Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Breast Cancer: Session 1

Thursday, June 3, 2021
5:00 PM – 6:00 PM ET

Faculty

Sara M Tolaney, MD, MPH
Allie Hershey, MSN, RN, ANP-BC, AOCNP

Moderator

Neil Love, MD

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Breast Cancer Faculty

Sara M Tolaney, MD, MPH
Associate Director
Susan F Smith Center for Women's Cancers
Director of Clinical Trials, Breast Oncology
Director of Breast Immunotherapy Clinical Research
Senior Physician
Breast Oncology Program
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Allie Hershey, MSN, RN, ANP-BC, AOCNP
Oncology Nurse Practitioner, Breast Oncology
Susan F Smith Center for Women's Cancers
Dana-Farber Cancer Institute
Boston, Massachusetts

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Commercial Support

This activity is supported by educational grants from Lilly, Novartis and Seagen Inc.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, Genentech, a member of the Roche Group, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Tolaney — Disclosures

Consulting Agreements	4D pharma plc, AstraZeneca Pharmaceuticals LP, Athenex, Bristol-Myers Squibb Company, Certara, Chugai Pharmaceutical Co Ltd, CytomX Therapeutics, Daiichi Sankyo Inc, Eisai Inc, Ellipses Pharma, G1 Therapeutics, Genentech, a member of the Roche Group, Gilead Sciences Inc, Immunomedics Inc, Infinity Pharmaceuticals Inc, Kyowa Kirin Co Ltd, Lilly, Merck, Mersana Therapeutics, NanoString Technologies, Nektar, Novartis, Odonate Therapeutics, OncoPep, OncoSec Medical, Pfizer Inc, Puma Biotechnology Inc, Samsung Bioepis, Sanofi Genzyme, Seagen Inc
Contracted Research	AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Cyclacel Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Immunomedics Inc, Lilly, Merck, NanoString Technologies, Nektar, Novartis, Odonate Therapeutics, Pfizer Inc, Sanofi Genzyme, Seagen Inc
Data and Safety Monitoring Board/Committee	Odonate Therapeutics

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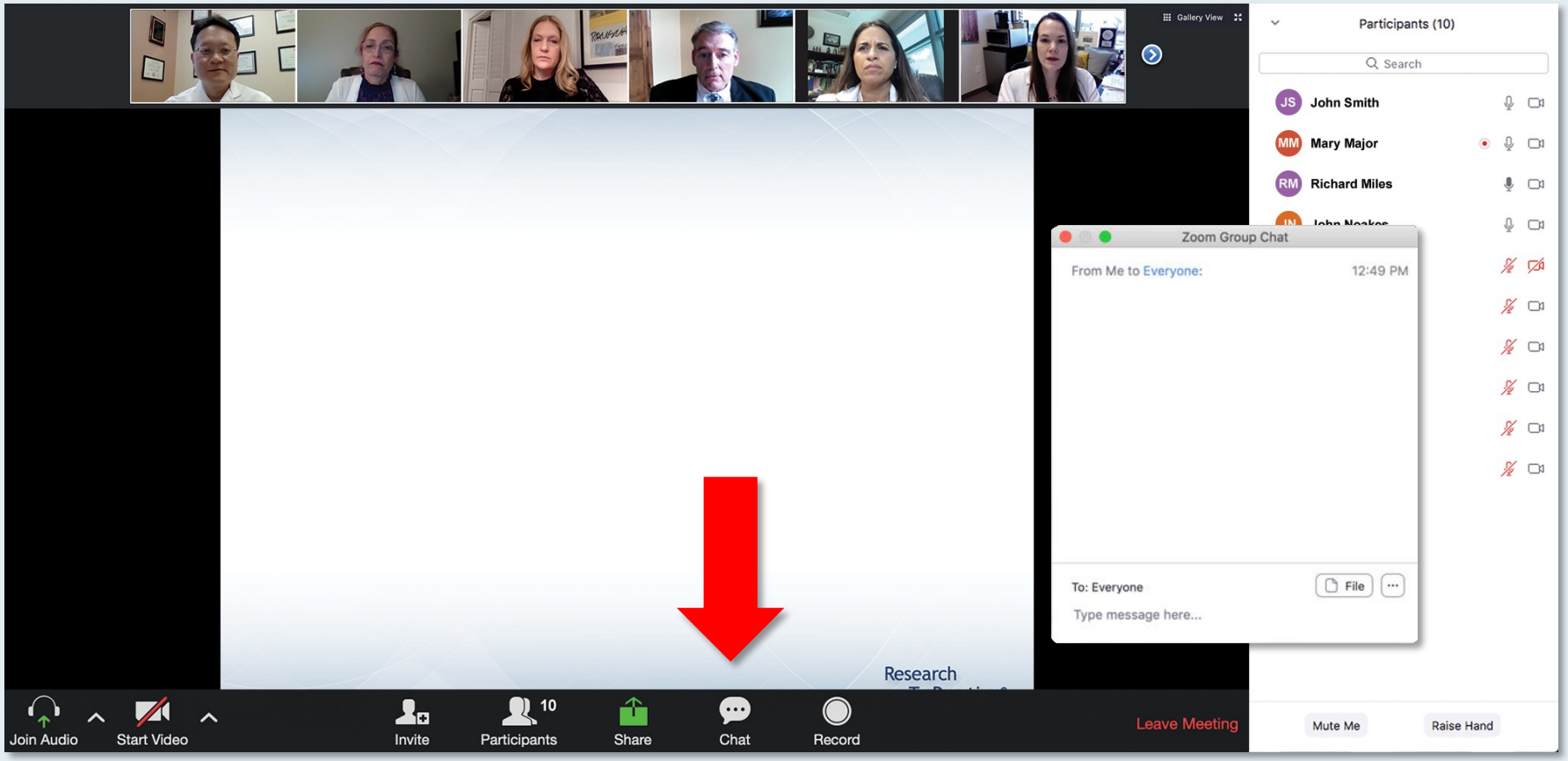
Ms Hershey — Disclosures

No relevant conflicts of interest to disclose.

We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

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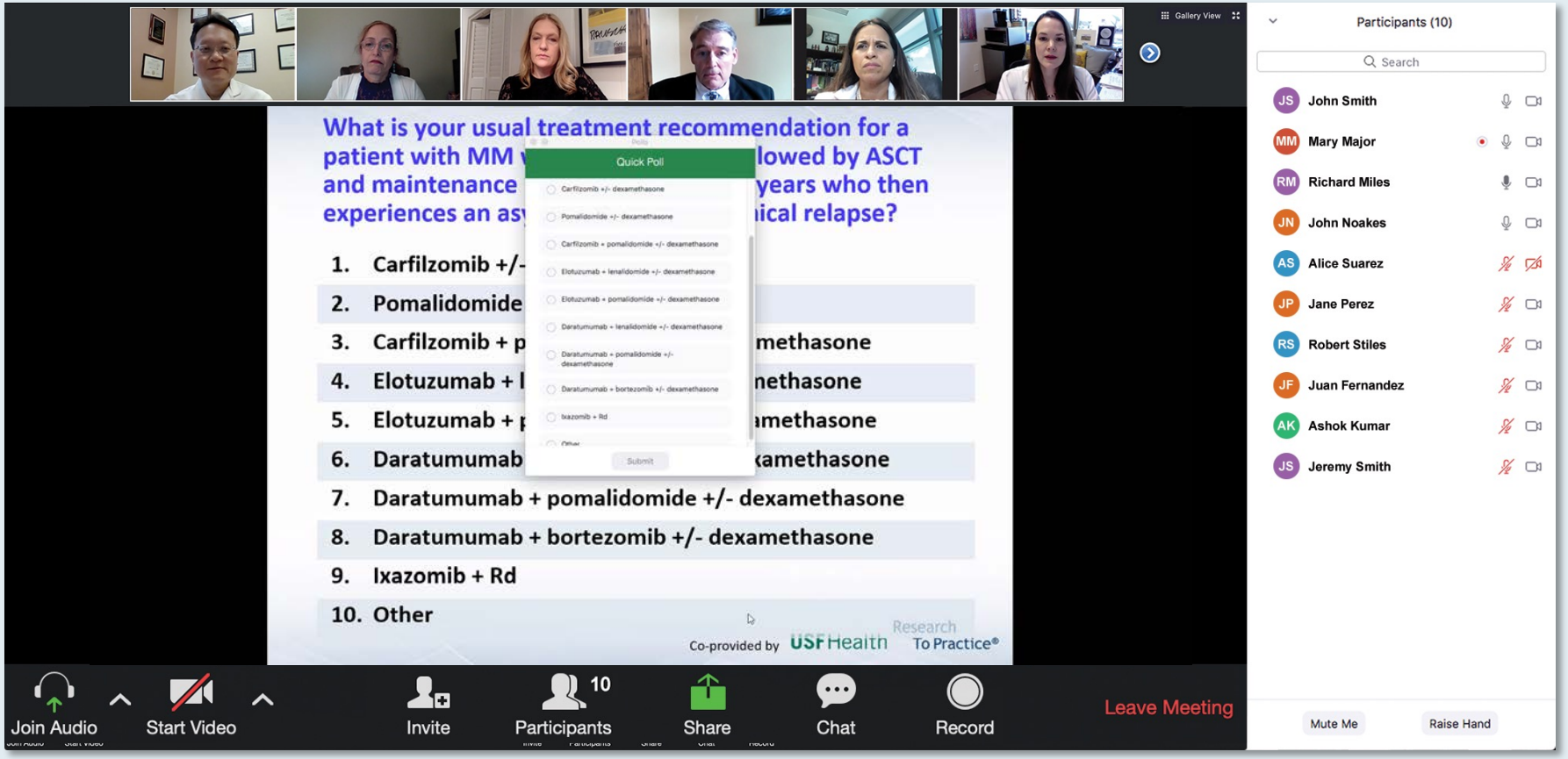
Familiarizing Yourself with the Zoom Interface

How to answer poll questions

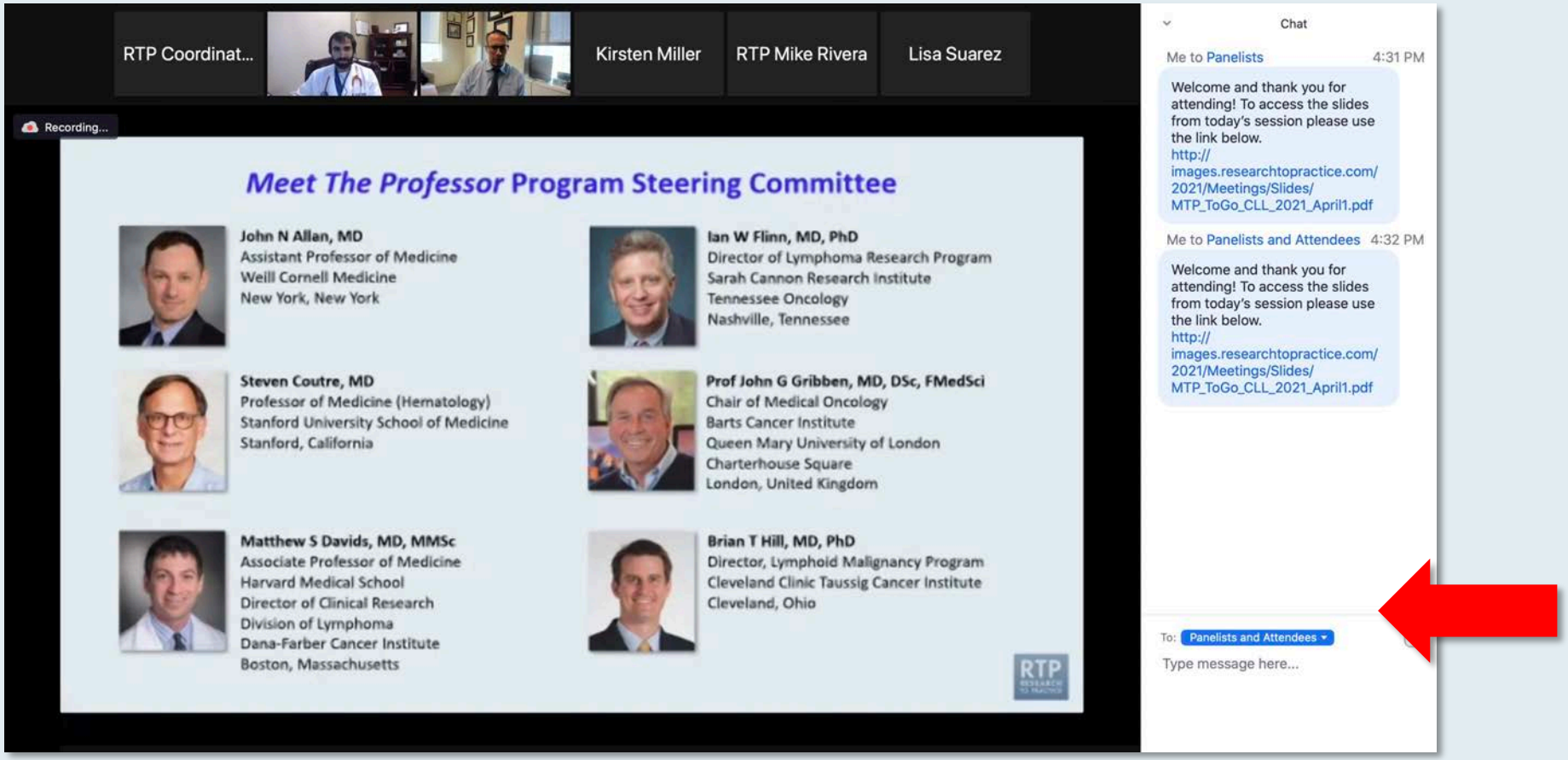


When a poll question pops up, click your answer choice from the available options.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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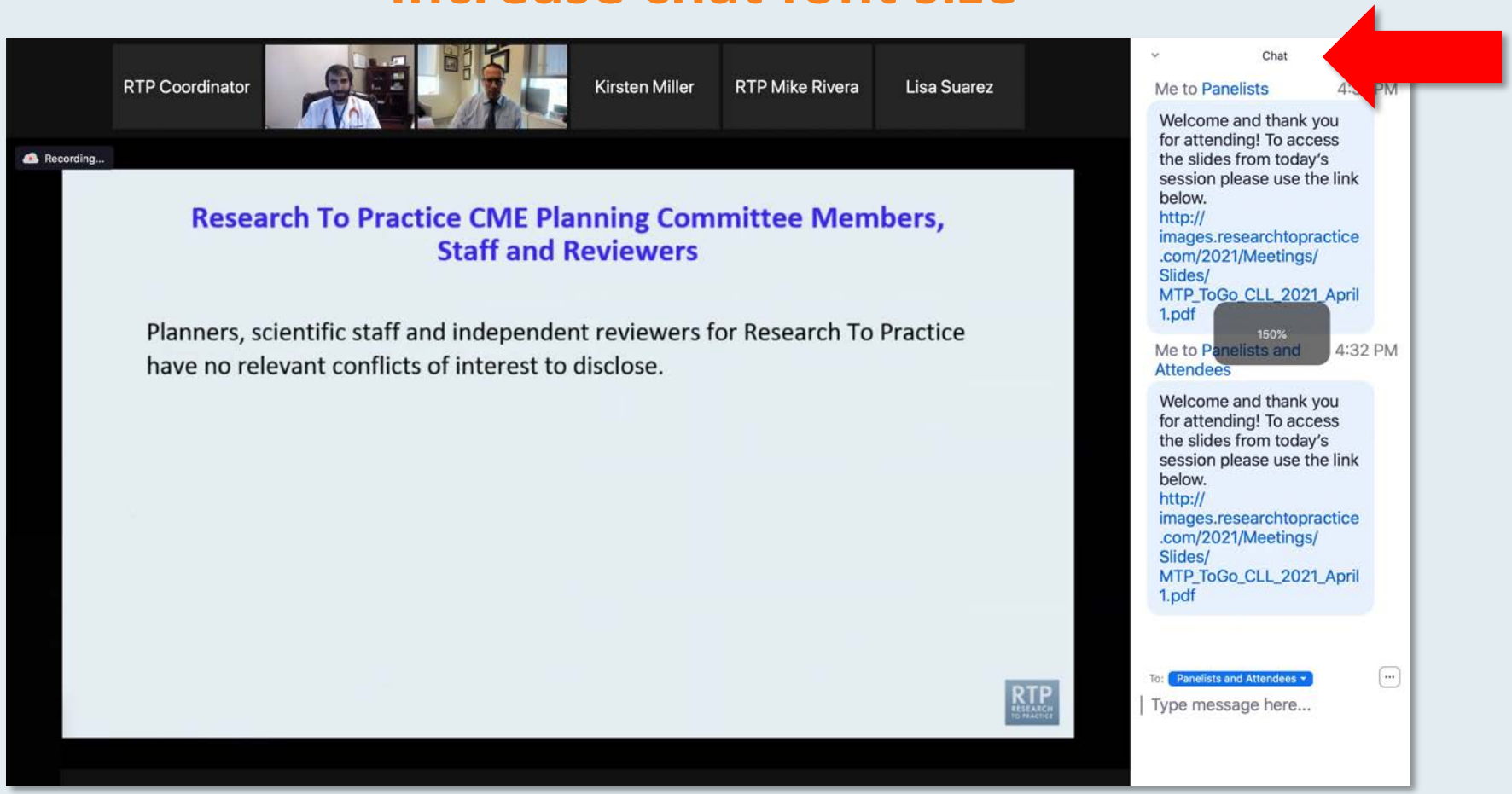
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

HER2-Positive Localized Breast Cancer

DR ADAM BRUFSKY
UNIVERSITY OF PITTSBURGH

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Monday, June 7, 2021
5:00 PM – 6:00 PM ET

Faculty

Kristen K Ciombor, MD, MSCI

Moderator

Neil Love, MD

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Summer Oncology Nursing Series

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Chronic Lymphocytic Leukemia: Session 1

Thursday, June 10, 2021
5:00 PM – 6:00 PM ET

Faculty

Jennifer Woyach, MD
Kristen E Battiato, AGNP-C

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor
Management of Ovarian Cancer

Tuesday, June 15, 2021
4:00 PM – 5:00 PM ET

Faculty
Susana Banerjee, MBBS, MA, PhD

Moderator
Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Wednesday, June 16, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas E Hutson, DO, PharmD

Moderator

Neil Love, MD

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Summer Oncology Nursing Series

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Hodgkin and Non-Hodgkin Lymphomas

Thursday, June 17, 2021
5:00 PM – 6:00 PM ET

Faculty

Carla Casulo, MD
Jacklyn Gideon, MSN, AGPCNP-BC

Moderator

Neil Love, MD

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Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Chimeric Antigen Receptor T-Cell Therapy in Multiple Myeloma

Thursday, June 24, 2021
5:00 PM – 6:00 PM ET

Faculty

Noopur Raje, MD
Alli McClanahan, MSN, APRN, ANP-BC

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

ASCO Highlights and More: Investigators Review Recent Data Sets and Provide Perspectives on Current Oncology Care

A Daylong Multitumor Educational Webinar in Partnership with the Texas Society of Clinical Oncology (TxSCO)

Saturday, June 26, 2021
8:00 AM – 3:00 PM Central Time
(9:00 AM – 4:00 PM Eastern Time)

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17 Exciting CME/MOC Events You Do Not Want to Miss

A Live Webinar Series Held in Conjunction with the 2021 ASCO Annual Meeting

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Tuesday, June 22
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ER-Positive and Triple-Negative Breast Cancer
Wednesday, June 23
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Chronic Lymphocytic Leukemia and Follicular Lymphoma
Tuesday, June 29
5:00 PM – 6:00 PM ET

Multiple Myeloma
Wednesday, June 30
5:00 PM – 6:00 PM ET

Ovarian Cancer
Wednesday, July 7
5:00 PM – 6:00 PM ET

Hormonal Therapy for Prostate Cancer
Monday, July 12
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Acute Myeloid Leukemia and Myelodysplastic Syndromes
Wednesday, July 14
5:00 PM – 6:00 PM ET

Metastatic Castration-Resistant Prostate Cancer
Tuesday, July 20
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Bladder Cancer
Wednesday, July 21
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Endometrial and Cervical Cancers
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Thank you for joining us!

NCPD credit information will be emailed to each participant within 3 business days.

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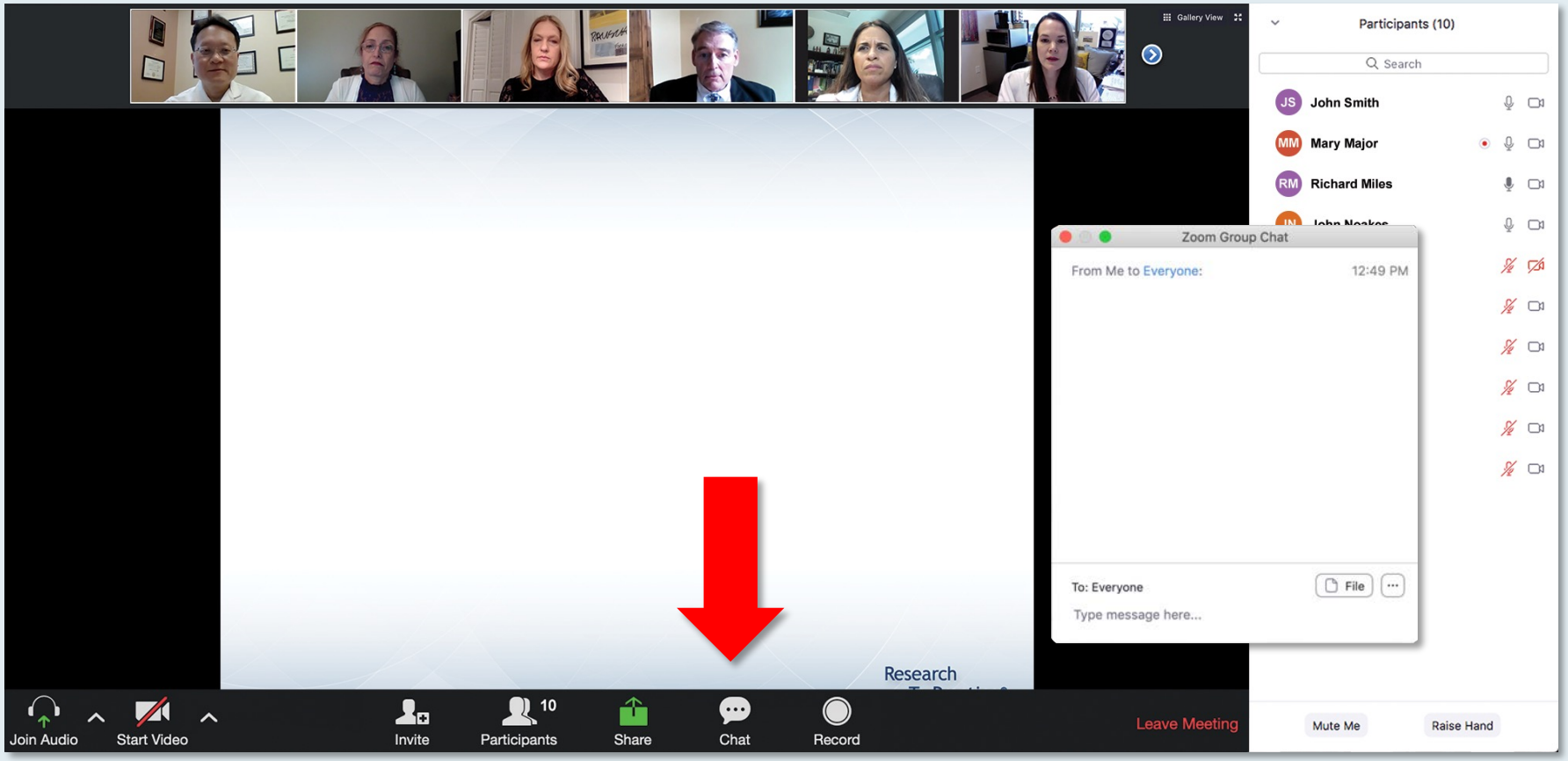

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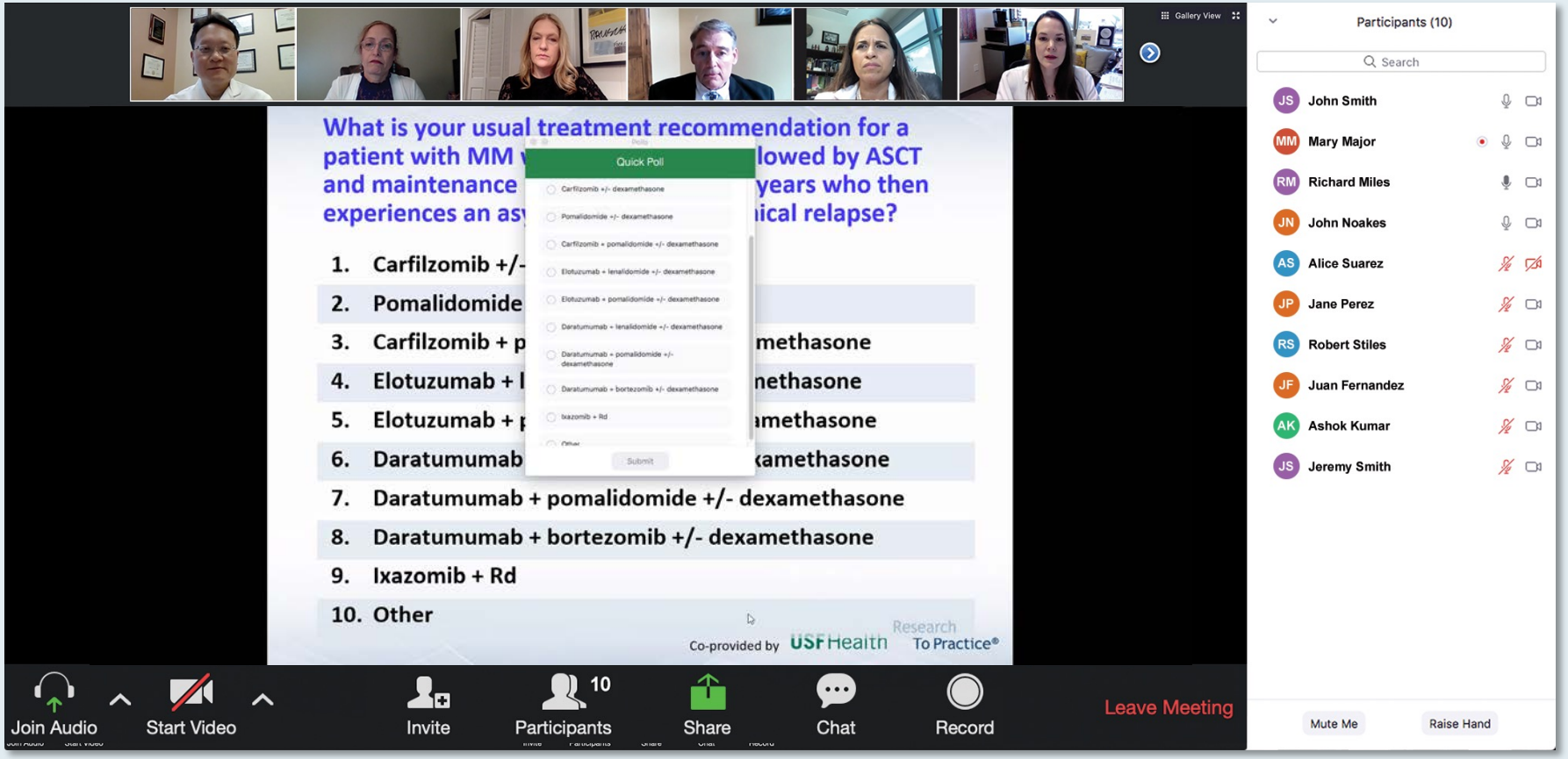

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Neil Love, MD

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Oncology Grand Rounds Nursing Webinar Series

April 2021

Monday	Tuesday	Wednesday	Thursday	Friday
19	20 Breast Ca 8:30 AM Lung Ca 5:00 PM	21 AML 12:00 PM CRC and GE Ca 4:45 PM	22 Prostate Ca 8:30 AM Lymphomas 5:00 PM	23
26	27 Multiple Myeloma 8:30 AM GYN 5:00 PM	28 Bladder Ca 12:00 PM	29 CLL 8:30 AM CAR-T 5:00 PM	30

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13th Annual Oncology Grand Rounds

A Complimentary NCPD Live Webinar Series
Held During the 46th Annual ONS Congress

Breast Cancer

Tuesday, April 20, 2021
8:30 AM – 10:00 AM ET

Medical Oncologists

Carey K Anders, MD
Kathy D Miller, MD
Sara M Tolaney, MD, MPH

Oncology Nurse Practitioners

Gretchen Santos Fulgencio, MSN, FNP-BC
Allie Hershey, MSN, RN, ANP-BC, AOCNP
Kelly Leonard, MSN, FNP-BC

Moderator

Neil Love, MD

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Kelly Leonard, MSN, FNP-BC


Gretchen Santos Fulgencio, MSN, FNP-BC


Allie Hershey, MSN, RN, ANP-BC, AOCNP

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Agenda

Module 1: ER-Positive, HER2-Negative

- Case 1 – Dr Tolaney: A 40-year-old woman with ER/PR-positive, HER2-negative, node-positive breast cancer
- Case 2 – Ms Hershey: A 63-year-old woman with hormone receptor-positive, node-positive breast cancer
- Case 3 – Dr Tolaney: A 42-year-old woman with hormone receptor-positive, HER2-negative metastatic breast cancer

Module 2: HER2-Positive

- Case 4 – Ms Hershey: A 44-year-old woman with hormone receptor-positive, HER2-positive metastatic breast cancer
- Case 5 – Dr Tolaney: A 36-year-old woman with ER-positive, HER2-positive metastatic breast cancer

Module 3: Triple-Negative

- Case 6 – Ms Hershey: A 52-year-old woman with metastatic triple-negative breast cancer

How long have you been in the field of oncology?

1. Less than 5 years
2. 5-10 years
3. 11-20 years
4. 21-30 years
5. 31-40 years
6. More than 40 years

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I feel emotionally drained by my work.

1. Never
2. A few times per year
3. Once a month
4. A few times per month
5. Once a week
6. A few times per week
7. Every day

I feel frustrated by my work.

1. Never
2. A few times per year
3. Once a month
4. A few times per month
5. Once a week
6. A few times per week
7. Every day

I feel very satisfied with my work.

1. Never
2. A few times per year
3. Once a month
4. A few times per month
5. Once a week
6. A few times per week
7. Every day

Agenda

Module 1: ER-Positive, HER2-Negative

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Module 3: Triple-Negative

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What effect was observed in the Phase III trial of adjuvant abemaciclib?

1. Fewer recurrences
2. Fewer deaths
3. Both

Case Presentation – Dr Tolaney: A 40-year-old woman with ER/PR-positive, HER2-negative, node-positive breast cancer

- Left breast mass with ipsilateral palpable axillary LN
  - US: 9 cm LN and 3 enlarged axillary LNs
  - Biopsy of the breast: Grade 3 IDC, ER+ PR+ HER2-
  - FNA of an axillary LN was positive for malignant cells
- Enrolled on a preoperative clinical trial of *nab* paclitaxel + pembrolizumab x 12 wks → AC x 4 wks → surgery
  - 9.2 cm of residual IDC with LVI, and 4/11 positive axillary LNs
- Radiation therapy → OS + AI, and adjuvant abemaciclib, along with zoledronic acid

Case Presentation – Dr Tolaney: A 40-year-old woman with ER/PR-positive, HER2-negative, node-positive breast cancer (continued)

What are the important factors you considered in managing this case?

1. High anatomic risk disease: large tumor, multiple axillary LNs
2. No response to preop chemotherapy with residual axillary node involvement
3. Young age
4. No significant comorbidities

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Which of the following toxicities is more common with palbociclib and ribociclib than with abemaciclib?

1. Gastrointestinal toxicity
2. Neutropenia
3. Anemia
4. Peripheral neuropathy
5. I don’t know

The PI3 kinase inhibitor alpelisib is used for patients with metastatic ER-positive, HER2-negative breast cancer with a…

1. PIK3CA germline mutation
2. PIK3CA somatic mutation
3. PIK3CA amplification
4. All of the above
5. I don’t know

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Case Presentation – Ms Hershey: A 63-year-old woman with hormone receptor-positive, node-positive breast cancer

- 2005: Diagnosed with HR-positive T2N1 breast cancer
- Mastectomy → ddAC-T and endocrine therapy x 5 years
- 2018: Hip/back pain → Evaluation delayed, admitted due to pain → T1 compression fracture and extensive bony metastases
  - Biopsy: ER-positive metastatic breast cancer
- Early 2019: Letrozole/palbociclib
- 12/2020: Fulvestrant/palbociclib
- 4/2021: Fulvestrant/alpelisib

Case Presentation – Ms Hershey: A 63-year-old woman with hormone receptor-positive, node-positive breast cancer (continued)

What are the important factors you considered in managing this case?

1. Indication for taking medication due to PIK3CA mutation (testing done 12/2020)
2. Side effects of therapy (hyperglycemia, diarrhea, rash, mouth sores, n/v, anorexia, weight loss, fatigue, muscle aches, decreased muscle strength)
3. Monitoring requirements, including baseline HgA1c/fasting glucose and weekly fasting glucose upon initiation
4. Initiation of daily antihistamine to decrease incidence and severity of rash
5. When to call the office

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Case Presentation – Dr Tolaney: A 42-year-old woman with hormone receptor-positive, HER2-negative metastatic breast cancer

- MD/PhD working in biotech with 3 young children – eldest 9 years old
- Recurrent breast cancer with spinal cord compression and dural-based mass, s/p adjuvant chemotherapy and endocrine therapy

What are the most important issues you planned to discuss with this patient?

1. Treatment approach for what to do now
2. Implications of living with metastatic disease
3. Discussion of overall life expectancy
4. Discussion of goals of care
5. Discussion of what to tell her children

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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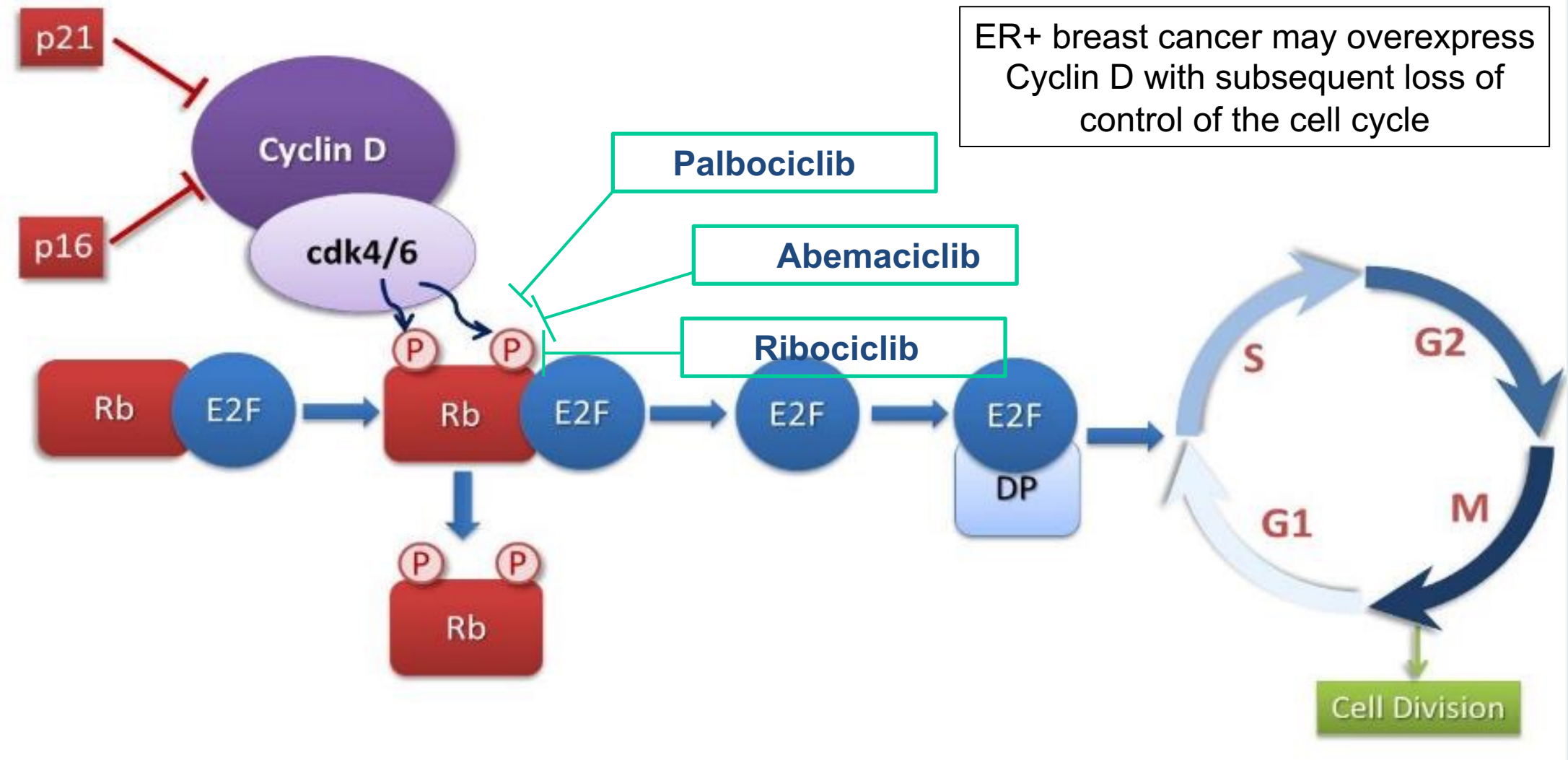
CDK4/6 Regulates Cell Cycle Progression



Adapted from Finn et al, 2016.

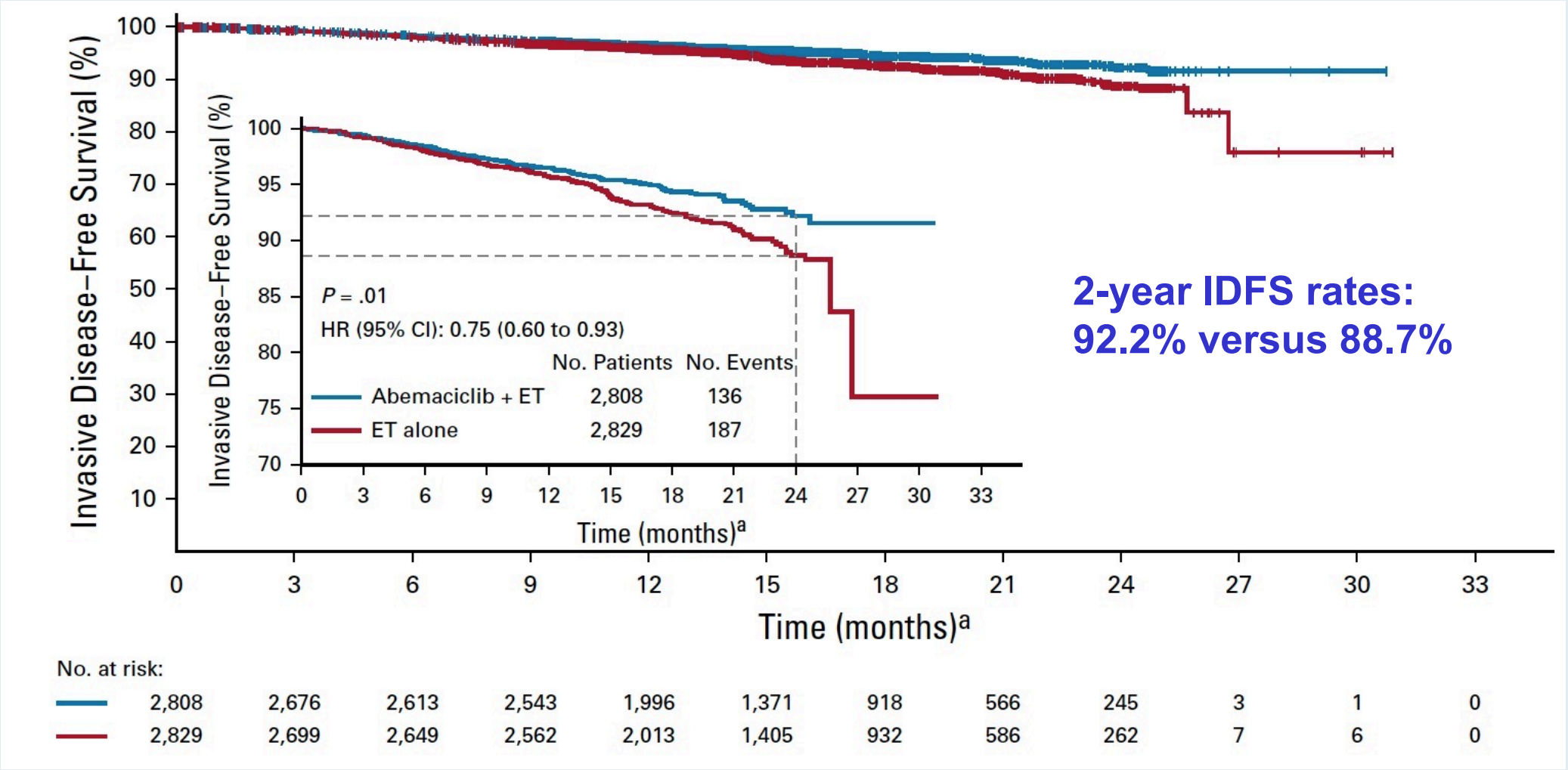
J Clin Oncol 2020;38(34):3987-98.

rapid communications

Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2−, Node-Positive, High-Risk, Early Breast Cancer (monarchE)

Stephen R. D. Johnston, MD, PhD[1]; Nadia Harbeck, MD, PhD[2]; Roberto Hegg, MD, PhD[3]; Masakazu Toi, MD, PhD[4]; Miguel Martin, MD, PhD[5]; Zhi Min Shao, MD[6]; Qing Yuan Zhang, MD, PhD[7]; Jorge Luis Martinez Rodriguez, MD[8]; Mario Campone, MD, PhD[9]; Erika Hamilton, MD[10]; Joohyuk Sohn, MD, PhD[11]; Valentina Guarneri, MD, PhD[12]; Morihito Okada, MD, PhD[13]; Frances Boyle, MD, MBBS, PhD[14]; Patrick Neven, MD, PhD[15]; Javier Cortés, MD, PhD[16]; Jens Huober, MD[17]; Andrew Wardley, MD, MBChB[18]; Sara M. Tolaney, MD, MPH[19]; Irfan Cicin, MD[20]; Ian C. Smith, MD[21,22]; Martin Frenzel, PhD[22]; Desirée Headley, MSc[22]; Ran Wei, PhD[22]; Belen San Antonio, PhD[22]; Maarten Hulstijn, PhD[22]; Joanne Cox, MD[22]; Joyce O'Shaughnessy, MD[23]; and Priya Rastogi, MD[24]; on behalf of the monarchE Committee Members and Investigators

monarchE: Invasive Disease-Free Survival (IDFS)
(Zoomed in to better show separation of curves)



Johnston SRD et al. *J Clin Oncol* 2020;38(34):3987-98.

Articles

Lancet Oncol 2021;22:212-22

Palbociclib with adjuvant endocrine therapy in early breast cancer (PALLAS): interim analysis of a multicentre, open-label, randomised, phase 3 study

Erica L Mayer, Amylou C Dueck, Miguel Martin, Gabor Rubovszky, Harold J Burstein, Meritxell Bellet-Ezquerra, Kathy D Miller, Nicholas Zdenkowski, Eric P Winer, Georg Pfeiler, Matthew Goetz, Manuel Ruiz-Borrego, Daniel Anderson, Zbigniew Nowecki, Sibylle Loibl, Stacy Moulder, Alistair Ring, Florian Fitzal, Tiffany Traina, Arlene Chan, Hope S Rugo, Julie Lemieux, Fernando Henao, Alan Lyss, Silvia Antolin Novoa, Antonio C Wolff, Marcus Vetter, Daniel Egle, Patrick G Morris, Eleftherios P Mamounas, Miguel J Gil-Gil, Aleix Prat, Hannes Fohler, Otto Metzger Filho, Magdalena Schwarz, Carter DuFrane, Debora Fumagalli, Kathy Puyana Theall, Dongrui Ray Lu, Cynthia Huang Bartlett, Maria Koehler, Christian Fesl, Angela DeMichele, Michael Gnant**

Randomized Trials of Endocrine Therapy +/- CDK4/6 Inhibition

Line	Trial	Schema	PFS HR compared to endocrine alone	OS HR compared to endocrine alone
First line	PALOMA-1	Letrozole ± palbociclib	0.49	0.897
	PALOMA-2	Letrozole ± palbociclib	0.58	NR
	MONALEESA-2	Letrozole ± ribociclib	0.56	0.75
	MONALEESA-3	Fulvestrant ± ribociclib	0.55	0.72
	MONALEESA-7 (premenopausal)	Goserelin + AI or tamoxifen ± ribociclib	0.55	0.71
	MONARCH 3	Letrozole or anastrozole, ± abemaciclib	0.54	NR
Second line	PALOMA-3	Fulvestrant ± palbociclib	0.46	0.75
	MONARCH 2	Fulvestrant ± abemaciclib	0.55	0.757

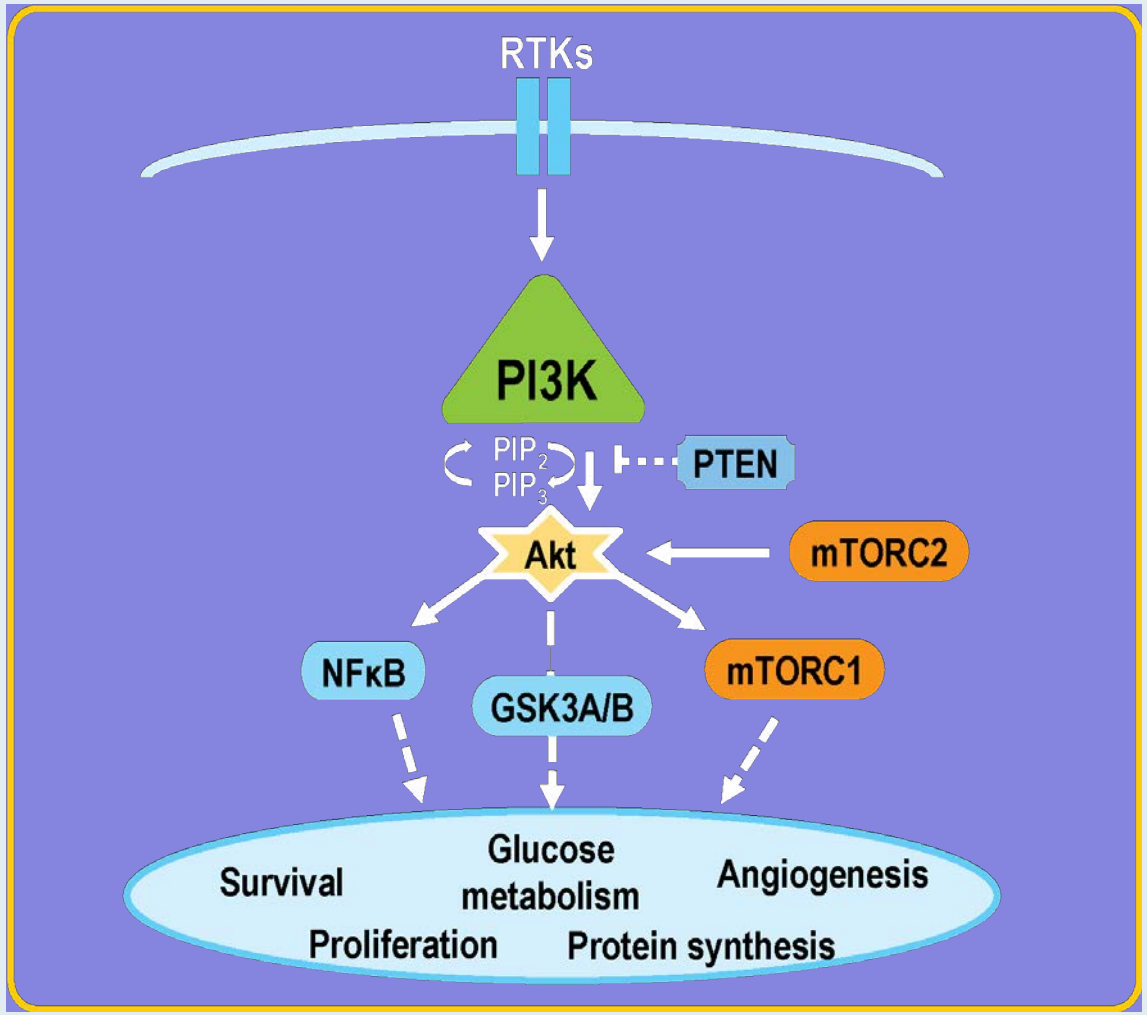
Courtesy of Dr Harold Burstein; Updated with MONALEESA-3 and MONALEESA-7

Common Side Effects and Dosing of CDK4/6 Inhibitors

	Palbociclib		Abemaciclib		Ribociclib	
Dosing	125 mg qd 3 wk on, 1 wk off		200 mg BID continuously		600 mg qd 3 wk on, 1 wk off	
Common adverse events	**All grades**	**Grade 3/4**	**All grades**	**Grade 3/4**	**All grades**	**Grade 3/4**
Neutropenia Thrombocytopenia	95% 76%	54% 19%	88% 42%	27% 2%	46% 37%	29% 10%
Diarrhea Nausea Vomiting	16% 23% 5%	0 0 0	90% 65% 35%	20% 5% 2%	22% 46% 25%	3% 2% 0

Barroso-Sousa R et al. *Breast Care* 2016;11:167-73.

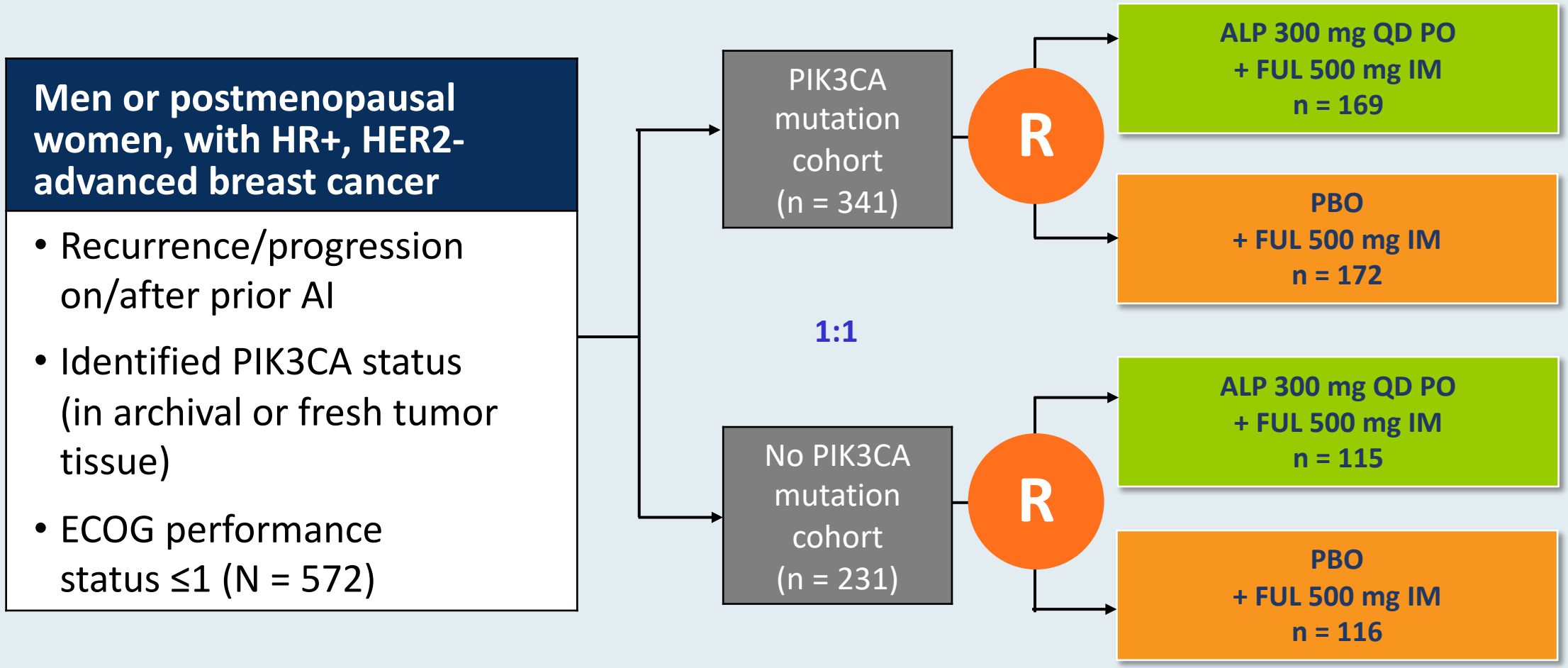
PI3K Inhibitors: Mechanism of Action



- PI3K is involved in the activation of Akt.
- Hyperactivation of the PI3K pathway is implicated in malignant transformation, cancer progression and endocrine therapy resistance.
- PIK3CA encodes the alpha isoform of the PI3K catalytic subunit.
- Around 40% of patients with HR+, HER- BC present with an activating PIK3CA tumor mutation.
- Alpelisib is a specific inhibitor of the PI3K alpha isoform.

André F et al. ESMO 2018;Abstract LBA3_PR.

SOLAR-1 Phase III Study Design



Primary endpoint: Locally assessed PFS in PIK3CA mutation cohort

André F et al. ESMO 2018;Abstract LBA3_PR.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Alpelisib plus fulvestrant for *PIK3CA*-mutated, hormone receptor-positive, human epidermal growth factor receptor-2—negative advanced breast cancer: final overall survival results from SOLAR-1

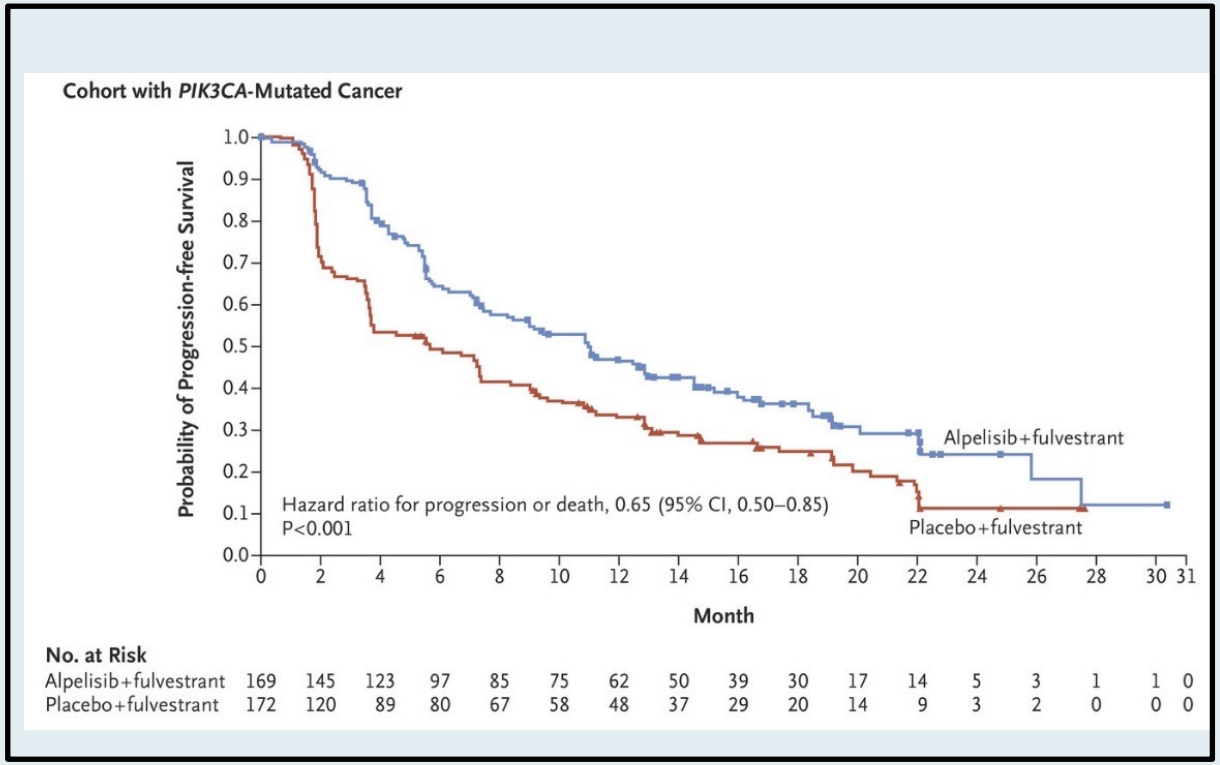
F. André[1*], E. M. Ciruelos[2], D. Juric[3], S. Loibl[4], M. Campone[5], I. A. Mayer[6], G. Rubovszky[7], T. Yamashita[8], B. Kaufman[9], Y.-S. Lu[10], K. Inoue[11], Z. Pápai[12], M. Takahashi[13], F. Ghaznawi[14], D. Mills[15], M. Kaper[14], M. Miller[14], P. F. Conte[16], H. Iwata[17] & H. S. Rugo[18]

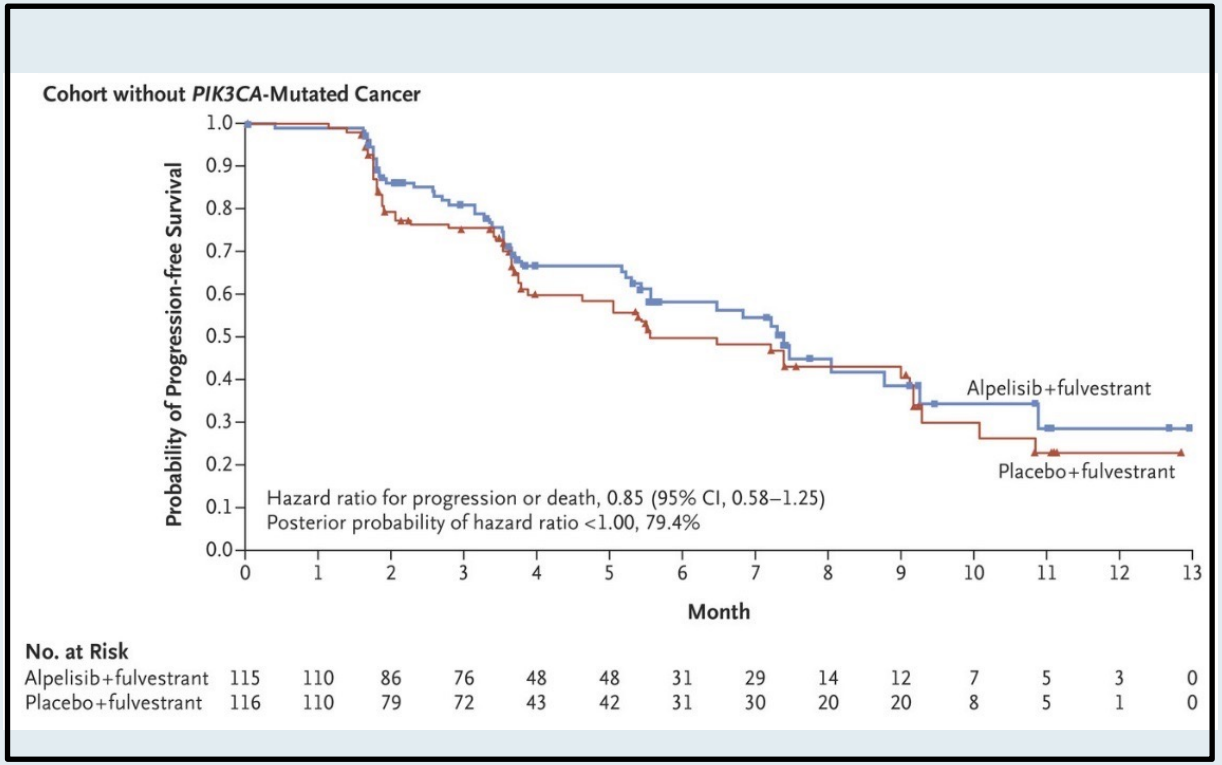
[1]Department of Medical Oncology, Institut Gustave Roussy, Villejuif and Paris Saclay University, Orsay, France; [2]Medical Oncology, Hospital Universitario 12 de Octubre, Madrid, Spain; [3]Department of Medicine, Massachusetts General Hospital Cancer Center, Boston, USA; [4]Department of Medicine and Research, German Breast Group, GBG Forschungs GmbH, Neu-Isenburg, Germany; [5]Medical Oncology, Institut de Cancerologie de l'Ouest, Saint-Herblain, Nantes Cedex, France; [6]Hematology/Oncology, Vanderbilt University, Nashville, USA; [7]Department of Medical Oncology and Clinical Pharmacology, National Institute of Oncology, Budapest, Hungary; [8]Department of Breast and Endocrine Surgery, Kanagawa Cancer Center, Yokohama, Japan; [9]Medical Oncology, Tel Aviv University, Sheba Medical Centre, Tel Hashomer, Israel; [10]Medical Oncology, National Taiwan University Hospital, Taipei, Taiwan; [11]Breast Surgery, Saitama Cancer Center, Saitama, Japan; [12]Medical Oncology, Hungarian Defence Forces Medical Centre, Budapest, Hungary; [13]Breast Surgery, NHO Hokkaido Cancer Center, Sapporo, Japan; [14]Novartis Pharmaceuticals Corporation, East Hanover, USA; [15]Novartis Pharma AG, Basel, Switzerland; [16]Medical Oncology, Universita di Padova and Oncologia Medica 2, Istituto Oncologico Veneto IRCCS, Padua, Italy; [17]Breast Oncology, Aichi Cancer Center Hospital, Aichi, Japan; [18]Breast Department, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, USA

Available online 25 November 2020

***Ann Oncol* 2021;32(2):208-17.**

SOLAR-1: PFS Outcomes by PIK3CA Mutation Status





André F et al. *N Engl J Med* 2019;380:1929-40.

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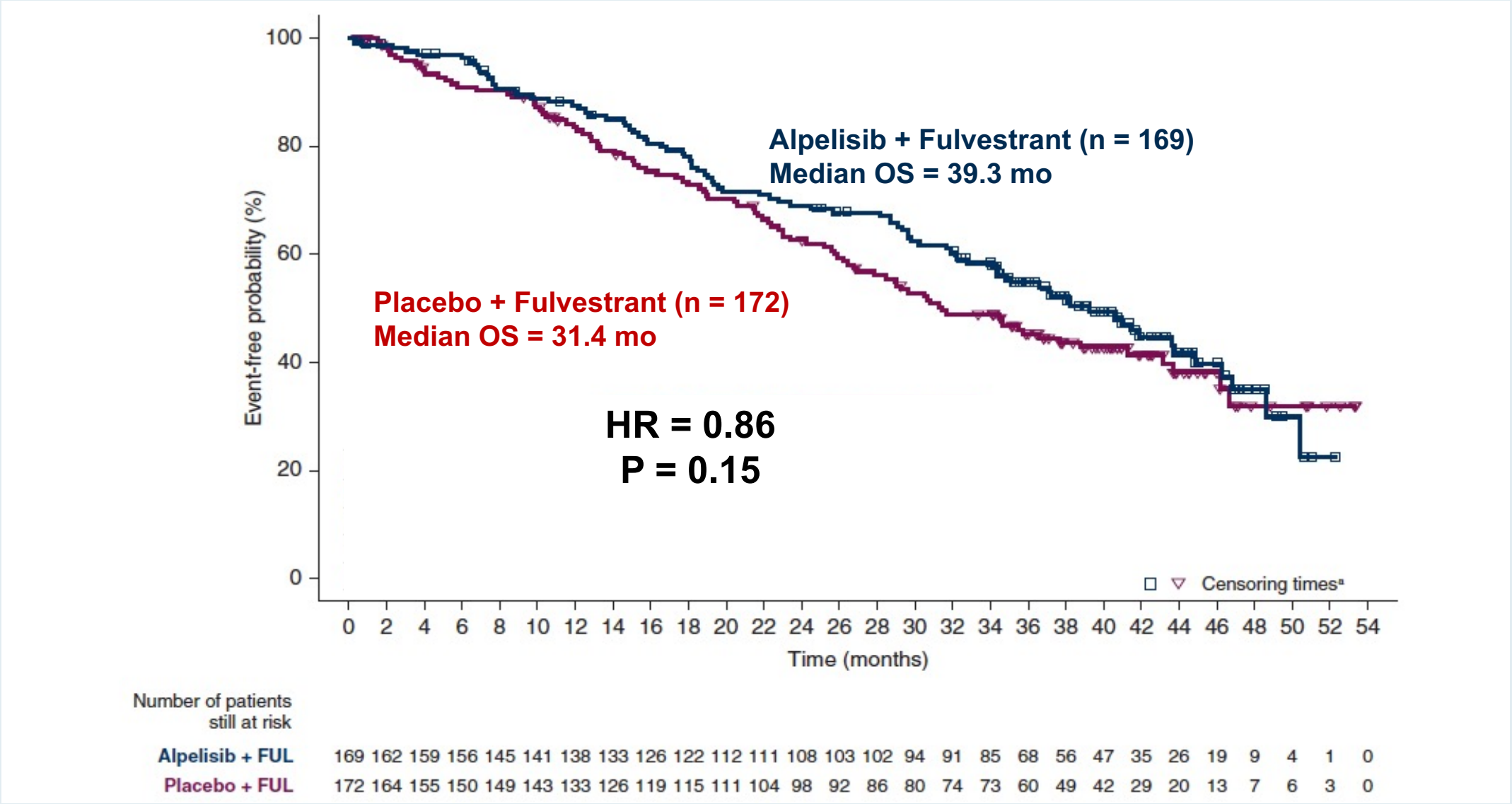
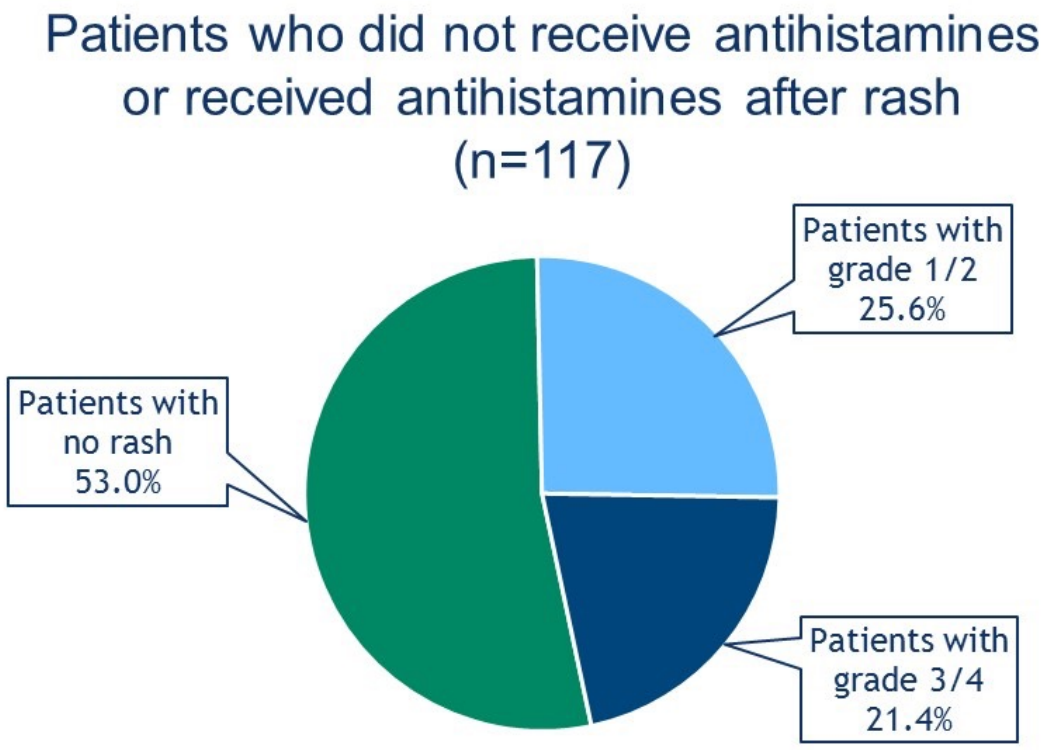
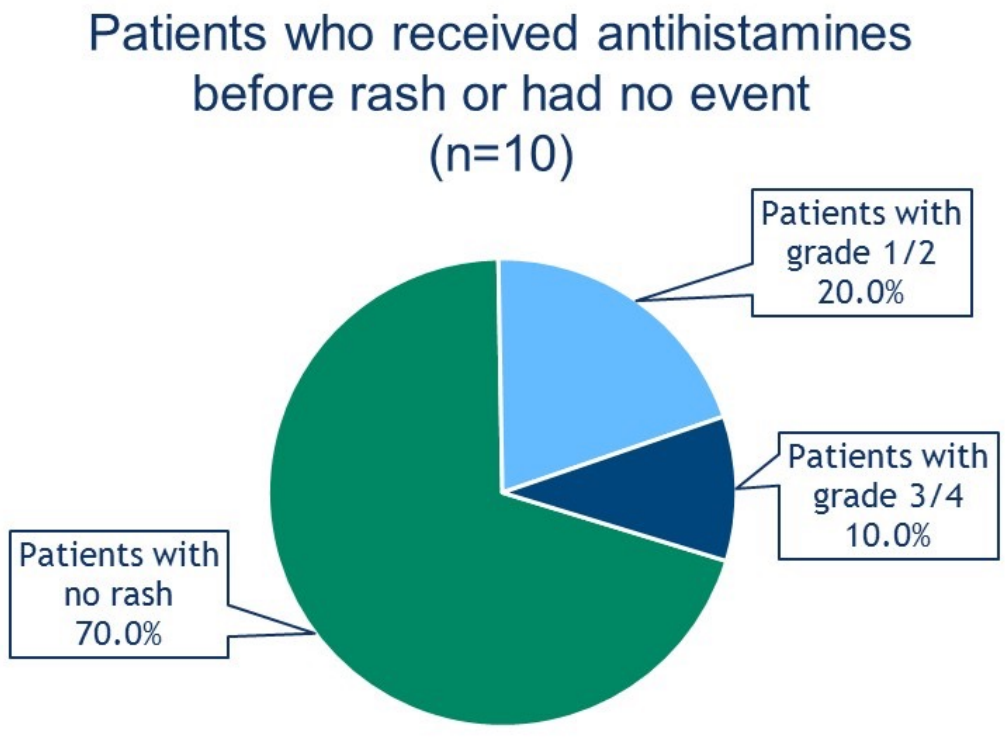
SOLAR-1: OS in Patients with Advanced BC with a PIK3CA Mutation



André F et al. *Ann Oncol* 2021;32(2):208-17.

BYLieve: Incidence of Rash with and without Prophylactic Antihistamines





Rugo HS et al. ASCO 2020;Abstract 1006.

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Agenda

Module 1: ER-Positive, HER2-Negative

- Case 1 – Dr Tolaney: A 40-year-old woman with ER/PR-positive, HER2-negative, node-positive breast cancer
- Case 2 – Ms Hershey: A 63-year-old woman with hormone receptor-positive, node-positive breast cancer
- Case 3 – Dr Tolaney: A 42-year-old woman with hormone receptor-positive, HER2-negative metastatic breast cancer

Module 2: HER2-Positive

- Case 4 – Ms Hershey: A 44-year-old woman with hormone receptor-positive, HER2-positive metastatic breast cancer
- Case 5 – Dr Tolaney: A 36-year-old woman with ER-positive, HER2-positive metastatic breast cancer

Module 3: Triple-Negative

- Case 6 – Ms Hershey: A 52-year-old woman with metastatic triple-negative breast cancer

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A patient with a HER2-positive IDC responds to neoadjuvant chemotherapy and trastuzumab/pertuzumab, but at surgery residual disease is detected. In general, the most common next treatment is…

1. Trastuzumab
2. Trastuzumab/pertuzumab
3. T-DM1
4. Any of the above
5. I don’t know

A Phase III trial evaluating the addition of tucatinib to trastuzumab/capecitabine for metastatic HER2-positive breast cancer resulted in an improvement in overall survival for all patients, including those with brain metastases.

1. Agree
2. Disagree
3. I don't know

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Case Presentation – Ms Hershey: A 44-year-old woman with hormone receptor-positive, HER2-positive metastatic breast cancer

- 2006: Initially diagnosed with breast cancer, s/p neoadjuvant AC/trastuzumab, tamoxifen + OS
- 2013: Recurrent disease
  - Lapatinib + trastuzumab (on protocol)
  - Trastuzumab, letrozole, OFS
  - Trastuzumab, fulvestrant, OFS
  - T-DM1
  - Capecitabine + trastuzumab
  - High dose trastuzumab + pertuzumab (on protocol)
  - Doxorubicin
  - Palbociclib (on protocol) + trastuzumab
  - Trastuzumab
  - Pembrolizumab (on protocol) + trastuzumab
  - Neratinib + capecitabine
  - Carboplatin + trastuzumab
  - GDC-0084 (PI3K inhibitor) + trastuzumab (on protocol)
  - Vinorelbine + trastuzumab + pertuzumab
  - Tucatinib + trastuzumab + capecitabine (June 2020)

Case Presentation – Ms Hershey: A 44-year-old woman with hormone receptor-positive, HER2-positive metastatic breast cancer (continued)

What are the most important things that you discussed with this patient prior to starting treatment?

1. Discussed challenge with progressive brain mets when other disease is stable
2. Reviewed HER2CLIMB data and BBB penetration
3. Focused on tucatinib education, as patient previously received trastuzumab and capecitabine
4. Discussed that other option would be local therapy with aggressive surgical procedure
5. Need for insurance approval, and possible challenges obtaining drug as so recently FDA approved

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Trastuzumab deruxtecan carries a black box warning for…

1. QT interval prolongation
2. Interstitial lung disease
3. Cardiovascular events
4. I don’t know

Case Presentation – Dr Tolaney: A 36-year-old woman with ER-positive, HER2-positive metastatic breast cancer

- De novo ER-positive, HER2-positive breast cancer with nodal and liver metastases
- THP → HP plus OS and AI maintenance → PD, with increase in liver metastases
- T-DM1 x 12 months → PD, with increase in liver metastases
- Trastuzumab deruxtecan

What are the important factors you considered in managing this case?

1. Lack of brain mets
2. Presence of visceral disease
3. 3L therapy

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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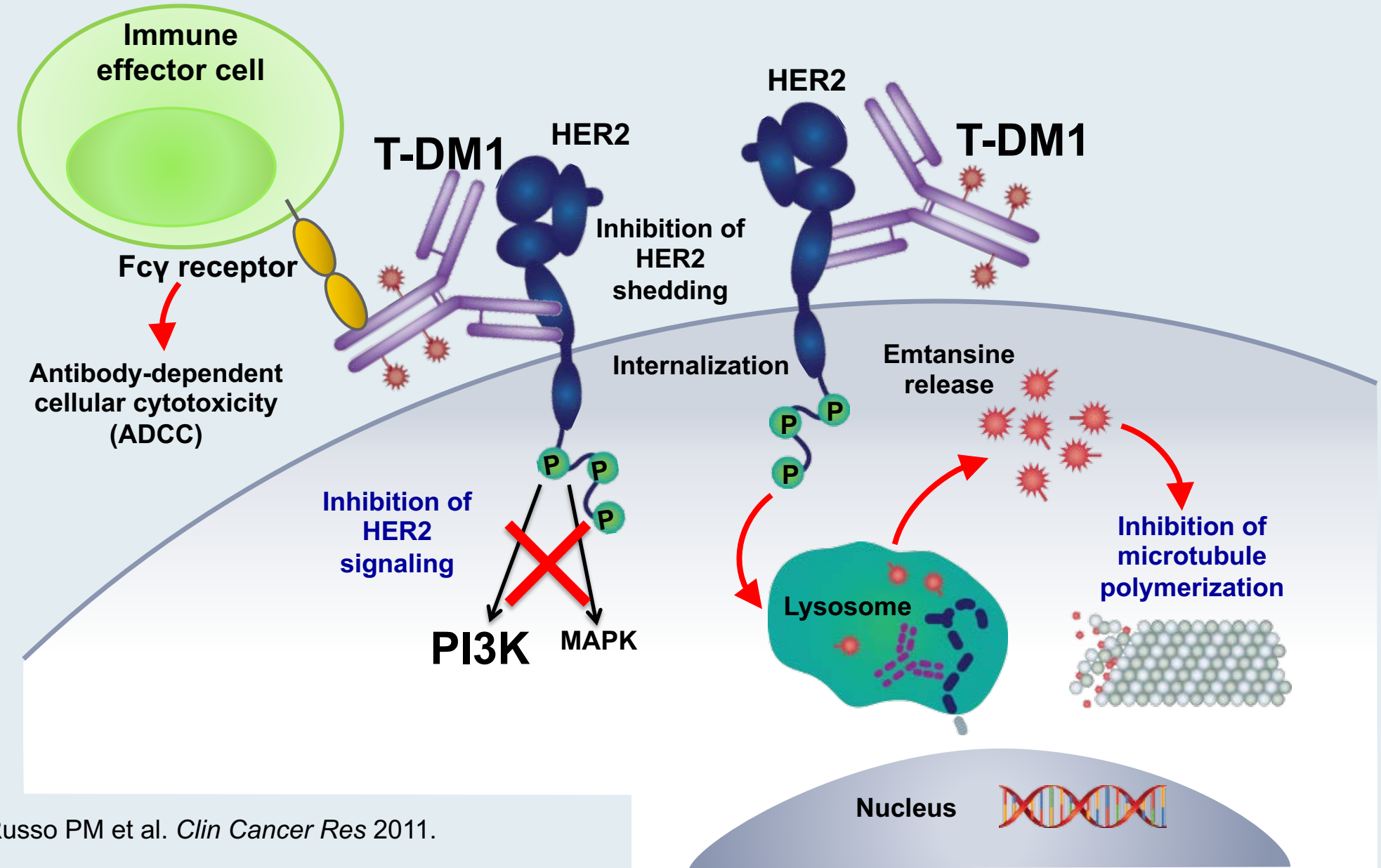
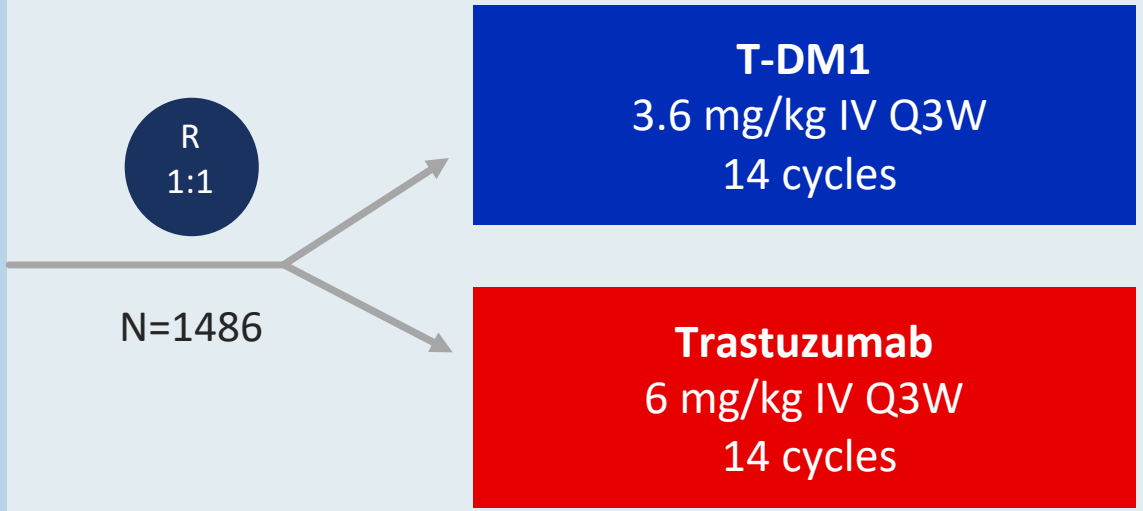
Trastuzumab Emtansine (T-DM1): Mechanisms of Action



Adapted from LoRusso PM et al. *Clin Cancer Res* 2011.

KATHERINE Study Design

- cT1-4/N0-3/M0 at presentation (cT1a-b/N0 excluded)
- Centrally confirmed HER2-positive breast cancer
- Neoadjuvant therapy must have consisted of
  - Minimum of 6 cycles of chemotherapy
    - Minimum of 9 weeks of taxane
    - Anthracyclines and alkylating agents allowed
    - All chemotherapy prior to surgery
  - Minimum of 9 weeks of trastuzumab
    - Second HER2-targeted agent allowed
- Residual invasive tumor in breast or axillary nodes
- Randomization within 12 weeks of surgery



Radiation and endocrine therapy per protocol and local guidelines

Stratification factors:

- Clinical presentation: Inoperable (stage cT4 or cN2–3) vs operable (stages cT1-3N0-1)
- Hormone receptor: ER or PR positive vs ER negative and PR negative/unknown
- Preoperative therapy: Trastuzumab vs trastuzumab plus other HER2-targeted therapy
- Pathological nodal status after neoadjuvant therapy: Positive vs negative/not done

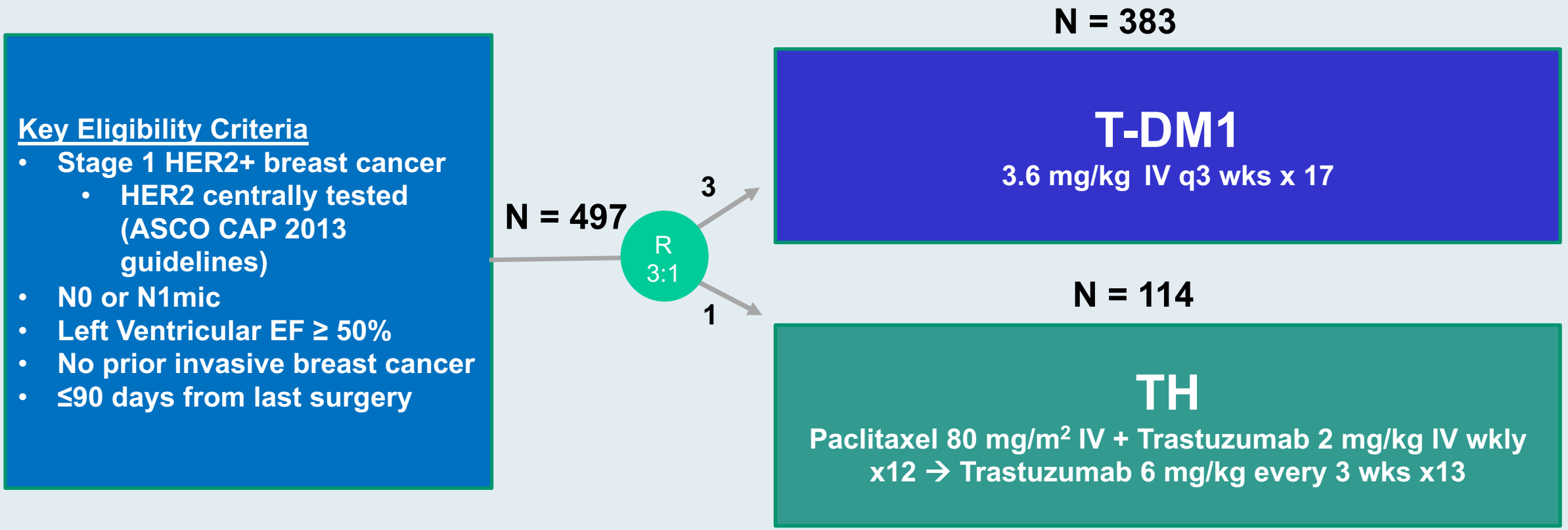
Geyer CE et al. SABCS® 2018;Abstract GS1-10.

KATHERINE: Invasive Disease-Free Survival (IDFS) Outcomes

IDFS	T-DM1 (n = 743)	Trastuzumab (n = 743)
IDFS events	12.2%	22.2%
3-year IDFS	88.3%	77.0%
	HR = 0.50; $p < 0.0001$	
Distant recurrence		
3-year event-free rate	89.7%	83.0%
	HR = 0.60	

Von Minckwitz G, et al. *N Engl J Med* 2019;380:617-28.

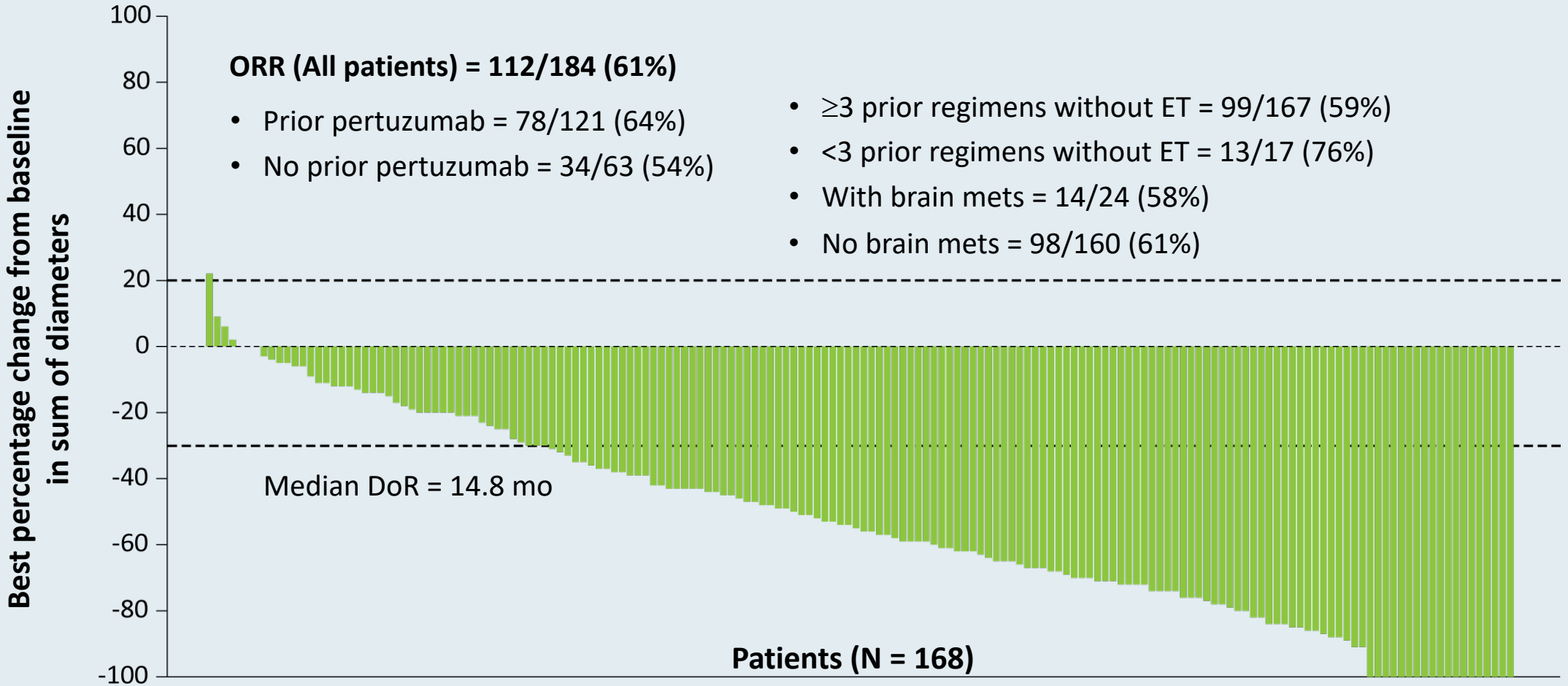
ATEMPT Study Schema



*Radiation and endocrine therapy could be initiated after 12 weeks on study therapy

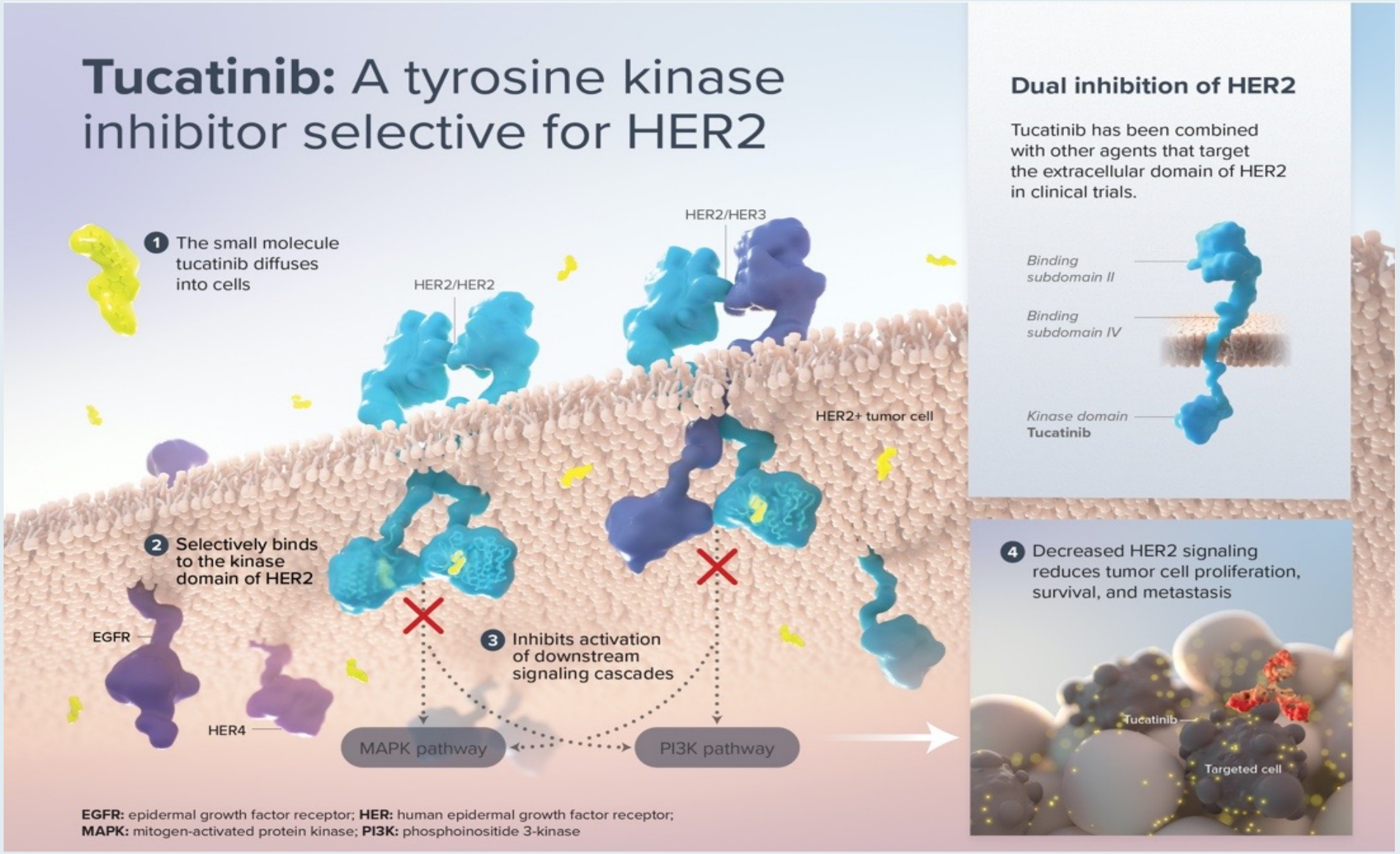
Tolaney S et al. SABCS 2019;Abstract GS1-05.

DESTINY-Breast01: Response According to Tumor Size and Subgroup Analyses



Modi S et al. *N Engl J Med* 2020;382(7):610-21.

Tucatinib Mechanism of Action



www.seagen.com/science/pipeline/tucatinib

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 13, 2020 VOL. 382 NO. 7

Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer

R.K. Murthy, S. Loi, A. Okines, E. Paplomata, E. Hamilton, S.A. Hurvitz, N.U. Lin, V. Borges, V. Abramson, C. Anders, P.L. Bedard, M. Oliveira, E. Jakobsen, T. Bachelot, S.S. Shachar, V. Müller, S. Braga, F.P. Duhoux, R. Greil, D. Cameron, L.A. Carey, G. Curigliano, K. Gelmon, G. Hortobagyi, I. Krop, S. Loibl, M. Pegram, D. Slamon, M.C. Palanca-Wessels, L. Walker, W. Feng, and E.P. Winer

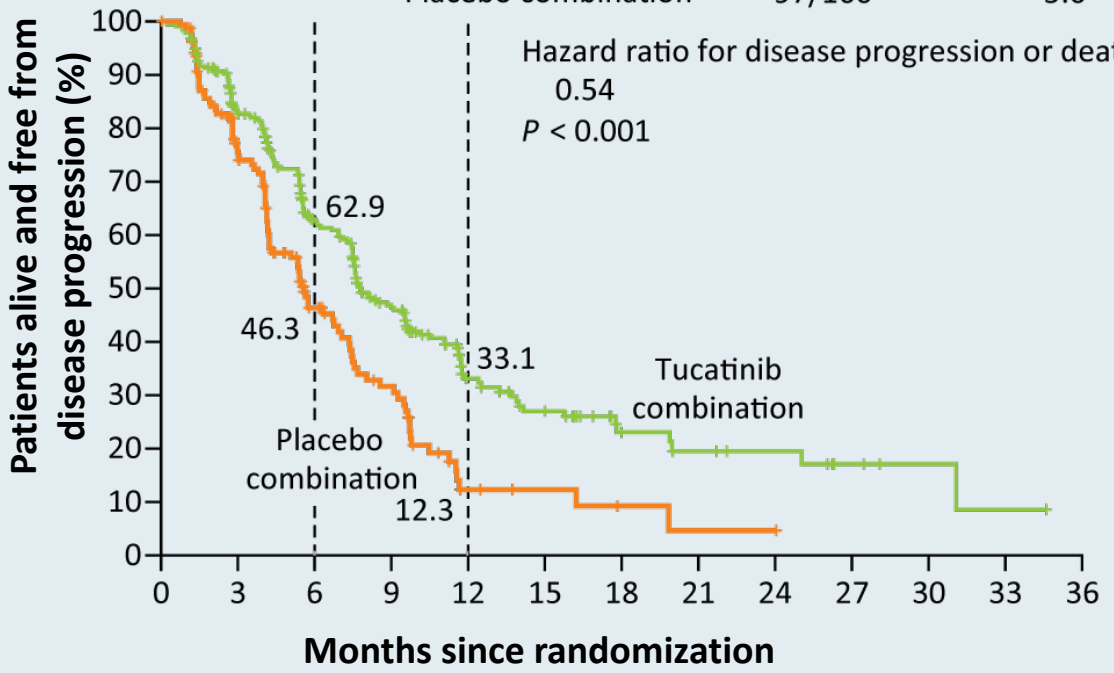
HER2CLIMB: Survival Outcomes

Among the patients with brain metastases:

- Median PFS = 7.6 mo (tucatinib) vs 5.4 mo (placebo)
  - HR = 0.48; $p < 0.001$
- 1-year PFS = 24.9% (tucatinib) vs 0% (placebo)

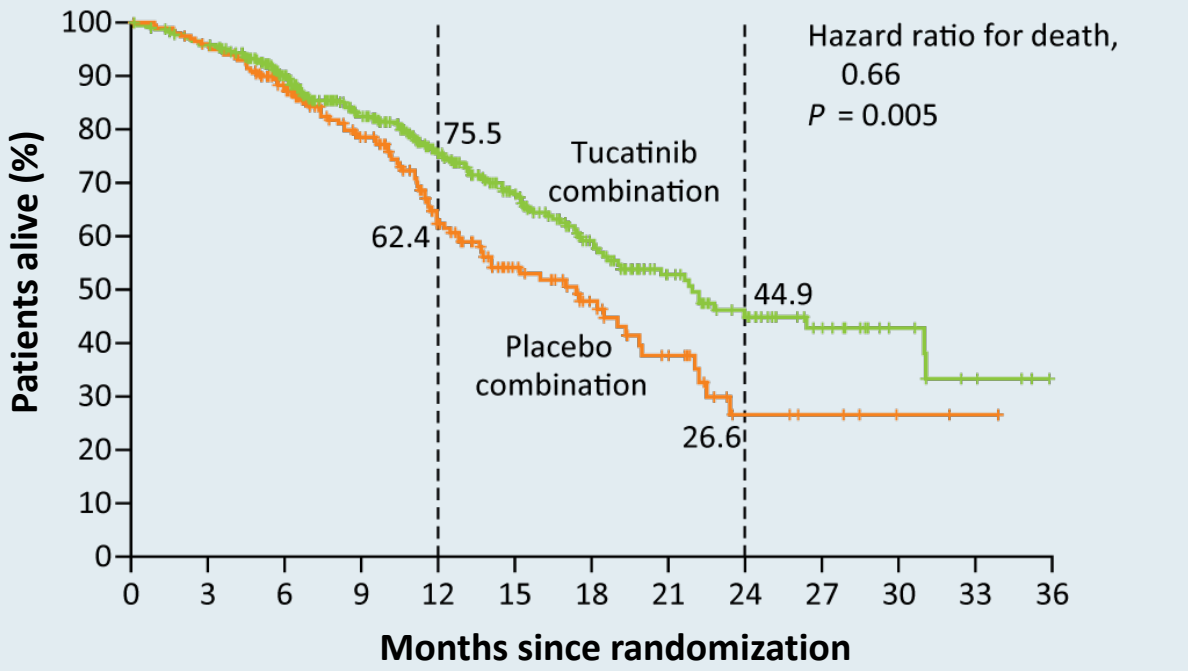
PFS

	No. of events/ No. of patients	Median duration *mo*
Tucatinib combination	178/320	7.8
Placebo combination	97/160	5.6



OS

	No. of deaths/ No. of patients	Median duration *mo*
Tucatinib combination	130/410	21.9
Placebo combination	85/202	17.4



Murthy R et al. San Antonio Breast Cancer Symposium 2019;Abstract GS1-01;
Murthy RK et al. *N Engl J Med* 2020;382(7):597-609.

RTP RESEARCH TO PRACTICE

rapid communications

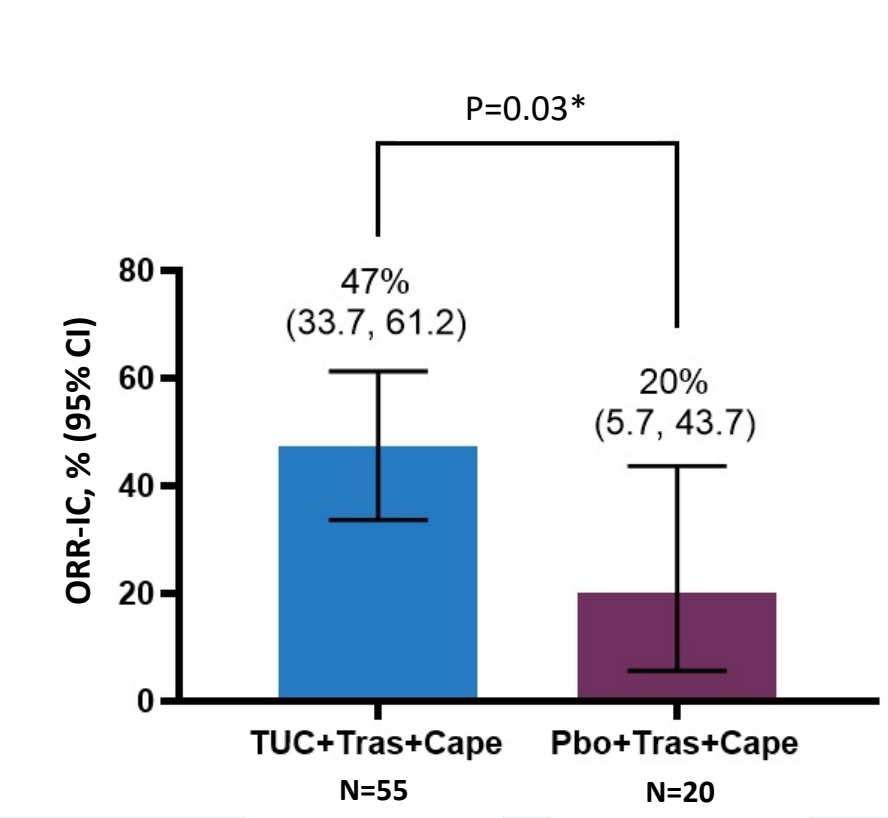
Intracranial Efficacy and Survival With Tucatinib Plus Trastuzumab and Capecitabine for Previously Treated HER2-Positive Breast Cancer With Brain Metastases in the HER2CLIMB Trial

Nancy U. Lin, MD[1]; Virginia Borges, MMSc, MD[2]; Carey Anders, MD[3]; Rashmi K. Murthy, MD, MBE[4]; Elisavet Paplomata, MD[5]; Erika Hamilton, MD[6]; Sara Hurvitz, MD[7]; Sherene Loi, MD, PhD[8]; Alicia Okines, MBChB, MD[9]; Vandana Abramson, MD[10]; Philippe L. Bedard, MD[11]; Mafalda Oliveira, MD, PhD[12]; Volkmar Mueller, MD[13]; Amelia Zelnak, MD[14]; Michael P. DiGiovanna, MD, PhD[15]; Thomas Bachelot, MD[16]; A. Jo Chien, MD[17]; Ruth O'Regan, MD[5]; Andrew Wardley, MBChB, MSc, MD[18]; Alison Conlin, MD, MPH[19]; David Cameron, MD, MA[20]; Lisa Carey, MD[21]; Giuseppe Curigliano, MD, PhD[22]; Karen Gelmon, MD[23]; Sibylle Loibl, MD, PhD[24]; JoAl Mayor, PharmD[25]; Suzanne McGoldrick, MD, MPH[25]; Xuebei An, PhD[25]; and Eric P. Winer, MD[1]

J Clin Oncol 2020;38(23):2610-9.

HER2CLIMB: Intracranial Response Rate (ORR-IC) in Patients with Active Brain Metastases and Measurable Intracranial Lesions at Baseline

Confirmed Objective Response Rate (RECIST 1.1)



*Stratified Cochran-Mantel-Haenszel P value

Best Overall Intracranial Response[a], n (%)		
Complete Response (CR)	3 (5.5)	1 (5.0)
Partial Response (PR)	23 (41.8)	3 (15.0)
Stable Disease (SD)	24 (43.6)	16 (80.0)
Progressive Disease (PD)	2 (3.6)	0
Not Available[b]	3 (5.5)	0
Subjects with Objective Response of Confirmed CR or PR, n	26	4
Duration of Intracranial Response (DOR-IC)[e] (95% CI)[f], months	6.8 (5.5, 16.4)	3.0 (3.0, 10.3)

(a) Confirmed Best overall response assessed per RECIST 1.1. (b) Subjects with no post-baseline response assessments. (c) Two-sided 95% exact confidence interval, computed using the Clopper-Pearson method (1934). (d Cochran-Mantel-Haenszel test controlling for stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. (e) As estimated using Kaplan-Meier methods. (f) Calculated using the complementary log-log transformation method (Collett, 1994).

Courtesy of Carey K Anders, MD

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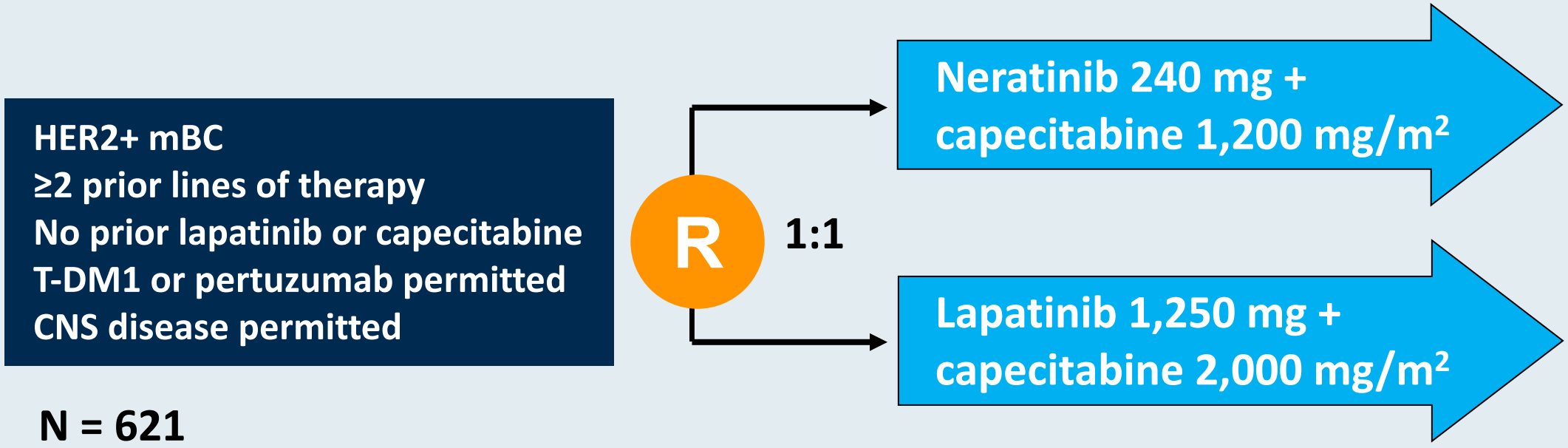
NALA: Phase III Trial Design



N = 621

Coprimary endpoints: PFS (central) and OS

Saura C et al. *J Clin Oncol* 2020;38(27):3138-49.

Research

JAMA Oncology | Original Investigation

Efficacy of Margetuximab vs Trastuzumab in Patients With Pretreated ERBB2-Positive Advanced Breast Cancer

A Phase 3 Randomized Clinical Trial

Hope S. Rugo, MD; Seock-Ah Im, MD, PhD; Fatima Cardoso, MD; Javier Cortés, MD, PhD; Giuseppe Curigliano, MD, PhD; Antonino Musolino, MD, PhD, MSc; Mark D. Pegram, MD; Gail S. Wright, MD; Cristina Saura, MD, PhD; Santiago Escrivá-de-Romaní, MD; Michelino De Laurentiis, MD, PhD; Christelle Levy, MD; Ursa Brown-Glaberman, MD; Jean-Marc Ferrero, MD; Maaike de Boer, MD, PhD; Sung-Bae Kim, MD, PhD; Katarína Petráková, MD, PhD; Denise A. Yardley, MD; Orit Freedman, MD, MSc; Erik H. Jakobsen, MD; Bella Kaufman, MD; Rinat Yerushalmi, MD; Peter A. Fasching, MD; Jeffrey L. Nordstrom, PhD; Ezio Bonvini, MD; Scott Koenig, MD, PhD; Sutton Edlich, MS, PA; Shengyan Hong, PhD; Edwin P. Rock, MD, PhD; William J. Gradishar, MD; for the SOPHIA Study Group

***JAMA Oncol* 2021;[Online ahead of print].**

Agenda

Module 1: ER-Positive, HER2-Negative

- Case 1 – Dr Tolaney: A 40-year-old woman with ER/PR-positive, HER2-negative, node-positive breast cancer
- Case 2 – Ms Hershey: A 63-year-old woman with hormone receptor-positive, node-positive breast cancer
- Case 3 – Dr Tolaney: A 42-year-old woman with hormone receptor-positive, HER2-negative metastatic breast cancer

Module 2: HER2-Positive

- Case 4 – Ms Hershey: A 44-year-old woman with hormone receptor-positive, HER2-positive metastatic breast cancer
- Case 5 – Dr Tolaney: A 36-year-old woman with ER-positive, HER2-positive metastatic breast cancer

Module 3: Triple-Negative

- Case 6 – Ms Hershey: A 52-year-old woman with metastatic triple-negative breast cancer

RTP RESEARCH TO PRACTICE

The anti-PD-L1 antibody atezolizumab is currently FDA approved in combination with *nab* paclitaxel as first-line treatment for…

1. All patients with metastatic breast cancer
2. Metastatic triple-negative breast cancer
3. Metastatic PD-L1-positive triple-negative breast cancer
4. I don’t know

Case Presentation – Ms Hershey: A 52-year-old woman with metastatic TNBC

- 1/2020: T2N1 left breast cancer, s/p neoadjuvant ddAC-T → left mastectomy + ALND and right-sided reduction mammoplasty
  - Left: 2.4-cm residual disease, 3 positive LNs
  - Delay in RT due to slow wound healing in right-sided reduction surgery
- After 3rd RT treatment, erythema in surgical excision → punch biopsy: TNBC
- Resection of 3.5-cm locally recurrent TNBC
- 4/2020: Concurrent capecitabine + RT
- Erythema in contralateral breast (right) at site of reduction surgery, with pain and heaviness and increased erythema of left chest wall at site of radiation field
  - Antibiotics
  - Biopsy of right, contralateral breast: Metastatic TNBC
- 6/2020: Atezolizumab/*nab*-paclitaxel
- 1/2021: Sacituzumab govitecan
- 4/2021: Carboplatin/gemcitabine

Case Presentation – Ms Hershey: A 52-year-old woman with metastatic TNBC (continued)

What are the most important issues you planned to discuss with this patient?

1. Had overall been tolerating 1st line tx well, but clinically appeared to have progression of skin findings (worsening erythema)
2. Difficult to monitor her disease with skin-only findings (no visceral disease), but concerned that current therapy was not adequately controlling her disease
3. Stepped out at one point to review with attending MD and recommended transition to new therapy – reviewed schedule and possible side effects
4. Patient appeared visibly upset, crying, so I asked what her concerns were
5. Patient acknowledged that information was difficult to hear; she was worried about lack of options moving forward. She said she feared dying and feeling unwell, having unmanaged pain
6. Called her husband, was able to have him come up from the car and join the conversation. Was also able to pull attending MD in to part of visit

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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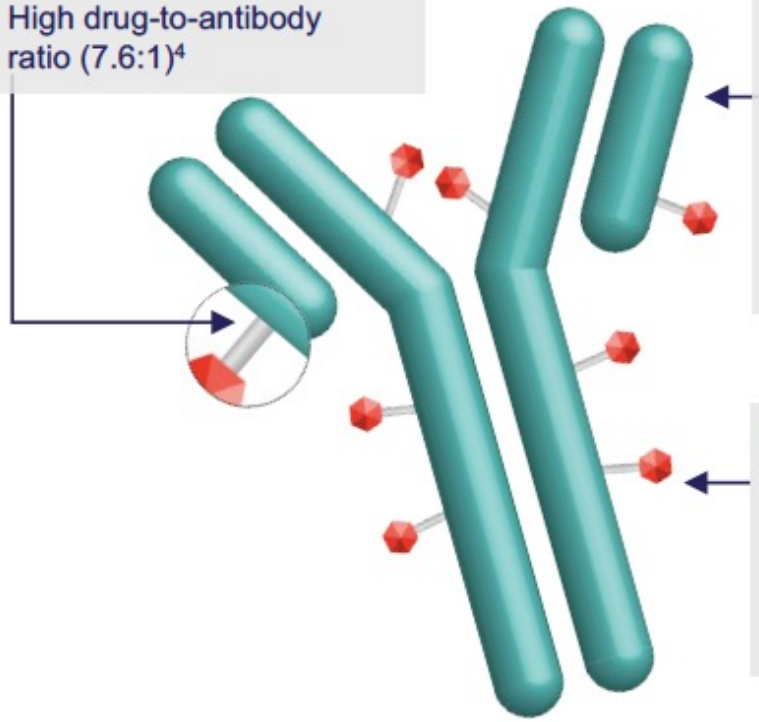
Sacituzumab Govitecan (SG) Is a First-in-Class Trop-2–Directed ADC

- SG is distinct from other ADCs[1-4]
  - Antibody highly specific for Trop-2
  - High drug-to-antibody ratio (7.6:1)
  - Internalization and enzymatic cleavage by tumor cell not required for SN-38 liberation from antibody
  - Hydrolysis of the linker also releases SN-38 extracellularly in the tumor microenvironment (bystander effect)
- Granted FDA accelerated approval for mTNBC[5]
- Landmark ASCENT study demonstrated a significant survival improvement of SG over chemotherapy, with a tolerable safety profile in pretreated mTNBC[6]
  - Median PFS of 5.6 vs 1.7 months (HR 0.41, *P*<0.0001)
  - Median OS of 12.1 vs 6.7 months (HR 0.48, *P*<0.0001)

Linker for SN-38
- Hydrolyzable linker for payload release
- High drug-to-antibody ratio (7.6:1)[4]



Humanized anti–Trop-2 antibody
- Directed toward Trop-2, an epithelial antigen expressed on many solid cancers

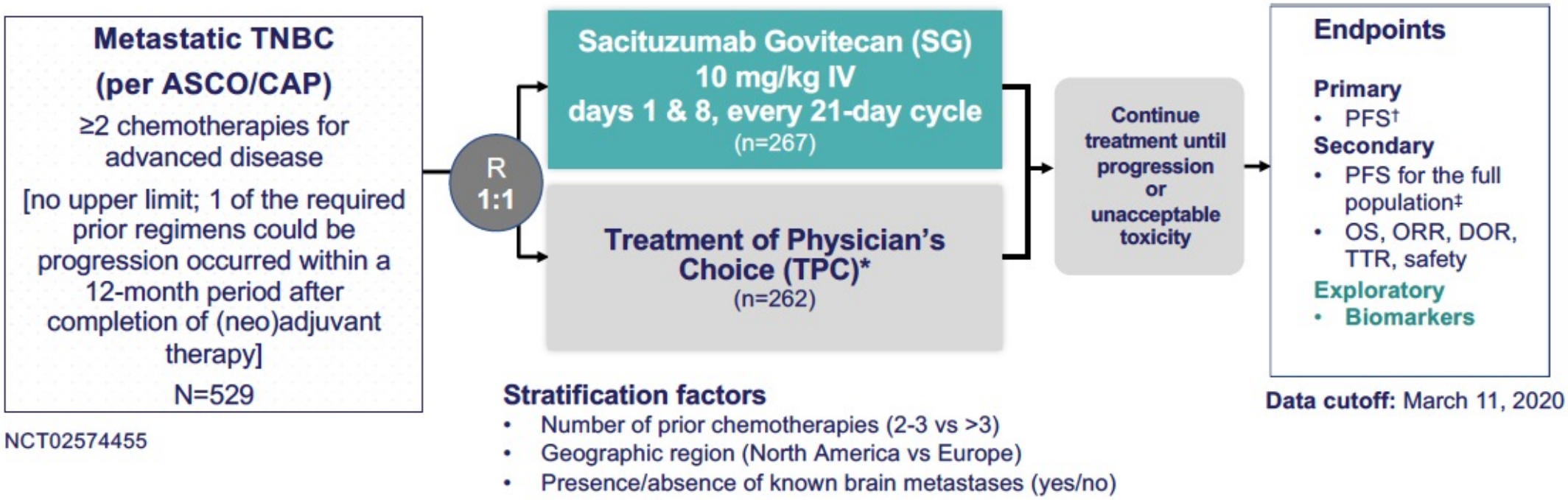
SN-38 payload
- SN-38 more potent than parent compound, irinotecan

ADC, antibody-drug conjugate; FDA, US Food and Drug Administration; OS, overall survival; PFS, progression-free survival; TNBC, triple-negative breast cancer; Trop-2, trophoblast cell surface antigen 2.

1. Goldenberg DM, et al. *Expert Opin Biol Ther.* 2020;20:871-885. 2. Nagayama A, et al. *Ther Adv Med Oncol.* 2020;12:1758835920915980. 3. Cardillo TM, et al. *Bioconjugate Chem.* 2015;26:919-931. 4. Goldenberg DM, et al. *Oncotarget.* 2015;6:22496-224512. 5. Press Release. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-sacituzumab-govitecan-hziy-metastatic-triple-negative-breast-cancer. Accessed August 26, 2020. 6. Bardia A, et al. ESMO 2020. Abstract LBA17.

Hurvitz SA et al. SABCS 2020;Abstract GS3-06.

ASCENT: A Phase 3 Confirmatory Study of Sacituzumab Govitecan in Refractory/Relapsed mTNBC



NCT02574455

Stratification factors
- Number of prior chemotherapies (2-3 vs >3)
- Geographic region (North America vs Europe)
- Presence/absence of known brain metastases (yes/no)

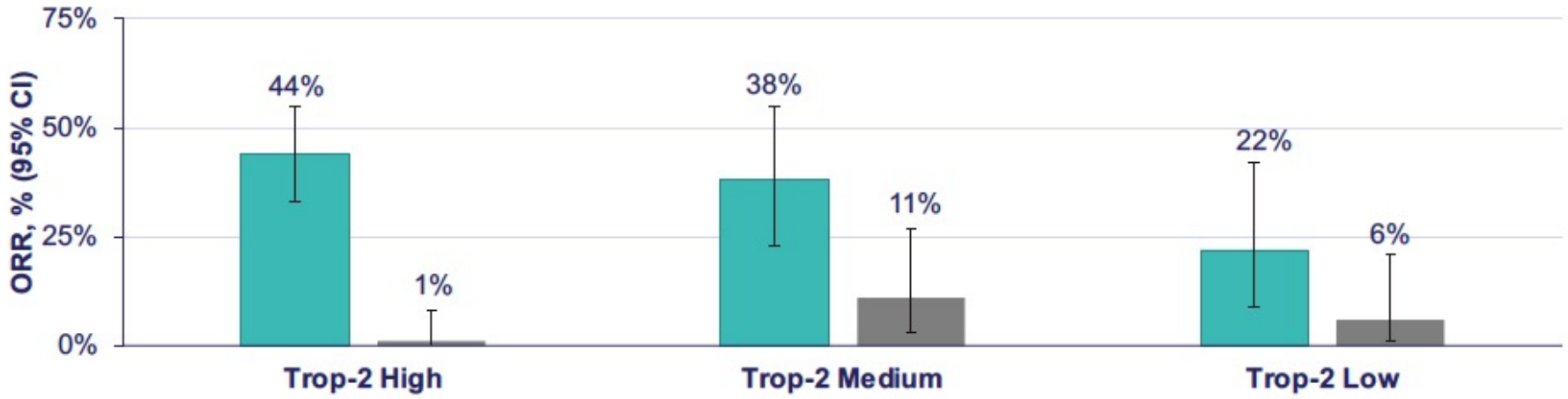
Data cutoff: March 11, 2020

We report the exploratory biomarker analysis in the brain metastases-negative (Brain Mets-Negative) population

*TPC: eribulin, vinorelbine, gemcitabine, or capecitabine. †PFS measured by an independent, centralized, and blinded group of radiology experts who assessed tumor response using RECIST 1.1 criteria in patients without brain metastasis. ‡The full population includes all randomized patients (with and without brain metastases). Baseline brain MRI only required for patients with known brain metastasis.
ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; DOR, duration of response; DSMC, Data Safety Monitoring Committee; IV, intravenous; mTNBC, metastatic triple-negative breast cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.
National Institutes of Health. https://clinicaltrials.gov/ct2/show/NCT02574455.

Hurvitz SA et al. SABCS 2020;Abstract GS3-06.

ORR by Trop-2 Expression



	Trop-2 High H-score: 200-300 (n=157)		Trop-2 Medium H-score: 100-200 (n=74)		Trop-2 Low H-score: <100 (n=59)	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
ORR—% (no.)	44% (37)	1% (1)	38% (15)	11% (4)	22% (6)	6% (2)
95% CI	33-55	0-8	23-55	3-27	9-42	1-21

Assessed in the brain metastases-negative population. ORR and PFS are assessed by BICR. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.
BICR, blind independent central review; H-score, histochemical-score; ORR, objective response rate; SG, sacituzumab govitecan; TPC, treatment of physician's choice; Trop-2, trophoblast cell surface antigen-2.

Hurvitz SA et al. SABCS 2020;Abstract GS3-06.

The PARP inhibitors olaparib and talazoparib are FDA approved for patients with metastatic breast cancer and a germline BRCA mutation…

1. As maintenance therapy after platinum chemotherapy
2. As monotherapy
3. Both a and b
4. I don’t know

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Phase III Olympia Trial of Adjuvant Olaparib for High-Risk HER2-Negative Localized Breast Cancer with a BRCA Mutation Crossed the Superiority Boundary for Invasive Disease-Free Survival

Press Release – February 17, 2021

"The OlympiA Phase III trial of [olaparib] will move to early primary analysis and reporting following a recommendation from the Independent Data Monitoring Committee (IDMC).

Based on the planned interim analysis, the IDMC concluded that the trial crossed the superiority boundary for its primary endpoint of invasive disease-free survival (iDFS) and demonstrated a sustainable, clinically relevant treatment effect for olaparib versus placebo for patients with germline BRCA-mutated (gBRCAm) high-risk human epidermal growth factor receptor 2 (HER2)-negative early breast cancer, and recommend primary analysis now take place.

In its communication, the IDMC did not raise any new safety concerns. The trial will continue to assess the key secondary endpoints of overall survival and distant disease-free survival."

https://www.astrazeneca.com/media-centre/press-releases/2021/olympia-trial-of-lynparza-idmc-recommend-early-analysis.html

OlympiA: A Phase III, Multicenter, Randomized, Placebo-Controlled Trial of Adjuvant Olaparib After (Neo)Adjuvant Chemotherapy in Patients with Germline BRCA1/2 Mutations and High-Risk HER2-Negative Early Breast Cancer

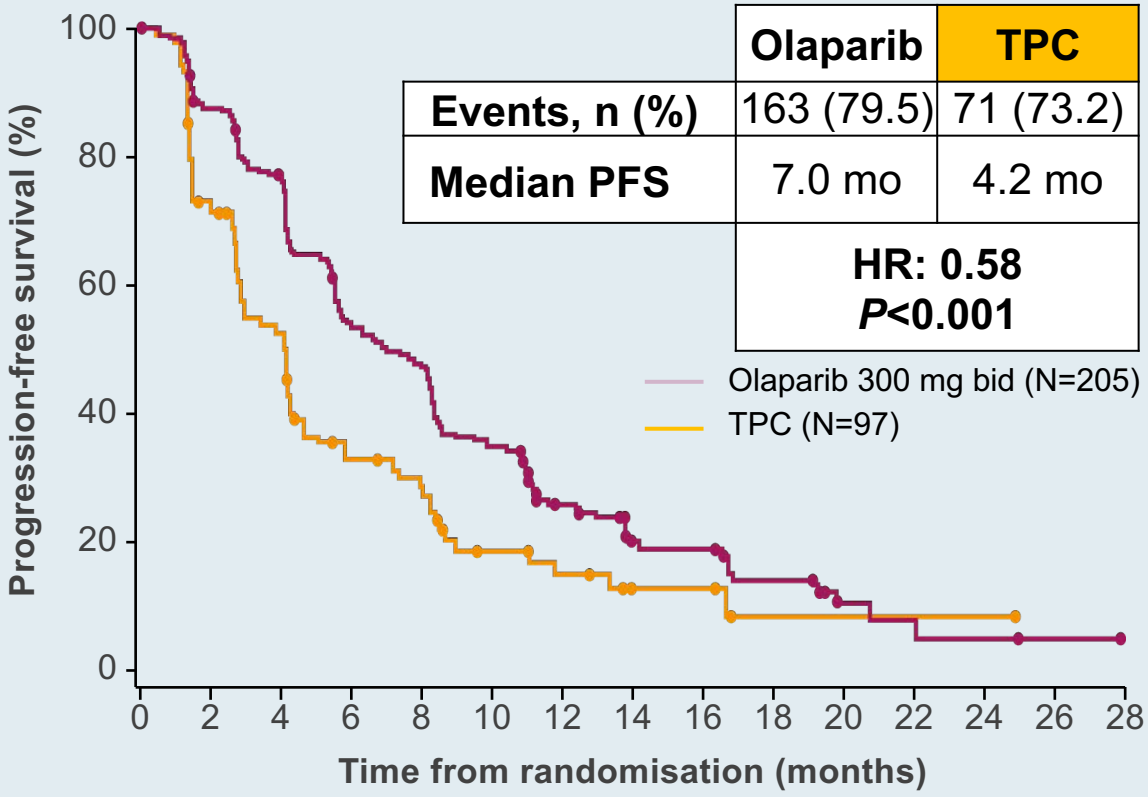
Tutt A et al.

ASCO 2021;Abstract LBA1.

Sunday, June 6, 1:00 PM - 4:00 PM EDT

Phase III Trials of PARP Inhibitors in gBRCA HER2-Negative Metastatic Breast Cancer

OlympiAD: Olaparib PFS[1,2]

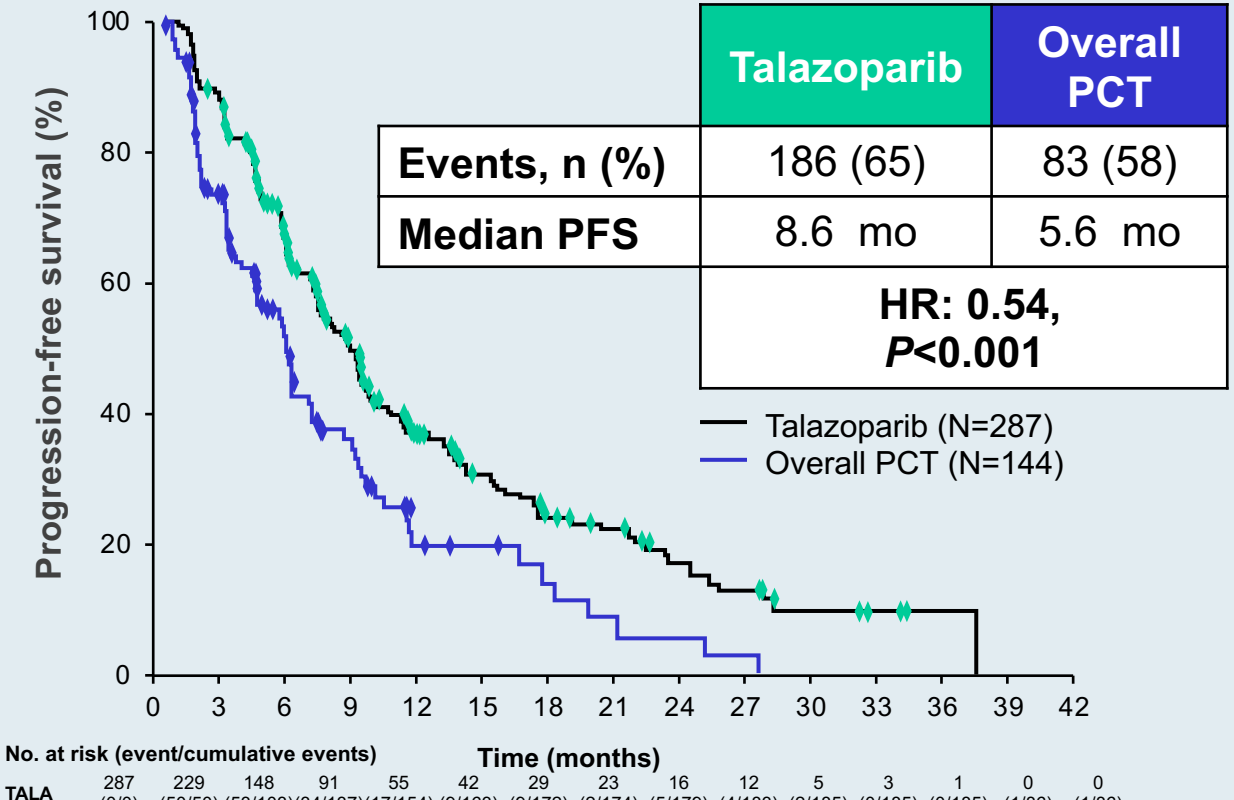


	Olaparib	TPC
Events, n (%)	163 (79.5)	71 (73.2)
Median PFS	7.0 mo	4.2 mo
	HR: 0.58 *P*<0.001	

Number at risk

Olaparib	205	201	177	159	154	129	107	100	94	73	69	61	40	36	23	21	21	11	11	11	4	3	3	2	2	1	1	1	0
TPC	97	88	83	46	44	29	25	24	21	13	11	11	8	7	4	4	4	1	1	1	1	1	1	1	1	0	0	0	0

EMBRACA: Talazoparib PFS[3]



	Talazoparib	Overall PCT
Events, n (%)	186 (65)	83 (58)
Median PFS	8.6 mo	5.6 mo
	HR: 0.54, *P*<0.001	

No. at risk (event/cumulative events)

TALA	287 (0/0)	229 (50/50)	148 (53/103)	91 (34/137)	55 (17/154)	42 (9/163)	29 (9/172)	23 (2/174)	16 (5/179)	12 (4/183)	5 (2/185)	3 (0/185)	1 (0/185)	0 (1/86)	0 (1/86)
PCT	144 (0/0)	68 (41/41)	34 (20/61)	22 (8/69)	9 (7/76)	8 (0/76)	4 (3/79)	2 (2/81)	2 (0/81)	1 (1/82)	0 (1/83)	0 (0/83)	0 (0/83)	0 (0/83)	0 (0/83)

1. Robson M, et al. *N Engl J Med* 2017;377:523-33; 2. Olaparib 150mg Film-Coated Tablets, SmPC. 2019;
3. Litton JK, et al. *N Engl J Med* 2018;379:753-63 (supplementary appendix)

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Monday, June 7, 2021
5:00 PM – 6:00 PM ET

Faculty

Kristen K Ciombor, MD, MSCI

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant within 3 business days.