MBC 101: Become Informed

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Oncology Medical Information Officer
Disclosures

I have received research funding from Pfizer.

I will note any unlabeled or non-FDA approved uses of drugs.
Who I am

- Medical oncologist in private practice in CA 1992-2009
- Joined Johns Hopkins 2009 – breast oncology, informatics/health IT
- Current interests/activities:
  - clinical care of breast cancer patients (Green Spring office)
  - electronic health records
  - consumer health informatics
  - healthcare-related social media (follow me on Twitter @rsm2800)
Tumor Initiation and Metastasis.

Tumor initiation: unlimited growth potential, survival, genomic instability
Genes: KRAS, BRAF, EGFR, HER2, PI3K (suppressors: APC, p53, PTEN, BRCA1, VHL1)

Metastasis initiation: invasion, marrow mobilization, angiogenesis, epithelial-to-mesenchymal transition
Genes: RHOC, LOX, VEGF, CSF-1, ID1, TWIST1, MET, FGFR, MMP-9, NEDD9

Metastasis progression: vascular remodeling, immune evasion, extravasation
Genes: EREG, COX-2, MMP-1, CCL5, ANGPTL4

Metastasis virulence: organ-specific functions
Genes: CXCR4, RANKL, CTGF, interleukin-11, endothelin-1

Case history

Kristin L is a 53 year old white female who had a lumpectomy in 2005 at age 47 for a 2.3 cm breast cancer with 3 positive nodes. The tumor was ER positive & HER2 negative.

She received chemotherapy x 20 wks with Adriamycin, Cytoxan, & Taxol (dose-dense AC-T). Following completion of chemo she had radiation x 6 weeks, then took tamoxifen through October 2010.
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Q: What type of tests should she be getting on a regular basis following treatment – scans, tumor markers, etc.?

A: Only breast imaging and physical exams.
Case history (cont.)

In July 2011 she began experiencing lower back pain, initially responsive to Aleve but then interfering with her ability to work out.
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Q: What type of symptoms should she be looking for?

A: Symptoms that are *progressive* and *anatomically persistent*. 
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She saw her oncologist who prescribed physical therapy. Her symptoms were no better after 3 weeks, so a bone scan was ordered. This showed multiple suspicious areas in the lumbar spine, ribs, and left femur. A CT of the chest/abd/pelvis showed 4 lesions in the liver, the largest 2.8 cm.
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Q: But she wasted 3 weeks doing physical therapy when it turned out she had metastatic breast cancer! Isn’t that harmful?

A: Probably no.
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She saw her oncologist who prescribed physical therapy. Her symptoms were no better after 3 weeks, so a bone scan was ordered. This showed multiple suspicious areas in the lumbar spine, ribs, and left femur. A CT of the chest/abdomen/pelvis showed 4 lesions in the liver, the largest 2.8 cm.

A biopsy of the largest liver lesion showed metastatic carcinoma compatible with a breast primary. ER was positive, and HER2 negative. CBC & chem panel were normal; CA 27.29 = 255. She was started on Arimidex and Zometa.
Initial workup for suspected metastatic breast cancer

- Staging studies – CT/bone scan/PET-CT
- Blood tests – CBC, chemistry panel (esp liver function tests), tumor markers CA27.29 (maybe)
- Biopsy (need to reassess ER/HER2 – 12% variance between primary site & mets)
- Assess for special sites of disease (bone, brain/spinal cord)
- Local recurrence only?
- Assess patient performance status (eg, ECOG)
- Define & individualize goals of treatment
Goals of therapy

- MBC = *treatable, although not curable*
- Palliate specific symptoms (eg, painful bone mets)
- Minimize treatment-related side effects
- Prolong life
- Help patient achieve specific personal goals
- Collaborate w/ patient, personalize therapy
Prognosis

“The median isn’t the message.”

--Stephen Jay Gould
“Providing patients with a single-point estimate of survival based on the median implies unwarranted precision and leaves little room for hope.”

--Kiely et al, JCO 2/1/11
Sites of First Distant Recurrence in Cases of Metastatic Triple-Negative Breast Cancer as Compared with Non–Triple-Negative Breast Cancer.

B  Hazard Rate for Distant Recurrence

Years after Diagnosis

Hazard Rate

Years after Diagnosis

0.30

0.25

0.20

0.15

0.10

0.05

0.00

0 1 2 3 4 5 6 7 8 9 10

Triple-negative breast cancers

Non-triple-negative breast cancers

Cumulative incidence curves of first distant metastasis by breast cancer subtype.

Kennecke H et al. JCO 2010;28:3271-3277

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Low vs. high risk MBC

**Low**

- Min/no symptoms
- Long disease-free interval
- No prior adjuvant therapy
- Bone/soft tissue predominance
- ER positive

**High**

- Symptomatic
- Shorter disease free interval
- Bone/liver/lung/brain mets
- ER negative
MBC Treatment Paradigm

- ER positive  ➔ hormonal therapy (at least 1%)
- HER2 positive ➔ Herceptin
- ER/HER2 neg ➔ chemotherapy
Hormonal Therapy

**Premenopausal**
- Tamoxifen
- Ovarian suppression
- AI + ovarian suppression
- Megace/Androgens

**Postmenopausal**
- AI
- Tamoxifen
- Faslodex
- Megace/Androgens

AI = aromatase inhibitor
Hormonal Therapy (cont.)

- First line hormonal therapy response rate 30-40%, overall clinical benefit (includes “stable” disease > 6 mos) 50-70%
- Can take > 3-4 mos to see response
- Lower response rate if HER2 pos
- Continue hormonal therapy as long as no progression; use sequential therapy (combination hormonal therapy no more effective)
HER2 positive

- Herceptin (IV) alone (not used much)
- Herceptin plus chemotherapy (e.g., Taxol, Taxotere*, Navelbine*, Xeloda*, etc.)
- 2nd line: Tykerb (lapatinib) oral + Xeloda
- 3rd line: Herceptin+Tykerb*, TDM-1 (experimental)

*non- FDA approved
Chemotherapy

- Sequential single agents preferred over combination regimens (Taxol, Taxotere, Abraxane, Doxil*, Xeloda, Gemzar, Navelbine*, Ixempra, Halaven)
- Response rates vary widely (usu ≤ 30%), depends on extent of prior therapy; complete responses very rare
- Role of Avastin (antibody to VEGF)

*non- FDA approved
Duration of chemotherapy for MBC

- *Continuous* (until disease progression or unacceptable toxicity) vs. *intermittent* (to maximal response then stop)
- No single correct or optimal answer
- Balancing benefits and toxicities – acute (e.g., fatigue, nausea) & chronic (e.g., neuropathy)
- Overall goal=palliation but patient wishes paramount
Progression-free survival.

<table>
<thead>
<tr>
<th>Study</th>
<th>HR + 95% CI</th>
<th>% Weight</th>
<th>HR</th>
<th>95% CI</th>
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<tr>
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<td>Gregory 1997</td>
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<td>0.31 to 0.68</td>
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<tr>
<td>Bastit 2000</td>
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<td>0.50 to 0.84</td>
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<tr>
<td>Nooij 2003</td>
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<td>0.50 to 0.90</td>
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<tr>
<td>Gennari 2006</td>
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<tr>
<td>Majordomo 2009</td>
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<td>0.57 to 1.05</td>
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<tr>
<td>Alba 2010</td>
<td>0.53</td>
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<td>0.37 to 0.76</td>
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<td><strong>Overall</strong></td>
<td><strong>0.64</strong></td>
<td><strong>100</strong></td>
<td><strong>0.55 to 0.76</strong></td>
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Test for heterogeneity, $P = .01$  
Test for treatment effect, $P < .001$

Gennari A et al. JCO 2011;29:2144-2149
Overall survival.

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<td>17</td>
<td>1.03</td>
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<td>7</td>
<td>0.94</td>
<td>0.67 to 1.32</td>
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<tr>
<td>Alba 2010</td>
<td></td>
<td>5</td>
<td>0.86</td>
<td>0.58 to 1.27</td>
</tr>
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**Overall**

- **Test for heterogeneity, \( P = .69 \)**
- **Test for treatment effect, \( P = .046 \)**

Gennari A et al. JCO 2011;29:2144-2149
Two special circumstances

• Bone metastases (Dr. Zellars) – role of bone-modifying agents (Zometa, Aredia, Xgeva), reduce “SRE’s” skeletal-related events

• Brain metastases (Dr. Hirose) – role of surgery, stereotactic radiosurgery, whole-brain radiation therapy
Thank you!

I am honored to speak with you today.

Follow me on Twitter @rsm2800.