pre/perimenopausal after 5 years of adjuvant tamoxifen: offer 10 years total duration of tamoxifen.
  – Postmenopausal after 5 years of adjuvant tamoxifen: continue tamoxifen or sequence to an AI for 10 years total adjuvant endocrine therapy.

• "It is important for clinicians and patients to discuss the trade-offs between potential risks of side effects and potential benefits of taking adjuvant endocrine therapy for up to 10 years.

• “Many women taking adjuvant tamoxifen experience side effects, and these appear to persist with longer duration. However, the trials did not find any new or unexpected side effects." – Jennifer Griggs, MD, MPH, co-chair of the ASCO guideline panel
Aromatase Inhibitors
Aromatase Inhibitors (AIs)

• Agents:
  • Letrozole (Femara) 2.5mg oral daily, nonsteroidal
  • Anastrozole (Arimidex) 1 mg oral daily, nonsteroidal
  • Exemestane (Aromasin) 25mg oral daily, steroidal

• Indications:
  • Primary hormonal therapy for postmenopausal women
  • May sequence after Tamoxifen

• Special considerations for intolerable side effects:
  • try other AIs
  • consider Tamoxifen
Aromatase Inhibitors: Trials

• RCT of 5 years letrozole vs placebo after 5 years tamoxifen (N=5170)
• Results: after median f/up 2.5 years
  – Lower rate of recurrence: 2.9% vs 4.9% (NNT 50)
  – Improved disease-free survival (primary outcome): event rates 3.6% vs 6.0%
  – Lower risk of distant metastases and contralateral breast cancer (statistical significance unclear)
  – Trend toward more fractures, not significant

Bottom line: Consider AI for 5 yrs following adjuvant tamoxifen

Goss et al. (2003). Randomized Trial of Letrozole Following Tamoxifen as Extended Adjuvant Therapy in Receptor-Positive Breast Cancer: Updated Findings from NCIC CTB AM.17. JNCI 97:1262-71

Memorial Sloan Kettering Cancer Center
Aromatase Inhibitors: Trials

- RCT (N= 1918) additional 5 years letrozole vs placebo after 5 years AI (which was mostly after 5 yrs tamoxifen)
- **At 10 years:**
  - No difference in disease-free or overall survival  
  - Lower rate of “recurrence or contralateral cancer”
    - Contralateral cancer: 1.4% vs 3.2%  
    - Recurrence: 5.7% vs 7.1%
  - More toxicity:
    - Bone: more fractures (14% vs 9%) and lower BMD  
    - More body pain and sexual dysfunction

**Bottom line:** MSK recommends extending AI treatment to 10 years

Hormonal Therapy: Side effects

- Bone/joint/muscle aches
- Fatigue
- Vaginal dryness/dyspareunia
- Hot flashes
- Hair thinning
- Bone loss
Hormonal Therapy: Clinical Management

- Vaginal dryness
  - non-hormonal moisturizers and lubricants
    - Hyalo GYN gel, Vitamin E, Coconut oil
    - Low dose vaginal estrogens (e.g. Vagifem, Estring)
- Hot flashes
  - Acupuncture
  - Avoid triggers
  - Venlafaxine (Effexor) 37.5mg to start
- Arthralgias
  - NSAIDs, glucosamine chondroitin, exercise
  - If progressive, consider imaging
Bone Health Issues
Aromatase Inhibitors and Bone Loss

- AIs cause bone loss and fracture
- Treatment with oral or IV bisphosphonates
  - Jaw necrosis- dental clearance suggested
  - Femoral fracture
- Oral
  - low compliance r/t to GI toxicity
- IV therapy
  - acute phase reactions
  - renal clearance
Bone Health: Clinical Implications

- Consult with oncologist
- Consider patient characteristics
  - risk of recurrence
  - risk vs benefit
- Bisphosphonates
  - clodronate, zoledronic acid, pamidronate, ibandronate
    - Zoledronic acid and clodronate are recommended for adjuvant therapy in breast cancer
- Denosumab

Bone Health: Management

- Screen with DEXA every 2 years starting at menopause
- AI therapy + diminished BMD
  - Consider denosumab or bisphosphonate
    - Dental assessment prior to starting bisphosphonates
- Wt bearing exercise, Ca+ rich diet, Vitamin D supp
- Smoking Cessation
- Decrease ETOH
- Following completion adjuvant AI
  - bone health managed by PCP, GYN or refer to endocrine or osteoporosis center
MSK Bone Modifying Agent Schema

Risk sufficient for adjuvant treatment

- NO
  - Osteoporosis
    - YES
      - Denosumab or zoledronate or oral bisphosphonate
    - NO
      - Osteopenia
        - YES
          - No treatment
        - NO
          - High risk for fracture by FRAX (3% hip/20% any)

- YES
  - AI planned
    - YES
      - Osteopenia/osteoporosis
        - YES
          - Denosumab (ABC56 publication pending, not encouraged by ASCO) or zoledronate
        - NO
          - No treatment
    - NO (e.g., ER)
      - Zoledronate

Zoledronate or off-label denosumab (ABC56 study, publication pending)
Life after cancer: Patient Perspectives

• Pervasive fear of recurrence
• Concerns about information sharing
  – treatment history
  – f/u plan
• Feel “unprepared” for transition
• Prefer slow taper of contact from oncologist
• Lack of clarity about
  – Expectations at end of treatment
  – Whom to contact for specific problems

Transition of Care

MSK provides patients with a *Transition Note* that includes relevant information to be shared with PCP

- Breast cancer and treatment history
- Persistent treatment-related side effects
- Radiology results
- Follow-up Plan
Transition of Care

- Patients may continue breast imaging at MSK if desired
- Plan for rapid return of patient to their oncology provider for recurrence or cancer-related issue
- Created patient education material
- Encourage patients to establish a relationship with a PCP
Thank you!!

Contact us at: survivorship@mskcc.org