Thank you for joining us.
The program will commence momentarily.

Meet The Professors

Nurse and Physician Investigators Discuss Existing and Emerging Treatment Strategies for Patients with Breast Cancer

Thursday, July 23, 2020

5:00 PM – 6:00 PM ET

Faculty

Joyce O'Shaughnessy, MD

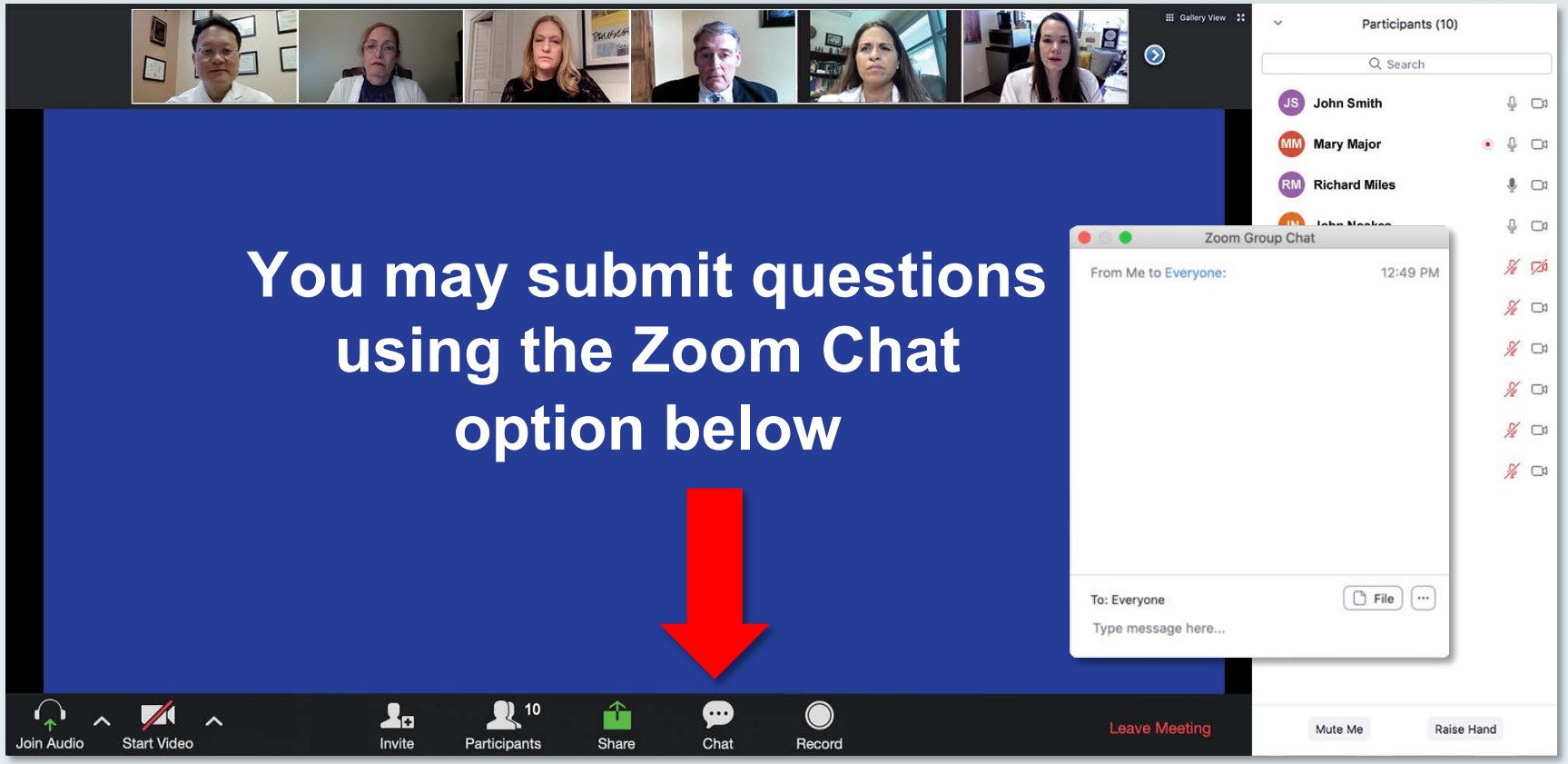
Marissa Marti, APRN, AGNP-C, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Dr Love and Faculty Encourage You to Ask Questions



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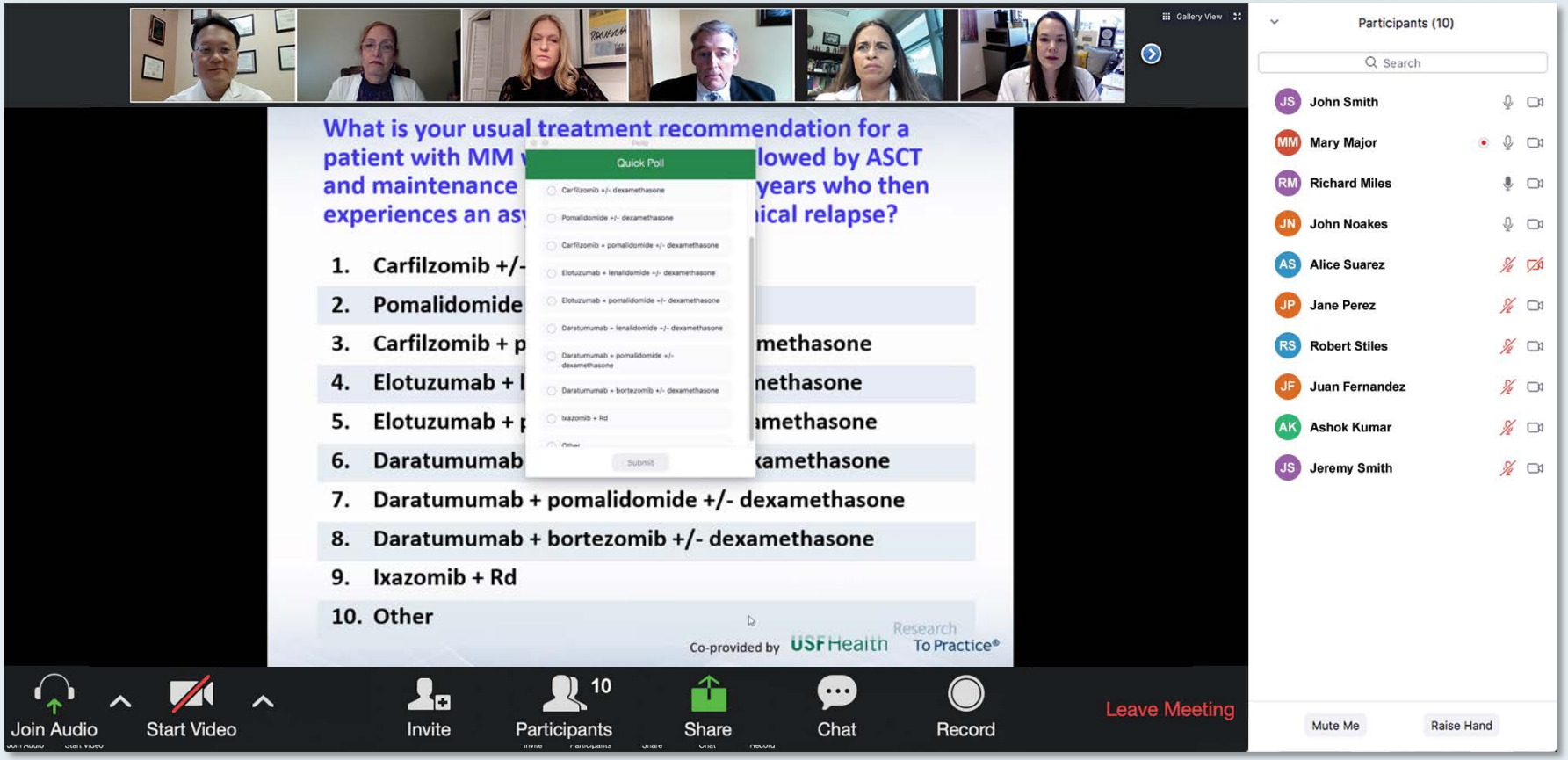
Familiarizing yourself with the Zoom interface
How to answer poll questions



When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.

Commercial Support

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Dr Love — Disclosures

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RTP CNE (NCPD) planning committee members, staff and reviewers

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

Dr O’Shaughnessy — Disclosures

Advisory Committee and Consulting Agreements	AbbVie Inc, Agendia Inc, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, Eisai Inc, Genentech, a member of the Roche Group, Genomic Health Inc, GRAIL, Halozyme Inc, Heron Therapeutics, Immunomedics Inc, Ipsen Biopharmaceuticals Inc, Jounce Therapeutics, Lilly, Merck, Myriad Genetic Laboratories Inc, Novartis, Odonate Therapeutics, Pfizer Inc, Puma Biotechnology Inc, Roche Laboratories Inc, Seattle Genetics, Syndax Pharmaceuticals Inc

Ms Marti — Disclosures

No financial interests or affiliations to disclose.

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

Prostate Cancer

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

Robert Dreicer, MD, MS

Victoria Sinibaldi, RN, MS, CS, CANP, BC

Bladder Cancer

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

Anastassia Daskalova, NP

Peter H O'Donnell, MD

All events moderated by Neil Love, MD

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RTP RESEARCH TO PRACTICE

Faculty

Joyce O'Shaughnessy, MD
Celebrating Women Chair in Breast Cancer Research
Baylor University Medical Center
Director, Breast Cancer Research Program
Texas Oncology
US Oncology
Dallas, Texas

Marissa Marti, APRN, AGNP-C, AOCNP
Texas Oncology-Baylor Charles A Sammons Cancer Center
Dallas, Texas

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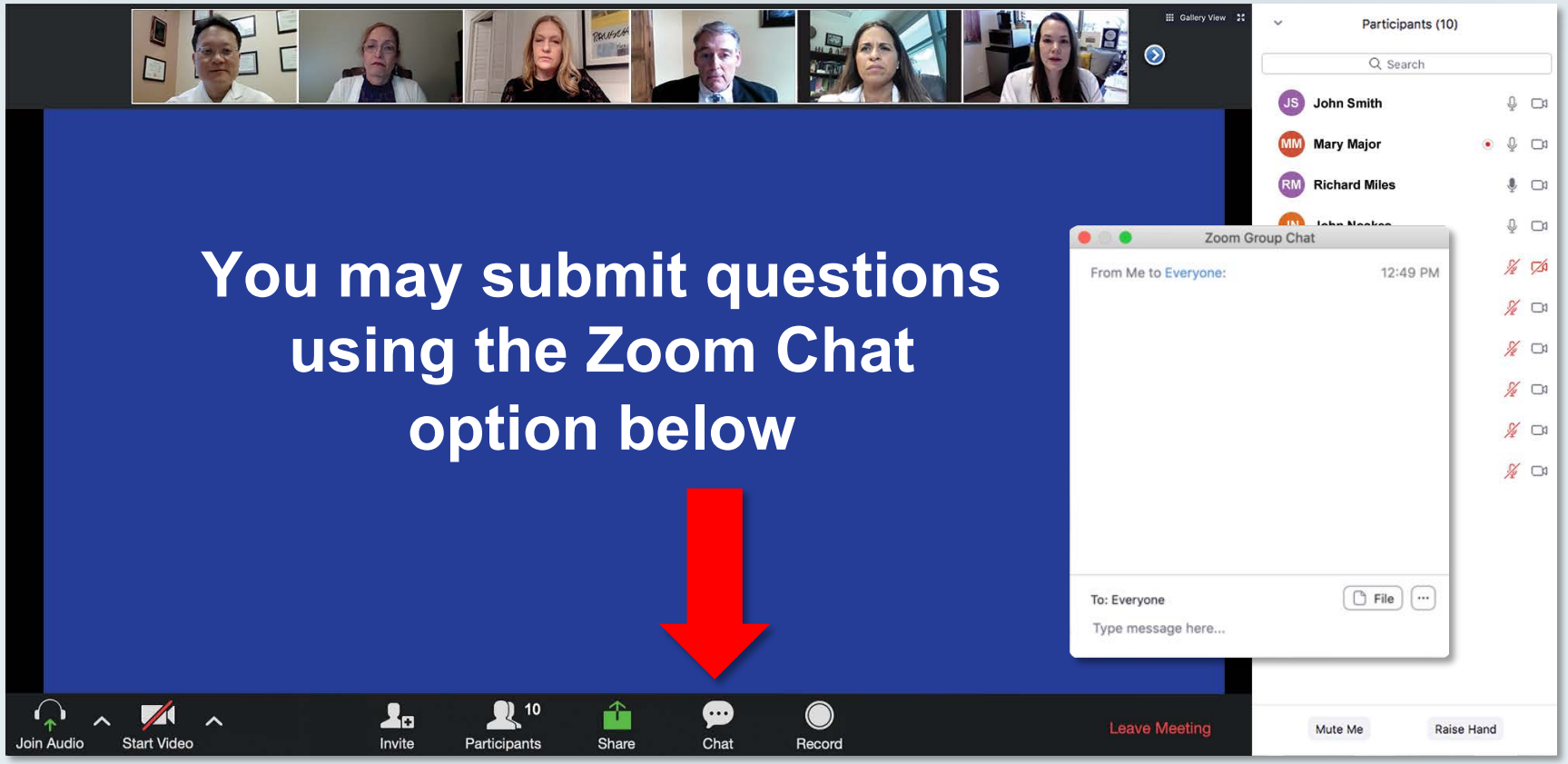

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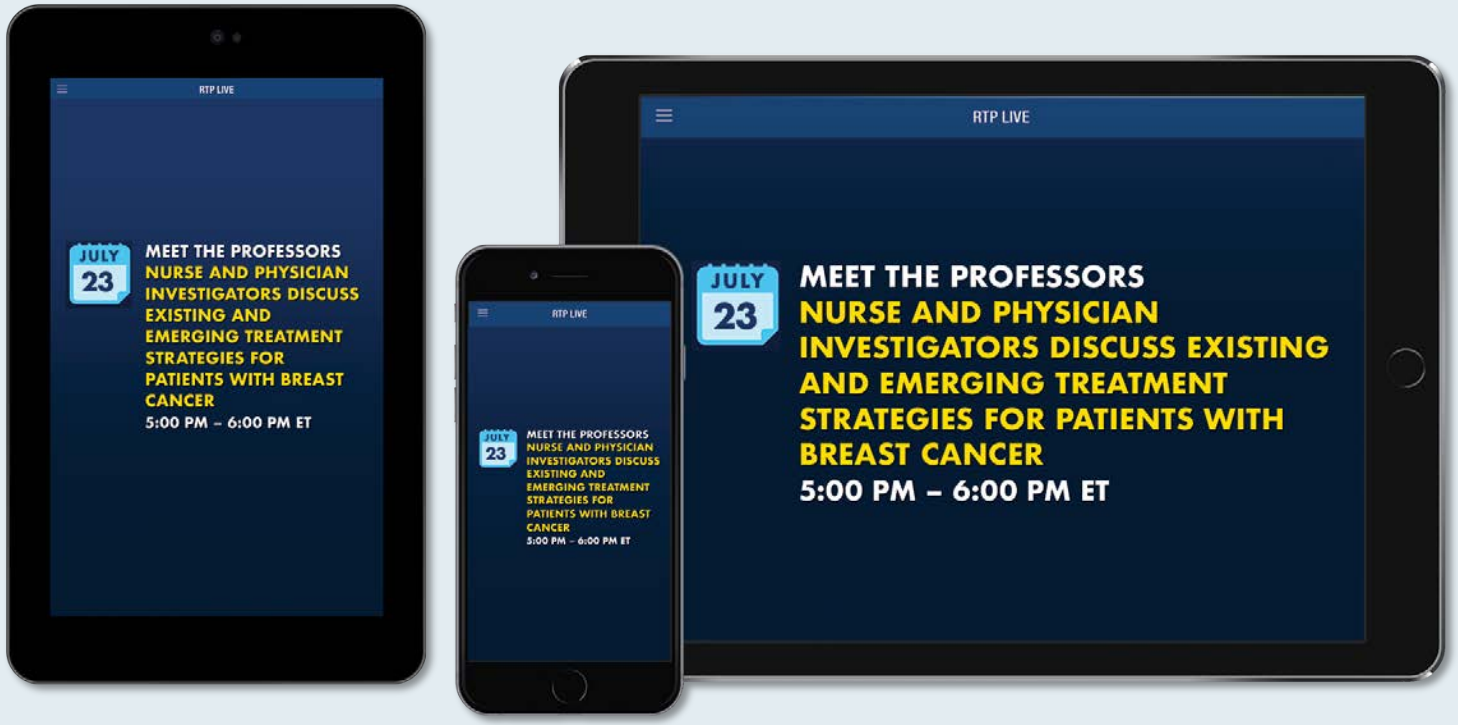
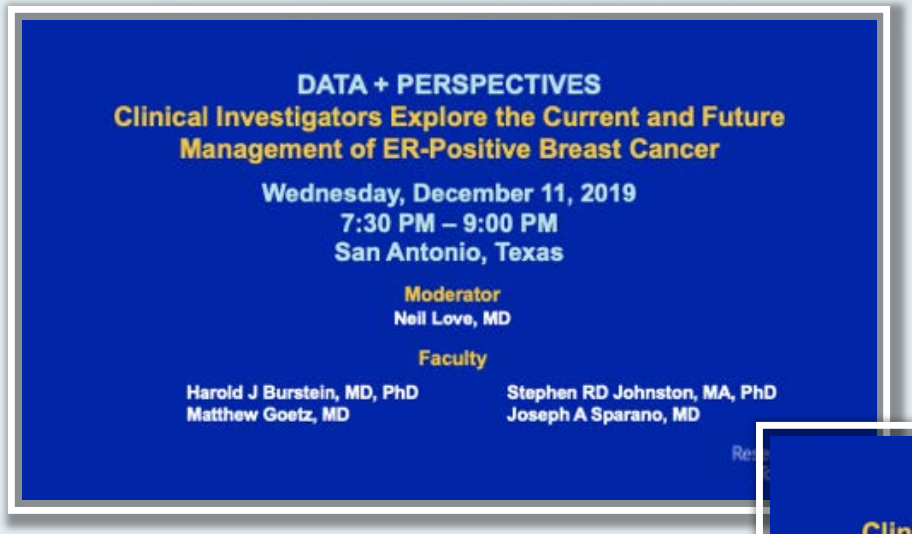
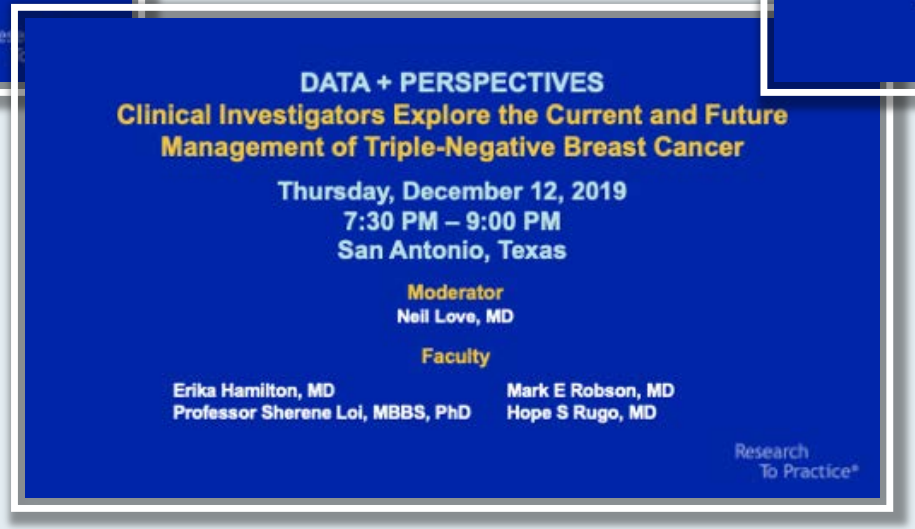
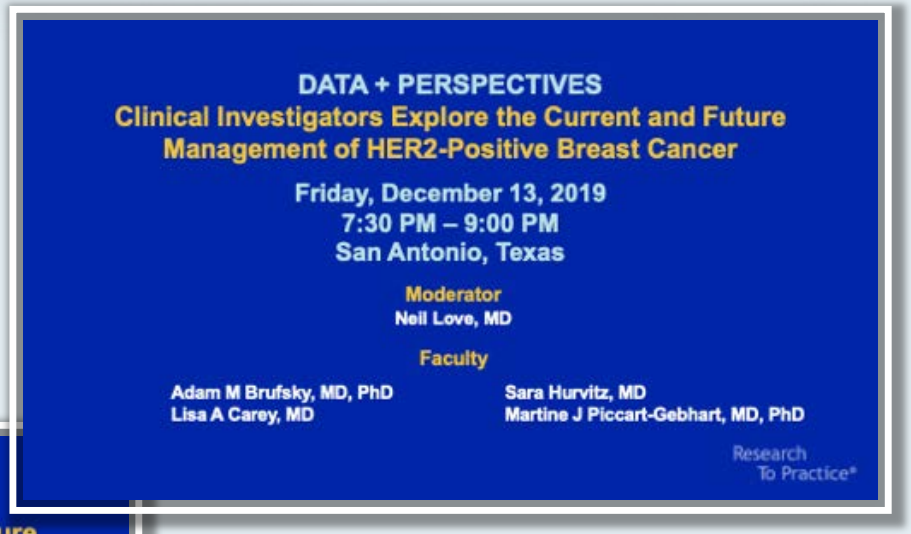


Research To Practice's 2019 San Antonio Breast Cancer Symposia







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RTP RESEARCH TO PRACTICE

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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?

- T-DM1 given for 16 cycles: grade 1 neuropathy, thrombocytopenia

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

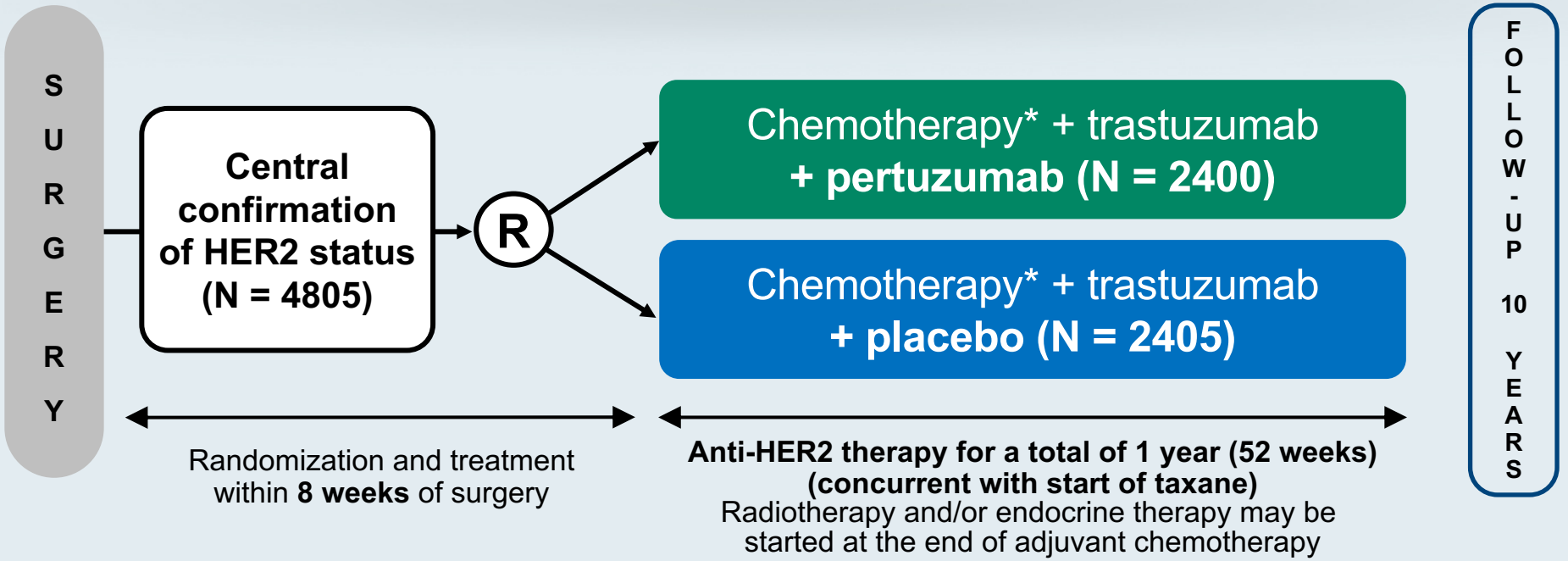
Decision 3: Post-adjuvant neratinib?

- 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

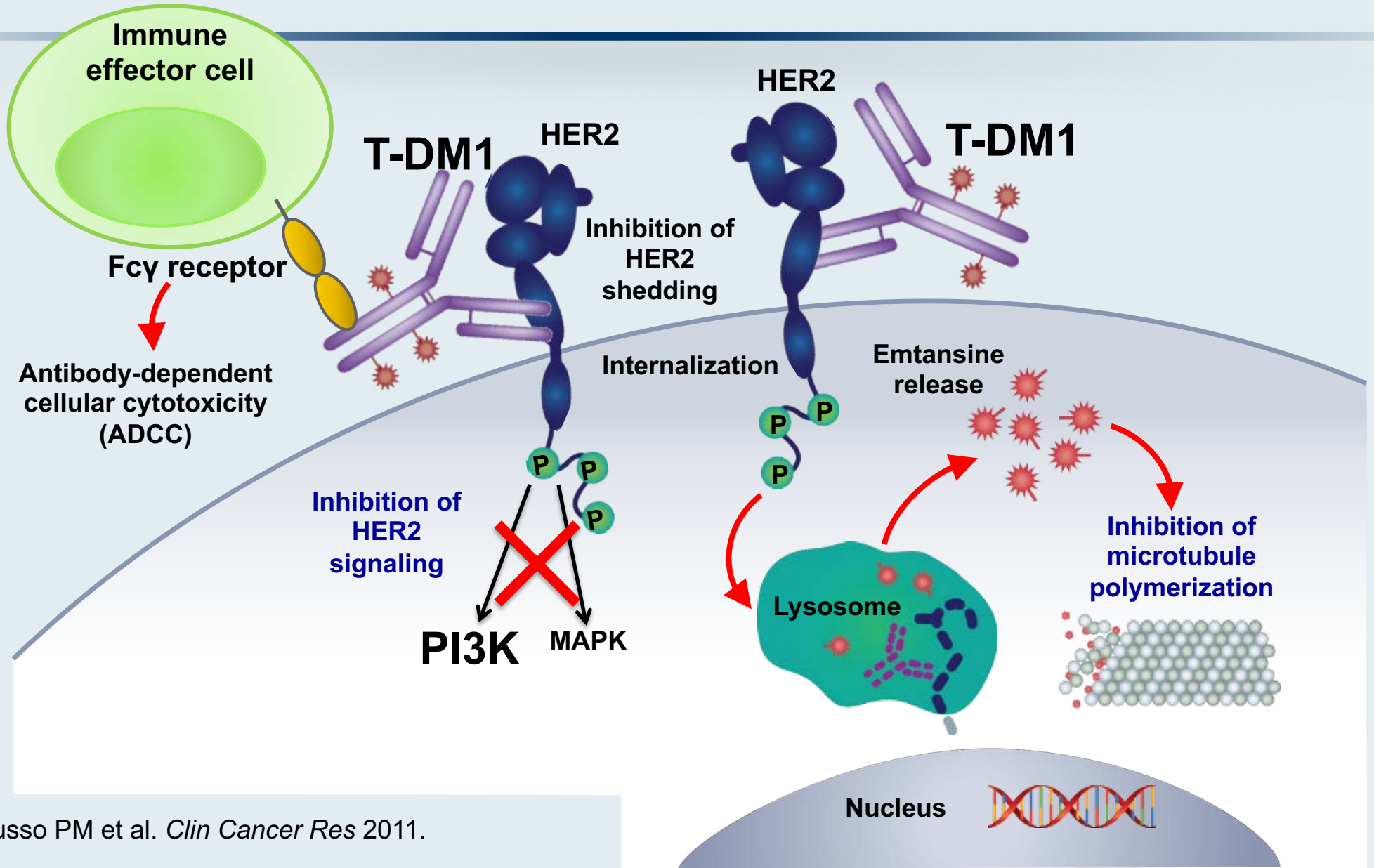
- **Primary endpoint:** IDFS (APHINITY definition differs from STEEP definition)
- **Secondary endpoint:** IDFS with 2nd primary non-breast primary cancers included, DFS, OS, RFI, DRFI, safety, and HRQoL
- **Stratification factors:** nodal status, HR status, chemotherapy regimen, geographic region, Protocol 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

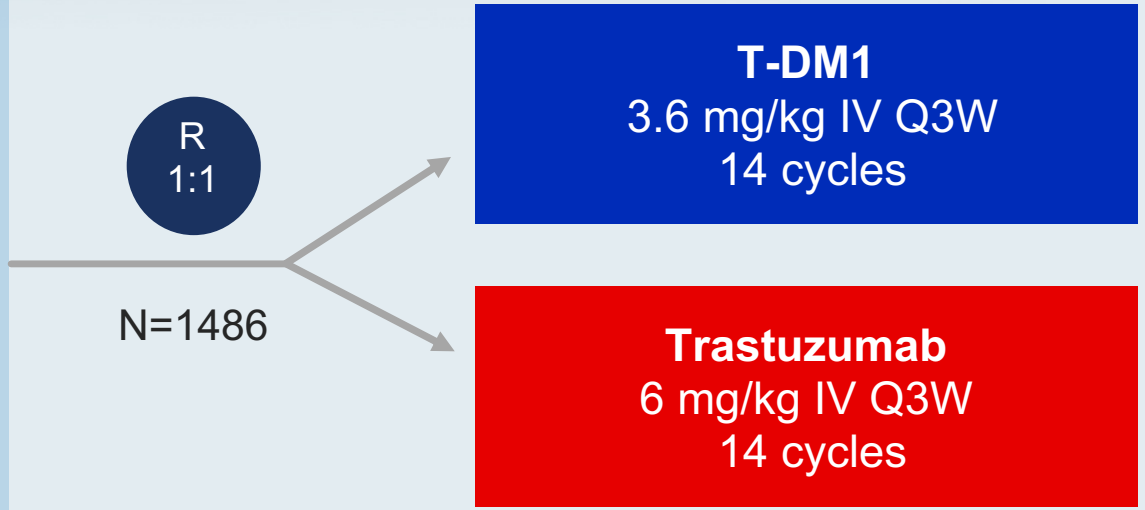
Trastuzumab Emtansine (T-DM1): Mechanisms of Action



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

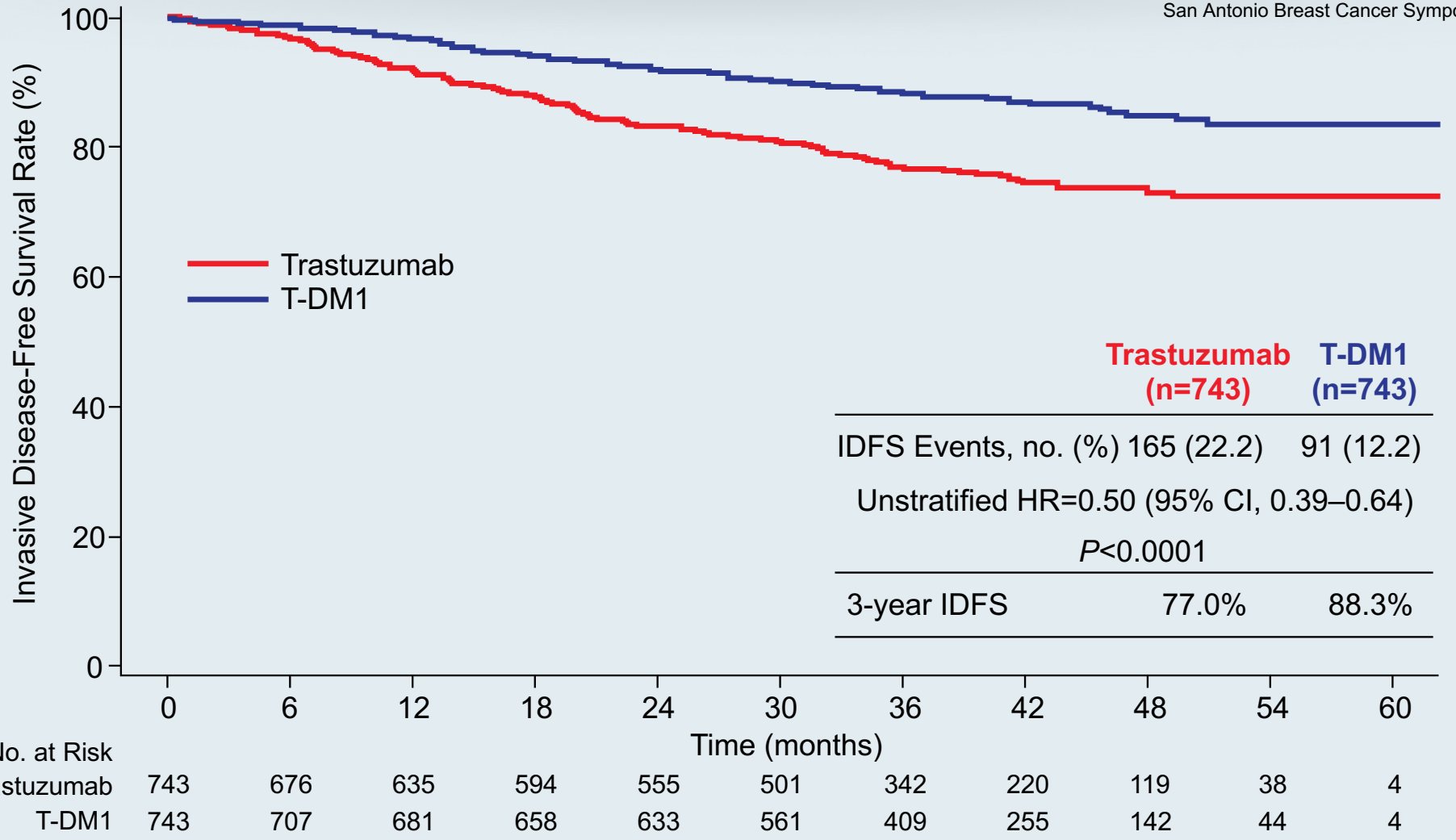
Geyer CE et al. SABCS 2018;Abstract GS1-10.

San Antonio Breast Cancer Symposium December 4–8, 2018

Courtesy of Virginia Kaklamani, MD DSc

Invasive Disease-Free Survival

San Antonio Breast Cancer Symposium December 4–8, 2018

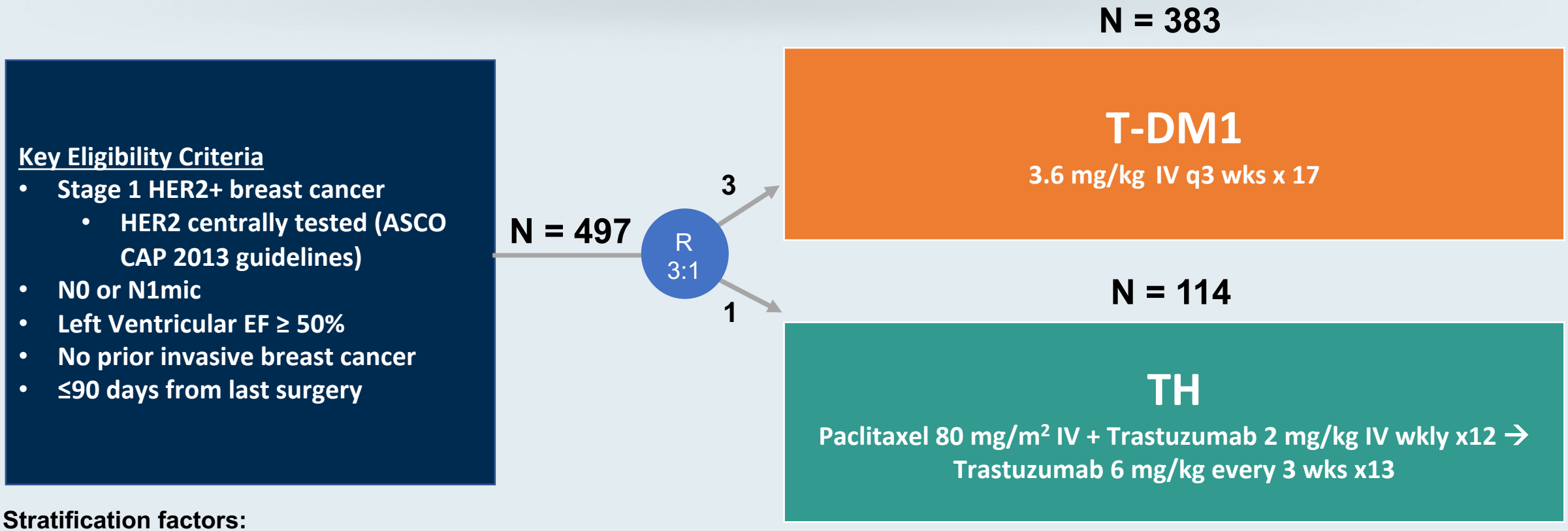


	Trastuzumab (n=743)	T-DM1 (n=743)
IDFS Events, no. (%)	165 (22.2)	91 (12.2)
Unstratified HR=0.50 (95% CI, 0.39–0.64)		
P<0.0001		
3-year IDFS	77.0%	88.3%

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

Courtesy of Virginia Kaklamani, MD DSc

Study Design: ATEMPT Trial



Stratification factors:

- **Age (<55, ≥55)**
- **Planned radiation (Yes/No)**
- **Planned hormonal therapy (Yes/No)**

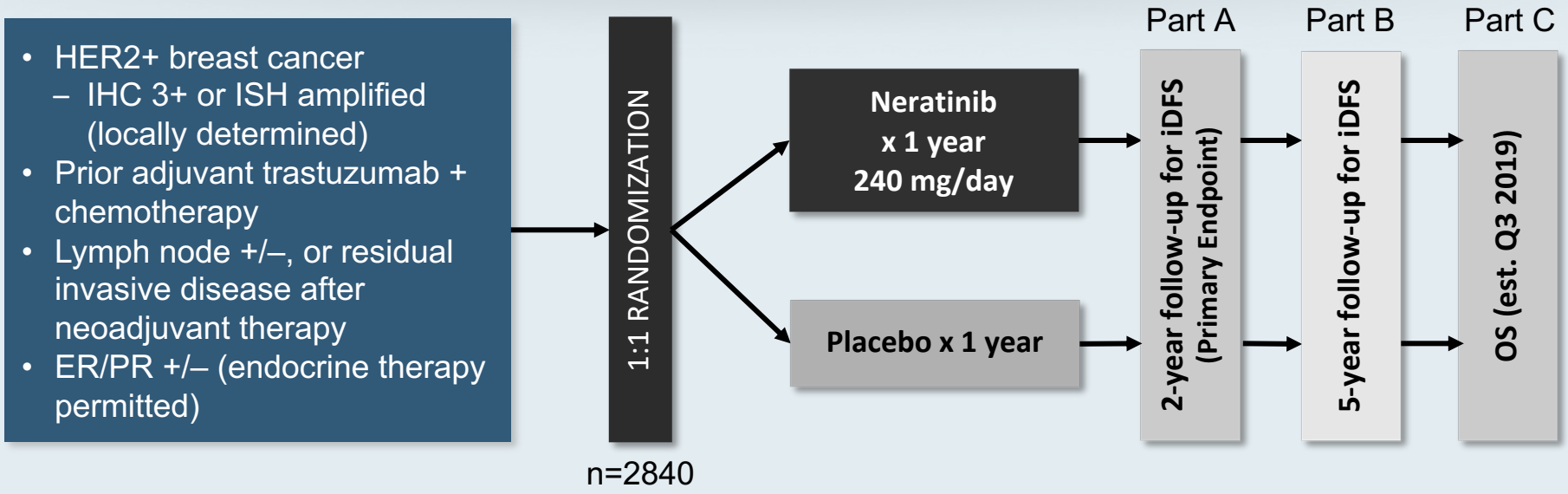
Radiation and endocrine therapy could be initiated after 12 weeks on study therapy

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

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

Courtesy of Virginia Kaklamani, MD DSc

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

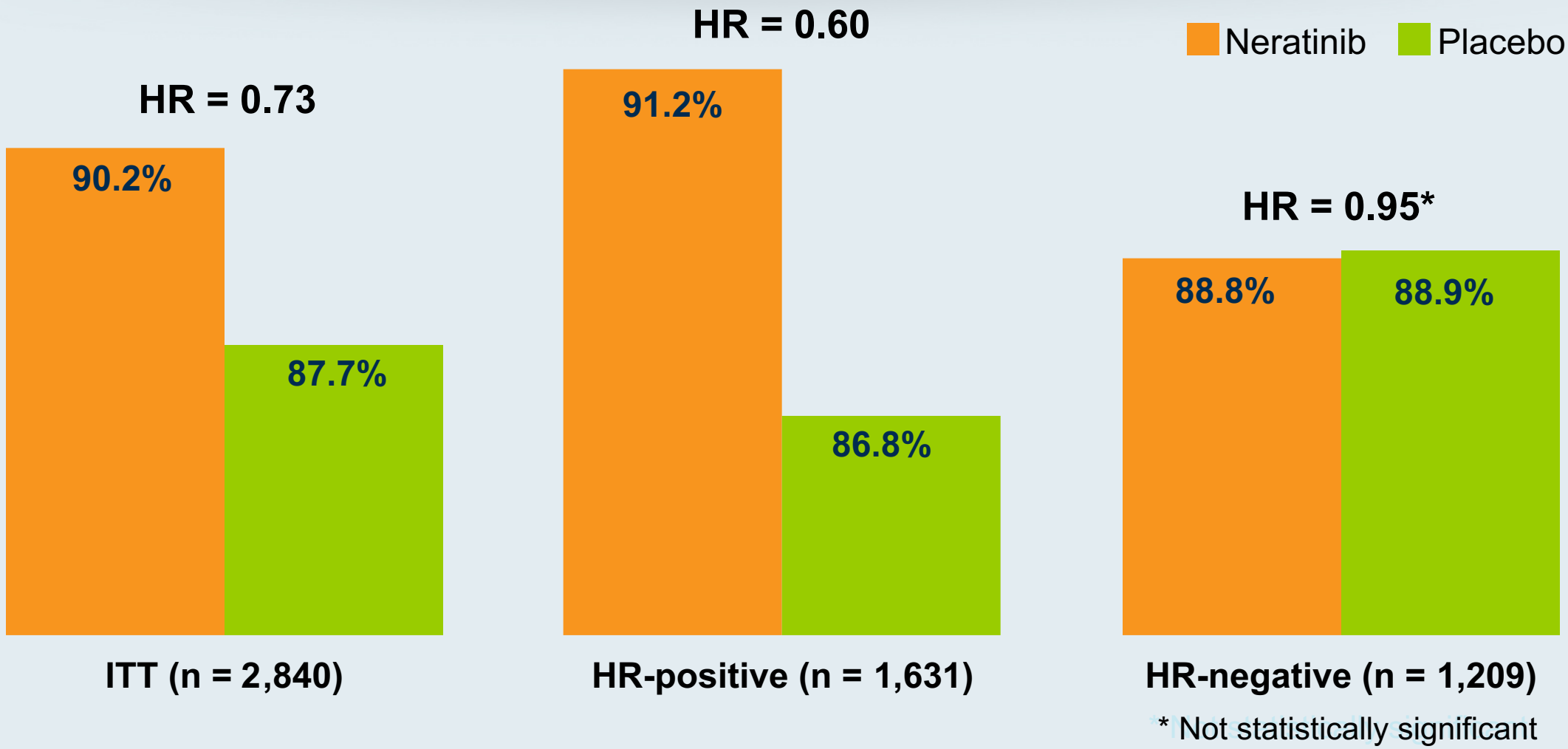
Follow-up for overall survival is ongoing (estimated: Q3 2019)

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

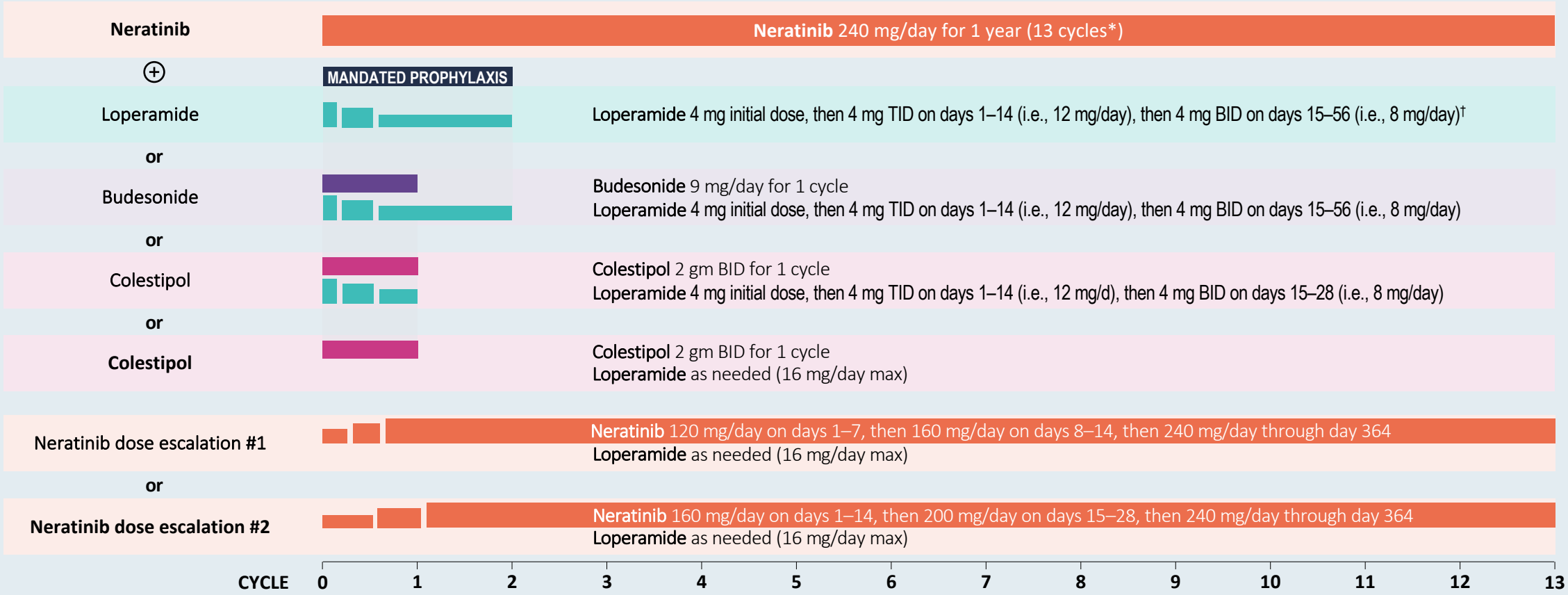
ExteNET: Five-Year Invasive Disease-Free Survival by Patient Population



Martin M et al. *Lancet Oncol* 2017;18(12):1688-700; Martin M et al. ESMO 2017;Abstract 149O.

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**



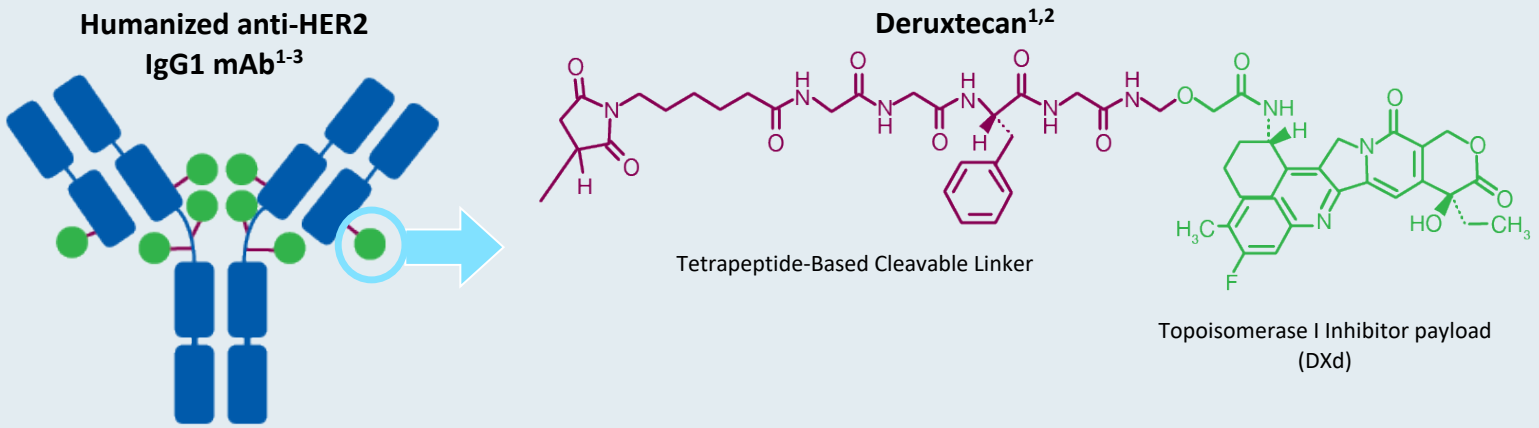
*One cycle=28 days. †Under the original protocol, subjects received loperamide 4 mg initial dose, 2 mg every 4 hours days 1–3, and 2 mg every 6 to 8 hours days 4–56 (n=28) before the "standard" loperamide regimen of 4 mg initial dose, 4 mg TID for 14 days and 4 mg BID days 14–56 was introduced (n=109). 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.

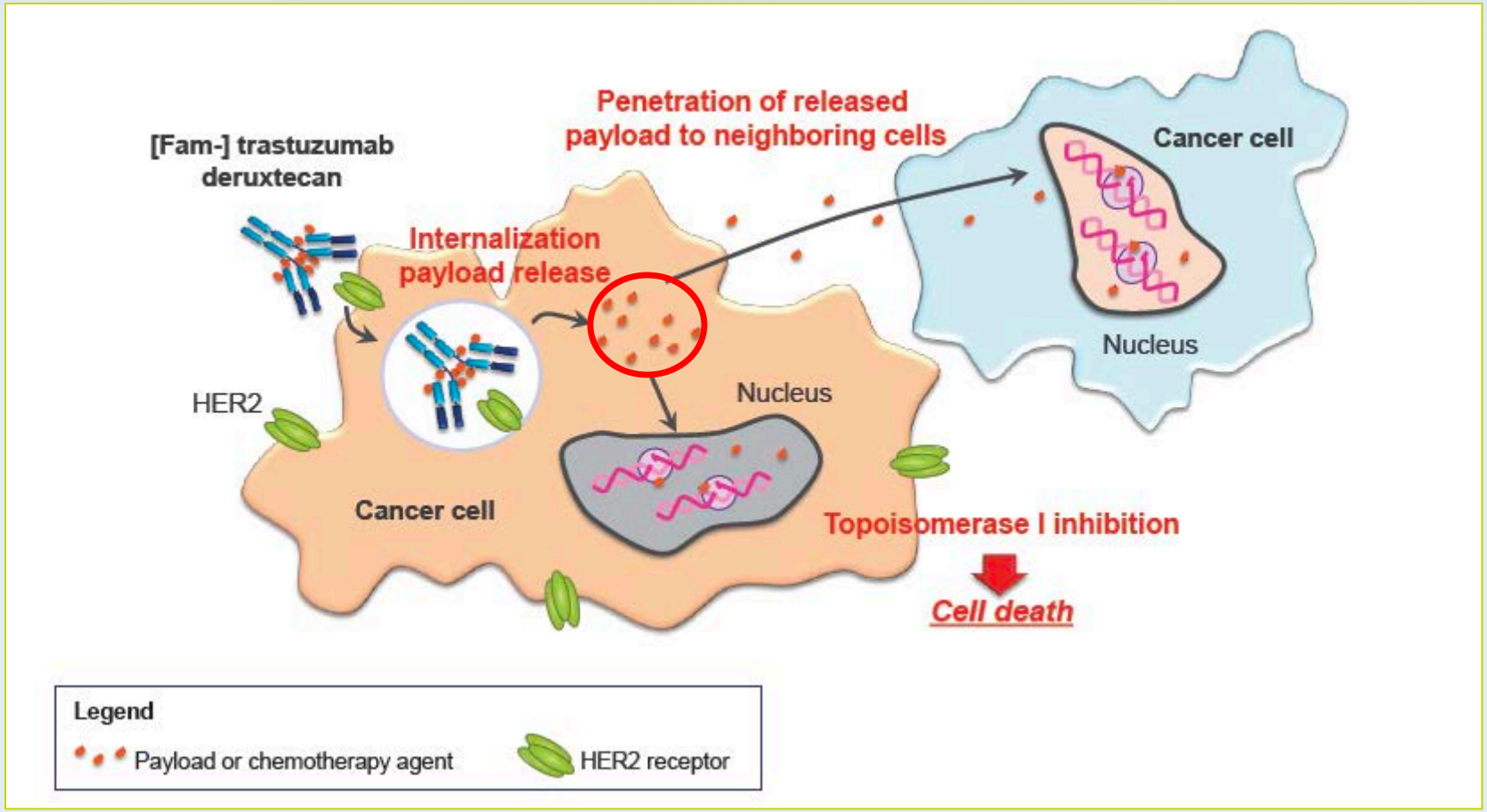
ADC, antibody-drug conjugate; MOA, mechanism of action.

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

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.

Courtesy of Ian E Krop, MD, PhD

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

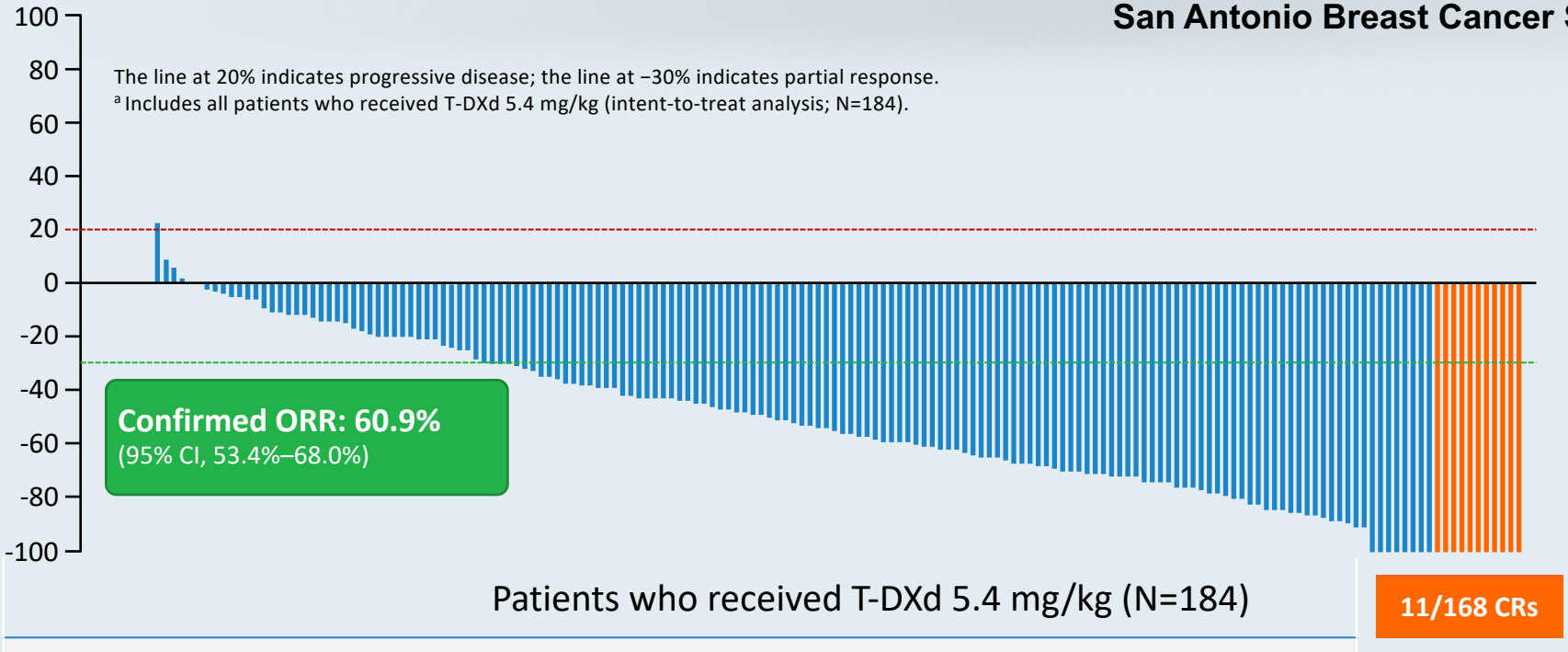


ADCC= antibody-dependent cellular cytotoxicity; HER2=human epidermal growth factor receptor 2; Topo-1=topoisomerase I.

1. Ogitani Y et al. *Cancer Sci*. 2016;107:1039–1046 . 2. Ogitani Y et al. *Clin Cancer Res*. 2016;22:5097–5108. Courtesy of Ian E Krop, MD, PhD

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

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



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)**

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

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

Courtesy of Virginia Kaklamani, MD DSc

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.

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

Courtesy of Ian E Krop, MD, PhD

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

R* (2:1)

N=410

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/m^2 PO BID (Days 1-14)

N=202

Placebo + Trastuzumab + Capecitabine
(21-day cycle)

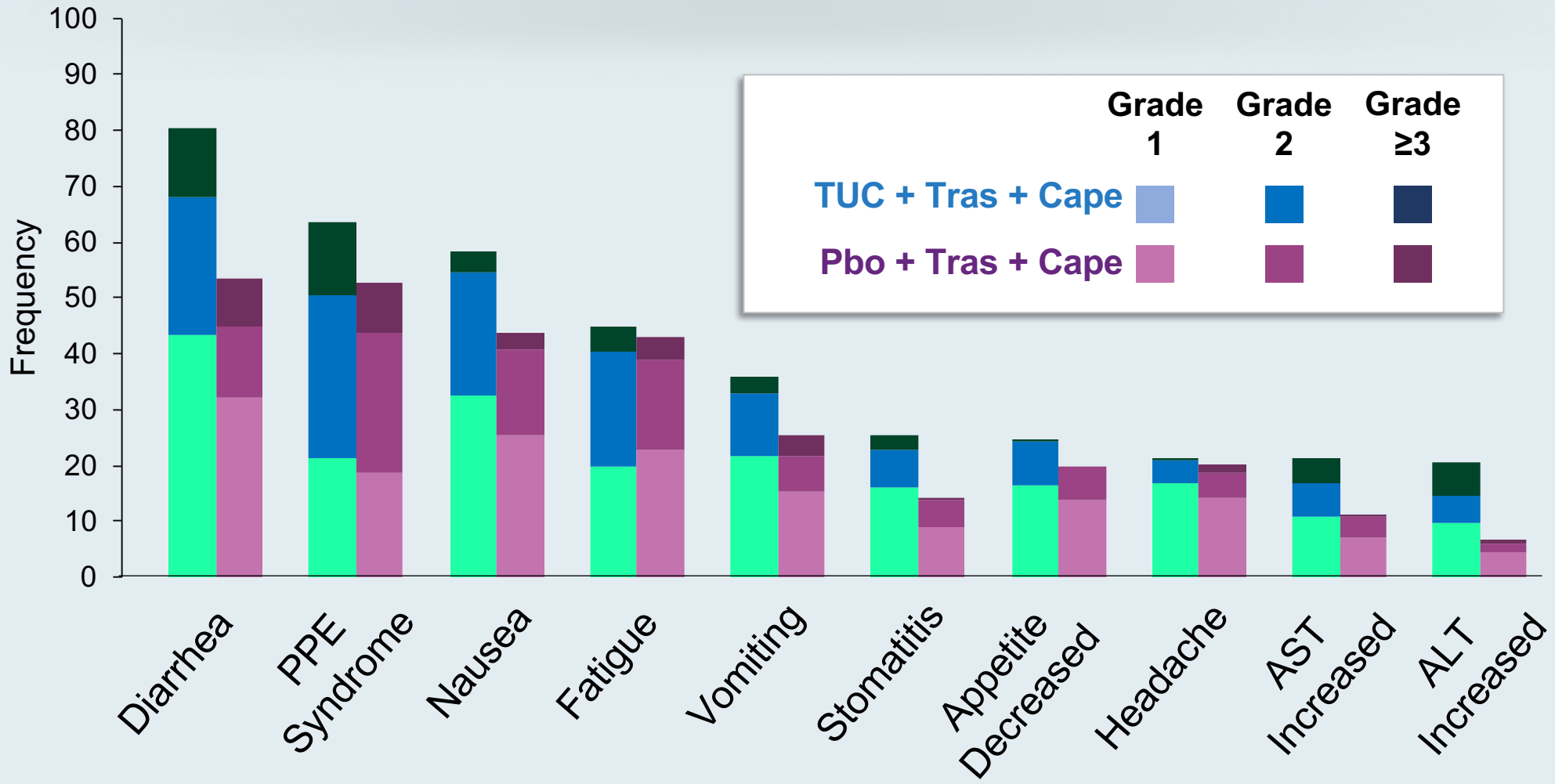
Placebo
+
Trastuzumab 6 mg/kg Q3W (loading dose 8 mg/kg C1D1)
+
Capecitabine 1000 mg/m^2 PO BID (Days 1-14)

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

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

Murthy R et al. SABCS 2019;Abstract GS1-01.
Courtesy of Virginia Kaklamani, MD DSc

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 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: 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 with 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 [≥ 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/m^2 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/m^2 IV
- On days 1, 8 and 15 of 28-day cycle

RECIST v1.1
PD or toxicity

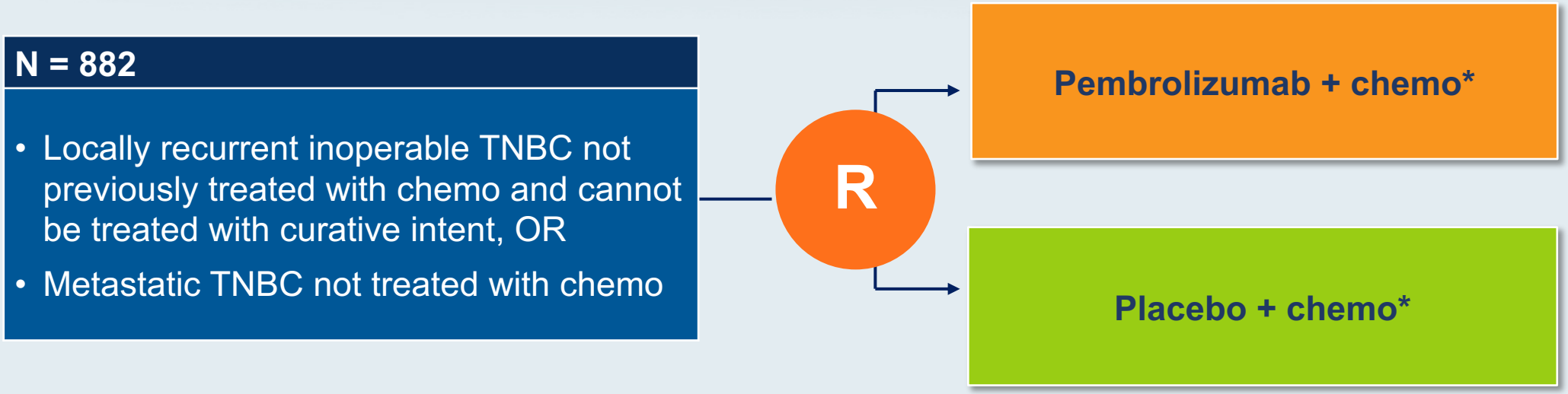
- Co-primary endpoints were PFS and OS in the ITT and PD-L1+ populations[d]
  - Key secondary efficacy endpoints (ORR and DOR) and safety were also evaluated

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).

Schmid P, et al. NEJM 2018, Schmid and Rugo et al, Lancet Oncol 2020

Courtesy of Joyce O'Shaughnessy, MD

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

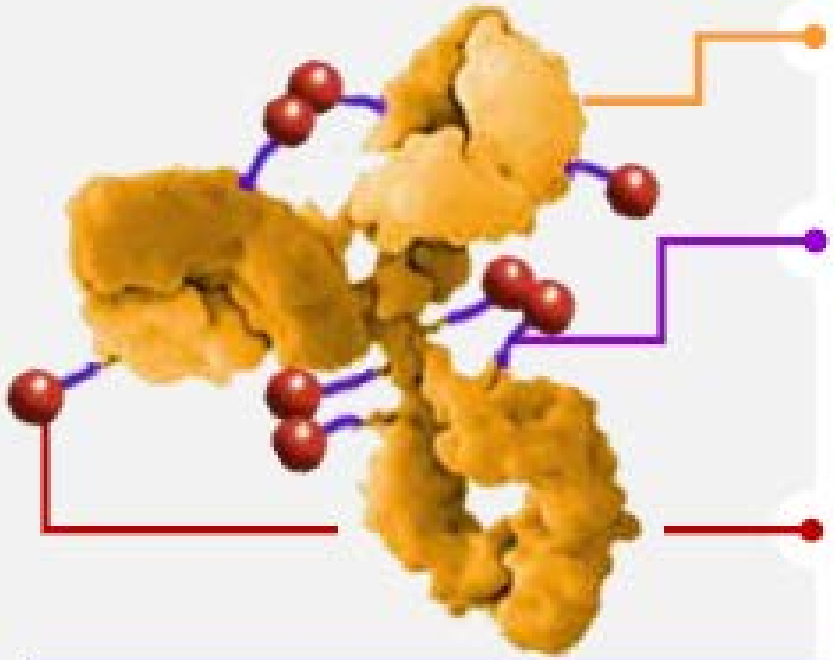


Primary endpoints: Progression-free and overall survival

- 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.

Cortes J et al. ASCO 2020;Abstract 1000. www.clinicaltrials.gov. Accessed May 24, 2020.

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

Courtesy of Joyce O'Shaughnessy, MD

FDA Grants Accelerated Approval to Sacituzumab Govitecan for Metastatic TNBC

Press Release – April 22, 2020

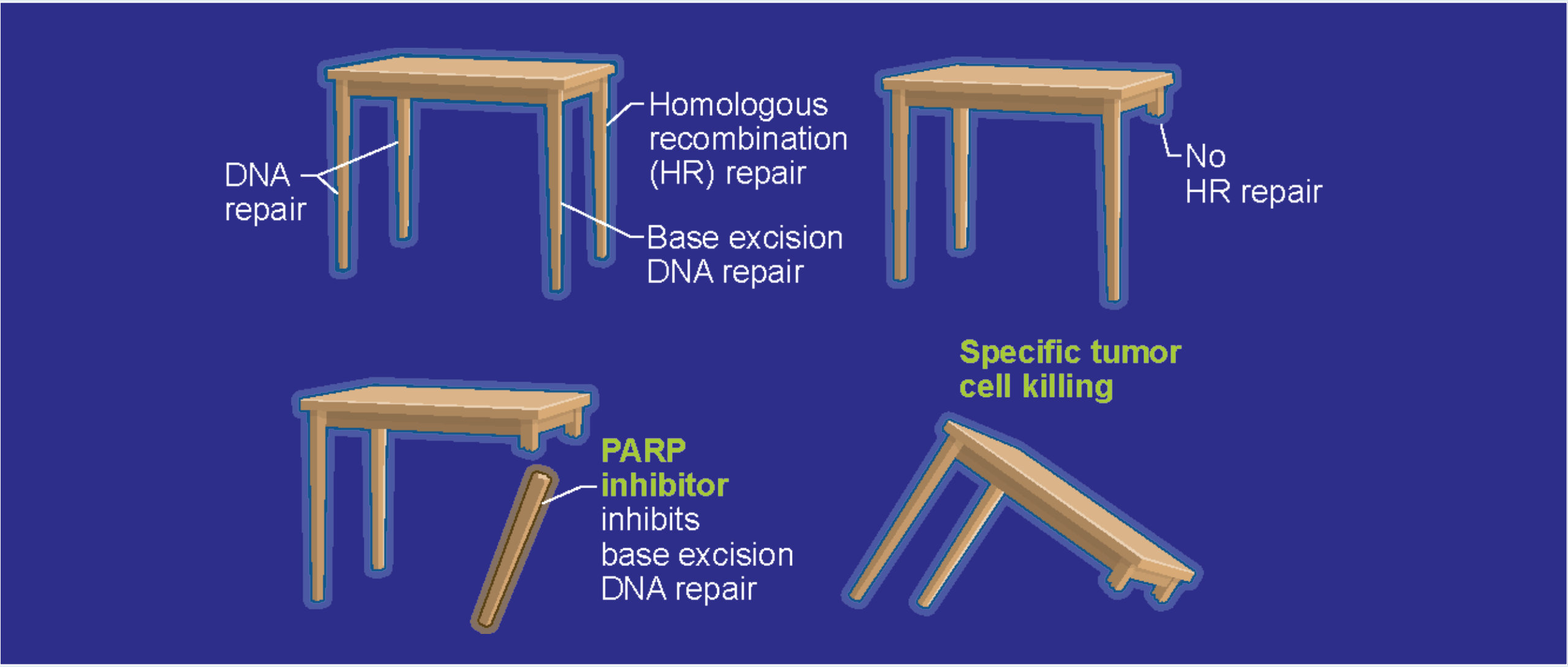
"The Food and Drug Administration granted accelerated approval to sacituzumab govitecan-hziy for adult patients with metastatic triple-negative breast cancer who received at least two prior therapies for metastatic disease.

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."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-sacituzumab-govitecan-hziy-metastatic-triple-negative-breast-cancer

Mechanism of Cell Death from Synthetic Lethality Induced by PARP Inhibition



Courtesy of Jenny C Chang, MD

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

Litton JK et al. *N Engl J Med* 2018;379(8):753-63.
Robson M et al. *N Engl J Med* 2017;377(6):523-33.

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

OlympiAD[1]

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)

EMBRACA[2]

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)

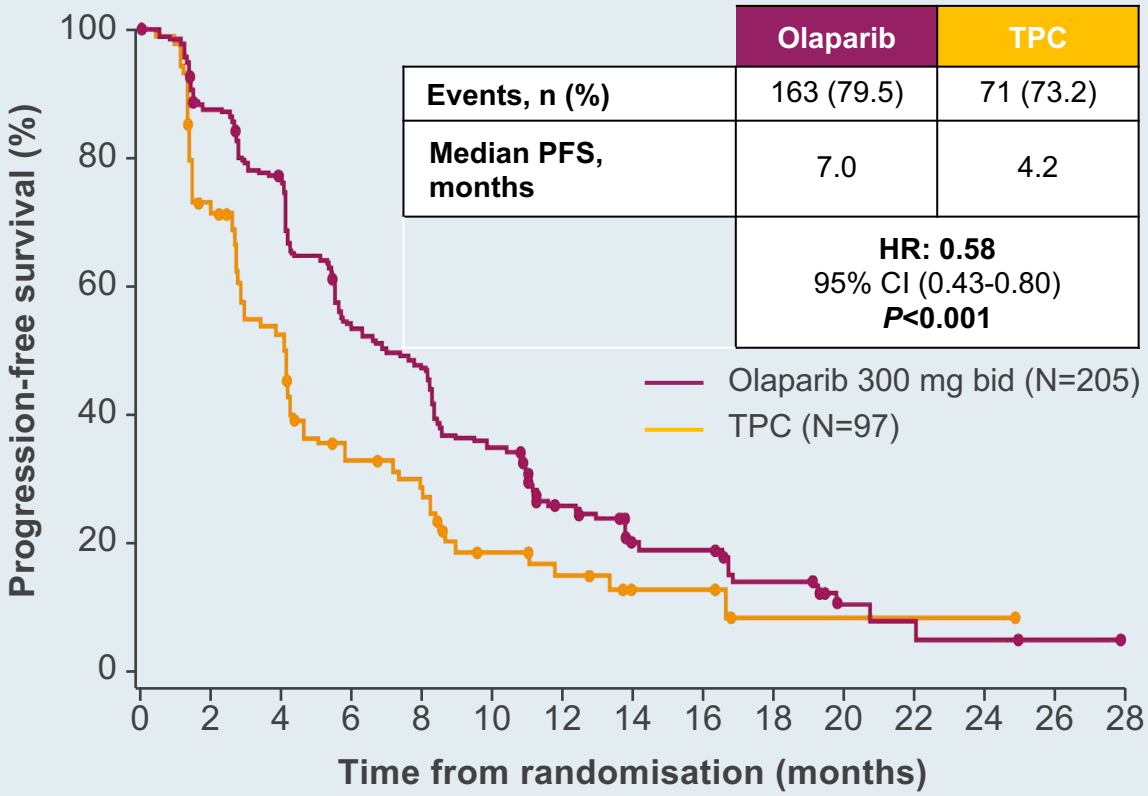
1. Robson et al. *N Engl J Med* 2017; 377:523-533;
2. Litton J et al. *N Engl J Med* 2018; 379:753-763

Courtesy of Joyce O'Shaughnessy, MD

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]

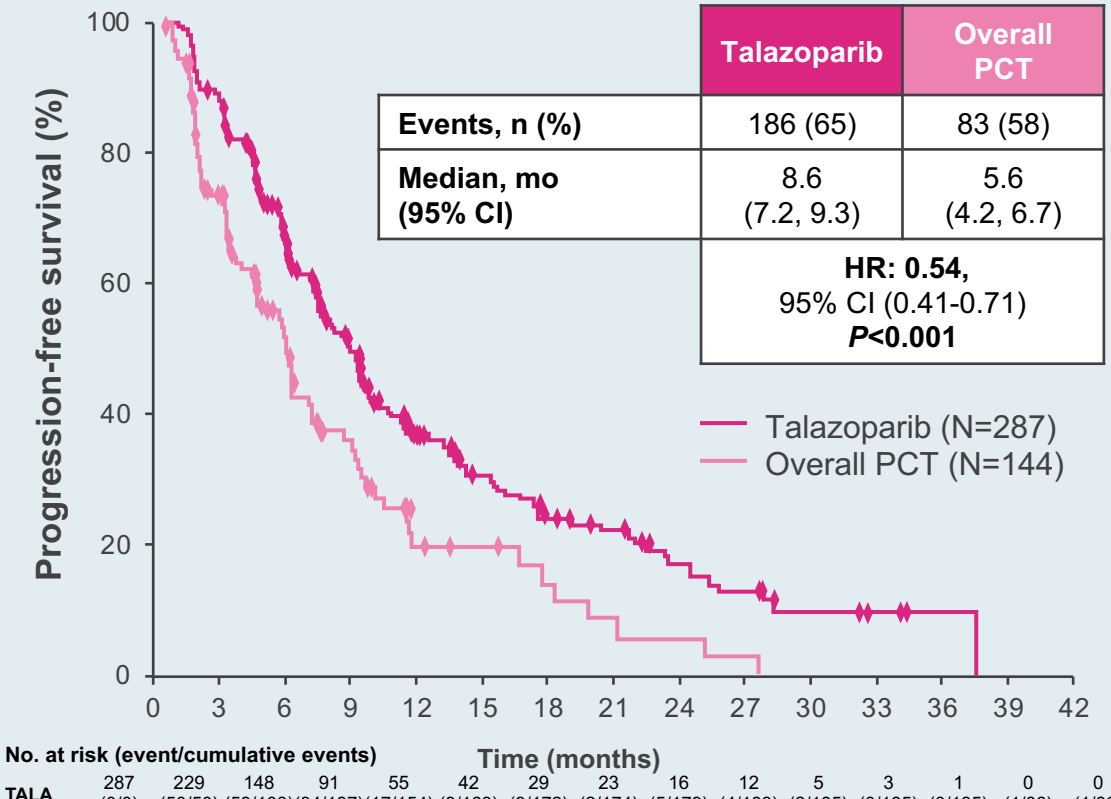


	Olaparib	TPC
Events, n (%)	163 (79.5)	71 (73.2)
Median PFS, months	7.0	4.2
	HR: 0.58 95% CI (0.43-0.80) *P*<0.001	

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, mo (95% CI)	8.6 (7.2, 9.3)	5.6 (4.2, 6.7)
	HR: 0.54, 95% CI (0.41-0.71) *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;377:523-533; 2. Olaparib 150mg Film-Coated Tablets, SmPC. 2019; 3. Litton JK, et al. N Engl J Med. 2018;379:753-763 (supplementary appendix)

Courtesy of Joyce O'Shaughnessy, 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)

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)?

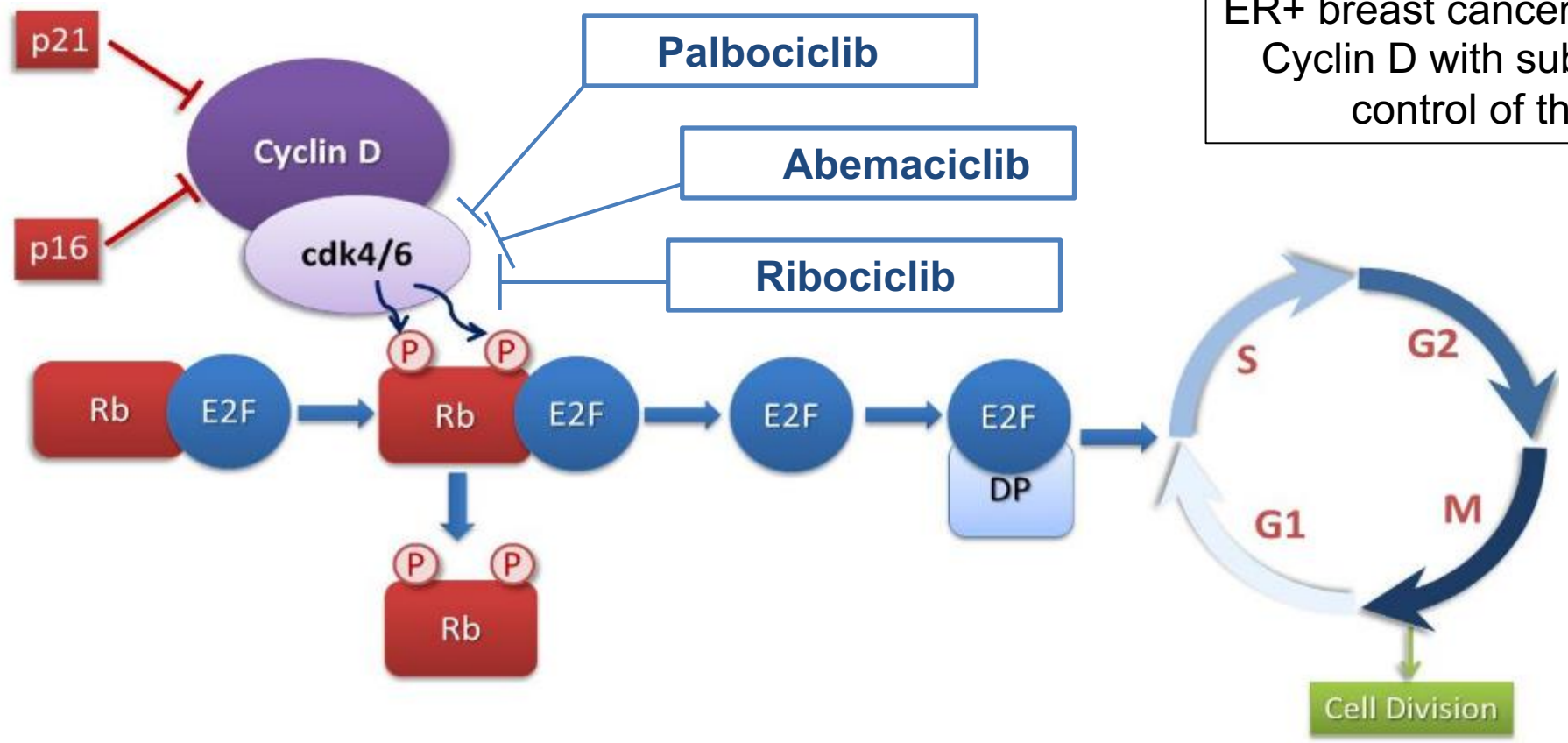
- Treated with fulvestrant and a CDK4/6 inhibitor
- Patient did well but disease progressed after 2 years, with new liver mets
- Patient was stable clinically
- PI3K mutation detected in the tumor

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

- Alpelisib, everolimus combinations

CDK4/6 Regulates Cell Cycle Progression

ER+ breast cancer may overexpress Cyclin D with subsequent loss of control of the cell cycle



M, mitosis; Rb, retinoblastoma.
Adapted from Finn et al, 2016.

Courtesy of Joyce O'Shaughnessy, MD

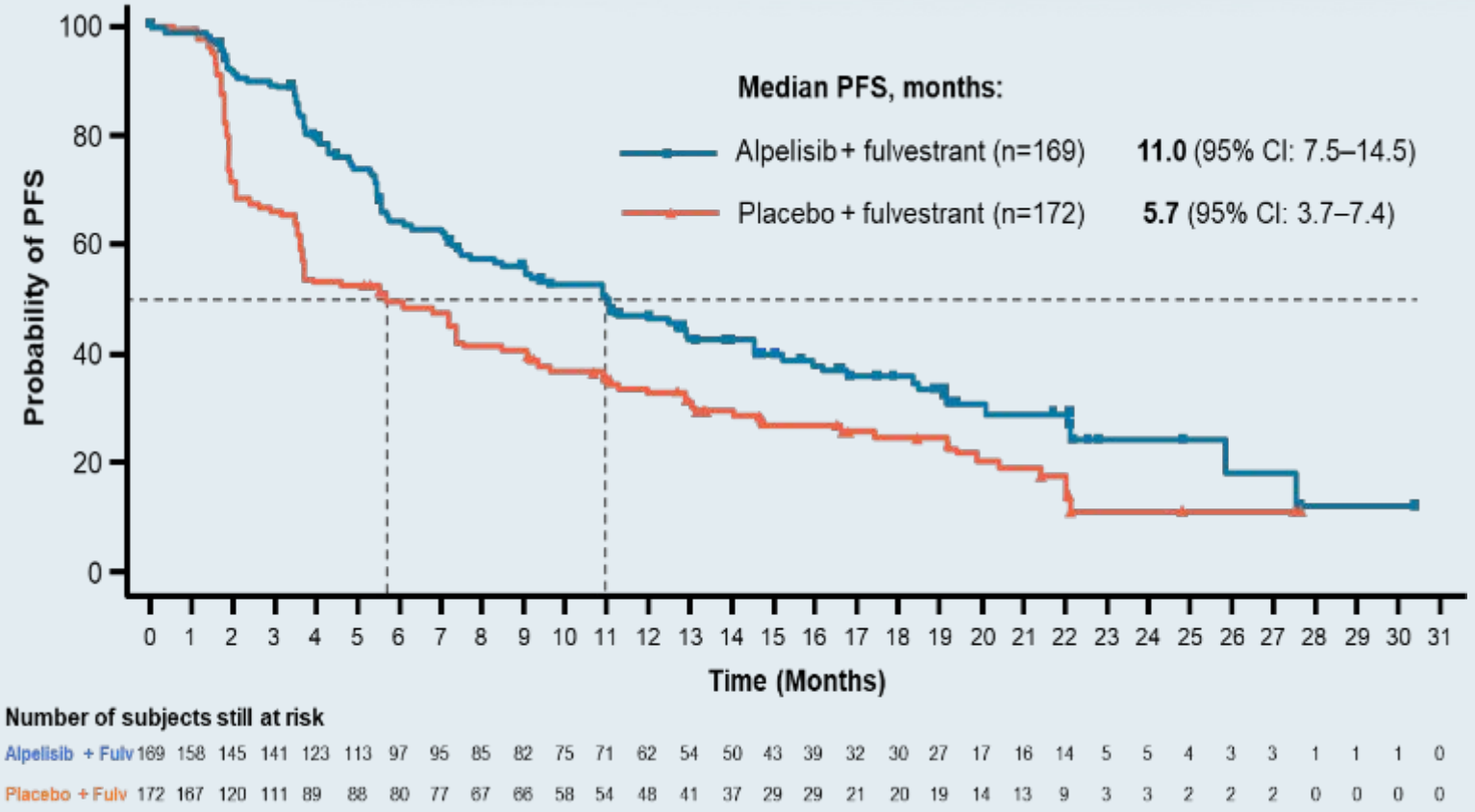
Common Side Effects and Dosing of CDK4/6 Inhibitors

	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.

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 *P* 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

Tuesday, July 28, 2020

5:00 PM – 6:00 PM ET

Faculty

Robert Dreicer, MD, MS

Victoria Sinibaldi, RN, MS, CS, CANP, BC

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Thank you for joining us!

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