Cancer Conference Update: What Happened at the 2020 San Antonio Breast Cancer Symposium®

Session 1: Triple-Negative Breast Cancer

Monday, January 11, 2021
5:00 PM – 6:00 PM ET

Faculty

P Kelly Marcom, MD

Moderator

Neil Love, MD

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Eisai Inc, Genentech, a member of the Roche Group, and Merck.

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 commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seagen Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc and Verastem Inc.

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

Dr Marcom — Disclosures

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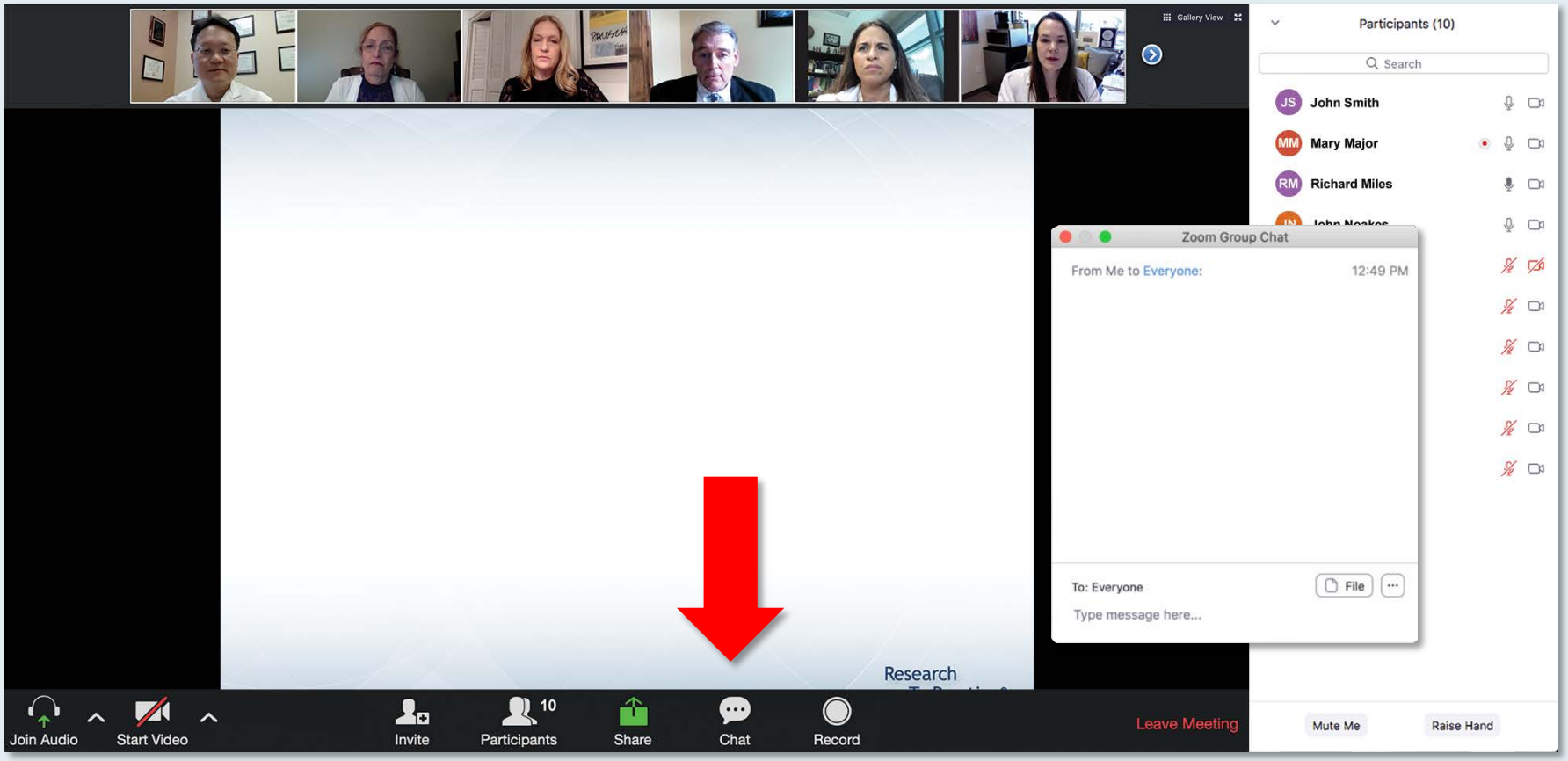
We Encourage Clinicians in Practice to Submit Questions



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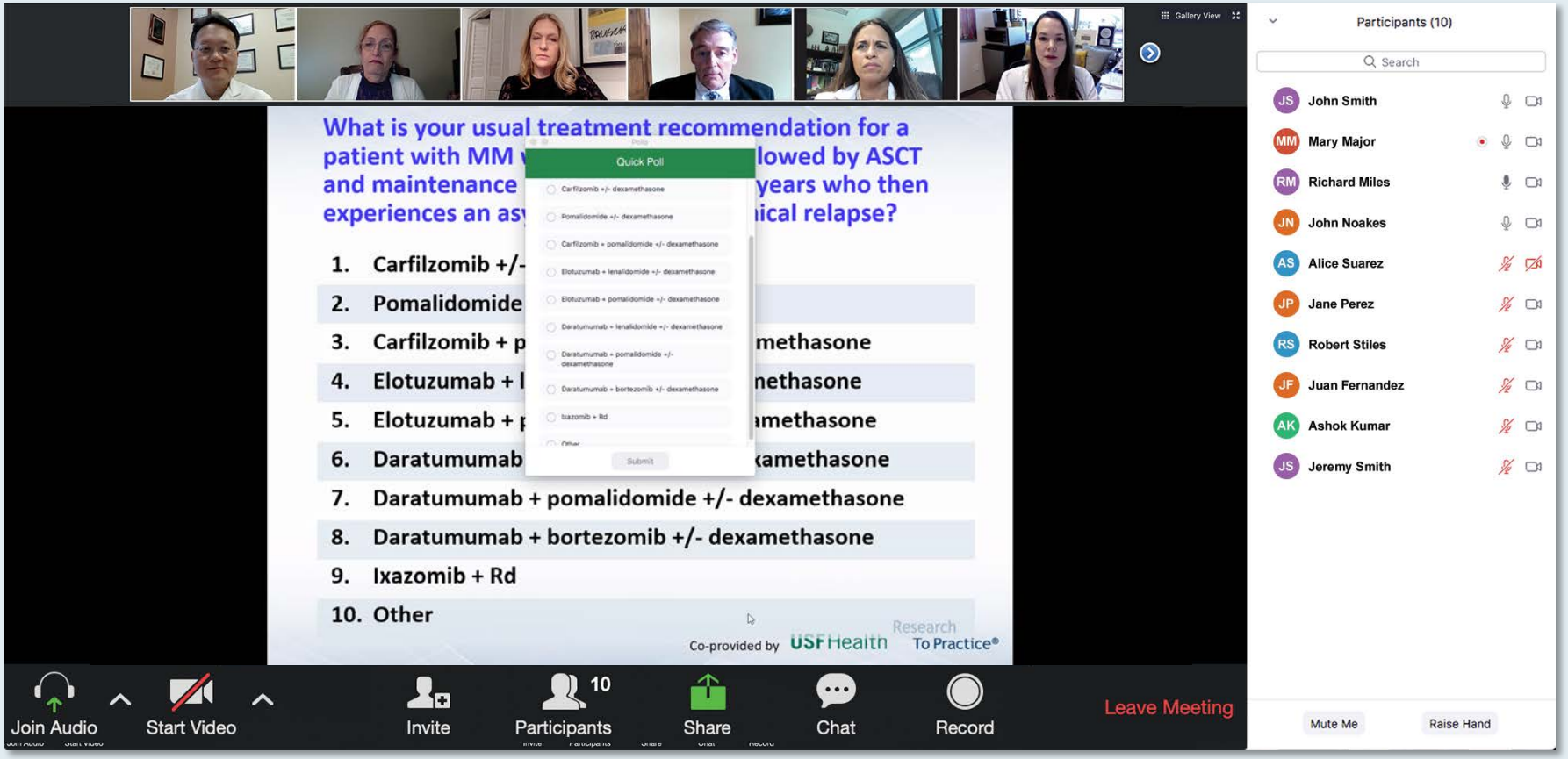
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

Gynecologic Cancers

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Sonali M Smith, MD

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Nontargeted Therapy for Lung Cancer

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Matthew Gubens, MD, MS
Suresh S Ramalingam, MD

Moderator

Neil Love, MD

RTP Year in Review 2021

Recent Advances in Hematologic Oncology: A 4-Part Live Webinar Series Reviewing Key Data and Presentations from the 62nd ASH Annual Meeting

Part 1 — Acute Myeloid Leukemia

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Chronic Lymphocytic Leukemia

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5:00 PM – 6:00 PM ET

Faculty

Matthew S Davids, MD, MMSc
Jennifer Woyach, MD

Moderator

Neil Love, MD

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Meet The Professor
Management of Ovarian Cancer

Friday, January 22, 2021
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Faculty
Erika Hamilton, MD

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Monday, February 22, 2021
5:00 – 6:00 PM ET

Faculty
Joyce O'Shaughnessy, MD

Session 2: HER2-Positive Breast Cancer
Monday, March 8, 2021
5:00 – 6:00 PM ET

Faculty
Mark D Pegram, MD

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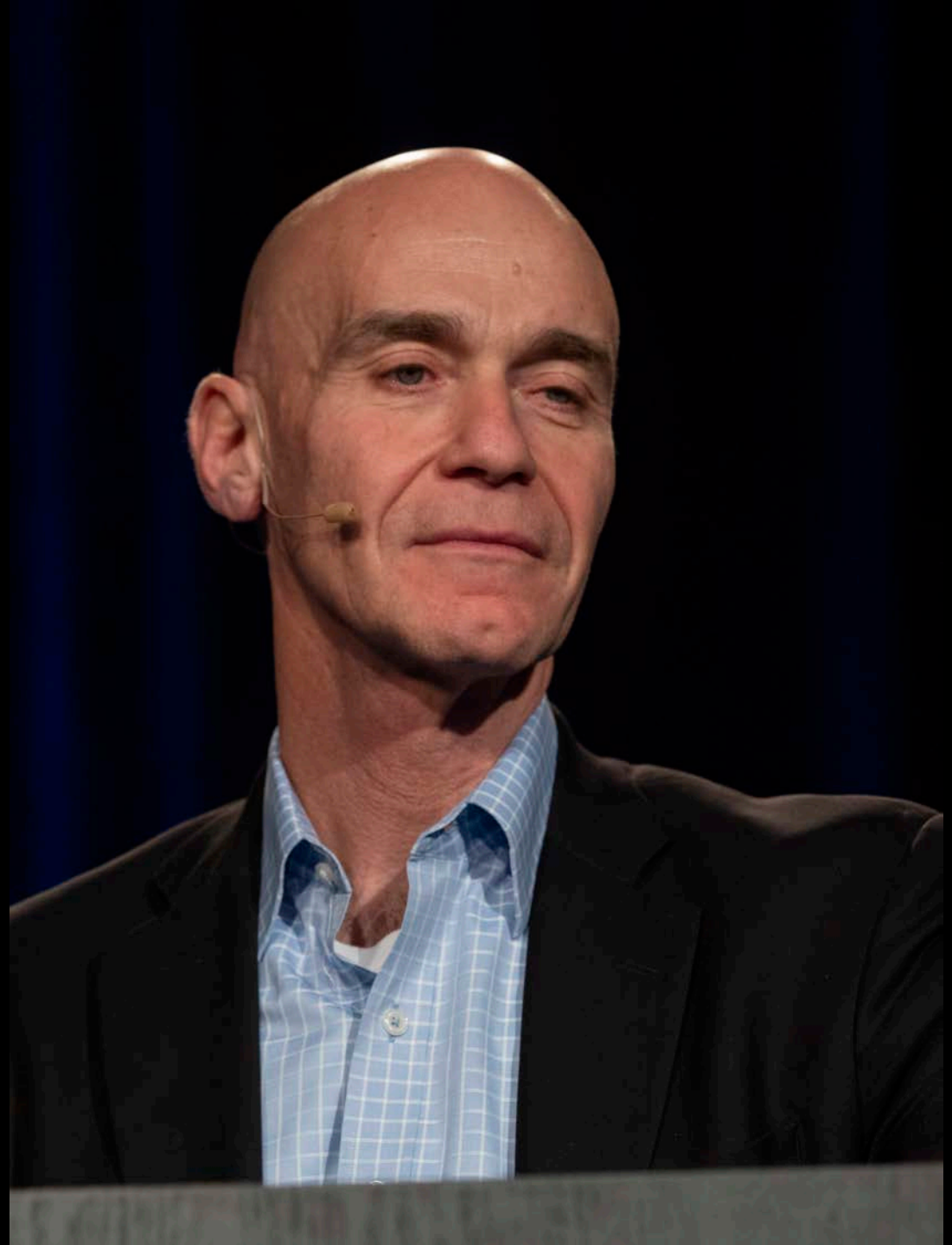
Thank you for joining us!

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


INSTITUT
JULES BORDET
INSTITUUT
Adjuvant and Extended-Adjuvant Therapy for Patients with Localized HER2-Positive Breast Cancer
Martine J Piccart-Gebhart, MD, PhD
Scientific Director




KEYNOTE 522: NEOADJUVANT CHEMO + PEMBROLIZUMAB IN TNBC
KEYNOTE 522: NEOADJUVANT CHEMO + PEMBROLIZUMAB IN TNBC


Management of Triple-Neg
Thursday, December 12, 2019
7:30 PM – 9:00 PM
San Antonio, Texas
Moderator
Neil Love, MD
Faculty
Erika Hamilton, MD


Sparano et al. N Engl J Med 2019;380(25):2395-2405.
Integrated Risk: Potential Clinical Utility of Integrated RS and Clinical Risk for Guiding Treatment in Women ≤ 50 Years
Integrated RS and Clinical Risk (CR)
Low Integrated Risk (58%)
< 5% Distant Recurrence
High Integrated Risk (31%)
> 10% Distant Recurrence
Tamoxifen alone adequate
No Chemotherapy
Consider chemotherapy or OFS + AI as an alternative to chemotherapy
Chemotherapy and consider OFS + AI in addition to chemotherapy
Prediction: Hazard Ratio for Chemotherapy Benefit as a Function of Continuous RS and Age (SEER)
Cox proportional hazards regression with propensity weighting (N=70,087)
Age ≤ 50 Years
Age > 50 Years


A 65-year-old postmenopausal woman completes 5 years of adjuvant anastrozole for an ER-positive, HER2-negative IDC but develops asymptomatic biopsy-proven bone and liver metastases 2 years later. Which systemic treatment would you most likely recommend?


Gene Expression Assays in Breast Cancer
Unsupervised analysis
Breast cancer is heterogeneous
Distinct subtypes
Prognosis varies by subtype (PAM50)
Supervised analysis
Several other prognostic assays (21-gene, 70-gene, others)
Lack of concordance in prognostic classification
Luminal A
Luminal B
ERBB2
Basal
Normal
C
D
E
F
G
Sorlie et al PNAS 2003; 100(14): 8418-8423
Bartlett JM et al. J Natl Cancer Inst. 2016;108(9)

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Triple-Negative Breast Cancer

Friday, December 11, 2020
8:30 PM – 10:00 PM ET

Faculty

P Kelly Marcom, MD
Joyce O'Shaughnessy, MD
Hope S Rugo, MD
Professor Peter Schmid, MD, PhD

Moderator

Neil Love, MD

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Presentation Library

Triple-Negative Breast Cancer, Friday, December 11, 2020

Optimal Integration of Immune Checkpoint Inhibitors into the Management of Metastatic Triple-Negative Breast Cancer (mTNBC)
Professor Peter Schmid, MD, PhD

Download Slides

Novel Applications of Immune Checkpoint Inhibitors for Patients with Early TNBC
Hope S Rugo, MD

Download Slides

Current and Future Role of PARP Inhibitors for Patients with TNBC and a BRCA Mutation
P Kelly Marcom, MD

Download Slides

Current and Future Management of PD-L1-Negative mTNBC
Joyce O'Shaughnessy, MD

Download Slides

Faculty

P Kelly Marcom, MD
Director, Breast Oncology Program
Professor of Medicine
Duke Cancer Institute
Durham, North Carolina

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

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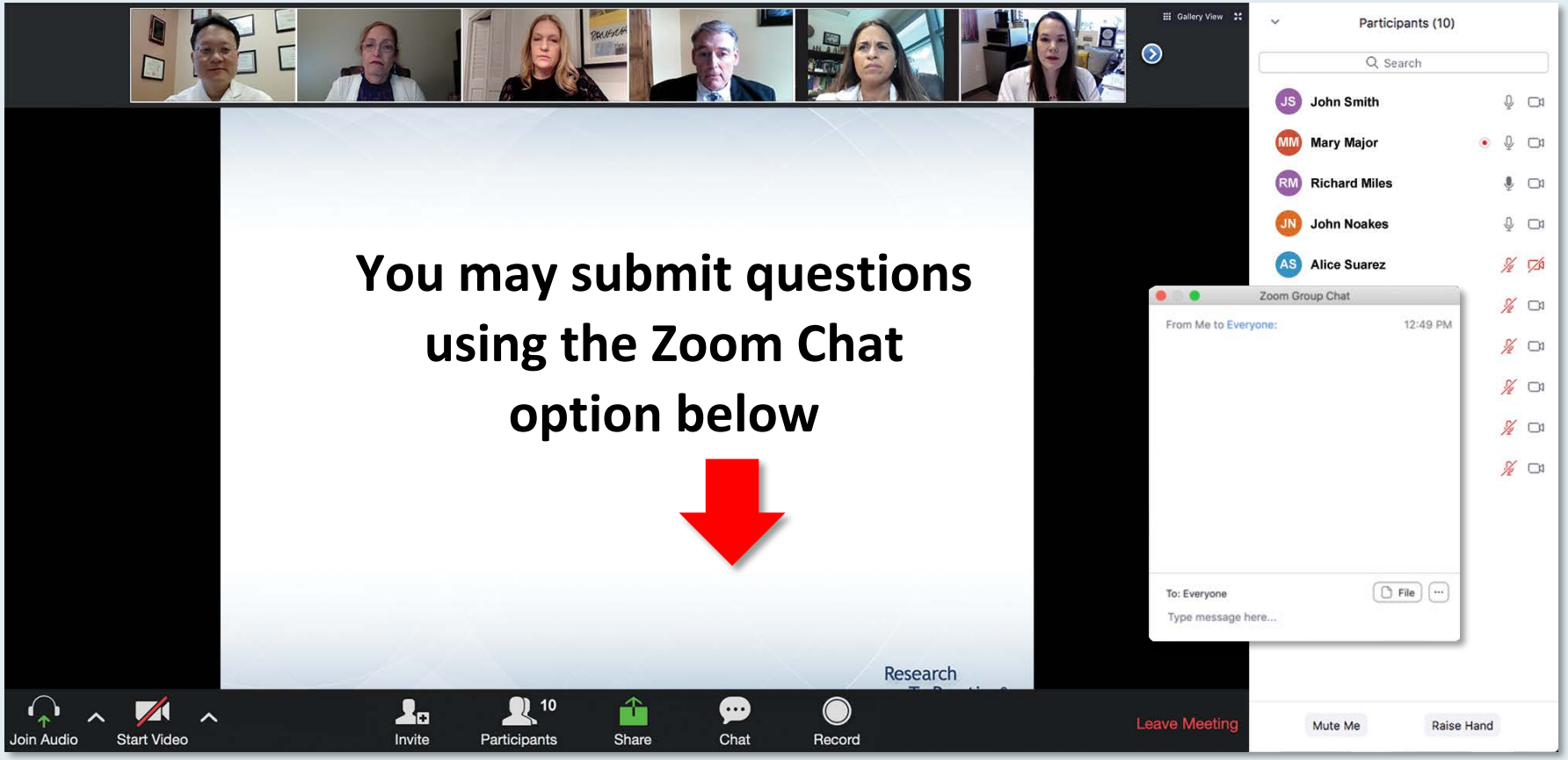
We Encourage Clinicians in Practice to Submit Questions



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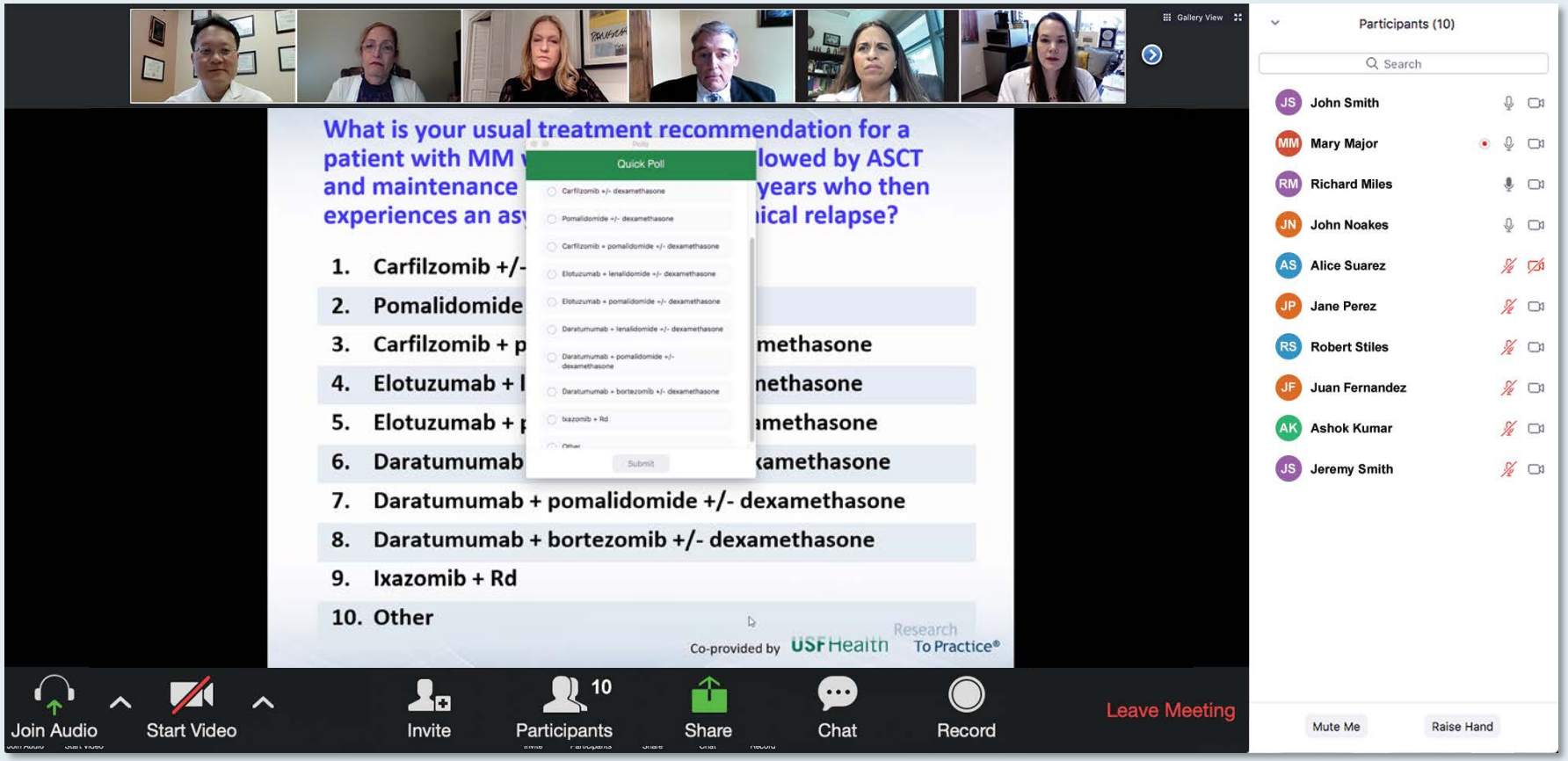

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ONCOLOGY TODAY

WITH DR NEIL LOVE

IMMUNE CHECKPOINT INHIBITION IN BREAST CANCER

DR SYLVIA ADAMS

PERLMUTTER CANCER CENTER

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Neil Love, MD

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Triple-Negative Breast Cancer Survey Participants

1. Sylvia Adams, MD
2. Carey K Anders, MD
3. Aditya Bardia, MD, MPH
4. Joanne L Blum, MD, PhD
5. Adam M Brufsky, MD, PhD
6. Howard A Burris III, MD
7. Harold J Burstein, MD, PhD
8. Lisa A Carey, MD
9. Matthew Goetz, MD
10. Erika Hamilton, MD
11. Sara Hurvitz, MD
12. Virginia Kaklamani, MD, DSc
13. Hannah M Linden, MD
14. P Kelly Marcom, MD
15. Jennifer M Matro, MD
16. Kathy D Miller, MD
17. Rita Nanda, MD
18. Ruth O'Regan, MD
19. Joyce O'Shaughnessy, MD
20. Mark D Pegram, MD
21. Lajos Pusztai, MD, DPhil
22. Hope S Rugo, MD
23. Professor Peter Schmid, MD, PhD
24. Joseph A Sparano, MD
25. Sara M Tolaney, MD, MPH

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Atif Hussein, MD, MMM
Program Director, Hematology/Oncology Fellowship
Medical Director, Oncology Clinical Research
Chairman, Cancer Committee
Memorial Healthcare System
Clinical Associate Professor
Florida International University Herbert Wertheim College of Medicine
Hollywood, Florida

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Agenda

Module 1: Optimal Integration of Immune Checkpoint Inhibitors into the Management of Metastatic Triple-Negative Breast Cancer (TNBC)

Module 2: Novel Applications of Immune Checkpoint Inhibitors for Patients with Early TNBC

Module 3: Current and Future Role of PARP Inhibitors for Patients with TNBC and a BRCA Mutation

Module 4: Current and Future Management of PD-L1-Negative Metastatic TNBC

SABCS 2020 Educational Session (ES4)

Triple-Negative Breast Cancer – Tuesday, December 8, 2020

Deconstructing Triple Negative Breast Cancer
Rebecca A Dent, MD, MSc

State of the Art Treatment for Neoadjuvant/Adjuvant Triple Negative Breast Cancer
Lisa A Carey, MD

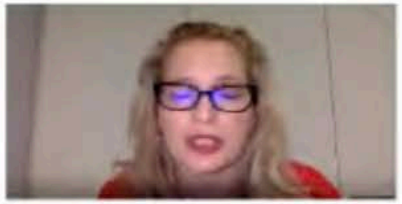
Metastatic TNBC – What's New on the Horizon?
Jennifer K Litton, MD

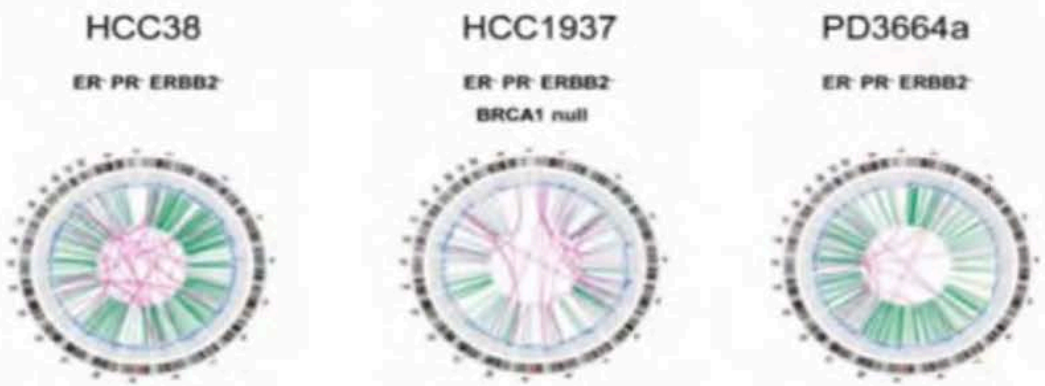
How and When to Use Immunotherapy and Related Toxicities
Javier Cortes, MD, PhD

Deconstructing

Triple Negative Breast Cancer

Rebecca A Dent, MD FRCP (Canada)
Head Dept of Medical Oncology
Senior Consultant
National Cancer Center Singapore
Associate Professor, Duke – NUS Medical School

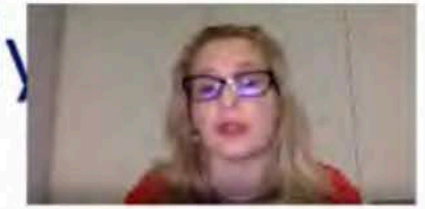




Dent R et al. SABCS 2020;Education Session ES4.

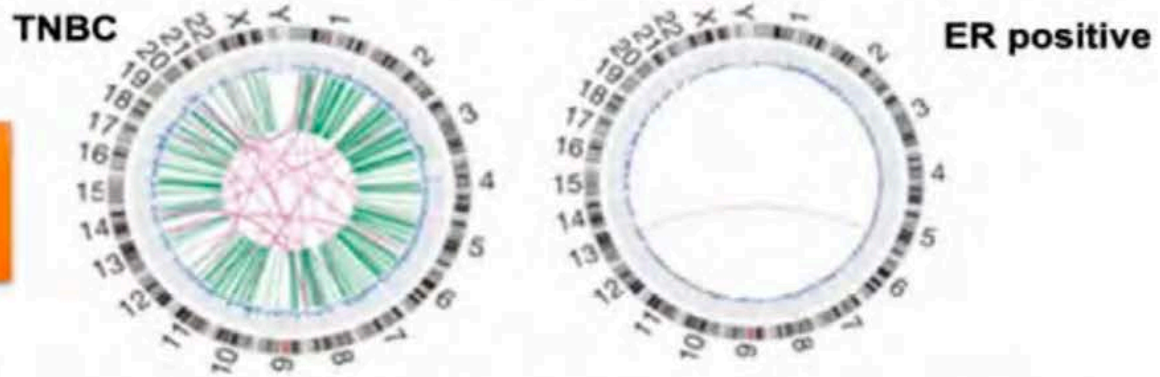
San Antonio Breast Cancer Symposium®, December 8-11, 2020

Not All Breast Cancers Are Equally Suitable for Immunotherapy

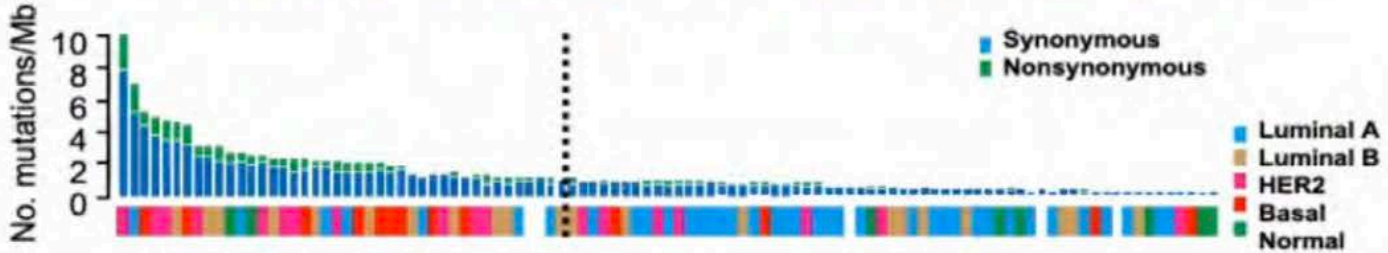


Somatic mutations in breast cancer subtypes

Quality as well as quantity
Of aberrations determine
Immune checkpoint sensitivity



Mutation rate higher in TNBC compared to other subtypes



Banerji
Nature. 2012

Dent R et al. SABCS 2020;Education Session ES4.

Carey LA et al. SABCS 2020;Education Session ES4.

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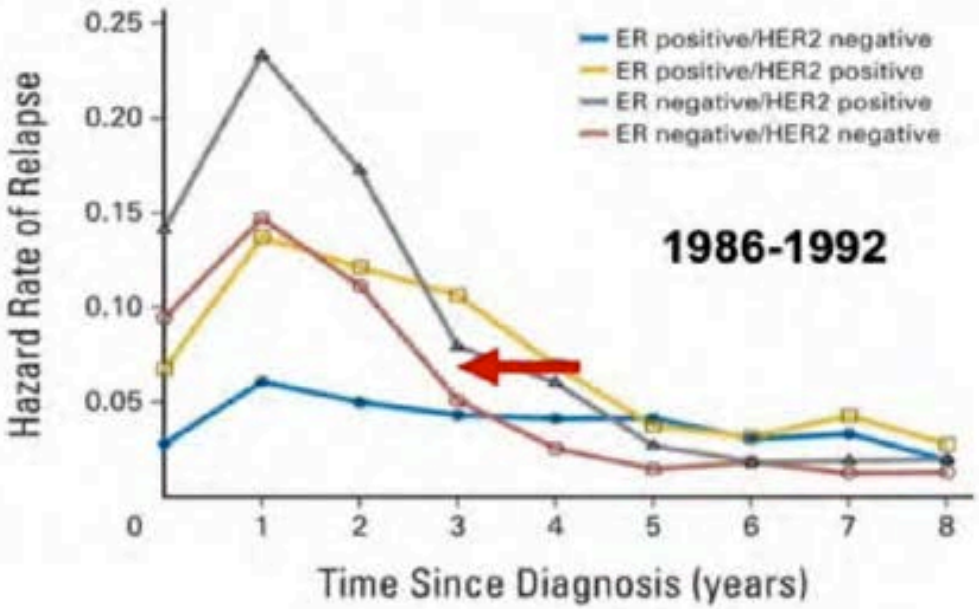
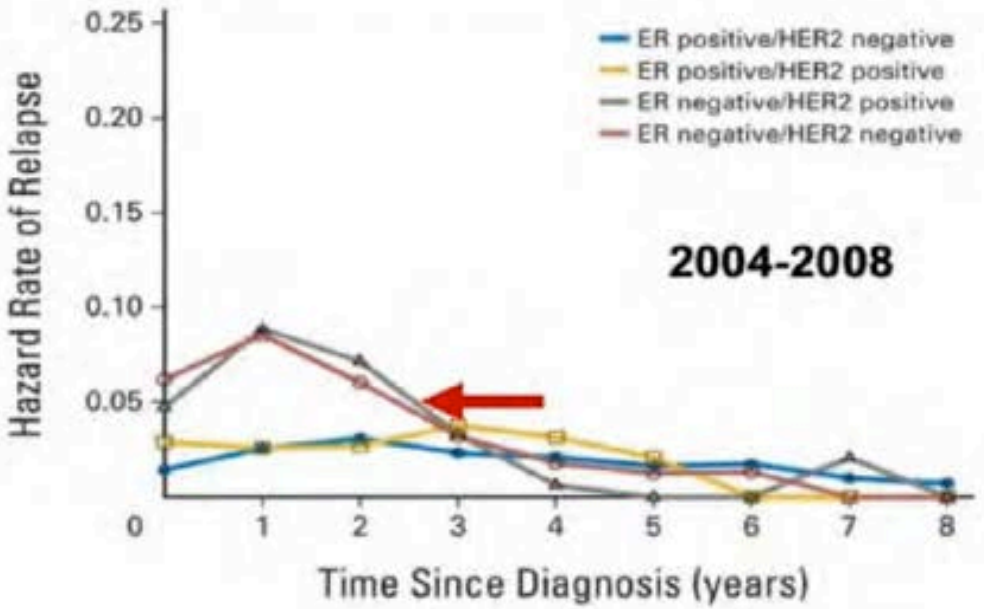
The Drugs Work! Early TNBC Relapse Rates over Time





Early relapse is the vast majority of all relapses
Decreased by 25-45% from years 0-6
However de novo is 20% of mTNBC in modern era

Cossetti R J et al. JCO 2015; File D et al, ASCO 2020

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

Carey LA et al. SABCS 2020;Education Session ES4.

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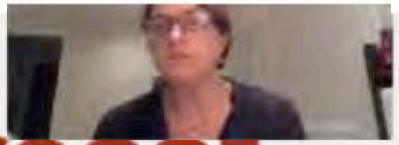
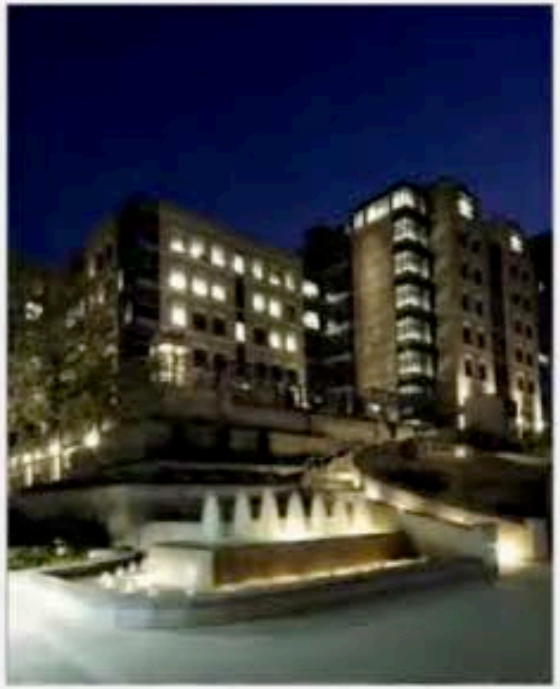


Metastatic Triple Negative Breast Cancer

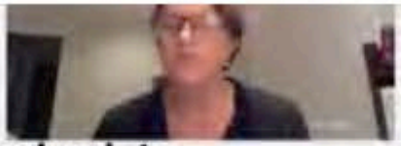


THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Jennifer Keating Litton, M.D.
Professor
Vice President Clinical Research *ad interim*
Department of Breast Medical Oncology

Litton JK et al. SABCS 2020;Education Session ES4.

Study Schema: SWOG 1416



Metastatic and/or loco-regionally recurrent TNBC[a]
or
***BRCA1* or *BRCA2* germline mutation-associated HER2-negative MBC**

0/1 prior cytotoxic chemotherapy for metastatic disease

R[b] (1:1)

- **Cisplatin 75 mg/m² Day 1 every 21 days**
  Veliparib 300 mg PO BID (D1-14) every 21 days
- **Cisplatin 75 mg/m² Day 1 every 21 days**
  Placebo PO BID (D1-14) every 21 days

Tumor Blood

Primary end point:

Progression- free survival in three pre-specified groups:

- g*BRCA*
- BRCA-like
- non-BRCA-like

Secondary end points:

- Overall survival
- Objective response rate
- Clinical benefit rate

Post-randomization germline and BRCA-like biomarker testing assigned patients into pre-specified groups

Germline *BRCA* testing

- **Deleterious germline *BRCA1/2* mutation detected** → **g*BRCA* group**
- **Deleterious germline *BRCA1/2* mutation not detected** → **BRCA-like Biomarker Analysis**

BRCA-like Biomarker Analysis (Primary tumor)

1. HRD genomic instability score ≥42
2. Somatic *BRCA1/2* mutation
3. *BRCA1* promoter methylation (PM)
4. Germline HR repair genes mutation (excluding *BRCA1/2*)

Positivity on any one of the above four marker/s placed patient in BRCA-like group

→ **BRCA-like group**
→ **Non-BRCA-like group**

[a]TNBC defined as estrogen receptor (ER) and progesterone receptor (PgR) immunohistochemical (IHC) nuclear staining of ≤1% and HER2 negative per ASCO/CAP guidelines
[b]Randomization stratified by number of prior cytotoxic regimens for metastatic disease (0 vs. 1)

Priyanka Sharma, MD ASCO 2020

SWOG

Litton JK et al. SABCS 2020;Education Session ES4.

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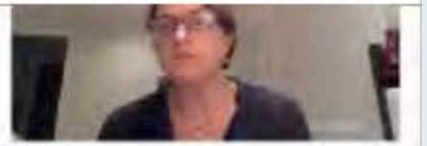
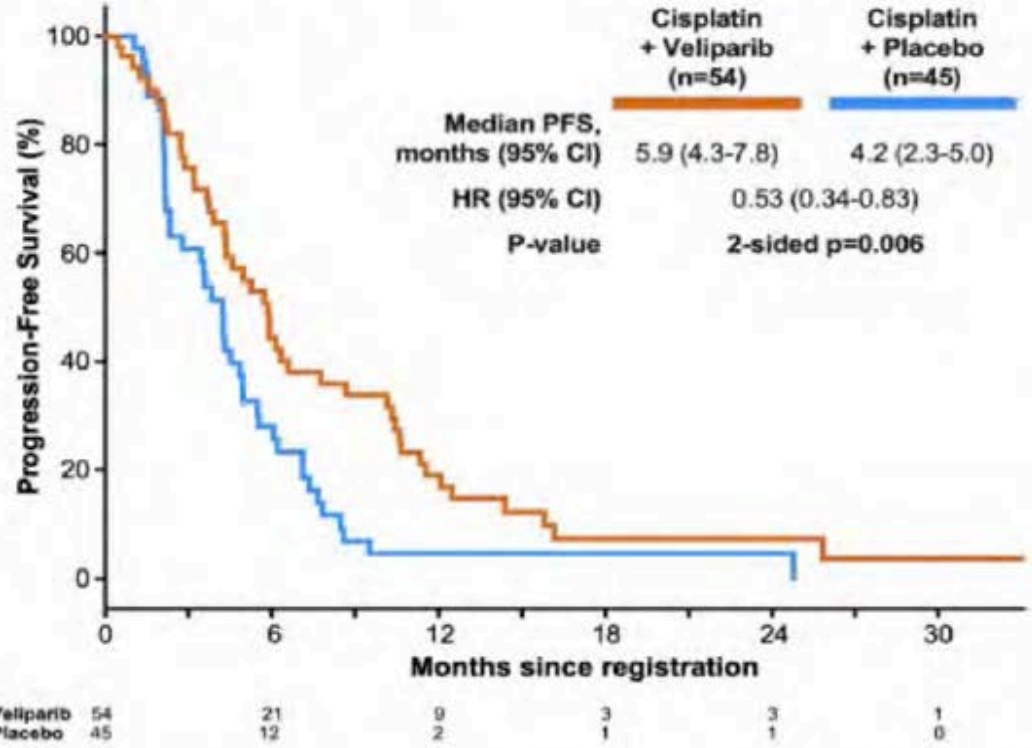
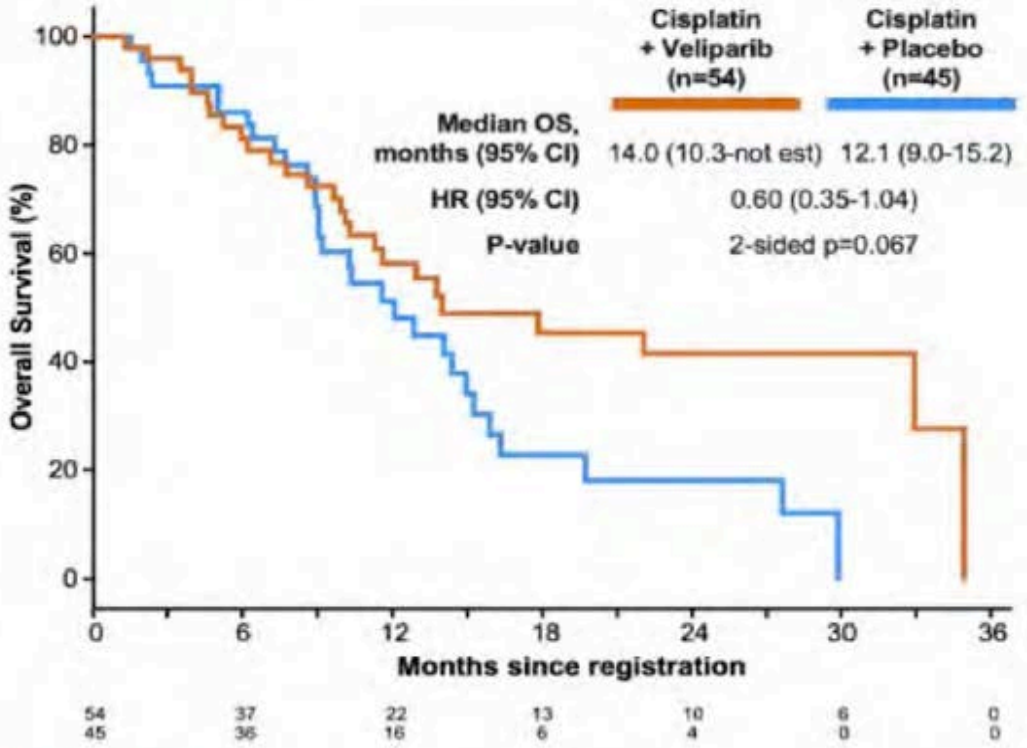
BRCA-like group



Progression-free survival



Overall survival



ORR (n=83): 45% vs 33%

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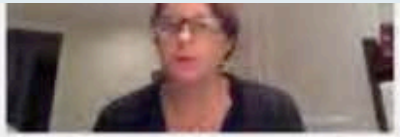
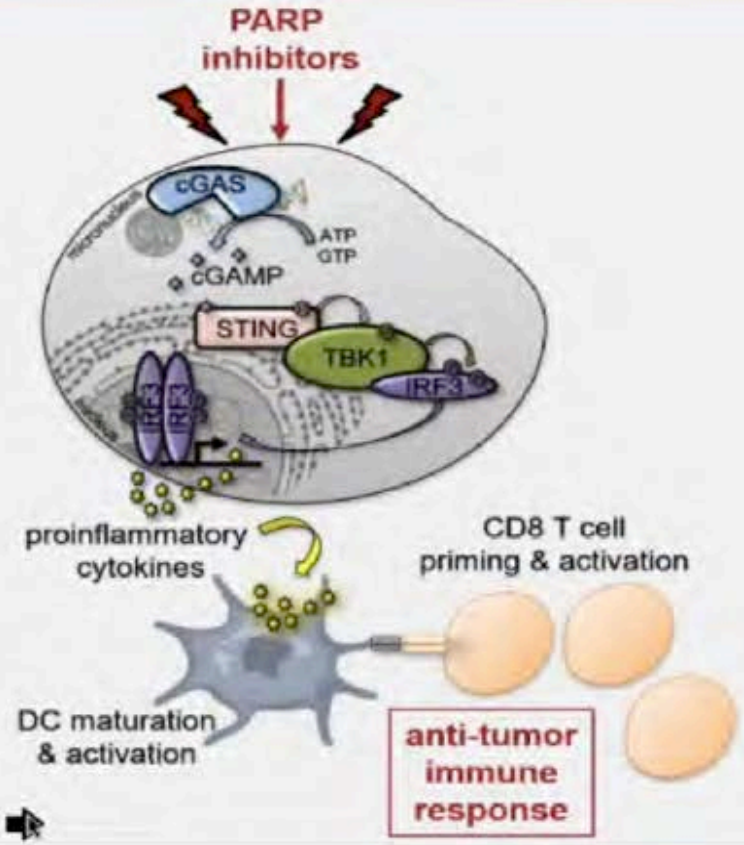


PARP Inhibitors

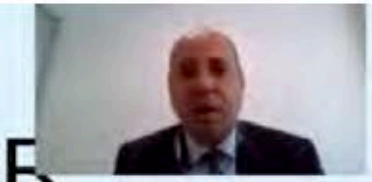


- PARP inhibition activates the cGAS/STING (stimulator of interferon genes) pathway
  - ↑ proinflammatory cytokines
  - ↑ Ag presentation
  - ↑ PD-L1 expression

Huang J, et al. *Biochem Biophys Res Commun* 2015;423:551-556
Jiao S, et al. *Clin Cancer Res* 2017;23:3711-3720
Sato H, et al. *Nat Commun* 2017;8:1751
Pantelidou C, et al. *Cancer Discov* 2019;9:722-737

Litton JK et al. SABCS 2020;Education Session ES4.

San Antonio Breast Cancer Symposium®, December 8-11, 2020



TRIPLE NEGATIVE BREAST CANCER

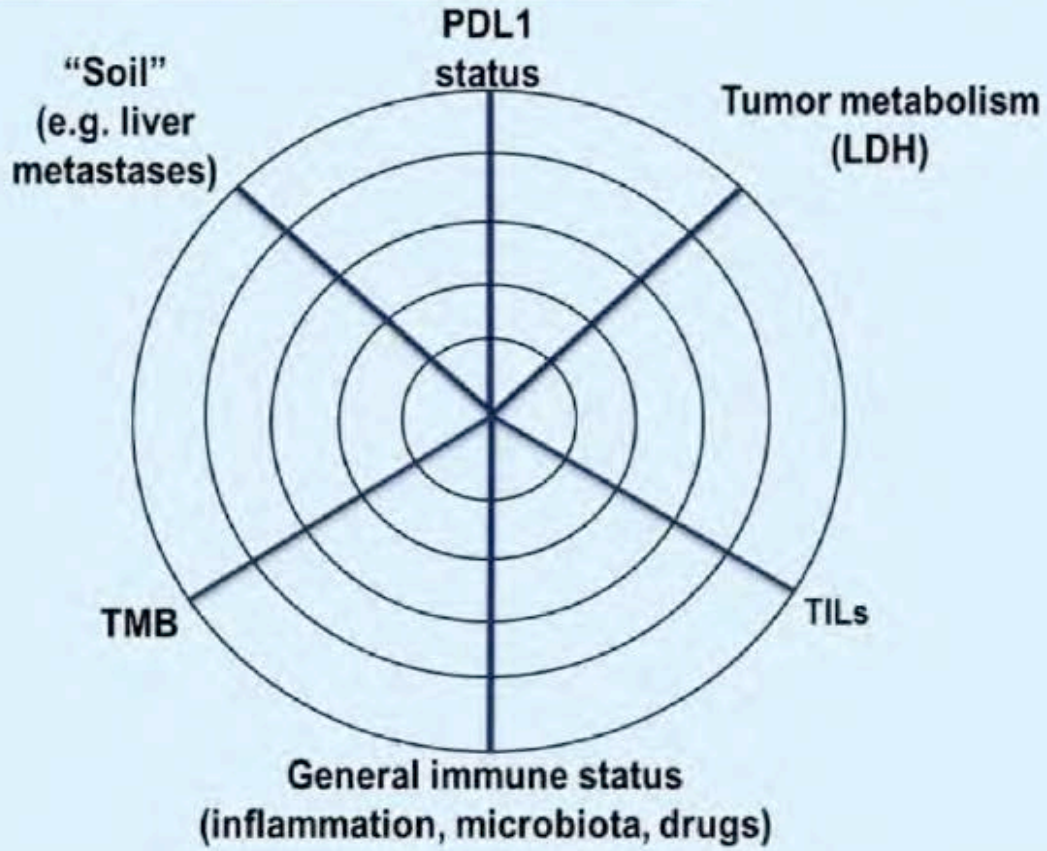
How and when to use immunotherapy and related toxicities in mTNBC

Javier Cortés
International Breast Cancer Center (IBCC), Madrid & Barcelona, Spain
Vall d´Hebron Institute of Oncology (VHIO), Barcelona, Spain
Medica Scientia Innovation Research (MedSIR), Valencia, Spain & New Jersey, US

Cortés J et al. SABCS 2020;Education Session ES4.

San Antonio Breast Cancer Symposium®, December 8-11, 2020

The "breast cancer immunogram" beyond PD



Courtesy of Giampaolo Bianchini

Cortés J et al. SABCS 2020;Education Session ES4.

When to rechallenge with ICI

Organ	Rechallenge	Do NOT Rechallenge
Skin	Grade ≤ 1 rash, pruritus	Grade 3/4 severe, life-threatening bullous disease
GI	Grade 2/3 PD-1/PD-L1–associated colitis*	Grade 3 CTLA-4–associated colitis; grade 4 colitis
Liver	Grade 2 transaminitis without elevated bilirubin*	Grade 3/4 hepatitis
Pancreatitis	Symptomatic grade 2	Grade 3/4 pancreatitis
Endocrine	After hormone repletion	Symptomatic pituitary inflammation
Lung	Grade 1/2, off steroids	Grade 3/4 pneumonitis
Renal	Grade 1/2*	Grade 3/4 proteinuria
Ocular	Grade 2	Grade 3/4 uveitis, episcleritis
Neurologic	Grade 1/2 peripheral neuropathy	GBS, encephalitis, transverse myelitis, grade 2-4 myasthenia gravis
Cardiovascular	Grade 1 myocarditis	Grade 2-4 myocarditis
Musculoskeletal	Resume after stabilization, adequate management	Severe inflammatory arthritis that impairs ADLs

*May resume once prednisone < 10 mg/day

Brahmer JR, et al. J Clin Oncol 2018; Haanen JB, et al. Ann Oncol 2017; ThompsonJA, et al. JNCCN 2020

Cortés J et al. SABCS 2020;Education Session ES4.

Agenda

Module 1: Optimal Integration of Immune Checkpoint Inhibitors into the Management of Metastatic (TNBC)

Module 2: Novel Applications of Immune Checkpoint Inhibitors for Patients with Early TNBC

Module 3: Current and Future Role of PARP Inhibitors for Patients with TNBC and a BRCA Mutation

Module 4: Current and Future Management of PD-L1-Negative Metastatic TNBC

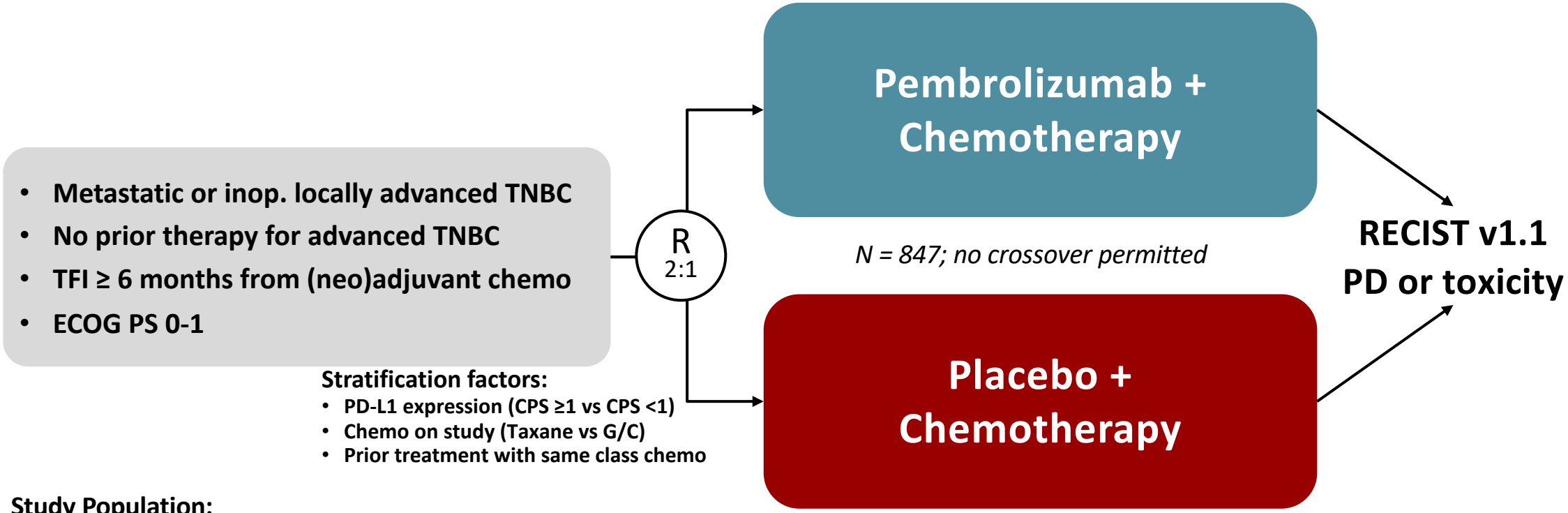
Additional Efficacy Endpoints from the Phase 3 KEYNOTE-355 Study of Pembrolizumab plus Chemotherapy vs Placebo plus Chemotherapy as First-Line Therapy for Locally Recurrent Inoperable or Metastatic Triple-Negative Breast Cancer

Rugo HS et al.

SABCS 2020;Abstract GS3-01.

Pembrolizumab (anti-PD-1) plus chemotherapy in TNBC

KEYNOTE-355 study design



- Metastatic or inop. locally advanced TNBC
- No prior therapy for advanced TNBC
- TFI ≥ 6 months from (neo)adjuvant chemo
- ECOG PS 0-1

Stratification factors:
- PD-L1 expression (CPS ≥1 vs CPS <1)
- Chemo on study (Taxane vs G/C)
- Prior treatment with same class chemo

Study Population:
- CPS≥10, 75%; CPS≥1, 38%; CPS <1, 25%
- Taxane, 45%; Gem/carboplatin, 55%
- Prior treatment with same class chemo, 22%
- De novo MBC, 30%; DFI 6-12, 21%; DFI >12, 49%

Nab-paclitaxel, 100 mg/m^2 IV on days 1, 8, and 15 every 28 days
Paclitaxel, 90 mg/m^2 IV on days 1, 8, and 15 every 28 days
Gemcitabine, 1000 mg/m^2/carboplatin AUC 2 on days 1 and 8 every 21 days

- **Co-primary endpoints were PFS and OS in the CPS ≥10, CPS ≥1, and ITT populations**

Statistical design: Overall alpha controlled at one-sided 0.025, split among PFS (0.005),OS (0.018), and ORR (0.002); hierarchical testing PFS (CSP10>CP1>ITT)

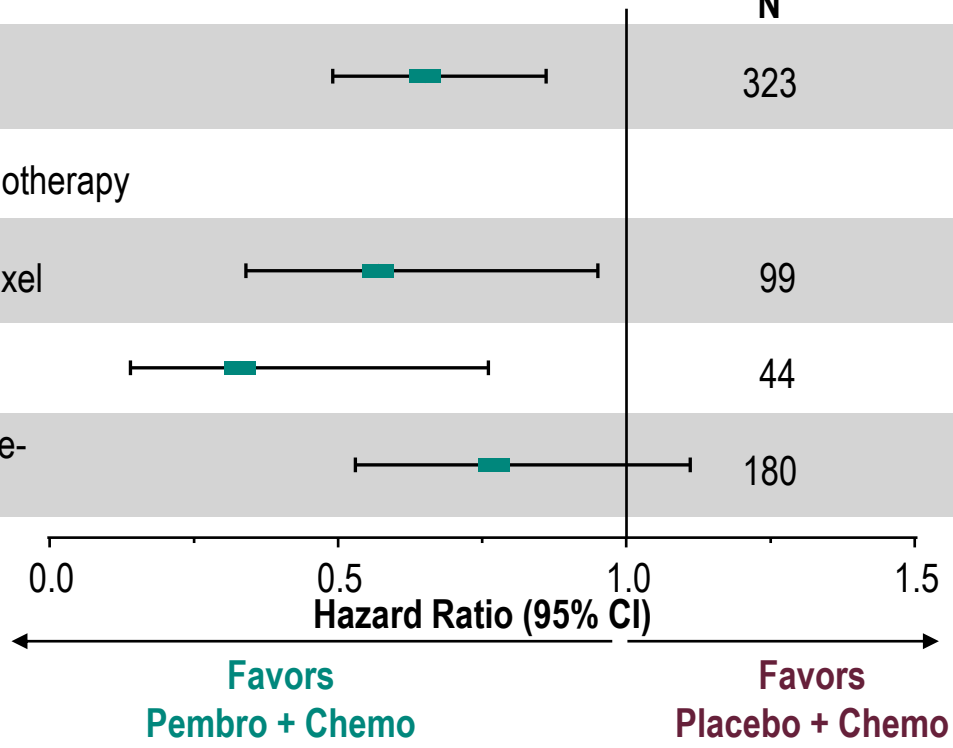
Courtesy of Professor Peter Schmid, MD, PhD

Cortes, et al. ASCO 2020

KEYNOTE-355: Progression-Free Survival in Subgroups by On-Study Chemotherapy

PD-L1 CPS ≥10

Subgroup	N	Median PFS (mo)		Hazard Ratio for Progression or Death (95% CI)
		Pembro + Chemo	Placebo + Chemo	
Overall	323	9.7	5.6	0.65 (0.49 to 0.86)
On-study chemotherapy				
Nab-Paclitaxel	99	9.9	5.5	0.57 (0.34 to 0.95)
Paclitaxel	44	9.6	3.6	0.33 (0.14 to 0.76)
Gemcitabine-Carboplatin	180	8.0	7.2	0.77 (0.53 to 1.11)

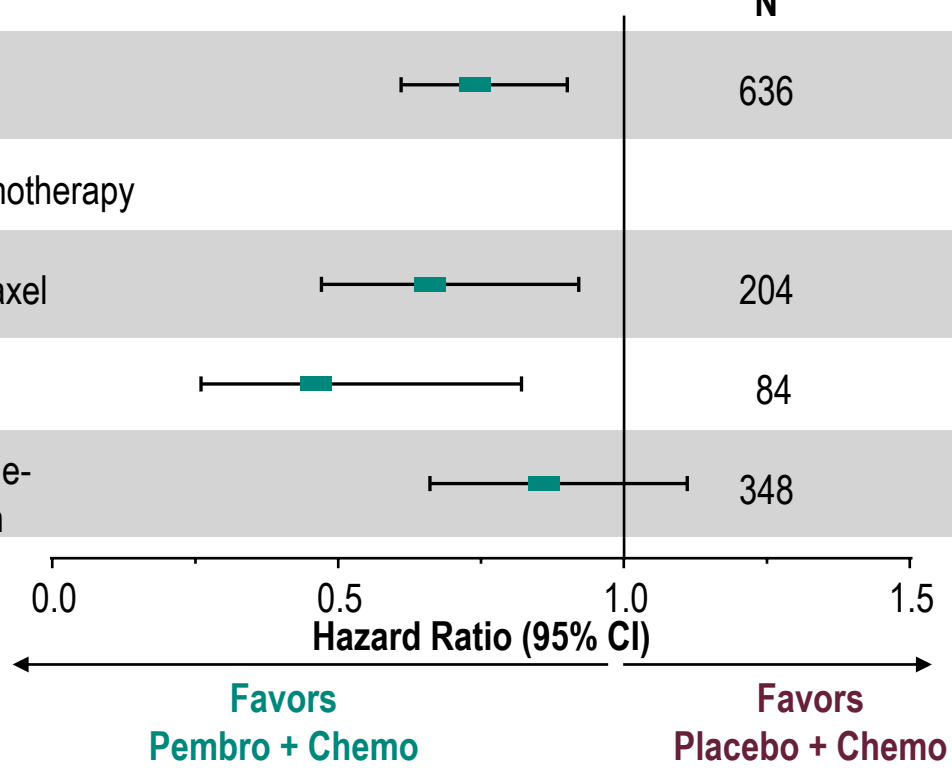


Rugo H et al. SABCS 2020;Abstract GS3-01.

KEYNOTE-355: Progression-Free Survival in Subgroups by On-Study Chemotherapy

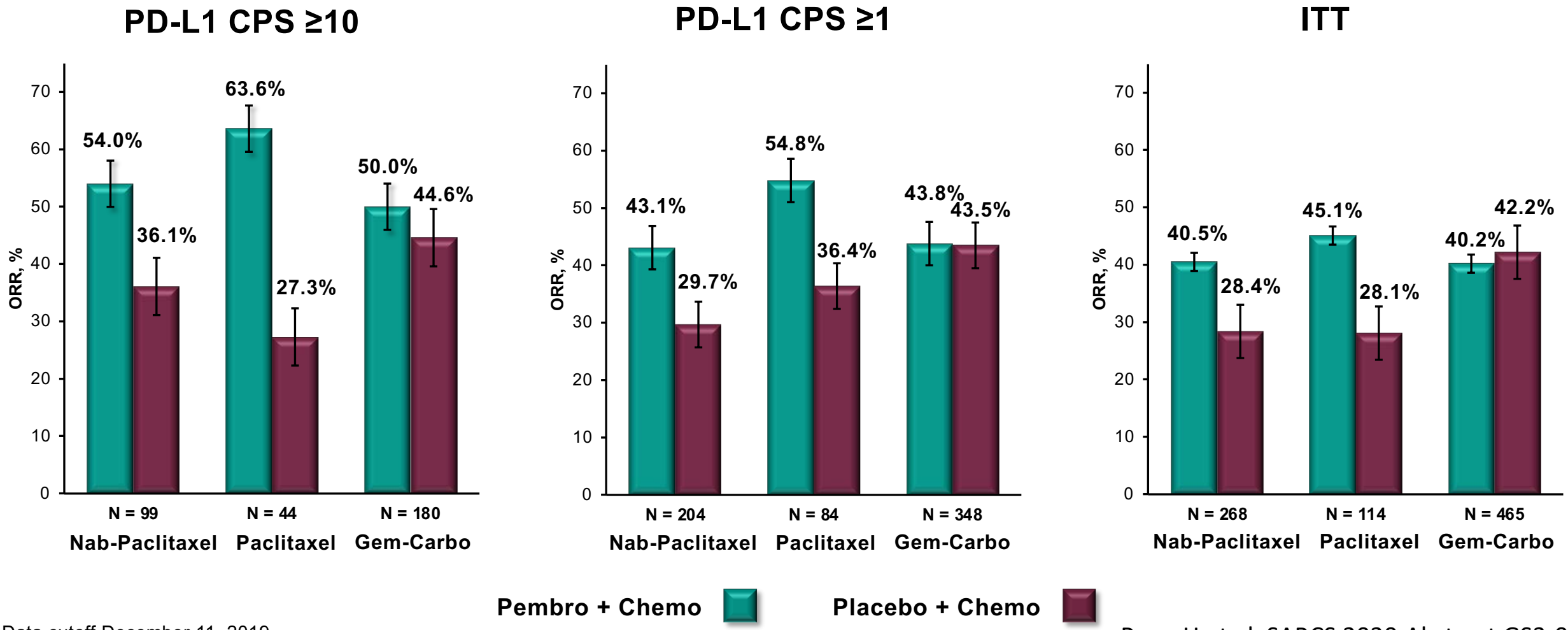
PD-L1 CPS ≥1

Subgroup	N	Median PFS (mo) Pembro + Chemo	Median PFS (mo) Placebo + Chemo	Hazard Ratio for Progression or Death (95% CI)
Overall	636	7.6	5.6	0.74 (0.61 to 0.90)
On-study chemotherapy				
Nab-Paclitaxel	204	6.3	5.3	0.66 (0.47 to 0.92)
Paclitaxel	84	9.4	3.8	0.46 (0.26 to 0.82)
Gemcitabine-Carboplatin	348	7.5	7.5	0.86 (0.66 to 1.11)



Rugo H et al. SABCS 2020;Abstract GS3-01.

KEYNOTE-355: Response Rate in Subgroups by On-Study Chemotherapy



Data cutoff December 11, 2019.

Rugo H et al. SABCS 2020;Abstract GS3-01.

Genomic Profiling and Clinical Outcomes with First-Line Atezolizumab and *Nab*-Paclitaxel in Triple-Negative Breast Cancer: An Exploratory Analysis from the Phase 3 IMpassion130 Trial

Emens L et al.

SABCS 2020;Abstract PD14-05.

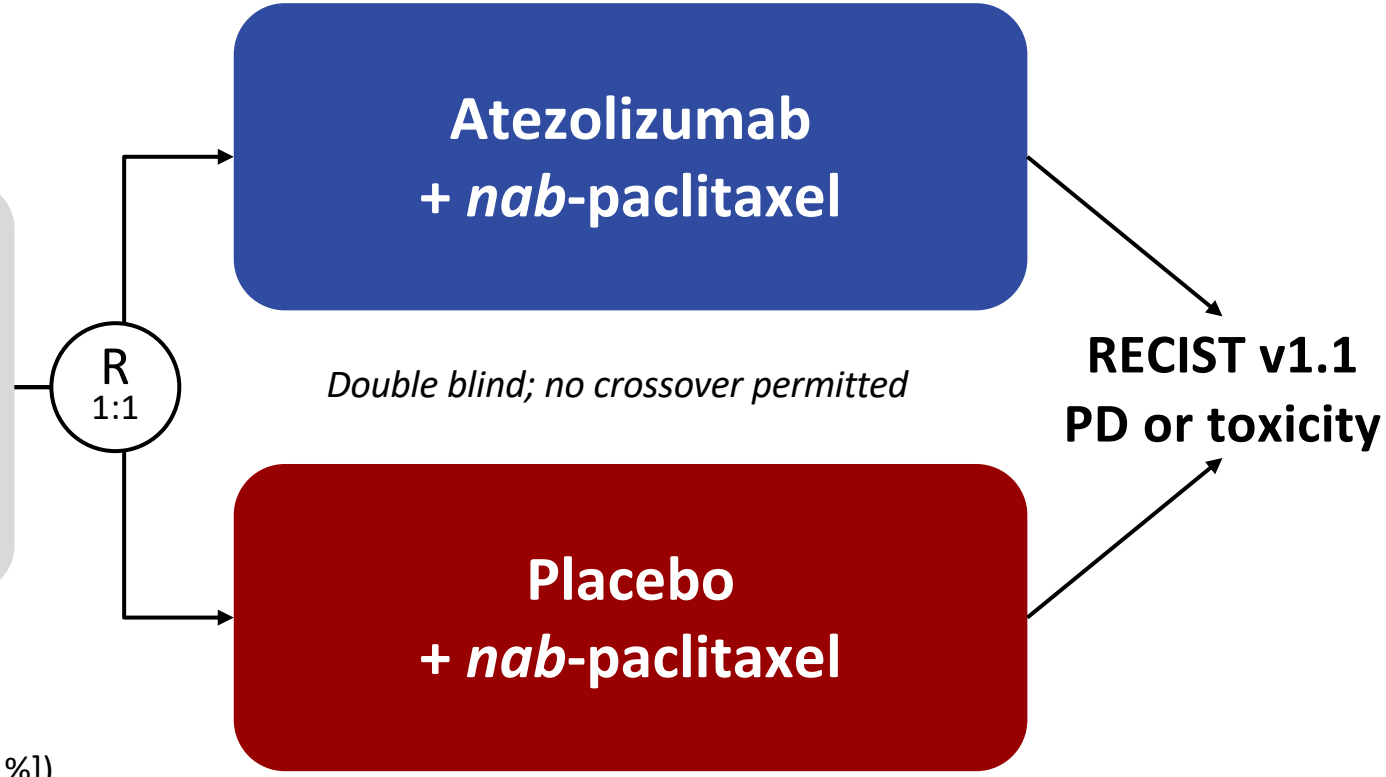
Atezolizumab (anti-PD-L1) plus chemotherapy in TNBC

IMpassion130 study design

- **Metastatic or inoperable locally advanced TNBC**
- **No prior therapy for advanced TNBC**
  - **Prior (neo)adjuvant chemo allowed if TFI ≥ 12 months**
- **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%])

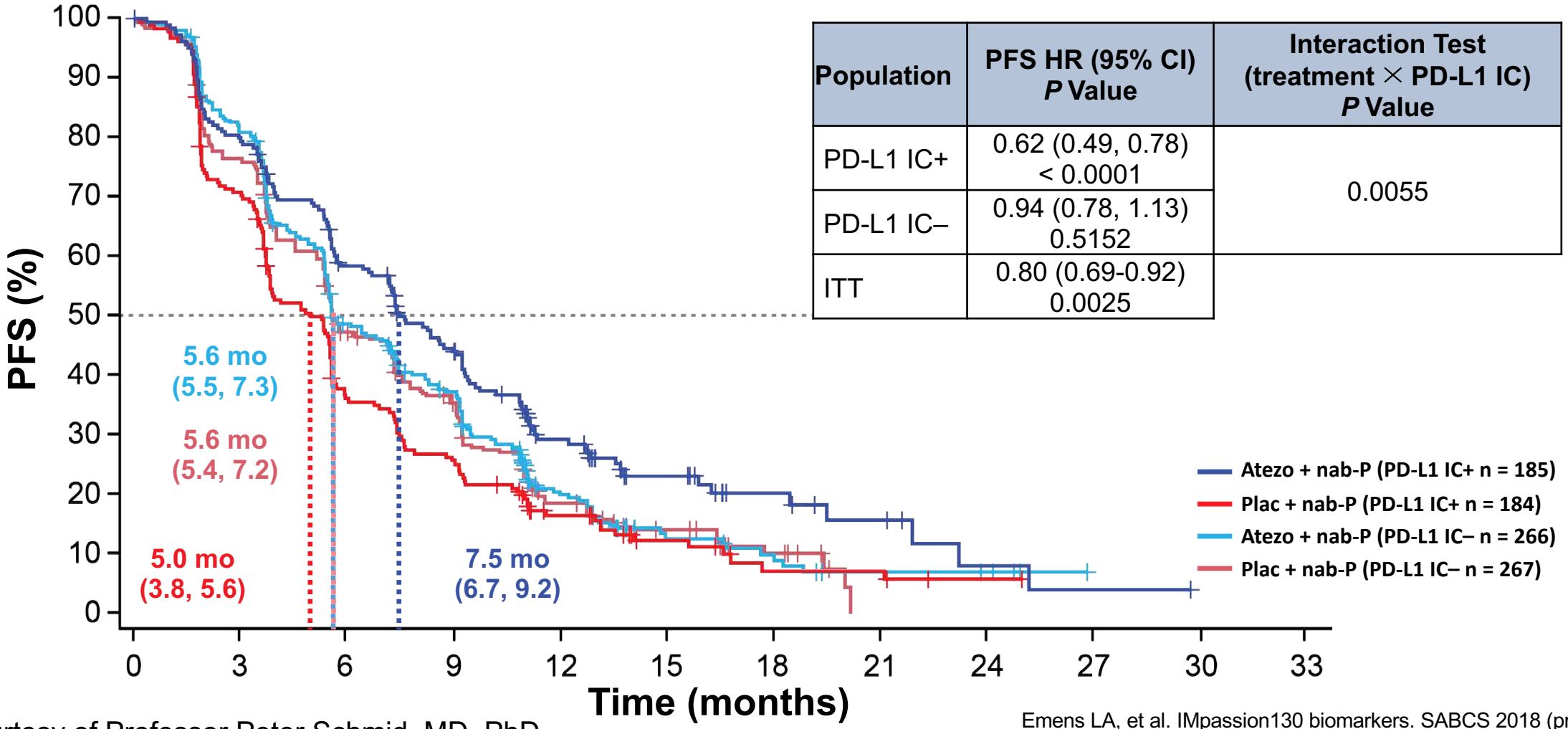


- **Co-primary endpoints were PFS and OS in the ITT and PD-L1+ populations**

Courtesy of Professor Peter Schmid, MD, PhD

Schmid P, et al. ESMO 2018 (LBA1); Schmid P, et al NEJM 2018

Progression-free survival: PD-L1 predicts benefit with atezolizumab



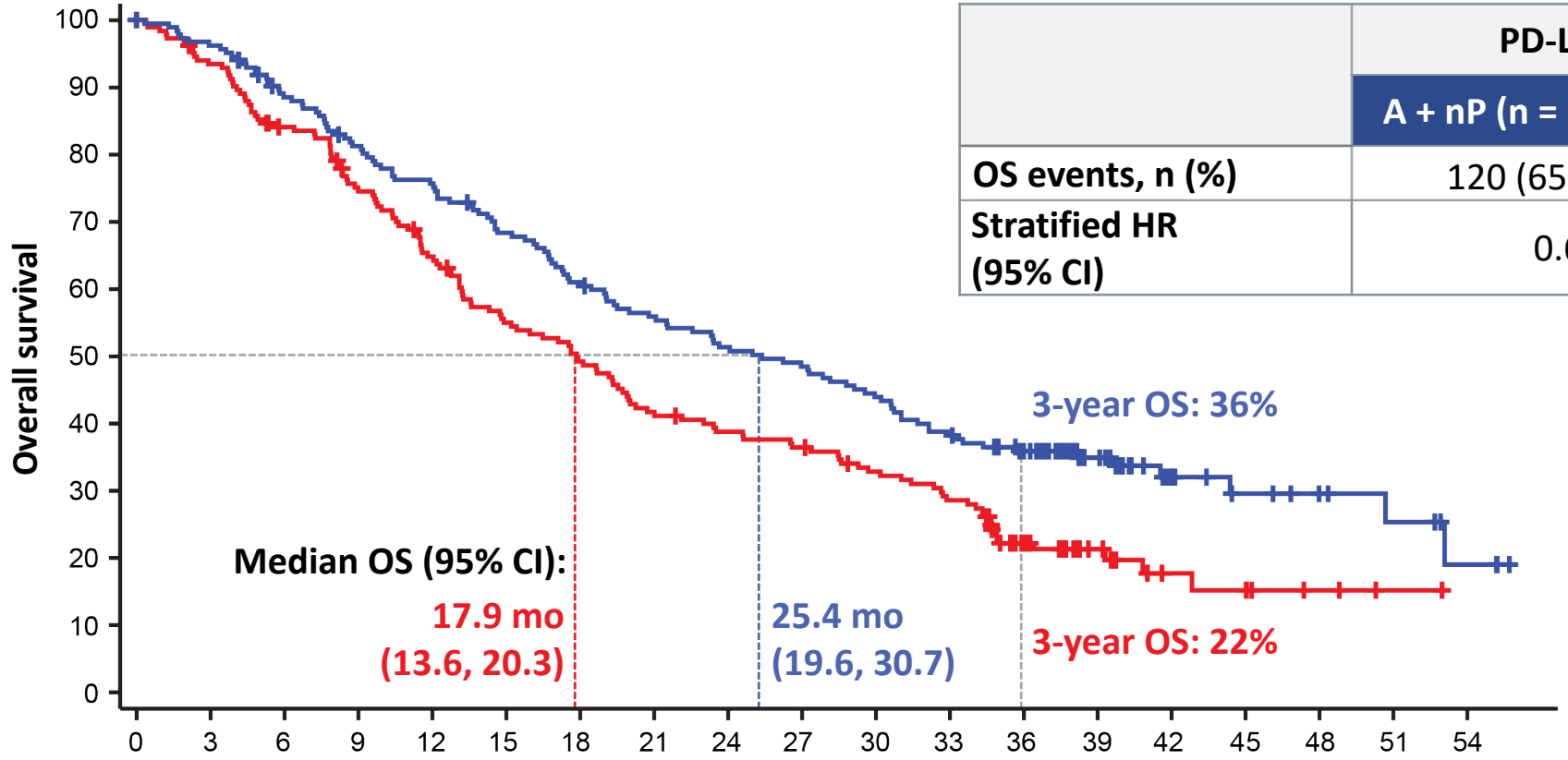
Population	PFS HR (95% CI) *P* Value	Interaction Test (treatment × PD-L1 IC) *P* Value
PD-L1 IC+	0.62 (0.49, 0.78) < 0.0001	0.0055
PD-L1 IC–	0.94 (0.78, 1.13) 0.5152	
ITT	0.80 (0.69-0.92) 0.0025	

Courtesy of Professor Peter Schmid, MD, PhD

Emens LA, et al. IMpassion130 biomarkers. SABCS 2018 (program #GS1-04); Schmid P, et al. ESMO 2018 (LBA1); Schmid P, et al NEJM 2018

Overall survival: PD-L1 status predicts benefit with atezolizumab

	PD-L1 IC+ population	
	A + nP (n = 185)	P + nP (n = 184)
OS events, n (%)	120 (65)	139 (76)
Stratified HR (95% CI)	0.67 (0.53, 0.86)[a]	



No. at risk (PD-L1+ population):																		
A + nP	185	177	160	145	135	121	108	98	90	86	77	67	56	32	17	11	9	6	3
P + nP	184	170	150	132	113	95	85	72	66	62	54	47	28	14	7	6	3	1	NE

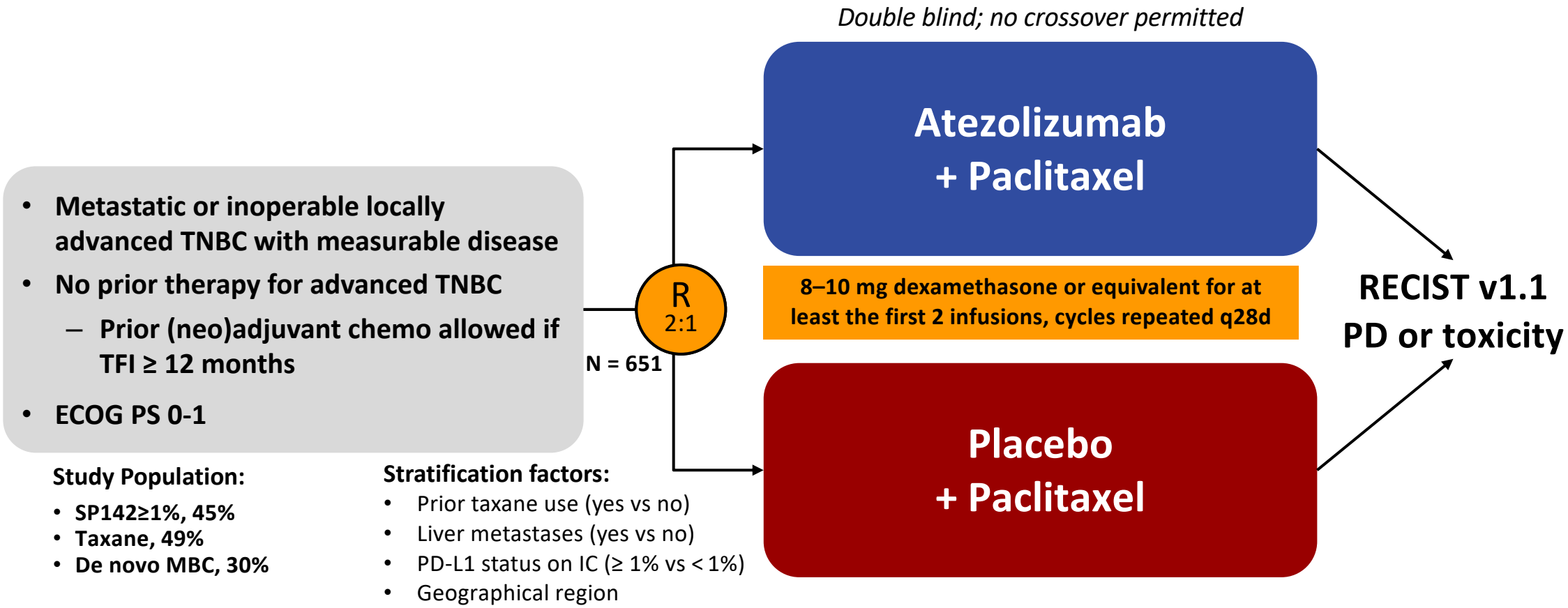
Courtesy of Professor Peter Schmid, MD, PhD

Data cutoff, 14 April 2020. NE, not estimable. [a] *P* value not formally tested per hierarchical study design.

Emens LA. ESMO 2020

Atezolizumab (anti-PD-L1) plus Paclitaxel in TNBC

IMpassion131 study design

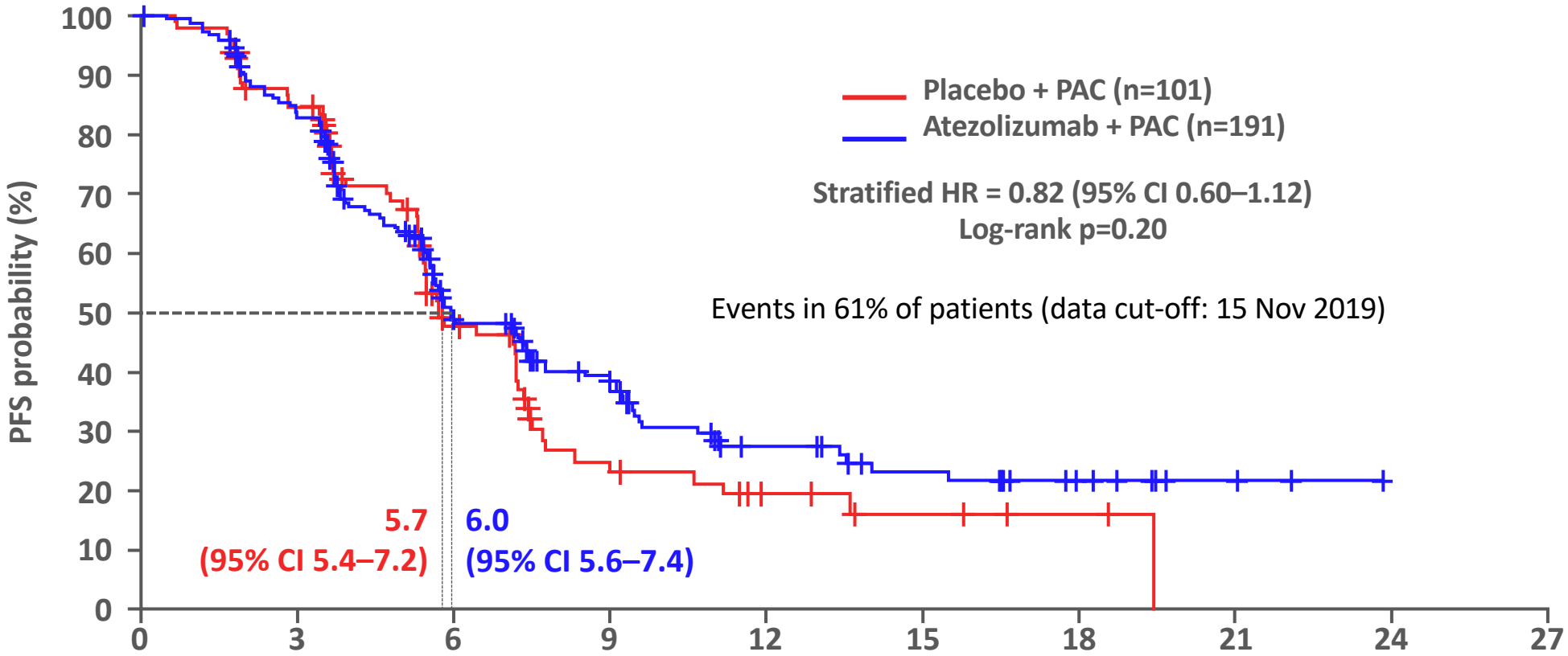


- **Co-primary endpoints were PFS (investigator assessed) in the PD-L1+ and ITT populations**

Courtesy of Professor Peter Schmid, MD, PhD

Miles D, et al. ESMO 2020

Atezolizumab plus Paclitaxel: Progression-free Survival in PD-L1+



Number at risk										
Placebo + PAC	101	81	33	14	7	4	2	0	0	0
Atezolizumab + PAC	191	152	69	44	22	15	8	3	0	0

Courtesy of Professor Peter Schmid, MD, PhD

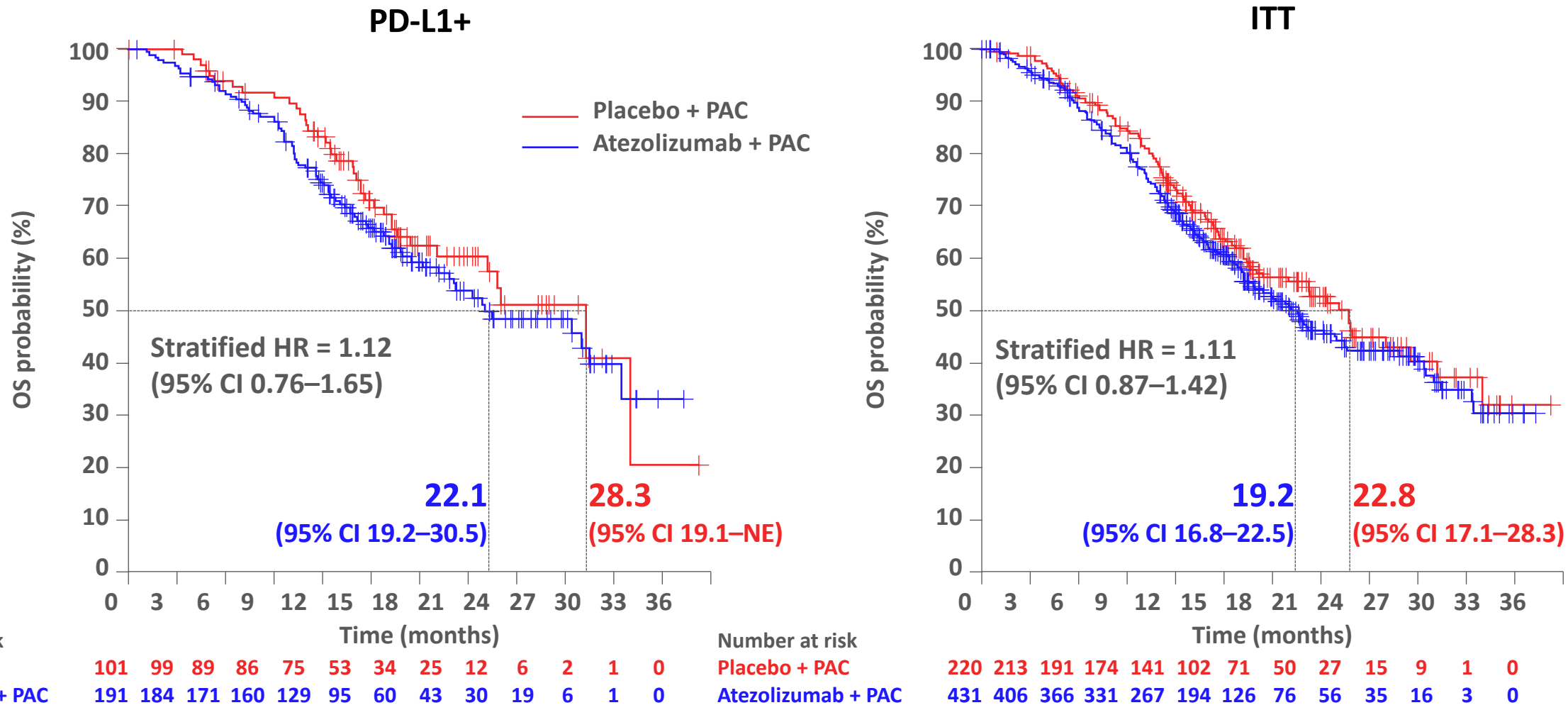
Median duration of follow-up: 8.6 months (placebo + PAC) vs 9.0 months (atezolizumab + PAC). CI = confidence interval

Miles D, et al. ESMO 2020

Atezolizumab plus Paclitaxel: Interim Survival Analysis

Updated interim OS analysis (data cut-off: 19 Aug 2020), events in 47% of the ITT population

Deaths in PD-L1+ 38 (38%) vs 82 (43%)

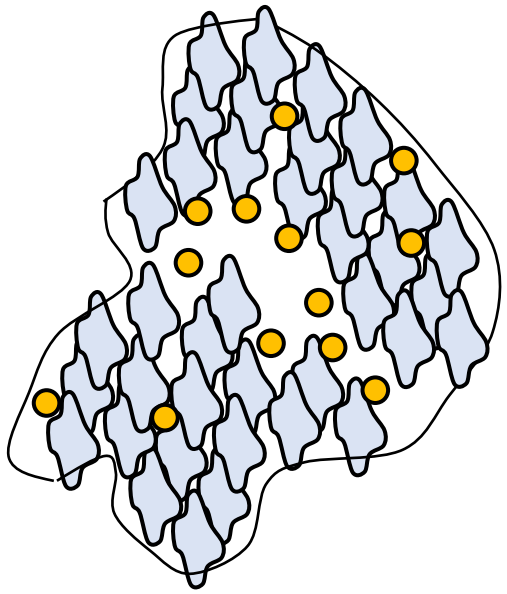


Median duration of follow-up: 14.5 months (placebo + PAC) vs 14.1 months (atezolizumab + PAC) in the ITT population

Prof. P. Schmid, Barts Cancer Institute

Courtesy of Professor Peter Schmid, MD, PhD

PD-L1 assessment: key variables to take into account



Tumor cells Immune cells

Type of cell to be considered

- Only tumor cells (TC)
- Only immune cells (IC)
- Both (e.g. CPS)

Modality of the scoring calculation

– Enumeration of positive cells (CPS)
– Area occupied by positive ICs (SP142)

Cut-off value

– ≥1, ≥10, ≥20, >50 …..

Primary antibody clones

– SP142, SP263 and 22C3

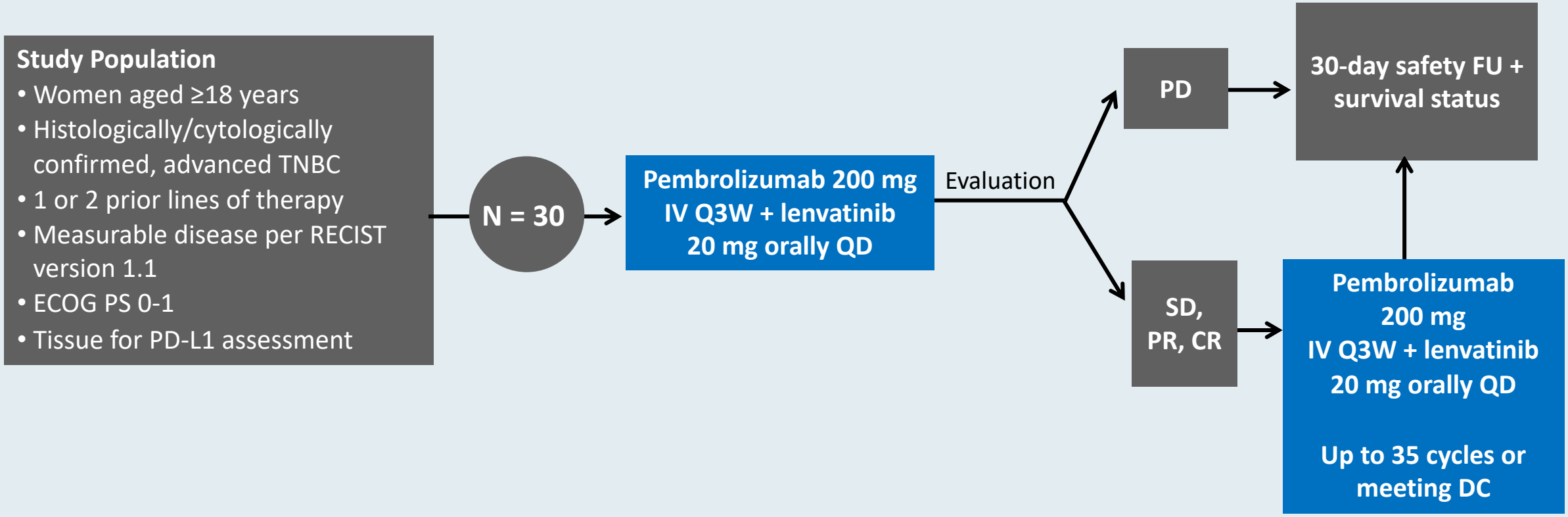
Courtesy of Professor Peter Schmid, MD, PhD

Lenvatinib plus Pembrolizumab for Previously Treated, Advanced Triple-Negative Breast Cancer: Early Results from the Multicohort Phase 2 LEAP-005 Study

Chung HC et al.

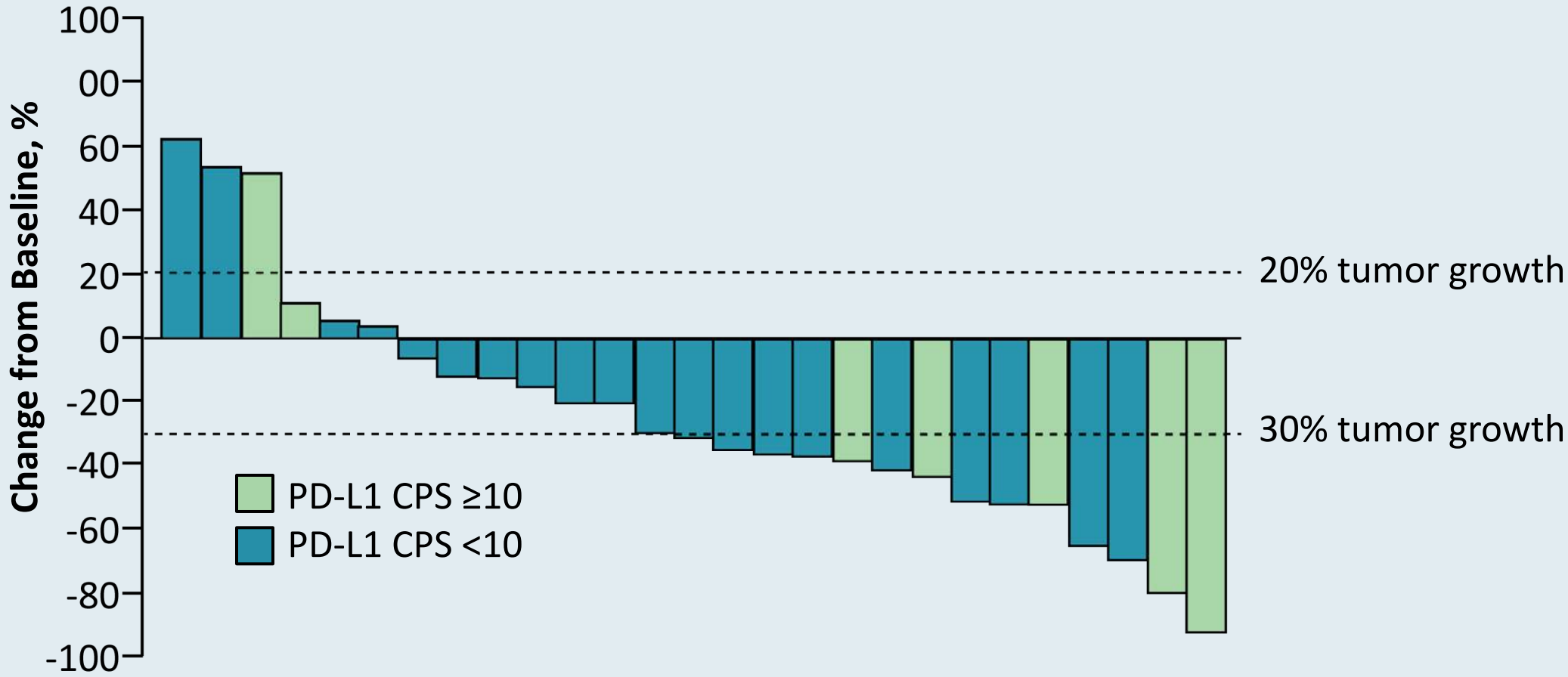
SABCS 2020;Abstract PS12-07.

LEAP-005 Study Design



Chung HC et al. SABCS 2020;Abstract PS12-07.

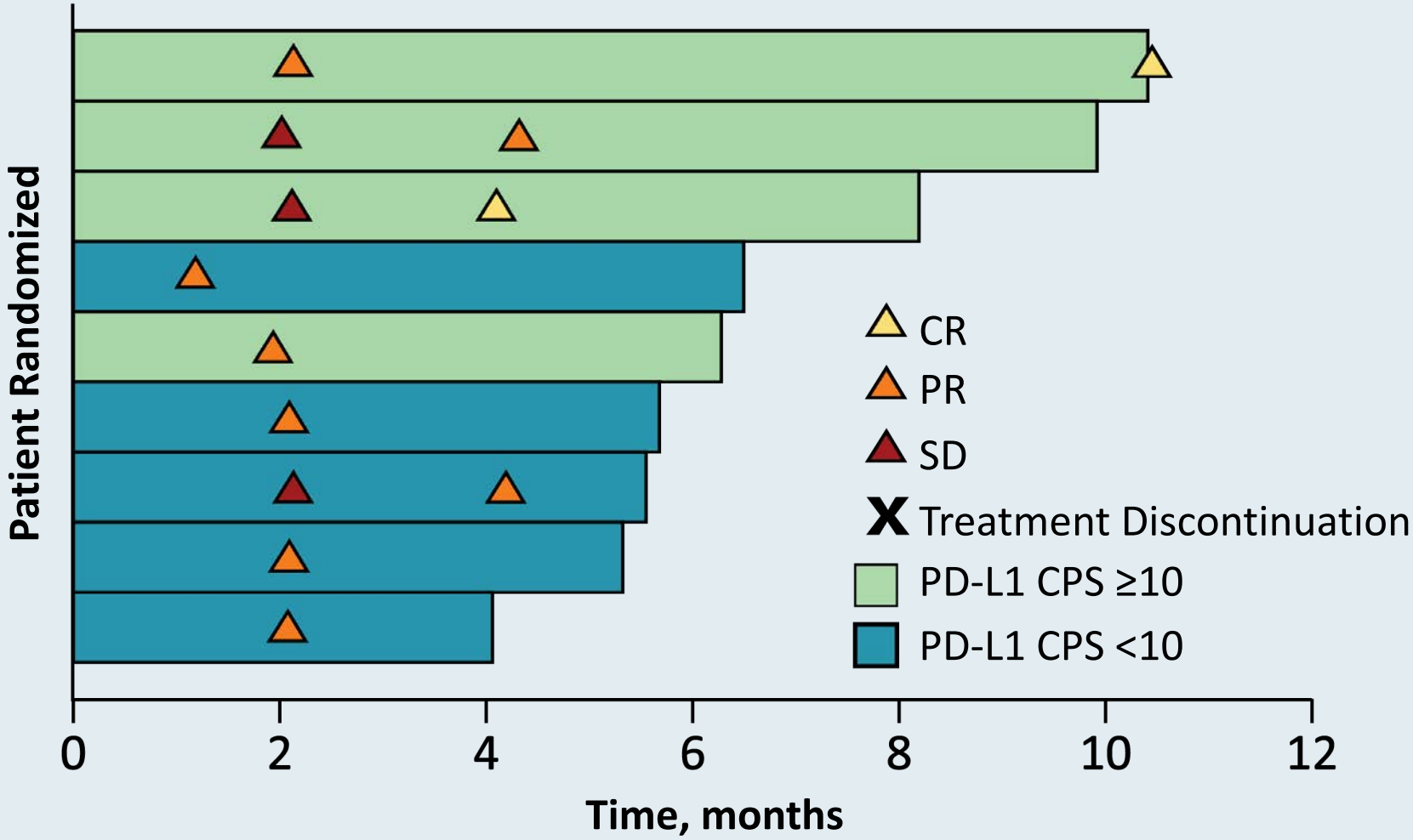
LEAP-005: Best Percentage Change from Baseline in Target Lesion Size



Includes patients with one or more evaluable post-baseline imaging assessment (n = 27).

Chung HC et al. SABCS 2020;Abstract PS12-07.

LEAP-005: Treatment Duration and Response Evaluation

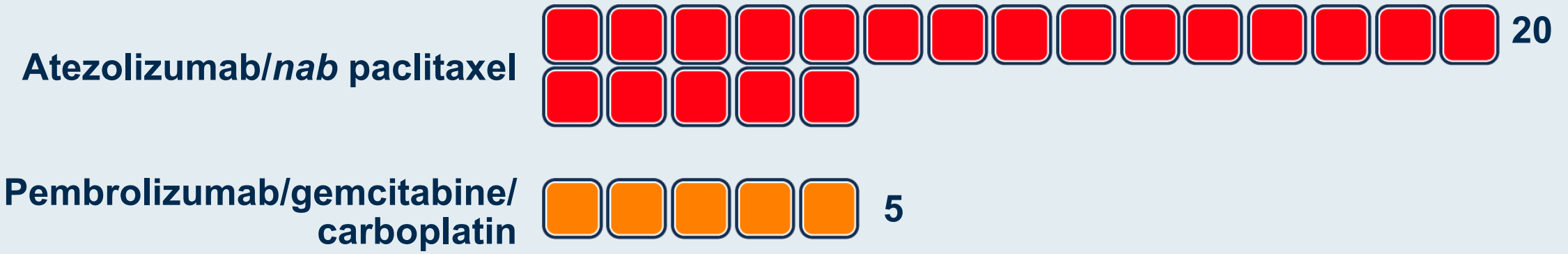


Chung HC et al. SABCS 2020;Abstract PS12-07.

A 32-year-old woman who completed neoadjuvant FEC/T and postoperative radiation therapy 21 months ago for localized TNBC now presents with small-volume liver and nodal metastases: BRCA wild type, PD-L1 positive. What therapy would you recommend?

1. Chemotherapy
2. Atezolizumab/*nab* paclitaxel
3. Atezolizumab/paclitaxel
4. Pembrolizumab/*nab* paclitaxel
5. Pembrolizumab/paclitaxel
6. Pembrolizumab/gemcitabine/carboplatin
7. Other

A 32-year-old woman who completed neoadjuvant FEC/T and radiation therapy 21 months ago for localized TNBC now presents with liver and nodal metastases. Biomarker assessment reveals BRCA WT, PD-L1-positive disease. What therapy would you recommend?



Survey of 25 breast cancer clinical investigators

Case Presentation: A very anxious 50-year-old woman with metastatic triple-negative breast cancer – PD-L1 of 1%

Atif Hussein, MD, MMM

- 2/2019: Diagnosed with ER/PR/HER2-negative, node-negative IDC
- Patient declines neoadjuvant therapy
- 3/2019: Genetic counseling unremarkable
- 5/2019: Left breast nipple sparing mastectomy + SLNB
  - 6/2019: Adjuvant paclitaxel/carboplatin weekly x 12 → dose-dense AC x 4
  - 7/2019 – 9/2019: Left chest wall RT
- 10/2020: Chest pain → Biopsy of right lung nodule: ER/PR/HER2-negative tumor compatible with mBC
  - 12/2020: NGS: PD-L1: 1%, CT abdomen/pelvis: No evidence of metastatic disease
- 12/15/2020: Atezolizumab/*nab*-paclitaxel (Cycle 1, Day 1)
  - 12/14/2020: Total bilirubin 0.7, ALP 141, AST 39, ALT 47
  - 12/22/2020: Total bilirubin 0.6, ALP 332, AST 235, ALT 398 (Cycle 1, Day 8)
  - 12/29/2020: Total bilirubin 1.0, ALP 471, AST 288, ALT 492
  - 1/05/2021: Total bilirubin 0.5, ALP 479, AST 88, ALT 254

Question

- What would you do next? Do I stop this regimen completely? Do I add some other chemotherapy to atezolizumab?

RTP RESEARCH TO PRACTICE

Agenda

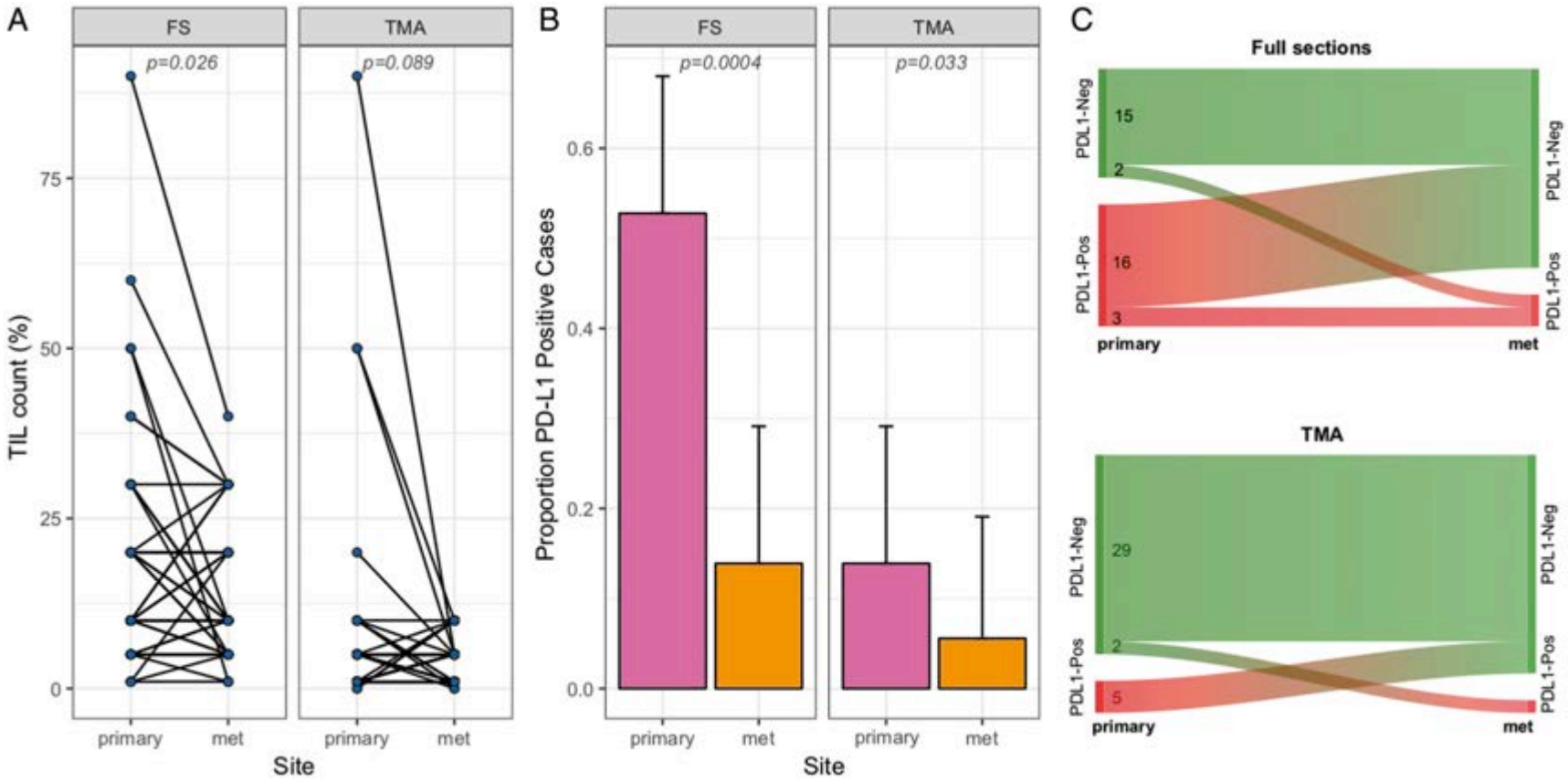
Module 1: Optimal Integration of Immune Checkpoint Inhibitors into the Management of Metastatic Triple-Negative Breast Cancer (TNBC)

Module 2: Novel Applications of Immune Checkpoint Inhibitors for Patients with Early TNBC

Module 3: Current and Future Role of PARP Inhibitors for Patients with TNBC and a BRCA Mutation

Module 4: Current and Future Management of PD-L1-Negative Metastatic TNBC

Immunologic Differences Between Primary and Metastatic Tumor Samples

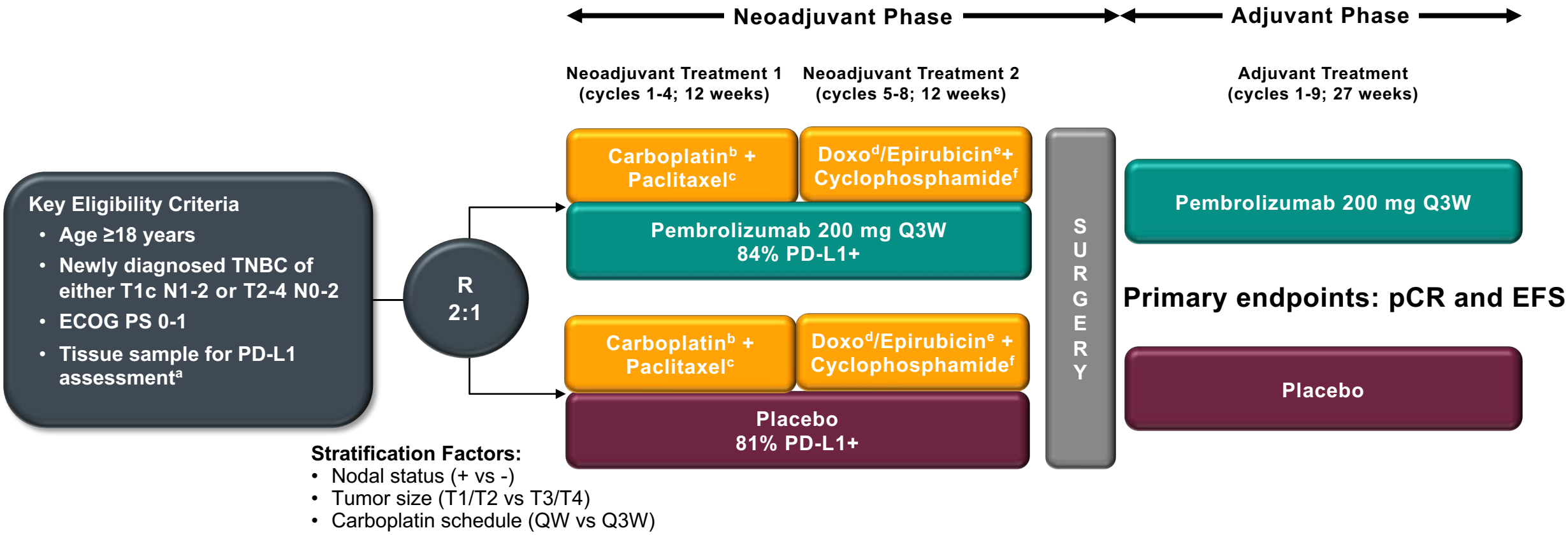


Percent TIL counts in full sections and TMAs.

Szekely, et al (Pusztai), Ann Oncol 2018

Courtesy of Hope S Rugo, MD

KEYNOTE-522 Study Design (NCT03036488)



Neoadjuvant phase: starts from the first neoadjuvant treatment and ends after definitive surgery (post treatment included)

Adjuvant phase: starts from the first adjuvant treatment and includes radiation therapy as indicated (post treatment included)

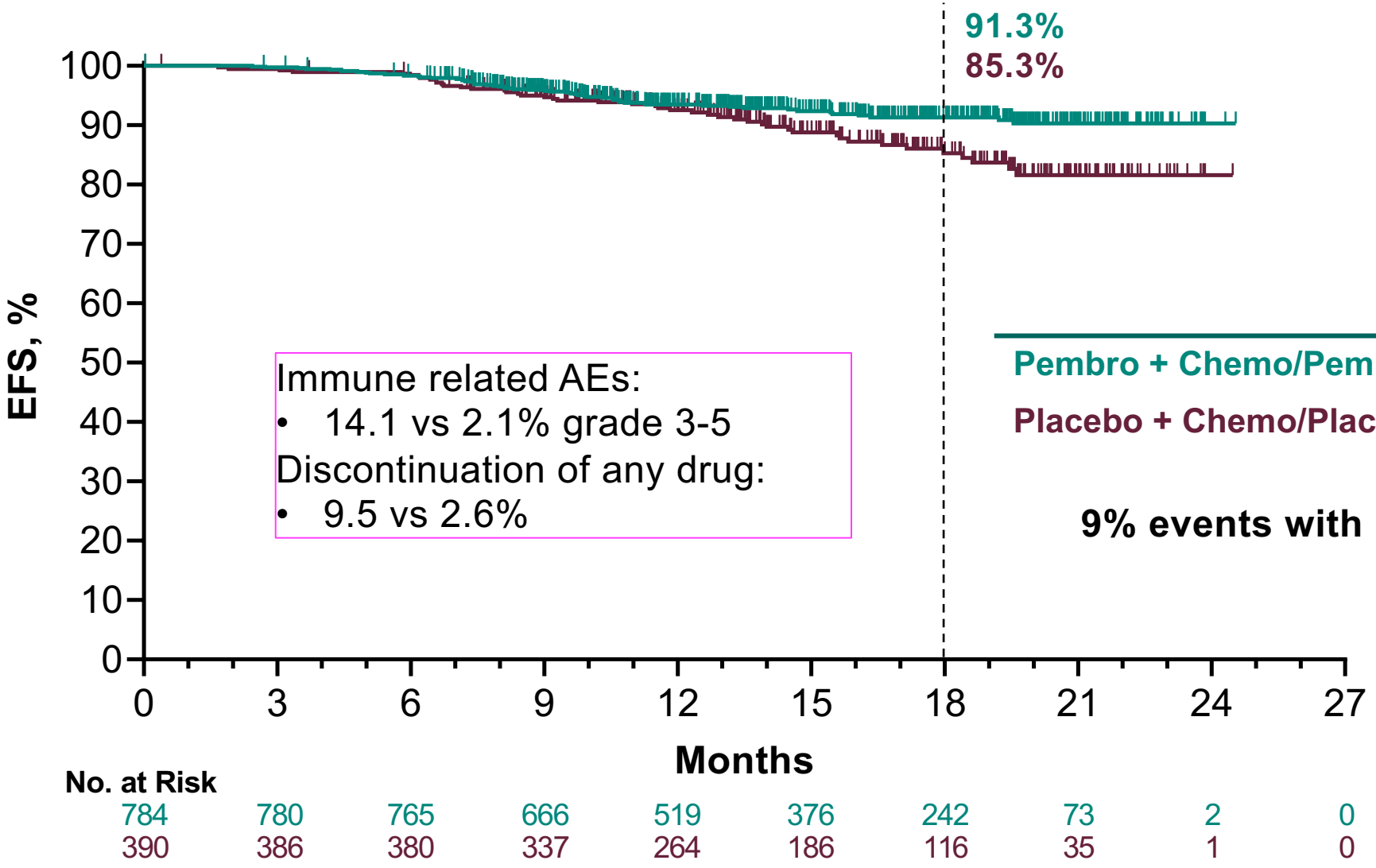
PD-L1 + defined by CPS ≥1

[a]Must consist of at least 2 separate tumor cores from the primary tumor.
[b]Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW.
[c]Paclitaxel dose was 80 mg/m^2 QW.
[d]Doxorubicin dose was 60 mg/m^2 Q3W.
[e]Epirubicin dose was 90 mg/m^2 Q3W.
[f]Cyclophosphamide dose was 600 mg/m^2 Q3W.

Courtesy of Hope S Rugo, MD
Schmid et al, NEJM 2020

Event-Free Survival at IA2: 1st Interim Analysis

P value boundary for significance 0.000051 (HR<0.4)



Immune related AEs:
- 14.1 vs 2.1% grade 3-5

Discontinuation of any drug:
- 9.5 vs 2.6%

	Events	HR (95% CI)
Pembro + Chemo/Pembro	7.4%	0.63[a] (0.43-0.93)
Placebo + Chemo/Placebo	11.8%	

9% events with median FU 15.5 months

Courtesy of Hope S Rugo, MD

[a]Prespecified *P* value boundary of 0.000051 not reached at this analysis (the first interim analysis of EFS). IA2: If pCR hypothesis successful at IA1, pCR will not be formally tested at IA2

HR (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by randomization stratification factors. **Data cutoff April 24, 2019; 24 mo after last pt enrolled**

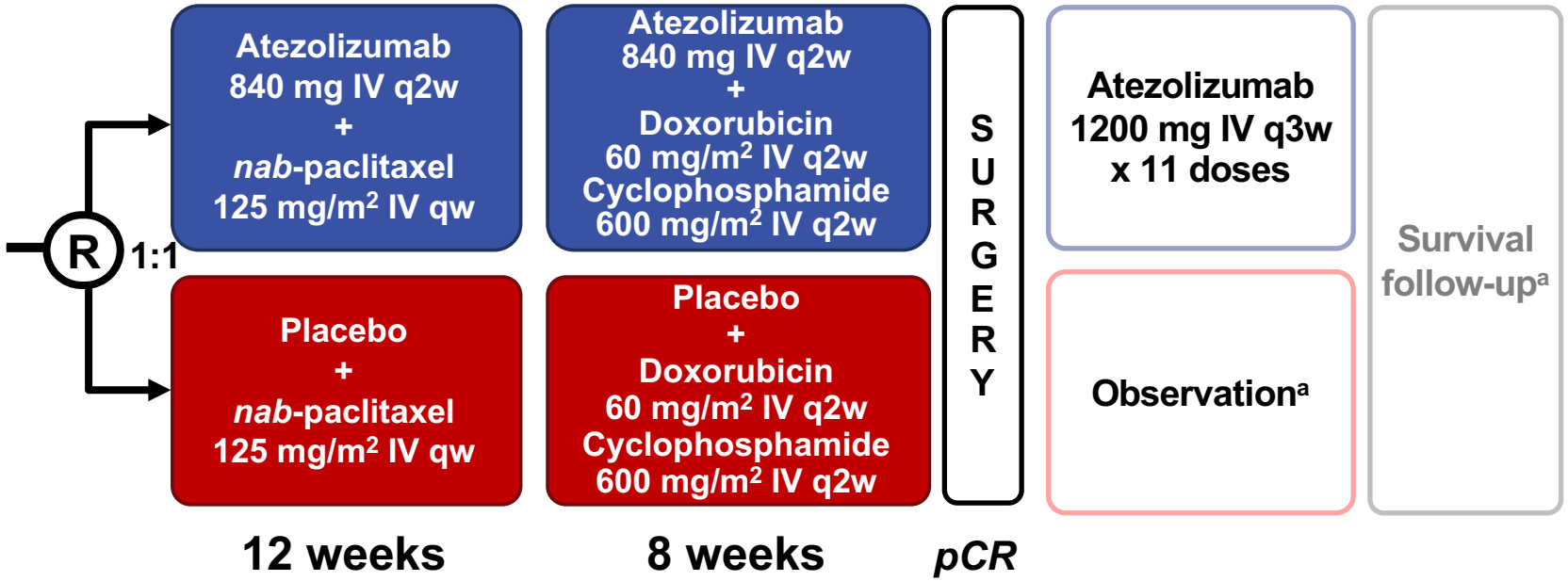
Patient-Reported Outcomes (PROs) from the Ph 3 IMpassion031 Trial of Neoadjuvant (NA) Atezolizumab + Chemo in Early Triple-Negative Breast Cancer (eTNBC)

Mittendorf EA et al.

SABCS 2020;Abstract GS3-02.

IMpassion031: Randomized Phase III Trial

- 333 patients with TNBC, T>2cm
- Co-primary endpoints: pCR in ITT and PD-L1+ (SP142)

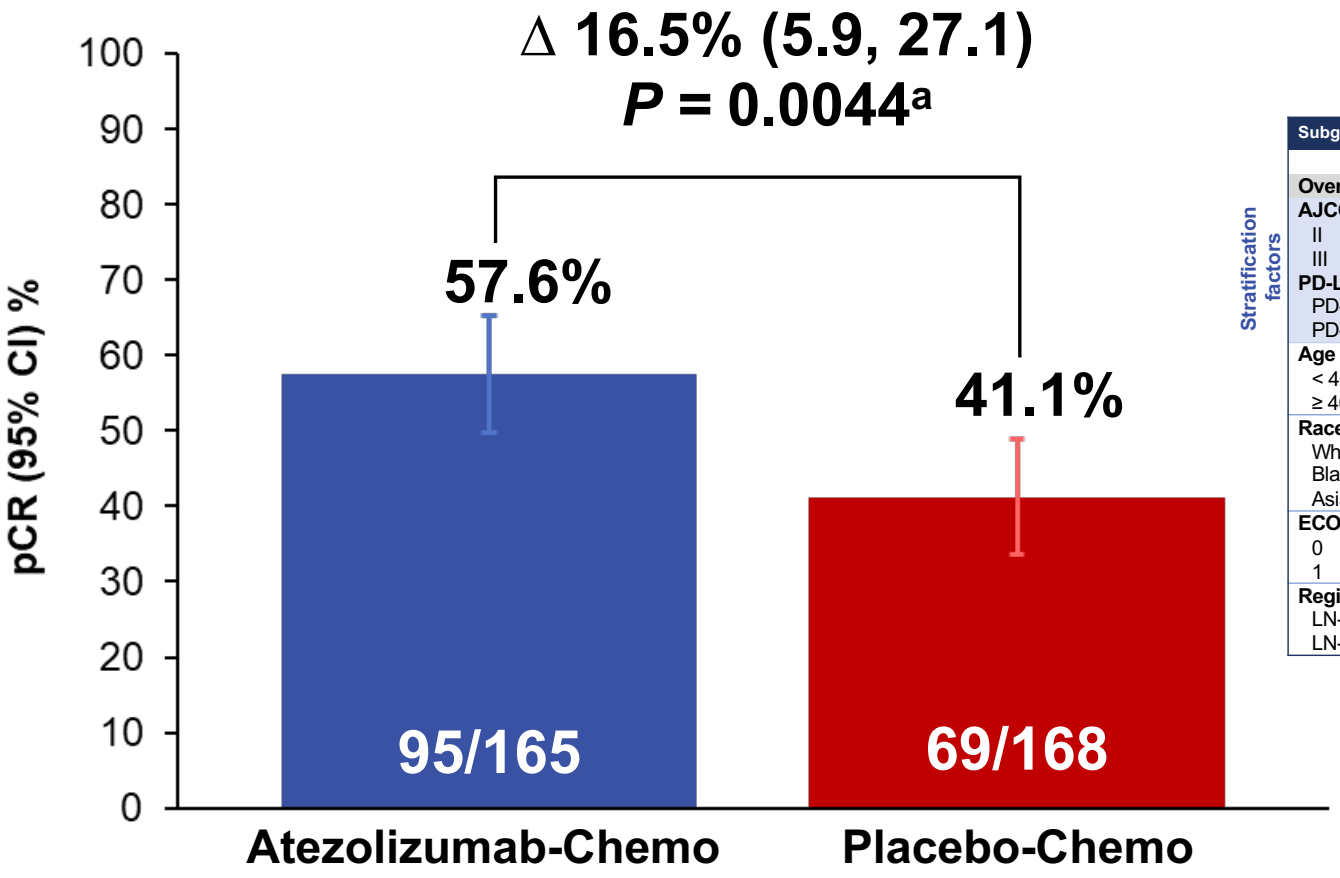


45-47% PD-L1+
76% stage II; 23% stage III
Median FU ~20 months

Courtesy of Hope S Rugo, MD

Harbeck et al, ESMO 2020 and Mittendorf et al, Lancet 2020

Primary Endpoint: pCR



Subgroup	Atezolizumab-Chemo		Placebo-Chemo			
	pCR (%)	n/n	pCR (%)	n/n	Difference in pCR (95% CI)	Δ (%) 95% CI
Overall	57.6	95/165	41.1	69/168		16.5 5.9, 27.1
AJCC BC Stage						
II	61.9	78/126	46.5	60/129		15.4 3.3, 27.5
III	44.7	17/38	23.1	9/39		21.7 1.1, 42.3
PD-L1 status[a]						
PD-L1-positive	68.8	53/77	49.3	37/75		19.5 4.2, 34.8
PD-L1-negative	47.7	42/88	34.4	32/93		13.3 −0.9, 27.5
Age group						
< 40 years	58.8	20/34	35.7	15/42		23.1 1.1, 45.1
≥ 40 years	57.3	75/131	42.9	54/126		14.4 2.3, 26.5
Race						
White	57.8	59/102	44.4	48/108		13.4 0, 26.8
Black	44.4	4/9	26.7	4/15		17.8 −21.7, 57.2
Asian	57.4	24/47	34.1	14/41		23.3 3.0, 43.6
ECOG PS						
0	57.7	90/156	43.1	66/153		14.6 3.5, 25.6
1	62.5	5/8	21.4	3/14		41 1.2, 80.9
Regional lymph node						
LN-negative	57.8	63/109	49	47/96		8.8 −4.8, 22.5
LN-positive	57.1	32/56	30.6	22/72		26.6 9.8, 43.4

Stratification factors

-30 -20 -10 0 10 20 30 40 50 60 70 80 90

Placebo better | Atezolizumab better

DFS and OS too early

AEs leading to discontinuation of any drug: 22.6 v 19.8%

AEs requiring corticosteroids: 12.8 v 9.6%

Harbeck et al, ESMO 2020 and Mittendorf et al, Lancet 2020

Courtesy of Hope S Rugo, MD

Ongoing Phase III Trials with IO in TNBC

Neoadjuvant/adjuvant	Adjuvant

• Atezolizumab
  • NSABP B59/GeparDouze (n=1520)
  • Pac/carbo → AC/EC
  • EFS NeoTRIPaPDL1 (n=272)
  • EFS IMpassion031 (n=333)
• Pembrolizumab
  • EFS KEYNOTE-522 (n=1174)
  • NeoPACT (n=100)
  • Docetaxel/carbo/pembro x 6
	• Atezolizumab
	  • IMpassion030 (n=2300)
	  • Pac → AC/EC
	• Avelumab
	  • A-Brave (n=335)
	  • Adjuvant and post NAC high risk: avelumab alone
	• Pembrolizumab
	  • SWOG S1418/NRG-BR006 (n=1000)
	  • Post NAC: Pembro vs Obs x 1 yr

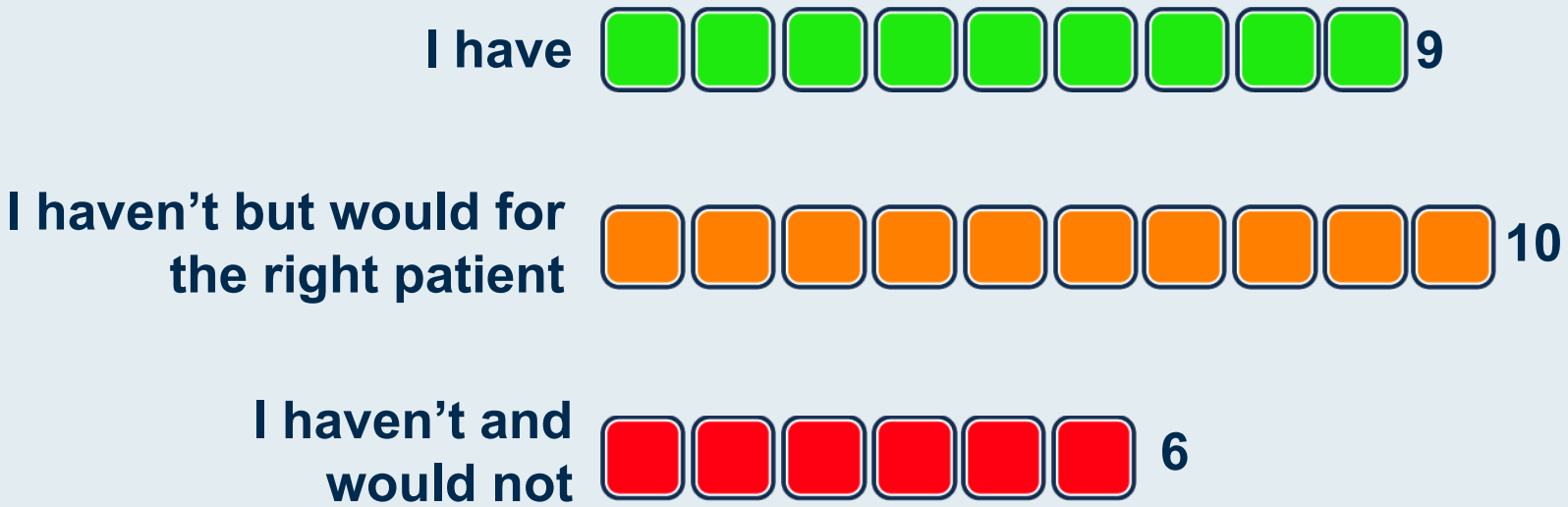
Courtesy of Hope S Rugo, MD

Regulatory and reimbursement issues aside, have you or would you attempt to access an anti-PD-1/PD-L1 antibody as part of neoadjuvant therapy for a 60-year-old patient with a 6-cm TNBC with 3 positive axillary nodes on biopsy (PD-L1 60%)?

1. I have
2. I haven't but would for the right patient
3. I haven't and would not

Have you or would you attempt to access an anti-PD-1/PD-L1 antibody as part of neoadjuvant therapy off protocol for a 60-year-old patient with TNBC with the following characteristics?

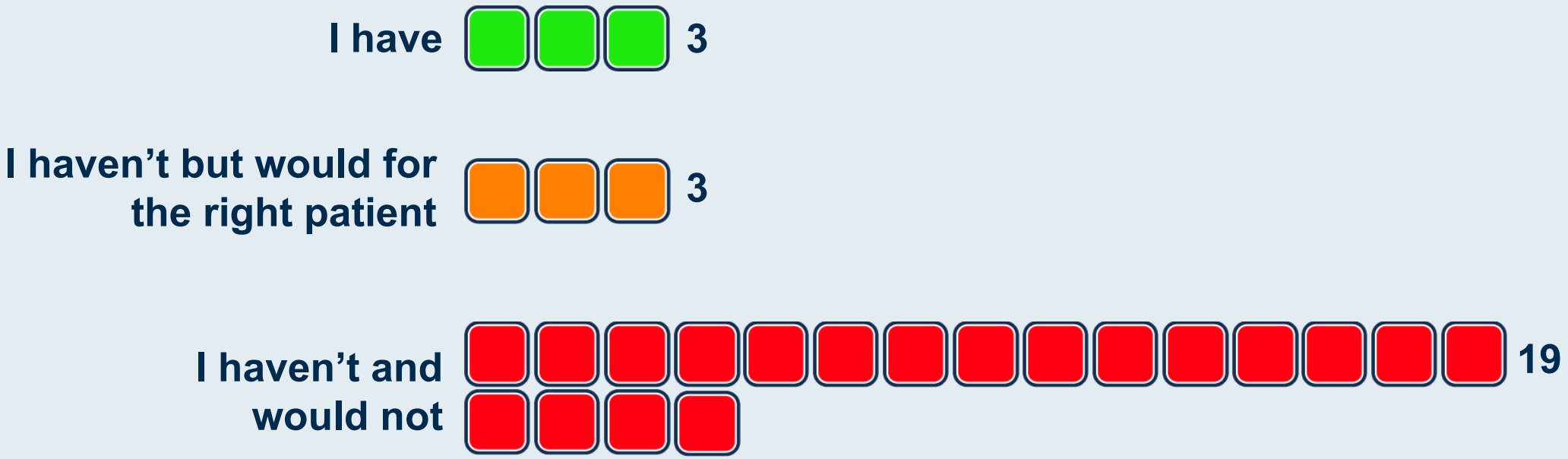
Tumor size: 6 cm, Nodal status: 3 positive nodes, PD-L1: 60%



Survey of 25 breast cancer clinical investigators

Regulatory and reimbursement issues aside, have you or would you attempt to access an anti-PD-1/PD-L1 antibody as part of neoadjuvant therapy off protocol for a 60-year-old patient with TNBC with the following characteristics?

Tumor size: 6 cm, Nodal status: node-negative, PD-L1: 10%



Survey of 25 breast cancer clinical investigators

Case Presentation: A 44-year-old woman with triple-negative, node-positive breast cancer – PD-L1 CPS 8

Atif Hussein, MD, MMM

- Right breast and axillary biopsies: 4.5-cm ER/PR/HER2-negative adenocarcinoma
- Imaging studies: No disease outside right breast and axilla
- PD-L1 CPS: 8

Questions

- What would you recommend as neoadjuvant treatment for this patient?
- After neoadjuvant pembrolizumab/carboplatin/paclitaxel, what type of adjuvant treatment would you give?
- How do you incorporate treatment with capecitabine, based on the adjuvant data?
- How do you incorporate immune checkpoint inhibitor therapy after surgery?

Agenda

Module 1: Optimal Integration of Immune Checkpoint Inhibitors into the Management of Metastatic Triple-Negative Breast Cancer (TNBC)

Module 2: Novel Applications of Immune Checkpoint Inhibitors for Patients with Early TNBC

Module 3: Current and Future Role of PARP Inhibitors for Patients with TNBC and a BRCA Mutation

Module 4: Current and Future Management of PD-L1-Negative Metastatic TNBC

TBCRC 048 Study: A Phase II study of olaparib monotherapy in metastatic breast cancer patients with germline or somatic mutations in homologous recombination (HR) pathway genes (Olaparib Expanded) (Nadine Tung, PI)

Hypothesis: Olaparib will have an overall response rate ≥ 20% in breast cancer patients with a germline or somatic mutation in DNA damage response (DDR) pathway genes associated with HR other than BRCA1/2 or with a somatic BRCA1/2 mutation.

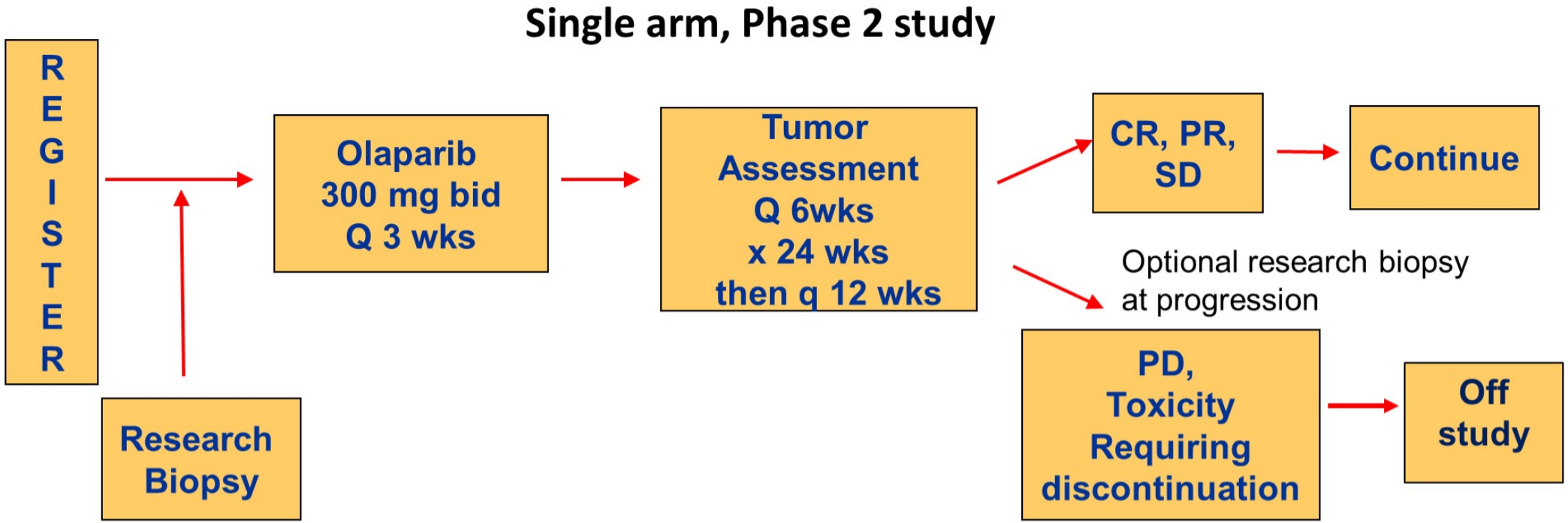
- Primary Aim: ORR (CR + PR by RECIST 1.1)
- Secondary Aim: CBR (CR + PR + SD ≥ 18 weeks), Duration of Response, Progression-Free Survival, Toxicity.

Eligibility: Measurable metastatic disease; no prior PARPi; No more than 2 prior chemotherapy regimens; Not platinum refractory.

Courtesy of P Kelly Marcom, MD

Tung, Journal of Clinical Oncology, Oct 29, 2020 https://dx.doi.org/10.1200/jco.20.02151

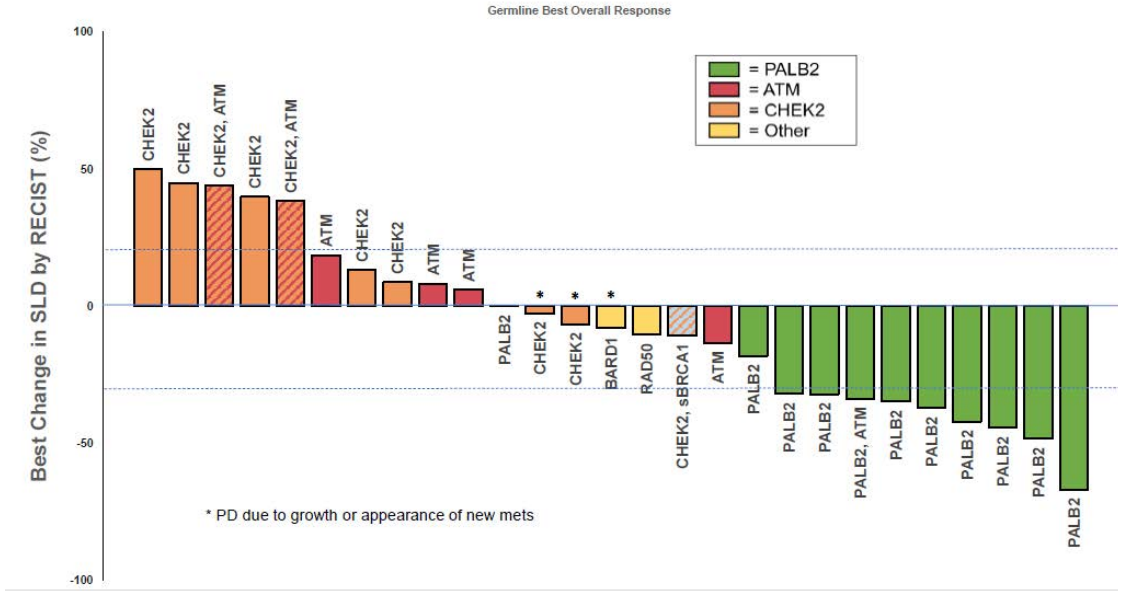
TBCRC 048 Trial Schema: Olaparib Expanded

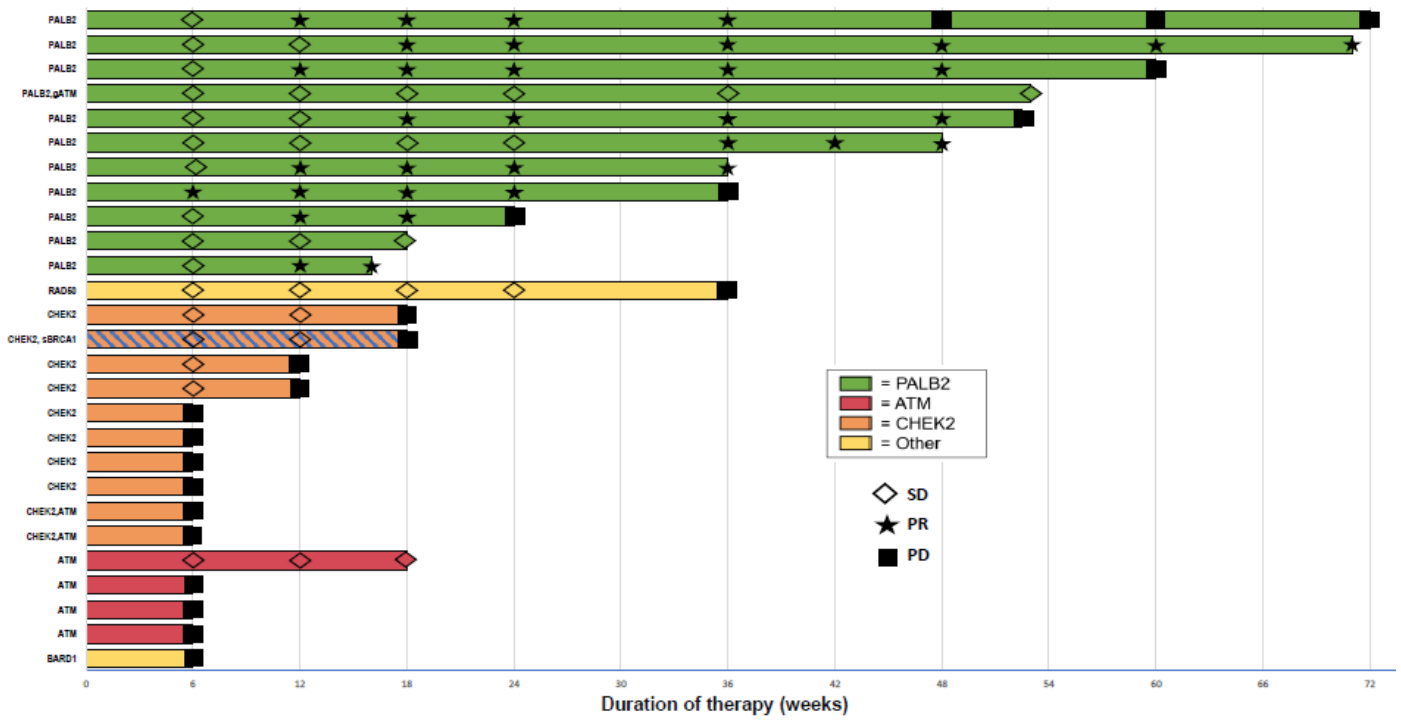


Tung NM et al. ASCO 2020;Abstract 1002.

Courtesy of P Kelly Marcom, MD

TBCRC 048 Trial Germline Cohort: Best Response and DOR

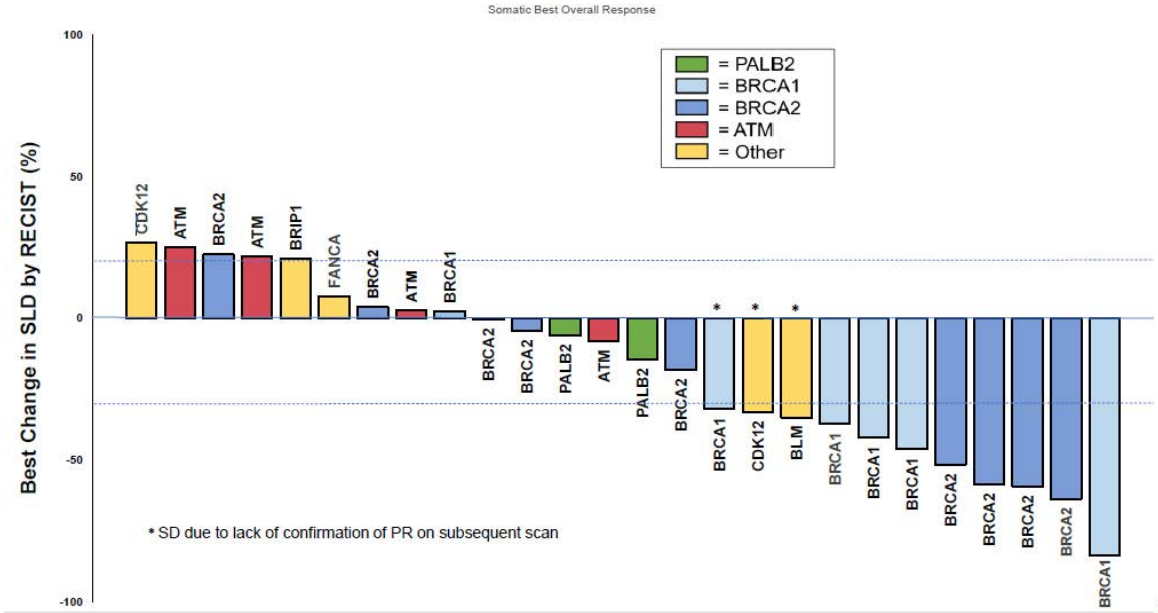


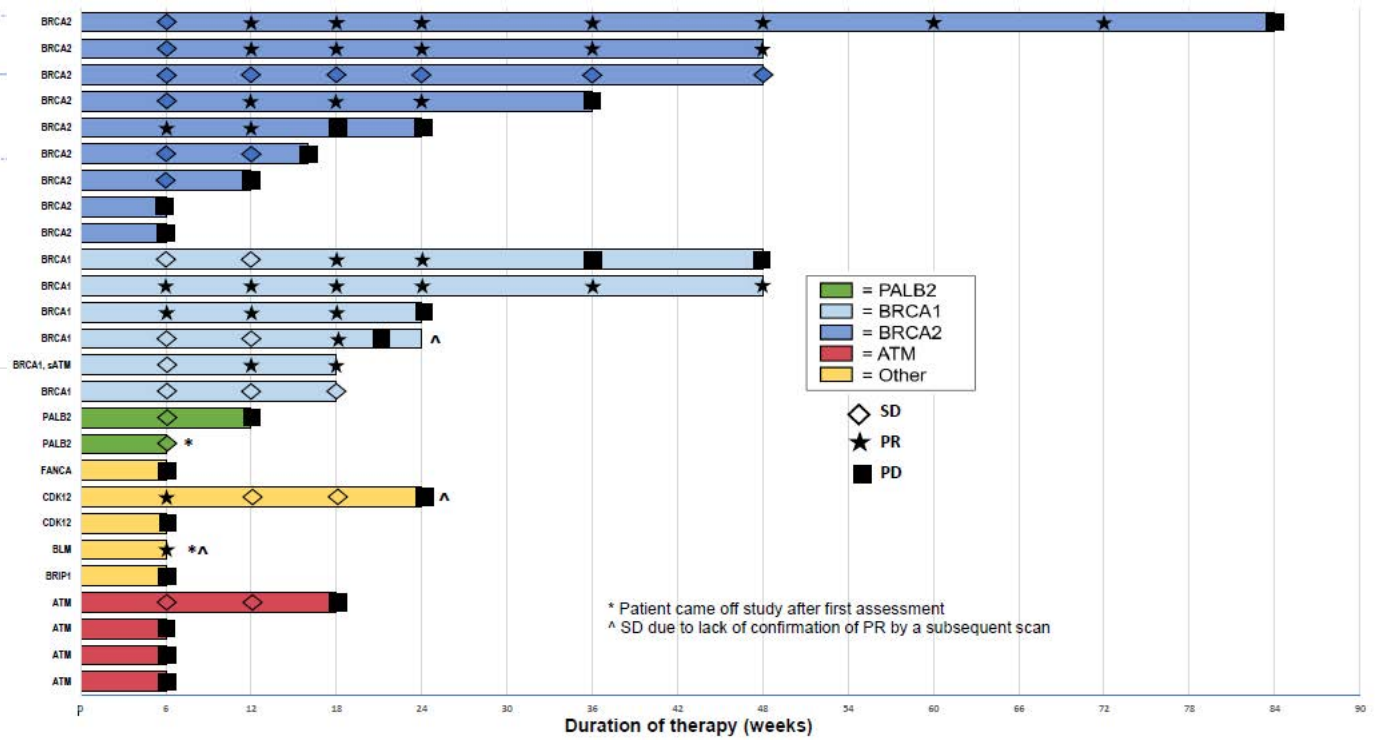


Tung NM et al. ASCO 2020;Abstract 1002.

Courtesy of P Kelly Marcom, MD

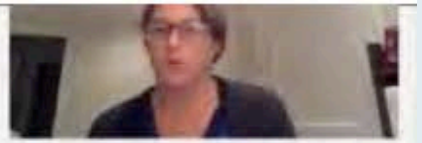
TBCRC 048 Trial Somatic Cohort: Best Response and DOR





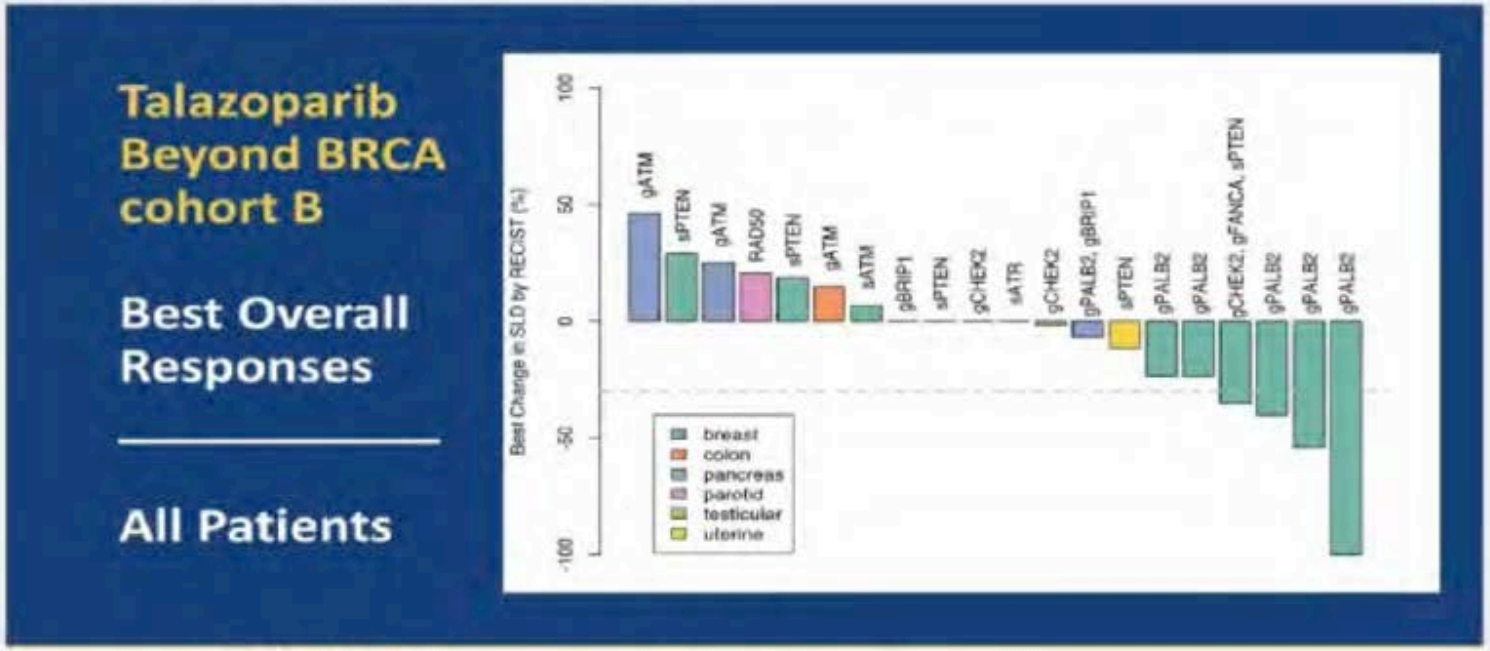
Tung NM et al. ASCO 2020;Abstract 1002.

Courtesy of P Kelly Marcom, MD



Talazoparib Beyond BRCA (TBB)

- 2 separate cohorts: A: HRD >42; B: Germline or somatic mutation in DDR pathway
- N=20 (13 germline, 7 somatic mutations)



Dent R et al. SABCS 2020;Education Session ES4.

PARPi (Neo) Adjuvant Trials

Preoperative Talazoparib Study:
Single Agent for 6 months gBRCA+

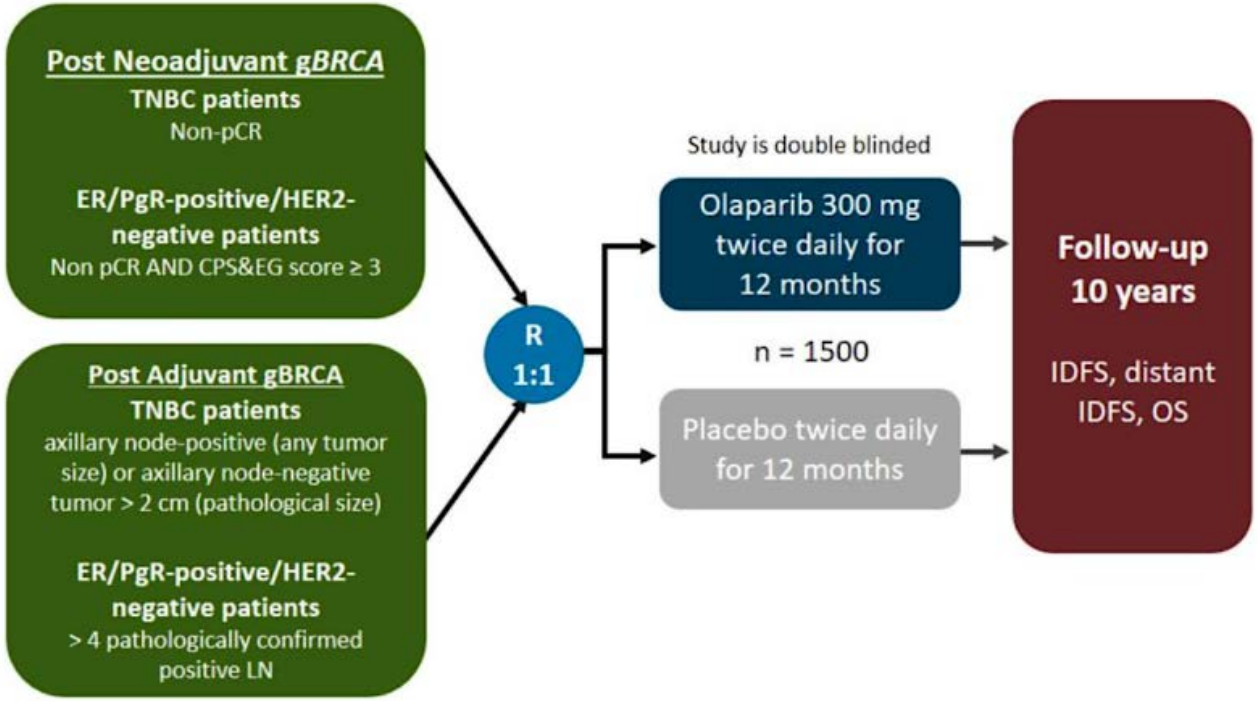
TABLE 1. Patient Characteristics

Characteristic	No. of Patients
Age, years	20
Median (range)	38 (23-58)
Race	
White	7
Black	5
Hispanic	5
Asian	3
BRCA	
1	16
2	4
Clinical stage	
I	5
II	12
III	3
Histology	
Ductal	18
Lobular	1
Metaplastic chondrosarcomatous	1
Tissue receptor subtype	
TNBC (ER and PR < 10%)	15
Hormone receptor positive (≥ 10%)	5

pCR 53%

OlympiA: Adjuvant Olaparib gBRCA+/HER2-

(NSABP B55/BIG 6-13)



Estimated primary completion date: November 18, 2020

Courtesy of P Kelly Marcom, MD

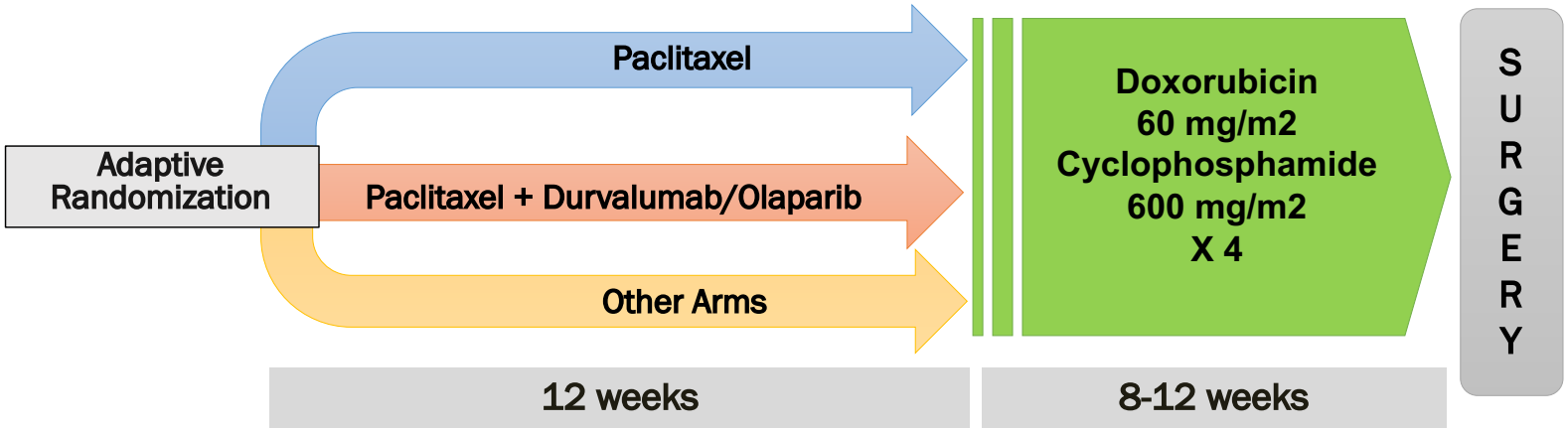
KEYLYNK-009: A Phase 2/3, Open-Label, Randomized Study of Pembrolizumab plus Olaparib vs Pembrolizumab plus Chemotherapy After Induction with First-Line Pembrolizumab plus Chemotherapy in Patients with Locally Recurrent Inoperable or Metastatic Triple-Negative Breast Cancer (TNBC)

Rugo H et al.

SABCS 2020;Abstract OT-30-01.

New Approaches: Durvalumab/Olaparib in I-SPY 2

- Rationale for combining PARPi/checkpoint inhibitor
  - Impaired nucleotide and base excision repair increase mutation and neoantigen load[1]
    - DNA fragments activate intracellular STING (Stimulator of Interferon Genes) pathway
    - PARP inhibition upregulates PD-L1 expression in breast cell lines



Control Arm
Paclitaxel 80 mg/m2 every wk x 12

Experimental Arm
Paclitaxel 80 mg/m2 every wk x 12
Durvalumab 1500 mg every 4 wks x 3
Olaparib 100 mg twice daily wks 1-11

Courtesy of Hope S Rugo, MD

Pusztai et al, AACR 2020

[1]Lancet Oncology. 2019 Mar 1;20(3):e175-86

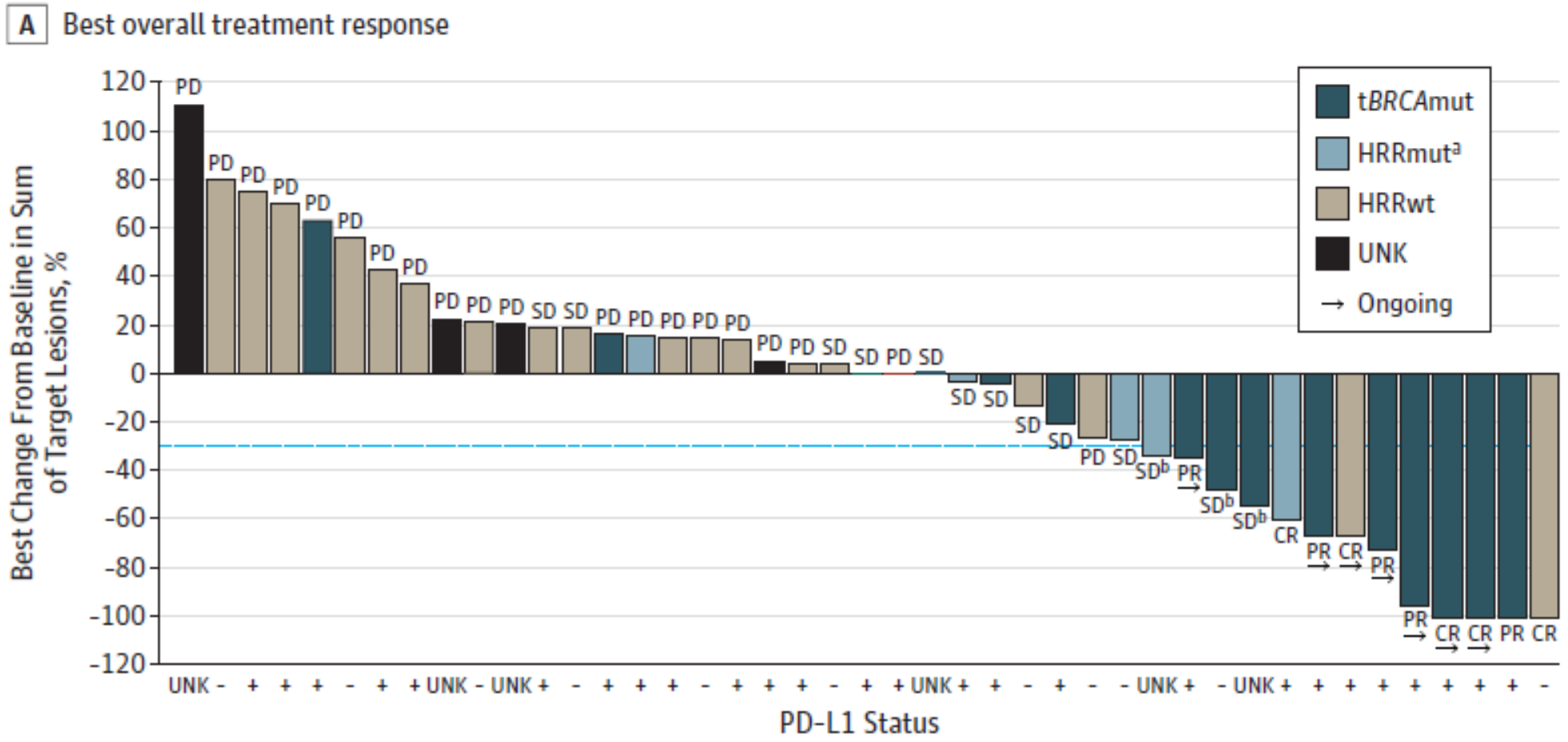
Novel Combinations: PARPi and Immune Checkpoints

- RATIONALE: PARPi activates intratumoral STING/c-GAS pathway causing CD8+ T-cell recruitment. IC might act synergistically with this activation.(Pantelidou, Cancer Discovery, 9: 722, 2019)

Trial	BRCA1/2 Status	Drugs	Eligibility	Cohort Size	Overall Response Rate
TOPACIO	Any BRCA or PD-L1 status	Niraparib Pembrolizumab	≤ 2 chemo	55	21%
MEDIOLA	gBRCA	Olaparib Durvalumab	≤ 2 chemo	30	63%

Courtesy of P Kelly Marcom, MD

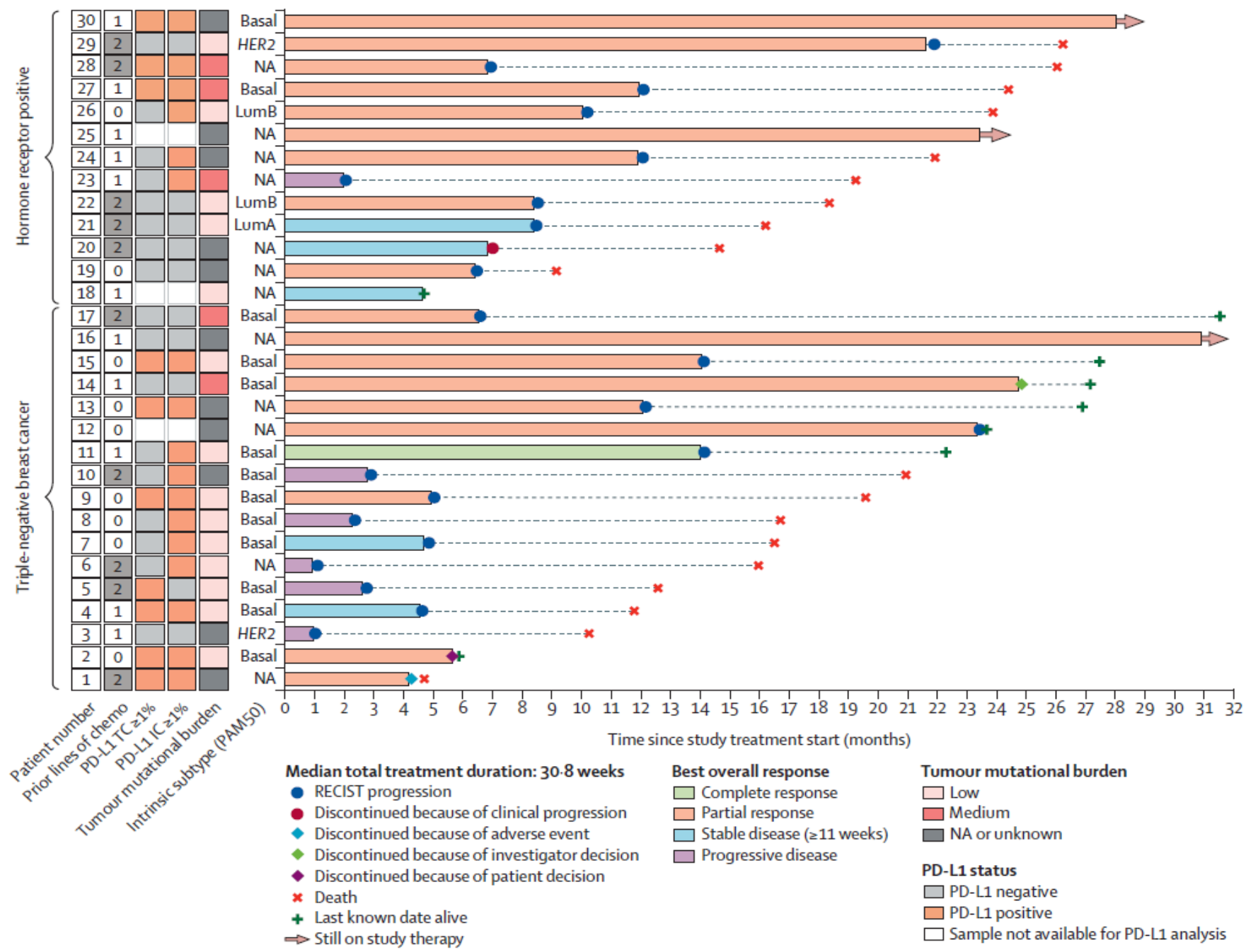
TOPACIO: Best Overall Response



Courtesy of P Kelly Marcom, MD

Vinayak, JAMA Oncol. 2019;5(8):1132-1140

MEDIOLA Trial



Courtesy of P Kelly Marcom, MD

Domchek, Lancet Oncol 2020; 21: 1155–64

Efficacy of Combined CDK4/6 Inhibitor and PARP Inhibitor in the Treatment of BRCA1 Mutant Triple Negative Breast Cancer

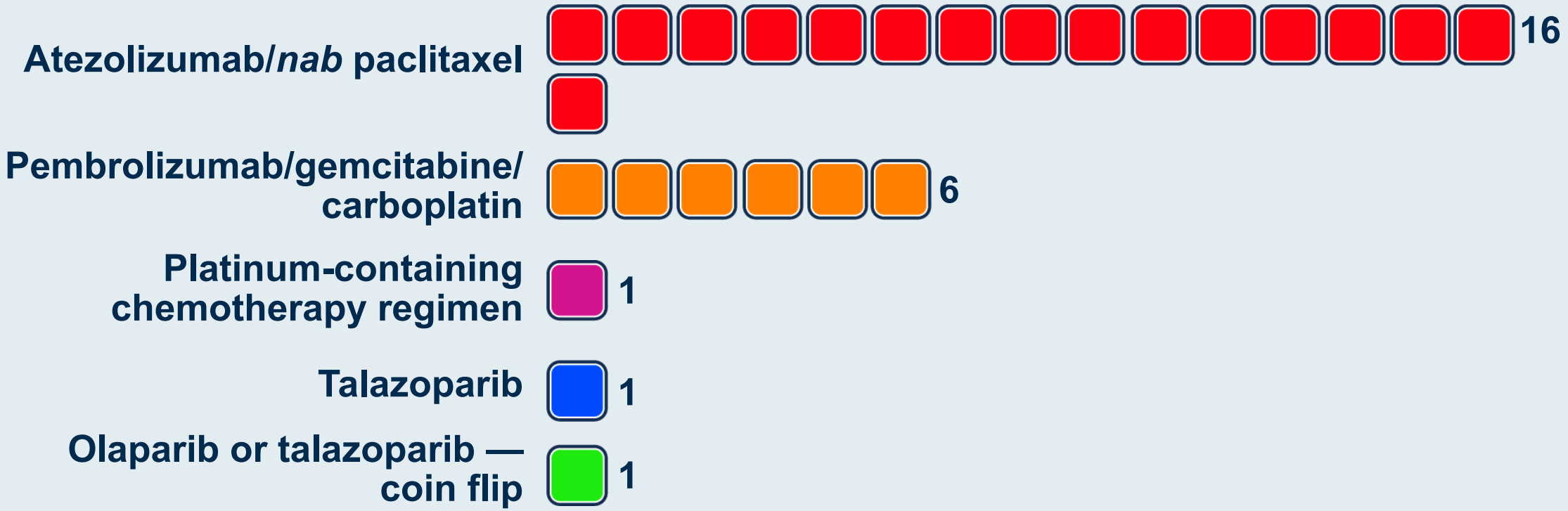
Zhu X et al.

SABCS 2020;Abstract PS4-39.

A 41-year-old woman with a gBRCA mutation who completed neoadjuvant AC/docetaxel and postoperative radiation therapy 21 months ago for localized TNBC now presents with liver, lung and nodal metastases. What therapy would you recommend if the tumor is PD-L1-positive?

1. Olaparib
2. Talazoparib
3. Olaparib or talazoparib — coin flip
4. Atezolizumab/*nab* paclitaxel
5. Pembrolizumab/chemotherapy
6. Chemotherapy
7. Chemotherapy followed by maintenance PARP inhibitor
8. Other

A 41-year-old woman with a gBRCA mutation who completed neoadjuvant AC/docetaxel and postoperative radiation therapy 21 months ago for localized TNBC now presents with liver, lung and nodal metastases. What therapy would you recommend if the tumor is PD-L1-positive?

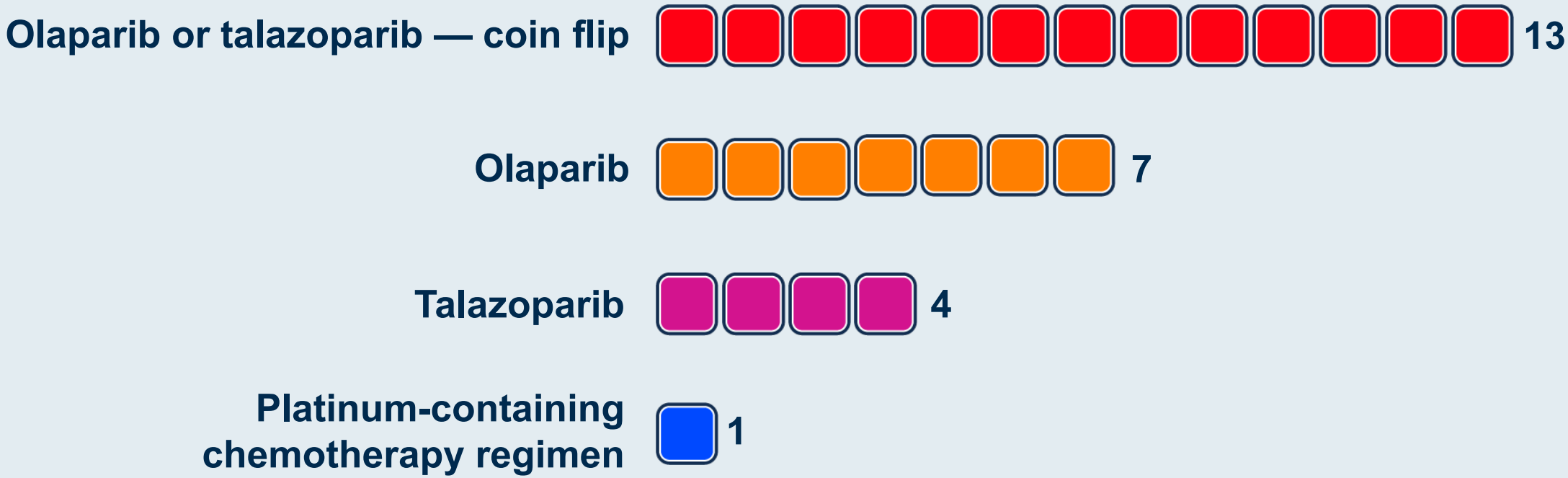


Survey of 25 breast cancer clinical investigators

The patient in the previous scenario receives first-line atezolizumab/*nab* paclitaxel but experiences disease progression after 29 months. What would you recommend next?

1. Olaparib
2. Talazoparib
3. Olaparib or talazoparib — coin flip
4. Nonplatinum chemotherapy
5. Platinum-containing chemotherapy
6. Chemotherapy followed by maintenance PARP inhibitor
7. Chemotherapy combined with a PARP inhibitor
8. Other

The patient in the previous scenario receives first-line atezolizumab/*nab* paclitaxel but experiences disease progression after 29 months. What would you recommend next?

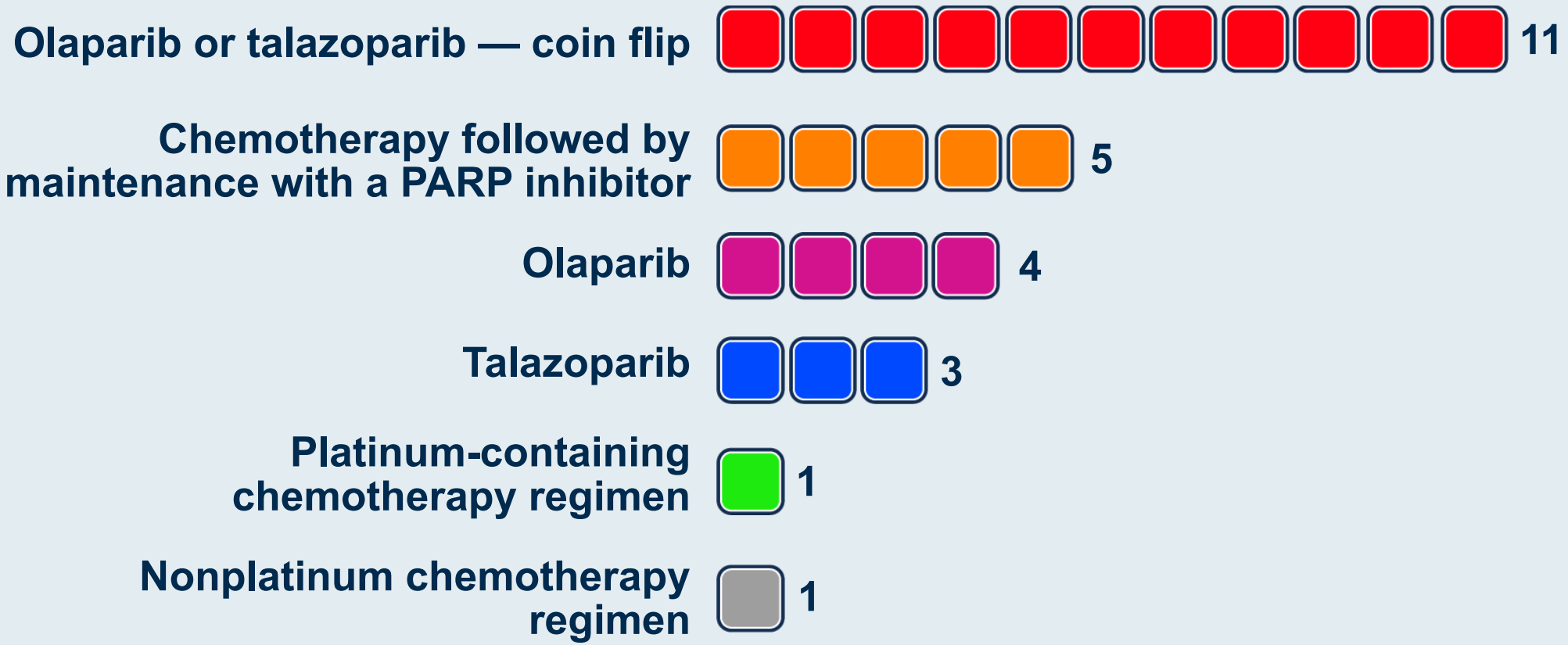


Survey of 25 breast cancer clinical investigators

What would be your preferred treatment approach for a 60-year-old patient with a BRCA germline mutation and de novo metastatic TNBC that is PD-L1-negative?

1. Olaparib
2. Talazoparib
3. Olaparib or talazoparib — coin flip
4. Nonplatinum chemotherapy
5. Platinum-containing chemotherapy
6. Chemotherapy followed by maintenance PARP inhibitor
7. Chemotherapy combined with a PARP inhibitor
8. Other

What would be your preferred treatment approach for a 60-year-old patient with a BRCA germline mutation and de novo metastatic TNBC that is PD-L1-negative?

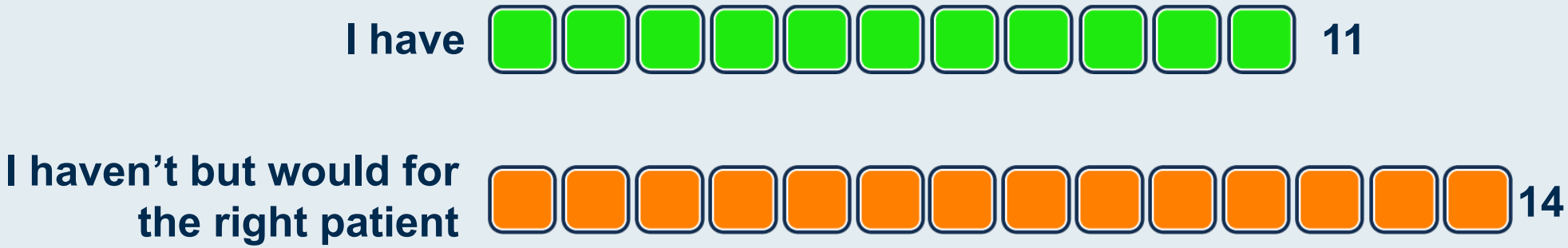


Survey of 25 breast cancer clinical investigators

Regulatory and reimbursement issues aside, have you or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a germline PALB2 mutation?

1. I have
2. I haven't but would for the right patient
3. I haven't and would not

Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a germline PALB2 mutation?

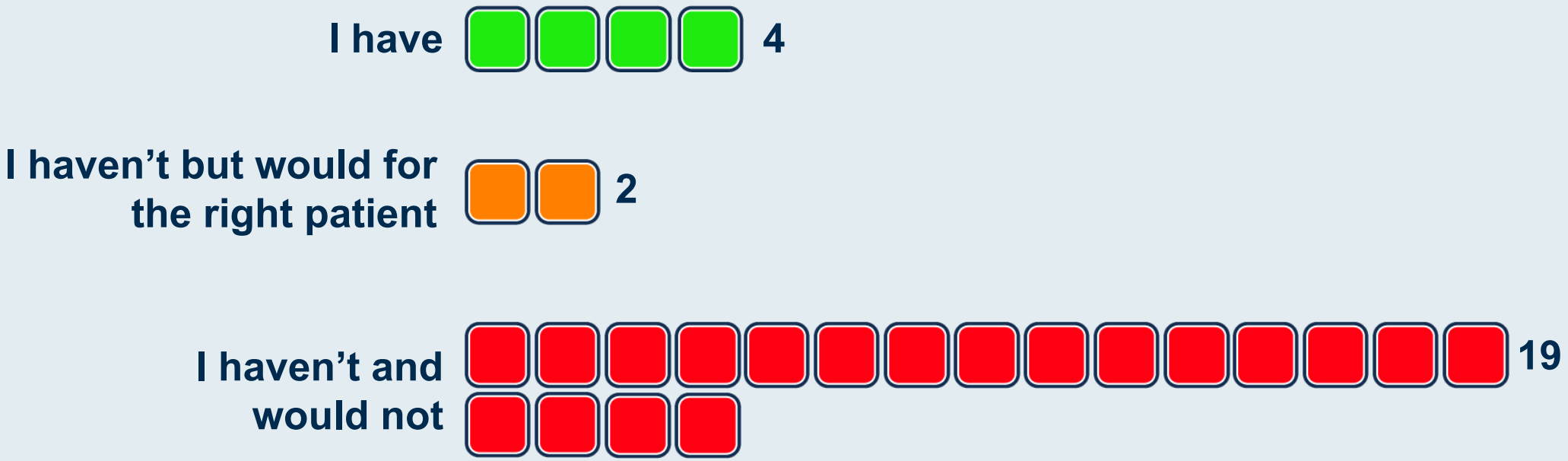


Survey of 25 breast cancer clinical investigators

Regulatory and reimbursement issues aside, have you or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a germline ATM mutation?

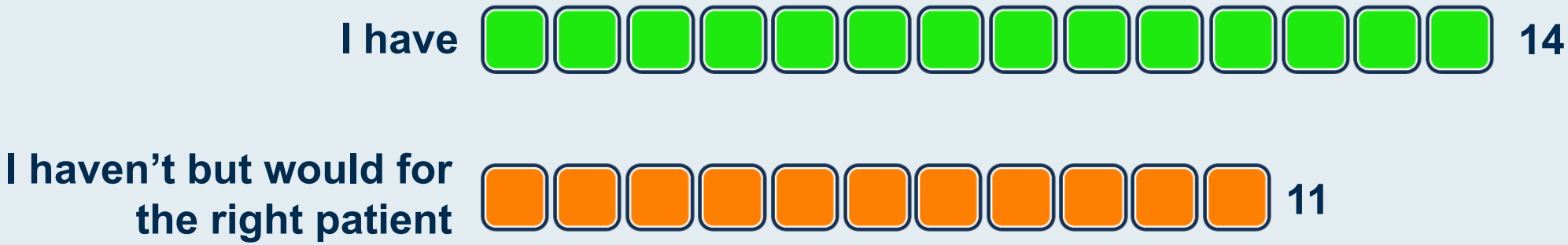
1. I have
2. I haven't but would for the right patient
3. I haven't and would not

Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a germline ATM mutation?



Survey of 25 breast cancer clinical investigators

Regulatory and reimbursement issues aside, have you attempted or would you attempt to access a PARP inhibitor for a patient with metastatic TNBC and a somatic BRCA mutation?



Survey of 25 breast cancer clinical investigators

Case Presentation: A 54-year-old woman with metastatic triple-negative breast cancer – gBRCA1m, PD-L1 of 2%

Atif Hussein, MD, MMM

- Diagnosed with 3-cm ER/PR/HER2-negative IDC of left breast
- CT/PET/CT guided biopsy: Hepatic metastatic triple-negative adenocarcinoma
- PD-L1: 2%
- Deleterious germline BRCA1 mutation
- Olaparib 300 mg BID, with mild nausea treated with ondansetron
  - After 3 months: 40% reduction in breast mass and hepatic lesions
  - Baseline Hgb: 11.9 → 9.8 → 10.8 g/dL and currently stable

Questions

- How do you incorporate PARP inhibitors in the treatment of triple-negative breast cancer? What line would you use a PARP inhibitor?
- What do we know about chemotherapy after a PARP inhibitor?

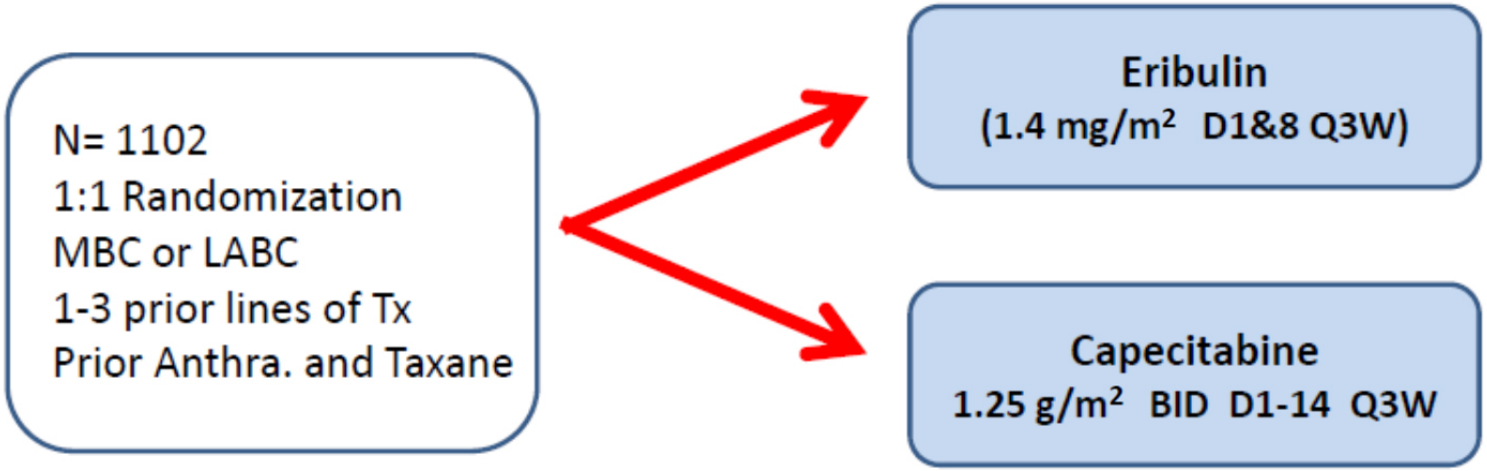
Agenda

Module 1: Optimal Integration of Immune Checkpoint Inhibitors into the Management of Metastatic Triple-Negative Breast Cancer (TNBC)

Module 2: Novel Applications of Immune Checkpoint Inhibitors for Patients with Early TNBC

Module 3: Current and Future Role of PARP Inhibitors for Patients with TNBC and a BRCA Mutation

Module 4: Current and Future Management of PD-L1-Negative Metastatic TNBC



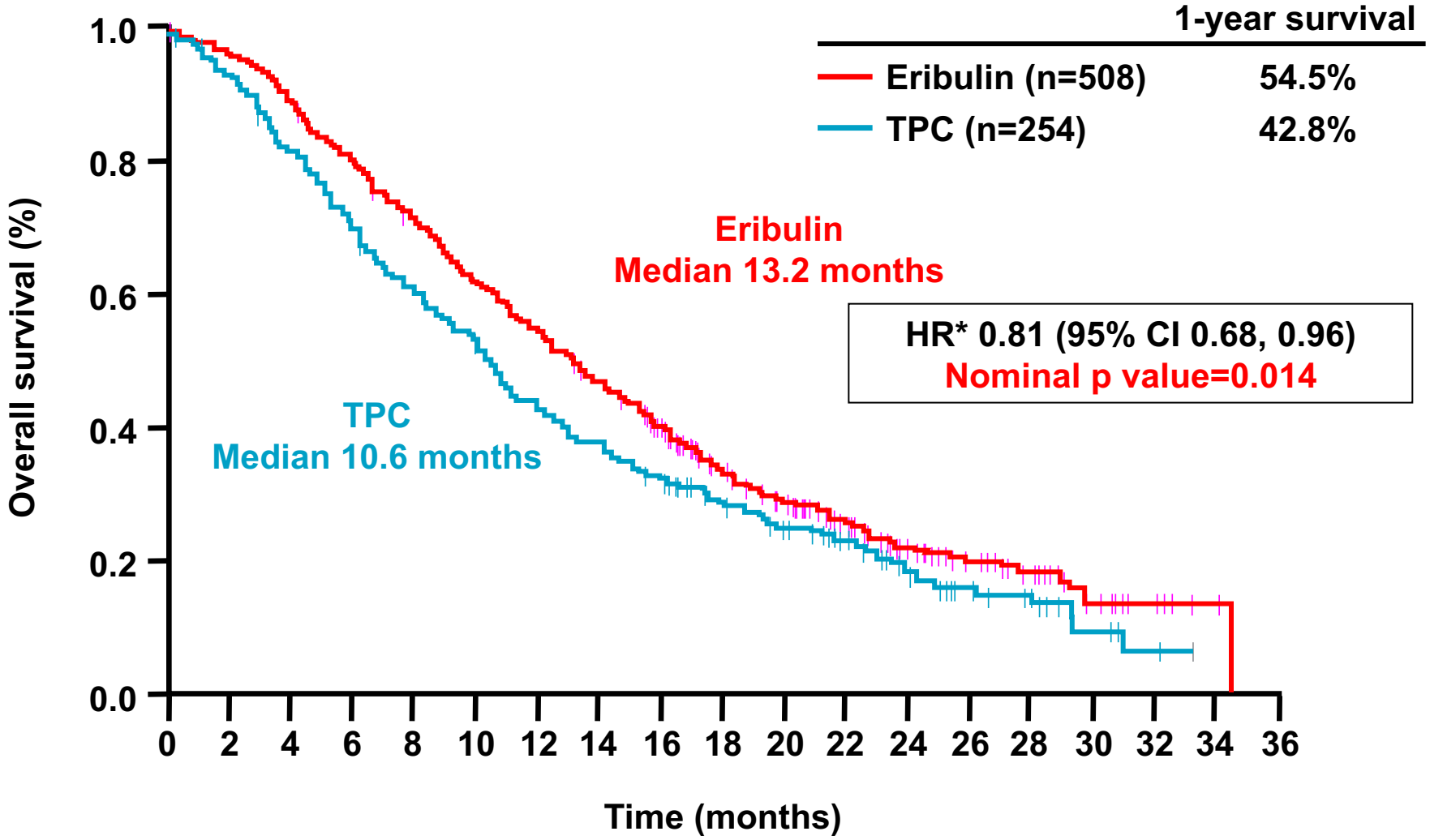
Study 301: eribulin vs capecitabine 2L MBC

Median OS	Eribulin	Cape	Hazard ratio
HER2 status			
Positive	14.3 mo	17.1 mo	0.965
Negative	15.9 mo	13.5 mo	0.838
ER status			
Positive	18.2 mo	16.8 mo	0.897
Negative	14.4 mo	10.5 mo	0.779
Triple-negative BC (TNBC)			
Yes	14.4 mo	9.4 mo	0.702
No	17.5 mo	16.6 mo	0.927
Overall	**15.9 mo**	**14.5 mo**	**0.879**

Courtesy of Joyce O'Shaughnessy, MD

Kaufman PA et al. J Clin Oncol 2015

EMBRACE: OS (ITT Population)
Eribulin vs Treatment of Physician's Choice



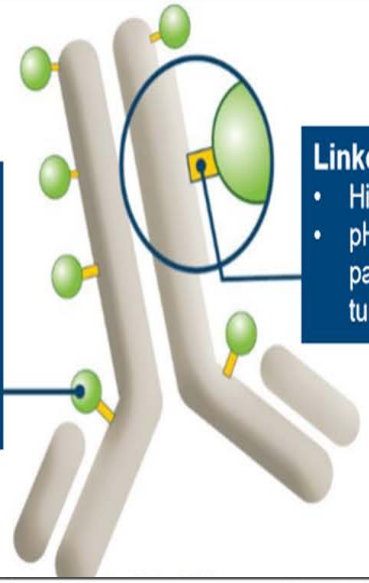
Courtesy of Joyce O'Shaughnessy, MD

Cortes J, et al. Lancet 2011;377:914-923.

Phase II Trial Sacituzumab Govitecan

Sacituzumab Antibody-Drug Conjugate (ADC)

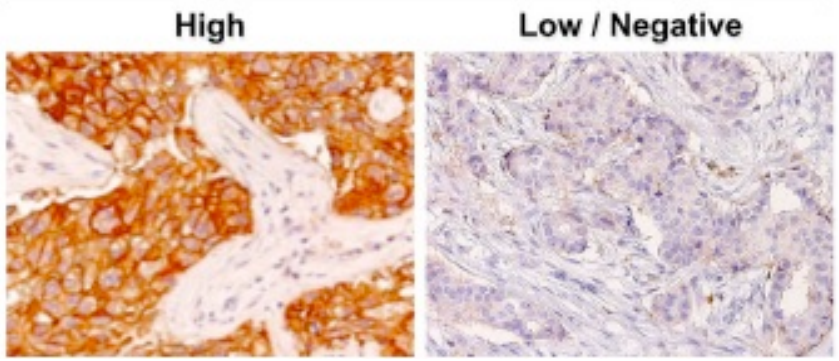
Humanized RS7 antibody
- Targets Trop-2, an epithelial antigen expressed on many solid cancers, including mTNBC



SN-38 payload
- Targets 136-fold more SN-38 than the parent compound, irinotecan (topoisomerase I inhibitor)
- ADCs unique chemistry avoids low solubility and selectively delivers SN-38 to the tumor

Linker for SN-38
- High drug-to-antibody ratio (7.6:1)
- pH-sensitive linker for rapid payload release at or inside the tumor

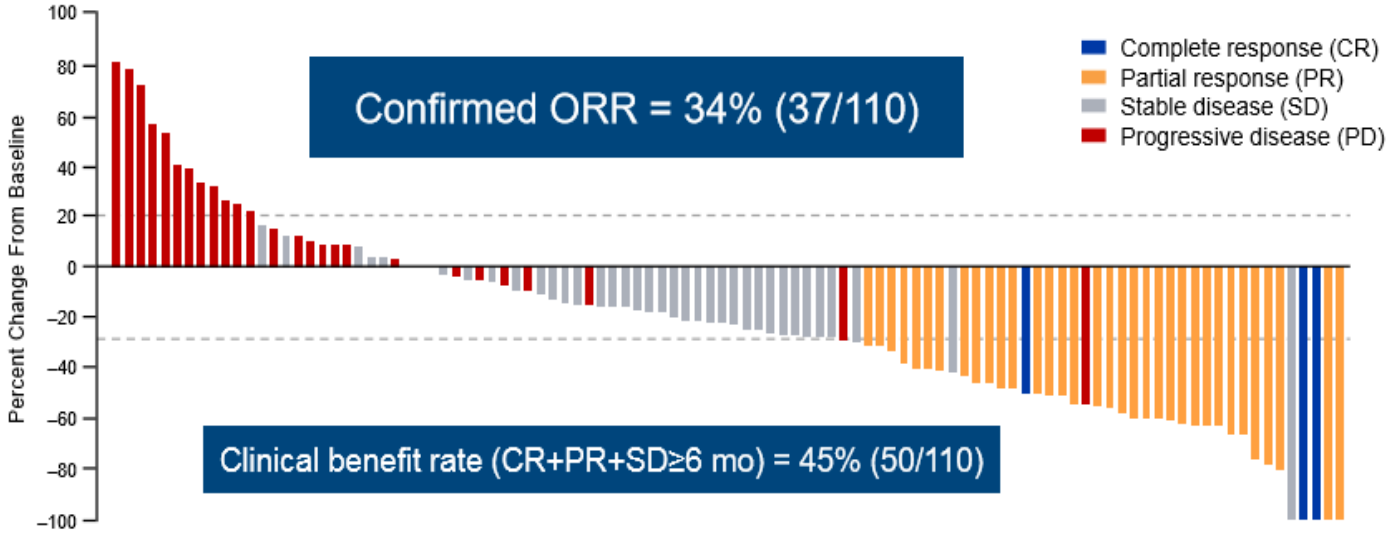
5



> 90% TNBCs express Trop-2

Met TNBC 3/4/5th-line Phase II

Tumor Response to Treatment



- 74% (75/102) of patients with at least one CT response assessment had reduction of target lesions (sum of diameters)
- 102 patients had ≥1 scheduled CT response assessment
- 8 patients withdrew prior to assessment (4 PD, 4 MRI brain mets)

11

Median DoR 7.6 mos
Med PFS 5.5 mos

Bardia A et al. SABCS 2017

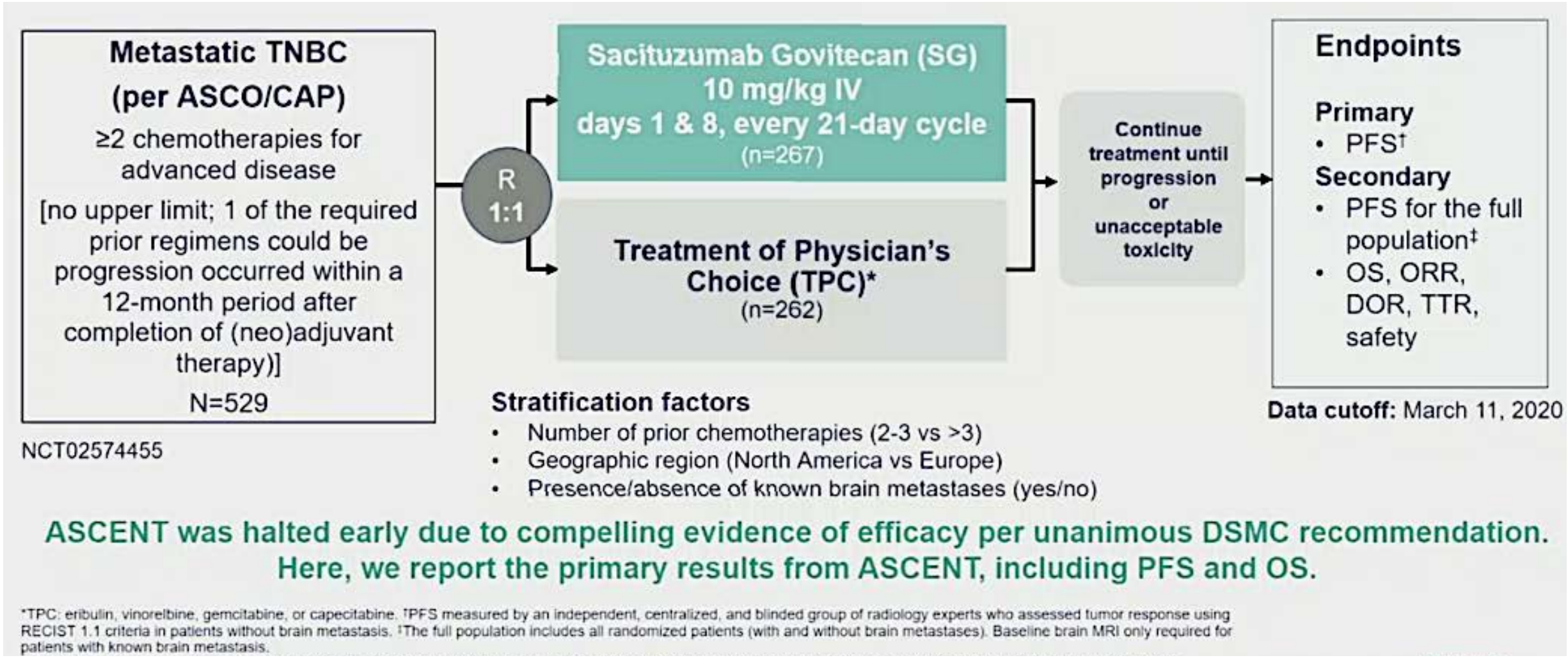
Courtesy of Joyce O'Shaughnessy, MD

Biomarker Evaluation in the Phase 3 ASCENT Study of Sacituzumab Govitecan versus Chemotherapy in Patients with Metastatic Triple-Negative Breast Cancer

Hurvitz SA et al.

SABCS 2020;Abstract GS3-06.

ASCENT (Phase III): Sacituzumab Govitecan (SG) vs Treatment of Physician´s Choice (TPC) in pretreated mTNBC (N=529) – *Study Design*



ASCENT was halted early due to compelling evidence of efficacy per unanimous DSMC recommendation. Here, we report the primary results from ASCENT, including PFS and OS.

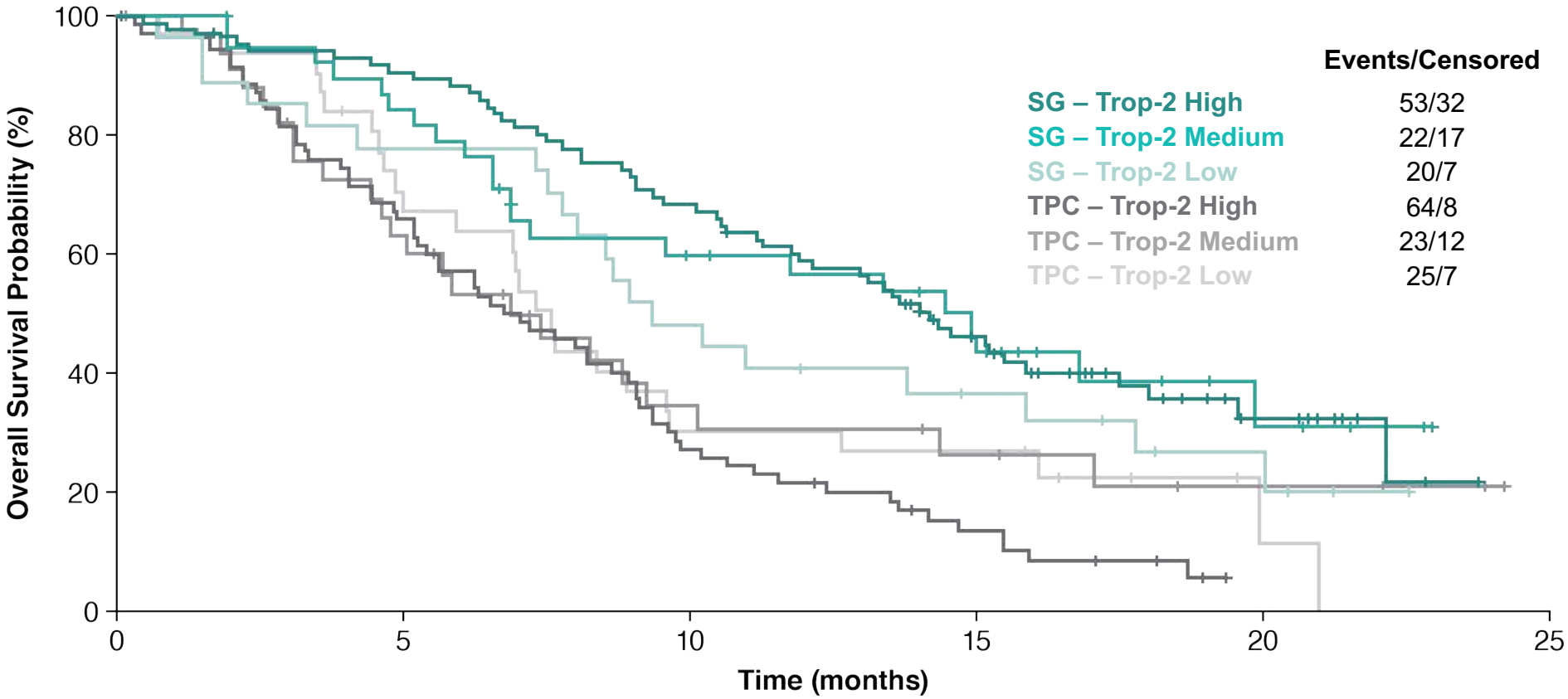
*TPC: eribulin, vinorelbine, gemcitabine, or capecitabine. †PFS measured by an independent, centralized, and blinded group of radiology experts who assessed tumor response using RECIST 1.1 criteria in patients without brain metastasis. ‡The full population includes all randomized patients (with and without brain metastases). Baseline brain MRI only required for patients with known brain metastasis.

Bardia A, et al. ESMO 2020 (LBA17)

Courtesy of Joyce O'Shaughnessy, MD

ASCENT Clinical Trial

Overall Survival by Trop-2 Expression

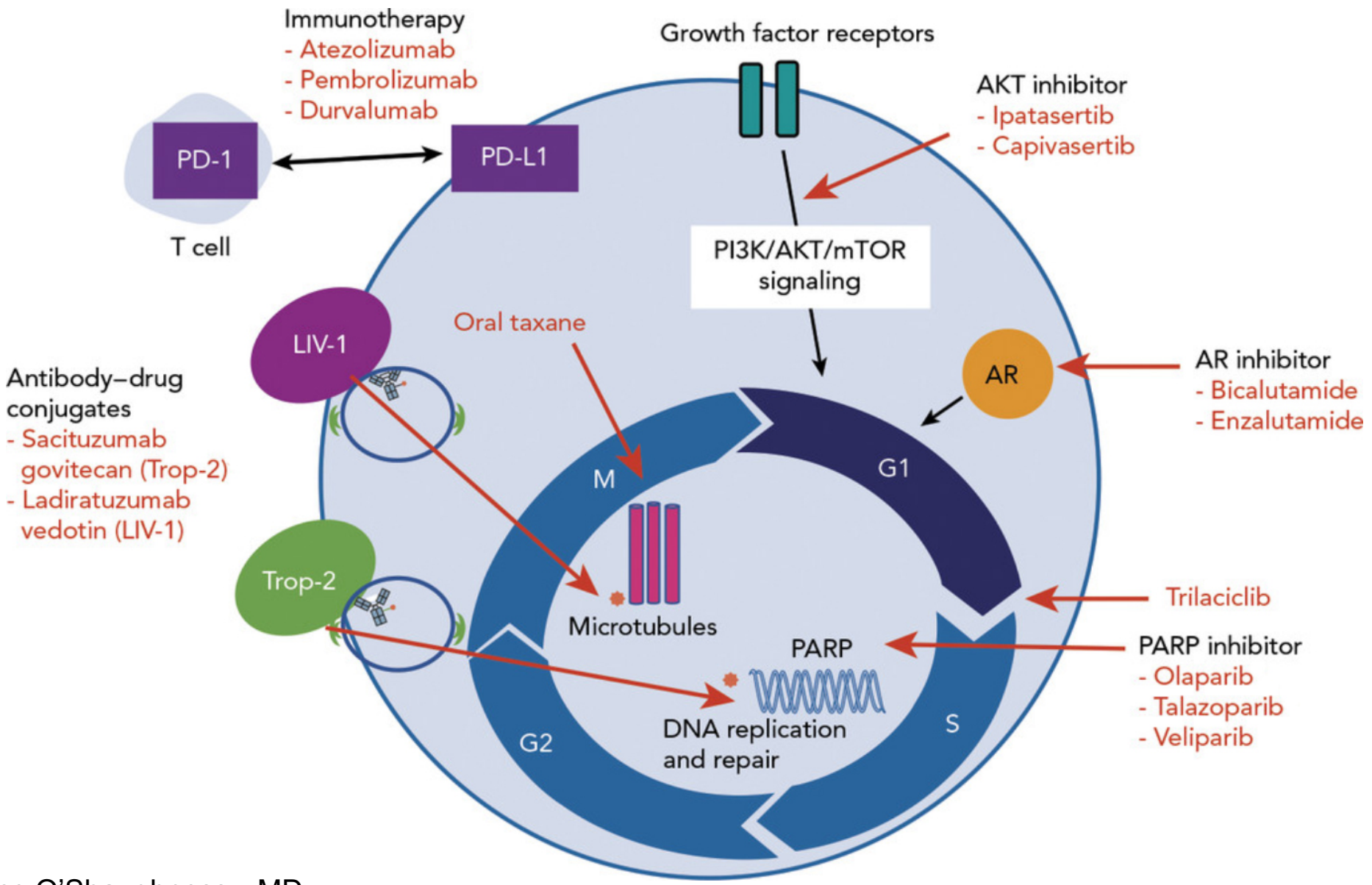


	Trop-2 High | H-score: 200-300		Trop-2 Medium | H-score: 100-200		Trop-2 Low | H-score: <100	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
Median OS—mo (95% CI)	14.2 (11.3-17.5)	6.9 (5.3-8.9)	14.9 (6.9-NE)	6.9 (4.6-10.1)	9.3 (7.5-17.8)	7.6 (5.0-9.6)

Assessed in brain metastases-negative population. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.
H-score, histochemical-score; OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice; Trop-2, trophoblast cell surface antigen-2.

Courtesy of Joyce O'Shaughnessy, MD

Novel Targets in Triple Negative Breast Cancer



Courtesy of Joyce O'Shaughnessy, MD

Double-Blind Placebo (PBO)-Controlled Randomized Phase III Trial Evaluating First-Line Ipatasertib (IPAT) Combined with Paclitaxel (PAC) for PIK3CA/AKT1/PTEN-Altered Locally Advanced Unresectable or Metastatic Triple-Negative Breast Cancer (aTNBC): Primary Results from IPATunity130 Cohort A

Dent R et al.

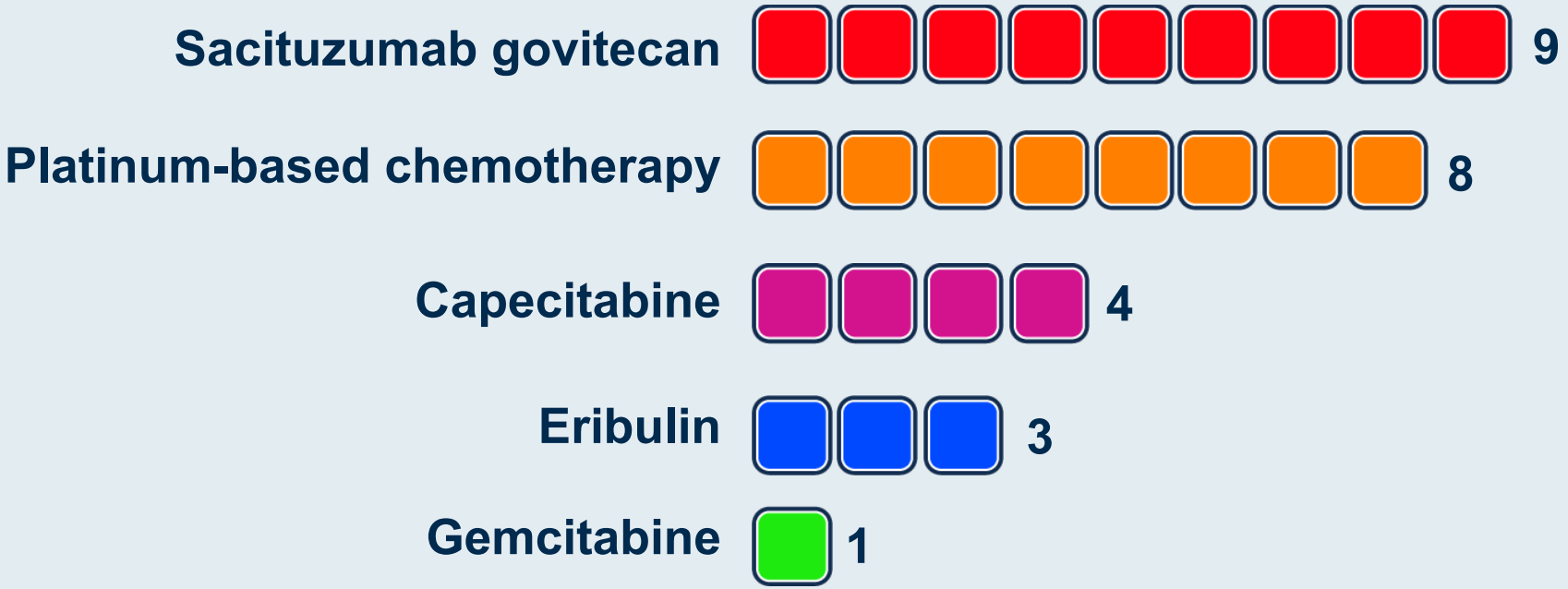
SABCS 2020;Abstract GS3-04.

What treatment would you recommend next for a 60-year-old woman with metastatic TNBC (BRCA wild-type, PD-L1-positive) who experiences disease progression after 7 months of first-line atezolizumab/*nab* paclitaxel?

1. Gemcitabine
2. Capecitabine
3. Vinorelbine
4. Eribulin
5. Sacituzumab govitecan
6. Platinum-based chemotherapy
7. Other chemotherapy
8. Other

RTP RESEARCH TO PRACTICE

What treatment would you recommend next for a 60-year-old woman with metastatic TNBC (BRCA WT, PD-L1-positive) who experiences disease progression after 7 months of first-line atezolizumab/*nab* paclitaxel?



Survey of 25 breast cancer clinical investigators

Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

Gynecologic Cancers

Tuesday, January 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Robert L Coleman, MD
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Moderator

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RTP Year in Review 2021

Thank you for joining us!

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

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