Conversations with Oncology Investigators
Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS
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OVERVIEW OF ACTIVITY
Breast cancer (BC) continues to be one of the most rapidly evolving fields in medical oncology. Results from numerous ongoing trials lead to the continual emergence of new therapeutic agents, treatment strategies and diagnostic and prognostic tools. In order to offer optimal patient care — including the option of clinical trial participation — the practicing cancer clinician must be well informed of these advances. Featuring information on the latest research developments along with expert perspectives, this CME activity is designed to assist medical oncologists, hematologist-oncologists and hematology-oncology fellows with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES
• Appraise available and emerging research evidence to individualize the selection and duration of neoadjuvant and adjuvant chemobiologic regimens for patients with HER2-overexpressing early BC.
• Develop an evidence-based algorithm for the treatment of advanced hormone receptor-positive BC, including the use of endocrine, biologic and chemotherapeutic agents.
• Recall the results of pivotal trials introducing effective new BC therapeutic agents, and identify their potential effect on existing treatment algorithms.
• Consider published data to guide the use of biomarkers and genomic assays to assess risk and individualize therapy for patients with hormone receptor-positive BC in the neoadjuvant, adjuvant and extended-adjuvant settings.
• Develop an understanding of the efficacy data and toxicity profiles of PARP inhibitors for patients with HER2-negative and BRCA-mutated advanced BC.
• Counsel appropriately selected patients with BC about participation in ongoing clinical trials.

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2.75 Medical Knowledge MOC points in the American Board of Internal Medicine’s (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider’s responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: medical oncology.

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**FACULTY** — Dr Burstein had no relevant conflicts of interest to disclose. The following faculty (and his spouse/partner) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

- **Dr Di Leo** — Advisory Committee: AstraZeneca Pharmaceuticals LP, Celgene Corporation, Daichi Sankyo Inc, Genomic Health Inc, Lilly, Novartis, Pfizer Inc, Roche Laboratories Inc; Consulting Agreements: Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Celgene Corporation, Eisai Inc, Genentech BioOncology, Genomic Health Inc, Lilly, Novartis, Pfizer Inc, Roche Laboratories Inc; Contracted Research: AstraZeneca Pharmaceuticals LP, Novartis, Pfizer Inc.


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| Track 1 | Case: A 57-year-old woman presents with ER-positive, PR-negative, HER2-positive metastatic breast cancer (mBC) |
| Track 2 | APHINITY: Results of a Phase III study evaluating the addition of pertuzumab to chemotherapy and trastuzumab as adjuvant therapy for patients with HER2-positive early BC |
| Track 3 | APT trial: Results after a 7-year follow-up of adjuvant paclitaxel and trastuzumab in patients with small, node-negative, HER2-positive BC |
| Track 4 | Postneoadjuvant therapy for patients with residual BC |
| Track 5 | CREATE-X: A Phase III study of adjuvant capecitabine for HER2-negative residual invasive disease after preoperative chemotherapy |
| Track 6 | Deescalating and escalating treatments for early-stage BC based on traditional risk factors |
| Track 7 | PALLAS Phase III trial of standard adjuvant endocrine therapy with or without palbociclib for ER-positive, HER2-negative early BC |
| Track 8 | Use of CDK4/6 inhibitors for patients with ER-positive, HER2-positive BC |
| Track 9 | Benefits of systemic chemotherapy with anti-HER2 therapy in ER-negative, HER2-positive BC |
| Track 10 | Results of the Phase III ExteNET study: Neratinib after trastuzumab-based adjuvant therapy for HER2-positive BC |
| Track 11 | Assessment of residual risk of recurrence in patients with HER2-positive BC after adjuvant therapy |
| Track 12 | Management of neratinib-associated gastrointestinal toxicity; risk-benefit ratio |
| Track 13 | Use of neratinib in HER2-positive BC with brain metastases |
| Track 14 | Delayed use of lapatinib in patients not receiving adjuvant trastuzumab |
| Track 15 | Case: A 56-year-old woman with an ER/PR-positive, HER2-negative, node-negative IDC and a 21-gene assay Recurrence Score® of 16 |
| Track 16 | Genomic assay selection in patients with ER-positive, HER2-negative disease |
| Track 17 | Case: A 63-year-old woman with heavily pretreated ER-positive mBC now considering CDK4/6 inhibitor therapy |
| Track 18 | Activity of CDK4/6 inhibitors alone or in combination with endocrine therapy for ER-positive mBC |
| Track 19 | Comparison of CDK4/6 inhibitors’ efficacy and tolerability |
| Track 20 | Potential role of biomarkers and treatment duration in CDK4/6 inhibitor therapy |
| Track 21 | Case: A 48-year-old woman with advanced-stage, poorly differentiated, triple-negative BC (TNBC) and a BRCA1 mutation receives olaparib on the Phase III OlympiAD trial |
| Track 22 | Activity and tolerability of olaparib |
| Track 23 | OlympiAD: Olaparib for patients with mBC and a germline BRCA mutation |
| Track 24 | Comparison of PARP inhibitors to standard chemotherapy for advanced BRCA-associated BC |
| Track 25 | Clinical experience with PARP inhibitors |
| Track 26 | Case: A 61-year-old woman with a history of early-stage BC presents with triple-negative neuroendocrine carcinoma within the breast |
| Track 27 | Systemic targeted therapy for neuroendocrine tumors with a lutetium radiolabeled agent |
Track 1  **Case:** A 57-year-old postmenopausal woman who received 5 years of adjuvant anastrozole presents with multiple lung metastases

Track 2  Use of adjuvant chemotherapy based on genomic risk assessment

Track 3  Activity of a CDK4/6 inhibitor alone or in combination with an aromatase inhibitor for patients with ER-positive mBC

Track 4  Similarities and differences among the side-effect profiles of CDK4/6 inhibitors

Track 5  Therapeutic options for patients with ER-positive mBC after disease progression on a CDK4/6 inhibitor

Track 6  Management of everolimus-associated mucositis and pneumonitis

Track 7  Ongoing trials investigating CDK4/6 inhibitors in the neoadjuvant and adjuvant settings

Track 8  **Case:** A 41-year-old premenopausal woman with progressive BRCA1 mutation-positive TNBC and multiple liver metastases

Track 9  Perspective on the use of bevacizumab for mTNBC

Track 10  Use of eribulin mesylate as late-line therapy for mBC

Track 11  OlympiAD: Results of a Phase III trial of olaparib monotherapy versus chemotherapy for patients with HER2-negative mBC and germline BRCA mutations

Track 12  Design limitations of the OlympiAD trial; sequencing of olaparib

Track 13  Tolerability of olaparib

Track 14  Effect of mBC diagnosis on family life and children

Track 15  **Case:** A 47-year-old premenopausal woman presents with an ER-negative, HER2-positive, node-positive Grade III IDC and vascular invasion

Track 16  Potential role of pertuzumab as a component of adjuvant therapy for patients with early-stage HER2-positive BC

Track 17  Estimating risk of recurrence in patients with BC

Track 18  Balancing magnitude of benefit and toxicity profiles of adjuvant pertuzumab and/or postadjuvant neratinib for early-stage HER2-positive BC

Track 19  **Case:** A 48-year-old premenopausal woman with an ER-positive, HER2-negative Grade II IDC and limited nodal involvement

Track 20  Comparison of available multigene assays

Track 21  Potential overestimation of disease relapse risk with genomic assays

Track 22  **Case:** A 55-year-old woman with ER-positive, node-positive BC receives CMF to avoid chemotherapy-related alopecia
SELECT PUBLICATIONS


Freedman R et al. TBCRC 022: Phase II trial of neratinib + capecitabine for patients (Pts) with human epidermal growth factor receptor 2 (HER2+) breast cancer brain metastases (BCBM). *Proc ASCO* 2017; Abstract 1005.


Tolaney S et al. Seven-year (yr) follow-up of adjuvant paclitaxel (T) and trastuzumab (H) (APT trial) for node-negative, HER2-positive breast cancer (BC). *Proc ASCO* 2017; Abstract 511.

1. Adding pertuzumab to adjuvant chemotherapy/trastuzumab in the Phase III APHINITY study reduced the relative risk of recurrence by about 20% for patients with node-positive or high-risk node-negative, HER2-positive early BC.
   a. True
   b. False

2. Results of the APT trial evaluating adjuvant paclitaxel/trastuzumab for node-negative, HER2-positive BC showed that the rate of distant recurrence after a 7-year follow-up analysis was approximately ___________.
   a. 1%
   b. 15%
   c. 50%

3. The Phase III CREATE-X trial demonstrated that the addition of adjuvant capecitabine after standard neoadjuvant chemotherapy elicited a benefit in terms of overall survival among patients with ___________ BC and residual invasive disease.
   a. HER2-positive
   b. HER2-negative

4. Which of the following groups derived a significant benefit from neratinib in the Phase III ExteNET study, which randomly assigned patients who received 1 year of adjuvant trastuzumab-based therapy to neratinib treatment or no further treatment?
   a. All patients with HER2-positive BC
   b. Patients with ER-positive, HER2-negative BC
   c. Patients with ER-negative, HER2-positive BC

5. The Phase III OlympiAD trial of olaparib monotherapy versus physician’s choice of chemotherapy for patients with HER2-negative mBC and a germline BRCA mutation demonstrated a statistically significant improvement in progression-free survival with olaparib.
   a. True
   b. False

6. In terms of treatment side effects, patients receiving abemaciclib may exhibit _________ neutropenia and __________ diarrhea compared to those undergoing treatment with palbociclib and ribociclib.
   a. Less, more
   b. Similar, similar
   c. Similar, more
   d. More, less

7. Treatment with which of the following CDK4/6 inhibitors requires patients to undergo EKG and liver function test monitoring?
   a. Abemaciclib
   b. Palbociclib
   c. Ribociclib
   d. All of the above

8. The CNS objective response rate for patients with HER2-positive BC brain metastases is increased approximately 5-fold for those who receive neratinib and capecitabine compared to neratinib alone.
   a. True
   b. False

9. In the OlympiAD trial for patients with HER2-negative, germline BRCA mutation-positive mBC, which of the following chemotherapies was not allowed as physician’s choice for comparison to olaparib?
   a. Capecitabine
   b. Vinorelbine
   c. Gemcitabine
   d. Carboplatin

10. At ESMO 2017, Cottu and colleagues presented a Phase II study demonstrating __________ activity with neoadjuvant letrozole and palbociclib versus chemotherapy for patients with luminal BC.
    a. Inferior
    b. Comparable
    c. Superior
EDUCATIONAL ASSESSMENT AND CREDIT FORM

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

**PART 1 — Please tell us about your experience with this educational activity**

How would you characterize your level of knowledge on the following topics?

<table>
<thead>
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<th>Topic</th>
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<td>evaluating olaparib versus chemotherapy for mBC with germline BRCA1/2 mutations</td>
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<td>of pertuzumab as a component of adjuvant therapy for patients with</td>
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<td>inhibitor into the clinical management of hormone receptor-positive,</td>
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<td>HER2-negative advanced BC</td>
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Practice Setting:
- [ ] Academic center/medical school
- [ ] Community cancer center/hospital
- [ ] Group practice
- [ ] Solo practice
- [ ] Government (eg, VA)
- [ ] Other (please specify): ...

Approximately how many new patients with breast cancer do you see per year? .................................... patients

Was the activity evidence based, fair, balanced and free from commercial bias?
- [ ] Yes
- [ ] No

If no, please explain: ..........................................................................................................................

Please identify how you will change your practice as a result of completing this activity (select all that apply).
- [ ] This activity validated my current practice
- [ ] Create/revise protocols, policies and/or procedures
- [ ] Change the management and/or treatment of my patients
- [ ] Other (please explain): ............................................................................................................

If you intend to implement any changes in your practice, please provide 1 or more examples:
..................................................................................................................................................................

The content of this activity matched my current (or potential) scope of practice.
- [ ] Yes
- [ ] No

If no, please explain: ..........................................................................................................................

Please respond to the following learning objectives (LOs) by circling the appropriate selection:

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<th>LO</th>
<th>4 = Yes</th>
<th>3 = Will consider</th>
<th>2 = No</th>
<th>1 = Already doing</th>
<th>N/M = LO not met</th>
<th>N/A = Not applicable</th>
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As a result of this activity, I will be able to:
- Appraise available and emerging research evidence to individualize the selection and duration of neoadjuvant and adjuvant chemobiologic regimens for patients with HER2-overexpressing early BC. ................................................. 4 3 2 1 N/M N/A
- Develop an evidence-based algorithm for the treatment of advanced hormone receptor-positive BC, including the use of endocrine, biologic and chemotherapeutic agents. ........................................ 4 3 2 1 N/M N/A
- Recall the results of pivotal trials introducing effective new BC therapeutic agents, and identify their potential effect on existing treatment algorithms. ........................................ 4 3 2 1 N/M N/A
As a result of this activity, I will be able to:

• Consider published data to guide the use of biomarkers and genomic assays to assess risk and individualize therapy for patients with hormone receptor-positive BC in the neoadjuvant, adjuvant and extended-adjuvant settings. ................................. 4 3 2 1 N/M N/A

• Develop an understanding of the efficacy data and toxicity profiles of PARP inhibitors for patients with HER2-negative and BRCA-mutated advanced BC. ................................. 4 3 2 1 N/M N/A

• Counsel appropriately selected patients with BC about participation in ongoing clinical trials. ................................................................. 4 3 2 1 N/M N/A

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:

Would you recommend this activity to a colleague?
☐ Yes ☐ No
If no, please explain: ........................................................................................................................................................................

PART 2 — Please tell us about the faculty and editor for this educational activity

<table>
<thead>
<tr>
<th>Faculty</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
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<tr>
<td>Harold J Burstein, MD, PhD</td>
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<td>Angelo Di Leo, MD, PhD</td>
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<td>Neil Love, MD</td>
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