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

FACULTY INTERVIEWS
Mark Robson, MD
Ian E Krop, MD, PhD

EDITOR
Neil Love, MD
OVERVIEW OF ACTIVITY
Breast cancer 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
• Implement a clinical plan for the management of metastatic HER2-positive breast cancer, incorporating existing and emerging targeted treatments.
• Develop an understanding of the efficacy data and toxicity profiles of PARP inhibitors for patients with HER2-negative and BRCA-mutated advanced breast cancer.
• Develop an evidence-based algorithm for the treatment of hormone-sensitive advanced breast cancer, including the use of endocrine, biologic and chemotherapeutic agents.
• Consider the use of available biomarkers and genomic assays to assess risk and individualize therapy for patients with breast cancer in the neoadjuvant and adjuvant settings.
• Recall the results of pivotal trials introducing effective new breast cancer therapeutic agents, and identify their potential effect on existing treatment algorithms.
• Counsel appropriately selected patients with breast cancer 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 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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This CME activity contains an audio component. To receive credit, the participant should review the CME information, listen to the audio tracks, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located in the back of this booklet or on our website at ResearchToPractice.com/BCU117/CME. The corresponding video program is available as an alternative at ResearchToPractice.com/BCU117/Video.

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CME INFORMATION

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process: Dr Robson — Advisory Committee, Consulting Agreement and Contracted Research: AstraZeneca Pharmaceuticals LP. Dr Krop — Advisory Committee: Genentech BioOncology, Roche Laboratories Inc, Seattle Genetics; Contracted Research: Roche Laboratories Inc.


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Track 1: Side effects associated with PARP inhibitors

Track 2: Efficacy of olaparib for patients with BRCA germline-mutant metastatic triple-negative breast cancer (mTNBC)

Track 3: OlympiAD: A Phase III trial of olaparib monotherapy versus chemotherapy for patients with HER2-negative metastatic breast cancer (mBC) and a germline BRCA mutation

Track 4: Somatic alterations in BRCA1/2 genes and response to PARP inhibitors

Track 5: BRCA testing for patients with BC

Track 6: Importance of genetic counseling for patients with germline mutations

Track 7: Clinical implications of the OlympiAD study results for patients with HER2-negative mBC

Track 8: TNT trial: Results of a Phase III study of carboplatin versus docetaxel for patients with metastatic or recurrent locally advanced triple-negative or BRCA1/2 mutation-associated BC

Track 9: Management of nausea and anemia associated with olaparib

Track 10: Case: A 49-year-old woman with BRCA-mutant mTNBC whose disease progresses through several lines of systemic therapy

Track 11: Mutational landscape of BC

Track 12: Ongoing trials of PARP inhibitors in the (neo)adjuvant setting

Track 13: 

Track 14: APHINITTY trial: 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 15: Adjuvant pertuzumab for patients with HER2-positive, node-positive mBC

Track 16: Case: A 65-year-old woman with ER-positive, HER2-negative mBC receives fulvestrant and palbociclib after disease relapse on exemestane

Track 17: Therapeutic options for patients with ER-positive, HER2-negative mBC after disease progression on a CDK4/6 inhibitor

Track 18: Targeting the androgen receptor in patients with mTNBC

Track 19: Case: A 54-year-old woman with bilateral ER/PR-positive, HER2-negative BC, 2 positive sentinel lymph nodes and a high genomic risk by the 70-gene assay

Track 20: Use of the 21-gene assay for patients with ER-positive, node-positive BC

Track 21: Case: A 49-year-old woman with BRCA mutation-positive mTNBC experiences rapid disease progression through several lines of therapy, including olaparib

Interview with Mark Robson, MD

Tracks 1-21

Track 1 Case: A 68-year-old woman with ER/PR-positive, HER2-negative, moderately differentiated IDC and 5 of 20 positive axillary nodes

Track 2 PALLAS: An ongoing Phase III trial evaluating the addition of palbociclib to adjuvant endocrine therapy for hormone receptor-positive, HER2-negative early BC

Track 3 Role of the 21-gene Recurrence Score® (RS) in the neoadjuvant setting

Track 4 Comparison of the 21-gene RS versus the 70-gene assay to determine benefit from chemotherapy in patients with ER-positive BC

Track 5 Updated ASCO clinical practice guidelines on the use of biomarkers to guide decisions on adjuvant systemic therapy for women with early-stage invasive BC

Track 6 MINDACT trial: Utility of the 70-gene assay in selecting patients with BC and 1 to 3 positive nodes for adjuvant chemotherapy

Interview with Ian E Krop, MD, PhD

Tracks 1-22

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Interview with Dr Krop (continued)

Track 7  **ABC trials: TC versus anthracycline/taxane-based chemotherapy for high-risk HER2-negative BC**

Track 8  **Role of anthracyclines in patients with HER2-positive BC**

Track 9  **Case: A 56-year-old woman with ER/PR-positive, HER2-negative invasive lobular BC and bone metastases**

Track 10  **Emergence of ESR1 mutations in patients with ER-positive mBC**

Track 11  **Clinical significance of ESR1 mutations in patients receiving fulvestrant for ER-positive mBC**

Track 12  **Detection of ESR mutations in the plasma of patients with ER-positive BC**

Track 13  **CDK4/6 inhibitors as first-line therapy for patients with ER-positive, HER2-negative mBC**

Track 14  **Efficacy and tolerability of CDK4/6 inhibitors for patients with ER-positive, HER2-negative mBC**

Track 15  **Activity and tolerability of abemaciclib**

Track 16  **Case: A 52-year-old woman with a Stage I, ER/PR-negative, HER2-positive, poorly differentiated IDC**

Track 17  **APT trial: Results after a 7-year follow-up of adjuvant paclitaxel/trastuzumab for lower-risk, HER2-positive BC**

Track 18  **Results of the APHINITY trial evaluating adjuvant pertuzumab**

Track 19  **ExteNET: Results of a Phase III trial investigating neratinib after trastuzumab-based adjuvant therapy for patients with HER2-positive BC**

Track 20  **ATEMPT: An ongoing Phase II trial evaluating T-DM1 versus trastuzumab/paclitaxel for Stage I, HER2-positive BC**

Track 21  **Efficacy of enzalutamide in BC**

Track 22  **Case: A 40-year-old woman with mTNBC and a BRCA1 mutation receives olaparib on the OlympiAD trial**

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**Video Program**

View the corresponding video interviews with (from left) Drs Robson and Krop by Dr Love at [www.ResearchToPractice.com/BCU117/Video](http://www.ResearchToPractice.com/BCU117/Video)

ALTERNate approaches for clinical stage II or III Estrogen Receptor positive breast cancer NeoAdjuvant TrEatment (ALTERNATE) in postmenopausal women: A phase III study (A011106). NCT01953588


Kuang Y et al. The emergence of ESR1 mutations is associated with aromatase inhibitor and fulvestrant therapy. Proc AACR 2017;Abstract 4950.

Love N et al. HER2 and estrogen receptor status drive decisions regarding the use of neoadjuvant chemotherapy. San Antonio Breast Cancer Symposium 2015;Abstract P1-14-20.

PALbociclib coLlaborative Adjuvant Study: A randomized phase III trial of palbociclib with standard adjuvant endocrine therapy versus standard adjuvant endocrine therapy alone for hormone receptor positive (HR+)/human epidermal growth factor receptor 2 (HER2)-negative early breast cancer (PALLAS). NCT02513394


Robson ME et al. OlympiAD: Phase III trial of olaparib monotherapy versus chemotherapy for patients (pts) with HER2-negative metastatic breast cancer (mBC) and a germline BRCA mutation (gBRCAm). Proc ASCO 2017;Abstract LBA4.


Sparano JA et al. Prospective trial of endocrine therapy alone in patients with estrogen receptor positive, HER2-negative, node-negative breast cancer: Results of the TAILORx low risk registry. San Antonio Breast Cancer Symposium 2015;Abstract P2-08-01.


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.

Von Minckwitz G et al. APHINITY trial (BIG 4-11): A randomized comparison of chemotherapy (C) plus trastuzumab (T) plus placebo (Pla) versus chemotherapy plus trastuzumab (T) plus pertuzumab (P) as adjuvant therapy in patients (pts) with HER2-positive early breast cancer (EBC). Proc ASCO 2017;Abstract LBA500.
QUESTIONS (PLEASE CIRCLE ANSWER):

1. The goal of the MINDACT trial, for which initial results were recently published, was to evaluate the benefit of genomic profiling with the ________ in addition to standard clinical-pathological criteria for identifying patients with early BC and 0 to 3 positive lymph nodes who might safely forgo chemotherapy without compromising outcome.
   a. PAM50 assay
   b. 70-gene signature
   c. 21-gene signature

2. The ongoing randomized Phase II ATEMPT trial is comparing ________ to trastuzumab/paclitaxel for patients with Stage I HER2-positive BC.
   a. Trastuzumab alone
   b. Trastuzumab emtansine (T-DM1)
   c. Pertuzumab/paclitaxel

3. The Phase III OlympiAD trial of olaparib monotherapy versus 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

4. Which of the following toxicities is exhibited to a greater extent in patients receiving abemaciclib than in those receiving palbociclib or ribociclib for ER-positive mBC?
   a. Diarrhea
   b. Neutropenia
   c. Myelosuppression
   d. All of the above

5. The Phase III ExteNET trial investigating neratinib versus placebo after trastuzumab-based adjuvant therapy for patients with HER2-positive BC ________ an invasive disease-free survival benefit with neratinib.
   a. Demonstrated
   b. Did not demonstrate

6. Which of the following drug types reflects the mechanism of action of fulvestrant?
   a. Selective estrogen receptor degrader
   b. Selective estrogen receptor modulator
   c. Both a and b
   d. Neither a nor b

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

8. Joint analysis of the ABC trials comparing a taxane with anthracycline to nonanthracycline-based regimens for HER2-negative, early BC demonstrated the benefit of anthracyclines in patients with ________ disease.
   a. Low-risk
   b. High-risk
   c. Both a and b

9. The Phase III TNT trial comparing carboplatin to docetaxel for mTNBC demonstrated that in a subgroup of patients with BRCA1/2 mutations, a significant difference was evident in ________ in favor of carboplatin.
   a. Overall response rate
   b. Progression-free survival
   c. Both a and b

10. Results of the Phase III APHINITY trial demonstrated that the addition of pertuzumab to trastuzumab and chemotherapy significantly improved invasive disease-free survival for patients with HER2-positive early BC.
    a. True
    b. False
EDUCATIONAL ASSESSMENT AND CREDIT FORM

Breast Cancer Update — Volume 16, Issue 1

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**

<table>
<thead>
<tr>
<th>How would you characterize your level of knowledge on the following topics?</th>
<th>BEFORE</th>
<th>AFTER</th>
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<tbody>
<tr>
<td>Olympic trial: Results of a Phase III trial evaluating olaparib versus chemotherapy for BRCA-mutant HER2-negative mBC</td>
<td>4 3 2 1</td>
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<td>Clinical implications of the Phase III APHINITY trial and the potential role of pertuzumab as a component of adjuvant therapy for patients with early-stage HER2-positive BC</td>
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<td>APT trial: Results after a 7-year follow-up of adjuvant paclitaxel/trastuzumab for node-negative, HER2-positive BC</td>
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<td>Updated ASCO guideline recommendation regarding the use of biomarkers to guide decisions on adjuvant systemic therapy for women with early-stage invasive BC</td>
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<td>Clinical significance of ESR1 mutations for patients with hormone receptor-positive mBC</td>
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**Practice Setting:**
- [ ] Academic center/medical school
- [x] 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?**
- [x] 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.**
- [x] Yes
- [ ] No
  - If no, please explain: .................................................................

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

<table>
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<tr>
<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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<td>As a result of this activity, I will be able to:</td>
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<td>- Implement a clinical plan for the management of metastatic HER2-positive breast cancer, incorporating existing and emerging targeted treatments.</td>
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<td>- Develop an understanding of the efficacy data and toxicity profiles of PARP inhibitors for patients with HER2-negative and BRCA-mutated advanced breast cancer.</td>
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<td>- Develop an evidence-based algorithm for the treatment of hormone-sensitive advanced breast cancer, including the use of endocrine, biologic and chemotherapeutic agents.</td>
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As a result of this activity, I will be able to:

• Consider the use of available biomarkers and genomic assays to assess risk and individualize therapy for patients with breast cancer in the neoadjuvant and adjuvant settings. ........................................................ 4 3 2 1 N/M N/A
• Recall the results of pivotal trials introducing effective new breast cancer therapeutic agents, and identify their potential effect on existing treatment algorithms. ........... 4 3 2 1 N/M N/A
• Counsel appropriately selected patients with breast cancer 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

4 = Excellent  3 = Good  2 = Adequate  1 = Suboptimal

<table>
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<tr>
<th>Faculty</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
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<td>Mark Robson, MD</td>
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<td>Ian E Krop, MD, PhD</td>
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<th>Editor</th>
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<td>Neil Love, MD</td>
<td>4 3 2 1</td>
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REQUEST FOR CREDIT — Please print clearly

Name: ...............................................................  Specialty: ...........................................
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I certify my actual time spent to complete this educational activity to be _________ hour(s).

Signature: .........................................................................  Date: ..............................

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