

Meet The Professors

Nurse and Physician Investigators

Discuss Existing and Emerging Treatment Strategies for Patients with Breast Cancer

Tuesday, July 14, 2020

5:00 PM – 6:00 PM ET

Faculty

Virginia Kaklamani, MD, DSc
Daniel G Pizana, MSN-FNP, OCN

Moderator

Neil Love, MD

Faculty



Virginia Kaklamani, MD, DSc

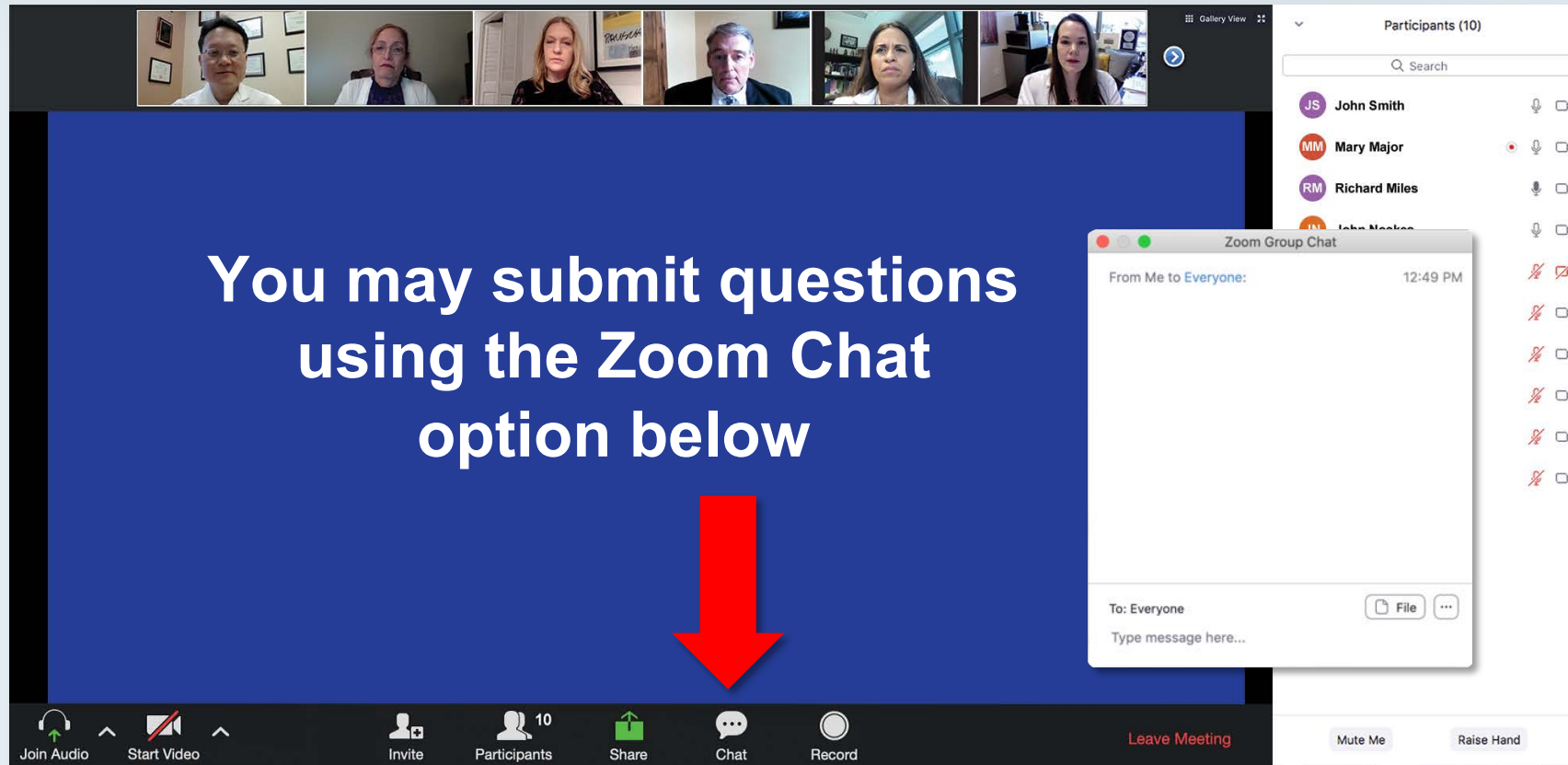
Professor of Medicine
Ruth McLean Bowman Bowers Chair in
Breast Cancer Research and Treatment
AB Alexander Distinguished Chair in Oncology
Associate Director for Clinical Research
Leader of the Breast Cancer Program
UT Health San Antonio
The University of Texas
MD Anderson Cancer Center
San Antonio, Texas



Daniel G Pizana, MSN-FNP, OCN

UT Health San Antonio Mays Cancer Center
Breast Oncology Clinic
San Antonio, Texas

Dr Love and Faculty Encourage You to Ask Questions



The screenshot displays a Zoom meeting interface. At the top, a gallery view shows six participants. The main area features a blue presentation slide with the text: "You may submit questions using the Zoom Chat option below". A large red arrow points from this text to the "Chat" button in the bottom toolbar. To the right, a "Zoom Group Chat" window is open, showing a list of participants (John Smith, Mary Major, Richard Miles, John Macken) and a message input field. The bottom toolbar includes buttons for "Join Audio", "Start Video", "Invite", "Participants" (showing 10), "Share", "Chat", and "Record". A "Leave Meeting" button is also visible on the right side of the toolbar.

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

Meet The Professors: Nurse and Physician Investigators Discuss Existing and Emerging Treatment Strategies for Patients with Bladder, Breast and Prostate Cancer

Bladder Cancer

Tuesday, July 21, 2020
5:00 PM – 6:00 PM ET

Arjun Balar, MD
Susan K Roethke, CRNP,
MSN, ANP-BC, AOCNP

Thursday, July 30, 2020
5:00 PM – 6:00 PM ET

Anastassia Daskalova, NP
Peter H O'Donnell, MD

Breast Cancer

Tuesday, July 14, 2020
5:00 PM – 6:00 PM ET

Virginia Kaklamani, MD, DSc
Daniel G Pizana,
MSN-FNP, OCN

Thursday, July 23, 2020
5:00 PM – 6:00 PM ET

Joyce O'Shaughnessy, MD
Marissa Marti, APRN,
AGNP-C, AOCNP

Prostate Cancer

Thursday, July 16, 2020
5:00 PM – 6:00 PM ET

Matthew R Smith, MD, PhD
Kara M Olivier, NP, APRN-BC

Tuesday, July 28, 2020
5:00 PM – 6:00 PM ET

Robert Dreicer, MD, MS
Victoria Sinibaldi, RN, MS,
CS, CANP, BC

All events moderated by Neil Love, MD

ONCOLOGY TODAY

WITH DR NEIL LOVE



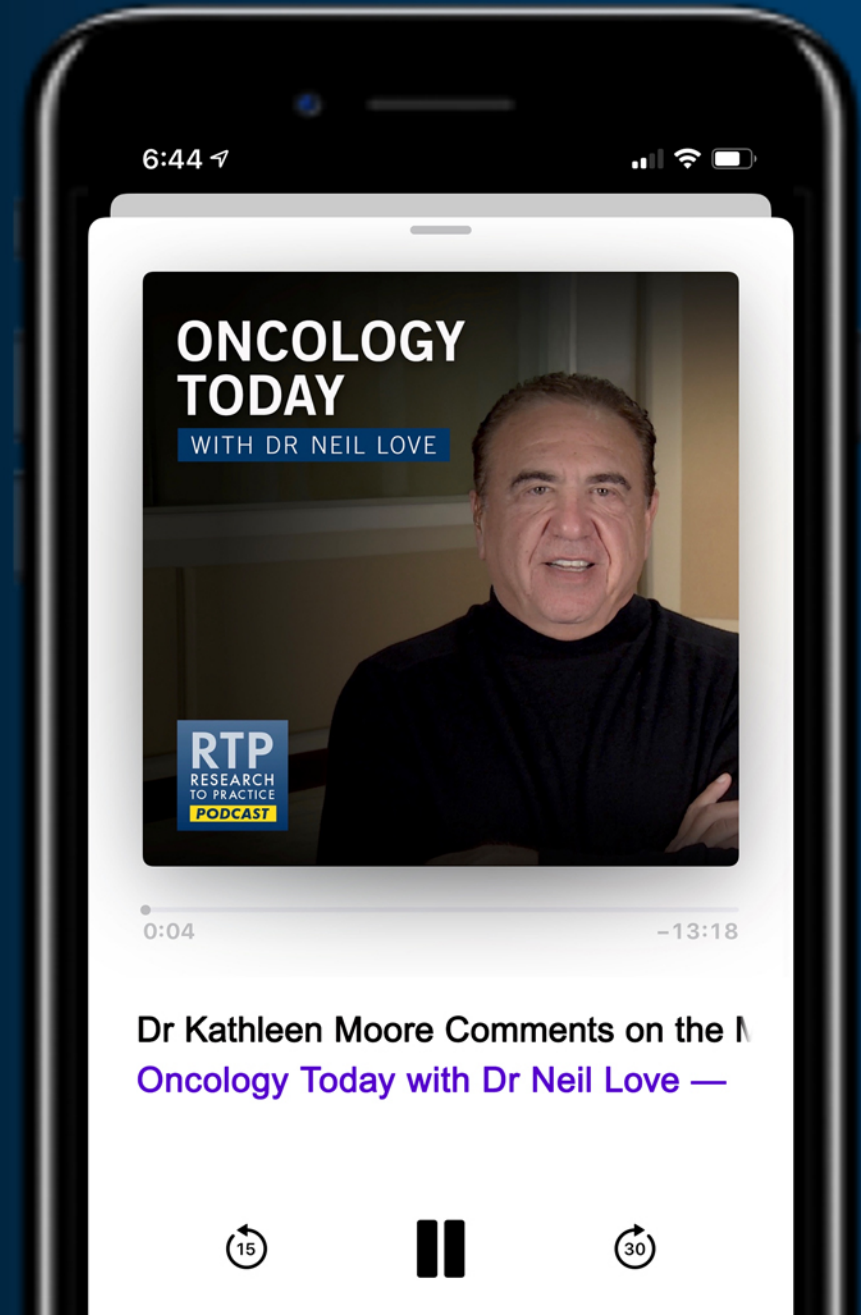
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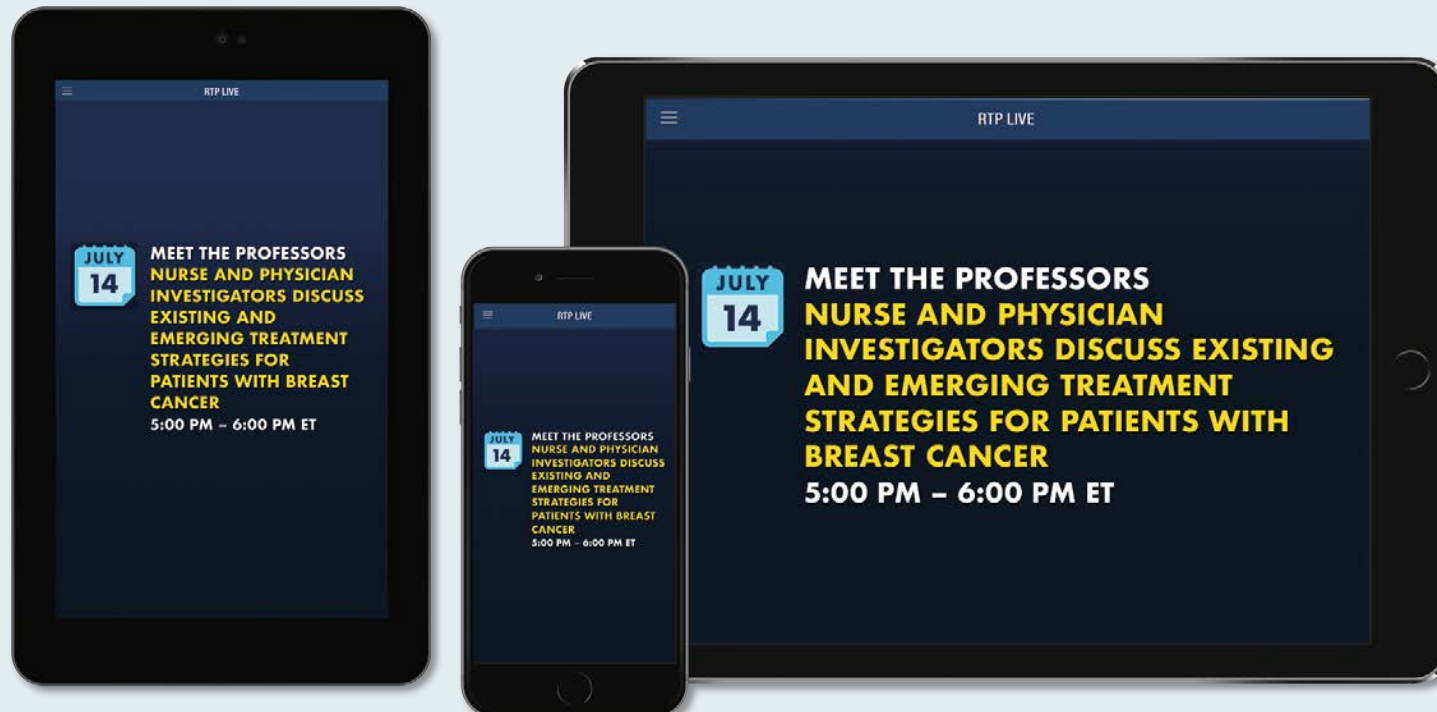
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www.ResearchToPractice.com/RTPLiveApp



Research To Practice's 2019 San Antonio Breast Cancer Symposia

DATA + PERSPECTIVES

Clinical Investigators Explore the Current and Future Management of ER-Positive Breast Cancer

Wednesday, December 11, 2019
7:30 PM – 9:00 PM
San Antonio, Texas

Moderator
Neil Love, MD

Faculty

Harold J Burstein, MD, PhD
Matthew Goetz, MD

Stephen RD Johnston, MA, PhD
Joseph A Sparano, MD

Research
To Practice®

DATA + PERSPECTIVES

Clinical Investigators Explore the Current and Future Management of HER2-Positive Breast Cancer

Friday, December 13, 2019
7:30 PM – 9:00 PM
San Antonio, Texas

Moderator
Neil Love, MD

Faculty

Adam M Brufsky, MD, PhD
Lisa A Carey, MD

Sara Hurvitz, MD
Martine J Piccart-Gebhart, MD, PhD

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To Practice®

DATA + PERSPECTIVES

Clinical Investigators Explore the Current and Future Management of Triple-Negative Breast Cancer

Thursday, December 12, 2019
7:30 PM – 9:00 PM
San Antonio, Texas

Moderator
Neil Love, MD

Faculty

Erika Hamilton, MD
Professor Sherene Loi, MBBS, PhD

Mark E Robson, MD
Hope S Rugo, MD

Research
To Practice®

Meet The Professors

Nurse and Physician Investigators

Discuss Existing and Emerging Treatment Strategies for Patients with Breast Cancer

Tuesday, July 14, 2020

5:00 PM – 6:00 PM ET

Faculty

Virginia Kaklamani, MD, DSc
Daniel G Pizana, MSN-FNP, OCN

Moderator

Neil Love, MD

Agenda

10 Decisions in Breast Cancer and Where New Agents and Strategies Fit In

Case 1: A 60-year-old woman with ER-positive, HER2-positive breast cancer

- Neoadjuvant, adjuvant treatment of localized disease
- New agents, regimens in metastatic disease

Case 2: A 38-year-old woman with triple-negative breast cancer (TNBC)

- Metastatic TNBC: Atezolizumab/*nab* paclitaxel, pembrolizumab/chemotherapy
- Neoadjuvant pembrolizumab/chemotherapy in localized TNBC
- Recent FDA approval of sacituzumab govitecan
- Germline and somatic mutation testing
- Indications for and selection of available PARP inhibitors (olaparib, talazoparib)

Case 3: An 80-year-old woman with ER-positive, HER2-negative breast cancer, with a low Recurrence Score

- Chemotherapy versus endocrine therapy for early breast cancer
- Current role of CDK4/6 inhibitors for pre- and postmenopausal women
- Alpelisib/fulvestrant (PIK3CA mutation)

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Case Presentation: A 60-year-old woman with ER-positive, HER2-positive breast cancer

Special Considerations

- Elementary school teacher, very frightened about the pandemic and future risks to herself and her students
- Also concerned that her cancer care may be compromised by the pandemic, resources, etc
- Divorced, no children. Close to family and church
- Palpates a 3 cm breast lump: ER-positive, HER2-positive
 - 1-cm axillary node (biopsy positive)



Decision 1: Surgery or neoadjuvant treatment?

- Paclitaxel/trastuzumab, pertuzumab given (subcutaneously?)
- Surgery: Residual tumor present

Decision 2: Adjuvant treatment?

- TDM-1 given for 16 cycles: grade 1 neuropathy, thrombocytopenia

Case Presentation: A 60-year-old woman with ER-positive, HER2-positive breast cancer (cont)

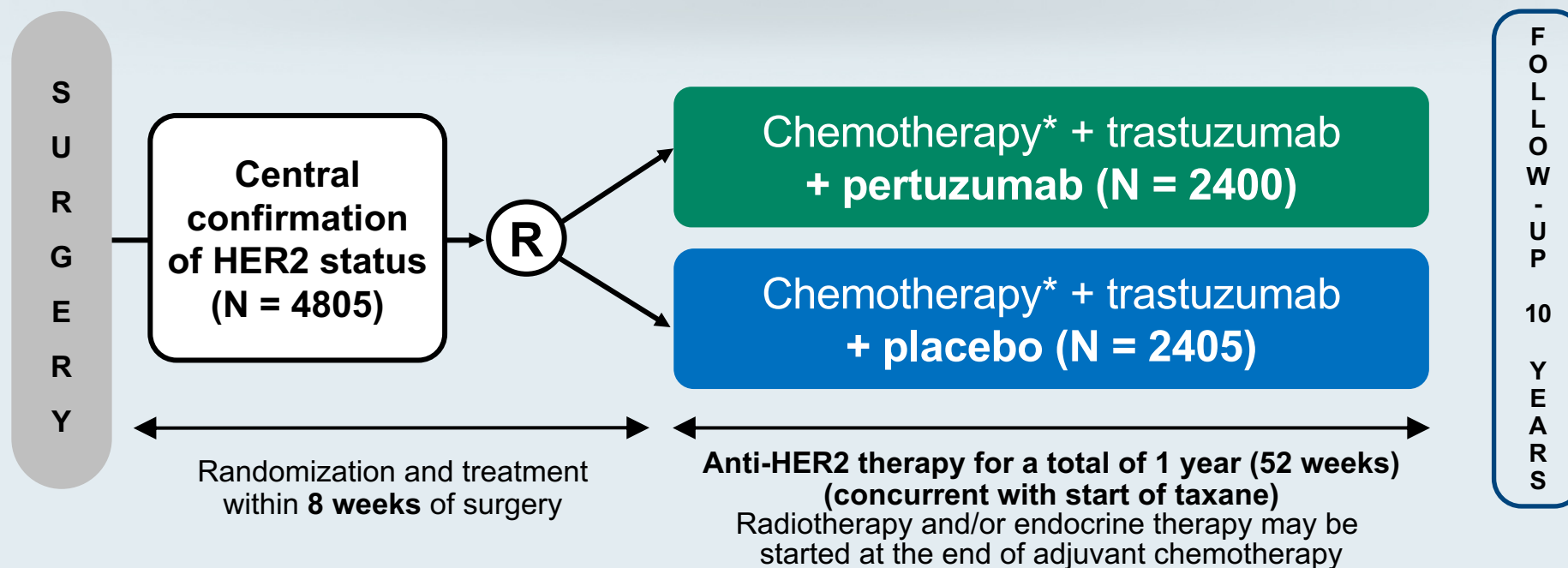
Decision 3: Post-adjuvant neratinib?

- Neratinib given
- 3 years later while on anastrozole: Bone metastases and 2 liver mets
- Treated with THP and responded but progressed in 18 months
- Responded to TDM-1 but later progressed with extensive bone and liver mets

Decision 4: Third-line treatment

- New roles for trastuzumab deruxtecan and trastuzumab/capecitabine/tucatinib

APHINITY: A Phase III adjuvant study investigating the benefit of pertuzumab when added to trastuzumab + chemotherapy



* Standard anthracycline or non-anthracycline (TCH) regimens were allowed: 3–4 x FEC (or FAC) → 3–4 x TH; 4 x AC (or EC) → 4 x TH; 6 x TCH

- **Primary endpoint:** IDFS (APHINITY definition differs from STEEP definition)
- **Secondary endpoint:** IDFS with 2nd primary non-breast primary cancers included, DFS, OS, RFI, DRFI, safety, and HRQoL
- **Stratification factors:** nodal status, HR status, chemotherapy regimen, geographic region, Protocol version (A vs. B)
- **Clinical cut off date (CCOD)** at the time of primary analysis was 19 Dec 2016, median follow up of 45.4 months

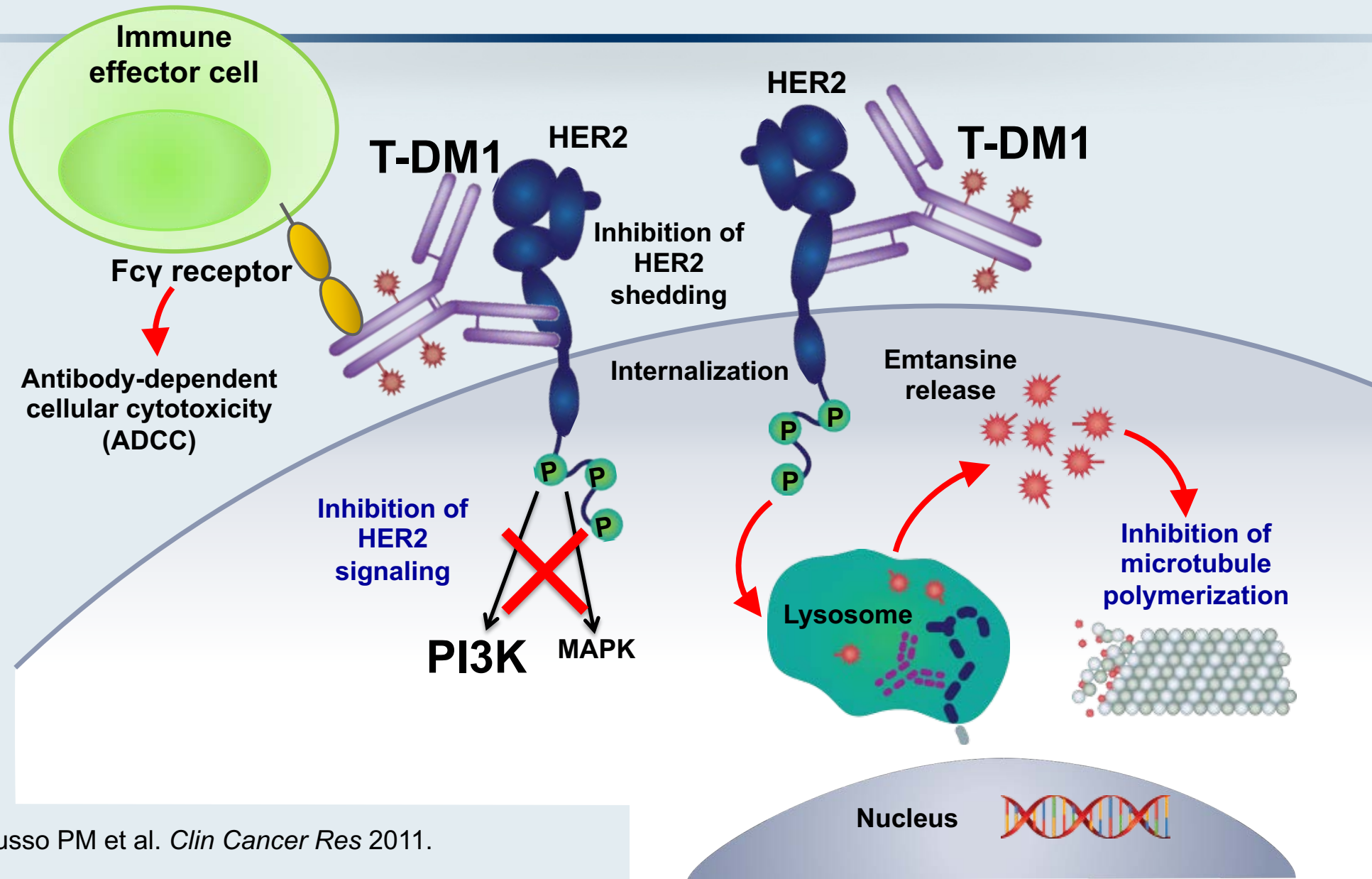
DFS, disease-free survival; DRFI, distant relapse-free interval; HR, hormone receptor; HRQoL, health-related quality of life;
IDFS, invasive disease-free survival; OS, overall survival; RFI, relapse-free interval

San Antonio Breast Cancer Symposium®, December 10-14, 2019
Adapted from von Minckwitz et al. N Engl J Med 2017
www.clinicaltrials.gov/ct2/show/NCT01358877

Courtesy of Virginia Kaklamani, MD DSc

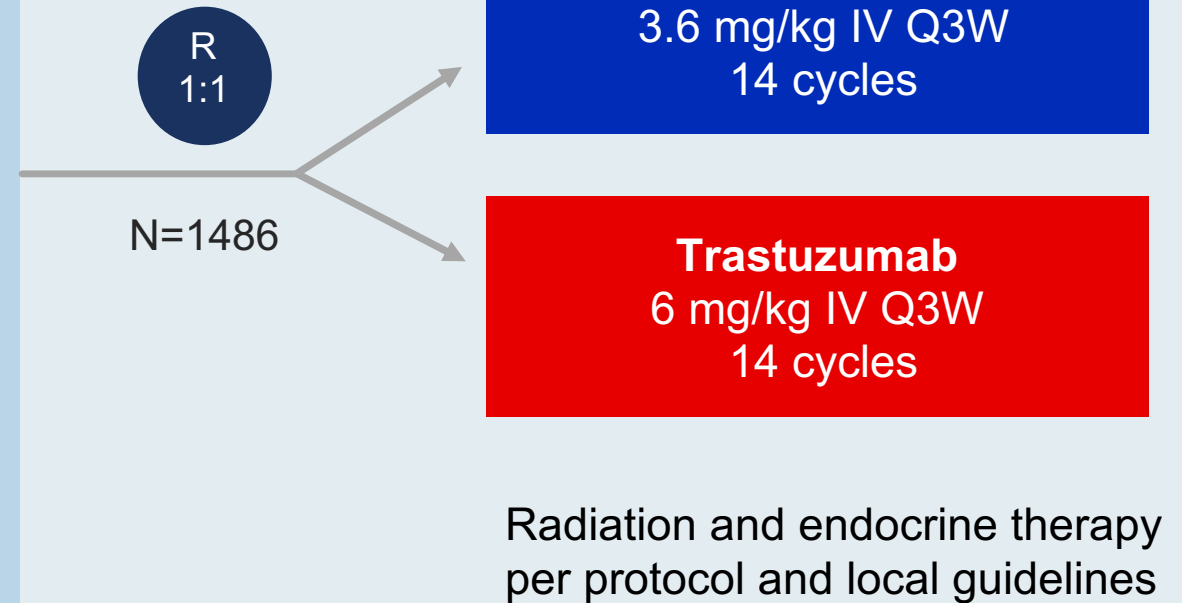
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Trastuzumab Emtansine (T-DM1): Mechanisms of Action



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



Stratification factors:

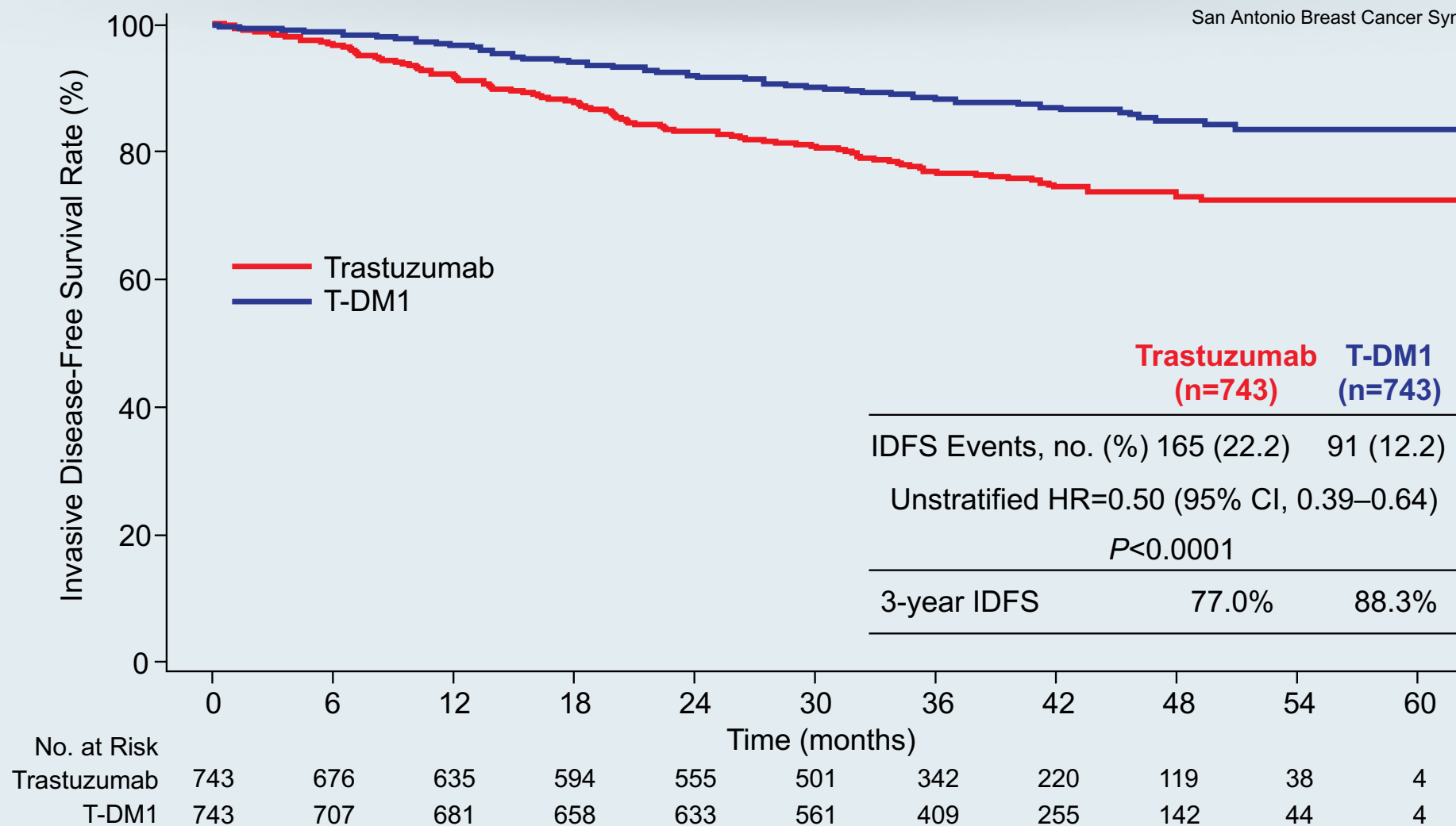
- Clinical presentation: Inoperable (stage cT4 or cN2–3) vs operable (stages cT1-3N0-1)
- Hormone receptor: ER or PR positive vs ER negative and PR negative/unknown
- Preoperative therapy: Trastuzumab vs trastuzumab plus other HER2-targeted therapy
- Pathological nodal status after neoadjuvant therapy: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

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

San Antonio Breast Cancer Symposium December 4–8, 2018

Courtesy of Virginia Kaklamani, MD DSc

Invasive Disease-Free Survival



Study Design: ATEMPT Trial

Key Eligibility Criteria

- Stage 1 HER2+ breast cancer
 - HER2 centrally tested (ASCO CAP 2013 guidelines)
- N0 or N1mic
- Left Ventricular EF \geq 50%
- No prior invasive breast cancer
- \leq 90 days from last surgery

N = 497



N = 383

T-DM1

3.6 mg/kg IV q3 wks x 17

N = 114

TH

Paclitaxel 80 mg/m² IV + Trastuzumab 2 mg/kg IV wkly x12 →
Trastuzumab 6 mg/kg every 3 wks x13

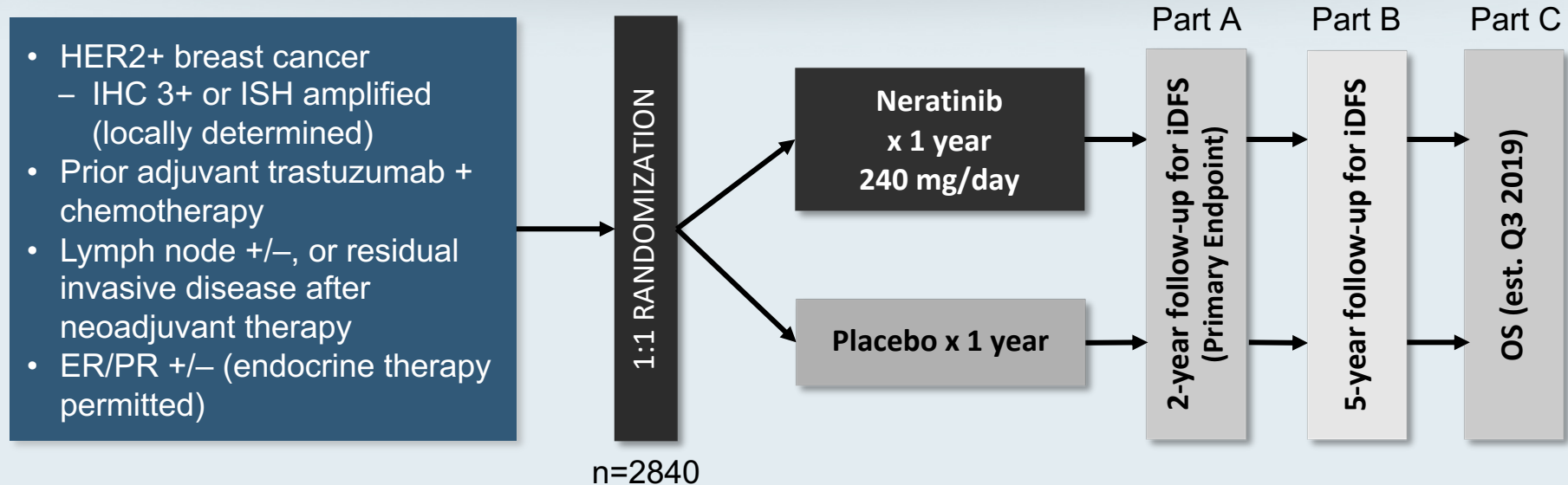
Stratification factors:

- Age (<55, \geq 55)
- Planned radiation (Yes/No)
- Planned hormonal therapy (Yes/No)

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

San Antonio Breast Cancer Symposium - Cancer Therapy and
Research Center at UT Health Science Center - December 10-14, 2019

ExteNET: Study Design



Primary endpoint: invasive disease-free survival (iDFS)

Secondary endpoints: DFS-DCIS, time to distant recurrence, distant DFS, CNS metastases, OS, safety

Other analyses: biomarkers, health outcome assessment (FACT-B, EQ-5D)

Stratified by: nodes 0, 1–3 vs. 4+, ER/PR status, concurrent vs. sequential trastuzumab

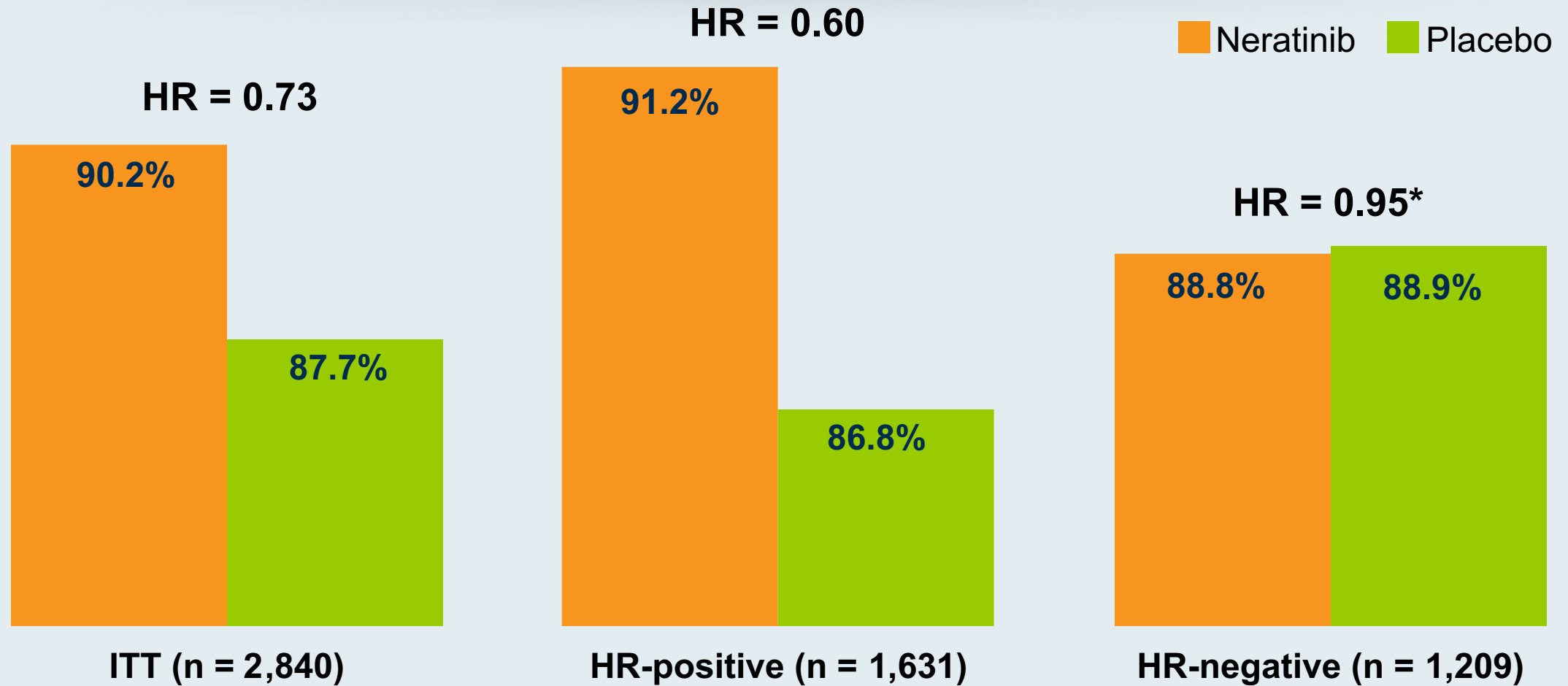
Follow-up for overall survival is ongoing (estimated: Q3 2019)

CNS=central nervous system; DCIS=ductal carcinoma in situ; ER=estrogen receptor; HER2=human epidermal growth factor receptor 2; IHC=immunohistochemistry; ISH=in situ hybridization; PR=progesterone receptor; OS=overall survival.

Martin et al. Lancet Oncol. 2017;18(12):1688-1700. NCT00878709

Courtesy of Virginia Kaklamani, MD DSc

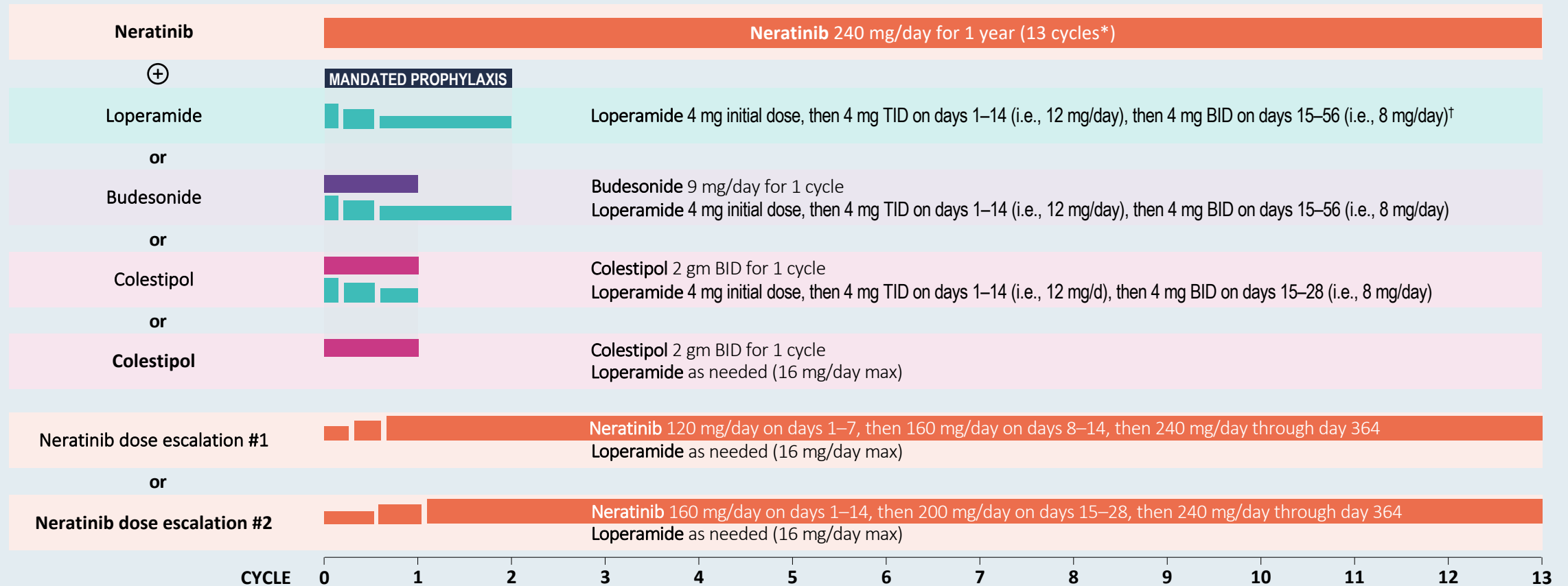
ExteNET: Five-Year Invasive Disease-Free Survival by Patient Population



* Not statistically significant

CONTROL Study Schema

- Prophylactic study to prevent and manage neratinib-associated diarrhea
 - Stage I-IIIc HER2+ disease; prior therapy allowed: endocrine therapy, **pertuzumab**, and **T-DM1**



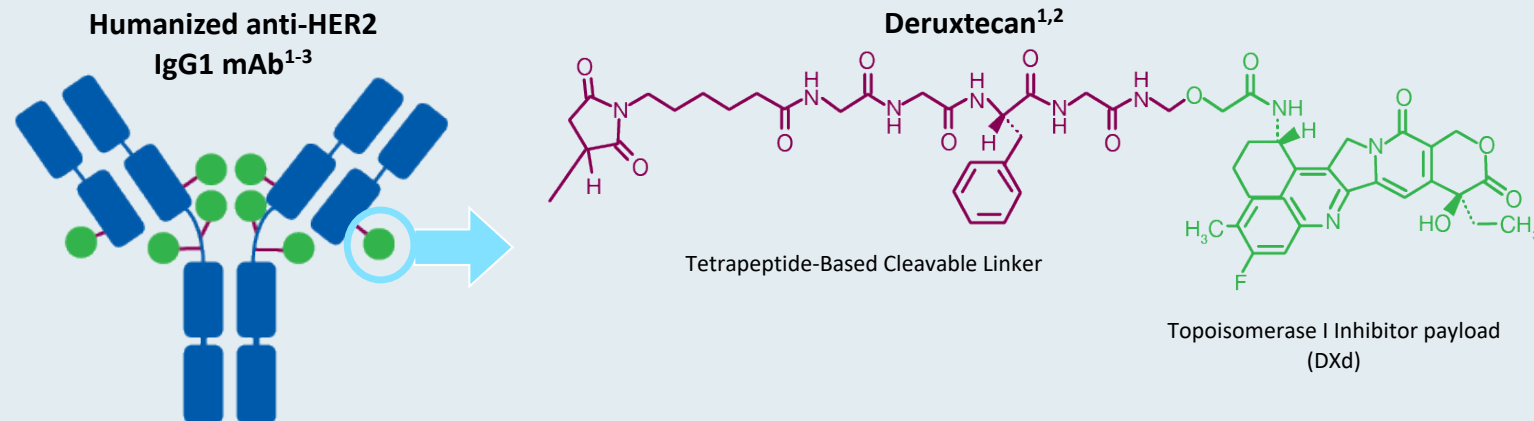
*One cycle=28 days. †Under the original protocol, subjects received loperamide 4 mg initial dose, 2 mg every 4 hours days 1–3, and 2 mg every 6 to 8 hours days 4–56 (n=28) before the “standard” loperamide regimen of 4 mg initial dose, 4 mg TID for 14 days and 4 mg BID days 14–56 was introduced (n=109). All subjects received loperamide as needed (16 mg/day max) after completion of mandated loperamide prophylaxis. Barcenas et al. ASCO 2019 #548.

Courtesy of Virginia Kaklamani, MD DSc

Trastuzumab Deruxtecan (DS-8201) is a Novel ADC Designed to Deliver an Optimal Antitumor Effect

Trastuzumab deruxtecan is an ADC composed of 3 components:

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



Payload MOA:
topoisomerase I inhibitor

High potency of payload

High drug to antibody ratio ≈ 8

Payload with short systemic half-life

Stable linker-payload

Tumor-selective cleavable linker

Membrane-permeable payload

The clinical relevance of these features is under investigation.

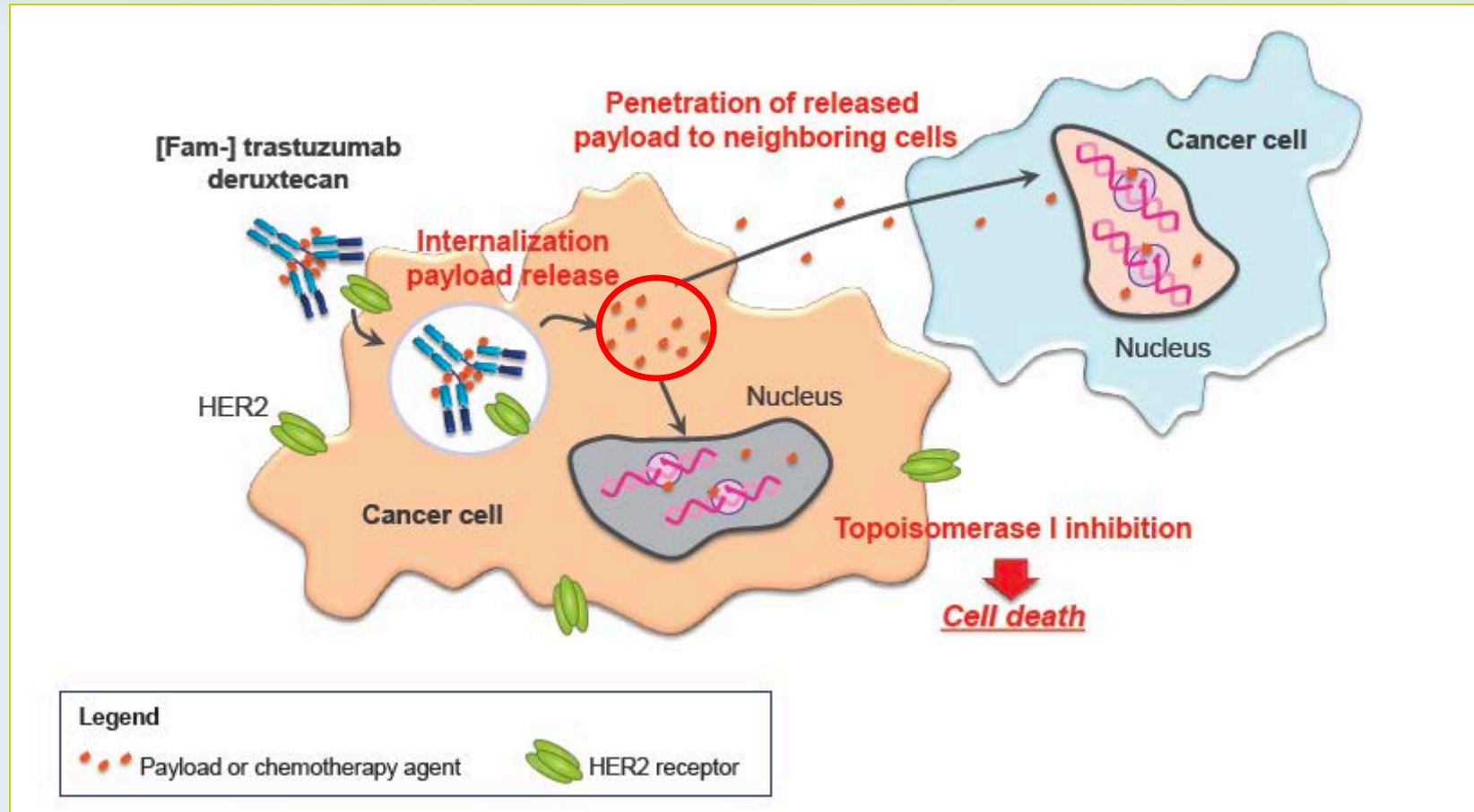
ADC, antibody-drug conjugate; MOA, mechanism of action.

1. Nakada T, et al. Chem Pharm Bull (Tokyo). 2019;67(3):173-185. 2. Ogitani Y, et al. Clin Cancer Res. 2016;22(20):5097-5108. 3. Trail PA, et al. Pharmacol Ther. 2018;181:126-142. 4. Ogitani Y, et al. Cancer Sci. 2016;107(7):1039-1046.

Krop IE et al. SABCS 2019;Abstract GS1-03.

Courtesy of Ian E Krop, MD, PhD

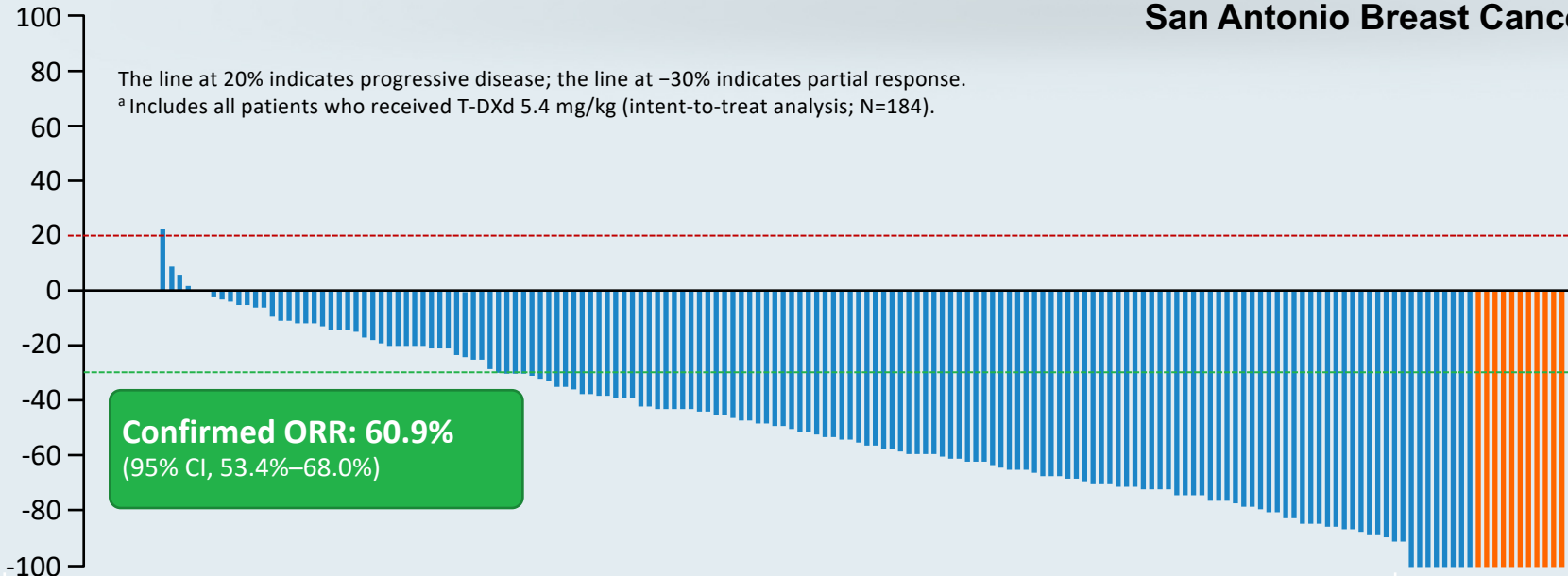
Trastuzumab Deruxtecan's Membrane-permeable Payload Can Attack Neighbouring Cancer Cells (i.e. a bystander effect)



ADCC= antibody-dependent cellular cytotoxicity; HER2=human epidermal growth factor receptor 2; Topo-1=topoisomerase I.

Trastuzumab Deruxtecan in HER2-Positive mBC Previously Treated with T-DM1: Best Tumor Size Response

Best % Change From Baseline in Sum of Diameters



Patients who received T-DXd 5.4 mg/kg (N=184)

11/168 CRs

Preferred Term, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/Total
Interstitial lung disease	5 (2.7)	15 (8.2)	1 (0.5)	0	4 (2.2)	25 (13.6)

Median time from the first infusion of T-DXd to onset of ILD was 27.6 weeks (range, 6-76 weeks)

DESTINY-Breast01: Adverse Events of Special Interest: Interstitial Lung Disease

Patients who received T-DXd 5.4 mg/kg (N=184)						
Preferred Term, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial lung disease	5 (2.7)	15 (8.2)	1 (0.5)	0	4 (2.2)	25 (13.6)

Drug related; ILD was determined by the Independent ILD Adjudication Committee based on 44 preferred terms.

Among the 25 total events:

- Median time to investigator-reported onset was 193 days (range, 42-535 days)
- 17 of 20 patients with grade ≥ 2 ILD received corticosteroids
- 7 patients recovered, 2 were recovering, 12 were either outcome unknown or not followed until resolution, and 4 died
- Of the 4 fatal cases, onset was from 63-148 days, 3 received steroids as part of treatment, and death occurred 9-60 days after diagnosis

Recommendations: Monitor for symptoms. Hold T-DXd and start steroids as soon as ILD is suspected

ILD, interstitial lung disease.

HER2CLIMB Trial Design

Key Eligibility Criteria

- HER2+ metastatic breast cancer
- Prior treatment with trastuzumab, pertuzumab, and T-DM1
- ECOG performance status 0 or 1
- Brain MRI at baseline
 - Previously treated stable brain metastases
 - Untreated brain metastases not needing immediate local therapy
 - Previously treated progressing brain metastases not needing immediate local therapy
- No evidence of brain metastases

N=410

R*
(2:1)

N=202

Tucatinib + Trastuzumab + Capecitabine

(21-day cycle)

Tucatinib 300 mg PO BID
+
Trastuzumab 6 mg/kg Q3W (loading dose 8 mg/kg C1D1)
+
Capecitabine 1000 mg/m² PO BID (Days 1-14)

Placebo + Trastuzumab + Capecitabine

(21-day cycle)

Placebo
+
Trastuzumab 6 mg/kg Q3W (loading dose 8 mg/kg C1D1)
+
Capecitabine 1000 mg/m² PO BID (Days 1-14)

*Stratification factors: presence of brain metastases (yes/no), ECOG status (0 or 1), and region (US or Canada or rest of world)

San Antonio Breast Cancer Symposium®, December 10-14, 2019

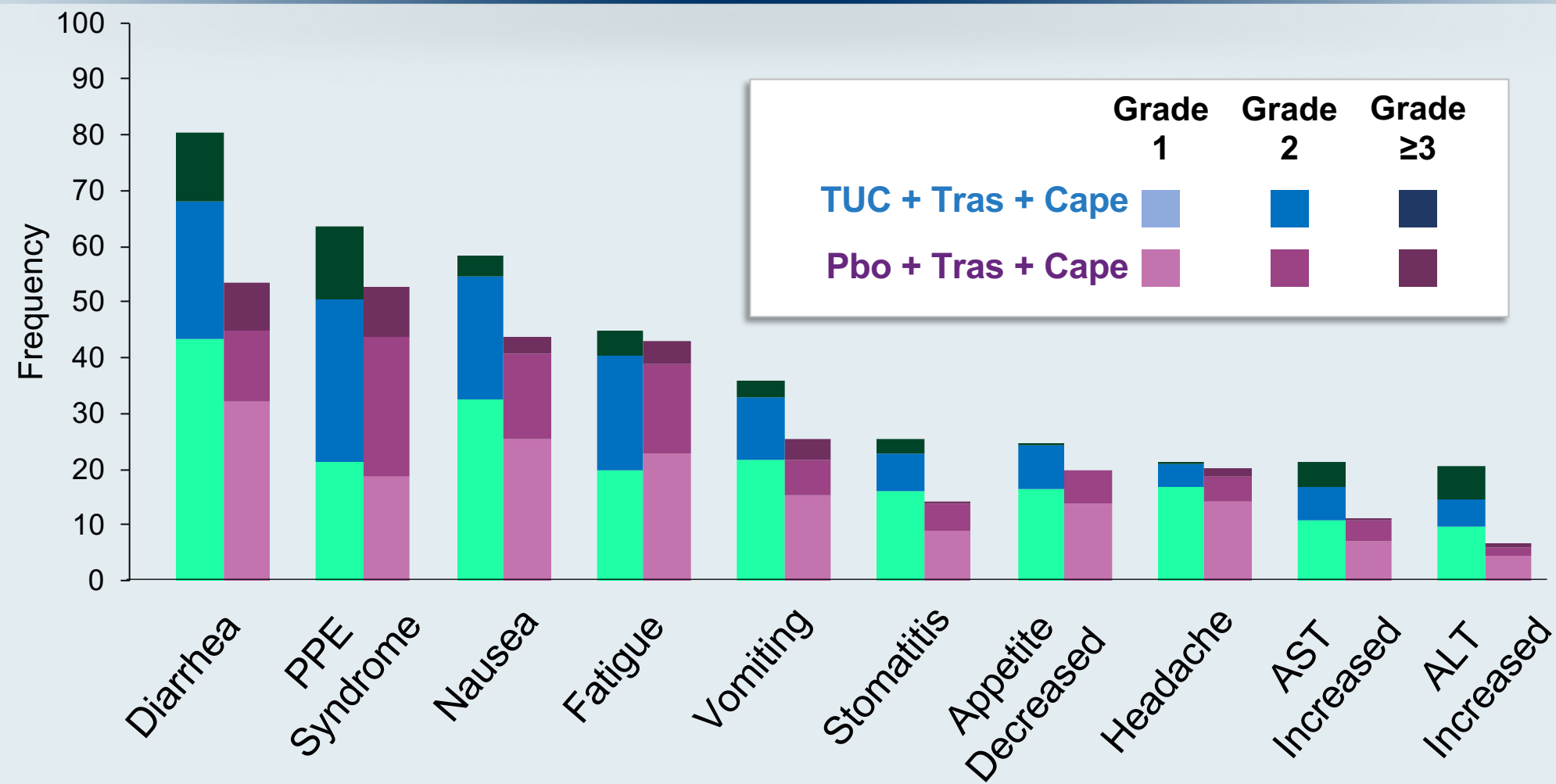
<https://clinicaltrials.gov/ct2/show/NCT02614794>

Murthy R et al. SABCS 2019; Abstract GS1-01.

Courtesy of Virginia Kaklamani, MD DSc

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Most Common Adverse Events (≥20% in the Tucatinib Arm)



PPE: palmar-plantar erythrodysesthesia, AST: aspartate transaminase, ALT: alanine transaminase

Murthy R et al. SABCS 2019;Abstract GS1-01.

Courtesy of Virginia Kaklamani, MD DSc

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Case Presentation: A 38-year-old woman with TNBC

Special considerations

- Speaks only Spanish (clinic staff are generally not bilingual)
- Day laborer with husband and 2 children, 11 and 14 years old.
- Drives 3 hours to the clinic
- Believes in nontraditional medicine
- Self palpates a 3-cm mass
- Biopsy: TNBC
- 2 small axillary nodes seen on ultrasound; biopsy positive



Decision 1: Neoadjuvant treatment or primary surgery?

- Anthracycline/taxane chemotherapy: Good response but residual disease at surgery

Decision 2: Post-neoadjuvant treatment?

- Capecitabine is given, but 9 months later: Bone and lung mets

Case Presentation: A 38-year-old woman TNBC (cont)

Decision 3: First-line mets. Role of genomic evaluation/PD-L1 levels?

- Atezolizumab + *nab*-paclitaxel given, followed by a PARP inhibitor maintenance
 - Patient doing well on olaparib maintenance therapy
- Genetic counseling and testing is offered to the family

IMpassion130 Study Design

Key IMpassion130 eligibility criteria^a:

- Metastatic or inoperable locally advanced TNBC
 - Histologically documented^b
- No prior therapy for advanced TNBC
 - Prior chemo in the curative setting, including taxanes, allowed if TFI ≥ 12 mo
- ECOG PS 0-1

Stratification factors:

- Prior taxane use (yes vs no)
- Liver metastases (yes vs no)
- PD-L1 status on IC (positive [$\geq 1\%$] vs negative [$< 1\%$])^c

R
1:1

Atezo + nab-P arm:

Atezolizumab 840 mg IV

- On days 1 and 15 of 28-day cycle

+ nab-paclitaxel 100 mg/m² IV

- On days 1, 8 and 15 of 28-day cycle

Double blind; no crossover permitted

Plac + nab-P arm:

Placebo IV

- On days 1 and 15 of 28-day cycle

+ nab-paclitaxel 100 mg/m² IV

- On days 1, 8 and 15 of 28-day cycle

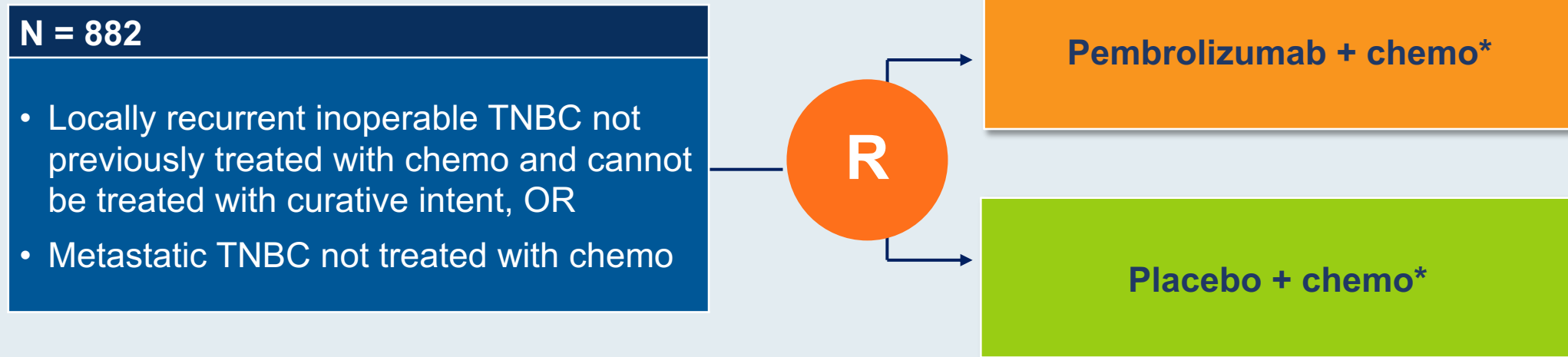
RECIST v1.1
PD or toxicity

- Co-primary endpoints were PFS and OS in the ITT and PD-L1+ populations^d
 - Key secondary efficacy endpoints (ORR and DOR) and safety were also evaluated

IC, tumour-infiltrating immune cell; TFI, treatment-free interval. ^a ClinicalTrials.gov: NCT02425891. ^b Locally evaluated per ASCO–College of American Pathologists (CAP) guidelines.

^c Centrally evaluated per VENTANA SP142 IHC assay (double blinded for PD-L1 status). ^d Radiological endpoints were investigator assessed (per RECIST v1.1).

KEYNOTE-355: A Phase III Study of Chemotherapy +/- Pembrolizumab

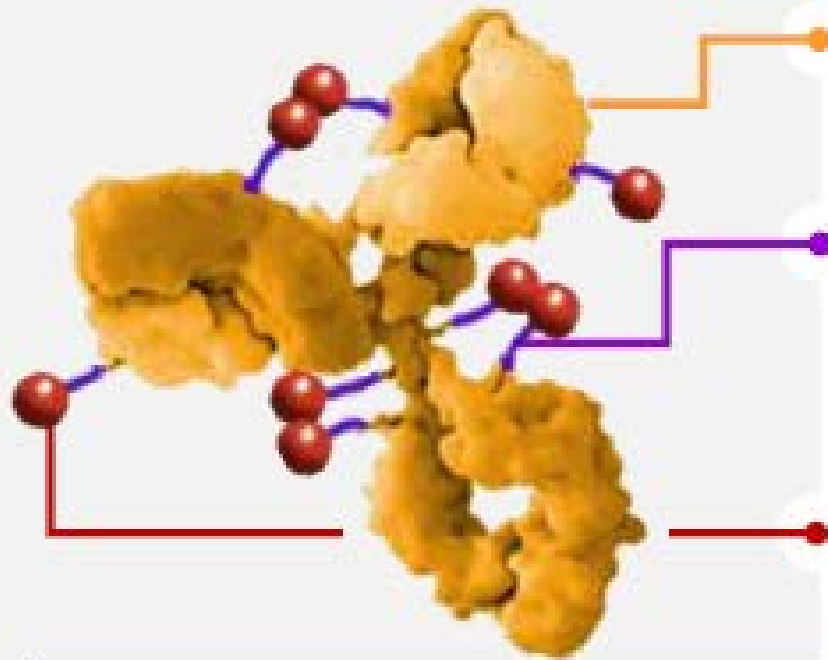


Primary endpoints: Progression-free and overall survival

- In Part 1, individual chemo regimens combined with pembrolizumab were evaluated.
- In Part 2, participants receive 1 of 3 chemo regimens: *nab* paclitaxel, paclitaxel or gemcitabine/carboplatin.

Sacituzumab Govitecan Mechanism of Action

– Trop-2-Directed Antibody-Drug Conjugate



1. Monoclonal antibody (hRS7)

- Binds to Trop-2, a cell surface antigen highly expressed by many cancers, including TNBC

2. Hydrolyzable linker (CL2A)

- Helps to ensure that an active concentration of SN-38 is maintained in the tumor
- Hydrolysis of the linker releases the cytotoxic payload intracellularly and in the tumor microenvironment to kill cells

3. Cytotoxic payload (SN-38)

- Topoisomerase I inhibitor that blocks DNA replication, leading to double-stranded DNA breaks via multiple mechanisms

Favorable Therapeutic Index

- SG has a high DAR (7.6:1 or 7-8 molecules of SN-38 per antibody), enhancing drug delivery to tumor
 - Other ADCs have 3 or 4 to 1 ratios^{2,3}
- Moderate drug potency mitigates toxicity, while increased intratumoral drug release enhances efficacy
 - Other ADCs have highly toxic payloads

FDA Grants Accelerated Approval to Sacituzumab Govitecan for Metastatic TNBC

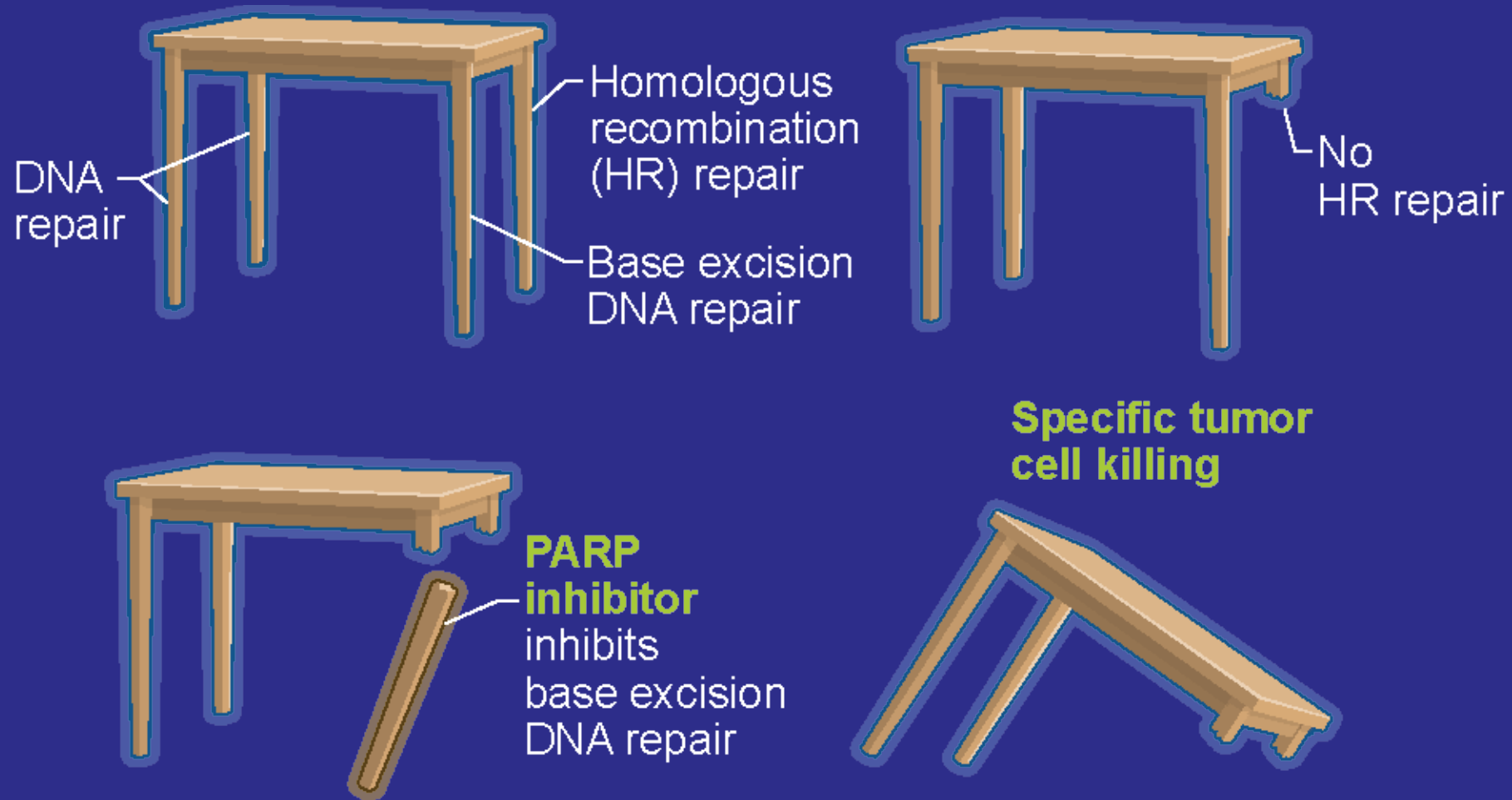
Press Release – April 22, 2020

“The Food and Drug Administration granted accelerated approval to sacituzumab govitecan-hziy for adult patients with metastatic triple-negative breast cancer who received at least two prior therapies for metastatic disease.

Efficacy was demonstrated in IMMU-132-01 (NCT 01631552), a multicenter, single-arm trial enrolling 108 patients with metastatic triple negative breast cancer (mTNBC) who received at least two prior treatments for metastatic disease. Patients received sacituzumab govitecan-hziy 10 mg/kg intravenously on days 1 and 8 every 21 days. Tumor imaging was obtained every 8 weeks, and patients were treated until disease progression or intolerance to therapy.

The primary efficacy outcome measures were investigator assessed overall response rate (ORR) using RECIST 1.1 and response duration. The ORR was 33.3%. The median response duration was 7.7 months.”

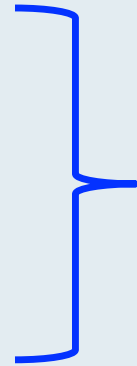
Mechanism of Cell Death from Synthetic Lethality Induced by PARP Inhibition



Common Side Effects of PARP Inhibitors Olaparib and Talazoparib

Hematologic

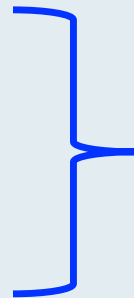
- Anemia
- Neutropenia
- Thrombocytopenia (more with talazoparib)



Grade ≥ 3 in 10% to 40% of patients

Nonhematologic

- Nausea
- Vomiting
- Fatigue



Mostly Grade 1 or 2

Phase III trials of PARP inhibitors in gBRCA HER2-negative metastatic breast cancer patients

OlympiAD¹

gBRCAm HER2- mBC

≤2 prior chemotherapy lines for mBC

Previous treatment with anthracycline and taxane in either the (neo)adjuvant or metastatic setting

Randomise 2:1

Olaparib

300mg *po* bid

**Treatment of
Physician's
Choice (TPC)**

Primary endpoint

PFS (BICR)

EMBRACA²

gBRCAm HER2- LABC or ABC

≤3 prior lines of chemotherapy

Previous treatment with a taxane, an anthracycline, or both, unless this treatment was contraindicated

Randomise 2:1

Talazoparib

1mg *po* qd

**Treatment of
Physician's
Choice (TPC)**

Primary endpoint

PFS (BICR)

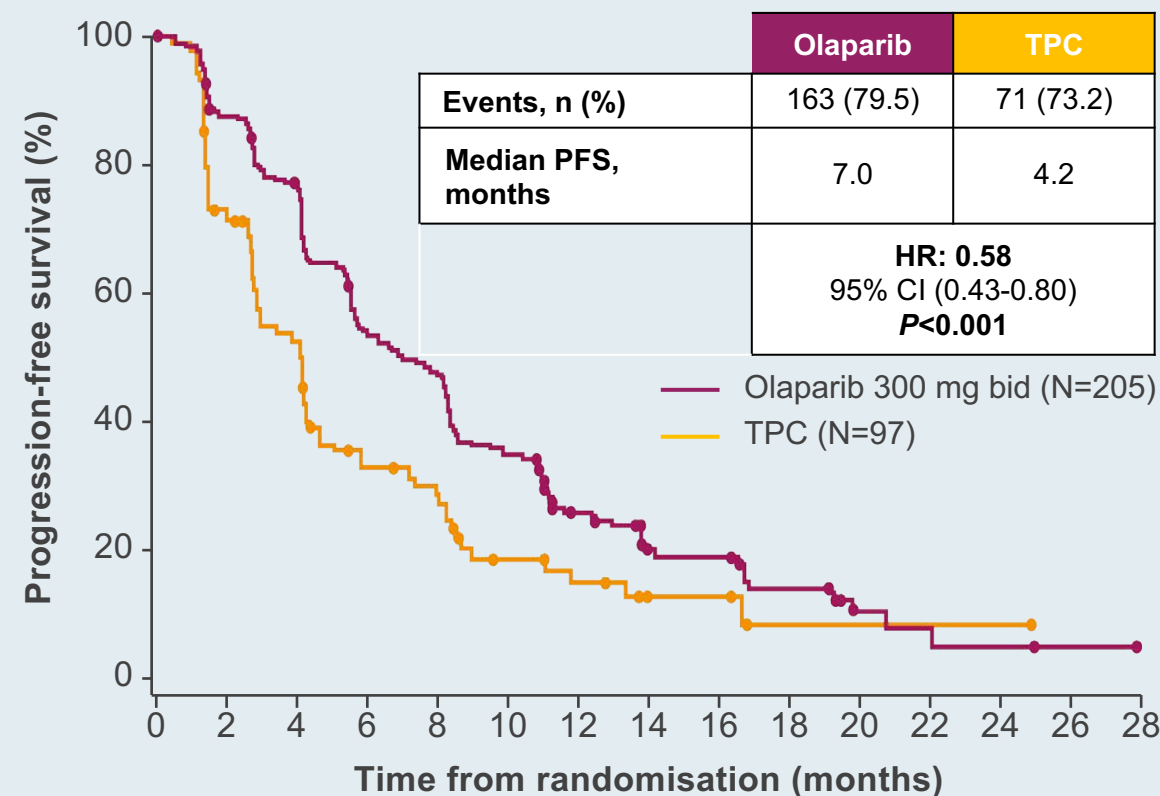
1. Robson et al. *N Engl J Med* 2017; 377:523-533;

2. Litton J et al. *N Engl J Med* 2018; 379:753-763

Phase III trials of PARP inhibitors in gBRCA HER2-negative metastatic breast cancer patients

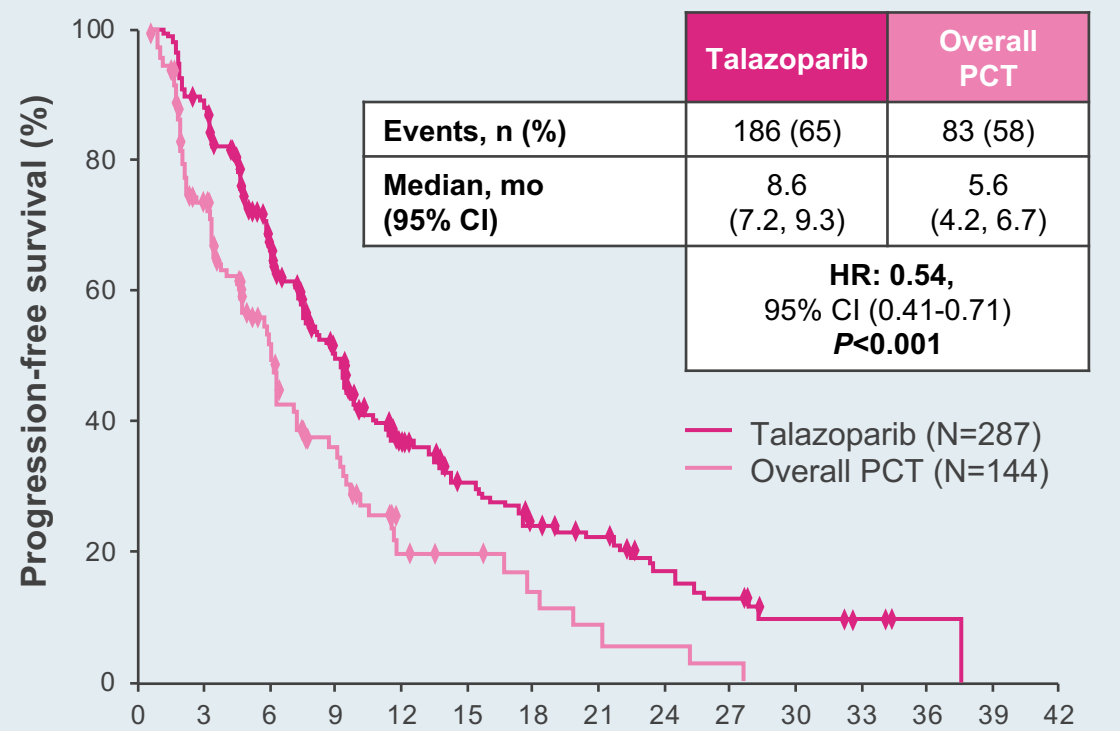
Olaparib and talazoparib both improve PFS in gBRCA mBC patients vs chemotherapy of physician's choice

OlympiAD: Olaparib PFS^{1,2}



Number at risk	
Olaparib	2052011771591541291071009473696140362321211111143322110
TPC	9788834644292524211311118744411111110000

EMBRACA: Talazoparib PFS³



No. at risk (event/cumulative events)		Time (months)															
TALA	287	229	148	91	55	42	29	23	16	12	5	3	1	0	0		
	(0/0)	(50/50)	(53/103)	(34/137)	(17/154)	(9/163)	(9/172)	(2/174)	(5/179)	(4/183)	(2/185)	(0/185)	(0/185)	(1/86)	(1/86)		
PCT	144	68	34	22	9	8	4	2	2	1	0	0	0	0	0		
	(0/0)	(41/41)	(20/61)	(8/69)	(7/76)	(0/76)	(3/79)	(2/81)	(0/81)	(1/82)	(1/83)	(0/83)	(0/83)	(0/83)	(0/83)		

Agenda

10 Decisions in Breast Cancer and Where New Agents and Strategies Fit In

Case 1: A 60-year-old woman with ER-positive, HER2-positive breast cancer

- Neoadjuvant, adjuvant treatment of localized disease
- New agents, regimens in metastatic disease

Case 2: A 38-year-old woman with triple-negative breast cancer (TNBC)

- Metastatic TNBC: Atezolizumab/*nab* paclitaxel, pembrolizumab/chemotherapy
- Neoadjuvant pembrolizumab/chemotherapy in localized TNBC
- Recent FDA approval of sacituzumab govitecan
- Germline and somatic mutation testing
- Indications for and selection of available PARP inhibitors (olaparib, talazoparib)

Case 3: An 80-year-old woman with ER-positive, HER2-negative breast cancer, with a low Recurrence Score

- Chemotherapy versus endocrine therapy for early breast cancer
- Current role of CDK4/6 inhibitors for pre- and postmenopausal women
- Alpelisib/fulvestrant (PIK3CA mutation)

Case Presentation: An 80-year-old woman with ER-positive, HER2-negative breast cancer, with a low Recurrence Score

Special considerations

- Husband died of lung cancer 4 years ago
- Currently, raising 2 grandchildren alone (8 and 12 years old)
- Overweight, with type 2 diabetes on insulin, antihypertensive and 3 other agents
- Disorganized about taking medications



Decision 1: Chemotherapy or not?

- Lumpectomy followed by anastrozole
- While on anastrozole, she is found to have moderately symptomatic bone mets
 - Focal radiation therapy

Case Presentation: An 80-year-old woman with ER-positive, HER2-negative breast cancer, with a low Recurrence Score (cont)

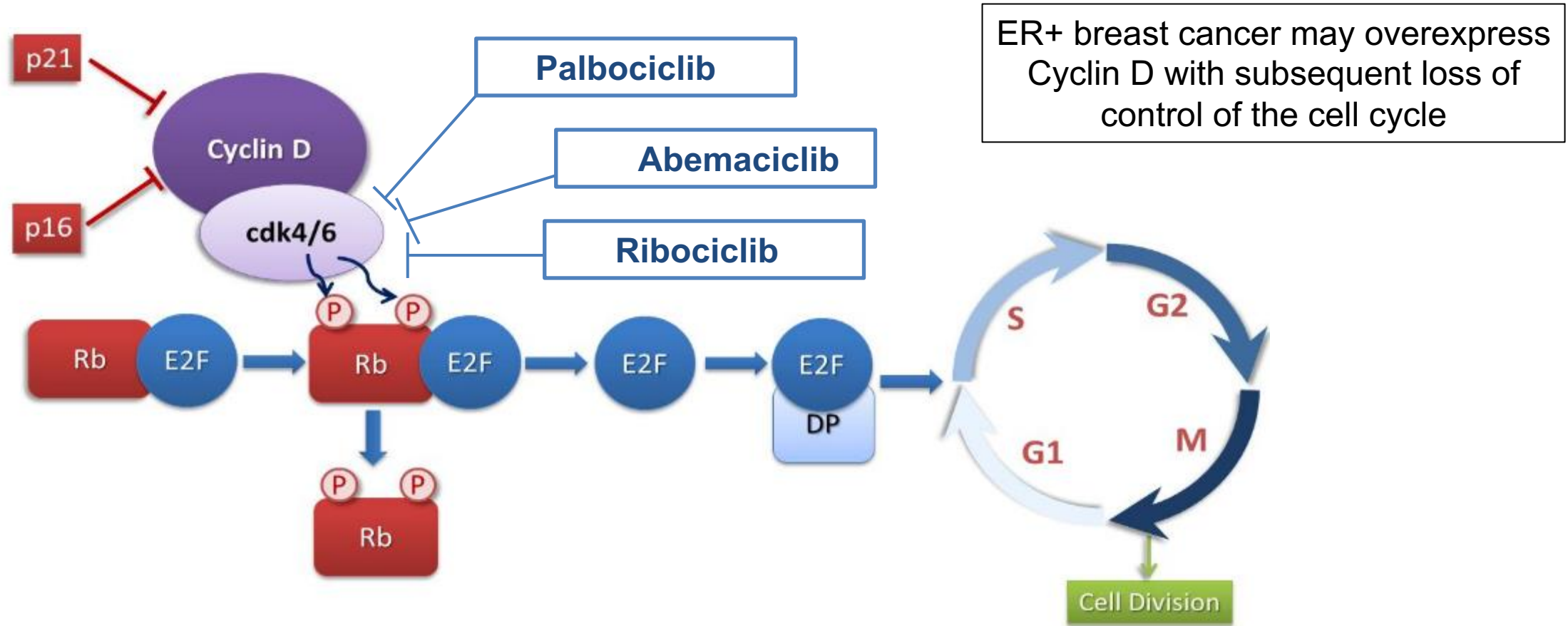
Decision 2: Chemotherapy or endocrine therapy (which endocrine therapy)?

- Treated with fulvestrant and a CDK4/6 inhibitor
- Patient did well but disease progressed after 2 years, with new liver mets
- Patient was stable clinically
- PI3K mutation detected in the tumor

Decision 3: Chemotherapy or endocrine therapy (which endocrine therapy)?

- Alpelisib, everolimus combinations

CDK4/6 Regulates Cell Cycle Progression

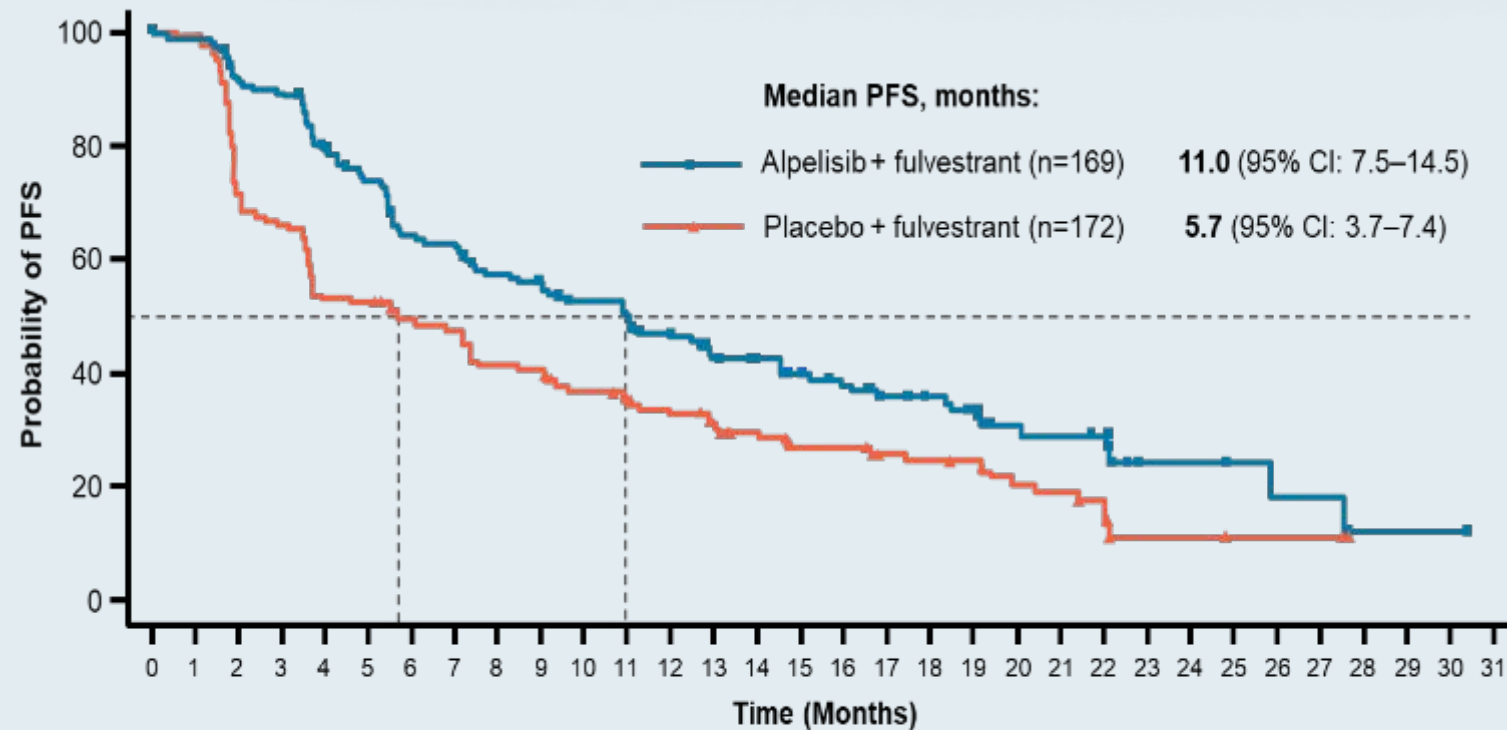


Common Side Effects and Dosing of CDK4/6 Inhibitors

	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

SOLAR-1: Alpelisib Improved PFS in the *PIK3CA*-mutant Cohort^{1,a}

Fulvestrant + Alpelisib or Placebo in ER+ HER2- mBC Patients Resistant to AI Therapy



Data cut-off: Jun 12, 2018	ALP + FUL (n = 169)	PBO + FUL (n = 172)
Number of PFS events, n (%)	103 (60.9)	129 (75.0)
Progression	99 (58.6)	120 (69.8)
Death	4 (2.4)	9 (5.2)
Censored	66 (39.1)	43 (25.0)
Median PFS (95% CI)	11.0 (7.5-14.5)	5.7 (3.7-7.4)
HR (95% CI)	0.65 (0.50-0.85)	
One-sided <i>P</i> value	0.00065	

CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

At final PFS analysis, superiority was declared if one-sided, stratified log-rank test *P* value was ≤ 0.0199 (Haybittle–Peto boundary).

^a Mutation status determined from tissue biopsy.

1. Andre F, et al. ESMO 2018. Abstract LBA3 [oral].

Courtesy of Joyce O'Shaughnessy, MD

Meet The Professors

Nurse and Physician Investigators

Discuss Existing and Emerging Treatment Strategies for Patients with Prostate Cancer

Thursday, July 16, 2020

5:00 PM – 6:00 PM ET

Faculty

**Matthew R Smith, MD, PhD and
Kara M Olivier, NP, APRN-BC**

Moderator

Neil Love, MD

Thank you for joining us!

**CNE (NCPD) credit information will be emailed
to each participant tomorrow morning.**