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Consensus or Controversy?

Clinical Investigators Provide Their Perspectives on Practical Issues and Research Questions in the Management of Breast Cancer

Saturday, June 4, 2011
7:00 PM – 9:00 PM
Chicago, Illinois

Moderator

Neil Love, MD

Faculty

Robert W Carlson, MD
John Crown, MD
Charles E Geyer Jr, MD
Joyce O'Shaughnessy, MD
Mark D Pegram, MD
Martine J Piccart-Gebhart, MD, PhD
Michael Untch, MD, PhD
Eric P Winer, MD

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MODULE 1

HER2-Positive Early-Stage Disease

What is your most common adjuvant treatment recommendation for a patient with ER-negative, HER2-positive early breast cancer and multiple positive nodes?

	Younger patient	85-year-old patient
 ROBERT W CARLSON, MD	AC → TH	None
 JOHN CROWN, MD	TCH	None or TCH
 CHARLES E GEYER JR, MD	AC → wkly TH	Wkly T x 4 + H or Wkly T/carbo x 4/H
 JOYCE O'SHAUGHNESSY, MD	AC → wkly TH	Wkly T/carbo/H
 MARK D PEGRAM, MD	AC → TH or TCH	Wkly T x 12 + H
 MARTINE J PICCART-GEBHART, MD, PHD	FEC100 → taxane/H	Taxane/H x 9 wks → FEC (FinHER)*
 MICHAEL UNTCH, MD, PHD	EC → wkly TH	Wkly TH
 ERIC P WINER, MD	AC → TH	TH

H = trastuzumab

* With the exception of FinHER, all other regimens use trastuzumab to completion of 1 year.

What is your most common adjuvant treatment recommendation for a patient with a small (5 mm) ER-negative, HER2-positive, node-negative breast tumor?

	Younger patient	85-year-old patient
 ROBERT W CARLSON, MD	AC → TH	None
 JOHN CROWN, MD	TCH	None
 CHARLES E GEYER JR, MD	TC x 4 + H	None
 JOYCE O'SHAUGHNESSY, MD	TCH	Wkly TH
 MARK D PEGRAM, MD	None or TCH	None or H mono
 MARTINE J PICCART-GEBHART, MD, PHD	FEC100 → taxane/H	None
 MICHAEL UNTCH, MD, PHD	EC → wkly TH	Wkly TH
 ERIC P WINER, MD	TH	None

What is your most common neoadjuvant treatment for younger patients with locally advanced ER-negative, HER2-positive breast cancer?

	Preferred neoadjuvant Rx?	Do you use trastuzumab/ lapatinib + chemo?
 ROBERT W CARLSON, MD	Wkly TH → FEC/H	No
 JOHN CROWN, MD	TCH	Not used, but would
 CHARLES E GEYER JR, MD	AC → wkly TH	Not used, but would
 JOYCE O'SHAUGHNESSY, MD	TH → FEC/H	Yes
 MARK D PEGRAM, MD	TCH	No
 MARTINE J PICCART-GEBHART, MD, PHD	FEC100 → taxane/H	No
 MICHAEL UNTCH, MD, PHD	EC → wkly TH	Not used, but would
 ERIC P WINER, MD	TH → AC	No

Ongoing Adjuvant Trials of Chemotherapy with Biologic Agents in HER2-Positive Breast Cancer

- **BETH** Chemotherapy + H → H
  or Chemotherapy + H + bev → H + bev
- **ALTTO** Chemotherapy (concurrent or sequential) + L alone *or* H alone *or* H → L *or* L + H
- **Dana Farber** Paclitaxel + H (node-negative)

www.ClinicalTrials.gov, June 2011.

Trials of Adjuvant Biologic Agents for HER2-Positive Breast Cancer

- **ExteNET*** Neratinib after trastuzumab
- **NCT00796978†** Trastuzumab alone (≥65 yo)
- **TEACH** Delayed lapatinib

*Goss PE et al. Proc ASCO 2011;Abstract TPS137. Monday, June 6, 8:00 am - 12:00 pm
†Owusu C et al. *Proc ASCO* 2011;Abstract TPS109. Monday, June 6, 8:00 am - 12:00 pm
www.ClinicalTrials.gov, June 2011.

Locoregional and Distant Relapse in Node-Negative Breast Cancer (≤1 cm)

Immunohistochemical subtype	HR
Luminal A (ER/PR+, HER2-neg)	1.00
Luminal B (ER/PR+, HER2-neg)	1.49
Luminal B (ER/PR+, HER2 +++)	3.12
HER2+++ (ER-/PR-)	**5.27**
Triple-negative	3.05

Cancello G et al. *Breast Cancer Res Treat* 2011;127:713-20.

TBCRC 006: Phase II Study of Neoadjuvant Lapatinib and Trastuzumab for HER2-Positive Breast Cancer (n = 66)

pCR: overall	28%
pCR: ER-positive	21%
pCR: ER-negative	42%

Chang JCN et al. *Proc ASCO* 2011;Abstract 505. Oral Session Sunday, June 5, 9:00 AM to 12:00 PM

GEPARQUINTO[1]

- Trastuzumab/EC-docetaxel: 50.4%
- Lapatinib/EC-docetaxel: 35.2%

NeoSphere[2]

- Docetaxel/trastuzumab/pertuzumab: 45.8%
- Docetaxel/trastuzumab: 29.0%
- Docetaxel/pertuzumab: 24.0%
- Trastuzumab/pertuzumab: 16.8%

NeoALTTO[3]

- Paclitaxel/trastuzumab/lapatinib: 51.3%
- Paclitaxel/trastuzumab: 29.5%
- Paclitaxel/lapitinib: 24.7%

[1]Untch M et al. *Proc SABCS* 2011;Abstract S3-1. [2]Gianni L et al. *Proc SABCS* 2010; Abstract S3-2. [3]Baselga J et al. *Proc SABCS* 2010;Abstract S3-3.

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MODULE 2

Special Issues in Early Breast Cancer

Do you offer zoledronic acid (or another bisphosphonate) as a component of adjuvant therapy to a woman with normal bone health?

	Do you use adjuvant bisphosphonates?	Has your practice changed since SABCS 2010?
 ROBERT W CARLSON, MD	No	No
 JOHN CROWN, MD	No	No
 CHARLES E GEYER JR, MD	No	No
 JOYCE O'SHAUGHNESSY, MD	No	No
 MARK D PEGRAM, MD	No	Yes
 MARTINE J PICCART-GEBHART, MD, PHD	Yes, per ABCSG-12	No
 MICHAEL UNTCH, MD, PHD	No	Yes
 ERIC P WINER, MD	Generally, no	Yes

Do you believe a complete axillary dissection may be avoided in patients with a positive sentinel lymph node biopsy?

	SLNB+, Avoid ALND?	Do you use genomic profiling in the decision re ALND?
 ROBERT W CARLSON, MD	Yes, Z-11 criteria	No
 JOHN CROWN, MD	Yes	No
 CHARLES E GEYER JR, MD	Yes, Z-11 criteria	No
 JOYCE O'SHAUGHNESSY, MD	Yes, Z-11 criteria	No
 MARK D PEGRAM, MD	Yes, Z-11 criteria	No
 MARTINE J PICCART-GEBHART, MD, PHD	Yes, select pts	No, but may be useful
 MICHAEL UNTCH, MD, PHD	Yes, select pts	No
 ERIC P WINER, MD	Yes, based on Z-11	No

AZURE: Adjuvant Zoledronic Acid versus Control in Stage II/III BC

Patient subset	Reduction in recurrence
Overall	2% (HR = 0.98)
Postmenopausal subset	24% (HR = 0.76)

Coleman RE et al. *Proc SABCS* 2010;Abstract S4-5.

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Overall Survival with Adjuvant Zoledronic Acid in Patients with Premenopausal Breast Cancer with Complete Endocrine Blockade: Long-Term Results from ABCSG-12

Gnant M et al.

Proc ASCO 2011;Abstract 520.

Poster Discussion, Tuesday, June 7, 11:30 AM – 12:30 PM

Key Maturing Trials of Adjuvant Bisphosphonates

- **NSABP-B34** — Clodronate *vs* placebo
- **SWOG-S0307** — Zoledronate *vs* clodronate *vs* ibandronate

www.ClinicalTrials.gov, June 2011.

Outcomes of ALND versus Not in 891 Patients with Positive SLNB (ACOSOG-Z0011)

5-yr in-breast recurrence*	3.7% *vs* 2.1% ($p = 0.16$)
5-yr nodal recurrence*	0.6% *vs* 1.3% ($p = 0.44$)
5-yr overall survival rate†	91.8% *vs* 92.5%

*Giuliano AE et al. *Proc ASCO* 2010;Abstract CRA506.
†Giuliano AE et al. *JAMA* 2011;305:569-75.

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MODULE 3

Genomic Predictors of Response to Adjuvant Chemotherapy

Would you offer/recommend a multigene assay (MammaPrint® or Oncotype DX®) for a patient with a node-positive tumor?

 ROBERT W CARLSON, MD	No
 JOHN CROWN, MD	No
 CHARLES E GEYER JR, MD	Generally no, but could be useful
 JOYCE O'SHAUGHNESSY, MD	Yes
 MARK D PEGRAM, MD	Yes
 MARTINE J PICCART-GEBHART, MD, PHD	Yes
 MICHAEL UNTCH, MD, PHD	No
 ERIC P WINER, MD	Yes, occasionally

Does the Onco*type* DX Recurrence Score® (RS) impact your selection of a particular chemotherapy regimen?

 ROBERT W CARLSON, MD	No
 JOHN CROWN, MD	No
 CHARLES E GEYER JR, MD	No
 JOYCE O'SHAUGHNESSY, MD	No
 MARK D PEGRAM, MD	No
 MARTINE J PICCART-GEBHART, MD, PHD	No
 MICHAEL UNTCH, MD, PHD	No, not off protocol
 ERIC P WINER, MD	No

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Meta-Analysis of the Decision Impact of the 21-Gene Breast Cancer Recurrence Score in Clinical Practice

Hornberger J and Chien R.

SABCS 2010;Abstract P2-09-06. (Poster)

Meta-Analysis of the Decision Impact of the 21-Gene Breast Cancer Recurrence Score (RS) in Clinical Practice

Rx plan before RS	Rx plan after RS	N = 912 (%)
Chemo	Chemo	271 (30%)
No chemo	No chemo	303 (33%)
No chemo	Chemo	41 (4%)
Chemo	No chemo	297 (33%)

37%

Hornberger J, Chien R. *Proc SABCS* 2010;Abstract P2-09-06 (Poster).

60 yo woman: 1.0-cm sentinel node-negative, ER-positive, HER2-negative IDC. Which adjuvant chemotherapy treatment would you recommend?

	Anthra → taxane	TC	AC	Other	None
Would order Oncotype DX (n = 82)					
High RS	30%	60%	6%	4%	0
Intermediate RS	7%	62%	4%	1%	26%
Low RS	0	4%	0	3%	93%
Would not order Oncotype DX (n = 18)	0	6%	0	6%	88%

Patterns of Care in Breast Cancer, Research To Practice 2010.

75 yo woman: 1.0-cm sentinel node-negative, ER-positive, HER2-negative IDC. Which adjuvant chemotherapy treatment would you recommend?

	Anthra → taxane	TC	AC	Other	None
Would order Oncotype DX (n = 46)					
High RS	22%	63%	11%	2%	2%
Intermediate RS	3%	37%	4%	4%	52%
Low RS	0	4%	0	2%	94%
Would not order Oncotype DX (n = 54)	0	11%	0	4%	85%

Patterns of Care in Breast Cancer, Research To Practice 2010.

Oncotype DX in Node-Positive BC: Retrospective Analysis of SWOG-8814

DFS benefit of CAF ➔ tamoxifen vs tamoxifen alone	
Recurrence Score	**DFS hazard ratio**
10	0.95
18	0.83
25	0.74
31	0.67
40	0.57

Albain K et al. *Lancet Oncol* 2010;11:55-65.

Recurrence Score-Pathology-Clinical (RSPC)

- Developed to augment decision-making with RS
- RSPC components:
  - RS
  - Tumor grade
  - Pathologic tumor size
  - Patient age at surgery

Tang G et al. *Proc SABCS* 2010;Abstract S4-9 and *Proc ASCO* 2010;Abstract 509.

SWOG-S1007 (RxPONDER): Invasive Breast Cancer and Recurrence Score (RS) ≤25

- ER- and/or PR-positive, HER2-negative invasive BC, 1-3 positive nodes
- Randomization:
  - Chemo + endocrine therapy
  - Endocrine therapy alone
- Primary endpoint: Invasive DFS
- Target enrollment: 4,000

www.Clinicaltrials.gov, June 2011.
Gonzalez-Angulo AM et al. *Proc ASCO* 2011;Abstract TPS104. Poster Session, Monday, June 6, 8:00 AM to 12:00 PM

MODULE 4

Triple-Negative and/or BRCA Mutation-Positive Breast Cancer

What is your usual preferred first-line systemic approach to a younger patient with metastatic, symptomatic triple-negative breast cancer (TNBC) with a known BRCA mutation and without?

	TNBC + BRCA+	TNBC + BRCA-
 ROBERT W CARLSON, MD	Carbo/gem or carbo/paclitaxel	Carbo/gem or carbo/paclitaxel
 JOHN CROWN, MD	Wkly paclitaxel	Wkly paclitaxel
 CHARLES E GEYER JR, MD	Wkly paclitaxel + carbo/bevacizumab	Wkly paclitaxel + bevacizumab
 JOYCE O'SHAUGHNESSY, MD	Carbo/gem	Paclitaxel or *nab* paclitaxel + bevacizumab
 MARK D PEGRAM, MD	Combo chemo or taxane/bevacizumab	Combo chemo or taxane/bevacizumab
 MARTINE J PICCART-GEBHART, MD, PHD	Docetaxel or wkly paclitaxel (± cape or gem)	Docetaxel or wkly paclitaxel (± cape or gem)
 MICHAEL UNTCH, MD, PHD	TAC or EC → wkly paclitaxel	Cisplatin-containing
 ERIC P WINER, MD	Taxane ± bevacizumab	Taxane ± platinum ± bevacizumab

What is your most common adjuvant treatment recommendation for a patient with TNBC and multiple positive nodes?

	Younger patient	85-year-old patient
 ROBERT W CARLSON, MD	dd AC → paclitaxel or dd AC → wkly paclitaxel	None or CMF or AC
 JOHN CROWN, MD	TC	None or TC x 4
 CHARLES E GEYER JR, MD	dd AC → paclitaxel or dd AC → wkly paclitaxel	Wkly paclitaxel x 9 → CMF x 3-4
 JOYCE O'SHAUGHNESSY, MD	dd AC → paclitaxel or dd AC → wkly paclitaxel	CMF → wkly paclitaxel
 MARK D PEGRAM, MD	TAC or dd AC → paclitaxel or AC → wkly paclitaxel	None, CMF or TC + G-CSF
 MARTINE J PICCART-GEBHART, MD, PHD	FEC → taxane or dd EC → wkly or q2wkly paclitaxel	EC75 x 4 or CMF x 3
 MICHAEL UNTCH, MD, PHD	TAC	EC → wkly paclitaxel
 ERIC P WINER, MD	AC → wkly or q2wkly paclitaxel	TC, AC, CMF or none

What is your most common neoadjuvant treatment recommendation for a younger patient with locally advanced TNBC?

 ROBERT W CARLSON, MD	CAF → wkly paclitaxel
 JOHN CROWN, MD	TC
 CHARLES E GEYER JR, MD	dd AC → wkly paclitaxel + carboplatin
 JOYCE O'SHAUGHNESSY, MD	dd AC → paclitaxel
 MARK D PEGRAM, MD	Cisplatin/taxane or AC → T
 MARTINE J PICCART-GEBHART, MD, PHD	FEC → taxane or dd EC → taxane
 MICHAEL UNTCH, MD, PHD	TAC
 ERIC P WINER, MD	AC → wkly or q2wkly paclitaxel

Phase III Trial of Iniparib (I) plus Gemcitabine (G)/ Carboplatin (C) in Metastatic TNBC

	GC n = 258	GCI n = 261	HR	*p*-value
Median OS, months	11.1	11.8	0.876	0.284
Median PFS, months	4.1	5.1	0.794	0.027

O'Shaughnessy J et al. *Proc ASCO* 2011;Abstract 1007. Oral Session Monday, June 6, 9:30 AM to 12:30 PM

Preclinical Pharmacodynamic and Pathway Analysis of Three Presumed Inhibitors of Poly (ADP-ribose) Polymerase: ABT-888, AZD2281 and BSI-201

- ABT-888 and AZD2281 are mediated by PARP1 or PARP2.
- Iniparib (BSI-201) suppressed genes in the telomere pathway, suggesting PARP5/6 as potential targets.

Ji J et al. *Proc AACR* 2011;Abstract 4527.

GEPARQUINTO: pCR Benefit of Neoadjuvant Chemo plus Bevacizumab in TNBC Subset of Patients

Patient population	pCR		
	EC-doc	EC-doc + bev	*p*-value
Overall (n = 968; 959)*	15%	17.5%	NS
TNBC subset (n = 345; 339)†	27.8%	36.4%	0.021

NS = not significant

*von Minckwitz G et al. *Proc SABCS* 2011;Abstract S4-6.

†Gerber B et al. *Proc ASCO* 2011;Abstract 1006. Oral Session Monday, June 6, 9:30 AM to 12:30 PM

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The Effect on pCR of Bevacizumab and/or Antimetabolites Added to Standard Neoadjuvant Chemotherapy: NSABP Protocol B-40

Bear HD et al.

Proc ASCO 2011;Abstract LBA1005.

Oral Session Monday, June 6, 9:30 AM – 12:30 PM

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Comparison of Subgroup Analyses of PFS from Three Phase III Studies of Bevacizumab in Combination with Chemotherapy in Patients with HER2-Negative Metastatic Breast Cancer

O'Shaughnessy J et al.
Proc SABCS 2009;Abstract 207. (Poster)

Improvement in PFS with Addition of Bevacizumab (B) in E2100, AVADO and RIBBON 1

Patient subgroup	Improvement in PFS, months		
	E2100 (n = 722)	AVADO* (n = 736)	RIBBON 1† (n = 1,237)
Overall	5.5 mos	0.8 mos 0.9 mos	2.9 mos 1.2 mos
Hormone receptor-positive	4.7 mos	1.1 mos 1.9 mos	3.0 mos 2.1 mos
Triple-negative	5.3 mos	0.8 mos 2.8 mos	1.9 mos 0.3 mos

*B 7.5 mg/kg, 15 mg/kg

† Capecitabine/B; taxane/anthracycline/B

O'Shaughnessy J et al. *Proc SABCS* 2009;Abstract 207.

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MODULE 5

Integration of Novel Agents into the Metastatic Setting

Should survival be the primary endpoint in trials evaluating systemic treatment for metastatic breast cancer (mBC)?

 ROBERT W CARLSON, MD	Yes
 JOHN CROWN, MD	No
 CHARLES E GEYER JR, MD	No
 JOYCE O'SHAUGHNESSY, MD	No
 MARK D PEGRAM, MD	Probably, yes
 MARTINE J PICCART-GEBHART, MD, PHD	No
 MICHAEL UNTCH, MD, PHD	No
 ERIC P WINER, MD	Not the only endpoint

Do you or would you like to be able to use ixabepilone in mBC?

	Ixabepilone?	Do you combine a biologic with ixabepilone?
 ROBERT W CARLSON, MD	Yes	No
 JOHN CROWN, MD	Yes	No
 CHARLES E GEYER JR, MD	Yes	Trastuzumab
 JOYCE O'SHAUGHNESSY, MD	Yes	Trastuzumab
 MARK D PEGRAM, MD	Yes	Trastuzumab
 MARTINE J PICCART-GEBHART, MD, PHD	No	—
 MICHAEL UNTCH, MD, PHD	No	—
 ERIC P WINER, MD	No	—

Do you or would you like to be able to use eribulin in mBC?

	Eribulin?	Do you combine a biologic with eribulin?
 ROBERT W CARLSON, MD	Yes	Trastuzumab
 JOHN CROWN, MD	Yes	No
 CHARLES E GEYER JR, MD	Yes	Trastuzumab
 JOYCE O'SHAUGHNESSY, MD	Yes	Trastuzumab
 MARK D PEGRAM, MD	Yes	Trastuzumab
 MARTINE J PICCART-GEBHART, MD, PHD	Yes	Trastuzumab
 MICHAEL UNTCH, MD, PHD	Yes	No
 ERIC P WINER, MD	Yes	Generally, no

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Relationship between OS and PFS in Metastatic Breast Cancer (MBC): Review of FDA Submission Data

Cortazar P et al.

Proc ASCO 2011;Abstract 1035.

(Poster Discussion, Saturday, June 4, 2 PM – 6 PM)

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Randomized Controlled Trials (RCTs) in the Era of Molecular Oncology: Methodology, Biomarkers and Endpoints

Kay A et al.

Proc ASCO 2011;Abstract 6049.

(Poster Session, Saturday, June 4, 8 AM – 12 PM)

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Calibrating Clinically Significant Effects in Survival and Response Endpoints in Cancer Clinical Trials

Dueck AC et al.
Proc ASCO 2011;Abstract 6130.
(Poster Session, Saturday, June 4, 8 AM – 12 PM)

Ixabepilone plus Capecitabine in Metastatic Breast Cancer Patients with Reduced Performance Status Previously Treated with Anthracyclines and Taxanes: A Pooled Analysis by Performance Status of Efficacy and Safety Data from 2 Phase III Studies

Roche H et al.

Breast Cancer Res Treat 2011;125(3):755-65.

A Phase II Trial of Trastuzumab plus Weekly Ixabepilone and Carboplatin in Patients with HER2-Positive Metastatic Breast Cancer: An Eastern Cooperative Oncology Group Trial

Moulder S et al.

Breast Cancer Res Treat 2010;119(3):663-71.

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Eribulin Monotherapy versus Treatment of Physician's Choice in Patients with Metastatic Breast Cancer (EMBRACE): A Phase 3 Open-Label Randomised Study

Cortes J et al.

Lancet 2011;377(9769):914-23.

EMBRACE Trial

- 762 women with locally recurrent or metastatic breast cancer
- 2-5 prior chemo regimens, including anthracycline and taxane
- Phase III: Eribulin vs treatment of physician's choice (vinorelbine, gemcitabine, capecitabine, taxanes, anthracyclines or other chemotherapy)

Cortes J et al. *Lancet* 2011;377(9769):914-23.

EMBRACE Trial: Efficacy

- Median OS = 13.1 vs 10.6 mos (HR = 0.81, *p* = 0.041)
- Median PFS = 3.6 vs 2.2 mos (HR = 0.76, *p* = 0.002)
- Objective response rate = 13% vs 7% (*p* = 0.028)
- Clinical benefit rate = 28% vs 20%

Cortes J et al. *Lancet* 2011;377(9769):914-23.

EMBRACE Trial: Toxicity

	Eribulin		TPC	
	All grades	Grade 3/4	All grades	Grade 3/4
Neutropenia	52%	45%	30%	21%
Anemia	19%	3%	23%	4%
Asthenia/fatigue	54%	9%	40%	10%
Peripheral neuropathy	35%	9%	16%	2%

Cortes J et al. *Lancet* 2011;377(9769):914-23.

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Comparison of Neuropathy-Inducing Effects of Eribulin Mesylate, Paclitaxel and Ixabepilone in Mice

Wozniak KM et al.
Cancer Res 2011 May 24;[Epub ahead of print].

"Overall, our findings indicate that eribulin mesylate induces less neuropathy in mice than paclitaxel or ixabepilone at equivalent MTD-based doses."

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The Relationship between Age and Survival Outcomes for Eribulin in Metastatic Breast Cancer

Twelves C et al.
Proc ASCO 2011;Abstract 1060.
(Poster Session, Monday, June 6, 1 PM – 5 PM)

Survival and PFS with Eribulin According to Age: EMBRACE Analysis

	ITT population		
Age at recruitment	N	OS (mos)	PFS (mos)
<50	161	11.8	3.5
50-59	174	13.6	3.7
60-69	129	13.8	3.8
≥70	44	14.2	4.2

Twelves C et al. *Proc ASCO* 2011;Abstract 1060.

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MODULE 6

HER2-Positive Advanced Disease

Should patients with HER2-positive metastatic disease generally be continued on some type of anti-HER2 therapy indefinitely?

 ROBERT W CARLSON, MD	Yes
 JOHN CROWN, MD	No, but prolonged
 CHARLES E GEYER JR, MD	Yes
 JOYCE O'SHAUGHNESSY, MD	Yes
 MARK D PEGRAM, MD	Probably, yes
 MARTINE J PICCART-GEBHART, MD, PHD	Yes
 MICHAEL UNTCH, MD, PHD	Yes
 ERIC P WINER, MD	Yes

Would you use T-DM1 if it were available?

 ROBERT W CARLSON, MD	Yes
 JOHN CROWN, MD	Yes
 CHARLES E GEYER JR, MD	Yes
 JOYCE O'SHAUGHNESSY, MD	Yes
 MARK D PEGRAM, MD	Yes
 MARTINE J PICCART-GEBHART, MD, PHD	Yes
 MICHAEL UNTCH, MD, PHD	Yes
 ERIC P WINER, MD	Yes

Have you combined or would you combine lapatinib or bevacizumab with trastuzumab?

	Trastuzumab/lapatinib?	Trastuzumab/ bevacizumab?
 ROBERT W CARLSON, MD	Yes	No
 JOHN CROWN, MD	Yes	No
 CHARLES E GEYER JR, MD	No, due to payers	Yes, in a few pts
 JOYCE O'SHAUGHNESSY, MD	Yes	No
 MARK D PEGRAM, MD	Yes	Not off protocol
 MARTINE J PICCART-GEBHART, MD, PHD	Yes	No
 MICHAEL UNTCH, MD, PHD	Yes	No
 ERIC P WINER, MD	Yes	No

PHEREXA: International, Multicenter, Randomized Phase II Study

- Patients with HER2-positive metastatic BC progressing on first-line trastuzumab-based therapy
- Randomization:
  - Trastuzumab + capecitabine
  - Trastuzumab + capecitabine + pertuzumab
- Primary endpoint: PFS

Munoz-Mateu M et al. *Proc ASCO* 2011;Abstract TPS118 (Trials in Progress Poster Session, Monday, June 6, 8 AM to 12 PM).

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Trastuzumab Beyond Progression in Human Epidermal Growth Factor Receptor 2-Positive Advanced Breast Cancer: A German Breast Group 26/ Breast International Group 03-05 Study

Von Minckwitz G et al.

J Clin Oncol 2009;27(12):1999-2006.

Phase II Study of Trastuzumab-DM1 (T-DM1) for the Treatment of HER2-Positive Metastatic Breast Cancer After Prior HER2-Directed Therapy

- 112 heavily pretreated patients with HER2+ metastatic BC
  - Median # systemic agents in all settings: 8
  - Median # systemic agents in metastatic setting: 5
- ORR = 25.9%; Median PFS = 4.6 mos
- Median duration of response not reached (F/U ≥12 mos)
- Most AEs Grade 1/2; No dose-limiting cardiotoxicity

Burris HA 3rd et al. *J Clin Oncol* 2011;29(4):398-405.

MARIANNE: Phase III Study of First-Line Therapy for HER2-Positive Progressive, Recurrent Locally Advanced or Metastatic Breast Cancer

- Randomization:
  - Trastuzumab + taxane (docetaxel or paclitaxel)
  - T-DM1 + pertuzumab
  - T-DM1 + placebo
- Primary endpoint: PFS
- Target enrollment: 1,092

Ellis PA et al. *Proc ASCO* 2011;Abstract TPS102 (Trials in Progress Poster Session, Monday, June 6, 8 AM to 12 PM).

EMILIA: Phase III Study in HER2-Positive, Locally Advanced or Metastatic Breast Cancer Previously Treated with Trastuzumab-Based Therapy

- Randomization:
  - T-DM1
  - Lapatinib + capecitabine
- Primary endpoint: PFS
- Target enrollment: 980

Verma S et al. *Proc ASCO* 2011;Abstract TPS116 (Trials in Progress Poster Session, Monday, June 6, 8 AM to 12 PM).

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Randomized Study of Lapatinib Alone or in Combination with Trastuzumab in Women with ErbB2-Positive, Trastuzumab-Refractory Metastatic Breast Cancer

Blackwell KL et al.

J Clin Oncol 2010;28(7):1124-30.

Phase III Study of Continued HER2 Suppression with Trastuzumab ± Lapatinib in HER2-Positive Metastatic Breast Cancer (Dana Farber)

- Patients with response or stable disease to 1st- or 2nd-line chemo/trastuzumab
- Randomization:
  - Maintenance lapatinib + trastuzumab
  - Maintenance trastuzumab alone
- Primary endpoint: PFS
- Target enrollment: 276

Lin NU et al. *Proc ASCO* 2011;Abstract TPS113 (Trials in Progress Poster Session, Monday, June 6, 8 AM to 12 PM).

Phase II Study of Bevacizumab, Trastuzumab and Capecitabine as First-Line Treatment of HER2-Positive Locally Advanced or Metastatic BC

	N	Overall response	Complete response	Partial response
ITT population	88	72.7%	6.8%	65.9%
Metastatic	74	73.0%	6.8%	66.2%
Locally advanced	13	76.9%	7.7%	69.2%
ER/PR+	37	70.3%	5.4%	64.9%
ER/PR-	51	74.5%	7.8%	66.7%

Tjulandin S et al. *Proc ASCO* 2011;Abstract 571. General Poster Session, Monday, June 6, 1 PM to 5 PM

BEVERLY2: Phase II Study of Neoadjuvant Chemotherapy, Trastuzumab and Bevacizumab in HER2-Positive Inflammatory Breast Cancer

- Pathologic complete response (n = 52): 67.3%
- Clinical response rate: 98%
- Postoperative events*
  - Seromas (n = 12)
  - Wound-healing complications (n = 5)
  - Infection (n = 2)

* Rouzier R et al. *Proc ASCO* 2011;Abstract 569. General Poster, Monday, June 6, 1 PM to 5 PM
Viens P et al. *Proc ASCO* 2011;Abstract 531. Poster Discussion, Tuesday, June 7, 8 AM to 12 PM

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MODULE 7

Rapid Fire

What is the most common endocrine treatment you use for a premenopausal woman who develops disease relapse while receiving tamoxifen?

 ROBERT W CARLSON, MD	Ovarian function suppression + AI
 JOHN CROWN, MD	Ovarian function suppression + AI
 CHARLES E GEYER JR, MD	Ovarian function suppression
 JOYCE O'SHAUGHNESSY, MD	Ovarian function suppression + AI
 MARK D PEGRAM, MD	Ovarian function suppression + AI
 MARTINE J PICCART-GEBHART, MD, PHD	Ovarian function suppression ± AI
 MICHAEL UNTCH, MD, PHD	Ovarian function suppression + AI
 ERIC P WINER, MD	Ovarian function suppression ± AI

What is the most common endocrine treatment you use for a postmenopausal woman who develops disease relapse while receiving a nonsteroidal AI?

 ROBERT W CARLSON, MD	Exemestane or fulvestrant
 JOHN CROWN, MD	Exemestane or fulvestrant
 CHARLES E GEYER JR, MD	Tamoxifen
 JOYCE O'SHAUGHNESSY, MD	Fulvestrant
 MARK D PEGRAM, MD	Exemestane
 MARTINE J PICCART-GEBHART, MD, PHD	Exemestane or fulvestrant
 MICHAEL UNTCH, MD, PHD	Exemestane
 ERIC P WINER, MD	Tamoxifen

Do you generally change your approach to adjuvant chemotherapy for patients diagnosed with breast cancer during late pregnancy, relevant to the issue of possibly delaying therapy until after delivery?

 ROBERT W CARLSON, MD	No, unless 4-8 wks to deliver
 JOHN CROWN, MD	No, unless few wks to deliver
 CHARLES E GEYER JR, MD	No, unless few wks to deliver
 JOYCE O'SHAUGHNESSY, MD	No, unless 2-4 wks to deliver
 MARK D PEGRAM, MD	No, depends on stage/pathology
 MARTINE J PICCART-GEBHART, MD, PHD	Prefer to delay
 MICHAEL UNTCH, MD, PHD	No
 ERIC P WINER, MD	No, unless short time to delivery

In a patient with TNBC who has significant residual disease at surgery after neoadjuvant anthracycline/taxane treatment, are there any systemic treatments you use?

 ROBERT W CARLSON, MD	Carboplatin/gemcitabine or CMF or capecitabine
 JOHN CROWN, MD	CMF + XRT
 CHARLES E GEYER JR, MD	No
 JOYCE O'SHAUGHNESSY, MD	Cisplatin if BRCA+, else capecitabine
 MARK D PEGRAM, MD	Low-dose capecitabine + XRT
 MARTINE J PICCART-GEBHART, MD, PHD	No
 MICHAEL UNTCH, MD, PHD	Cisplatin
 ERIC P WINER, MD	No

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313 Patients with Breast Cancer During Pregnancy — Results from a Prospective and Retrospective Registry (GBG-20/BIG02-03)

Loibl S et al.

Proc SABCS 2010;Abstract S6-2.

Chemotherapy During and After Pregnancy: Fetal and Patient Outcomes

- Premature delivery, which increases fetal morbidity and unfavorable long-term outcome, is unnecessary
- Patients should be treated as closely as possible to standard recommendations for nonpregnant women.

Loibl S et al. *Proc SABCS* 2010;Abstract S6-2.