Margaret Chen  MD, FACS  Assistant Professor of Clinical Surgery, Breast Surgery, Department of Surgery
Disclosure
(preceding 12 months)

Research grants:
  • Novian Health
  • Agendia

Consultant + speaker:
  • Global Health Pass
Overview

• Breast surgery
• Axillary surgery

Neoadjuvant chemotherapy
Breast cancer surgery evolution

2010’s: tailor surgery based on individualized risk of locoregional recurrence (LRR)
Two treatment approaches to reduce LRR

Neoadjuvant chemotherapy (NC) does not improve survival
Preoperative Chemotherapy in Patients With Operable Breast Cancer: Nine-Year Results From National Surgical Adjuvant Breast and Bowel Project B-18

Norman Wolmark, Jiping Wang, Eleftherios Mamounas, John Bryant, Bernard Fisher

- NC downstages the breast and axilla, allowing less surgery and less morbidity, without compromising LRR
- Tumors that show pathologic complete response (PCR) have better overall, disease free and relapse free survival. Thus, PCR is a surrogate endpoint for long term survival.
Invasive Breast Cancer

PREOPERATIVE SYSTEMIC THERAPY

Stage IIA
T2, N0, M0

Stage IIB
T2, N1, M0
T3, N0, M0

Stage IIIA
T3, N1, M0

Stage IIIB
T0, N2, M0
T1, N2, M0
T2, N2, M0
T3, N2, M0

Stage IIIC
Any T, N3, M0

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Clinically negative axillary lymph node(s) consider axillary imaging; suspicious nodes should be sampled by FNA or core biopsy prior to preoperative systemic therapy

Core biopsy with placement of image-detectable marker(s), if not previously performed, must be done to demarcate the tumor bed for post-chemotherapy surgical management

Clinically positive axillary lymph node(s) should be sampled by FNA or core biopsy prior to preoperative systemic therapy

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Paradoxically, increased PCR did not lead to fewer mastectomies

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Rates of pCR to NACT and BCS in randomized trials</th>
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<tbody>
<tr>
<td>Trial and treatment</td>
<td>pCR (%)</td>
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<tr>
<td><strong>NSABP B-27</strong>&lt;sup&gt;14&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>Doxorubicin and cyclophosphamide (4 cycles)</td>
<td>13.7</td>
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<tr>
<td>Doxorubicin and cyclophosphamide plus docetaxel (4 cycles)</td>
<td>26.1</td>
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<tr>
<td><strong>GeparQuinto GBG 44</strong>&lt;sup&gt;17&lt;/sup&gt; (HER2-positive disease)</td>
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<tr>
<td>Epirubicin, cyclophosphamide and docetaxel (4 cycles) plus trastuzumab</td>
<td>44.6</td>
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<tr>
<td>Epirubicin, cyclophosphamide and docetaxel (4 cycles) plus lapatinib</td>
<td>30.2</td>
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<tr>
<td><strong>CHER-LOB</strong>&lt;sup&gt;16&lt;/sup&gt;</td>
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<tr>
<td>Paclitaxel (12 cycles) plus trastuzumab, and FEC (4 cycles)</td>
<td>25</td>
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<tr>
<td>Paclitaxel (12 cycles) plus lapatinib, and FEC (4 cycles)</td>
<td>26</td>
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<tr>
<td>Paclitaxel (12 cycles) plus trastuzumab and lapatinib, and FEC (4 cycles)</td>
<td>47</td>
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<tr>
<td><strong>NeoALTTO</strong>&lt;sup&gt;15&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>Lapatinib plus paclitaxel (12 cycles)</td>
<td>24.7</td>
</tr>
<tr>
<td>Trastuzumab plus paclitaxel (12 cycles)</td>
<td>29.5</td>
</tr>
<tr>
<td>Lapatinib and trastuzumab plus paclitaxel (12 cycles)</td>
<td>51.3</td>
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</tbody>
</table>

Response and survival of breast cancer intrinsic subtypes following multi-agent neoadjuvant chemotherapy

Aleix Prat1,2,3*, Cheng Fan4, Aranzazu Fernández2,3, Katherine A. Hoadley4, Rossella Martinello2,3, Maria Vidal1, Margarita Viladot2,3, Estela Pineda2,3, Ana Arance2,3, Montserrat Muñoz2,3, Laia Paré2,3, Maggie C. U. Cheang5, Barbara Adamo2,3 and Charles M. Perou4,6,7

- Breast cancer molecular subtypes influence response to NC
- 957 patients were treated with neoadjuvant anthracycline and taxane/exabepilone. PCR rates differed among subtypes - luminal A (6%), luminal B (16%), HER2 (37%), basal (38%)
- Unifocal, high grade, ER-, HER2+, TN may achieve higher PCR and be eligible for lumpectomy
Gene Expression Profiles in Paraffin-Embedded Core Biopsy Tissue Predict Response to Chemotherapy in Women With Locally Advanced Breast Cancer

Luca Gianni, Milvia Zambetti, Kim Clark, Joffre Baker, Maureen Cronin, Jenny Wu, Gabriella Mariani, Jaime Rodriguez, Marialuisa Carcangiu, Drew Watson, Pinuccia Valagussa, Roman Rouzier, W. Fraser Symmans, Jeffrey S. Ross, Gabriel N. Hortobagyi, Lajos Pusztai, and Steven Shak
Identification of SNPs associated with response of breast cancer patients to neoadjuvant chemotherapy in the EORTC-10994 randomized phase III trial
V Le Morvan¹, S Litière¹, A Laroche-Clary¹, S Ait-ouferoukh¹, R Bellott¹, C Messina², D Cameron³, H Bonnefoi¹ and J Robert¹

• Efficacy of anticancer drugs is highly variable among individuals, in part due to every patient’s genetic features
• Single nucleotide polymorphisms in certain genotypes (CYP1B1, MDM2, MDM4, TP53BP1, ADH1C, R272Q) have been found to be associated with chemosensitivity, and can influence PCR
Agreement between MRI and pathologic breast tumor size after neoadjuvant chemotherapy, and comparison with alternative tests: individual patient data meta-analysis

Michael L. Marinovich, Petra Macaskill, Les Inwig, Francesco Sardanelli, Eleftherios Mamounas, Gunter von Minckwitz, Valentina Guarnieri, Savannah C. Partidge, Frances C. Wright, Jae Hyuck Choi, Madhumita Bhattacharyya, Laura Martinich, Eren Yeh, Viviana Londero and Nehmat Houssami

BMC Cancer (2015) 15:662
Impact of Preoperative Versus Postoperative Chemotherapy on the Extent and Number of Surgical Procedures in Patients Treated in Randomized Clinical Trials for Breast Cancer

Boughey, Judy C. MD; Peintinger, Florentia MD; Meric-Bernstam, Funda MD; Perry, Allison C. MS, PA-C; Hunt, Kelly K. MD; Babiera, Gildy V. MD; Singletary, S E. MD; Bedrosian, Isabelle MD; Lucci, Anthony MD; Buzdar, Aman U. MD; Pusztai, Lajos MD, PhD; Kuerer, Henry M. MD, PhD

• Extent of lumpectomy resection does not need to include the original breast tissue volume occupied by the tumor prior to NC
Surgical issues in patients with breast cancer receiving neoadjuvant chemotherapy

Tari A. King and Monica Morrow

• NSABP B18, using no ink on tumor, showed no higher LRR with lumpectomy post NC, compared with lumpectomy and adjuvant chemotherapy
• No ink on tumor is probably adequate margin
• Swiss chess pattern of tumor regression or multiple scattered tumor foci post NC increased LRR, and may warrant re-excision if close margin
Diagnosis of pathological complete response to neoadjuvant chemotherapy in breast cancer by minimal invasive biopsy techniques

Joerg Heil, Sherko Kümmel, Benedikt Schaefgen, Stefan Paepke, Christoph Thomssen, Geraldine Rauch, Beyhan Ataseven, Regina Große, Volker Dreesmann, Thorsten Kühn, Sibylle Loibl, Jens-Uwe Blohmer and Gunter von Minckwitz

- Tumors that show PCR could potentially require no surgery, but will require accurate diagnosis of PCR
- MRI is insufficient to detect residual, scattered tumor foci (median sensitivity 0.92, median specificity 0.6)
- 164 patients with clinical complete response had core needle biopsies at clip sites. NPV for PCR 71.3%, FNR 49.3%. Biopsy is inaccurate to predict PCR.
- Currently, surgery is obligatory for all patients to diagnose PCR and resect residual disease

Laser ablation to treat T1 breast cancer achieved complete ablation in 45/60 (75%) patients

Ongoing studies show PCR may be higher when combined with adjuvant therapies

Potential use post NC in future studies in place of surgery
Among women with cN1 breast cancer who received NC and had 2 or more SLNs examined, the FNR was 12.6% (90% BCI, 9.85%-16.05%) with SLN surgery

SLN surgery may be an alternative to ALND in this patient population
Alliance A11202: A Randomized Phase III Trial Evaluating The Role of Axillary Lymph Node Dissection in Breast Cancer Patients (cT1-3 N1) Who Have Positive Sentinel Lymph Node Disease After Neoadjuvant Chemotherapy

Bret Taback, MD, Site PI, Columbia University Medical Center
Pilot study utilizing master regulator analysis to prioritize treatment of residual disease following neoadjuvant chemotherapy for breast cancer in patient-derived tumor xenografts

Kevin Kalinsky MD, PI, Columbia University Medical Center
Conclusion

- Tailoring breast and axillary surgery may be feasible in neoadjuvant chemotherapy
- The opportunity to treat without surgery using ablation and targeted therapies will require precise imaging and clinical trials
Thank you