TUESDAY, SEPTEMBER 22, 2020

This activity is provided by Med Learning Group.
This activity is co-provided by Ultimate Medical Academy/Complete Conference Management (CCM).
Supported by educational grants from AstraZeneca, Daiichi Sankyo, Inc., and Merck & Co, Inc.

ONQ ONCOLOGY NURSES QUALITY Improvement Series

The Roles of Oncology Nurses in Next-generation Approaches to the Management of Advances HER2-Positive Breast Cancer

FACULTY

Andrea Rodriguez, CRNP, AOCNP
Women's Cancer Center
Magee-Women's Cancer Hospital
University of Pittsburgh Medical Center
Pittsburgh, VA

PROGRAM OVERVIEW

This case-based live virtual activity will cover the treatment and management of patients with HER2-positive breast cancer.

TARGET AUDIENCE

This initiative is designed to meet the educational needs of U.S.-based nurse practitioners, physician assistants, clinical nurse specialists, advanced degree nurses, oncology and hematology nurses, pharmacists, and physicians involved in the management of patients with breast cancer (BC).

LEARNING OBJECTIVES

Upon completion of the program, attendees should be able to:

- Identify the mechanisms underlying resistance to monoclonal antibodies currently approved as for first-line treatment of advanced HER2-positive breast cancer
- Discuss next-generation second-line approaches to the treatment of advanced HER2-positive breast cancer including antibody–drug conjugate technology
- Describe the mechanisms of action and clinical profiles of approved and emerging antibody–drug conjugates used to treat advanced HER2-positive breast cancer in the second-line setting
- Review the various roles for oncology nurses in the management of patients with advanced HER2-positive breast cancer who are treated or eligible for treatment with antibody–drug conjugates

ACCREDITATION STATEMENT

Med Learning Group is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. This CME activity was planned and produced in accordance with the ACCME Essentials.

CREDIT DESIGNATION STATEMENT

Med Learning Group designates this live virtual activity for a maximum of 1.0 *AMA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the live virtual activity.

NURSING CREDIT INFORMATION

Purpose: This program would be beneficial for nurses involved in the management or treatment of patients with breast cancer. **CNE Credits:** 1 ANCC Contact Hour.

CNE ACCREDITATION STATEMENT

Ultimate Medical Academy/CCM is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Awarded 1.0 contact hour of continuing nursing education for RNs and APNs.

ONCC STATEMENT

The program content has been reviewed by the Oncology Nursing Certification Corporation (ONCC) and is acceptable for recertification points.

DISCLOSURE POLICY STATEMENT

In accordance with the Accreditation Council for Continuing Medical Education (ACCME) Standards for Commercial Support, educational programs sponsored by Med Learning Group must demonstrate balance, independence, objectivity, and scientific rigor. All faculty, authors, editors, staff, and planning committee members participating in a MLG-sponsored activity are required to disclose any relevant financial interest or other relationship with the manufacturers of any commercial products and/or providers of commercial services that are discussed in an educational activity.

DISCLOSURE OF CONFLICTS OF INTEREST

Andrea Rodriguez, CRNP, AOCNP has nothing to disclose.

CME Content Review

The content of this activity was independently peer-reviewed.
The reviewer of this activity has nothing to disclose.

CNE Content Review

The content of this activity was peer-reviewed by a nurse reviewer.
The reviewer of this activity has nothing to disclose.

The staff, planners and managers reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME/CE activity:
Matthew Frese, General Manager of Med Learning Group has nothing to disclose.
Christina Gallo, SVP, Educational Development of Med Learning Group has nothing to disclose.
Ana Maria Albino, Senior Program Manager of Med Learning Group has nothing to disclose.
Nicole Longo, DO, FACOI, Director of Medical and Scientific Services of Med Learning Group has nothing to disclose.
Lauren Welch, MA, VP of Accreditation and Outcomes of Med Learning Group has nothing to disclose.
Brianna Hanson, Accreditation and Outcomes Coordinator for Med Learning Group, has nothing to disclose.

DISCLOSURE OF UNLABELED USE

Med Learning Group requires that faculty participating in any CME activity disclose to the audience when discussing any unlabeled or investigational use of any commercial product or device not yet approved for use in the United States.

During this lecture, faculty may mention the use of medications for both FDA-approved and non-approved indications.

ONQ ONCOLOGY NURSES QUALITY Improvement Series

METHOD OF PARTICIPATION

There are no fees for participating and receiving CME/CNE credit for this live virtual activity. To receive CME/CNE credit participants must:

1. Read the CME/CNE information and faculty disclosures
2. Participate in the live virtual activity
3. Complete the posttest and online evaluation form

You will receive your certificate as a downloadable file.

DISCLAIMER

Med Learning Group makes every effort to develop CME activities that are science-based. This activity is designed for educational purposes. Participants have a responsibility to use this information to enhance their professional development in an effort to improve patient outcomes. Conclusions drawn by the participants should be derived from careful consideration of all available scientific information. The participant should use his/her clinical judgment, knowledge, experience, and diagnostic decision-making before applying any information, whether provided here or by others, for any professional use.

For CME questions, please contact: Med Learning Group at info@medlearninggroup.com
Contact this CME provider at Med Learning Group for privacy and confidentiality policy statement information at: www.medlearninggroup.com/privacy-policy/

AMERICANS WITH DISABILITIES ACT

Staff will be glad to assist you with any special needs. Please contact Med Learning Group prior to participating info@medlearninggroup.com

Med Learning Group | UMA

This activity is provided by Med Learning Group.

Complete Conference Management | UMA
A DIVISION OF ULTIMATE MEDICAL ACADEMY

This activity is co-provided by Ultimate Medical Academy/Complete Conference Management (CCM).

This activity is implemented in partnership with the Boston ONS Chapter.

Supported by an educational grant from AstraZeneca and Daiichi Sankyo, Inc.

ONCOLOGY NURSES QUALITY Improvement Series

The Roles of Oncology Nurses in Next-generation Approaches to the Management of Advances HER2-Positive Breast Cancer

I. HER2-positive BC: An Overview

- a. Biology of HER2-positive
- b. Role of HER2 in BC
- c. New HER2 testing guidelines and definition of low HER2
- d. Standard of care treatment options
  - i. AEs associated with first-line mAbs
  - ii. Resistance to first-line mAbs

II. Next-generation Approaches to HER2-positive BC Treatment

- a. Strategies to overcome resistance and decrease toxicity in second-line setting
- b. ADCs, TKIs, mAbs
  - i. Architecture of ADCs
  - ii. MOAs of ADCs

III. Approved and Emerging Second-line Therapeutic Options for the Treatment of HER2-positive BC

- a. Approved
  - i. T-DM1
  - ii. Clinical trial efficacy and safety results
- b. HER2-directed ADCs in clinical development
  - i. Trastuzumab deruxtecan clinical trial efficacy and safety results
  - ii. SYD985 clinical trial efficacy and safety results
  - iii. Clinical trial efficacy and safety results from additional investigational agents
- c. Non-HER2-directed ADCs in clinical development
  - i. Non-HER2 targets
  - ii. Clinical trial efficacy and safety results

IV. Multidisciplinary Oncology Team – Optimizing Patient Care and Survivorship Through Shared Decision Making

- a. Educational strategies for the oncology patient
- b. Ongoing, routine communication throughout treatment – shared decision making and decision aids in practice
- c. Oncology nurses as integral members of the cancer care team

V. Case studies

VI. Conclusions and Questions and Answers

The Roles of Oncology Nurses in Next-Generation Approaches to the Management of Advanced HER2-Positive Breast Cancer

Andrea Rodriguez, CRNP, AOCNP
Women's Cancer Center
Magee-Women's Hospital
University of Pittsburgh Medical Center
Pittsburgh, PA

1

Disclosures

- Andrea Rodriguez, CRNP, AOCNP has nothing to disclose.
- During the course of this lecture, the faculty may mention the use of medications for both US FDA-approved and non-approved indications.

This activity is supported by educational grants from

AstraZeneca and Daiichi Sankyo, Inc.

2

Learning Objectives

- Identify the mechanisms underlying resistance to monoclonal antibodies currently approved for first-line treatment of advanced HER2-positive breast cancer
- Discuss next-generation second-line approaches to the treatment of advanced HER2-positive breast cancer, including antibody-drug conjugate technology
- Describe the mechanisms of action and clinical profiles of approved and emerging antibody-drug conjugates used to treat advanced HER2-positive breast cancer in the second-line setting
- Review the various roles for oncology nurses in the management of patients with advanced HER2-positive breast cancer who are treated or eligible for treatment with antibody-drug conjugates

3

AJCC TNM Staging for Breast Cancer (BC)

T Category	T Criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤20 mm in greatest dimension (subgroups 1mi, 1a, 1b, 1c)
T2	Tumor >20 mm but ≤50 mm in greatest dimension
T3	Tumor >50 mm in greatest dimension
T4	Tumor of any size with direct extension to chest wall and/or skin (ulceration or macroscopic nodules); invasion of dermis alone does not qualify as T4. Subgroups 4a (chest wall extension), 4b (skin ulceration/ipsilateral macroscopic satellite nodules ± edema), 4c (4a & 4b present), 4d (inflammatory carcinoma)

cN Category	cN Criteria
cNX	Regional LN cannot be assessed (eg, previously removed)
cN0	No regional LN metastases (by imaging or clinical examination)
cN1	Metastases to movable ipsilateral Level I, II axillary LN; subgroup 1mi (micrometastases)
cN2	Metastases in ipsilateral Level I, II axillary lymph nodes that are clinically fixed or matted; subgroups 2a (axillary LN), 2b (mammary LN)
cN3	Metastases in ipsilateral infraclavicular (Level III axillary) LN(s) ± Level I, II axillary LN involvement; ***OR*** in ipsilateral internal mammary LN) with Level I, II axillary LN metastases; ***OR*** metastases in ipsilateral supraclavicular LN(s) ± axillary or internal mammary LN involvement; subgroups 3a (ipsilateral infraclavicular LN), 3b (ipsilateral internal mammary and axillary LN), 3c (ipsilateral supraclavicular LN)

M Category	M Criteria
M0	No clinical or radiographic evidence of distant metastases
cM0(i+)	No clinical or radiographic evidence of distant metastases in presence of tumor cells or deposits ≤0.2 mm detected microscopically or by molecular techniques *in a patient without symptoms or signs of metastases*
cM1	Distant metastases detected *clinically or radiographically*
pM1	Any *histologically proven* metastases in distant organs or metastases greater than 0.2 mm (if in non-regional nodes)

AJCC = American Joint Committee on Cancer; LN = lymph node.

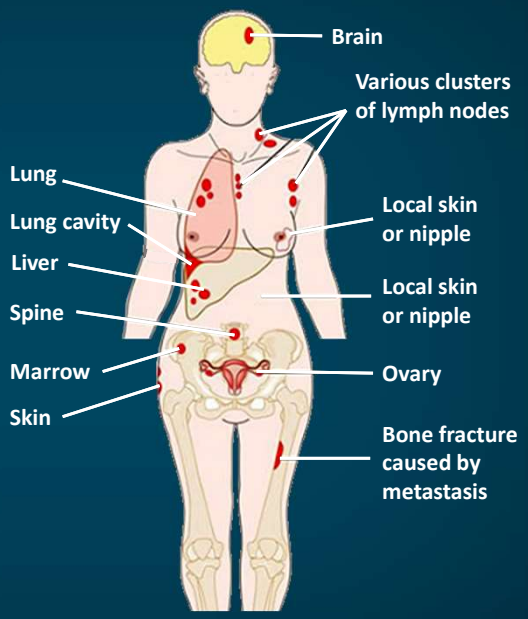
Hortobagyi et al. In: Amin MB, Edge SB, Greene FL, et al (eds.). *AJCC Cancer Staging Manual, 8th edition.* New York: Springer, 2017.

4

NL8

Advanced Breast Cancer

- M1 = metastatic
- Stage IV
- 20–30% of early stage will metastasize
- 26% of new breast cancers are metastatic at diagnosis
  - De novo
  - Statistics based on de novo as recurrences hard to track
- 5-year survival rate improving for women with de novo metastatic BC
  - 1994 = 18%
  - 2012 = 36%



Metastatic Breast Cancer Network (MBCN). Incidence and incidence rates. (http://mbcn.org/incidence-and-incidence-rates/). Mariotto AB, et al. *Cancer Epidemiol Biomarkers Prev.* 2017;26:809-815. Image (https://breast360.org/news/2016/04/01/initial-surgery-survival-metastatic-breast). URLs accessed 8/11/2020.

5

Prognostic Biomarkers

Biomarkers			
Hormone receptor status		HER2	
ER	PR	Immunochemistry	in situ hybridization (ISH)
Determined primarily to identify benefit from hormonal therapy		ERBB2 testing	Fluorescence (FISH), Chromogenic (CISH) Silver-enhanced (SISH)
Receptor status is a weak prognostic factor		Protein overexpression usually due to gene amplification (correlates in >95% cases)	Most assays = CEP17 to determine ratio of HER2 signals to copies of chromosome 17
Substantial survival benefit with endocrine therapy among ER+ tumors	True ER–/PR+ tumors are rare	Overexpression is prognostic and predictive	Some assays = single probe to detect the number of present gene copies

ER = estrogen receptor; PR = progesterone receptor; HER2 = human epidermal growth factor receptor 2; FISH = fluorescence ISH; CISH = chromogenic ISH; SISH = silver-enhanced ISH; CEP17 = chromosome 17 centromere.

College of American Pathologists. Breast biomarkers 1.2.0.1. 2018. (https://documents.cap.org/protocols/cp-breast-biomarker-20-1400.pdf). Accessed 8/11/2020.

6

Slide 5

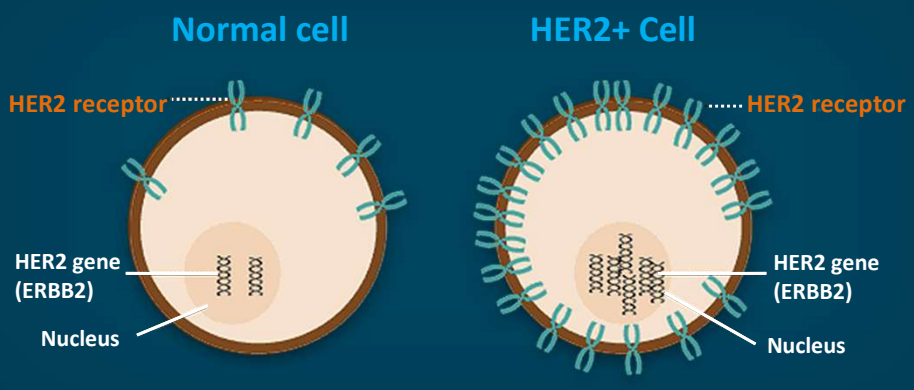
NL8 4th bullet point updated from 6% to 26% (Mariotto)
Nicole Longo, 8/21/2020

HER2-Positive Breast Cancer: An Overview

7

Biology of HER2-Positive Breast Cancer

HER2 protein overexpression allows uncontrolled growth of cells



Amplification—multiple HER2 genes
Overexpression—many HER2 receptors

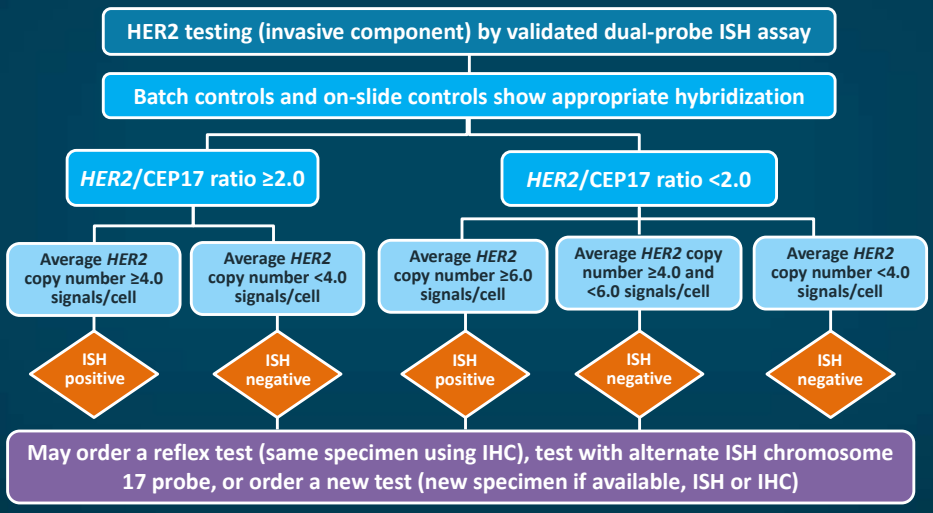
ERBB2 = Erb-B2 receptor tyrosine kinase 2, ie, HER2.

Wilson C. *J Adv Pract Oncol.* 2016 (www.advancedpractitioner.com/narratives/her2/). Accessed 8/11/2020.

8

Algorithm for Evaluating *HER2* Gene Amplification

In situ hybridization assay of the invasive component of a BC specimen using a dual-signal HER2 gene assay (dual-probe ISH)



IHC = immunohistochemistry.

Wolff AC, et al. *J Clin Oncol.* 2018;36:2105-2122.

9

Role of HER2 Gene in Breast Cancer Development

- HER2-positive breast cancer is more aggressive
  - More likely to recur
    - Usually within 5 years
- Provides a target for treatment
  - Trastuzumab was the first targeted agent
- High propensity for brain metastases

Gridhar K. Mayo Clinic website. 2020 (www.mayoclinic.org/breast-cancer/expert-answers/faq-20058066). URL accessed 8/11/2020. Loibl S, Gianni L. *Lancet.* 2017;389(10087):2415-2429. Maurer C, et al. *ESMO Open.* Yu S, et al. *Exp Hematol Oncol.* 2017;6:31. 2018;3:e000440. Wangchinda P, Ithimakin S. *World J Surg Oncol.* 2016;14:233.

10

Nursing Implications—HER2+ BC Basics

- 20% of breast cancers are HER2-positive
- Common metastatic sites
  - lung, liver, brain
- 5-year relative survival dependent on stage at diagnosis (SEER 18 2010-2016) NL9

Subtype	Localized	Regional	Distant
HR+/HER2+	98.7%	89.5%	43.5%
HR-/HER2+	96.1%	81.7%	36.8%

- Brain metastases
  - Hardest to treat/control
  - Likely cause of death in HER2-positive mBC

mBC = metastatic breast cancer.

Gridhar K. Mayo Clinic website. 2020 (www.mayoclinic.org/breast-cancer/expert-answers/faq-20058066). National Cancer Institute (NCI). Metastatic cancer. 2017 (www.cancer.gov/types/metastatic-cancer). URLs accessed 8/11/2020. NCI. Cancer Stat Facts: Female Breast Cancer Subtypes. 2020 (https://seer.cancer.gov/statfacts/html/breast-subtypes.html). Accessed August 21, 2020. Nieder C. *Lancet Oncol.* 2013;14:e2-e3. Montemurro F, et al. *Annal Oncol.* 2020;S0923-7534(20)39930-0.

11

Anti-HER2 Therapies

- **Monoclonal antibodies**
  - Bind to HER2 and block activation
    - Trastuzumab, pertuzumab, margetuximab, biosimilars, and subcutaneous biosimilars
- **Tyrosine kinase inhibitors**
  - Binds to EGFR inside cell to inhibit growth
    - Lapatinib, neratinib, tucatinib
- **Antibody-drug conjugates**
  - Binds to HER2 then releases the chemotherapy portion (payload)
  - trastuzumab emtansine (T-DM1), trastuzumab deruxtecan (DS 8201), trastuzumab-duocarmycin (SYD985)

EGFR = epidermal growth factor receptor.

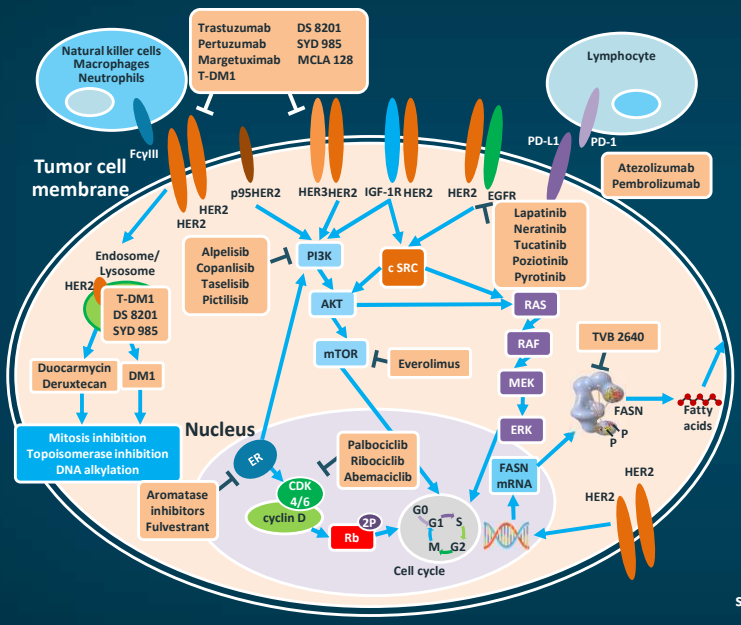
Yu S, et al. *Exp Hematol Oncol.* 2017;6:31. Broderick JM. *OncLive.* 2019. (www.onclive.com/view/fda-approval-sought-for-margetuximab-in-her2-metastatic-breast-cancer). Segovia-Mendoza M, et al. *Am J Cancer Res.* 2015;5: 2531-2561. National Center for Biotechnology Information (NCBI). Tucatinib. 2020. (https://pubchem.ncbi.nlm.nih.gov/compound/Tucatinib). Modi S, et al. *N Engl J Med.* 2020;382: 610-621. NCI. 2019. (www.cancer.gov/news-events/cancer-currents-blog/2019/kadcyla-fda-breast-her2-adjuvant). Costa RLB, Czerniecki BJ. *NPJ Breast Cancer.* 2020;6:10. URLs accessed 8/11/ 2020.

12

Slide 11

NL9 3rd bullet point amended (previous 2-5 year life expectancy) in order to allow for reference citation.
Nicole Longo, 8/21/2020

Signaling Pathways



CDK 4/6 = cyclin-dependent kinase 4/6; DM1 = derivative of maytansine 1; DNA = deoxyribonucleic acid; FASN = fatty-acid synthase; IGF-1R = insulin-like growth factor 1 receptor; mRNA = messenger ribonucleic acid; mTOR = mammalian target Of rapamycin; PI3K = phosphoinositide 3-kinase; PD1 = programmed death 1; PD-L1 = PD1 ligand; Rb = retinoblastoma protein.

Vernieri C, et al. *Crit Rev Oncol Hematol.* 2019;139:53-66.

13

Standard-of-Care Treatment Options: First-line mAbs

Trastuzumab	Pertuzumab	Margetuximab	Biosimilars	Combinations
Anti-HER2 antibody • Binds to HER2 receptor, causing G1 arrest • Downregulates growth signal activation • Blocks ligand-independent HER2 activation • Recruits immune system: ADCC	**Anti-HER2 antibody** • Dimerization inhibitor • Interrupts proliferation and survival pathways by preventing HER2/HER3 binding • Blocks ligand-dependent HER2 activation	**Anti-HER2 antibody (Investigational)** • Fc optimization • Modulation of HER2 signaling • Tumor destruction via ADCC	**Biosimilar to *trastuzumab:*** • Trastuzumab-dkst • Trastuzumab-pkrb • Trastuzumab-dttb • Trastuzumab-qyyp • Trastuzumab-anns	• Trastuzumab + hyaluronidase • Trastuzumab + pertuzumab + hyaluronidase

mAb = monoclonal antibody; ADCC = antibody-dependent cellular cytotoxicity.

Trastuzumab (Herceptin®). Proposed mechanism of action (MOA) (www.herceptin.com/hcp/treatment/moa). Gajria D, Chandarlapaty S. *Expert Rev Anticancer Ther.* 2011;11:263-275. Pertuzumab (Perjeta®). MOA and safety (www.perjeta.com/hcp/breast-cancer/about-perjeta.html). Margetuximab. (www.macrogenics.com/margetuximab-anti-her2/). American Cancer Society (ACS). Targeted therapy, 2020 (www.cancer.org/cancer/breast-cancer/treatment/ targeted-therapy-for-breast-cancer.html). ACS. mAbs, 2019 (www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/monoclonal-antibodies.html). Accessed 8/11/2020.

14

Standard-of-Care Treatment Options

Systemic treatment of recurrent or stage IV (M1) disease: ER– and/or PR+; HER2+

Systemic therapy + HER2-targeted therapy with:

- Pertuzumab + trastuzumab + taxane (preferred)

OR

- Ado-trastuzumab emtansine (T-DM1)

OR

- Fam-trastuzumab deruxtecan-nxki

OR

- Trastuzumab + chemotherapy

OR

Endocrine therapy + HER2-targeted therapy (if premenopausal, consider ovarian ablation or suppression)

OR

Other HER2-targeted therapies

→ Continue therapy until progression of unacceptable toxicity

National Comprehensive Cancer Network (NCCN). NCCN guidelines version 5.2020. Invasive breast cancer. 2020. (www.nccn.org/professionals/physician_gls/pdf/breast.pdf). Accessed 8/11/2020.

15

Adverse Events (AEs) Associated with First-Line mAbs

Adverse events after the discontinuation of docetaxel in safety population.*

Adverse Events	Control Group (N=261)	Pertuzumab Group (N=306)
Most common events of any grade — no. of patients (%)		
Alopecia	6 (2.3)	5 (1.6)
Diarrhea	37 (14.2)	86 (28.1)
Neutropenia	13 (5.0)	10 (3.3)
Nausea	30 (11.5)	39 (12.7)
Fatigue	25 (9.6)	41 (13.4)
Rash	21 (8.0)	56 (18.3)
Asthenia	23 (8.8)	41 (13.4)
Decreased appetite	14 (5.4)	22 (7.2)
Peripheral edema	32 (12.3)	28 (9.2)
Vomiting	17 (6.5)	30 (9.8)
Myalgia	19 (7.3)	25 (8.2)
Mucosal inflammation	4 (1.5)	11 (3.6)
Headache	32 (12.3)	52 (17.0)
Constipation	18 (6.9)	17 (5.6)
Upper respiratory tract infection	32 (12.3)	56 (18.3)
Pruritus	15 (5.7)	42 (13.7)
Febrile neutropenia	0	0
Dry skin	10 (3.8)	10 (3.3)
Muscle spasm	6 (2.3)	24 (7.8)

Swain S, et al. *N Engl J Med.* 2015;372:724-734.

*Data for patients receiving ≥1 dose of study drug after completing docetaxel treatment.

16

Sources of Resistance to First-Line mAbs

- Escaping antibody-dependent cell-mediated cytotoxicity
- Expression of other TKRs and proteins in the cellular membrane
- Crosstalk between estrogen receptor and HER2 pathways
- Intrinsic alterations in HER2
- Aberrant activation of PI3K/Akt/mTOR pathway
- Alterations in apoptosis and cell-cycle control

TKR = tyrosine kinase receptor; PI3K = phosphoinositide 3-kinase.

Luque-Cabal M, et al. *Clin Med Insights Oncol.* 2016;10(suppl 1):21-30

17

Nursing Implications—First-Line mAbs

- Monitor LVEF
  - subclinical and clinical cardiac failure, presenting as CHF or decreased LVEF
- Side-effect management
  - GI
  - Fatigue
- HER2-positive BC is heterogenous
- Some will respond well for long periods, others will not
  - Focus of research

LVEF = left ventricular ejection fraction; CHF = congestive heart failure; GI = gastrointestinal.

Buckley NE, et al. *Sci Rep.* 2016; 6:23383. ACS. mAb side effects. 2019 (www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/monoclonal-antibodies.html). Trastuzumab (Herceptin®) PI, 2018 (www.gene.com/download/pdf/herceptin_prescribing.pdf). Pertuzumab (Perjeta®) PI, 2020 (www.gene.com/download/pdf/perjeta_prescribing.pdf). All URLs accessed 8/11/2020. Luque-Cabal et al. *Clin Med Insights Oncol.* 2016;10(suppl 1):21-30.

18

Next-Generation Approaches to HER2-Positive Breast Cancer Treatment

19

Overcoming Resistance in Second-Line Setting

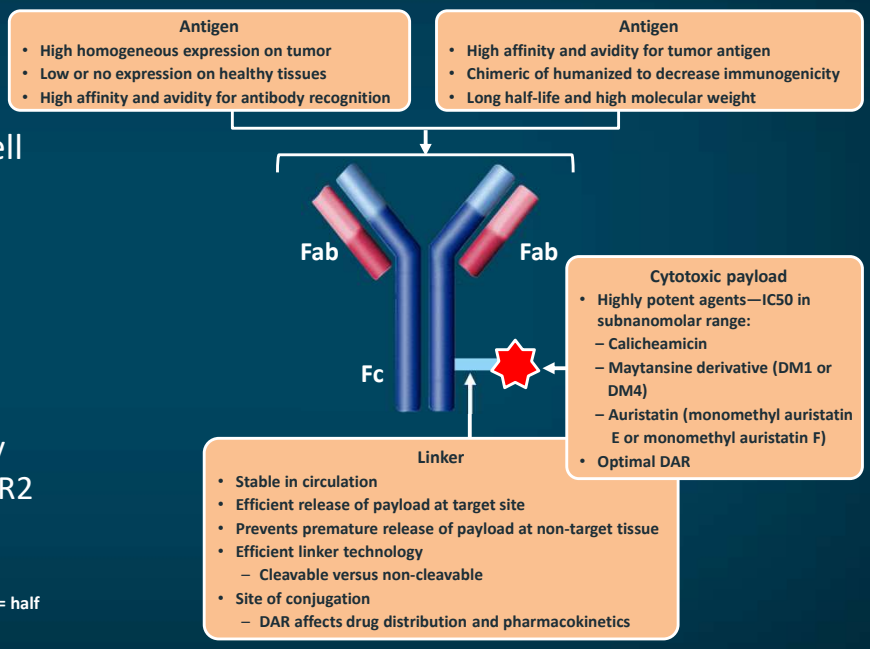
- HER2 resistance can be reversed by acting on the escape route
  - Antibody-drug conjugate
- Non-cross-resistant drugs
- Combination therapy
- Sequential therapy

D'Souza A, et al. *J Hematol Oncol.* 2018;11:80. Lavaud P, Andre F. *BMC Med.* 2014:12:132. Mohd Sharial MSN, et al. *Ann Oncol.* 2012;23:3007-3016.

20

Antibody-Drug Conjugates (ADCs)

- Binds to HER2
- Releases payload in cancer cell
  - Improves efficacy
  - Decreases toxicity
- 2nd generation is membrane permeable
  - Can leave cell and kill nearby cancer cells regardless of HER2 expression

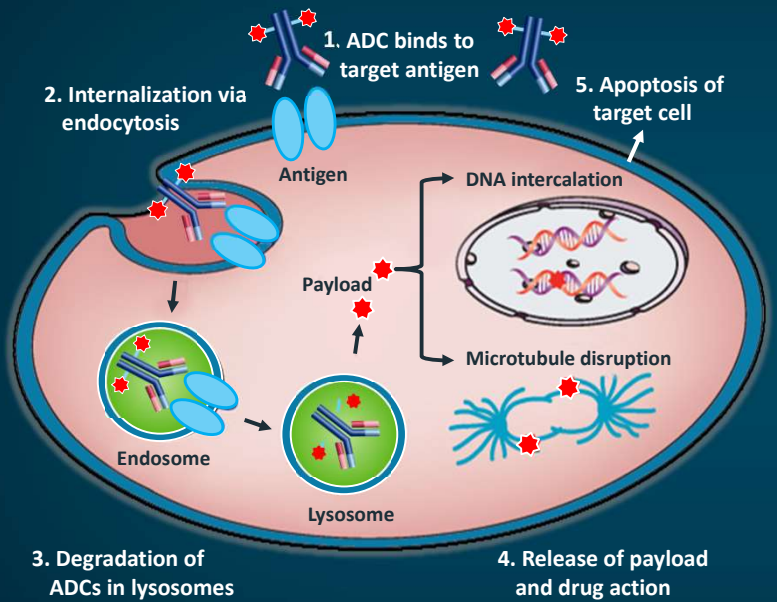


Fab = antigen-binding fragment; Fc = constant fragment; IC50 = half maximal inhibitory concentration; DAR = drug-antibody ratio.

Chau CH, et al. *Lancet*. 2019;394:793-804.

21

MOA of ADCs



Mechanisms of resistance in:

1. ADC binding to target antigen
   - Target downregulation
   - Loss of antigen expression
   - Mutated antigen affects target recognition
2. Receptor-mediated ADC internalization:
   - Reduced cell-surface trafficking causing insufficient ADC internalization
   - Defects in internalization and trafficking pathways
3. Degradation of ADCs in lysosomes
   - Impaired lysosomal function (eg, acidification)
   - Reduced lysosomal proteolytic activity
4. Payload release to cytosol
   - Loss of lysosomal transporter expression (eg, SLC46A3)
   - Overexpression of drug efflux transporters
5. Apoptosis of target cell
   - Loss of bystander effect

MOA = mechanism of action; SLC46A3 = solute carrier family 46 member 3.

Chau CH, et al. *Lancet*. 2019;394:793-804.

22

Mitigating Toxicity with Second-Line Therapy

Adverse Events in the Safety Population		
	Trastuzumab Emtansine (T-DM1) (N = 490)	
Adverse event, no. (%)	Events—Any Grade	Events—Grade 3 or Above
Any event	470 (95.9)	200 (40.8)
Specific events		
Diarrhea	114 (23.3)	8 (1.6)
PPE	6 (1.2)	0
Vomiting	93 (19.0)	4 (0.8)
Neutropenia	29 (5.9)	10 (2.0)
Hypokalemia	42 (8.6)	11 (2.2)
Fatigue	172 (35.1)	12 (2.4)
Nausea	192 (39.2)	4 (0.8)
Mucosal inflammation	33 (6.7)	1 (0.2)
Anemia	51 (10.4)	13 (2.7)
Elevated ALT	83 (16.9)	14 (2.9)
Elevated AST	110 (22.4)	21 (4.3)
Thrombocytopenia	137 (28.0)	63 (12.9)

PPE = palmar-plantar erythrodysesthesia; ALT = alanine aminotransferase; AST = aspartate aminotransferase.

Verma S, et al. *N Engl J Med.* 2012;367:1783-1791.

23

Nursing Implications—ADCs

- Combination chemotherapy/monoclonal antibody
- Lock and key
  - HER2 protein (lock) and HER2 antibody (key)
  - Unlock membrane to allow chemotherapy into the cell
- Lower dose of chemotherapy when targeted
  - Fewer side effects
- Monitor for toxicities of mAB and chemotherapy
  - Monitor LFTs, CBC
- Fatigue, quality of life, goals
- Self-management patient education

LFT = liver-function test; CBC = complete blood (cell) count.

Pondé N, et al. *Curr Treat Options Oncol.* 2019;20:37. Birrer MJ, et al. *J Natl Cancer Inst.* 2019;111:538-549. Bourdeanu L, Luu T. *Clin J Oncol Nurs.* 2013;17:E58-62. Tariman JD, et al. *Clin J Oncol Nurs.* 2016;20:560-563.

24

Approved and Emerging Second-line Therapeutic Options for HER2-positive Breast Cancer

25

T-DM1

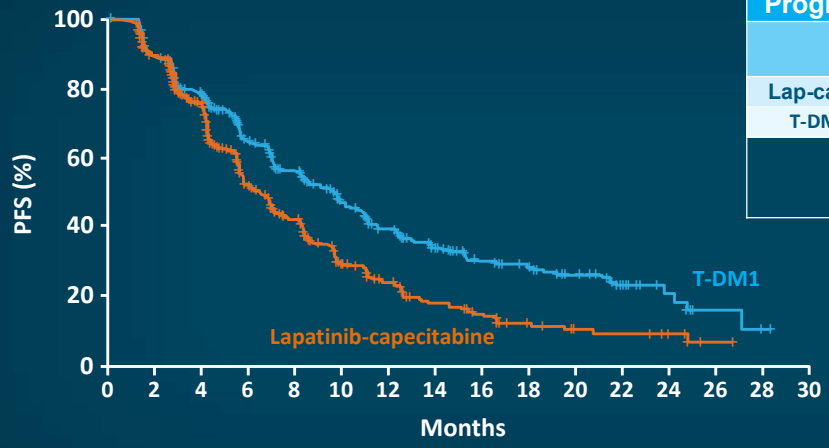
- Trastuzumab + emtansine
- Emtansine too toxic on its own
  - Lower dose when targeted
- T-DM1 binds to HER2 and releases emtansine
- Not membrane-permeable
  - Only effective on HER2-expressing cells

Verma S, et al. *N Engl J Med.* 2012;367:1783-1791. Bourdeanu L, Luu T. *Clin J Oncol Nurs.* 2013;17:E58-62. Pondé N, et al. *Curr Treat Options Oncol.* 2019;20:37.

26

T-DM1: Progression-Free Survival

PFS (ITT population)



Progression-Free Survival		
	mPFS mo	No. of Events
Lap-cap	6.4	304
T-DM1	9.6	265
Stratified HR = 0.65 (95% CI, 0.55–0.77) ***P* <.001**		

No. at risk																
Lap-Cap	496	404	310	176	129	73	53	35	25	14	9	8	5	1	0	0
T-DM1	495	419	341	236	183	130	101	72	54	44	30	18	9	3	1	0

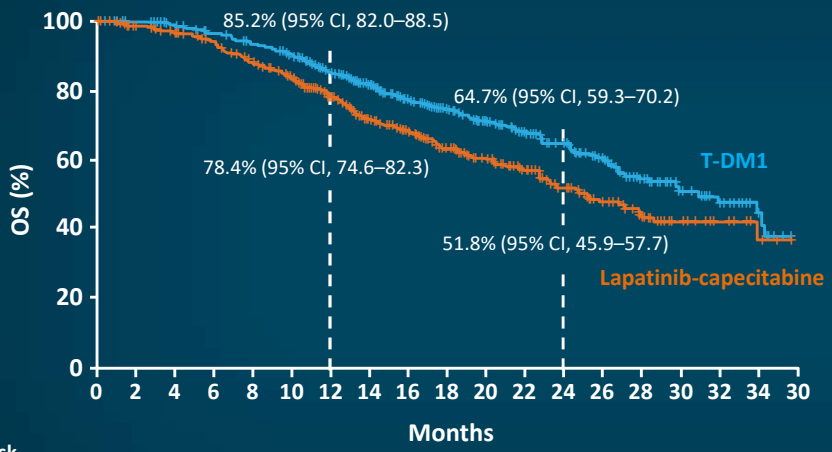
PFS = progression-free survival; mPFS = median PFS, mo = month(s); ITT = intention to treat; HR = hazard ratio; CI = confidence interval; Lap = lapatinib; Cap = capecitabine.

Verma S, et al. *N Engl J Med.* 2012;367:1783-1791.

27

T-DM1: Overall Survival

OS (second interim analysis)



Overall Survival		
	mOS mo	No. of Events
Lap-Cap	25.1	182
T-DM1	30.9	149
Stratified HR = 0.68 (95% CI, 0.55–0.85) ***P* <.001** Efficacy stopping boundary *P*= .0037 or HR = 0.73		

No. at risk																	
Lap-Cap	496	471	453	435	403	368	297	240	204	159	133	110	86	63	45	27	17	7	4
T-DM1	495	485	474	457	439	418	349	293	242	197	164	136	111	86	62	38	28	13	5

OS = overall survival; mOS = median OS.

Verma S et al. *N Engl J Med.* 2012;367: 1783-1791

28

T-DM1 Safety

Adverse Events in the Safety Population				
	Lapatinib + Capecitabine n = 488		Trastuzumab Emtansine (T-DM1) n = 490	
	Grade			
Adverse event, no. (%)	Any	≥3	Any	≥3
Any event	477 (97.7)	278 (57.0)	470 (95.9)	200 (40.8)
Specific events				
Diarrhea	389 (79.7)	101 (20.7)	114 (23.3)	8 (1.6)
PPE	283 (58.0)	80 (16.4)	6 (1.2)	0
Vomiting	143 (29.3)	22 (4.5)	93 (19.0)	4 (0.8)
Neutropenia	42 (8.6)	21 (4.3)	29 (5.9)	10 (2.0)
Hypokalemia	42 (8.6)	20 (4.1)	42 (8.6)	11 (2.2)
Fatigue	136 (27.9)	17 (3.5)	172 (35.1)	12 (2.4)
Nausea	218 (44.7)	12 (2.5)	192 (39.2)	4 (0.8)
Mucosal inflammation	93 (19.1)	11 (2.3)	33 (6.7)	1 (0.2)
Anemia	39 (8.0)	8 (1.6)	51 (10.4)	13 (2.7)
Elevated ALT	43 (8.8)	7 (1.4)	83 (16.9)	14 (2.9)
Elevated AST	46 (9.4)	4 (0.8)	110 (22.4)	21 (4.3)
Thrombocytopenia	12 (2.5)	1 (0.2)	137 (28.0)	63 (12.9)

Verma S et al. *N Engl J Med.* 2012;367: 1783-1791

29

Nursing Implications—T-DM1

- T-DM1 every 3 weeks until progression or toxicity
- Thrombocytopenia—assess for signs of bleeding at each visit
- Transaminitis—monitor LFTs
- Fatigue strategies
- Most side effects grade 1–2
- Grade 3 may require dose delay or reduction

Trastuzumab emtansine (Kadcyla®) PI, 2019 (www.gene.com/download/pdf/kadcyla_prescribing.pdf). Accessed 8/11/2020.

30

Tyrosine Kinase Inhibitors (TKIs)

Lapatinib	Neratinib	Tucatinib
• Binds to HER2 and EGFR inside cell • Inhibits tumor cell growth	• Pan-HER and EGFR binding inside cell • Inhibits tumor cell growth • Crosses BBB	• Inhibits phosphorylation of HER2 and HER3, inhibiting tumor cell growth • More selective to HER2 • Crosses BBB

BBB = blood brain barrier.

Lapatinib (Tykerb®). MOA (www.hcp.novartis.com/products/tykerb/her2-abc-mbc/mechanism-of-action/). Neratinib (Nerlynx®) tablets. MOA (https://nerlynx.com/hcp/mechanism). Tucatinib (Tukysa®) PI, 2020 (https://seagendocs.com/TUKYSA_Full_Ltr_Master.pdf). NCI. mHER+BC (www.cancer.gov/news-events/cancer-currents-blog/2020/tucatinib-trastuzumab-deruxtecan-her2-positive-metastatic-breast-cancer). All URLs accessed 8/11/2020. OncLive. 2020. (https://www.onclive.com/view/tucatinib-lead-researcher-explains-significance-of-fda-approval-in-her2-positive-breast-cancer). Accessed August 21, 2020.

31

Neratinib + Capecitabine

- Neratinib + capecitabine in 3rd line
  - vs lapatinib + capecitabine
- Risk of progression or death decreased by 24%
- PFS = 8.8 months vs 6.6 months with lapatinib + capecitabine
- Grade 3 diarrhea 24% vs 13%
- Otherwise similar adverse events
  - Higher capecitabine dose in lapatinib arm

Helwick C. *The ASCO Post*. 2019. (www.ascopost.com/issues/july-10-2019/nala-trial/). Accessed 8/11/2020.

32

Tucatinib + Trastuzumab + Capecitabine

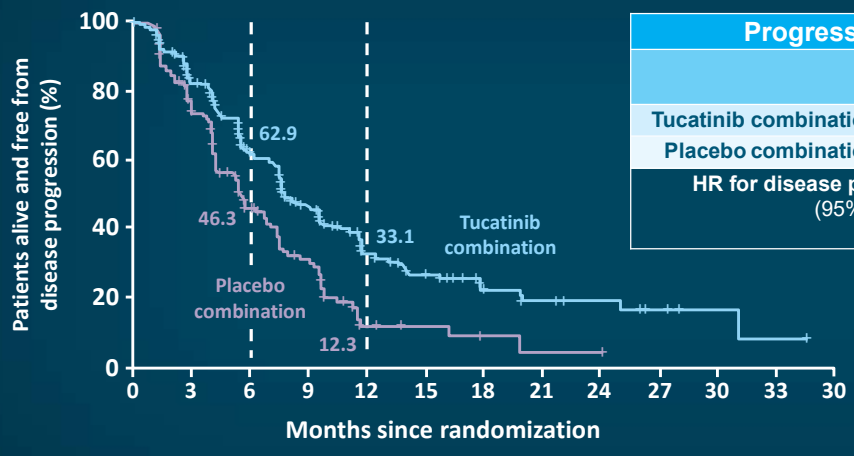
- Patients previously treated with trastuzumab, pertuzumab, and trastuzumab emtansine were randomly assigned to tucatinib + trastuzumab + capecitabine vs placebo + trastuzumab + capecitabine
- In the tucatinib-combination group:
  - Lower risk of disease progression or death among patients with brain metastases
  - 4.5 month longer overall survival
  - Patients with brain metastases got the same benefit as those without

Murthy RK, et al. *N Engl J Med.* 2020;382:597-609.

33

Tucatinib + Trastuzumab + Capecitabine: PFS

Kaplan-Meier Estimates of PFS



Progression-Free Survival		
	Events/ Patients	mPFS (95% CI) mo
Tucatinib combination	178/320	7.8 (7.5–9.6)
Placebo combination	97/160	5.6 (4.2–7.1)

HR for disease progression or death = 0.54
(95% CI, 0.42–0.71)
***P* <.001**

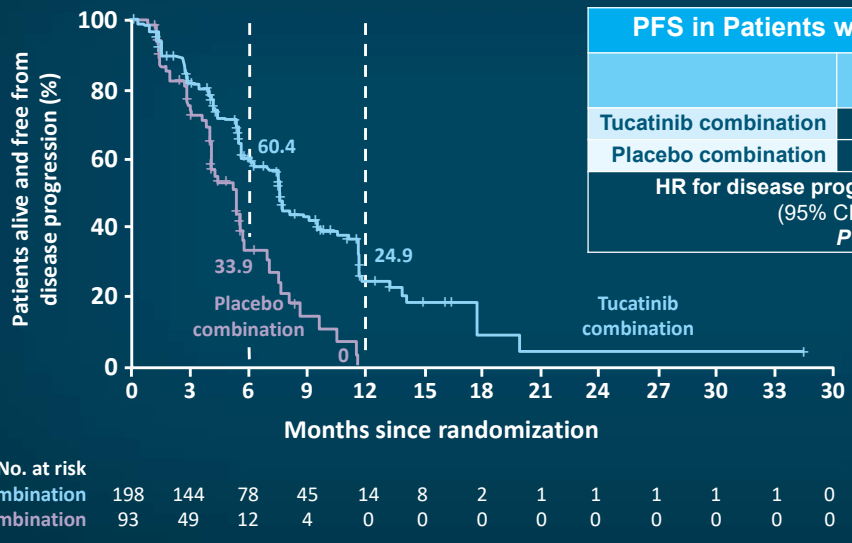
No. at risk													
Tucatinib combination	320	235	152	98	40	29	15	10	8	4	2	1	0
Placebo combination	160	94	45	27	6	4	2	1	1	0	0	0	0

Murthy RK, et al. *N Engl J Med.* 2020;382:597-609.

34

Tucatinib + Trastuzumab + Capecitabine: PFS in Brain Metastases

Kaplan-Meier estimates of PFS among patients with brain metastases



PFS in Patients with Brain Metastases		
	Events/ Patients	mPFS (95% CI) mo
Tucatinib combination	106/198	7.6 (6.2–9.5)
Placebo combination	51/93	5.4 (4.1–5.7)
HR for disease progression or death = 0.48 (95% CI, 0.34–0.69) *P* <.001		

No. at risk													
Tucatinib combination	198	144	78	45	14	8	2	1	1	1	1	1	0
Placebo combination	93	49	12	4	0	0	0	0	0	0	0	0	0

Murthy RK et al. *N Engl J Med.* 2020;382:597-609.

35

Tucatinib + Capecitabine + Trastuzumab: Safety

Most Common Adverse Events*				
	Tucatinib Combination Group n = 404		Placebo Combination Group n = 197	
	Grade			
Adverse event, no. (%)	Any	≥3	Any	≥3
Any event	401 (99.3)	223 (55.2)	191 (97.0)	96 (48.7)
Specific events				
Diarrhea	327 (80.9)	52 (12.9)	105 (53.3)	17 (8.6)
PPE syndrome	256 (63.4)	53 (13.1)	104 (52.8)	18 (9.1)
Nausea	236 (58.4)	15 (3.7)	86 (43.7)	6 (3.0)
Fatigue	182 (45.0)	19 (4.7)	85 (43.1)	8 (4.1)
Vomiting	145 (35.9)	12 (3.0)	50 (25.4)	7 (3.6)
Stomatitis	103 (25.5)	10 (2.5)	28 (14.2)	1 (0.5)
Decreased appetite	100 (24.8)	2 (0.5)	39 (19.8)	0
Headache	87 (21.5)	2 (0.5)	40 (20.3)	3 (1.5)
Elevated AST	86 (21.3)	18 (4.5)	22 (11.2)	1 (0.5)
Elevated ALT	81 (20.0)	22 (5.4)	13 (6.6)	1 (0.5)

* Listed are adverse events reported in at least 20% of the patients in the tucatinib-combination group. Safety analyses included all the patients who received at least one dose of any trial drug or placebo.

Murthy RK, et al. *N Engl J Med.* 2020;382:597-609.

36

Nursing Implications—Tucatinib

- Diarrhea
  - Grading
  - Diet—low fiber, low fat, avoid spicy foods
  - Loperamide as needed, prophylaxis not needed
- Nausea
- Fatigue
- Monitor LFTs and renal function
- Oral therapy compliance/adherence
- Used in patients with brain metastases

Murthy RK, et al. *N Engl J Med.* 2020;382:597-609. Tipton JM. *Clin J Oncol Nurs.* 2015;19(3 suppl):37-40. Benson AB, et al. *J Clin Oncol.* 2004;22:2918-2926.

37

Trastuzamab Deruxtecan

- Accelerated FDA approval
  - DESTINY-Breast01 study
  - Must continue to study, especially risk and mitigation strategies for interstitial lung disease
- 3rd-line metastatic HER2 positive
  - Already received trastuzumab, pertuzumab, and T-DM1
- Deruxtecan
  - Topoisomerase I inhibitor
- Membrane permeable
  - Bystander effect
- Increased drug-to-antibody ratio (8:1 vs 3.5:1 in T-DM1)

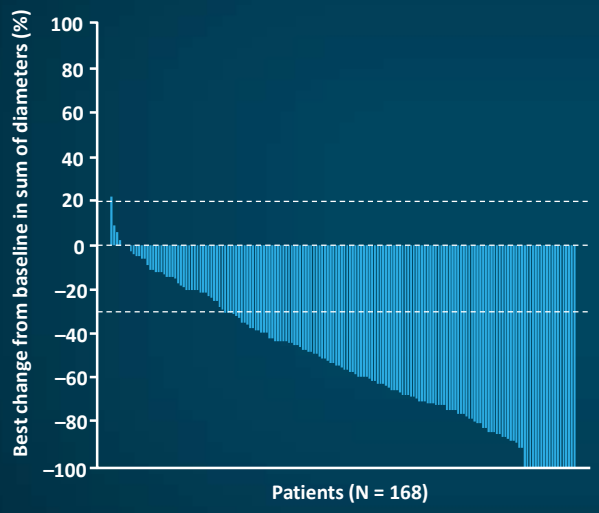
FDA = US Food and Drug Administration.

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

38

Trastuzamab Deruxtecan

Change from baseline in tumor size



Objective response in prespecified subgroups

Subgroup	Events/ Patients	Objective response (95% CI) %
All patients	112/184	61 (53–68)
Previous pertuzumab use		
Yes	78/121	64 (55–73)
No	34/63	54 (41–67)
Hormone receptors		
Positive	56/97	58 (47–68)
Negative	55/83	66 (55–76)
No. of regimens excluding HT		
≥3	99/167	59 (51–67)
<3	13/17	76 (50–93)
Brain metastasis		
Yes	14/24	58 (37–78)
No	98/160	61 (53–69)
Presence of visceral disease		
Yes	102/169	60 (53–68)
No	10/15	67 (38–88)
Geographic region		
Asia	37/63	59 (46–71)
North America	33/53	62 (48–75)
Europe	42/68	62 (49–73)
ECOG performance-status score		
0	67/102	66 (56–75)
1	45/81	56 (44–67)
Trastuzumab deruxtecan therapy immediately after T-DM1		
Yes	36/56	64 (50–77)
No	76/128	59 (50–68)
HER2- positive tumor		
IHC 3+	97/154	63 (55–71)
IHC 1+ or 2+, or ISH-positive	13/28	46 (28–66)

HT = hormone therapy; ECOG = Eastern Cooperative Oncology Group.

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

39

Trastuzumab Deruxtecan: LVEF

Left ventricular ejection fraction decreased in 3 patients

- Asymptomatic
- Recovery after an interruption in study treatment; no patients discontinued treatment because of lowered LVEF
- No LVEF <40%
- No decrease >20%

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

40

Trastuzamab Deruxtecan: safety

Adverse Events in Overall Population of 184 Patients			
	Any Grade	Grade 3	Grade 4
Any AE	183 (99.5)	89 (48.4)	7 (3/8)
Nausea	143 (77.7)	14 (7.6)	0
Fatigue	91 (49.5)	11 (6.0)	0
Alopecia	89 (48.4)	1 (0.5)	0
Vomiting	84 (45.7)	8 (4.3)	0
Constipation	66 (35.9)	1 (0.5)	0
Decreased neutrophil count/neutropenia	64 (34.8)	36 (19.6)	2 (1.1)
Decreased appetite	57 (31.0)	3 (1.6)	0
Anemia	55 (29.9)	15 (8.2)	1 (0.5)
Diarrhea	54 (29.3)	5 (2.7)	0
Decreased white-cell count	39 (21.2)	11 (6.0)	1 (0.5)
Decreased platelet count	39 (21.2)	7 (3.8)	1 (0.5)
Headache	36 (19.6)	0	0
Cough	35 (19.0)	0	0
Abdominal pain	31 (16.8)	2 (1.1)	0
Decreased lymphocyte count	26 (14.1)	11 (6.0)	1 (0.5)
AEs of special interest			
Interstitial lung disease	25 (13.6)	1 (0.5)	0
Prolonged QT interval	9 (4.9)	2 (1.1)	0
Infusion-related reaction	4 (2.2)	0	0
Decreased LVEF	3 (1.6)	1 (0.5)	0

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

41

Trastuzamab Deruxtecan and Interstitial Lung Disease (ILD)

- 25 patients (13.6%) had interstitial lung disease
  - 4 deaths attributed to ILD
- Median time to onset of ILD was 193 days (42–535 days)
- In follow-up
  - 7 recovered
  - 2 recovering
  - 10 ongoing ILD
  - 4 died
  - 2 unknown
- Recovery onset median 34 days (3–179)

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

42

Trastuzamab Deruxtecan and ILD

- **Early detection**
- Suspect ILD
  - Dyspnea
  - Fever
  - Cough
- CT scan and pulmonology consult
- Dose interruption regardless of grade
- Glucocorticoids, dose reductions

CT = computed tomography.

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

43

Nursing Implications—Trastuzumab Deruxtecan and ILD

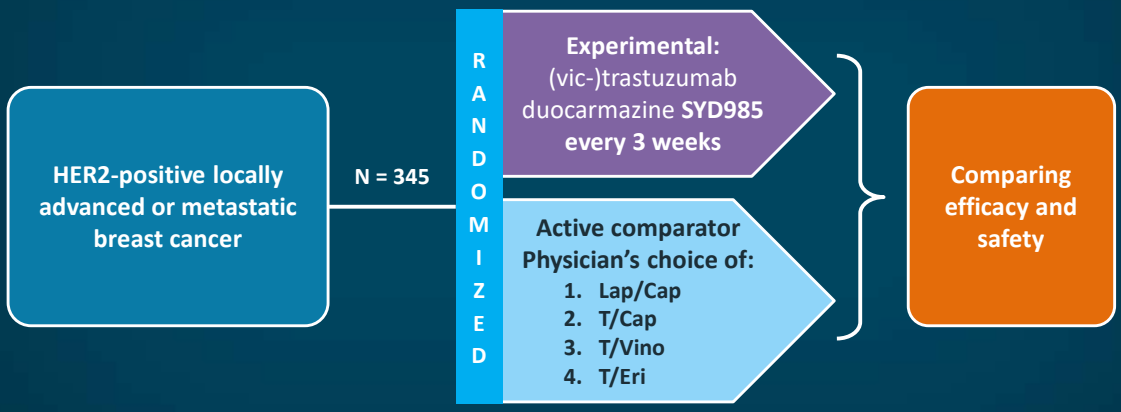
- Monitor for dyspnea, cough, fever at every encounter
- High suspicion for ILD always
- Patients with ILD may or may not recover
- Neutropenia, anemia, fatigue

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

44

SYD985 (Investigational)

- Trastuzumab-duocarmazine
- TULIP trial



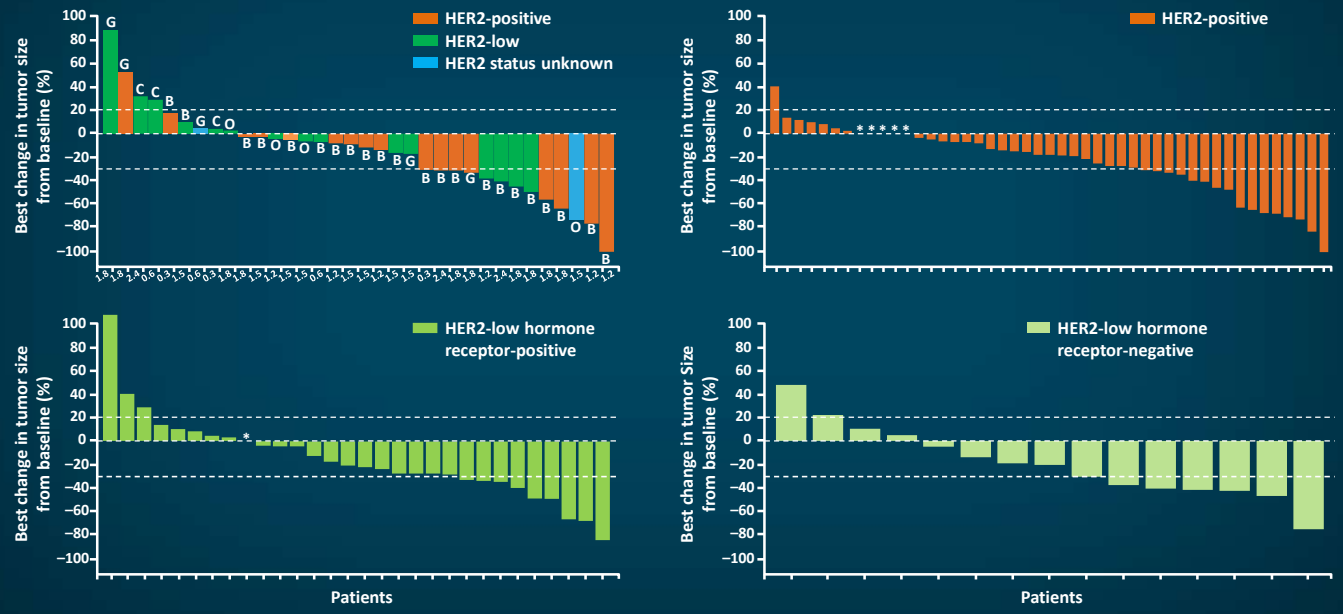
T/Cap = trastuzumab = capecitabine; T/Vino = trastuzumab = vinorelbine; T/Eri = trastuzumab + eribulin.

NCT03262935 (TULIP) (https://clinicaltrials.gov/ct2/show/NCT03262935?term=trastuzumab%2C+duocarmazine&cond=breast+cancer&draw=2&rank=1). Accessed 8/14/2020. Banerji U, et al. *Lancet Oncol*. 2019;20:1124-1135.

45

Trastuzumab Duocarmazine (SYD985)

Best percentage change in tumor size from baseline



Banerji U, et al. *Lancet Oncol*. 2019;20:1124-1135.

46

SYD985: Safety

Adverse Events in Dose-Expansion Cohorts			
	Grades 1–2	Grade 3	Grade 4
Fatigue	29%	3%	0
Conjunctivitis	28%	3%	0
Dry eye	30%	1%	0
Lacrimation increased	20%	0	0
Dry skin	18%	0	0
Decreased appetite	18%	1%	0
Alopecia	18%	0	0
Nausea	18%	0	0
Keratitis	17%	2%	0
Stomatitis	16%	0	0
Infusion-related reaction	9%	1%	0
Neutropenia	10%	6%	0
Anemia	9%	1%	0
Pyrexia	6%	0	0

Banerji U, et al. *Lancet Oncol*. 2019;20:1124-1135.

47

Nursing Implications—SYD985

- Under investigation in phase 3 trial
- IV every 3 weeks
- Included HER2 “low” (1+ or 2+ on IHC)
- Ocular toxicities
- Fatigue

IV = intravenous (administration).

Banerji U et al. *Lancet Oncol*. 2019;20(8):1124-1135.

48

Additional HER2-Directed Investigational Agents

- ADCs in development
- Different linkers and payloads
- Looking at effectiveness of ADCs in "HER2-low" (IHC 1+ or 2+)
- XMT-1522
  - ADC with mAb + dolaflexin
- RC48-ADC
  - mAb + auristatin

Pondé N, et al. *Curr Treat Options Oncol.* 2019;20:37

49

Additional HER2-Directed Investigational Agents (continued)

- Margetuximab
  - Monoclonal antibody
    - Designed to alter Fc-gamma receptor affinities
    - Increases affinity to *CD16A*-158F allele
  - SOPHIA trial
    - Margetuximab + chemotherapy vs trastuzumab + chemotherapy
    - Modest benefit, particularly enhanced in patients with *CD16A*-158F allele

The ASCO Post. Phase III SOPHIA Trial. 2020. (www.ascopost.com/issues/march-10-2020-supplement-conference-highlights-sabcs-2019/margetuximab-plus-chemotherapy-vs-trastuzumab-plus-chemotherapy-for-her2-positive-breast-cancer/). Accessed 8/11/2020

50

New and Investigational Agents With Non-HER2 Targets

- Sacituzumab govitecan in TNBC FDA approved this year
  - 3rd line
  - Anti-TROP-2 + govitecan
- SAR566658 studies in TNBC
  - Anti-CA6 antibody + DM4 (anti-microtubule)
- Ladiratuzumab vedotin SGN-LIV1A studies in all phenotypes
  - Anti-LIV-1 antibody + auristatin analogue

TNBC = triple-negative breast cancer; TROP = trophoblast cell-surface antigen.

Pondé N, et al. *Curr Treat Options Oncol.* 2019;20:37

51

Nursing Implications—New and Investigational Agents

- Heterogeneity of breast cancers
- Signaling pathways
- Later lines of therapy = shorter progression-free interval

52

Individualizing the Sequencing of Care for Patients with HER2-Positive BC

53

Patient-Specific Factors Affecting Outcomes

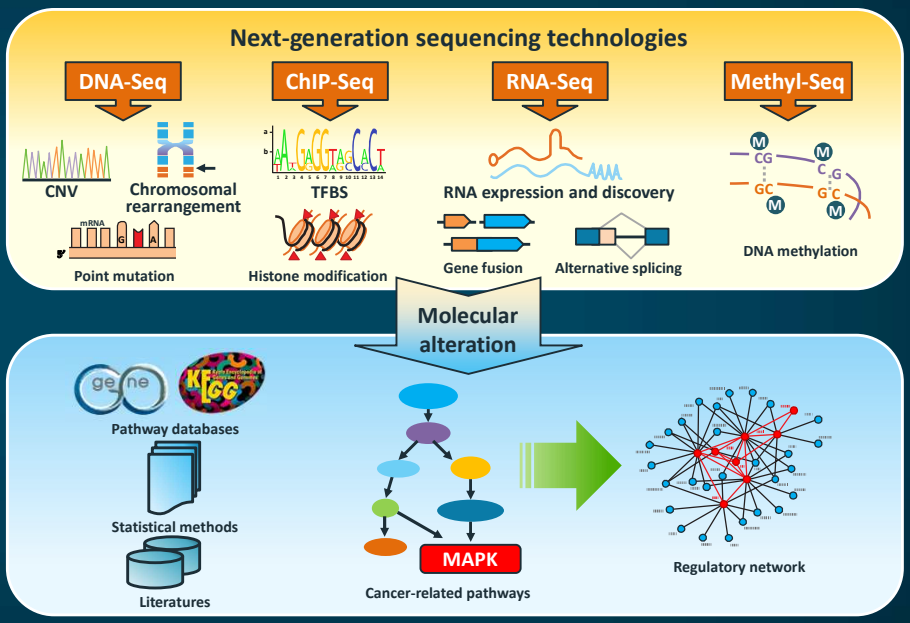
- HER-2 positive breast cancer is heterogenous
- Hormone-receptor status
- Newer ADCs are studying effect in heavily pre-treated patients
- ADCs have fewer toxicities, but they are still present
- Brain metastases
- Performance status
- Patient goals
- Shared decision-making

Verma S, et al. *N Engl J Med.* 2012;367:1783-1791. Murthy RK, et al. *N Engl J Med.* 2020;382:597-609. Modi S, et al. *N Engl J Med.* 2020;382:610-621.

54

Next-Generation Sequencing

- Tumor or liquid biopsy
- Analyzes tumor mutations
- Identifies targets



Seq = sequencing; RNA = ribonucleic acid; CNV = copy number alterations; ChIP = interactome-based; TFBS = transcription factor-binding sites; MAPK = mitogen-activated protein kinase.

Qin D. *Cancer Biol Med.* 2019;16:4-10. Chen J, et al. *Biomed Res Int.* 2013;2013:901578.

55

Roles of Emerging Agents in Established Treatment Algorithms

- No algorithm beyond 2nd line
  - Physician's choice
- 2nd-line T-DM1
  - Newer agents looking at 3rd-line therapies
  - Order of treatment
- Typically, 3–6 months PFS on 3rd-line treatment

56

NCCN Guidelines for Stage IV, ER-Negative, HER2-Positive

Systemic treatment of recurrent or stage IV (M1) disease: ER– and/or PR–, HER2+

Systemic therapy + HER2-targeted therapy with:

- Pertuzumab + trastuzumab + taxane (preferred)

or

- Ado-trastuzumab emtansine (T-DM1)

or

- Fam-trastuzumab deruxtecan-nxki

or

- Trastuzumab + chemotherapy

or

Other HER2-targeted therapies

→ Continue therapy until progression of unacceptable toxicity → Progression → Another line of systemic therapy + HER2-targeted therapy → Most patients will be candidates for multiple lines of systemic therapy to palliate advanced BC. At each reassessment, clinicians should assess value of ongoing treatment, risks and benefits of an additional line of systemic therapy, patient performance status, and patient preferences through shared decision-making process. → Consider no further HER2-targeted therapy and continue supportive care

See NCCN guidelines for palliative care and for supportive care

NCCN guidelines version 5.2020. Invasive breast cancer. 2020. (www.nccn.org/professionals/physician_gls/pdf/breast.pdf). Accessed 8/11/2020.

57

Role of Patient Preferences in Treatment Considerations

- Every 3-week dosing
- Emerging and investigational therapies
- Clinical trials
- Shared decision-making
- Patient- and family-centered care

Panje CM, et al. *JCO Clin Cancer Inform.* 2018;2:1-10. Tariman JD, et al. *Clin J Oncol Nurs.* 2016;20:560-563. Banerji U, et al. *Lancet Oncol.* 2019;20:1124-1135. NCCN guidelines version 5.2020. Invasive breast cancer. 2020. (www.nccn.org/professionals/physician_gls/pdf/breast.pdf). Accessed 8/11/2020.

58

Nursing Implications—Counseling and Monitoring

- Goals are quality of life and buying time
  - 1 year? 3 years? 10 years?
- Patient education
- Goals-of-care discussions
- Facilitating shared decision-making
- Monitoring pulmonary symptoms, lab abnormalities, fatigue, diarrhea

Panje CM, et al. *JCO Clin Cancer Inform.* 2018;2:1-10. Tariman JD, et al. *Clin J Oncol Nurs.* 2016;20:560-563. NCCN guidelines version 5.2020. Invasive breast cancer. 2020. (www.nccn.org/professionals/physician_gls/pdf/breast.pdf). Accessed 8/11/2020.

59

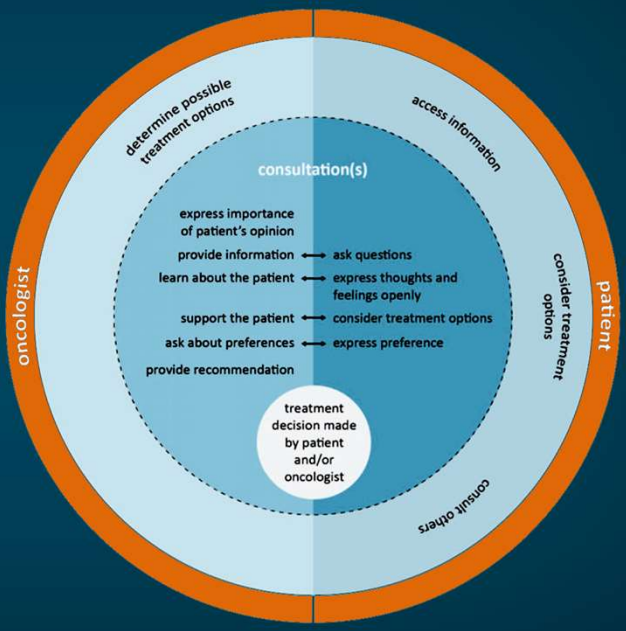
The Multidisciplinary Oncology Team

Optimizing Patient Care and Survivorship Through Shared Decision-Making

60

Shared Decision-Making in Oncology—What Is It?

- SDM is a dynamic process in which both patients and oncologists have complimentary roles *during* and *outside* the medical encounter
- Patients play an *active* role
- SDM should not be imposed on patients but should be encouraged through supportive means



SDM = shared decision-making.

Bomhof-Roordink H, et al. *Psychooncology.* 2019;28:139-146.

61

5 Essential Steps of SDM

SHARE Approach

1. **S**eek your patient's participation
2. **H**elp your patient explore and compare treatment options
3. **A**ssess your patient's values and preferences
4. **R**each a decision with your patient
5. **E**valuate your patient's decision

It's all about communication!

AHRQ Share Approach (www.ahrq.gov/sites/default/files/publications/files/share-approach_factsheet.pdf). Accessed 8/11/2020.

62

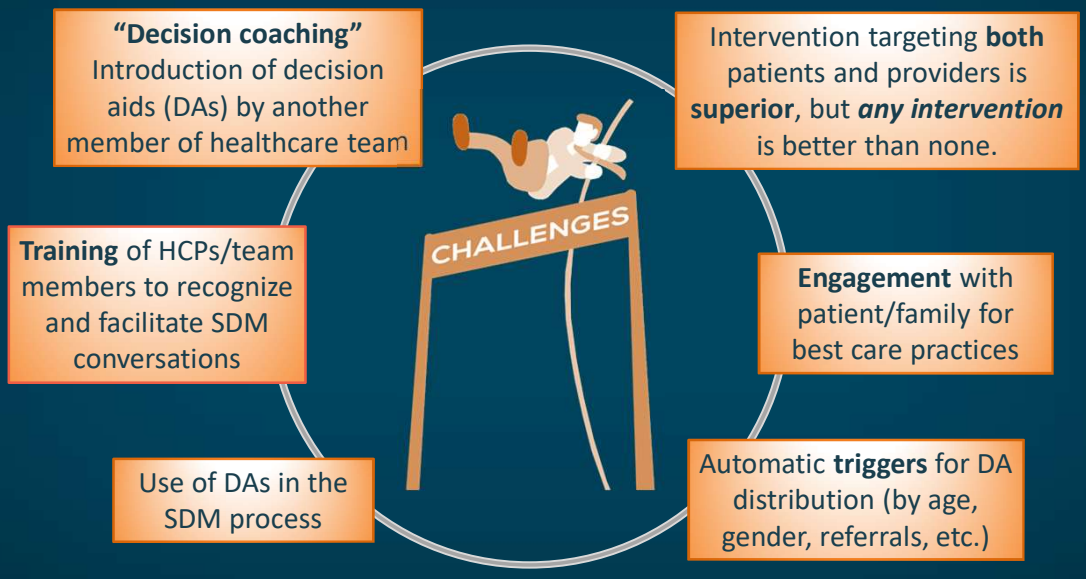
Educational Strategies for the Oncology Patient

- All patients are at risk for low literacy
- Adult education theory
- Multiple modes
- Demonstration and teach-back most effective
  - Written materials and audio-visual tools next
- Not one-size-fits-all
- Direct to reputable sites
  - cancer.gov/about-cancer/managing-care/using-trusted-resources

Blecher C et al. *Standards of Oncology Education: Patient/Significant Other and Public, 4th ed.* Oncology Nursing Society. 2016.

63

Overcoming Barriers



HCP = healthcare provider.

AHRQ. SHARE curriculum. 2015 (www.ahrq.gov/sites/default/files/wysiwyg/professionals/education/curriculum-tools/shareddecisionmaking/webinars/sharewebinar518-slides.pdf). Accessed 8/11/2020.

64

Oncology Nursing in the Care Team

- Professional identity
- Power of nursing
  - Connecting with the patient
  - Personalized coordination
  - Realizing the patient's potential
- Reduce disparities
- "The nurse owes the same duties to self as to others" —Nurse's code of ethics provision 5

Payne K, Murphy-Ende K. *Current Trends in Oncology Nursing, 2nd ed.* Oncology Nursing Society. 2019.

65

Nursing Implications—Summary

- Heterogeneity of breast cancers, heterogeneity of subtypes
- Lines of treatment in metastatic breast cancer
- Actively monitor for adverse events
- New directions in therapy for HER2-positive advanced breast cancers
- Promising strategies leading to accelerated FDA approvals
- Extending life expectancy of patients with HER2-positive metastatic breast cancer
- Brain metastases

66

Case Study 1

- SH is a 40-year-old female with de novo metastatic breast cancer, metastases to the liver, bone, and ovaries. She noted a right breast mass in May 2018.
- Ultrasound-guided core breast biopsy revealed invasive ductal carcinoma, grade 3, ER+, PR+, and HER2 equivocal by IHC (2+) and negative by FISH, with ratio 1.44 and copy #5.
- She underwent a liver biopsy that revealed IDC, ER+, PR+; IHC was 2+, but this sample was amplified by FISH with ratio 1.94 and copy #6.3.
- 1st-line therapy was paclitaxel + trastuzumab + pertuzumab.
- She progressed after 3 months on therapy and was changed to T-DM1 as 2nd-line therapy.
- After 13 months, she progressed again and was placed on trastuzumab + vinorelbine*.
- She remained on fulvestrant for anti-estrogen therapy.
- She was on trastuzumab + vinorelbine for 3 months before progression.

IDC = invasive ductal carcinoma.

*Not FDA approved for use in breast cancer.

67

Case Study 1—Question 1

- SH rapidly progressed through multiple therapies.
- What do you suspect in this patient?

  A. Trastuzumab resistance

  B. 1st-generation ADC resistance

  C. Estrogen therapy resistance

  D. A and B

68

Case Study 1—Question 2

- At that time, trastuzumab deruxtecan had just received FDA approval, and she started treatment with that agent in January 2020
- Currently with stable disease, she reports her only side effect is fatigue, but she remains active as a single mother and working full-time
- What is the nurse monitoring for at every visit?
  A. Dyspnea, cough, fever
  B. Numbness/tingling in extremities
  C. Neutropenic fever
  D. Decreased LVEF

69

Case Study 2

- ML is a 59-year-old female with metastatic breast cancer to the lung, liver, and brain.
- She was originally diagnosed with a stage IIA left breast IDC in 2014 that was ER–, PR–, and HER2+ (3+ on IHC).
- She underwent neoadjuvant TCHP, followed by bilateral total mastectomy, and completed one year of trastuzumab therapy that ended in 2015.
- In November 2018, she reported a persistent cough to her PCP. A chest X-Ray had abnormal findings and led to a CT scan that revealed suspicious pulmonary nodules and liver lesions. A liver biopsy revealed metastatic breast cancer, ER–, PR–, HER2 3+.
- She was placed on 1st-line THP, then progressed after 12 months.
- She was changed to 2nd-line T-DM1. While on T-DM1, she developed brain metastases that were treated with radiation. She remained on T-DM1 as systemic therapy.
- After 5 months on T-DM1, she progressed further in the liver.

TCHP = docetaxel + carboplatin + trastuzumab + pertuzumab; PCP = primary care provider; THP = paclitaxel + trastuzumab + pertuzumab.

70

Case Study 2—Question

- ML has heard from the internet and her support groups that HER2+ breast cancer is more aggressive, and she is worried that she is running out of options.
- Which of the following responses to her concerns is best?
  A. We have several new drugs that we can use, and even more are being studied
  B. There is only one more line of treatment left
  C. We should discuss why you want to continue treatment
  D. Now that you have brain metastases, there are no medications we can use

71

HER2-Positive BC: Take-Aways

- HER2-targeted therapies are changing natural history of HER2-positive breast cancer
- Adverse-event monitoring for early identification and intervention is a ***critical*** component to all HER2-targeted therapy
- HER2-targeted therapies are evolving
- Expect more therapies
- HER2-positive breast cancers are heterogenous, providing more and different targets
- Educate the public, patients, peers, and yourself

You are leaders!

72

SDM Take-Aways

- Involve the patient and other members of the healthcare team in the SDM process
- Intervention options should be **neutrally presented** and include discussion of risks, benefits, and no intervention
- Use decision aids to enhance patient understanding and communication with the healthcare team
- Complete **all steps** in the SDM process

73

Thank you!

74


Build your own complimentary poster for the office!
Supplement your Course Learning. It's fast and easy.
We'll ship it to you directly free of charge
For more information and additional resources please visit
ONQ.POSTERPROGRAM.COM
ONQ
ONCOLOGY
NURSES
QUALITY
Improvement Series

75