TV-116-091620-65

SYLLABUS AND COURSE GUIDE

Targeted Therapy for HER2 and HER3-Positive Breast Cancer: Navigating the Evolving Treatment Landscape

A Free, 90-Minute Live and OnDemand Activity
Premiere Date: Wednesday, September 16, 2020
6:30 PM - 8:00 PM ET (live)
Credit Expiration Date: Thursday, September 16, 2021

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#treatBC

LIVE FACULTY: Shanu Modi, MD and Michael F. Press, MD, PhD
MODERATOR: Sara A. Hurvitz, MD

Take advantage of our LIVE Q&A segment during this webcast!

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INFORMATION FOR PARTICIPANTS

Statement of Need

Breast cancer (BC) is a heterogeneous disease with human epidermal growth factor receptor 2 (HER2) overexpression and/or amplification observed in 20%-30% of cases. HER2-positive (+) BC correlates with poor clinical outcomes unless appropriately treated with targeted therapy. Despite significant therapeutic advances, many patients experience disease progression with resistance to targeted agents developing over the course of treatment.

This CME Outfitters Live and OnDemand webcast will provide up-to-date education on this rapidly evolving field, in order to better tailor treatment strategies, leading to improved patient outcomes. Additionally, faculty will discuss COVID-19 and its impact on patients with BC.

Learning Objectives

At the end of this CME/CE activity, participants should be able to:

- Apply HER2 testing guidelines for improved treatment selection in breast cancer.
- Evaluate clinical trial data for novel and emerging therapies for the management of patients with low HER2 expression, resistant to HER2-directed therapies, and HER3+ BC.
- Expand use of telemedicine in BC care.

The following learning objectives pertain only to those requesting CNE or CPE credit:

- Summarize HER2 testing guidelines for improved treatment selection in BC.
- Evaluate clinical trial data for novel and emerging therapies for the management of patients with low HER2 expression, resistant to HER2-directed therapies, and HER3+ BC.
- Describe ways to expand use of telemedicine in BC care.

Target Audience

Hematologists/oncologists, OB/GYNs, surgeons, pathologists, PAs, nurse practitioners, nurses, and pharmacists

Financial Support

Supported by an educational grant from Daiichi Sankyo, Inc.

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Universal Activity Number: Live: 0376-0000-20-108-L01-P; Enduring: 0376-0000-20-108-H01-P
Type: Knowledge-based

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.5 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.

Learning Formats: Live activity; Enduring material

Royal College MOC

Through an agreement between the Accreditation Council for Continuing Medical Education and the Royal College of Physicians and Surgeons of Canada, medical practitioners participating in the Royal College MOC Program may record completion of accredited activities registered under the ACCME's "CME in Support of MOC" program in Section 3 of the Royal College's MOC Program.

MIPS Improvement Activity

This activity counts towards MIPS Improvement Activity requirements under the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA). Clinicians should submit their improvement activities by attestation via the CMS Quality Payment Program website.

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Post-tests, credit request forms, and activity evaluations must be completed online (requires free account activation), and participants can print their certificate or statement of credit immediately (75% pass rate required). This website supports all browsers except Internet Explorer for Mac. For complete technical requirements and privacy policy, visit https://www.cmeoutfitters.com/privacy-and-confidentiality-policy.

There is no fee for participation in this activity. The estimated time for completion is 90 minutes. Questions? Please call **877.CME.PROS**.

FACULTY BIOS & DISCLOSURES

Sara A. Hurvitz, MD (Moderator)

Dr. Hurvitz is Professor of Medicine at the University of California, Los Angeles (UCLA); Co-director of the Santa Monica-UCLA Outpatient Oncology Practice; Medical Director of the Clinical Research Unit of the Jonsson Comprehensive Cancer Center at UCLA; and Director of Breast Oncology. Dr. Hurvitz earned her MD from the University of Southern California. She served internship/residency at UCLA 1999-2002, was Chief Resident of internal medicine in 2003-2004, and completed a hematology-oncology fellowship at UCLA in 2006. Dr. Hurvitz earned board-certification in internal medicine, hematology, and medical oncology.

In the 14 years since joining the faculty at UCLA, Dr. Hurvitz has gained international recognition as an academic expert in breast oncology. She not only has an active clinical practice but also has extensive experience designing and leading first-in-human through phase III clinical trials. She has served as UCLA principle investigator on over 50 interventional clinical trials, has been chair of six international and four national studies, on the steering committee for 15 international trials, and on the Data Safety Monitoring Board for four studies of novel therapeutics. She has personally designed, co-written, obtained funding, and completed multiple phase II and III clinical trials of novel targeted therapies (including TRIO B07, KRISTINE, and neoMONARCH). She serves on the Department of Defense Breast Cancer Research Program Programmatic Panel, is on the Scientific Committee for TRIO (Translational Research in Oncology, formerly BCIRG, an academic not-for-profit CRO), is on the editorial board for several peer-reviewed journals, including *Journal of Clinical Oncology*, and serves as a reviewer for numerous high-impact medical journals including the *New England Journal of Medicine, Lancet Oncology, Journal of Clinical Oncology, JAMA-Oncology*, and *Clinical Cancer Research*. In addition to her expertise in the clinical development of novel therapeutics, Dr. Hurvitz also has been extensively involved in laboratory-based research. She has been awarded and successfully led and completed several government-funded basic science projects. Additionally, she co-directs the preclinical evaluation of novel targeted therapeutics for breast cancer in the UCLA-JCCC/Translational Oncology Research Laboratory (TORL). Dr. Hurvitz is committed to the translation of basic laboratory science into innovative clinical testing and the movement of important clinical questions into the laboratory. Her understanding of both bench and bedside makes her uniquely positioned to lead the successful translation of new discoveries into the clinical realm.

Shanu Modi, MD

Dr. Modi is Associate Professor of Medicine in the Department of Medicine at Weill Cornell Medical College in New York, New York. She is also Associate Member of the Breast Medicine Service at Memorial Sloan Kettering Cancer Center (MSKCC) in New York, New York. Dr. Modi received her medical degree from the University of Alberta in Edmonton, Canada where she also completed a residency in internal medicine. She followed this with subspecialty training in medical oncology at the Cross Cancer Institute and subsequently completed a 4-year fellowship in breast cancer research at MSKCC. She has been a full-time faculty member of the Breast Medicine Service at MSKCC since 2005.

Dr. Modi has been chair and member of the Scientific Program Committee for HER2 Positive Breast Cancer from 2013 to 2016 and member of the Grants Selection Committee for the American Society of Clinical Oncology (ASCO) from 2013 to 2015. She received the Conquer Cancer Foundation Advanced Clinical Research Award in 2009 for her work in Heat Shock Protein Inhibition. Dr. Modi was awarded and held the Patricia and James Cayne Chair for Junior Faculty at MSKCC from 2009 to 2012.

She has had a clinical research career in the development of HER2-targeted therapies and is currently the Section Head for HER2 Positive Breast Cancer for the Breast Medicine Service at MSKCC. Dr. Modi is also a member of the Expert Committee to establish Guidelines for Patients with Advanced HER2+ Breast Cancer, where she serves on the Breast Cancer Consensus Panel. She is also a member of the Scientific Committee for the European Society of Medical Oncology (ESMO) as part of the metastatic breast cancer track responsible for abstract selection.

She is an ad hoc reviewer for *Journal of Clinical Oncology, Clinical Breast Cancer, Breast Cancer Research and Treatment*, and *Journal of Surgical Oncology*. She has authored or co-authored more than 50 peer-reviewed articles as well as books, book chapters, and reviews.

Dr. Modi holds memberships in ASCO, ESMO, the American Association for Cancer Research, ALLIANCE for Clinical Trials in Oncology, and the Translational Breast Cancer Consortium. She has been an invited speaker for national and international congresses, meetings, and symposiums.

Michael F. Press, MD, PhD

Dr. Press is a Professor in the Department of Pathology and holds the Harold E. Lee Chair in Cancer Research at the University of Southern California (USC) Norris Comprehensive Cancer Center. He is a board-certified pathologist, directs the USC Breast Cancer Analysis Laboratory as well as the Central Laboratory for the Translational Research in Oncology (TRIO)/Cancer International Research Group (CIRG), and is Leader of the USC Clinical Laboratories. His laboratory evaluates prognostic and predictive markers used in making treatment decisions for women with breast cancer. It has served as the Central Laboratory for either retrospective or prospective analyses of tissue specimens for 28 clinical trials that collectively accrued more than 13,000 patients. Dr. Press' area of research interest is in molecular alterations of breast and gynecologic cancers, especially those that have the potential to be important in either diagnostic or therapeutic decision-making for patient management. His research has been continuously funded by research grants for more than 35 years. He is the author or co-author of more than 250 peer-reviewed publications. The most prominent area of activity for his laboratory has been in the study of the human epidermal growth factor receptor type 2 (HER2) in breast and other cancers. He published his first paper in this area in 1989 (*Science* 1989;244:707-712) and his laboratory is still actively contributing to this area as well as to the conduct of clinical trials evaluating HER2 as a target for therapy.

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Dr. Modi reports that she receives research support from AstraZeneca; Daiichi Sankyo, Inc.; Genentech, Inc.; Novartis; and Seattle Genetics, Inc. She is on the advisory committee for AstraZeneca; Daiichi Sankyo, Inc.; and MacroGenics, Inc. She is a consultant for AstraZeneca; Daiichi Sankyo, Inc.; Genentech, Inc.; and Seattle Genetics, Inc. She served as a speaker or a member of a speakers bureau for AstraZeneca; Daiichi Sankyo, Inc.; Genentech, Inc.; and Seattle Genetics, Inc.

Dr. Press reports that he is a consultant for Puma Biotechnology, Inc.; Science Branding Communications; and Zymeworks. He is on the advisory board for AstraZeneca; Biocartis; Cepheid; Eli Lilly and Company; Lilly USA, LLC; Merck & Co., Inc.; and Novartis. He receives honoraria from Science Branding Communications and is a stock shareholder for TORL Biotherapeutics, LLC.

Jeffrey Helfand, DO (peer reviewer) has no disclosures to report.

Mae Ochoa, RPh (peer reviewer) has no disclosures to report.

Poshala Tish Aluwihare, PhD (planning committee) has no disclosures to report.

Susan Perry (planning committee) has no disclosures to report.

Jan Perez (planning committee) has no disclosures to report.

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Targeted Therapy for HER2 and HER3-Positive Breast Cancer: Navigating the Evolving Treatment Landscape

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Sara A. Hurvitz, MD

Professor of Medicine
University of California, Los Angeles (UCLA)
Co-Director, Santa Monica-UCLA Outpatient Oncology Practice
Medical Director, Clinical Research Unit
Jonsson Comprehensive Cancer Center at UCLA
Director of Breast Oncology
Simms/Mann UCLA Center for Integrative Oncology
Los Angeles, CA

Shanu Modi, MD

Associate Professor of Medicine, Department of Medicine
Weill Cornell Medical College
Associate Member
Section Head, HER2 Positive Breast Cancer,
Breast Medicine Service
Memorial Sloan Kettering Cancer Center
New York, NY

Michael F. Press, MD, PhD

Professor
Department of Pathology
Harold E. Lee Chair in Cancer Research
Norris Comprehensive Cancer Center
Keck School of Medicine
The University of Southern California
Los Angeles, CA

Learning Objective 1

Apply HER2 testing guidelines for improved treatment selection in breast cancer (BC).

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Learning Objective 2

Evaluate clinical trial data for novel and emerging therapies for the management of patients with low HER2 expression, resistant to HER2-directed therapies, and HER3+ BC.

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Learning Objective 3

Expand use of telemedicine in BC care.

Evaluating HER2 Status

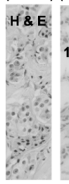
Case Study: 61-year-old woman with MBC

- Left biopsy (March 2015): IDC
  - ER: positive (100%)
  - PR: positive (35%)
  - HER2 IHC: **IHC 3+** ("40% strong, complete membrane staining") (Dako HercepTest, FDA-approved)
  - *HER2* FISH: *HER2* ratio = *HER2*/CEP17 = 3.8/1.6 = 2.3 ("**FISH positive**") (PathVysion FISH assay, FDA-approved)
- Metastatic carcinoma in pleural fluid (September 2019)
  - ER: not provided
  - PR: not provided
  - HER2 IHC: **IHC 2+** (Dako HercepTest, FDA-approved)
  - *HER2* FISH: *HER2* ratio = *HER2*/CEP17 = 2.0/2.0 = 1.0 ("**FISH negative**")
- Patient tissue referral for HER2 assessment second opinion – two separate samples provided (C26712 and C26727)

CEP17 = centromere enumerator probe 17; ER = estrogen receptor; FDA = U.S. Food and Drug Administration; FISH = fluorescence in situ hybridization; HER2 = human epidermal growth factor receptor 2; IDC = invasive ductal carcinoma; IHC = immunohistochemistry; MBC = metastatic breast carcinoma; PR = progesterone receptor

Case Study: 61-year-old woman with MBC

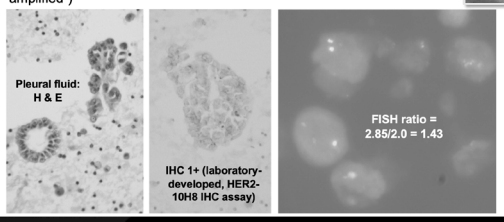
- Left breast biopsy (March 2015): IDC (USC, **C26712**, 09/2019)
  - HER2 IHC: **IHC 2+** (Dako HercepTest, FDA-approved)
  - HER2 IHC: IHC 1+ (LDA 10H8 HER2 IHC)
  - *HER2* FISH: *HER2* ratio = *HER2*/CEP17 = 2.5/1.5 = 1.67 ("*HER2*-not-amplified") (PathVysion FISH assay, FDA-approved)



H & E = hematoxylin and eosin; LDA = laboratory-developed assay

Case Study: 61-year-old woman with MBC

- Metastatic carcinoma in pleural fluid (September 2019): USC, **C26727**, 09/2019
  - HER2 IHC: IHC 1+ (HER2-10H8 assay, laboratory-developed IHC)
  - *HER2* FISH: *HER2* ratio = *HER2*/CEP17 = 2.85/2.0 = 1.43 ("*HER2*-not-amplified")

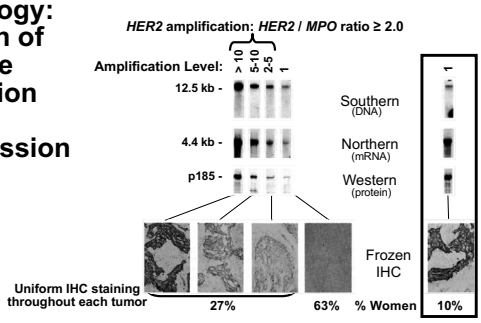


HER2/ERBB2 Testing in Breast Carcinomas

- *HER2/ERBB2* amplification is directly correlated with HER2 overexpression in frozen tissues
- HER2 status by FISH is significantly more accurate than by IHC
- ASCO-CAP Guidelines for HER2 Testing in Breast Cancer (2007, 2013/2014, and 2018)
- Summarize data related to each ASCO-CAP FISH group according to 2013/2014 and 2018 breast cancer guidelines
- Assess the use of alternative control FISH probes for HER2 "ISH-equivocal" breast cancers

ASCO = American Society of Clinical Oncology; CAP = College of American Pathologists

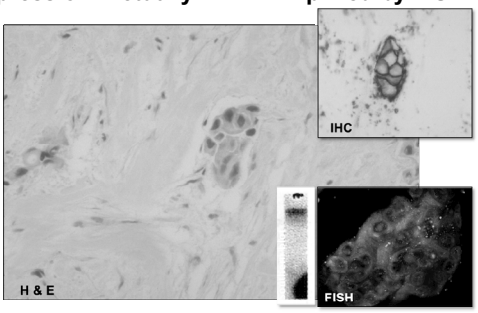
HER2 Biology: Correlation of *HER2* Gene Amplification with Overexpression



MPO = myeloperoxidase

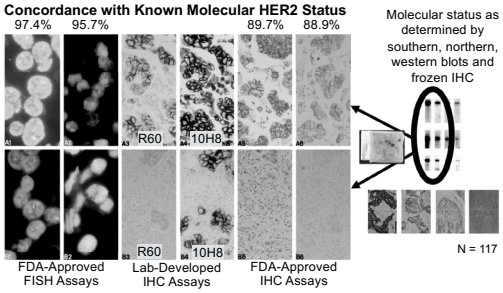
Slamon DJ, et al. *Science*. 1989;244:707-712.

HER Biology: Southern Blot "Single Copy or Not-Amplified" Overexpression: Actually HER2-Amplified by FISH



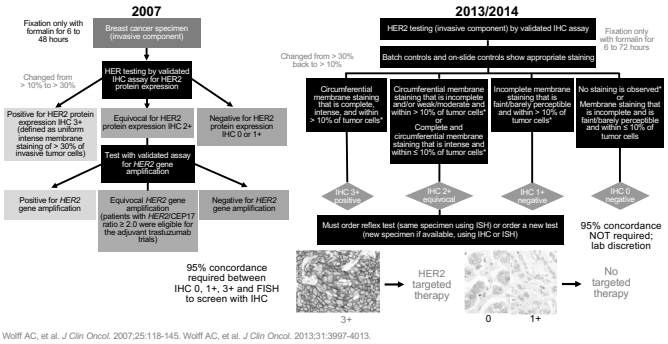
Slamon DJ, et al. *Science*.1989;244:707-712. Pauletti G, et al. *Oncogene*. 1996;13:63-72.

Comparison of Six Different HER2 Assays in HER2 Molecularly Characterized Breast Cancers



Press MF, et al. *J Clin Oncol*. 2002;20:3095-3105.

Algorithm for HER2 Testing by IHC



Wolff AC, et al. *J Clin Oncol*. 2007;25:118-145. Wolff AC, et al. *J Clin Oncol*. 2013;31:3997-4013.

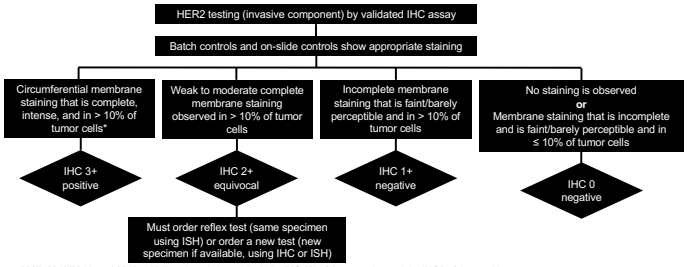
Concordance Between IHC and FISH: Prevalence of *HER2* Gene Amplification by IHC Category (2008-2014)

HER2 Gene Amplification Rate (%) in Each IHC Staining Category by Study						
IHC 0 (%)	IHC 1+ (%)	IHC 2+ (%)	IHC 3+ (%)	Number	IHC Method	Reference
0%	8.3%	22.9%	56.3%	661	**Dako HercepTest (FDA)**	Rasmussen 2008
1.6%		21.1%	64%	697	**A0485 (Dako)**	Grimm 2010
12.2%		66.6%	93.9%	175	**3B5 antibody (LDT)**	Panjwani 2010
3.3%		57.9%	95.2%	100	**Dako HercepTest (FDA)**	Tsuda 2010
0%	3.3%	15.2%	84.1%	200	**4B5 antibody, LDT**	Lambein 2011
0%	3.2%	21.5%	91%	681	**Dako HercepTest (FDA)**	Jørgensen 2011
12.8%		43.8%	97.8%	291	**A0485 (Dako), LDT**	Bernasconi 2012
0%	10%	25%	100%	216	**CB11 antibody**	Martin 2012
3.3%	7.1%	49.2%	88.4%	543	**CB11 antibody**	Lee 2012
0%	12.5%	76.5%	97.3%	125	**Dako HercepTest (FDA)**	Kiyose 2012
2.4%		39.9%	98.1%	1,437	**Dako HercepTest (FDA)**	Vergara-Lluri 2012
9.6%		38.9%	87.2%	396	**CB11 (Biogenix)**	Kokate 2012
2.6%	4.6%	28.1%	93.6%	950	**A0485 (Dako), LDT**	Park 2012
0%	1%	19%	92%	154	**Dako HercepTest (FDA)**	Minot 2012
10%	5%	13%	69%	1,024	**CB11 (Ventana)**	Varga 2013
0%	2.6%	29.4%	100%	150	**4B5 (Ventana) (FDA)**	Lambein 2013
9.4%	6.4%	13.5%	55.1%	628	**A0485 (Dako), LDT**	Fasching 2014
1.7%	3.3%	12.4%	81.1%	2,590	**Dako HercepTest (FDA)**	Schalper 2014

Less than 95% concordance of IHC with FISH assay results

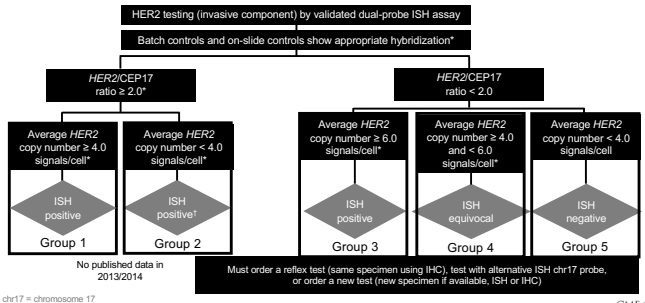
LDT = lab-developed test

HER2 Testing by IHC: 2018 Guidelines (Unchanged from 2013/2014)



2007, 2013/2014, and 2018 guidelines largely ignore both the IHC 0/1+ false-negative and the IHC3+ false-positives
Wolff AC, et al. *J Clin Oncol*. 2018;36(20):2105-2122.

Optimal ASCO-CAP Algorithm for HER2 Testing by FISH: *HER2* Probe with a Control CEP17 Probe



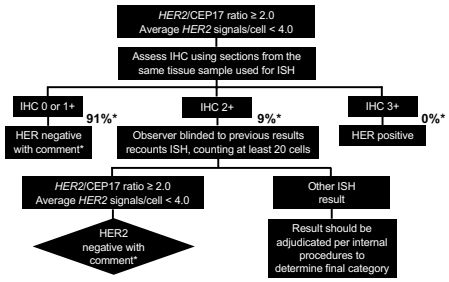
chr17 = chromosome 17
*Observed in a homogeneous and contiguous population; †See data supplement 2E in Wolff 2014 reference for more information on these rare scenarios
Wolff AC, et al. *J Clin Oncol*. 2013;31:3997-4013. Wolff AC, et al. *Arch Pathol Lab Med*. 2014;138(2):241-256.

Assessment of HER2 by FISH According to 2014 ASCO-CAP Guidelines by Group

		Consultation Study		CIRG Trials Study	
Group	**Description of FISH Category**	**No. of Cases**	**Overall %**	**No. of Cases**	**Overall %**
1	Ratio ≥ 2.0 HER2 average ≥ 4.0	1,328	**17.7%**	4,269	**40.8%**
2	Ratio ≥ 2.0 HER2 average < 4.0	31	**0.4%**	71	**0.7%**
3	Ratio < 2.0 HER2 average ≥ 6.0	48	**0.6%**	55	**0.5%**
4	Ratio < 2.0 HER2 average ≥ 4.0, < 6.0	345	**4.6%**	432	**4.1%**
5	Ratio < 2.0 HER2 average < 4.0	5,774	**76.7%**	5,641	**53.9%**
Totals		7,526*	**100%**	10,468	**100%**

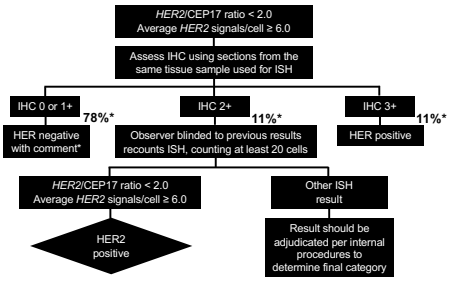
*86 cases (1.1%) with *HER2* genomic heterogeneity were excluded
Press MF, et al. *Arch Pathol Lab Med*. 2016;140:1250-1258. Press MF, et al. *J Clin Oncol*. 2016;34(29):3518-3528.

Evaluation of FISH Group 2



*Press MF, et al. *J Clin Oncol*. 2016;34(29):3518-3528. Wolff AC, et al. *J Clin Oncol*. 2018;36(20):2105-2122.

Evaluation of FISH Group 3



*Press MF, et al. *J Clin Oncol*. 2016;34(29):3518-3528. Wolff AC, et al. *J Clin Oncol*. 2018;36(20):2105-2122.

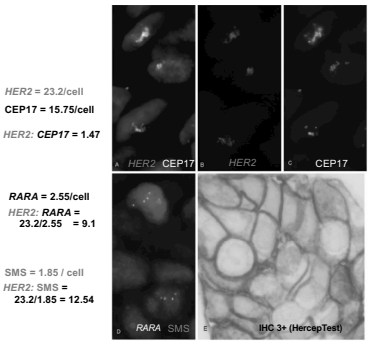
HER2 Gene Amplification Status vs. HER2 Protein Expression in ASCO-CAP Group 3 Patients in a BCIRG Trial

ASCO-CAP Group (Ratio < 2.0 and Average HER2 Copies ≥ 6.0)	*HER2* BCIRG FISH Status	Mean of Average *HER2* Copy Numbers	IHC 0	IHC 1+	IHC 2+	IHC 3+	Totals
Group 3A	**Amplified**	Average 16.38	1 (17%)	0 (0%)	3 (50%)	2 (33%)	6 (24%)
Group 3N	**Not Amplified**	Average 7.43	8 (42%)	9 (47%)	2 (11%)	0 (0%)	19 (76%)
Totals			9	9	5	2	25 (100%)

There is a significant difference between Group 3A and Group 3N in terms of IHC staining
Group 3A: 83% IHC 2+/3+; Group 3N: 89% IHC 0/1+ (p = .002)

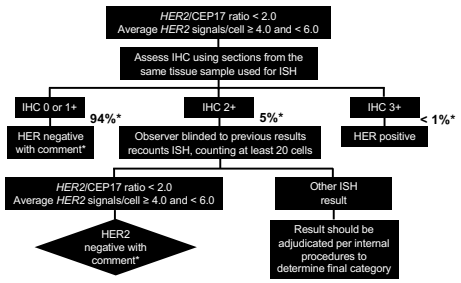
BCIRG = Breast Cancer International Research Group
Press MF, et al. *J Clin Oncol*. 2016;34(29):3518-3528.

Minority of ASCO-CAP FISH Group 3 Breast Cancers ("Group 3A") Show *HER2* Gene Amplification and HER2 Protein Overexpression



Press MF, et al. *Arch Pathol Lab Med*. 2016;140(11):1250-1258.

Evaluation of FISH Group 4



*Press MF, et al. *J Clin Oncol*. 2016;34(29):3518-3528. Wolff AC, et al. *J Clin Oncol*. 2018;36(20):2105-2122.

Chr17 Regional Gene Copy Gains/Losses Among Alternative Control Genomic Sites vs. *HER2*/*ERBB2* Gene Copy Gains/Losses

Alternative Control (Region)	HER2 Loss		Total HER2 Copy Number Status HER2 Normal		HER2 Gain		HER2 Amp		Total	
LIS1										
Gain	9	2.48%	25	2.67%	61	18.71%	13	4.47%	108	5.64%
Normal	46	12.67%	622	66.52%	64	19.63%	87	29.90%	819	42.77%
Loss	308	84.85%	288	30.80%	201	61.66%	191	65.64%	988	51.59%
Total	363	100%	935	100%	326	100%	291	100%	1,915	100%
TP53										
Gain	3	0.83%	15	1.60%	60	18.40%	4	1.37%	82	4.28%
Normal	41	11.29%	624	66.74%	59	18.10%	81	27.84%	805	42.04%
Loss	319	87.88%	296	31.66%	207	63.50%	206	70.79%	1,028	53.68%
Total	363	100%	935	100%	326	100%	291	100%	1,915	100%
D17S122 (TEKT3)										
Gain	10	2.75%	11	1.18%	55	16.87%	8	2.75%	84	4.39%
Normal	50	13.77%	643	68.77%	67	20.55%	84	28.87%	844	44.07%
Loss	303	83.47%	281	30.05%	204	62.58%	199	63.38%	987	51.54%
Total	363	100%	935	100%	326	100%	291	100%	1,915	100%
RAI1										
Gain	7	1.93%	39	4.17%	78	23.93%	35	12.03%	159	8.30%
Normal	57	15.70%	640	68.45%	64	19.94%	89	30.58%	851	44.44%
Loss	299	82.37%	256	27.38%	183	56.13%	167	57.39%	905	47.26%
Total	363	100%	935	100%	326	100%	291	100%	1,915	100%
SMS (TOP3A)										
Gain	12	3.31%	42	4.49%	79	24.23%	41	14.09%	174	9.09%
Normal	54	14.88%	647	69.20%	71	21.78%	94	32.30%	866	45.22%
Loss	297	81.82%	246	26.31%	176	53.99%	156	53.61%	875	45.69%
Total	363	100%	935	100%	326	100%	291	100%	1,915	100%
TOP2A/RARA (TOP2A)										
Gain	2	0.55%	19	2.03%	284	87.12%	117	40.21%	422	22.04%
Normal	22	6.06%	899	96.15%	36	11.04%	77	26.46%	1,034	53.99%
Loss	339	93.39%	17	1.82%	6	1.84%	97	33.33%	459	23.97%
Total	363	100%	935	100%	326	110%	291	100%	1,915	100%

METABRIC Cohort
(N = 1,915)

Press MF, et al. *JAMA Oncol*. 2019;5(3):366-375.

Comparison of FISH Groups with FDA-Approved Status, ASCO-CAP Guidelines, HER2 Expression by IHC, and BCIRG Clinical Trials

Group	Ratio	Average *HER2*	%	FDA	ASCO-CAP 2014 2018	HER2 Protein	Prognosis BCIRG-005	Trastuzumab Response BCIRG-006	BCIRG/TRIO
1	≥ 2.0	≥ 4.0	40.8	Amplified	ISH +	Overexpression	-	Significant improvement	Amplified
2	≥ 2.0	< 4.0	0.7	Amplified	ISH+ IHC	Low expression	-	Not significant	Not amplified
3	< 2.0	≥ 6.0	0.5	Not amplified	ISH+ IHC	Mixed	Undetermined	Undetermined	Mixed
4	< 2.0	≥ 4.0, < 6.0	4.1	Not amplified	ISH? IHC	Low expression	Not worse	-	Not amplified
5	< 2.0	< 4.0	53.9	Not amplified	ISH -	Low expression	Reference	-	Not amplified

Press MF, et al. *J Clin Oncol*. 2016;34(29):3518-3528; Press MF, et al. *JAMA Oncol*. 2019;5(3):366-375.

Management of Treatment-Resistant HER2+ Breast Cancer

Standard of Care for HER2+ Advanced Breast Cancer

First Line

- Trastuzumab + Pertuzumab + Taxane — CLEOPATRA

Second Line

- Trastuzumab emtansine (T-DM1) — EMILIA
- Tucatinib + Trastuzumab + Capecitabine — HER2CLIMB

Third Line

- Trastuzumab + Chemotherapy
  Lapatinib + Capecitabine
  Trastuzumab + Lapatinib — EGF104900, EGF100151
- Trastuzumab deruxtecan (T-DXd) — DESTINY 01
- Neratinib + Capecitabine — NALA

Giordano SH, et al. *J Oncol Pract*. 2018;14(8):501-504. National Comprehensive Cancer Network. Invasive Breast Cancer (Version 5.2020). https://www.nccn.org/professionals/physician_gls/pdf/breast_blocks.pdf.

New HER2-Targeted Agents

- Antibody drug conjugates (ADCs)
  - Trastuzumab deruxtecan (T-DXd)*
  - Trastuzumab duocarmazine (SYD985)
- Tyrosine kinase inhibitors
  - Neratinib*
  - Tucatinib*
- Re-engineered HER2 monoclonal antibody
  - Margetuximab

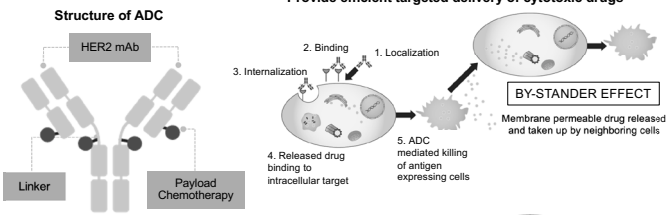
*Agents approved by the FDA

HER2-Directed ADCs

Combine antigen specificity and potent cytotoxicity in a single molecule

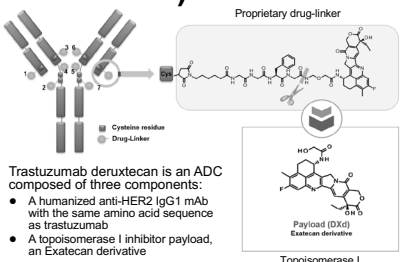
- T-DM1 prototype ADC for HER2+ breast cancer
- New linker technologies and novel potent payloads
- Over 60 ADCs in clinical trials today

Provide efficient targeted delivery of cytotoxic drugs



Trail PA, et al. *Pharmacol Ther.* 2018;181:126-142. Tsuchikama K, An Z. *Protein Cell.* 2018;9(1):33-46.

Trastuzumab Deruxtecan (T-DXd; DS8201a) Is a Novel HER2 ADC



Trastuzumab deruxtecan is an ADC composed of three components:

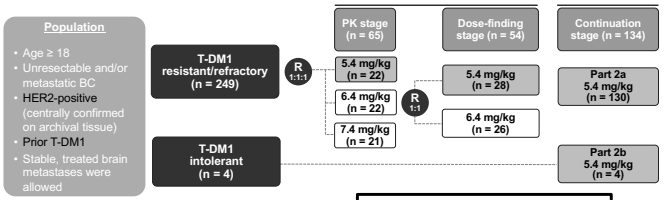
- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an Exatecan derivative
- A tetrapeptide-based cleavable linker

DAR = drug antibody ratio

	T-DXd	T-DM1
Antibody	Anti-HER2 mAb	Trastuzumab
Payload	Topoisomerase I inhibitor	Tubulin inhibitor
DAR	7-8	3.5
Membrane Permeability	Yes (by-stander effect)	No

Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185. Pondé N, et al. *Curr Treat Options Oncol.* 2019;20(5):37.

DESTINY-Breast01 Trial: Phase II Study of T-DXd in HER2-Positive MBC



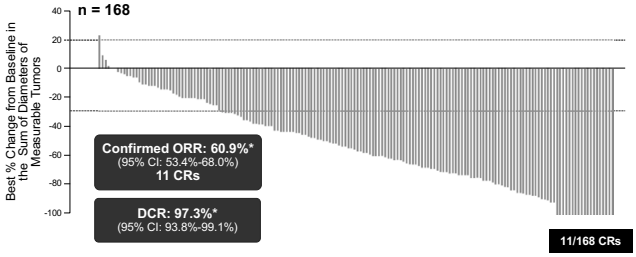
- **Primary:** confirmed ORR by independent review
- **Secondary:** investigator-assessed ORR, DCR, DOR, CBR, PFS, OS, PK, and safety

CBR = clinical benefit rate; DCR = disease control rate; DOR = duration of response; ORR = objective response rate; PFS = progression-free survival; PK = pharmacokinetic

Median lines of therapy = 6 (range: 2-27)
- 100% received prior trastuzumab
- 100% received prior T-DM1
- 66% received prior pertuzumab
- 54% received other HER2 therapies

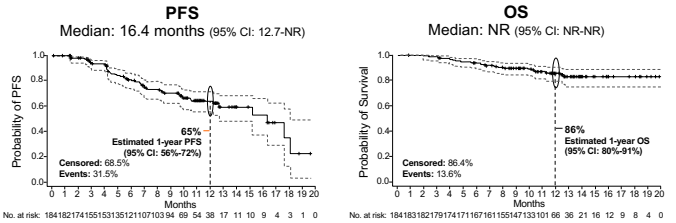
Modi S, et al. *N Engl J Med.* 2020;382(7):610-621.

DESTINY-Breast 01: Best Change in Tumor Size



The line at 20% indicates progressive disease; the line at −30% indicates partial response
*Includes all patients who received T-DXd 5.4 mg/kg (intent-to-treat [ITT] analysis; N = 184)
Modi S, et al. *N Engl J Med.* 2020;382(7):610-621.

DESTINY 01: PFS and OS

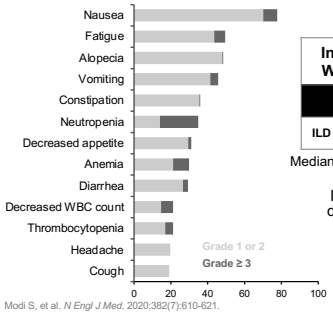


Median DOR 14.8 months

Median PFS in the 24 patients with brain metastases was 18.1 months (95% CI: 6.7-18.1 months)

NR = not reached
Modi S, et al. *N Engl J Med.* 2020;382(7):610-621.

Treatment-Emergent Adverse Events (AEs) in > 15% of Patients



Interstitial Lung Disease (ILD) in Patients Who Received T-DXd 5.4 mg/kg (N = 184)

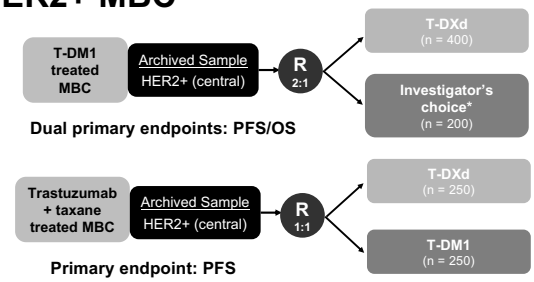
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
ILD	5 (2.7)	15 (8.2)	1 (0.5)	0	4 (2.2)	**25 (13.6)**

Median to onset of ILD was 27.6 weeks (range: 6-76 weeks)

ILD requires awareness via monitoring, dose interruptions and modification, and adherence to management guidelines

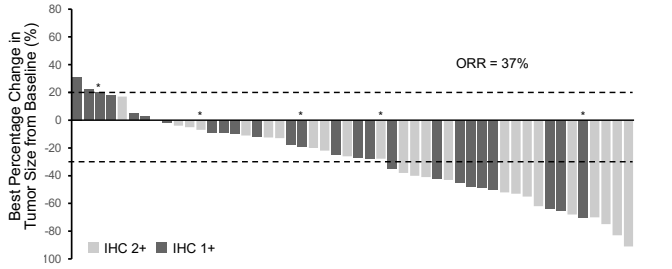
Modi S, et al. *N Engl J Med.* 2020;382(7):610-621.

DESTINY-Breast02 and Breast03 for HER2+ MBC



*Trastuzumab + capecitabine OR lapatinib + capecitabine
ClinicalTrials.gov Identifier: NCT03529110 and NCT03523585.

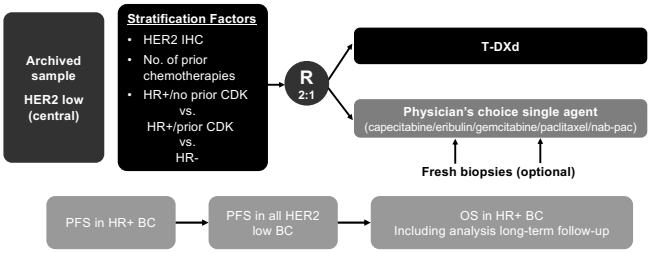
Phase I Trial of Trastuzumab Deruxtecan: Tumor Regression in HER2 Low BC (N = 54)



*HR negative

Modi S, et al. *J Clin Oncol*. 2020;38(17):1887-1896.

DESTINY-Breast04: Study Design for HER2 Low MBC



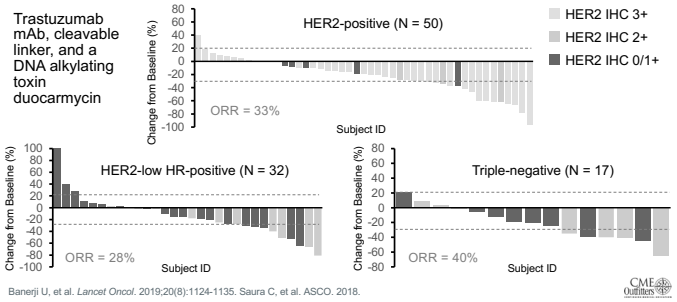
CDK = cyclin-dependent kinase; HR = hormone receptor

Modi S, et al. SABCS 2019; Abstract OT1-07-02. ClinicalTrials.gov Identifier: NCT03734029.

Trastuzumab Duocarmazine (SYD985): HER2 ADC

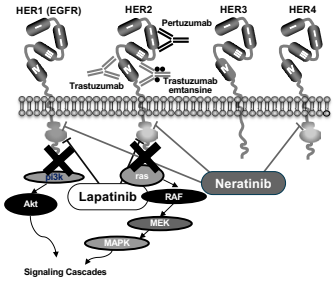
Trastuzumab mAb, cleavable linker, and a DNA alkylating toxin duocarmycin

Best Percentage Change from Baseline in Target Lesions



Banerji U, et al. *Lancet Oncol*. 2019;20(8):1124-1135. Saura C, et al. ASCO. 2018.

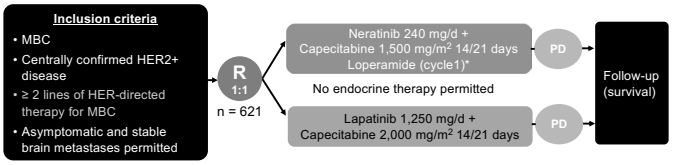
Tyrosine Kinase Inhibitors for HER2+ BC



	Binding	Targets
Lapatinib	Reversible	HER1, HER2
Neratinib	Irreversible	Pan-HER
Pyrotinib	Irreversible	Pan-HER
Poziotinib	Irreversible	Pan-HER
Tucatinib	Reversible	HER2 specific

Baselga J, et al. *Crit Rev Oncol Hematol*. 2017;119:113. Kim JY, et al. *Int J Cancer*. 2019;145(6):1669-1678. Kunte S, et al. *Cancer*. 2020;10.1002/cncr.33102. doi:10.1002/cncr.33102. Xuhong JC, et al. *Am J Cancer Res*. 2019;9(10):2103-2119.

NALA: Phase III Trial of Neratinib for HER2+ MBC



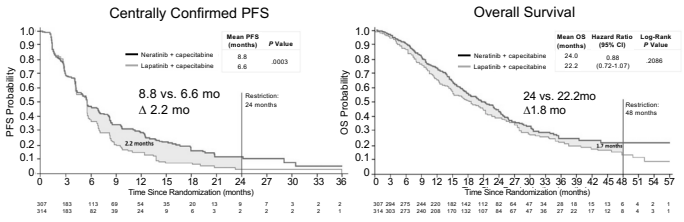
Stratification variables
- Number of prior HER2 therapies for MBC
- Disease location
- HR status
- Geographic location

Endpoints
- Co-primary: PFS (centrally confirmed) and OS
- Secondary: PFS (local), ORR, DOR, CBR, intervention for CNS metastases, safety, health outcomes

*Loperamide 4 mg with first dose of neratinib, followed by 2 mg every 4 hours for the first 3 days, then loperamide 2 mg every 6-8 hours until end of cycle 1; thereafter as needed

Nasrazadani A, et al. *Future Oncol*. 2020;16(7):247-254. Saura C, et al. 2019 ASCO Annual Meeting. Abstract 1002.

NALA: Co-Primary Endpoints of PFS and OS

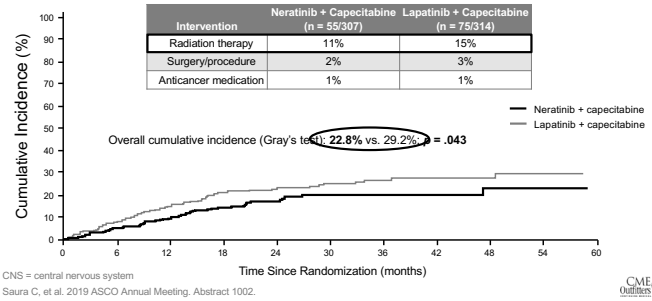


1-yr PFS: 29% vs. 15%
ORR: 33% vs. 27% (p = .1201)
Median DOR: 8.5 mo vs. 5.6 mo (HR: 0.50; 95% CI: 0.33-0.74; p = .0004)

Saura C, et al. 2019 ASCO Annual Meeting. Abstract 1002.

Time to Intervention for CNS Metastases

Intervention	Neratinib + Capecitabine (n = 55/307)	Lapatinib + Capecitabine (n = 75/314)
Radiation therapy	11%	15%
Surgery/procedure	2%	3%
Anticancer medication	1%	1%



CNS = central nervous system

Saura C, et al. 2019 ASCO Annual Meeting. Abstract 1002.

NALA: Most Frequent Treatment-Emergent AEs (TEAEs)

Safety Outcome	Neratinib + Capecitabine (n = 303)		Lapatinib + Capecitabine (n = 311)	
	All Grades, %	Grade 3/4, %	All Grades, %	Grade 3/4, %
Any TEAE	100	61	99	60
Diarrhea	83	24	66	13
Hand-foot syndrome	46	10	56	11
Hypokalemia	12	5	14	6
Nausea	53	4	42	3
Vomiting	46	4	31	2
Fatigue	34	3	31	3
Neutropenia	7	3	5	2
Asthenia	12	3	12	2
Decreased appetite	35	3	22	2
Dehydration	6	2	6	2

Treatment discontinuations due to TEAE: N+C = 10.9% vs. L+ C = 14.5%

Saura C, et al. 2019 ASCO Annual Meeting. Abstract 1002.

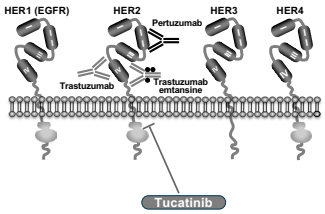
CONTROL Study: Grade 3 Diarrhea Rates

Neratinib Dose Escalation* n = 60 % (no.)	Loperamide n = 137 % (no.)	Budesonide + Loperamide n = 64 % (no.)	Colestipol + Loperamide n = 136 % (no.)
15 (9)	31 (42)	28 (18)	21 (28)

*Median duration per Grade 3 episode was 1-2 days; no Grade 4 diarrhea has been reported in the dose-escalation cohort in CONTROL

Barcenas CH, et al. *Ann Oncol*. 2020;31(9):1223-1230.

Tucatinib: A HER2 Selective TKI



Phase Ib tucatinib/capecitabine/trastuzumab n = 60

Prior treatment:
- 100% trastuzumab
- 65% pertuzumab
- 97% T-DM1
- 55% lapatinib
- 56% with CNS metastasis

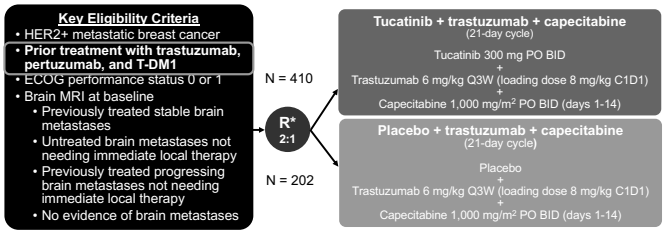
ORR: 61% (n= 14/23)
42% (5/12) in CNS metastasis

PFS: 7.8 months
6.7 months in CNS metastasis

Diarrhea: 33% Grade 1-2
0% Grade 3-4

Murthy R, et al. *Lancet Oncol*. 2018;19(7):880-888.

HER2CLIMB Trial Design: Randomized Phase II Trial



Primary endpoint: PFS

*Stratification factors: presence of brain metastases (yes/no), Eastern Cooperative Oncology Group (ECOG) status (0 or 1), and region (United States or Canada or rest of world)

MRI = magnetic resonance imaging; Q3W = every 3 weeks

Murthy R, et al. *N Engl J Med*. 2020;382(7):597-609.

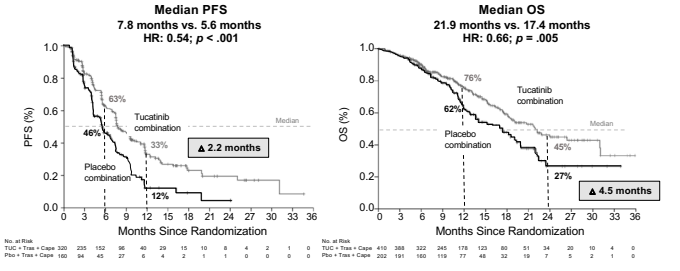
HER2CLIMB: Balanced Baseline Demographics

Characteristic, n (%)		Total Population, N = 612 TUC + Tras + Cape n = 410	Pbo + Tras + Cape n = 202
Female		407 (99)	200 (99)
Age (years), median (range)		55 (22, 80)	54 (25, 82)
ECOG performance status	0	204 (50)	94 (47)
	1	206 (50)	108 (54)
Stage IV at initial diagnosis		143 (35)	77 (39)
Hormone receptor status	ER- and/or PR-positive	243 (60)	127 (63)
	ER- and PR-negative	161 (40)	75 (37)
Prior lines of therapy, median (range)	Overall	4 (2, 14)	4 (2,17)
	Metastatic setting	3 (1, 14)	3 (1, 13)
Presence/history of brain metastases		198 (48)	93 (46)
Treated, stable		118 (59.6)	55 (59.1)
Untreated		44 (22.2)	22 (23.7)
Treated progressing		36 (18.2)	16 (17.2)

Cape = capecitabine; Pbo = placebo; Tras = trastuzumab; TUC = tucatinib

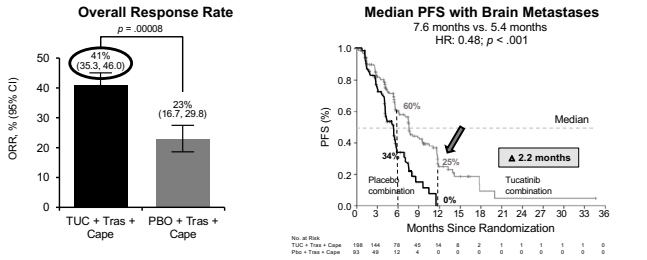
Murthy R, et al. *N Engl J Med*. 2020;382(7):597-609.

HER2CLIMB: Tucatinib Improves PFS and OS



Murthy R, et al. *N Engl J Med*. 2020;382(7):597-609.

HER2CLIMB: Additional Secondary Endpoints



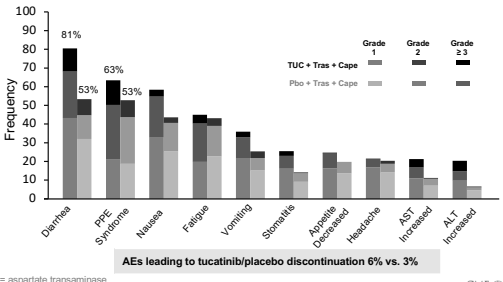
Murthy R, et al. *N Engl J Med*. 2020;382(7):597-609.

Most Common AE (≥ 20% in the Tucatinib Arm)

Diarrhea:
Grade ≥ 3:
13% vs. 9%

Liver function tests:
Grade ≥ 3 AST:
4.5% vs. 0.5%
Grade ≥ 3 ALT:
5.4% vs. 0.5%

Palmar-plantar erythrodysesthesia:
Grade ≥ 3: **13% vs. 9%**



AEs leading to tucatinib/placebo discontinuation 6% vs. 3%

ALT = alanine transaminase; AST = aspartate transaminase

Murthy R, et al. *N Engl J Med*. 2020;382(7):597-609.

HER2CLIMB-02: Randomized Phase III Trial of Tucatinib + T-DM1 vs. T-DM1

Key Eligibility Criteria
- HER2+ MBC
- Prior trastuzumab and taxane (pertuzumab permitted)
- Patients with or without brain metastasis

R 1:1

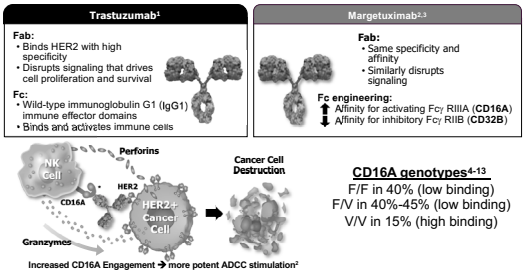
n = 460

- Tucatinib (300 mg orally BID) + T-DM1 (3.6 mg/kg IV Q3W)
- Placebo (orally BID) + T-DM1 (3.6 mg/kg IV Q3W)

Primary endpoint: PFS

Clinical trial NCT03975647.

Margetuximab: A Novel HER2 mAb with a Modified Fc Domain

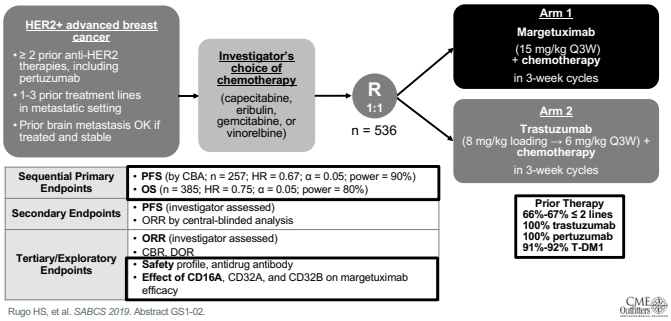


CD16A genotypes[4-13]
F/F in 40% (low binding)
F/V in 40%-45% (low binding)
V/V in 15% (high binding)

ADCC = antibody-dependent cell-mediated cytotoxicity; F= phenylalanine; Fab = fragment, antigen binding; Fc = fragment, crystallizable; V= valine

1. Pohlmann PR, et al. *Clin Cancer Res*. 2009;15(24):7479-7491. 2. Nordstrom JL, et al. *Breast Cancer Res*. 2011;13(6):R123. 3. Stavenhagen JB, et al. *Cancer Res*. 2007;67(18):8882-8890. 4. Lehrnbecher T, et al. *Blood*. 1999;94:4220-4232. 5. Tanaka Y, et al. *Nephrol Dial Transplant*. 2005;20:2439-2445. 6. Stavenhagen JB, et al. *Cancer Res*. 2007;67:8882-8890. 7. Koene HR, et al. *Blood*. 1997;90:1109-1114. 8. Musolino A, et al. *J Clin Oncol*. 2008;26:1789-1796. 9. Nordstrom JL, et al. *Breast Cancer Res*. 2011;13:R123. 10. Shields JM, et al. *J Biol Chem*. 2002;277:9790-9799. 11. Varchetta S, et al. *Cancer Res*. 2007;67:11991-11998. 12. Gavin PG, et al. *JAMA Oncol*. 2017;3:335-341. 13. Musolino A, et al. *Pharmacogenomics J*. 2016;16:472-477.

SOPHIA Study: Phase III Design

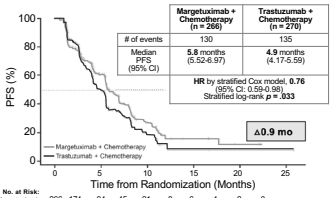


Sequential Primary Endpoints	• **PFS** (by CBA; n = 257; HR = 0.67; α = 0.05; power = 90%) • **OS** (n = 385; HR = 0.75; α = 0.05; power = 80%)
Secondary Endpoints	• **PFS** (investigator assessed) • ORR by central-blinded analysis
Tertiary/Exploratory Endpoints	• **ORR** (investigator assessed) • CBR, DOR • **Safety** profile, antidrug antibody • **Effect of CD16A**, CD32A, and CD32B on margetuximab efficacy

Rugo HS, et al. *SABCS 2019*. Abstract GS1-02.

SOPHIA: Primary PFS and Interim OS Analyses

Primary PFS Analysis
(ITT population, N = 536)



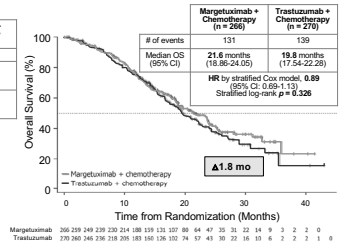
	Margetuximab + Chemotherapy (n = 266)	Trastuzumab + Chemotherapy (n = 270)
# of events	130	135
Median PFS (95% CI)	**5.8** months (5.52-6.97)	**4.9** months (4.17-5.59)

HR by stratified Cox model, **0.76** (95% CI: 0.59-0.98)
Stratified log-rank ***p* = .033**

No. at Risk:										
Margetuximab	266	174	94	45	21	8	6	4	2	0
Trastuzumab	270	158	74	33	13	2	2	1	1	1

24% risk reduction of disease progression

Second Interim OS Analysis (September 2019 Cutoff)*



	Margetuximab + Chemotherapy (n = 266)	Trastuzumab + Chemotherapy (n = 270)
# of events	131	139
Median OS (95% CI)	**21.6** months (18.86-24.05)	**19.8** months (17.54-22.28)

HR by stratified Cox model, **0.89** (95% CI: 0.69-1.13)
Stratified log-rank ***p* = 0.326**

Margetuximab	266	259	249	239	230	214	188	159	135	107	89	64	47	35	31	22	14	9	3	2	2	0
Trastuzumab	270	260	246	236	218	205	183	160	126	102	74	57	43	30	22	16	10	6	2	2	2	1	0

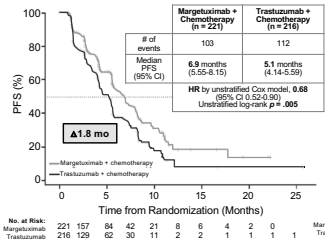
*OS analysis performed, as of September 10, 2019 data cutoff, after 270 (70%) of 385 events needed for final OS analysis had occurred

Rugo, et al. *ASCO 2019*. Rugo HS, et al. *SABCS 2019*. Abstract GS1-02.

SOPHIA: Exploratory PFS and OS in CD16A-185 F Carriers

CD16A FF or FV, n = 437 of 506 genotyped (86%)

PFS

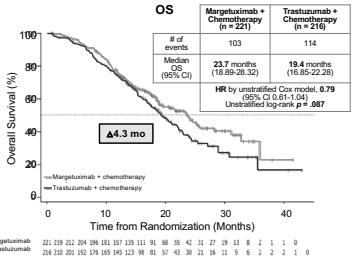


	Margetuximab + Chemotherapy (n = 221)	Trastuzumab + Chemotherapy (n = 216)
# of events	103	112
Median PFS (95% CI)	**6.9** months (5.55-8.15)	**5.1** months (4.14-5.59)

HR by unstratified Cox model, **0.68** (95% CI 0.52-0.90)
Unstratified log-rank ***p* = .005**

No. at Risk:										
Margetuximab	221	157	84	42	21	8	6	4	2	0
Trastuzumab	216	129	62	30	11	2	2	1	1	1

OS



	Margetuximab + Chemotherapy (n = 221)	Trastuzumab + Chemotherapy (n = 216)
# of events	103	114
Median OS (95% CI)	**23.7** months (18.89-28.32)	**19.4** months (16.85-22.28)

HR by unstratified Cox model, **0.79** (95% CI 0.61-1.04)
Unstratified log-rank ***p* = .087**

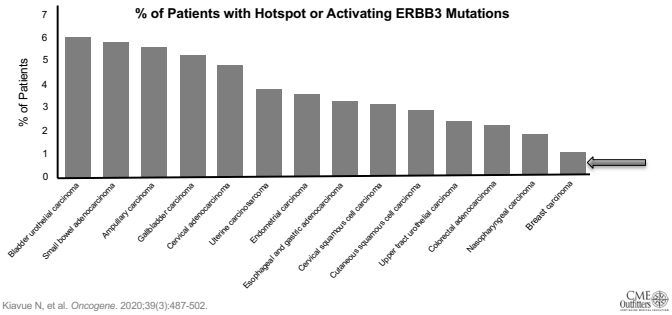
Margetuximab	221	219	212	204	196	181	157	135	111	91	68	55	42	31	27	19	13	8	2	1	1	0	
Trastuzumab	216	210	201	192	176	165	145	123	98	81	57	43	30	21	16	11	9	6	2	2	2	1	0

Rugo, et al. ASCO 2019. Rugo, et al. SABC 2019.

HER3 in Breast Cancer

HER3-Initiated Signaling
An Animated Tour

Prevalence of *ERBB3* Somatic Mutations



Kiavue N, et al. *Oncogene*. 2020;39(3):487-502.

HER3 in HER2-Amplified BC

- Development of tumors in transgenic mice due to overexpression of a HER2 transgene in mammary tissue is significantly averted by Cre-mediated deletion of the endogenous *ERBB3* gene in mammary tissue
- In HER2-amplified breast cancer cell lines, the experimental transcriptional repression of HER3 expression stops tumor cell growth and proliferation
- The in vivo tumorigenic growth of HER2-amplified breast cancers can be stopped using shRNA knockdown of HER3 in the tumors or Crispr-mediated knockout of HER3 in the tumors
- EGFR or HER4 do not seem to supplant the requirement for HER3 as the requisite partner for HER2 in these tumors

Kumar R, et al. *Adv Cancer Res*. 2020;147:109-160.

HER3: Resistance to Hormonal and Targeted Therapy

- Hormonal therapy
  - Co-expression of *HER2* and *HER3* linked to tamoxifen resistance
  - ER+ BC cells when treated with fulvestrant induce protein expression and activity of *HER3*
- Targeted therapy
  - Increased *HER3* expression linked to trastuzumab resistance
  - HER3 upregulation linked to lapatinib resistance

Mishra R, et al. *Oncol Rev*. 2018;12(1):355.

New and Emerging Treatments

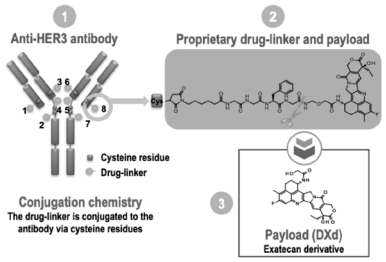
Select HER3-Targeting Agents in Clinical Development

Drug	MOA	Phase (NCT)	Result
U3-1402	ADC – anti-HER3 antibody conjugated to topoisomerase 1 inhibitor	I/II (NCT02980341)	Ongoing
MCLA-128	Bispecific antibody targeting HER2/HER3	II (NCT03321981)	Ongoing
CDX-3379	Anti-HER3 antibody	II (NCT03254927)*	Ongoing
ISU 104	Anti-HER3 antibody	I (NCT03552406)	Ongoing
LJM716	Anti-HER3 antibody	I (NCT02167854)	Ongoing

*In head and neck squamous cell carcinoma
MOA = mechanism of action

U3-1402: HER3-Targeting ADC

- High-potency payload with a different MOA and short half-life
- By-stander effect
- Stable linker-payload
- Tumor-selective cleavable linker
- High drug-to-antibody ratio



Hashimoto Y, et al. *Clin Cancer Res*. 2019;25(23):7151-7161. Masuda N, et al. San Antonio Breast Cancer Symposium (SABCS); 2018. Abstract PD1-03. Yonemori K, et al. *Ann Oncol*. (2019;30(suppl 3):iii47-iii64.

U3-1402 in HER3-Overexpressing MBC: Phase I/II

- U3-1402 showed promising antitumor activity in heavily-pretreated patients with HER3-overexpressing MBC
  - Confirmed ORR: 42.9%
  - Median DOR
  - Median PFS: 8 months
- Efficacy seen regardless of MBC subtype
  - 50% HR+ HER2-
  - 24% triple-negative BC
  - 17% HER2+

Masuda N, et al. SABCS; 2018. Abstract PD1-03. Yonemori K, et al. *Ann Oncol*. 2019;30 suppl 3):iii47-iii64.

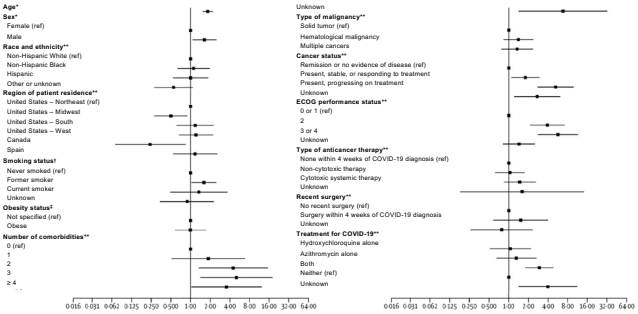
COVID-19 and Breast Cancer

Outpatient Visit Priorities for BC: ESMO Guidance

High Priority	Medium Priority	Low Priority
Postoperative unstable clinical scenario	New diagnosis of non-invasive cancer: *convert as many visits as possible to telemedicine*	Established patients with no new issues: *refer to telemedicine*
New diagnosis of invasive BC	Postoperative visits in patients with no complications	Survivorship follow-up: *refer to telemedicine*
BC diagnosis during pregnancy		Follow-up for patients at high risk of BC
On-treatment patients with new symptoms or side effects: *convert as many visits as possible to telemedicine*		Psychological support visits: *convert to telemedicine*

ESMO = European Society for Medical Oncology
de Azambuja E, et al. *ESMO Open*. 2020;5(Suppl 3):e000793.

30-Day All-Cause Mortality in Patients with COVID-19 and Cancer: A Cohort Study



*Adjusted for sex, smoking status, and obesity; **Adjusted for age, sex, smoking status, and obesity; †Adjusted for age, sex, and obesity; ‡Adjusted for age, sex, and smoking status.
Kuderer NM, et al. *Lancet*. 2020;395(10241):1907-1918.

Considerations for Patients Age ≥ 70 with BC During COVID-19

Disease Setting	Treatment Considerations*
HER2+ disease	• Limit use of neo/adjuvant chemotherapy in small tumors • Use hormonal therapy when also HR+ • Select and modify neo/adjuvant chemotherapy regimens and supportive medications to minimize immunosuppression† • Consider T-DM1, T-DM1 plus pertuzumab, or weekly paclitaxel-trastuzumab (+/-) pertuzumab if neo/adjuvant treatment required • Consider cessation of trastuzumab before 1 year when appropriate or use of subcutaneous administration to limit infusion time
Metastatic disease	• Discuss goals of care • Consider postponement of or dose-reduced CDK 4/6 inhibition until COVID-19 exposure risks decline • Consider oral therapy when appropriate • Select and modify any neo/adjuvant chemotherapy regimens and supportive medications to minimize immunosuppression†

*Consider patient priorities, preferences, concerns, competing comorbidity, life expectancy, frailty, and functional status in decision-making; discuss anticipated benefits and harms of treatments
†Limit steroid use, use growth factor, avoid anthracyclines, modify sequence of therapy
Freedman RA, et al. *J Natl Cancer Inst.* 2020;djaa079.

SMART Goals

Specific, **M**easurable, **A**ttainable, **R**elevant, **T**imely

- Optimize HER2 testing to guide treatment decisions
- Identify HER2 low and HER3+ patients who may benefit from new and emerging therapies
- Sequence new ≥ third-line agents for advanced HER2+ breast cancer
- Tailor breast cancer treatment during the COVID-19 pandemic according to stage, tumor biology, comorbidities, age, patient preferences, and available hospital resources

To Ask a Question

Please click on the *Ask Question* tab and type your question. Please include the faculty member's name if the question is specifically for them.

To Receive Credit

To receive CME/CE credit click on the *Request Credit* tab to complete the post-test and evaluation online.

Be sure to fill in your **ABIM ID number** and **DOB** (MM/DD) on the evaluation so we can submit your credit to ABIM.

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- Complete activity post-test and evaluation at the link provided
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CME Outfitters will send you confirmation of your participation to submit to CMS attesting to your completion of a CME for MIPS Improvement Activity

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IMPROVEMENT ACTIVITY

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for clinical information and
certified educational activities

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TV-116-091620-65

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Activity Title and Faculty:

Targeted Therapy for HER2 and HER3-Positive Breast Cancer: Navigating the Evolving Treatment Landscape

with Sara A. Hurvitz, MD (Moderator); Shanu Modi, MD; Michael F. Press, MD, PhD

Site/Institution Name: ____

Practice Setting: ❑ Office-Based ❑ Hospital ❑ Clinic ❑ Managed Care ❑ Small Group Practice (less than 5) ❑ Large Group Practice (more than 5) ❑ Other: ______________________________

Address: ____

City: ______________________________ State: ________ ZIP: __________________

Site Coordinator: ______________________________ Phone: ______________________________

Fax: ______________________________ Email: ______________________________

Completion Date: _____________ We participated in: ______________________________

Attendee Name (please print)	Please Circle Discipline						
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