Treatment Decision Making: The Road Map for Breast Cancer Management

Presenter: Robert J. Brooks, MD
Disclosure

I have nothing to disclose
Objectives

- Discuss indications/decision making process for post-operative/adjuvant treatment for breast cancer patients.
- Discuss anti HER-2 therapy as part of breast cancer treatments.
- Discuss current guidelines for breast screening/imaging.

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Breast Cancer Screening and Diagnosis

- Breast self exam
- Mammography
  - 2D Digital
  - 3D for Dense Breast Tissue
- MRI for newly diagnosed and those at high risk (i.e. BRCA mutation)
- Core needle biopsy preferred diagnostic test
THE CANCER DIAGNOSIS

- SCARY
- OVERWHELMING
- LIFE-CHANGING
- EXISTENTIAL CRISIS!

“What is going to happen to me?”

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WHO ARE YOU GOING TO CALL?

- Support network: family, friends, spiritual
- The internet, Dr. Oz
- Tertiary Care Center – often out of town, may be “less personal”
- Community Cancer Center - in your neighborhood, better continuity?

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THE FIRST VISIT

- No matter who you are or what disease you have, the first visit is always the worst
- A new doctor to meet
- Entering a cancer clinic with a very scary looking group of people in the lobby
- Hopefully the patient is not alone
- This is the ultimate unknown for most
Who is on the team?

Medical Oncology
- Overall treatment plan
- Chemotherapy
- Biologics
- Hormonal Therapy
- Immunotherapy

Surgical Oncology
- Surgical management for tumors that are surgically curable, staging, palliation, intravenous catheters

Radiation Oncology
- Primary or adjuvant therapy, palliation

Palliative Care Oncology
- Symptom management, pain control, spiritual/psychosocial support

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ONE DOCTOR’S APPROACH

- Be prepared and know the previously obtained records/history
- Always remember you are caring for a person with cancer not the cancer
- Make certain that patient understands their diagnosis
- Make certain that patient understands their likely prognosis
- Try to get a feel for patient’s “value system”
- Discuss treatment options in the context of perceived values…allopathic, integrative, side effects profile, “what is the end game?”
- What we think might be best is not always what the patient thinks might be best

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- Are you sure I have cancer? Show me the pathology report.
- How did I get this cancer?
- What is my cancer’s stage?
- What are my treatment options?
- What treatment do you recommend?
- I read this on the internet, my sister told me, I know somebody who knew somebody who…..
- What are the short-term and long-term side effects?

- How will this treatment affect my daily life? Will I be able to work, exercise, and perform my usual activities?
- What is my prognosis?
- How are you going to follow me after the treatment is done?
EDUCATION – The substance of the visit

Methodical approach: Diagnosis → Prognosis → Treatment → Survivorship

- **Diagnosis**
  - “Tissue is the issue” Review the path report
  - Is a second opinion path review needed?
  - Explain patient’s cancer

- **Prognosis** – “What are my chances, doc?”
  - Tools: Adjuvant Online, Oncotype, etc.

- **Treatment**
  - Guidelines (NCCN, ACS, USON, etc)
  - Pathways

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Education (continued)

- Survivorship
  - “What happens after my treatment is done?”

- Psychosocial - How does the new diagnosis affect your patient’s future?
  - Long term side effects
  - Follow-up plan

- Nutrition

- Second Opinions

All delivered with empathy and compassion in the setting of rapidly increasing burdens to the doctor and “system” – Time constraints, EHR inefficiencies, Insurance restrictions, Cost containment
HOPE VS HONESTY-A JUGGLING ACT!

- Better drugs with more specific targeting
- Better Management of Side Effects “Do you know somebody who has had chemotherapy?”
- More Breakthroughs
- More Victories
- Most patients need and appreciate honesty even if news is bad
THE WORKUP AND STAGING
**NCCN Guidelines Version 1.2012**

**Invasive Breast Cancer**

**CLINICAL STAGE**

- Stage I
  - T1, N0, M0
  - or
  - Stage IIA
  - T0, N1, M0
  - T1, N1, M0
  - T2, N0, M0
  - or
  - Stage IIB
  - T2, N1, M0
  - T3, N0, M0
  - or
  - Stage IIA
  - T3, N1, M0

**WORKUP**

- History and physical exam
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review
- Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER2 status
- Genetic counseling if patient is high risk for hereditary breast cancer
- Breast MRI (optional)
- Consider fertility counseling if indicated

For clinical stage I-IB, consider additional studies only if directed by signs or symptoms:
- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvic diagnostic CT or MRI indicated if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, or abnormal physical examination of the abdomen or pelvis
- Chest diagnostic CT (if pulmonary symptoms present)

If clinical stage IIA (T3, N1, M0) consider:
- Chest diagnostic CT
- Abdominal ± pelvic diagnostic CT or MRI
- Bone scan or fluoride PET/CT (category 2B)
- FDG PET/CT (optional, category 2B)

See Locoregional Treatment (BINV-2)
Stage Determines Prognosis and Treatment

Pre-invasive/in situ stage 0.
Treatment goal=PREVENTION OF NEW CANCER.

Early stage (I-III).
Treatment goal=PREVENTION OF RECURRENCE.

Advanced/stage IV.
Treatment goal=MANAGING AS A CHRONIC ILLNESS, “buying time”, all while maintaining QOL.

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Stage 0

Local treatment is curative for vast majority of women

Excision +/- radiation

Further treatment is aimed at prevention
  Tamoxifen
  Exemestane
INVASIVE BREAST CANCER SUBTYPES

• Luminal A  
  ER+ and/or PR+, HER2-, low Ki67  40%

• Luminal B  
  ER+ and/or PR+, HER2+/-(high Ki67)  20%

• Triple Negative/Basal Type  
  ER-, PR-, HER2-  15-20%

• HER2 type  
  ER-, PR-, HER2+  10-15%
Evolution of the Shared Decision Making Process

- Historically: Benevolent Paternalism.
- Evolving Shift toward Individual Empowerment.
- Internet: Gives Patients the Impression they can manage their own Medical Affairs with Physicians as Consultants.
- Shared Decision Making approach: Healthier balance of power with Physicians being seen as having expertise and authority over matters of medical science, whereas patients hold sway over questions of values and preferences.
- Growing role of third parties

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The Stakeholders

1. PATIENT
2. Those who love the patient
3. Employer
4. Physician/healthcare system/PHARMA
5. Payers
6. Government

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GENERAL APPROACH TO ADJUVANT THERAPY

Early stage/low risk ER+/HER2- disease=hormonal therapy when possible

Locally advanced/high risk (large tumor/node+/"bad biology") ER+/HER2-
disease=chemotherapy +hormonal therapy

ER-/triple negative=chemotherapy

HER2+ disease=Herceptin (trastuzumab)/Perjeta (pertuzumab) based
chemotherapy+hormonal therapy when ER+
Treatment Decision Tools

- Historical data set, clinical trials, experience
- Tumor boards, institutional and virtual
- Academic, community and payer guidelines: (evidence based medicine…NCCN, USON)
- Risk Models
  - Adjuvant Online (population based)
  - Oncotype DX (“personalized medicine”)

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**Patient Information**

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<th>Age:</th>
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<td>ER Status:</td>
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<tr>
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<tr>
<td>Tumor Size:</td>
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<td>Relapse</td>
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<td>10 Year Risk:</td>
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**Adjuvant Therapy Effectiveness**

<table>
<thead>
<tr>
<th>Horm:</th>
<th>Aromatase Inhibitor for 5 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemo:</td>
<td>2nd Generation Regimens</td>
</tr>
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</table>

**No additional therapy:**
- 67.5 alive and without cancer in 10 years.
- 25.0 relapse.
- 7.5 die of other causes.

**With hormonal therapy:** Benefit = 12.5 without relapse.

**With chemotherapy:** Benefit = 6.5 without relapse.

**With combined therapy:** Benefit = 15.3 without relapse.

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“Personalized Medicine” – OncoType DX

The Recurrence Score reflects an individual’s unique tumor biology

- **Low Risk**
  - Group Average: 7%
  - 95% CI: 4%–20%

- **Intermediate Risk**
  - Group Average: 14%
  - 95% CI: 8%–29%

- **High Risk**
  - Group Average: 31%
  - 95% CI: 24%–37%

**High Recurrence Score disease:**
- Aggressive
- Less sensitive to hormone therapy
- Large chemotherapy benefit

**Low Recurrence Score disease:**
- Indolent
- Hormone therapy–sensitive
- Minimal, if any, chemotherapy benefit

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Treatment decisions**

37% changed

63% confirmed

*This analysis included 912 patients with node-negative, ER-positive early-stage invasive breast cancer.

†Patients with unclear treatment decisions were excluded from this meta-analysis. Additionally, patients who did not want CT, those with poor performance status, and those who could not tolerate CT were excluded.

‡CT=chemotherapy; HT=hormone therapy.
EXAMPLES: Patient # 1

- 70-year-old woman
- Screening mammogram: suspicious
- Biopsy: grade 2 ductal carcinoma
- Bilateral mastectomies (personal choice) (same year Christina Applegate declared “Cancer-Free After Double Mastectomy”)
  - 1.1 cm mass, poorly differentiated
  - 0/10 + nodes
  - ER + / PR +
  - HER 2 Neu not amplified

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Decision: No Additional Therapy

- 59 out of 100 women are alive and without cancer in 10 years.
- 30 out of 100 women relapse.
- 11 out of 100 women die of other causes.

Decision: Hormonal Therapy

- 10 out of 100 women are alive and without cancer because of therapy.

Decision: Chemotherapy

- 7 out of 100 women are alive and without cancer because of therapy.

Decision: Combined Therapy

- 15 out of 100 women are alive and without cancer because of therapy.
Recurrence Score = 37

Test Results should be interpreted using the Clinical Experience information contained in this report which is derived from clinical studies involving patient populations with specific clinical features as noted in each section of the Clinical Experience. It is unknown whether the findings summarized in the Clinical Experience are applicable to patients with features different from those described.

**CLINICAL EXPERIENCE: PROGNOSIS FOR NODE NEGATIVE, ER-POSITIVE PATIENTS**

The Clinical Validation study included female patients with Stage I or II, Node Negative, ER-Positive breast cancer treated with 5 years of tamoxifen. Those patients who had a Recurrence Score of 37 had an Average Rate of Distant Recurrence of 25% (96% CI: 18%-31%).

The following results are from a clinical validation study of 588 patients from the NSABP B-14 study, N Engl J Med 2004; 351: 2817-26.

**Recurrence Score vs Distant Recurrence in NODE NEGATIVE, ER-Positive Breast Cancer Prognosis**

- **Low Risk**
  - Group Average: 7%
  - 95% CI: 4%-10%

- **Intermediate Risk**
  - Group Average: 14%
  - 95% CI: 8%-20%

- **High Risk**
  - Group Average: 31%
  - 95% CI: 21%-37%

*for Recurrence Score > 30, group average rate of distant recurrence is 30% at 10 years of tamoxifen treatment.
Decision: Patient #1

- Adjuvant TC x 4
- Adjuvant Arimidex
- NED
Patient #2

- 52 woman, school counselor
- Two years of nipple thickening
- Biopsy: IDC
- Lumpectomy (9/2/2010)
  - 2.1 cm, well differentiated
  - 1/1 + (sentinel node)
  - ER + / PR +
  - HER 2 Neu not amplified
- Stage: IIIB (pT4b pN1c M0)
Decision: No Additional Therapy
- 58 out of 100 women are alive and without cancer in 10 years.
- 39 out of 100 women relapse.
- 3 out of 100 women die of other causes.

Decision: Hormonal Therapy
- 13 out of 100 women are alive and without cancer because of therapy.

Decision: Chemotherapy
- 18 out of 100 women are alive and without cancer because of therapy.

Decision: Combined Therapy
- 26 out of 100 women are alive and without cancer because of therapy.
RESULTS

**Breast Cancer Recurrence Score = 17**

The findings summarized in the Clinical Experience sections of this report are applicable to the patient populations defined in each section. It is unknown whether the findings apply to patients outside those criteria.

**Clinical Experience: Prognosis for Node Negative, ER-Positive Patients**

The Clinical Validation study included female patients with Stage I or II, Node Negative, ER-Positive breast cancer treated with 5 years of tamoxifen. Those patients who had a Recurrence Score of 17 had an Average Rate of Distant Recurrence of 11.9% (95% CI: 8.4%-15%).

The following results are from a clinical validation study of 663 patients from the NSABP B-14 study, N Engl J Med 2004; 351: 2017-25.

**Recurrence Score vs Distant Recurrence in Node Negative, ER-Positive Breast Cancer Prognosis**

- **Low Risk**
  - Group Average: 7%
  - CI: 3% - 11%
- **Intermediate Risk**
  - Group Average: 12%
  - CI: 8% - 16%
- **High Risk**
  - Group Average: 31%
  - CI: 24% - 37%

**Note:**
- The Recurrence Score is used to predict the risk of distant recurrence and can be used to guide treatment decisions.
- The CI represents the confidence interval for the estimated average rate of distant recurrence.

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Decision: Patient #2

- Elected not to receive adjuvant chemotherapy.
- Radiation therapy
- Tamoxifen
- NED
Principles of Therapy for Metastatic Breast Cancer

Goal is treatment as a chronic disease, prolongation of life while maintaining QOL (minimizing side effects, balancing benefits and risks) with patient as active participant

For non life threatening/non visceral ER+ metastatic disease, hormonal therapy is treatment of choice

For life threatening/visceral disease regardless of ER status, chemotherapy is usually indicated

For HER2+ metastatic disease:
First line-Herceptin (trastuzumab), Perjeta (pertuzumab), Taxotere
Second line-Kadcyla (ado-trastuzumab emtansine)

With thoughtful sequencing of treatments, many women will survive many years with GOOD QOL!
SURVEILLANCE

After the treating
I’m still following you
SURVIVORSHIP

For most patients, transitioning off of active treatment is a scary time!

Survivorship care plan

Acknowledge “new normal”

Greatest challenge faced by most survivors is finding balance between hypervigilence and delay in seeking care when new symptoms (not sure when to call/what’s “normal”?)

Most survivors prefer to be followed by their oncology provider for reassurance, new information, late side effects

Presenter: Robert J. Brooks, MD