Exploring the Role of Immune Checkpoint Inhibitor Therapy and Other Novel Strategies in Gynecologic Cancers

A Meet The Professor Series

David M O'Malley, MD
Professor
Division Director, Gynecologic Oncology
Co-Director, Gyn Oncology Phase I Program
The Ohio State University and The James Cancer Center
Columbus, Ohio

Commercial Support

These activities are supported by educational grants from Eisai Inc, Merck, Seattle Genetics and Tesaro, A GSK Company.

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Dr Love — Disclosures

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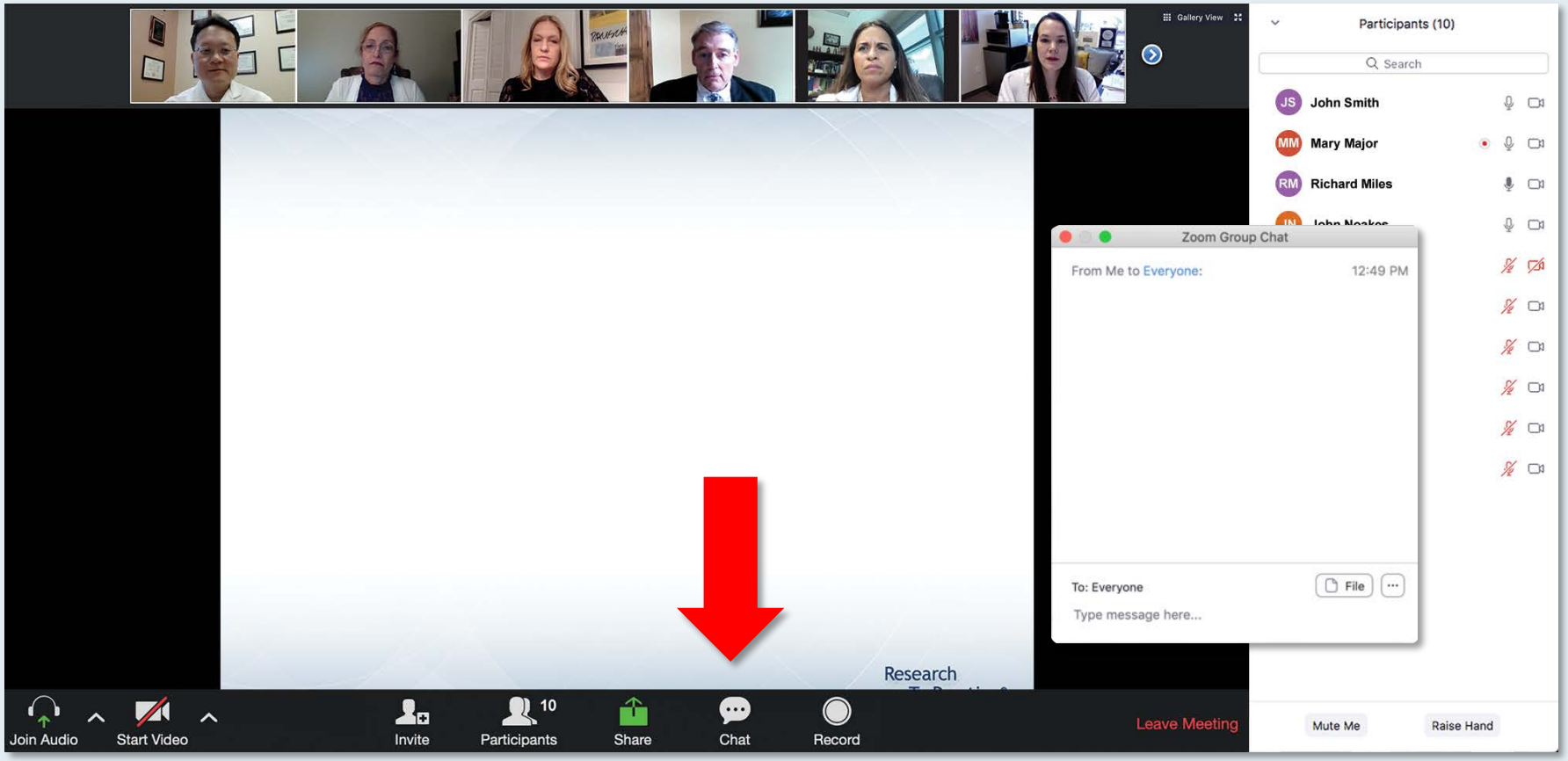

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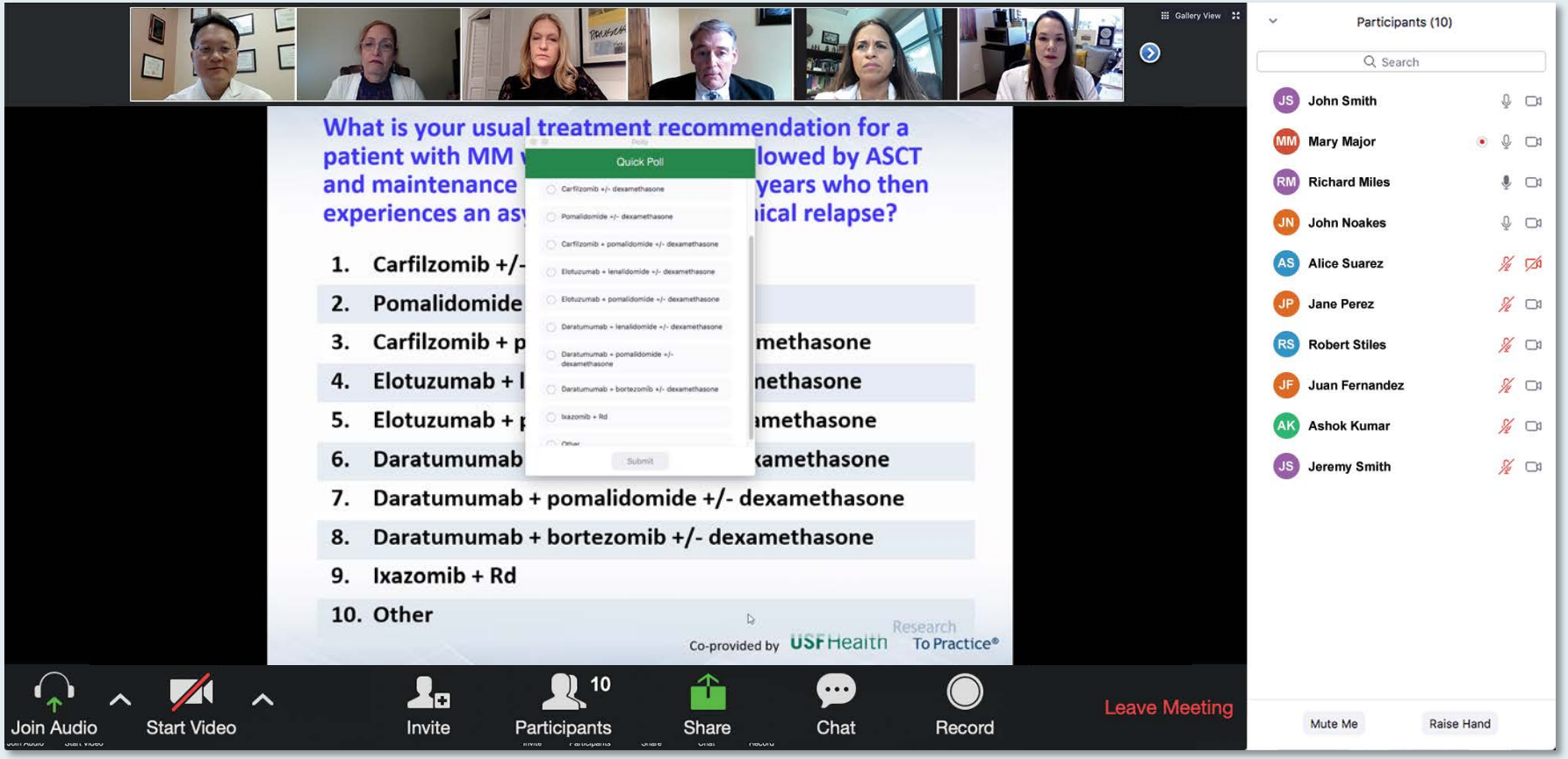

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Upcoming Live Webinars

Tuesday, September 29, 2020
12:00 PM – 1:00 PM ET

Current Questions and Controversies in the Management of Lung Cancer

Faculty
Benjamin Levy, MD

Moderator
Neil Love, MD

Wednesday, September 30, 2020
3:00 PM – 4:00 PM ET

Clinical Investigator Perspectives on the Current and Future Management of Multiple Myeloma

Faculty
S Vincent Rajkumar, MD

Moderator
Neil Love, MD

Upcoming Live Webinars

Thursday, October 1, 2020
12:00 PM – 1:00 PM ET

Clinical Investigator Perspectives on the Current and Future Role of PARP Inhibition in the Management of Ovarian Cancer

Faculty
Ursula Matulonis, MD

Moderator
Neil Love, MD

Friday, October 2, 2020
12:00 PM – 1:00 PM ET

Optimizing the Selection and Sequencing of Therapy for Patients with Chronic Lymphocytic Leukemia

Faculty
William G Wierda, MD, PhD

Moderator
Neil Love, MD

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 days.

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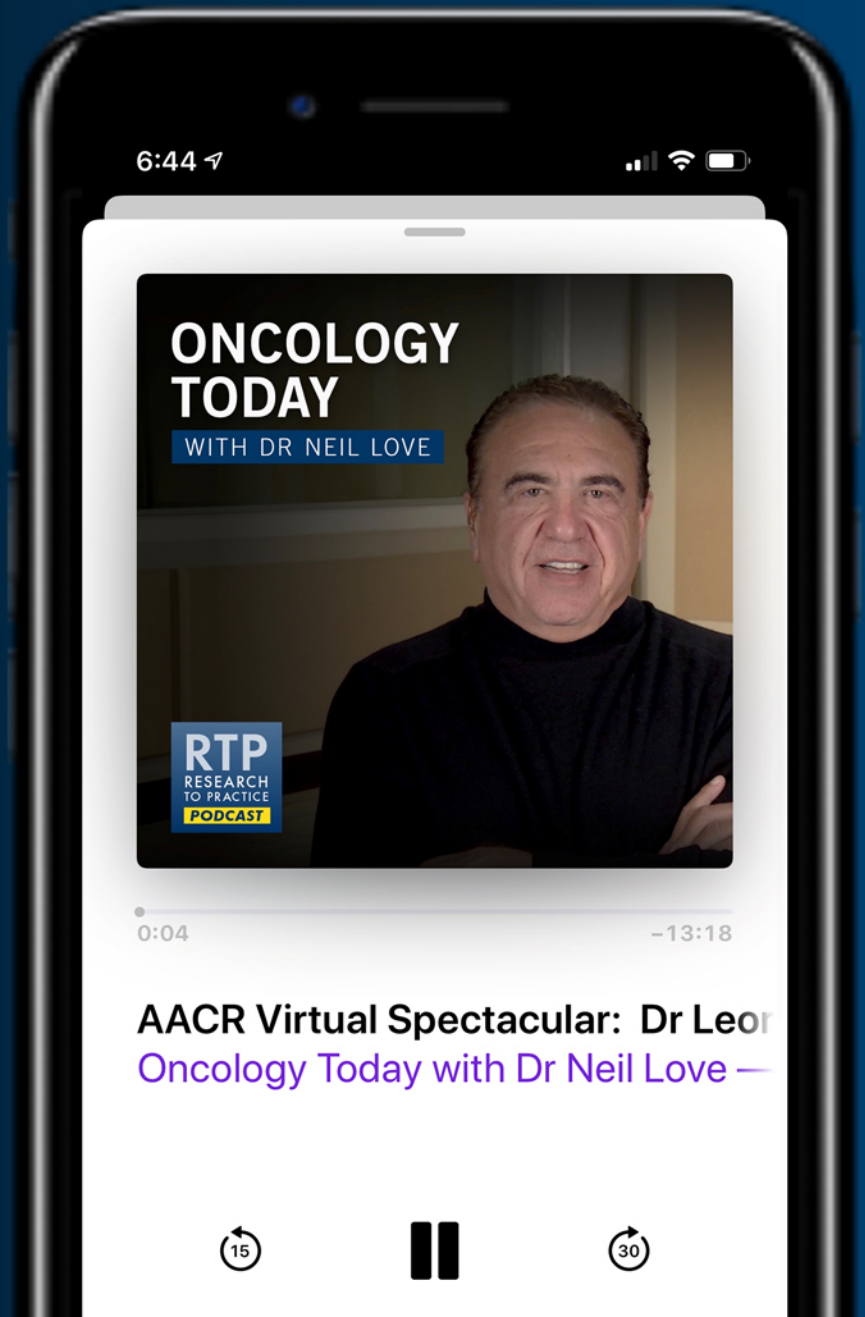

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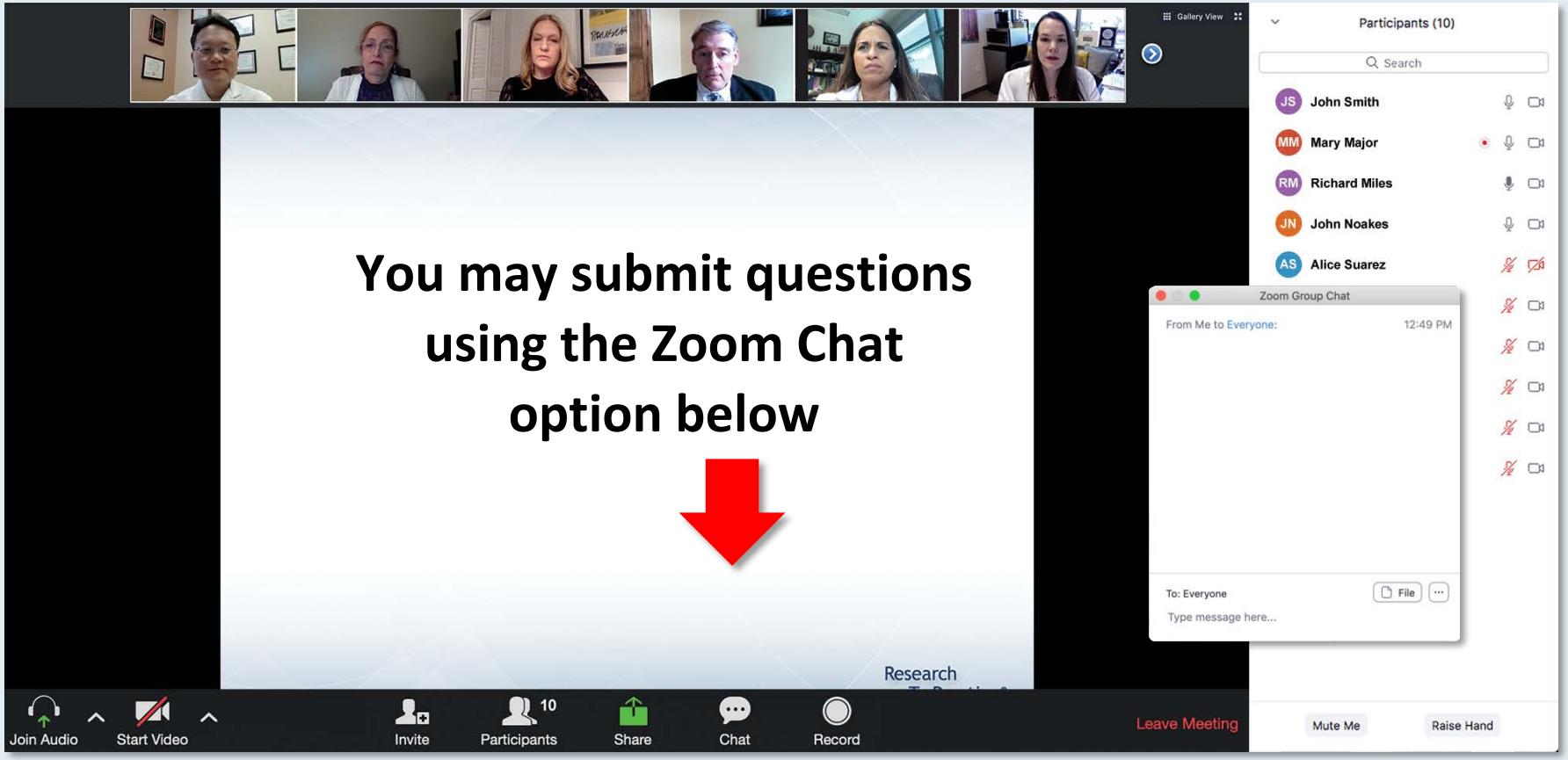

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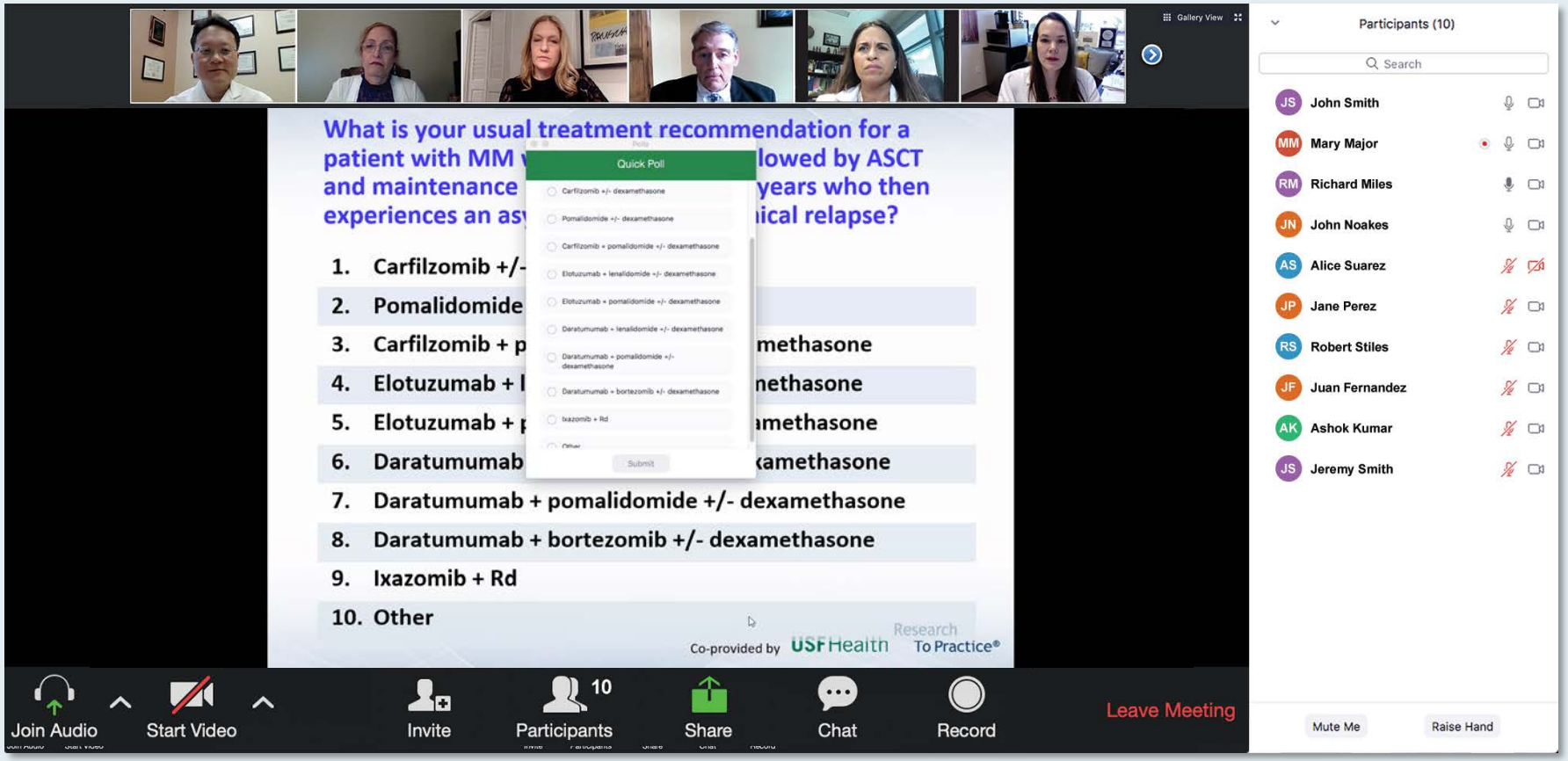

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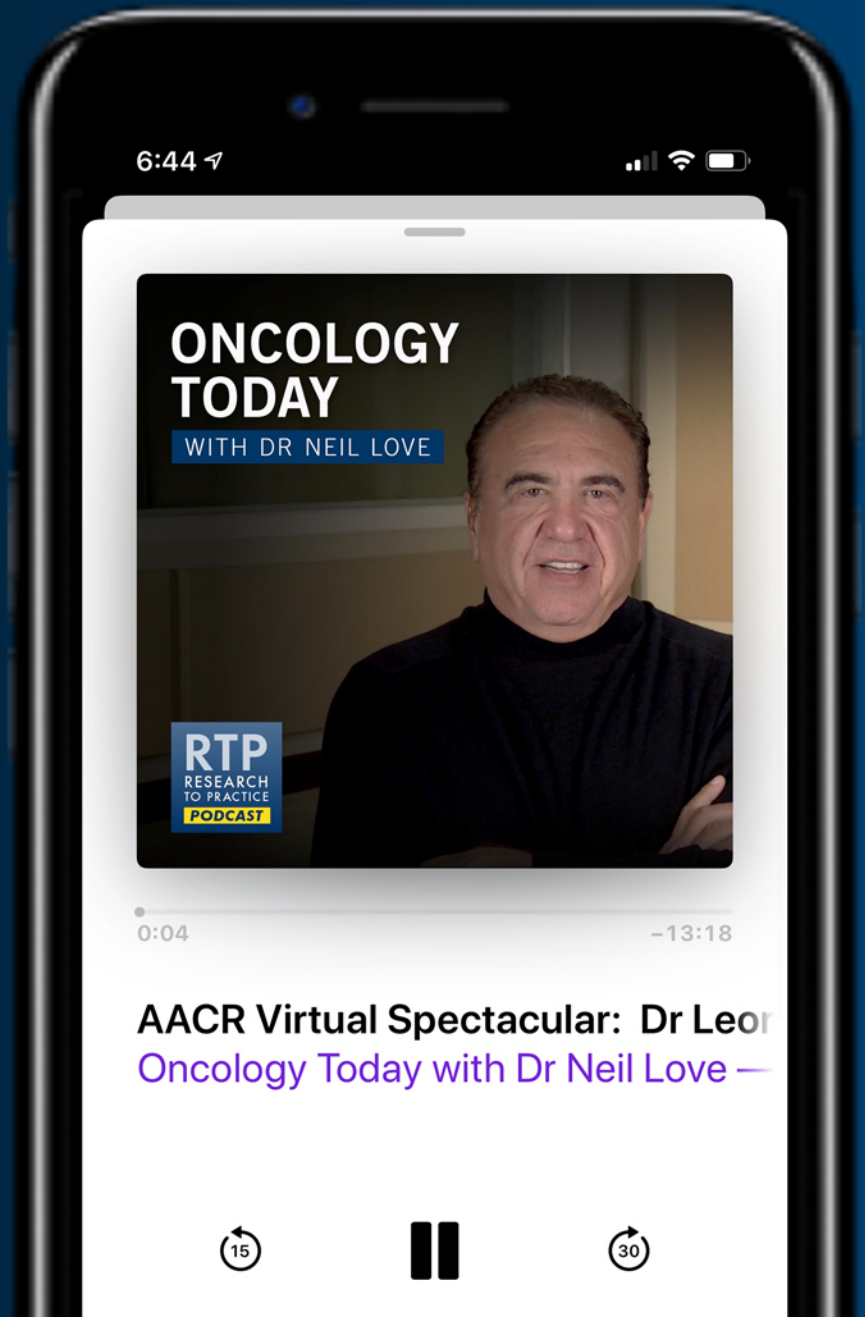

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Meet The Professor with Dr O'Malley

MODULE 1: Cases from Dr Mirza

- Questions and Comments: NSGO-PALEO trial — Palbociclib/letrozole for ER-positive advanced or recurrent endometrial cancer
- Questions and Comments: Tisotumab vedotin in cervical cancer; management of ophthalmic toxicity
- A 68-year-old woman with advanced, recurrent endometrial cancer – Microsatellite instability high (MSI-H)
- A 68-year-old woman with advanced, recurrent endometrial cancer – Microsatellite stable (MSS)
- A 68-year-old woman with advanced, recurrent endometrial cancer – ER-positive, MSS
- A 65-year-old woman with advanced, recurrent endometrial cancer – MSS, hypertension with pembrolizumab/lenvatinib
- Questions and Comments: Management of pembrolizumab/lenvatinib-associated diarrhea
- A 68-year-old woman with advanced, recurrent endometrial cancer – ER-positive, MSI-H
- A 68-year-old woman with unresectable endometrial cancer and lung metastases – MSI-H
- Questions and Comments: Immune checkpoint inhibitors in platinum-resistant ovarian cancer after multiple lines of chemotherapy

MODULE 2: Gynecologic Oncology Journal Club with Dr O'Malley

MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Data Sets

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Endocrine therapy combined with a CDK4/6 inhibitor for metastatic ER-positive endometrial cancer

1. Has not been studied in a randomized trial
2. Has been studied but is not very effective
3. Has been studied and is very effective
4. I DON'T KNOW!

Questions and Comments: NSGO-PALEO/ENGOT-EN3 trial of palbociclib/letrozole for ER+ advanced or recurrent endometrial cancer (ESMO 2020)

Dr Mansoor Raza Mirza

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Questions and Comments: Tisotumab vedotin in cervical cancer; management of ophthalmic toxicity

Dr Mansoor Raza Mirza

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Based on your clinical experience and/or the published literature, how would you characterize the tolerability of tisotumab vedotin in the treatment of metastatic cervical cancer?

 MICHAEL J BIRRER, MD, PHD	Well tolerated except for epistasis
 ROBERT L COLEMAN, MD	Similar to other single-agent chemotherapy
 ANA OAKNIN, MD, PHD	Moderate toxicity
 DAVID M O'MALLEY, MD	Reasonable toxicity
 RICHARD T PENSON, MD, MRCP	Excited by it
 MATTHEW A POWELL, MD	Reasonable toxicity
 BRIAN M SLOMOVITZ, MD	Well tolerated; ocular side effects
 KRISHNANSU S TEWARI, MD	Relatively well tolerated so far
 PROFESSOR IGNACE VERGOTE	Good tolerability

A patient with PD-L1-positive metastatic cervical cancer experiences disease progression on platinum-based therapy and has significant symptoms from her disease. If tisotumab vedotin were approved, what would likely be your next line of treatment?

1. Pembrolizumab
2. Tisotumab vedotin
3. Other

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Tisotumab Vedotin in Previously Treated Recurrent or Metastatic Cervical Cancer: Results from the Phase II innovaTV 204/GOG-3023/ENGOT-cx6 Study

Coleman RL et al.

ESMO 2020;Abstract LBA32.

Phase Ib/II Trial of Tisotumab Vedotin (TV) ± Bevacizumab (BEV), Pembrolizumab (PEM), or Carboplatin (CBP) in Recurrent or Metastatic Cervical Cancer (innovaTV 205/ENGOT-cx8/GOG-3024)

Vergote I et al.

ASCO 2020;Abstract TPS6095.

Case Presentation – Dr Mirza: A 68-year-old woman with advanced, recurrent endometrial cancer – MSI-H

Dr Mansoor Raza Mirza

- Diagnosed with Stage 3C endometrial cancer (serous adenocarcinoma), MSI-H, p53 mutation
- Upfront surgery, with complete resection → adjuvant carboplatin/paclitaxel x 6
- Relapsed disease 15 months later with multiple lung and abdominal metastases

Questions

- What treatment would you recommend, and why?

Case Presentation – Dr Mirza: A 68-year-old woman with advanced, recurrent endometrial cancer – MSS

Dr Mansoor Raza Mirza

- Diagnosed with Stage 3C endometrial cancer (serous adenocarcinoma), MSS, p53 mutation
- Upfront surgery, with complete resection → adjuvant carboplatin/paclitaxel x 6
- Relapsed disease 15 months later with distant metastases

Questions

- What treatment would you recommend, and why?
- If you decide to treat with pembrolizumab/lenvatinib, with what dose of lenvatinib would you start?

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Case Presentation – Dr Mirza: A 68-year-old woman with advanced, recurrent endometrial cancer – ER-positive, MSS

Dr Mansoor Raza Mirza

- Diagnosed with Stage 3C endometrial cancer (serous adenocarcinoma), ER-positive, MSS, p53 mutation
- Upfront surgery, with complete resection → adjuvant carboplatin/paclitaxel x 6
- Relapsed disease 15 months later with distant metastases

Questions

- What treatment would you recommend?
  - Would you recommend endocrine treatment, and if so, what would you choose?
  - What about re-challenging with carboplatin/paclitaxel?
  - Would you recommend lenvatinib/pembrolizumab?

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Case Presentation – Dr Mirza: A 65-year-old woman with advanced, recurrent endometrial cancer – MSS

Dr Mansoor Raza Mirza

- Diagnosed with Stage 3C endometrial cancer (serous adenocarcinoma), MSS
- Complete resection → adjuvant carboplatin/paclitaxel x 6
- Relapsed disease 18 months later with multiple lung metastases
- Pembrolizumab/lenvatinib
  - Grade III hypertension
  - Grade III diarrhea

Questions

- How would you manage this patient? Would you treat the hypertension and continue the same dose of lenvatinib? Would you pause the lenvatinib and re-start at a lower dose?
  Or would you discontinue lenvatinib and continue with pembrolizumab?

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Questions and Comments: Management of pembrolizumab/lenvatinib-associated diarrhea

Dr Mansoor Raza Mirza

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Case Presentation – Dr Mirza: A 68-year-old woman with unresectable endometrial cancer and lung metastases – MSI-H

Dr Mansoor Raza Mirza

- Diagnosed with unresectable endometrial cancer (serous adenocarcinoma) and lung metastases
  - MSI-H

Questions

- Regulatory and reimbursement issues aside, what treatment would you recommend?
  - Would you recommend chemotherapy or immunotherapy?
- What would you recommend if the patient's disease was MSS?

Questions and Comments: Use of immune checkpoint inhibitors for platinum-resistant ovarian cancer after multiple lines of chemotherapy

Dr Mansoor Raza Mirza

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Meet The Professor with Dr O'Malley

MODULE 1: Cases from Dr Mirza

MODULE 2: Gynecologic Oncology Journal Club with Dr O'Malley

- COVID-19 and ovarian cancer: Exploring alternatives to IV therapies
- Carboplatin/paclitaxel/trastuzumab in recurrent uterine serous carcinoma
- Antibody-drug conjugates for the treatment of ovarian cancer (OC)
- innovaTV 205 trial in progress: Tisotumab vedotin +/- bevacizumab, pembrolizumab or carboplatin for cervical cancer
- MOONSTONE: Niraparib + dostarlimab for platinum-resistant OC
- MEDIOLA: Olaparib + durvalumab and bevacizumab for platinum-sensitive relapsed OC without germline BRCA mutation
- GARNET: Dostarlimab for advanced or recurrent mismatch repair deficient or proficient endometrial cancer

MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Data Sets

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CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

Randomized Phase II Trial of Carboplatin–Paclitaxel Compared with Carboplatin–Paclitaxel–Trastuzumab in Advanced (Stage III–IV) or Recurrent Uterine Serous Carcinomas that Overexpress Her2/Neu (NCT01367002): Updated Overall Survival Analysis

Amanda N. Fader[1], Dana M. Roque[2], Eric Siegel[3], Natalia Buza[4], Pei Hui[4], Osama Abdelghany[4], Setsuko Chambers[5], Angeles Alvarez Secord[6], Laura Havrilesky[6], David M. O'Malley[7], Floor J. Backes[7], Nicole Nevadunsky[8], Babak Edraki[9], Dirk Pikaart[10], William Lowery[11], Karim ElSahwi[12], Paul Celano[13], Stefania Bellone[4], Masoud Azodi[4], Babak Litkouhi[14], Elena Ratner[4], Dan-Arin Silasi[4], Peter E. Schwartz[4], and Alessandro D. Santin[4]

Clin Cancer Res 2020;26:3928–35

MOONSTONE/GOG-3032: A Phase II, Open-Label, Single-Arm Study to Evaluate the Efficacy and Safety of Niraparib + Dostarlimab in Patients with Platinum-Resistant Ovarian Cancer

Randall LM et al.

ESMO 2020;Abstract 883TiP.

Phase II Study of Olaparib (O) plus Durvalumab (D) and Bevacizumab (B) (MEDIOLA): Initial Results in Patients (pts) with Non-Germline BRCA-Mutated (Non-gBRCAm) Platinum Sensitive Relapsed (PSR) Ovarian Cancer (OC)

Drew Y et al.

ESMO 2020;Abstract 814MO.

Safety and Antitumor Activity of Dostarlimab in Patients (pts) with Advanced or Recurrent DNA Mismatch Repair Deficient (dMMR) or Proficient (MMRp) Endometrial Cancer (EC): Results from GARNET

Oaknin A et al.

ESMO 2020;Abstract LBA36.

GARNET: Primary Endpoint Analysis

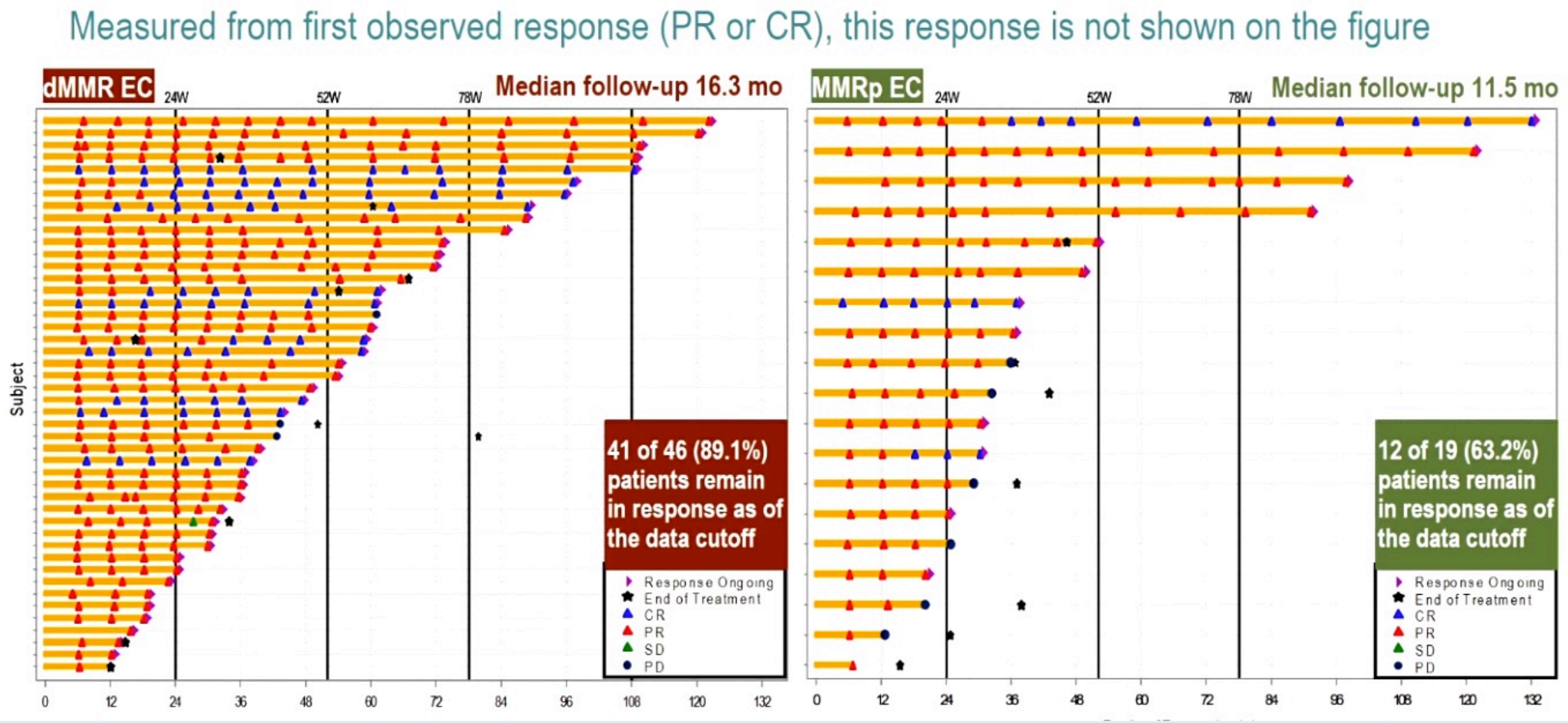
ORR was 44.7% in patients with dMMR EC, and 13.4% in patients with MMRp EC

Variable	dMMR EC, n=103	MMRp EC, n=142
Median follow-up time, mo	**16.3**	**11.5**
Objective response rate*, n (%, 95% CI)	**46 (44.7%, 34.9–54.8)**	**19 (13.4%, 8.3–20.1)**
Complete response, n (%)	11 (10.7)	3 (2.1)
Partial response, n (%)	35 (34.0)	16 (11.3)
Stable disease, n (%)	13 (12.6)	31 (21.8)
Progressive disease, n (%)	39 (37.9)	77 (54.2)
Not evaluable, n (%)	3 (2.9)	0
Not done, n (%)	2 (1.9)	15 (10.6)
Disease control rate†, n (%, 95% CI)	**59 (57.3%, 47.2–67.0)**	**50 (35.2%, 27.4–43.7)**
Response ongoing, n (%)	**41 (89.1)**	**12 (63.2)**
Median duration of response, (range) mo	**Not reached (2.63–28.09+)**	**Not reached (1.54+–30.36+)**
Kaplan–Meier estimated probability of remaining in response		
at 6 mo, %	97.8	83.0
at 12 mo, %	90.6	61.3
at 18 mo, %	79.2	61.3

*Responses required confirmation at a subsequent scan; SD had to be observed at ≥12 weeks on study to qualify as SD; †Includes confirmed CR, PR or SD at ≥12 weeks.

Oaknin A et al. ESMO 2020;Abstract LBA36.

GARNET: Duration of Response



Duration of Response

Duration of Response

Oaknin A et al. ESMO 2020;Abstract LBA36.

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MODULE 4: Key Recent Data Sets

- Pembrolizumab (KEYNOTE-158 trial) or dostarlimab (GARNET trial) for MSI-H or dMMR endometrial cancer (EC)
- KEYNOTE-146 trial: Pembrolizumab/lenvatinib for EC without MSI-H/dMMR; ongoing studies (KEYNOTE-775, LEAP-001)
- FDA approval of pembrolizumab for cervical cancer; ongoing studies (BEATcc, KEYNOTE-826, CALLA)
- KEYNOTE-100 trial: Pembrolizumab for advanced recurrent ovarian cancer
- Emerging data from the JAVELIN Ovarian 200, TOPACIO and MEDIOLA trials in ovarian cancer
- Key ongoing studies (FIRST, MOONSTONE, ATHENA, DUO-O) in ovarian cancer
- Randomized Phase II trial of carboplatin/paclitaxel +/- trastuzumab for HER2-positive uterine serous carcinoma
- Emerging clinical trial data with tisotumab vedotin; ongoing innovaTV 205 study

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In general, what treatment would you recommend for a patient with microsatellite-stable metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel?

1. Cisplatin/doxorubicin
2. Carboplatin/docetaxel
3. Lenvatinib/pembrolizumab
4. Test for PD-L1 combined positive score (CPS) and administer pembrolizumab if 1% or higher
5. Pembrolizumab
6. Other chemotherapy
7. Other

In general, what treatment would you recommend for a patient with MSI-high metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel?

1. Cisplatin/doxorubicin
2. Carboplatin/docetaxel
3. Lenvatinib/pembrolizumab
4. Pembrolizumab
5. Other chemotherapy
6. Other

In general, what treatment would you recommend for a patient with metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel if their disease was…

	Microsatellite stable (MSS)	MSI high (MSI-H)
 MICHAEL J BIRRER, MD, PHD	Lenvatinib/pembrolizumab	Pembrolizumab
 ROBERT L COLEMAN, MD	Lenvatinib/pembrolizumab	Pembrolizumab
 ANA OAKNIN, MD, PHD	Lenvatinib/pembrolizumab	Dostarlimab
 DAVID M O'MALLEY, MD	Lenvatinib/pembrolizumab	Pembrolizumab
 RICHARD T PENSON, MD, MRCP	Lenvatinib/pembrolizumab	Pembrolizumab
 MATTHEW A POWELL, MD	Lenvatinib/pembrolizumab	Pembrolizumab
 BRIAN M SLOMOVITZ, MD	Lenvatinib/pembrolizumab	Pembrolizumab
 KRISHNANSU S TEWARI, MD	Lenvatinib/pembrolizumab	Pembrolizumab
 PROFESSOR IGNACE VERGOTE	Lenvatinib/pembrolizumab	Pembrolizumab

For a patient with MSI-high metastatic endometrial cancer, outside of a clinical trial setting and regulatory and reimbursement issues aside, what is the earliest point at which you would introduce an anti-PD-1/PD-L1 antibody? Which regimen would you generally use?

	Earliest timing	Regimen
 MICHAEL J BIRRER, MD, PHD	Second line	Pembrolizumab
 ROBERT L COLEMAN, MD	Second line	Pembrolizumab
 ANA OAKNIN, MD, PHD	Second line	Dostarlimab
 DAVID M O'MALLEY, MD	First line	Pembrolizumab
 RICHARD T PENSON, MD, MRCP	First line	Pembrolizumab
 MATTHEW A POWELL, MD	Second line	Pembrolizumab
 BRIAN M SLOMOVITZ, MD	Second line	Pembrolizumab
 KRISHNANSU S TEWARI, MD	Second line	Pembrolizumab
 PROFESSOR IGNACE VERGOTE	First line	Pembrolizumab

In general, what would be your preferred first-line therapy for a patient with MSS metastatic cervical cancer who has received no prior systemic treatment?

 MICHAEL J BIRRER, MD, PHD	Cisplatin/paclitaxel/bevacizumab
 ROBERT L COLEMAN, MD	Cisplatin/paclitaxel/bevacizumab
 ANA OAKNIN, MD, PHD	Carboplatin/paclitaxel
 DAVID M O'MALLEY, MD	Cisplatin/paclitaxel/bevacizumab
 RICHARD T PENSON, MD, MRCP	Cisplatin/paclitaxel/bevacizumab
 MATTHEW A POWELL, MD	Cisplatin/paclitaxel/bevacizumab
 BRIAN M SLOMOVITZ, MD	Cisplatin/paclitaxel/bevacizumab
 KRISHNANSU S TEWARI, MD	Cisplatin/paclitaxel/bevacizumab
 PROFESSOR IGNACE VERGOTE	Carboplatin/paclitaxel/bevacizumab

In general, what would be your preferred first-line therapy for a patient with MSS metastatic cervical cancer who experienced relapse 12 months after receiving cisplatin-based chemoradiation therapy for Stage IIIB disease?

 MICHAEL J BIRRER, MD, PHD	Carboplatin/paclitaxel/bevacizumab
 ROBERT L COLEMAN, MD	Carboplatin/paclitaxel/bevacizumab
 ANA OAKNIN, MD, PHD	Cisplatin/paclitaxel/bevacizumab
 DAVID M O'MALLEY, MD	Carboplatin/paclitaxel/bevacizumab
 RICHARD T PENSON, MD, MRCP	Cisplatin/paclitaxel/bevacizumab
 MATTHEW A POWELL, MD	Carboplatin/paclitaxel/bevacizumab
 BRIAN M SLOMOVITZ, MD	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 KRISHNANSU S TEWARI, MD	Carboplatin/paclitaxel/bevacizumab
 PROFESSOR IGNACE VERGOTE	Carboplatin/paclitaxel/bevacizumab

CPS = combined positive score

In general, what would be your preferred second-line therapy for a patient with MSS metastatic cervical cancer who experiences disease progression on carboplatin/paclitaxel/bevacizumab?

1. Other chemotherapy
2. Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
3. Pembrolizumab
4. Other

In general, what would be your preferred second-line therapy for a patient with MSS metastatic cervical cancer who experienced disease progression on carboplatin/paclitaxel/bevacizumab?

 MICHAEL J BIRRER, MD, PHD	Pembrolizumab
 ROBERT L COLEMAN, MD	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 ANA OAKNIN, MD, PHD	Anti-PD-1/PD-L1 antibody in general
 DAVID M O'MALLEY, MD	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 RICHARD T PENSON, MD, MRCP	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 MATTHEW A POWELL, MD	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 BRIAN M SLOMOVITZ, MD	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 KRISHNANSU S TEWARI, MD	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 PROFESSOR IGNACE VERGOTE	Tisotumab vedotin

Do you generally evaluate microsatellite instability status in your patients with advanced ovarian cancer?

1. Yes
2. No

Do you generally evaluate microsatellite instability status in your patients with advanced ovarian cancer?

 MICHAEL J BIRRER, MD, PHD	Yes
 ROBERT L COLEMAN, MD	Yes
 ANA OAKNIN, MD, PHD	No
 DAVID M O'MALLEY, MD	Yes
 RICHARD T PENSON, MD, MRCP	Yes
 MATTHEW A POWELL, MD	Yes
 BRIAN M SLOMOVITZ, MD	No
 KRISHNANSU S TEWARI, MD	No
 PROFESSOR IGNACE VERGOTE	No

Meet The Professor with Dr O'Malley

MODULE 1: Cases from Dr Mirza

MODULE 2: Gynecologic Oncology Journal Club with Dr O'Malley

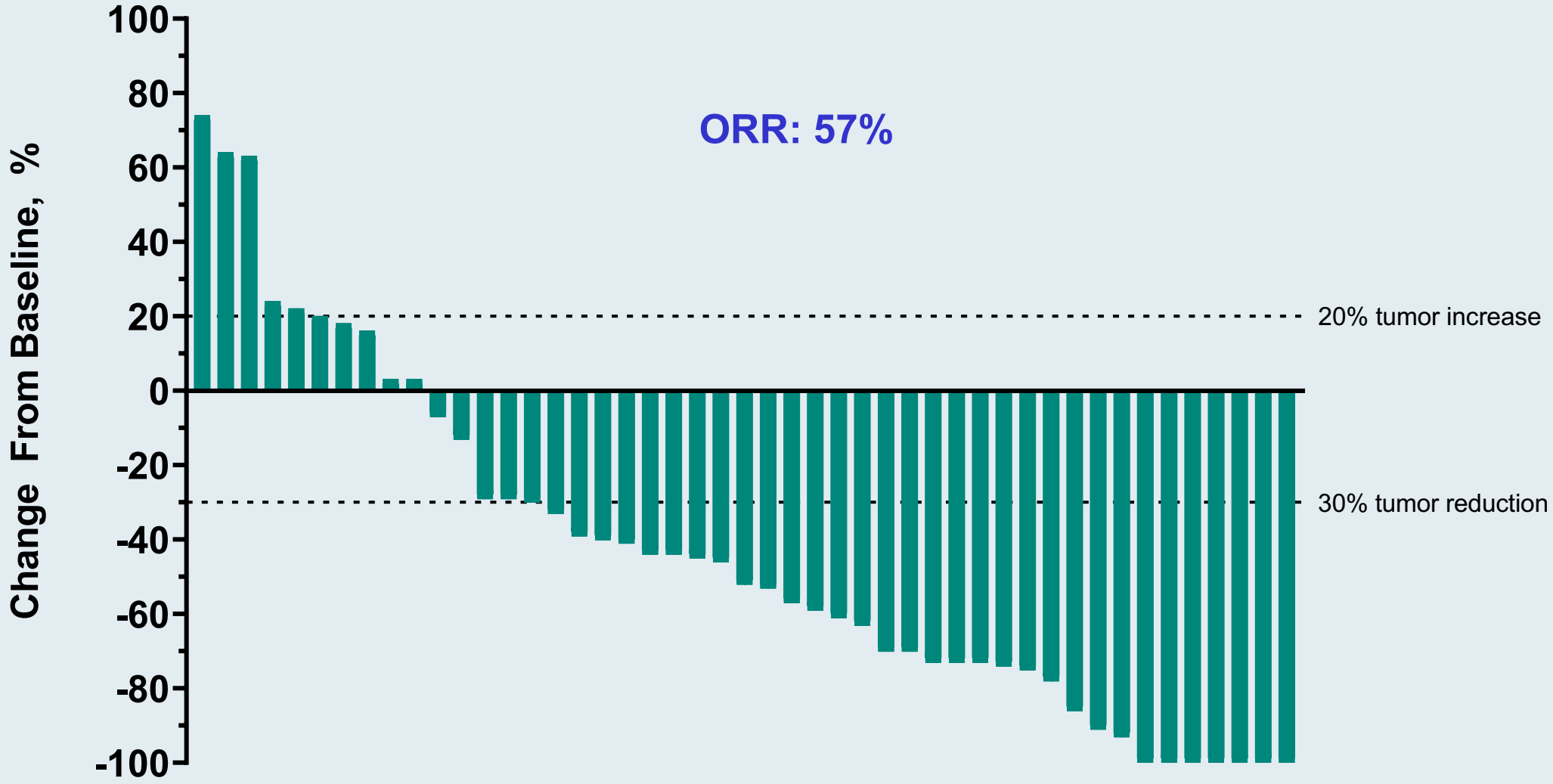
MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Data Sets

- Pembrolizumab (KEYNOTE-158 trial) or dostarlimab (GARNET trial) for MSI-H or dMMR endometrial cancer (EC)
- KEYNOTE-146 trial: Pembrolizumab/lenvatinib for EC without MSI-H/dMMR; ongoing studies (KEYNOTE-775, LEAP-001)
- FDA approval of pembrolizumab for cervical cancer; ongoing studies (BEATcc, KEYNOTE-826, CALLA)
- KEYNOTE-100 trial: Pembrolizumab for advanced recurrent ovarian cancer
- Emerging data from the JAVELIN Ovarian 200, TOPACIO and MEDIOLA trials in ovarian cancer
- Key ongoing studies (FIRST, MOONSTONE, ATHENA, DUO-O) in ovarian cancer
- Randomized Phase II trial of carboplatin/paclitaxel +/- trastuzumab for HER2-positive uterine serous carcinoma
- Emerging clinical trial data with tisotumab vedotin; ongoing innovaTV 205 study

RTP RESEARCH TO PRACTICE

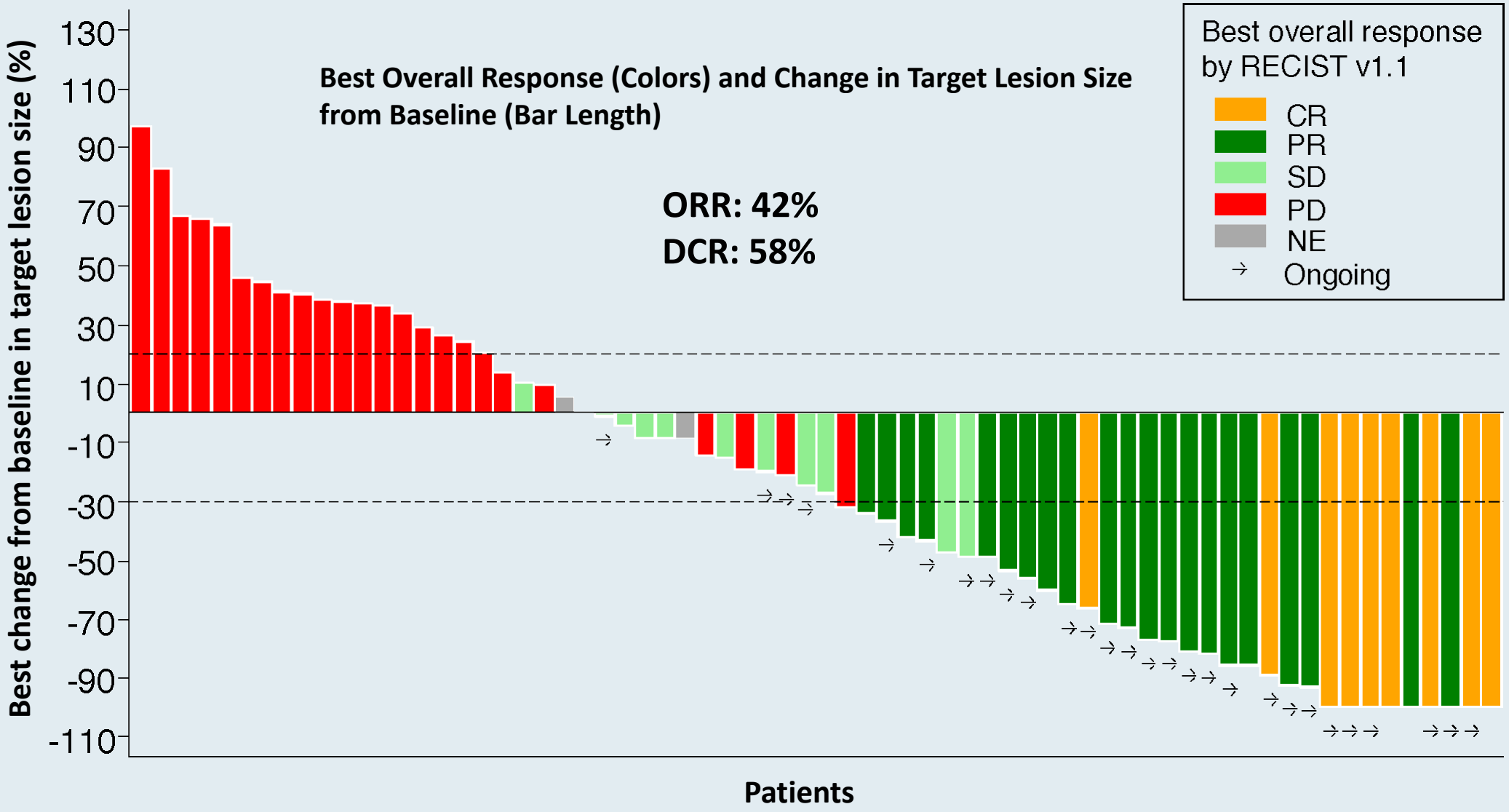
KEYNOTE-158: Best Percentage Change from Baseline in Target Lesion Size with Pembrolizumab Monotherapy in MSI-H Endometrial Cancer



O'Malley DM et al. ESMO 2019;Abstract 1044P.

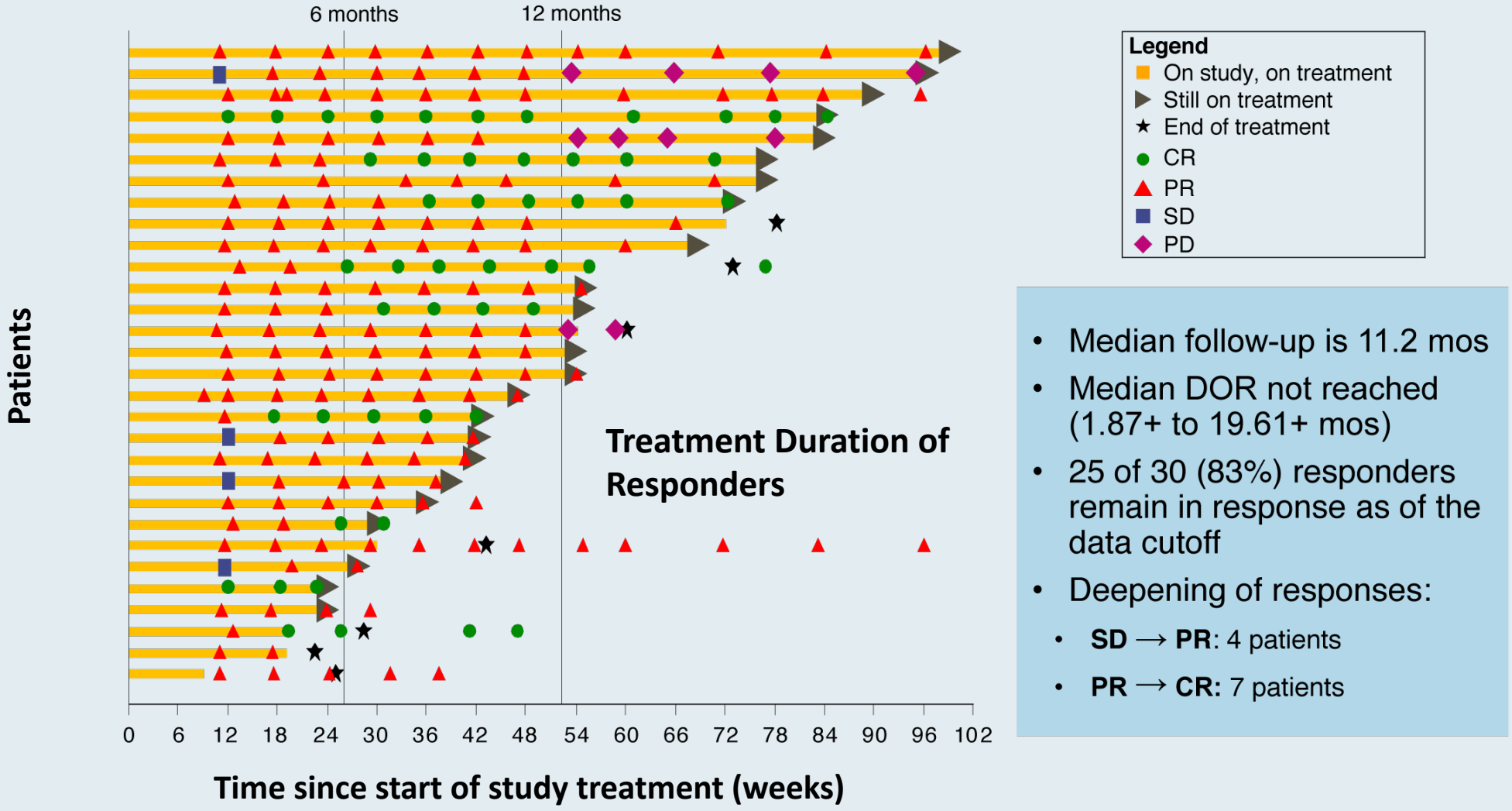
RTP RESEARCH TO PRACTICE

GARNET: Dostarlimab in Recurrent or Advanced dMMR Endometrial Cancer



Oaknin A et al. SGO 2020;Abstract LBA9.

GARNET: Dostarlimab in Recurrent or Advanced dMMR Endometrial Cancer

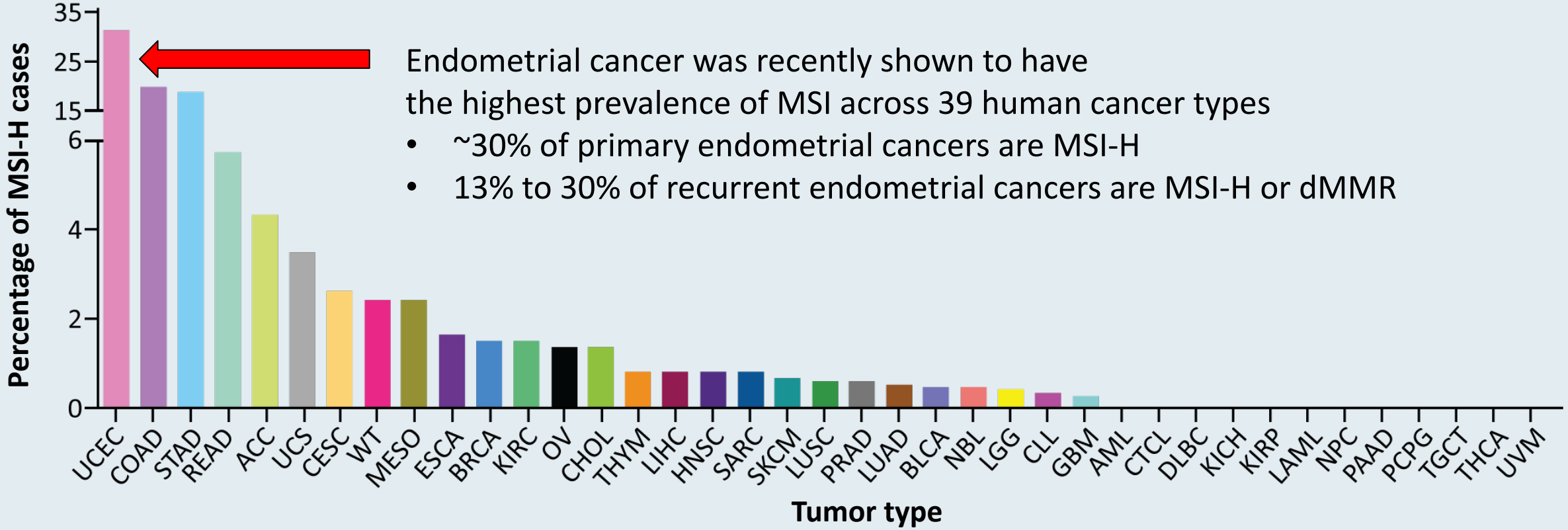


- Median follow-up is 11.2 mos
- Median DOR not reached (1.87+ to 19.61+ mos)
- 25 of 30 (83%) responders remain in response as of the data cutoff
- Deepening of responses:
  - **SD → PR**: 4 patients
  - **PR → CR:** 7 patients

Oaknin A et al. SGO 2020;Abstract LBA9.

MSI-High Across 39 Cancer Types

Whole-exome data from 11,139 tumor-normal pairs from The Cancer Genome Atlas and Therapeutically Applicable Research to Generate Effective Treatments projects



Endometrial cancer was recently shown to have the highest prevalence of MSI across 39 human cancer types

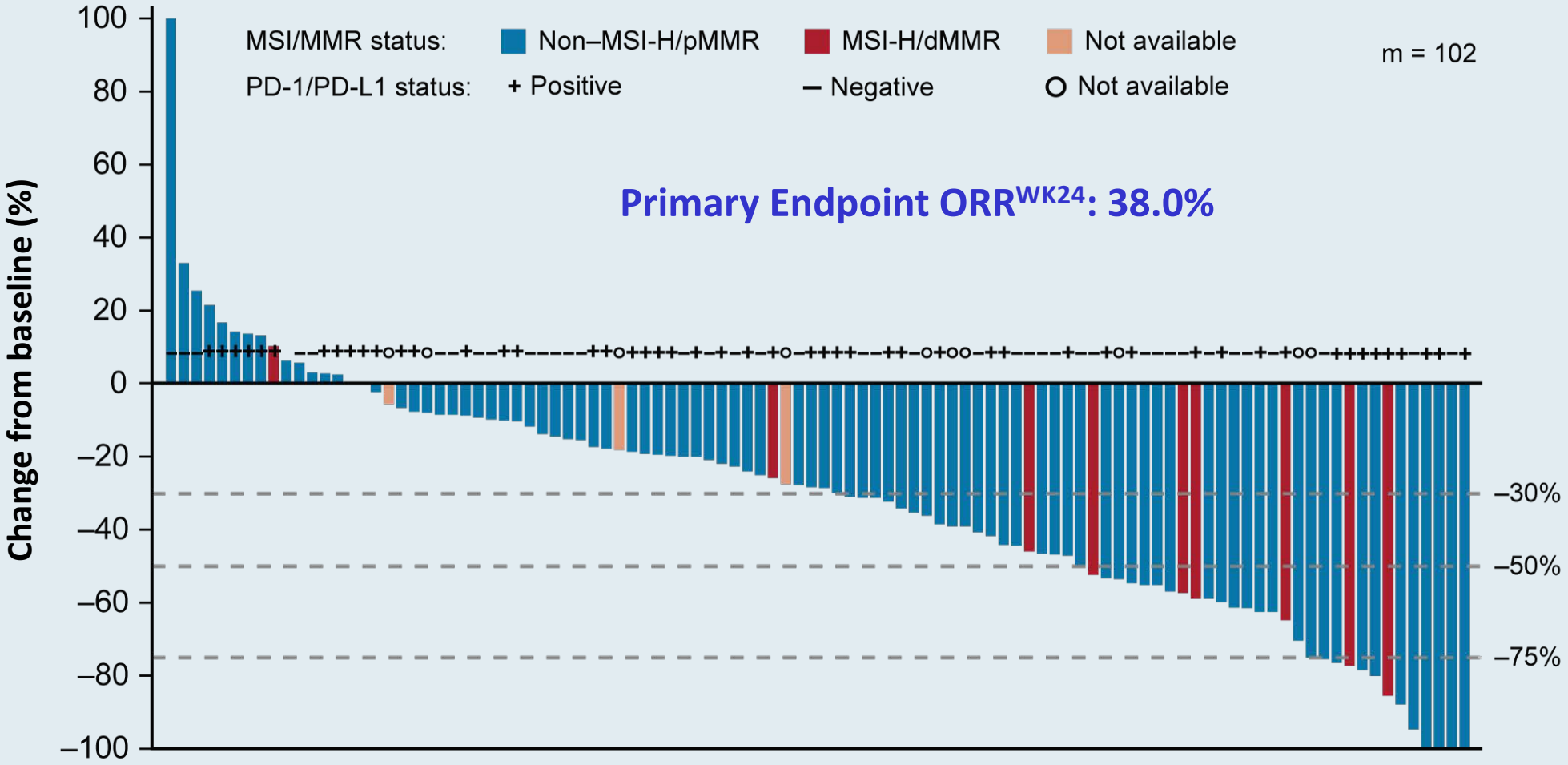
- ~30% of primary endometrial cancers are MSI-H
- 13% to 30% of recurrent endometrial cancers are MSI-H or dMMR

UCEC = uterine corpus endometrial carcinoma

Bonneville R et al. *JCO Precis Oncol* 2017;2017:10.1200/PO.17.00073; Green AK et al. *ASCO Educational Book* 2020.

RTP RESEARCH TO PRACTICE

KEYNOTE-146: Pembrolizumab/Lenvatinib in Advanced Endometrial Cancer That Is *Not* MSI-H or dMMR After Disease Progression on Prior Systemic Therapy



Makker V et al. *J Clin Oncol* 2020;[Online ahead of print].

RTP RESEARCH TO PRACTICE

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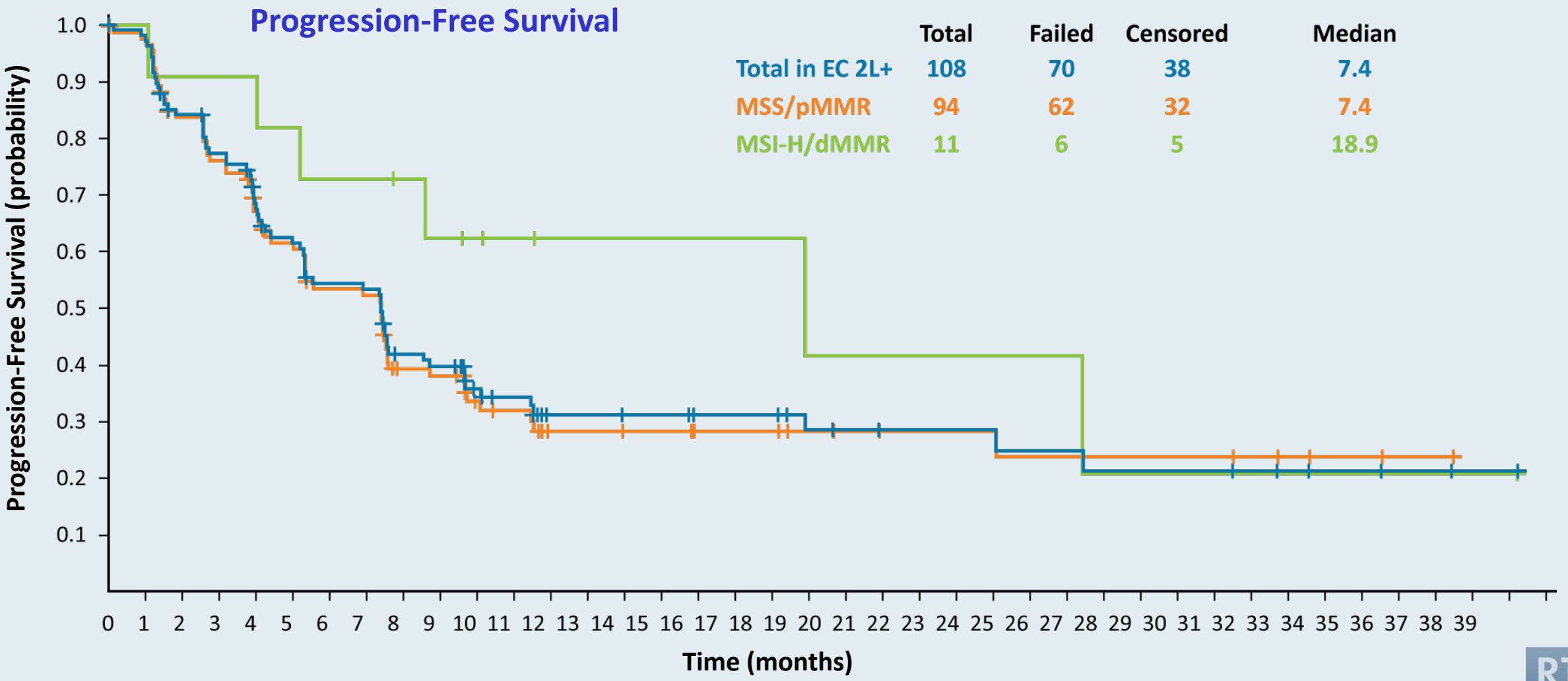
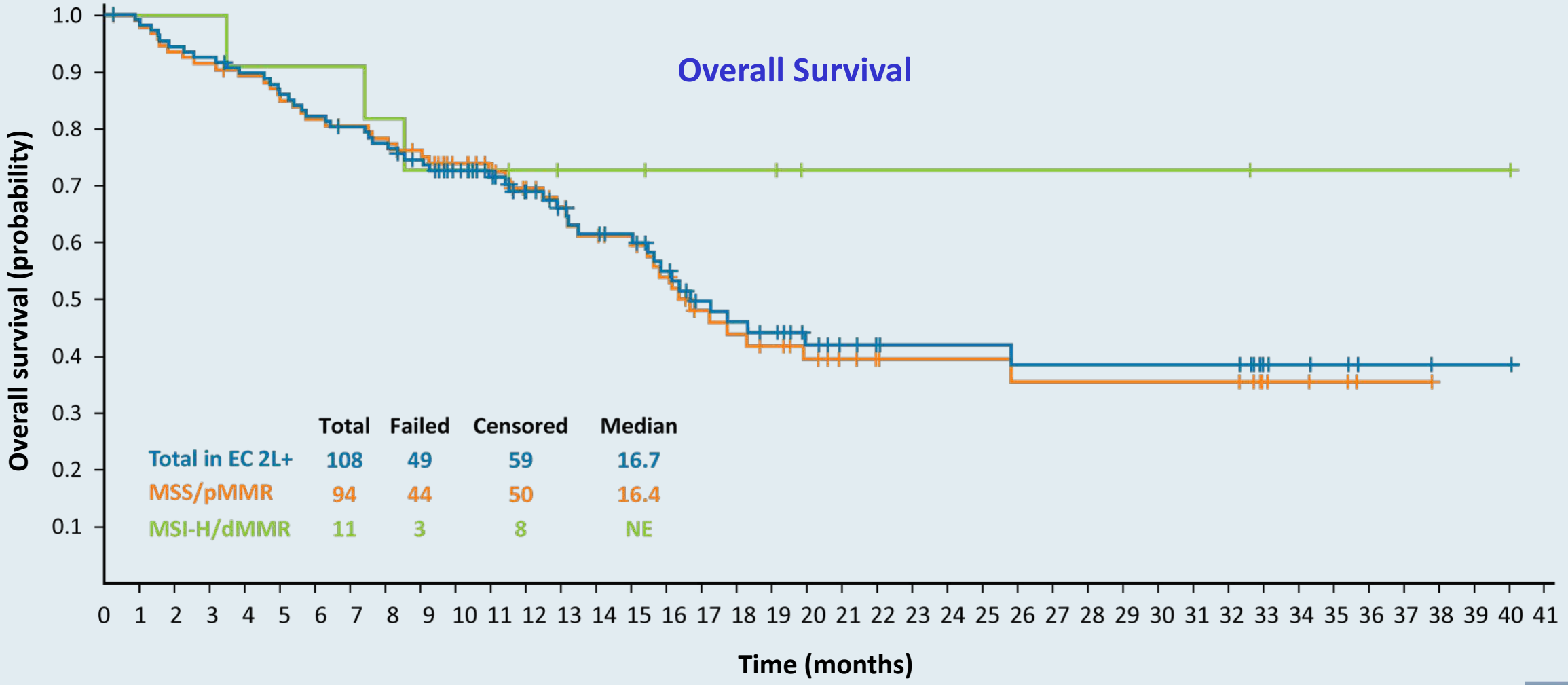


Makker V et al. *J Clin Oncol* 2020;[Online ahead of print].

RTP RESEARCH TO PRACTICE

KEYNOTE-146: Pembrolizumab/Lenvatinib in Advanced Endometrial Cancer That Is *Not* MSI-H or dMMR After Progression on Prior Systemic Therapy



Makker V et al. *J Clin Oncol* 2020;[Online ahead of print].

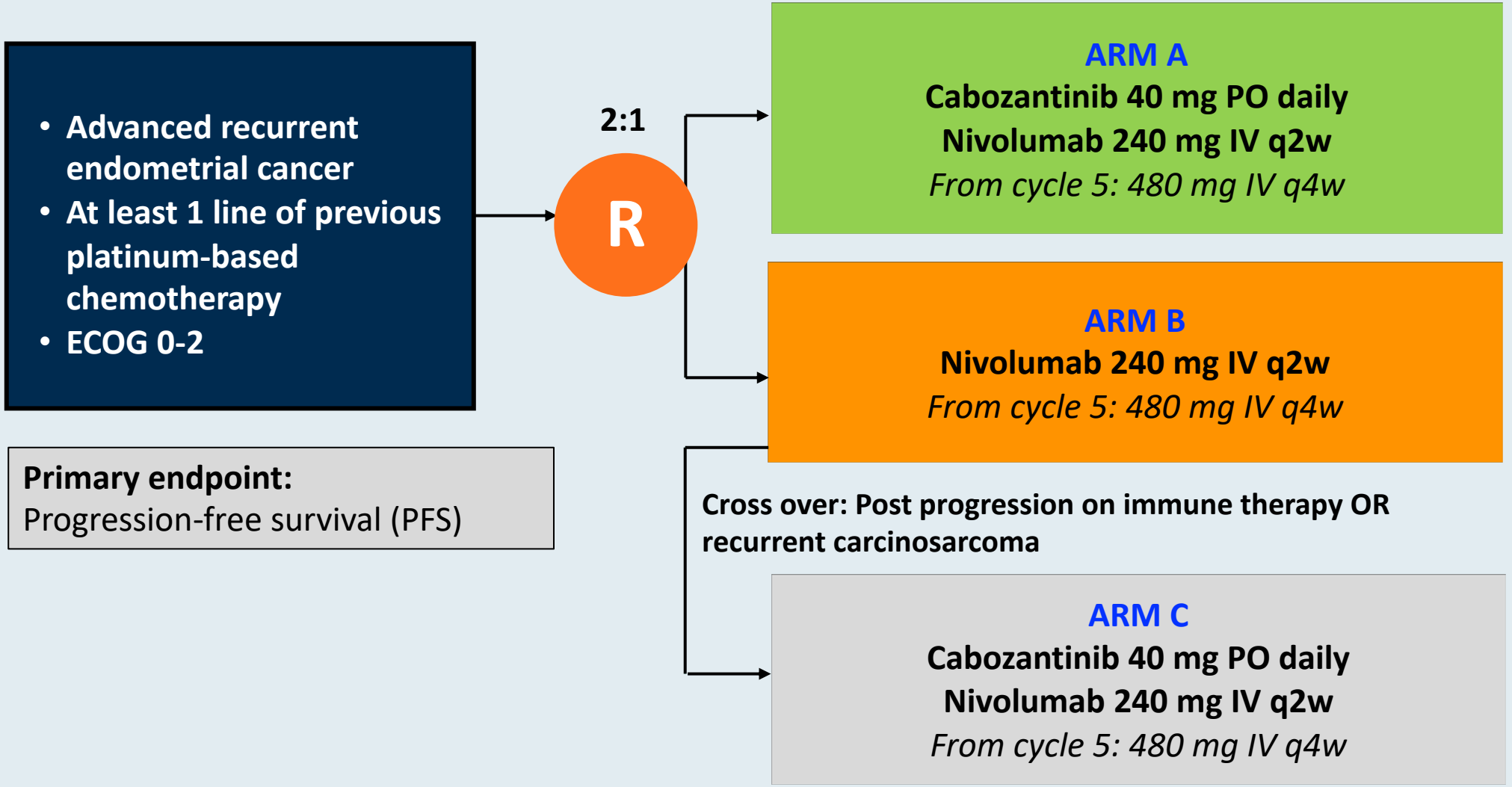
RTP RESEARCH TO PRACTICE

NCI 10104: A Randomized Phase 2 Study of Cabozantinib in Combination with Nivolumab in Advanced, Recurrent Metastatic Endometrial Cancer

Lheureux S et al.

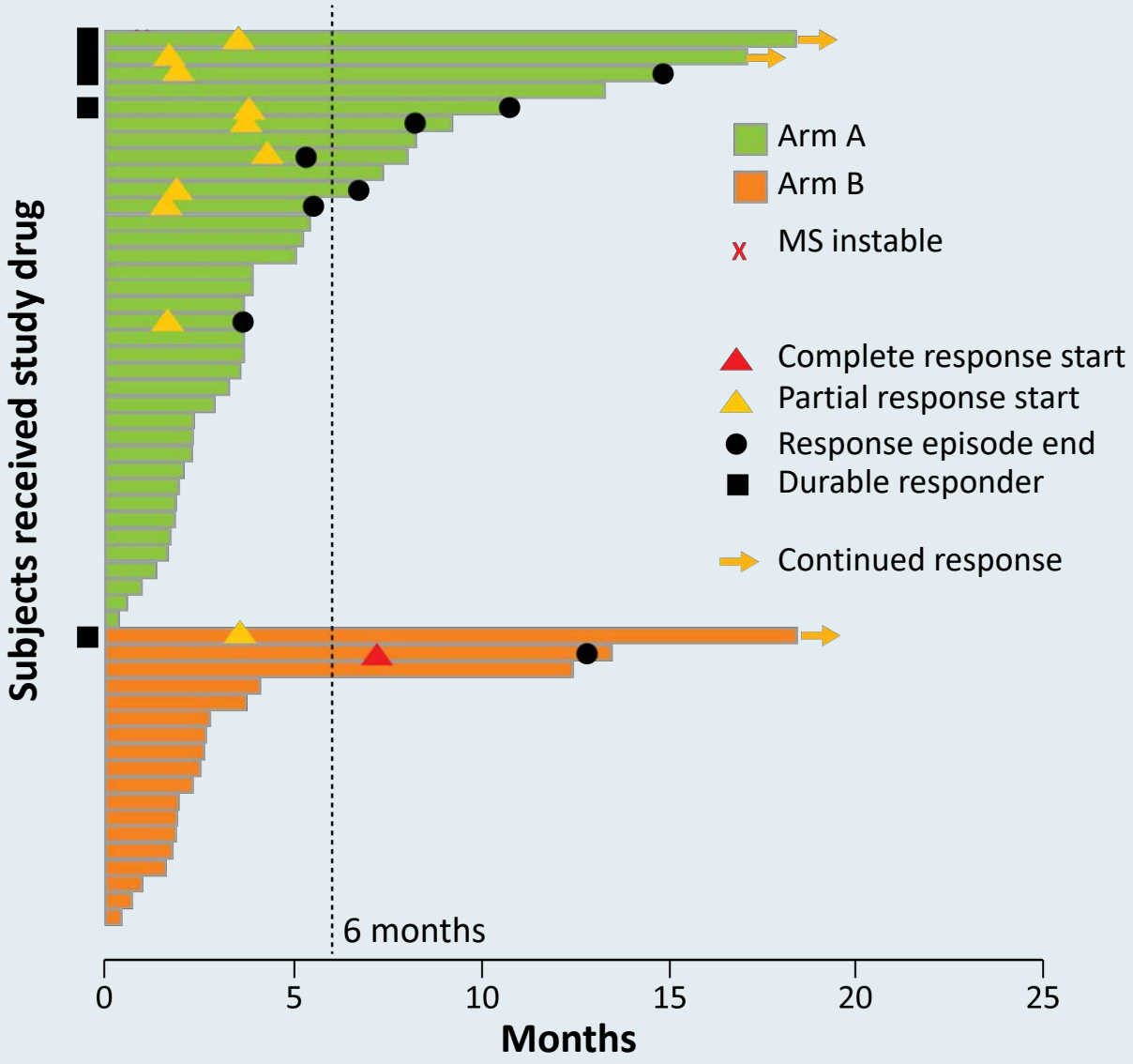
ASCO 2020;Abstract 6010.

NCI 10104 Phase II Study Schema



Lheureux S et al. ASCO 2020;Abstract 6010.

NCI 10104: Response Rate and Duration and Survival Analyses



	Arm A Cabo/nivolumab (n = 36)	Arm B Nivolumab (n = 18)
ORR	25%	11%
SD as best response	44%	11%
CBR	69%	22%
Median PFS*	5.3 mo	1.9 mo
Median OS†	13.0 mo	7.9 mo

* HR: 0.59, significant

† Immature, 55% events

Lheureux S et al. ASCO 2020;Abstract 6010.

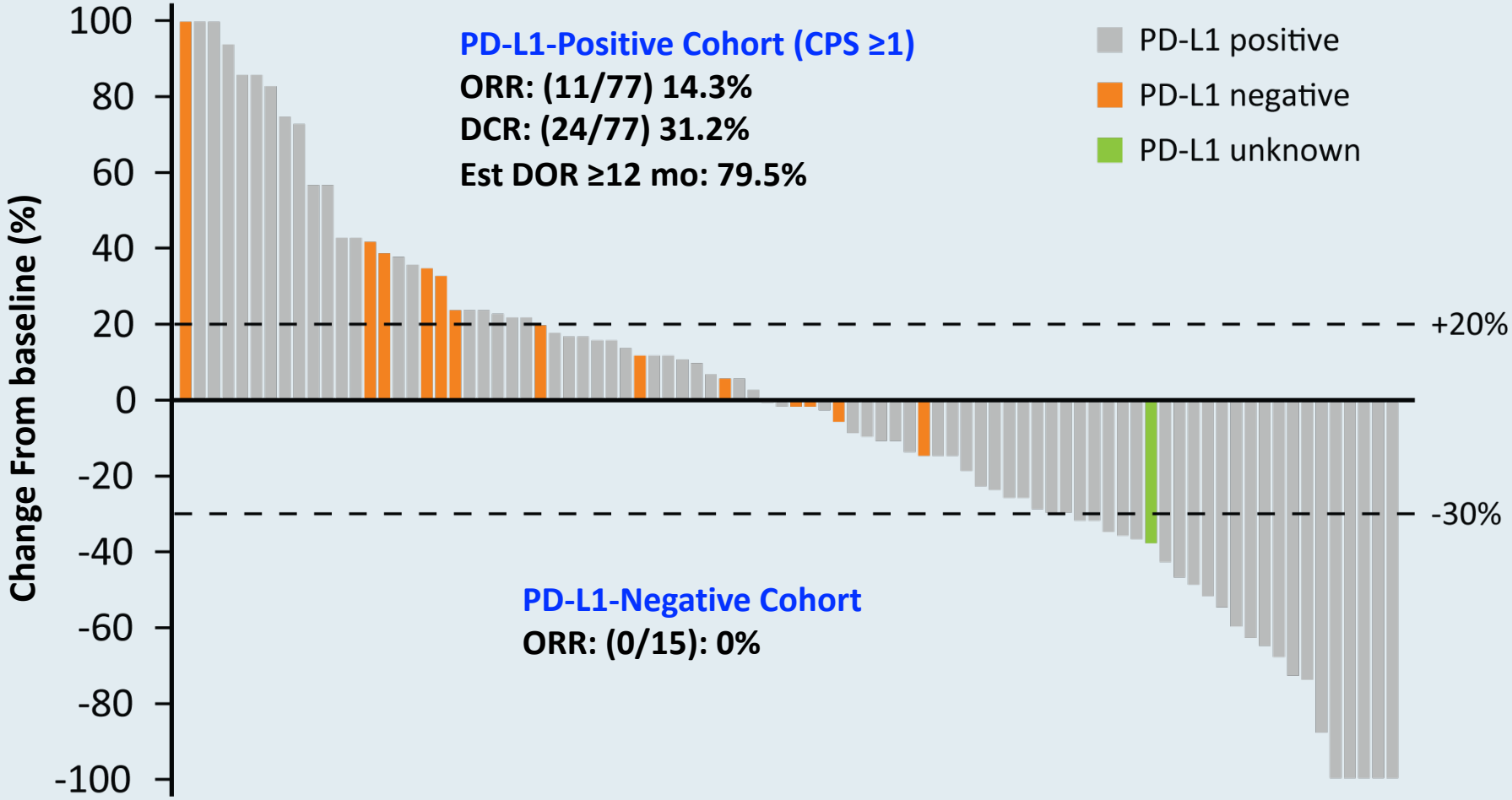
Select Ongoing Phase III Immune Checkpoint Inhibitor Combination Studies

Trial	N	Eligibility	Randomization
KEYNOTE-775	780	• Advanced, recurrent or metastatic EC • PD after 1 prior platinum-based chemo regimen	• Pembro + lenvatinib • Paclitaxel + carboplatin
LEAP-001	720	• Stage III, IV or recurrent EC • May have received 1 prior line of platinum-based adjuvant or neoadjuvant chemo	• Pembro + lenvatinib • Paclitaxel + carboplatin
NRG-GY018	810	• Stage III, IVA or IVB or recurrent EC • No prior chemo for EC, except adjuvant	• Pembro + paclitaxel + carboplatin → Pembro • Placebo + paclitaxel + carboplatin → Placebo
RUBY	470	• Stage III, IV or first recurrent EC	• Dostarlimab + paclitaxel + carboplatin • Placebo + paclitaxel + carboplatin
AtTEnd	550	• Newly dx with residual disease after surgery, OR inoperable Stage III-IV naïve to first-line systemic treatment	• Atezolizumab + paclitaxel + carboplatin • Placebo + paclitaxel + carboplatin

Clinicaltrials.gov. Accessed August 18, 2020; Green AK et al. *ASCO Ed Book* 2020.

Anti-PD-1/PD-L1 Antibodies in Cervical Cancer

Phase II KEYNOTE-158: Pembrolizumab in Previously Treated Advanced Cervical Cancer

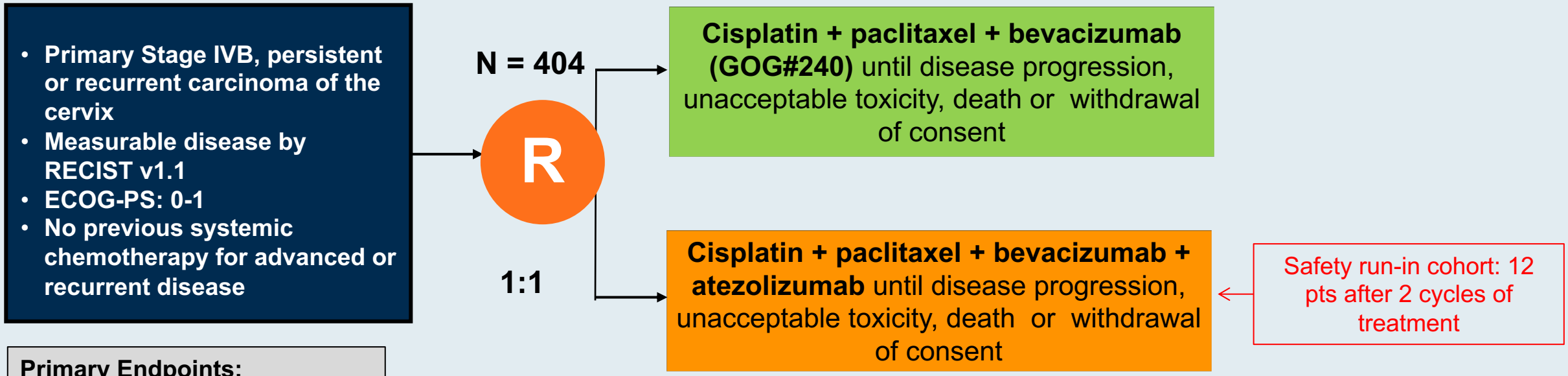


Combined Positive Score (CPS) = PD-L1+ cells (tumor cells, lymphocytes, macrophages) / Total number of tumor cells x 100

Chung HC et al. *J Clin Oncol* 2019;37:1470-8.

RTP RESEARCH TO PRACTICE

BEATcc Phase III Randomized Front-Line Trial of Atezolizumab



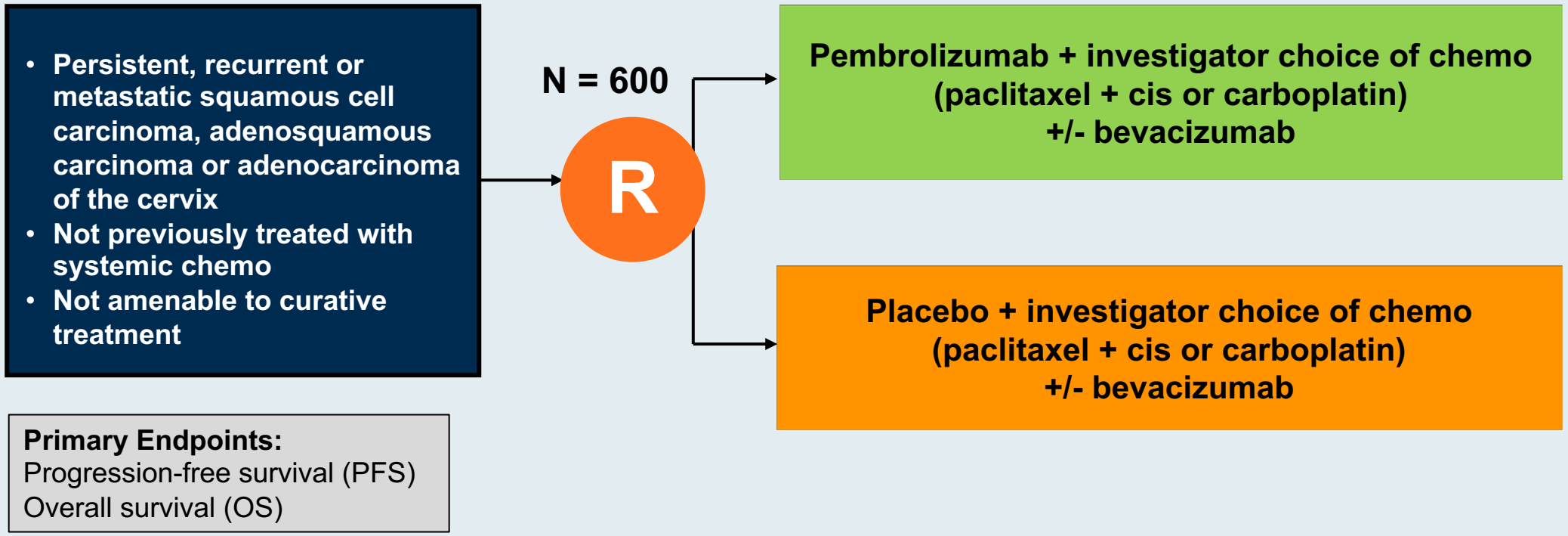
Primary Endpoints:
Overall survival (OS)
Secondary Endpoints:
- PFS
- ORR
- DOR
- Safety
- HR-QOL

Stratification Factors:
- Prior concurrent Cisplatin-RDT
- Histology: SCC vs ADK (including AdenoSquamous)
- Chemotherapy Backbone: Cisplatin vs Carboplatin

ClinicalTrials.gov Identifier: NCT03556839

Courtesy of Krishnansu S Tewari, MD

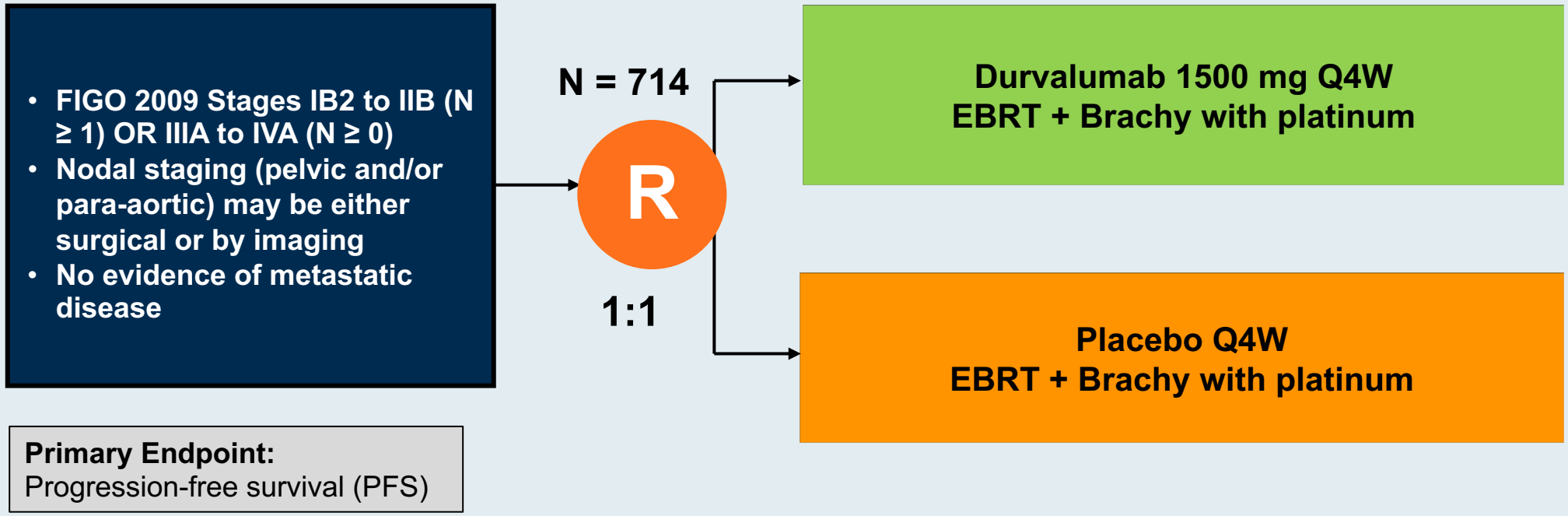
KEYNOTE-826 Phase III Schema



Primary Endpoints:
Progression-free survival (PFS)
Overall survival (OS)

ClinicalTrials.gov Identifier: NCT03635567, Accessed August 18, 2020

CALLA Phase III Schema



Primary Endpoint:
Progression-free survival (PFS)

Mayadev J et al. *Int J Gynecol Cancer* 2020;30:1065-1070.

Anti-PD-1/PD-L1 Antibodies in Ovarian Cancer

FDA-Approved Indications for Immunotherapy in Ovarian Cancer

Pembrolizumab: 2017 FDA approval for MSI-high/MMR deficient cancers

- The incidence of germline MMR gene mutations in high grade serous cancers is 1-8%
- MMR deficiency is more common in non-serous ovarian cancer

2020 ASCO ovarian cancer genetics guidelines re MMR testing:

- Women diagnosed with clear cell, endometrioid, or mucinous ovarian cancer should be offered somatic tumor testing for mismatch repair deficiency
- Testing for MMR deficiency may be offered to women diagnosed with other histologic types of epithelial ovarian cancer

Xiao X, et al. *Gynecol Oncol.* 2014.; Morice P, et al. *N Engl J Med.* 2019.; Konstantinopoulos PA, et al. *J Clin Oncol.* 2020; Murphy MA Cancer 2011

Courtesy of Ursula Matulonis, MD

Final Results from the KEYNOTE-100 Trial of Pembrolizumab in Patients with Advanced Recurrent Ovarian Cancer

Matulonis UA et al.

ASCO 2020;Abstract 6005.

KEYNOTE-100 Phase II, 2-Cohort Study Schema

Patients (N = 376)

- Recurrent, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer
- ECOG PS 0 or 1
- Provision of a tumor sample for biomarker analysis

Key exclusion criteria

- Mucinous histology
- No bowel obstruction within 3 months
- No active autoimmune disease
- No active CNS metastases and/or carcinomatous meningitis

Cohort A
1-3 prior lines
PFI or TFI of 3-12 months

Total enrollment: n = 285

Pembrolizumab 200 mg IV q3wk until PD, prohibitive toxicity, death, or completion of 2 years

Cohort B
4-6 prior lines
PFI or TFI of ≥3 months

Total enrollment: n = 91

PFI = platinum-free interval; TFI = treatment-free interval

Matulonis UA et al. ASCO 2020;Abstract 6005.

KEYNOTE-100: Summary of Efficacy, Including by PD-L1 Status

Endpoint	Cohort A 1-3 prior lines PFI/TFI 3-12 months			Cohort B 4-6 prior lines PFI/TFI ≥3 months			Cohorts A + B All comers		
	All n = 285	CPS ≥1 n = 101	CPS ≥10 n =43	All n = 91	CPS ≥1 n = 49	CPS ≥10 n = 22	All n = 376	CPS ≥1 n = 150	CPS ≥10 n = 65
ORR	8.1%	6.9%	11.6%	9.9%	10.2%	18.2%	8.5%	8.0%	13.8%
DoR	8.3 mo	Not reported	Not reported	23.6 mo	Not reported	Not reported	10.2 mo	Not reported	Not reported
OS	18.7 mo	20.6 mo	21.9 mo	17.6 mo	20.7 mo	24.0 mo	Not reported	Not reported	Not reported

Matulonis UA et al. ASCO 2020;Abstract 6005.

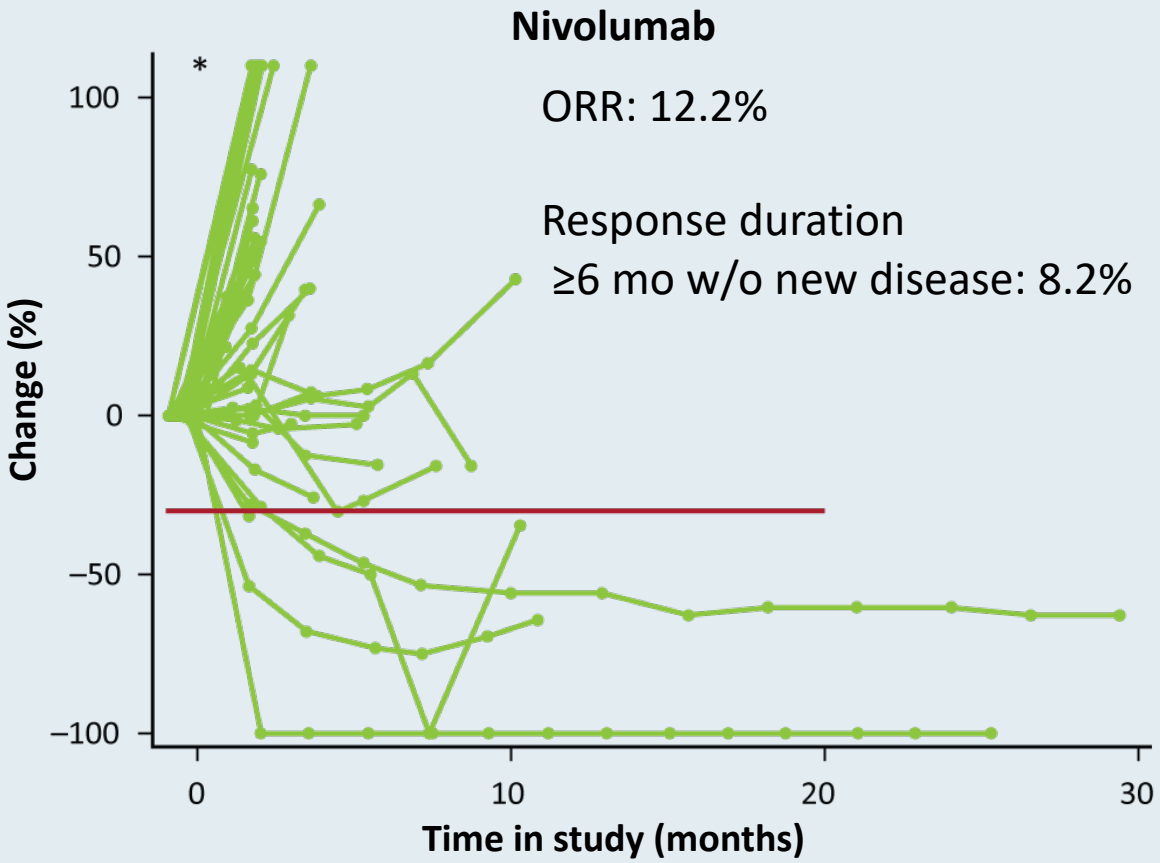
JAVELIN Ovarian 200: Avelumab Alone or in Combination with Pegylated Liposomal Doxorubicin (PLD) versus PLD Alone in Platinum-Resistant or Refractory OC

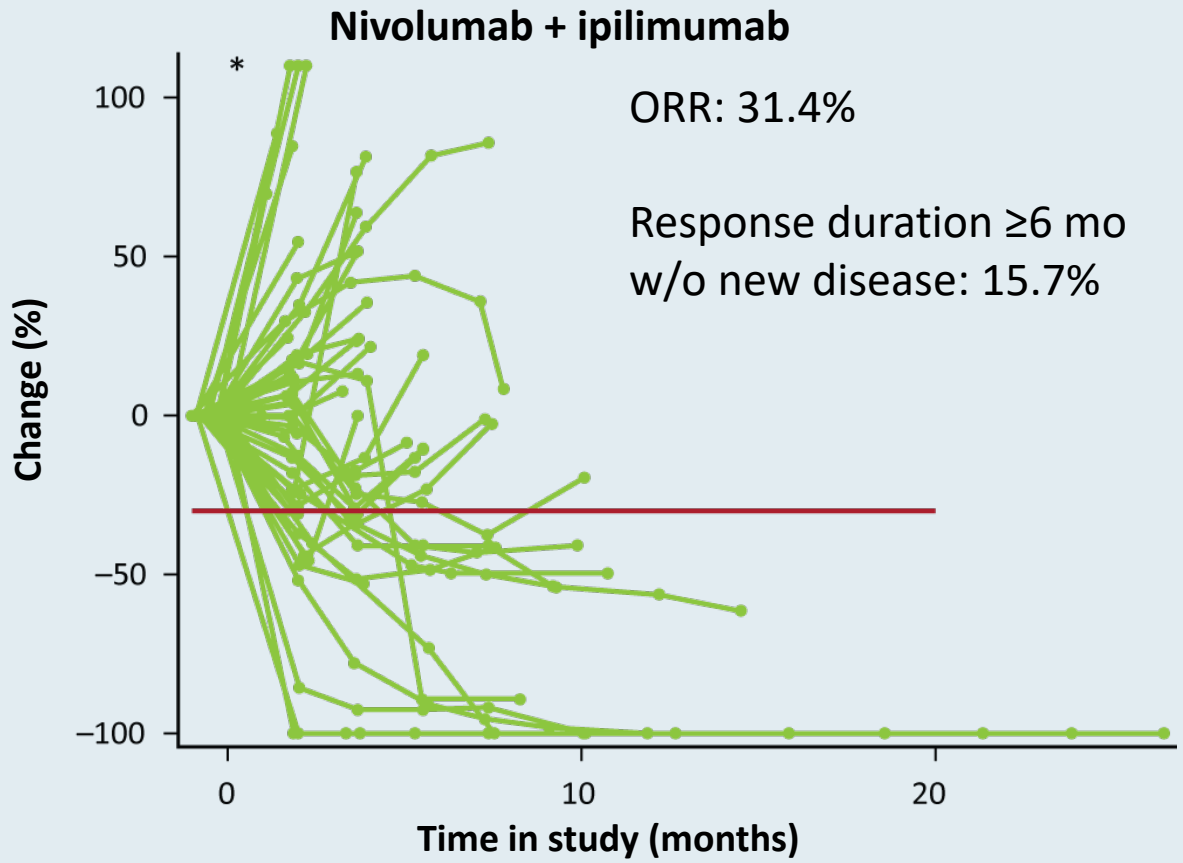
	Avelumab (n = 188)		Avelumab + PLD (n = 188)		PLD (n = 190)	
All patients						
Median OS	11.8 mo		15.7 mo		13.1 mo	
	HR: 1.14, *p* = 0.83		HR: 0.80, *p* = 0.21		Reference	
Median PFS	1.9 mo		3.7 mo		3.5 mo	
	HR: 1.68, *p* > 0.99		HR: 0.78, *p* = 0.03		Reference	
PD-L1 evaluable	**PD-L1+ (n = 91)**	**PD-L1- (n = 62)**	**PD-L1+ (n = 92)**	**PD-L1- (n = 58)**	**PD-L1+ (n = 73)**	**PD-L1- (n = 66)**
Median OS	13.7 mo	10.5 mo	18.4 mo	12.7 mo	13.8 mo	13.1 mo
	HR: 0.80	HR: 1.4	HR: 0.72	HR: 1.1	Ref	Ref
Median PFS	1.9 mo	1.8 mo	3.7 mo	3.9 mo	1.9 mo	3.7 mo
	HR: 1.3	HR: 1.8	HR: 0.59	HR: 0.92	Ref	Ref

Pujade-Lauraine E et al. SGO 2019; Abstract LBA1.

NRG GY003 Phase II Study of Nivolumab with or without Ipilimumab in Recurrent or Persistent OC

(PFI <6 months: 62%, ≥2 prior cytotoxic regimens: 70%+ of patients)

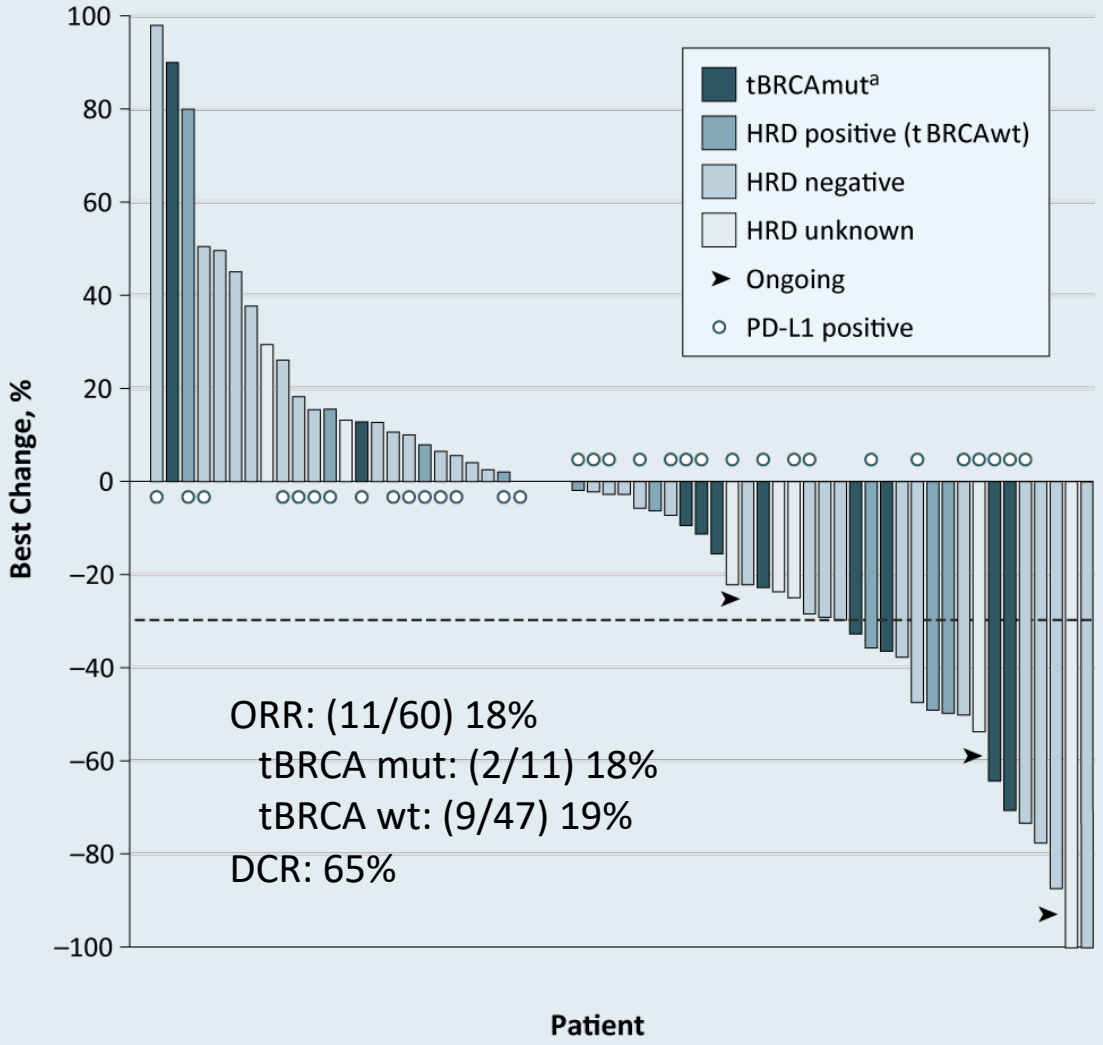


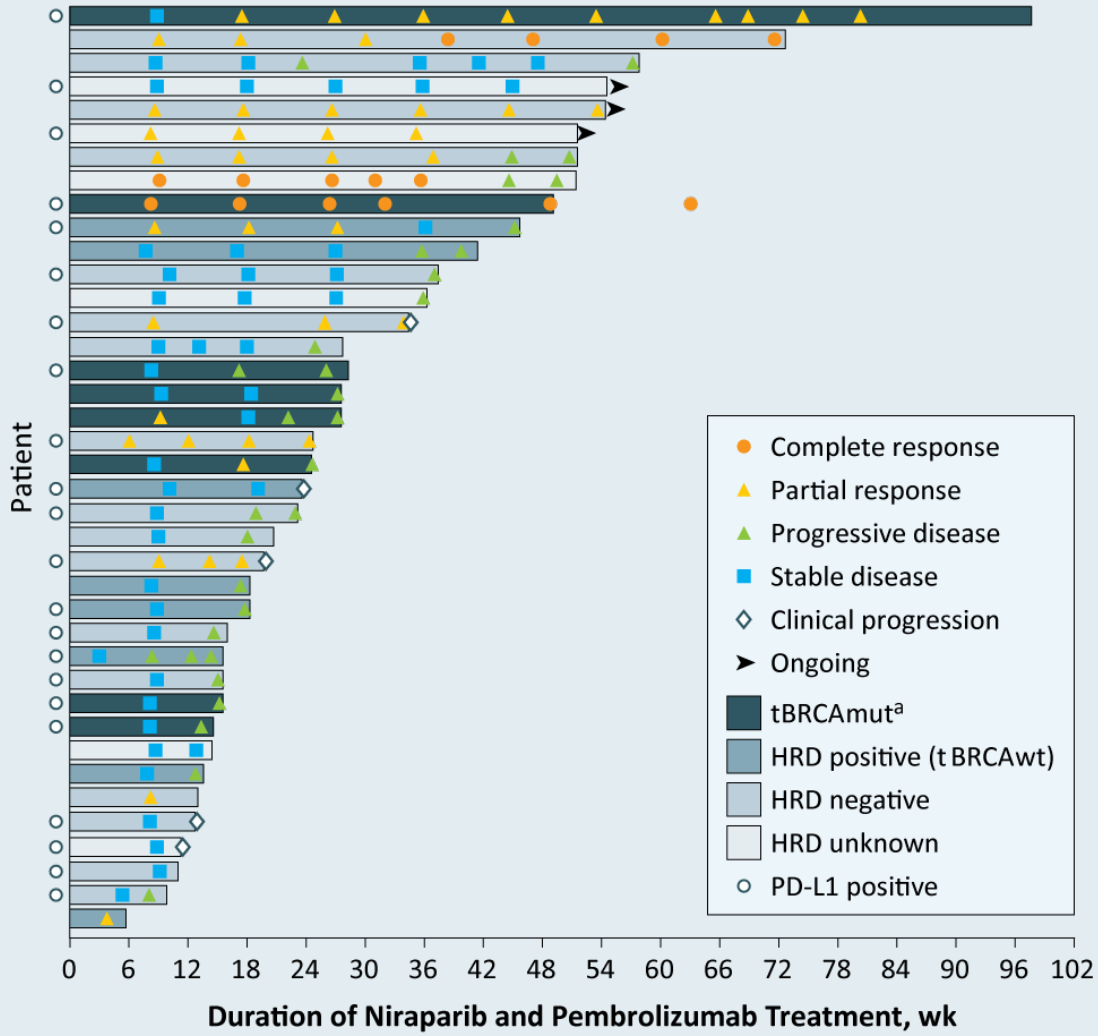


PD-L1 expression was not significantly associated with response in either treatment group

Zamarin D et al. *J Clin Oncol* 2020;38:1814-23.

TOPACIO/KEYNOTE-162: Niraparib and Pembrolizumab in Recurrent Platinum-Resistant Ovarian Cancer

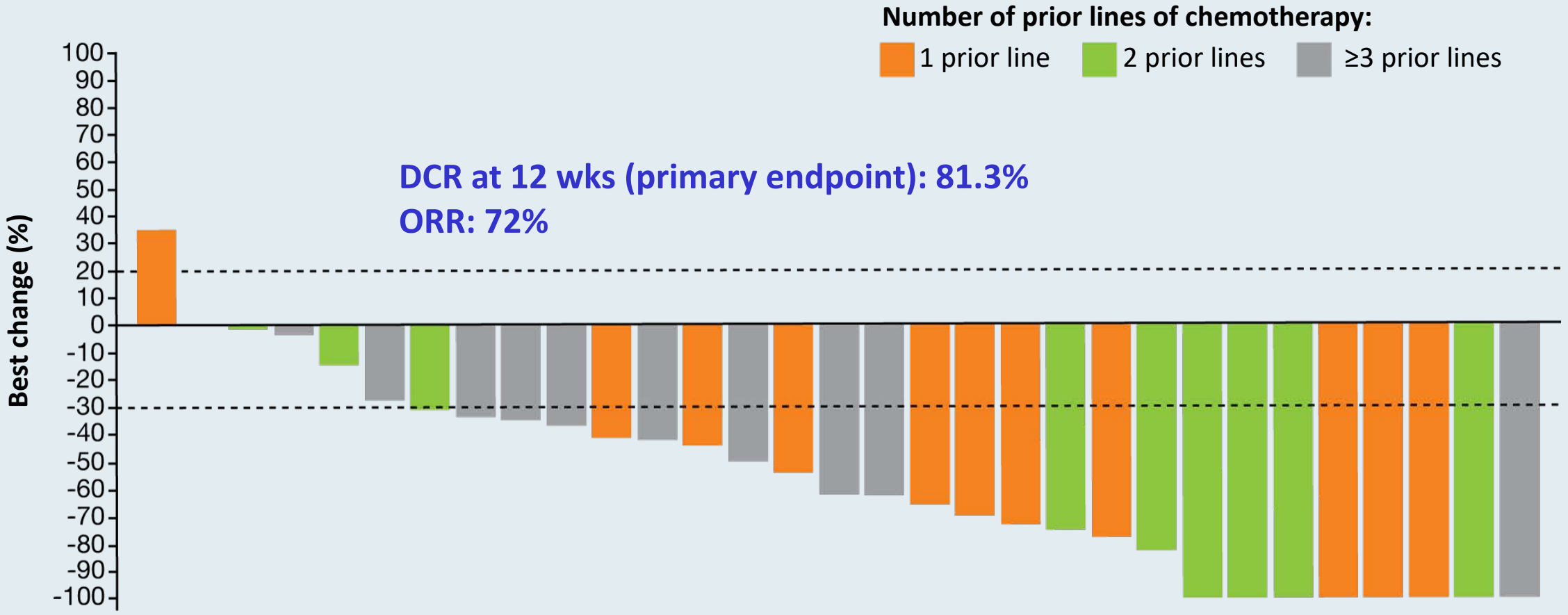




Konstantinopoulos PA, et al. *JAMA Oncol* 2019;5(8):1141-9.

RTP RESEARCH TO PRACTICE

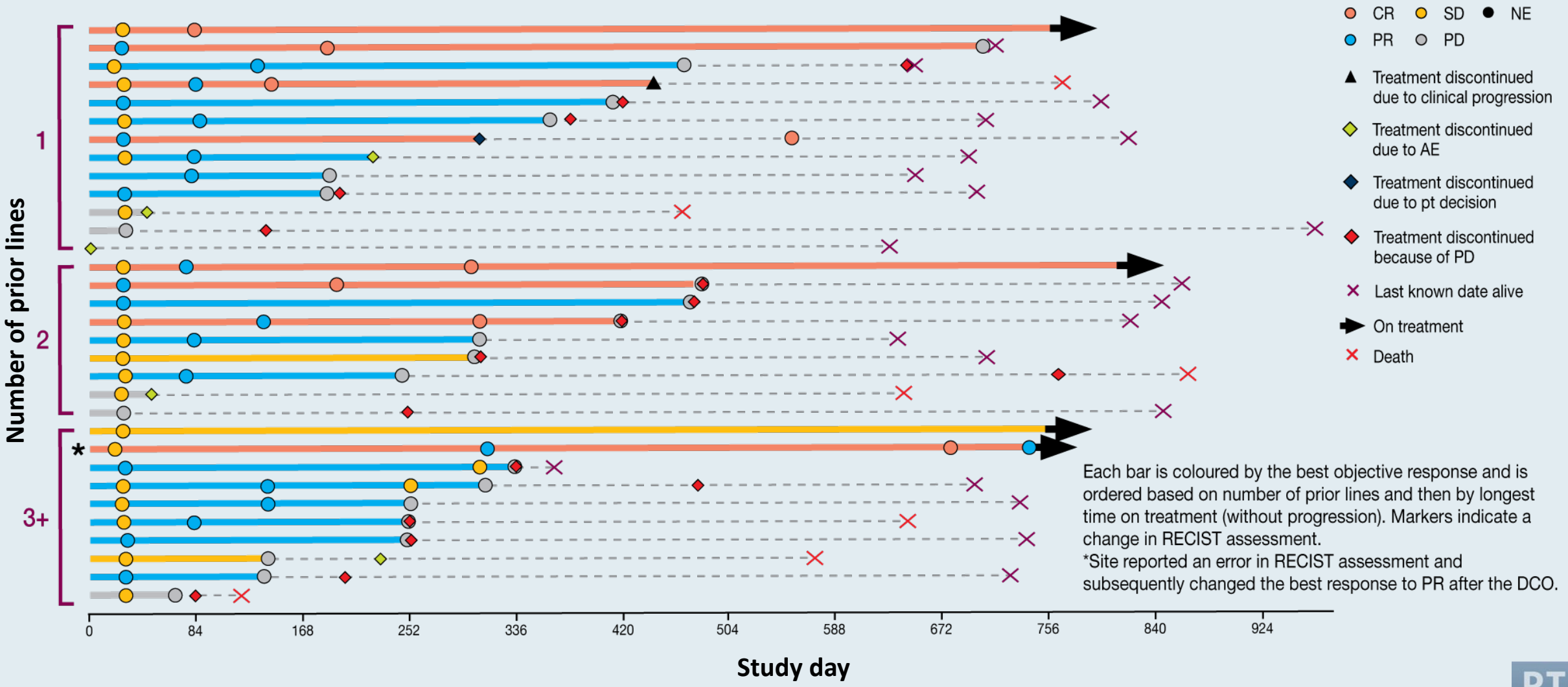
MEDIOLA: A Phase II Study of Olaparib and Durvalumab in gBRCA-Mutated Platinum-Sensitive Relapsed OC



Drew Y et al. ESMO 2019;Abstract 1190PD.

RTP RESEARCH TO PRACTICE

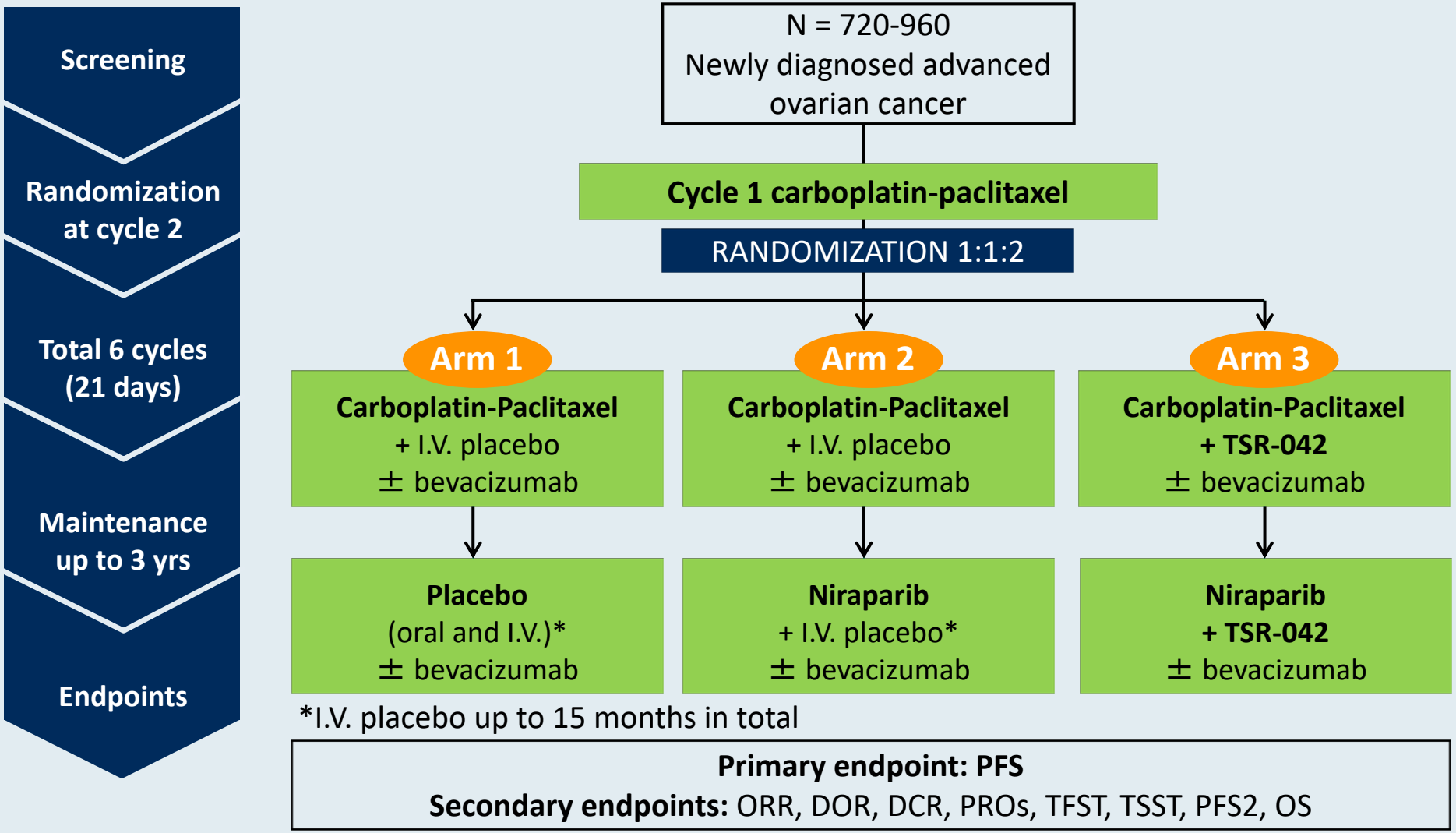
MEDIOLA: Time to Disease Progression or Treatment Discontinuation, Based on Number of Prior Lines of Therapy



Drew Y et al. ESMO 2019;Abstract 1190PD.

RTP RESEARCH TO PRACTICE

FIRST Phase III Trial of Dostarlimab (TSR-042) in Newly Diagnosed Ovarian Cancer



www.clinicaltrials.gov/ct2/show/NCT03602859

Courtesy of Ursula Matulonis, MD

Phase II MOONSTONE Study Design

Eligibility

- Completed 1-3 prior lines of therapy for advanced or metastatic ovarian cancer
- Previously treated with platinum-based chemo, taxane and bevacizumab
- Resistant to last administered platinum agent
- No known BRCA 1 or 2 mutation

N=150

Niraparib + Dostarlimab

Primary endpoint: ORR
Secondary endpoints: DOR, PFS, OS, DCR

https://clinicaltrials.gov/ct2/show/NCT03955471?term=MOONSTONE&draw=2&rank=1

Select Ongoing Phase III Trials of Immunotherapy in Combination with PARP Inhibitors

Trial name (Trial identifier)	N	Setting	Treatment arms
ATHENA (NCT03522246)	1,012	Maintenance therapy after 1L platinum-based chemo	• Rucaparib + nivolumab • Rucaparib + placebo • Nivolumab + placebo • Placebo
DUO-O (NCT03737643)	1,056	Maintenance therapy after 1L platinum-based chemo/bev ± durvalumab	• Bevacizumab • Bevacizumab + durvalumab • Bevacizumab + durvalumab + olaparib

www.clinicaltrials.gov. Accessed August 2020.

HER2-Positive Endometrial Cancer

HER2 Testing in Endometrial Serous Carcinoma

Current Criteria (Approved or Proposed) for HER2 Positivity by Immunohistochemistry (IHC) and Fluorescence In Situ Hybridization (FISH) in Different Tumor Types

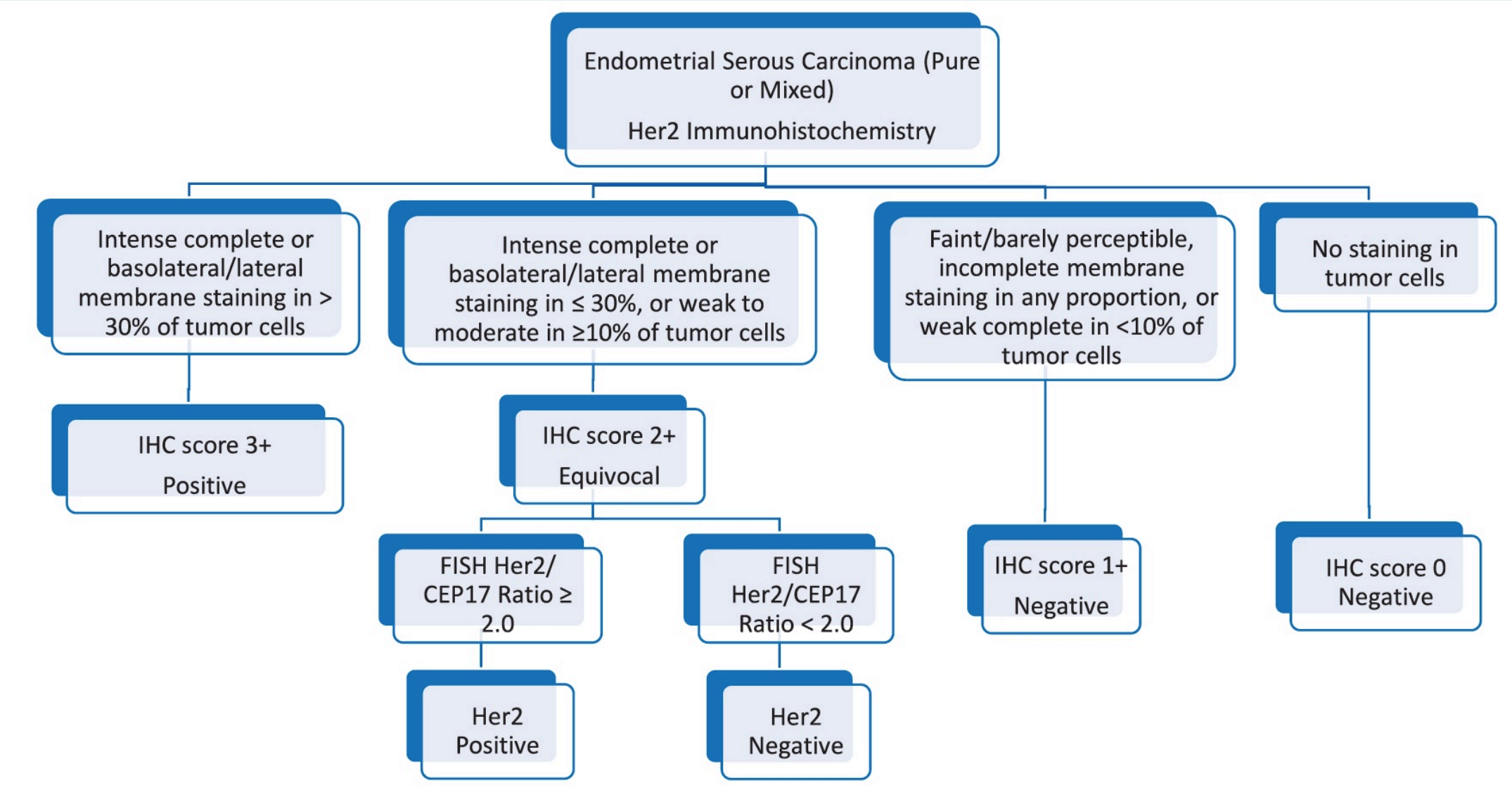
	Breast (ASCO/CAP 2018)[23]	Gastric (ASCO/CAP 2016)[36]	Colorectal (HERACLES Trial)[39]	Endometrial Serous (Fader et al Clinical Trial)[21]
HER2 IHC 3+	>10% circumferential, strong, complete	≥10%, strong complete, or basolateral/lateral	≥50% strong complete, or basolateral/lateral	>30% strong complete or basolateral/lateral
HER2 FISH amplification	*HER2*/CEP17 ratio ≥2.0 and *HER2* signal ≥4.0 per nucleus OR ratio <2.0 and *HER2* signal ≥6.0 per nucleus (if IHC score 2+ or 3+)	*HER2*/CEP17 ratio ≥2.0 OR ratio <2.0 and *HER2* signal >6.0 per nucleus	*HER2*/CEP17 ratio ≥2.0 in ≥50% of cells	*HER2*/CEP17 ratio ≥2.0

Abbreviations: ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists.

Buza N. *Arch Pathol Lab Med* 2020;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Proposed HER2 Testing Algorithm for Endometrial Serous Carcinoma



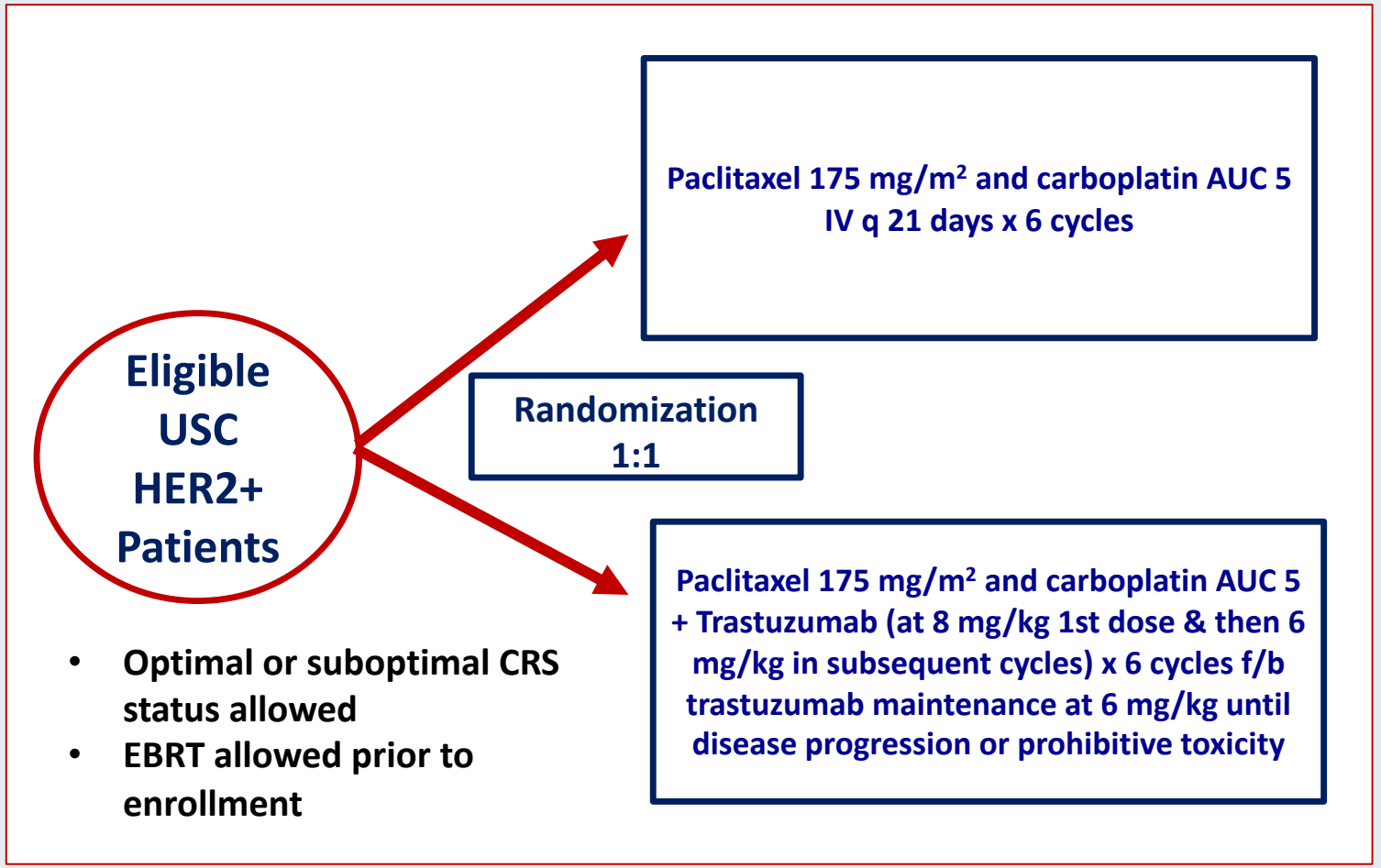
Buza N. *Arch Pathol Lab Med* 2020;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Randomized Phase II Trial of Carboplatin/Paclitaxel versus Carboplatin/Paclitaxel/Trastuzumab for Uterine Serous Carcinoma That Overexpresses HER2/Neu: Updated Survival Analysis

Eligibility

- FIGO Stage III-IV USC or recurrent USC
- HER2/neu+ USC as defined by IHC score of 3+ (ASCO/CAP 2007 criteria) or 2+ with gene amplification confirmed by FISH
- Patients diagnosed with recurrence were required to have measurable disease, defined as at least one target lesion per RECIST 1.1
- Patients with recurrent disease may not have received >3 prior chemotherapies for treatment of their EC, and a treatment-free interval of >6 months from last C/T was required for patients with recurrent disease

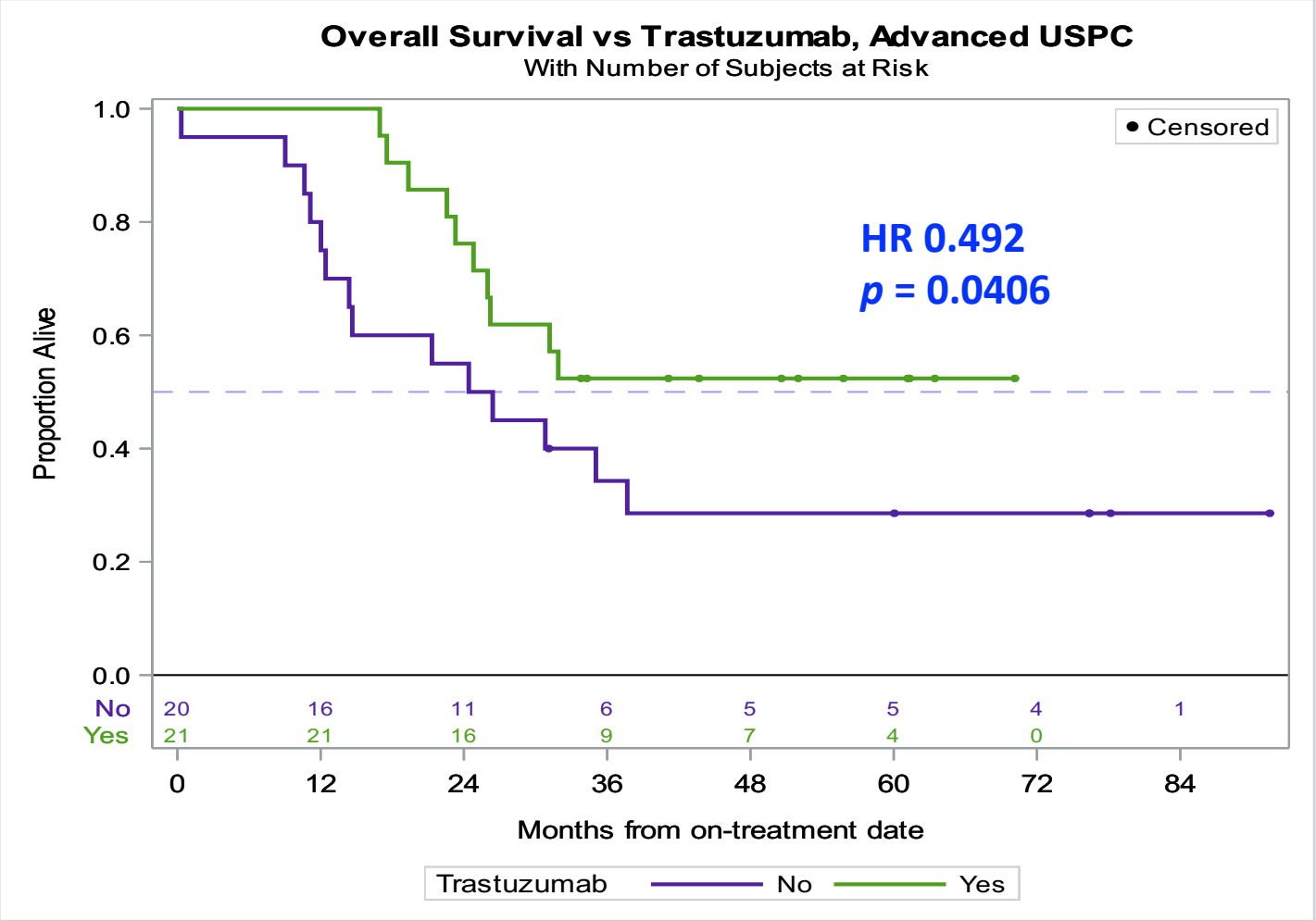


Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

Courtesy of David M O'Malley, MD

Overall Survival with the Addition of Trastuzumab to Carboplatin/ Paclitaxel for Advanced Uterine Serous Papillary Carcinoma (USPC)

- Benefit was particularly striking in the Stage III-IV pts, with a median OS of 25.4 mo (control) compared with an unreached median OS (experimental; *p* = 0.0406, HR 0.492)



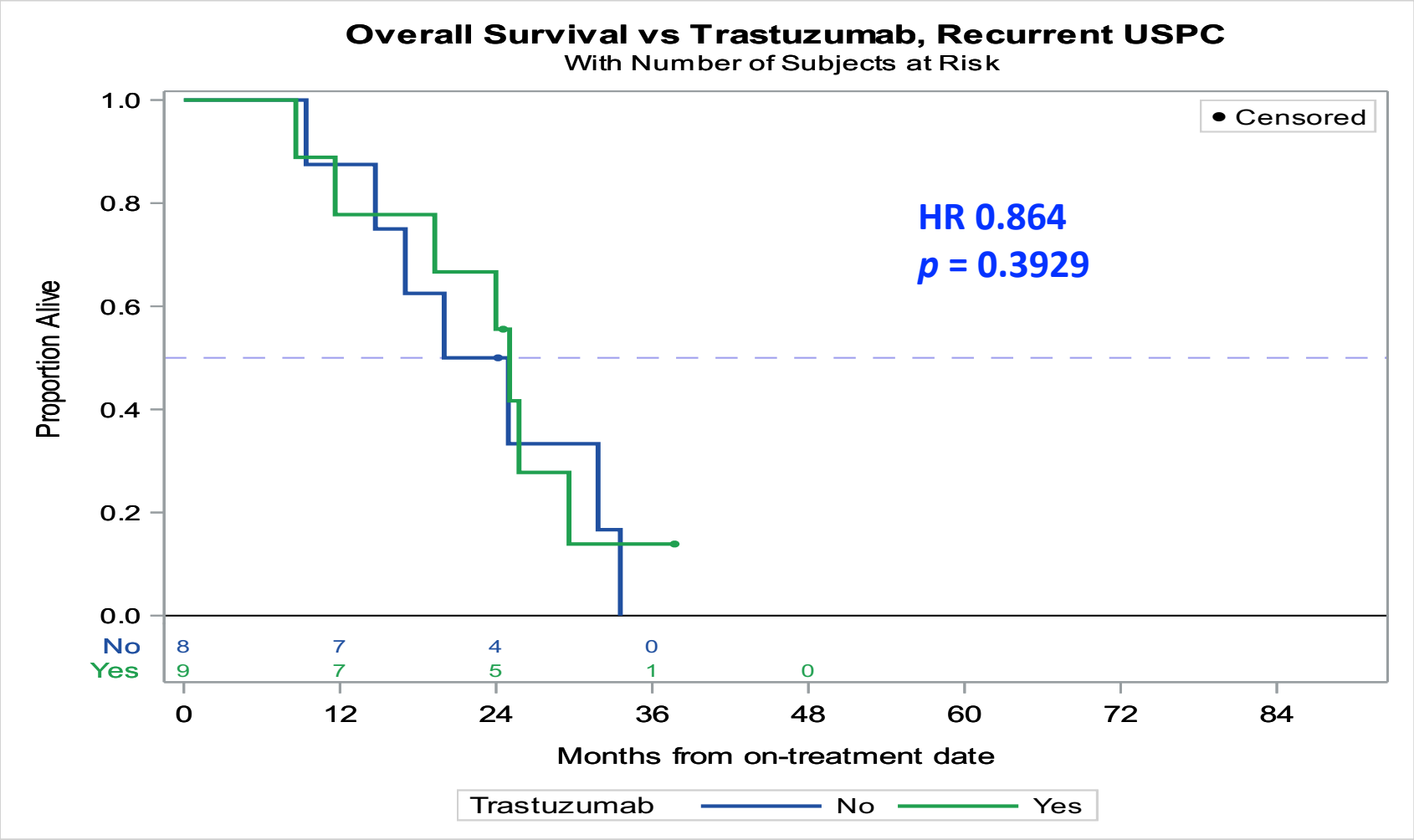
Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

Courtesy of David M O'Malley, MD

RTP RESEARCH TO PRACTICE

Overall Survival with the Addition of Trastuzumab to Carboplatin/Paclitaxel for Recurrent USPC

- No significant OS benefit was observed in the recurrence cohort



Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

Courtesy of David M O'Malley, MD

Carboplatin/Paclitaxel/Trastuzumab: Summary

- First trial of targeted therapy in USC ONLY patients
- Demonstration that HER2 is an important prognostic and actionable target in USC
- NCCN designation of C/T/Trastuzumab as a preferred regimen in HER2+ USC (Level IIA)

Fader AN et al. SGO 2020

Courtesy of David M O'Malley, MD

Phase II DESTINY-PanTumor02 Study Design

Trial Identifier: NCT04482309 (Not yet recruiting)
Estimated Enrollment: 280

Eligibility

- Locally advanced, unresectable or metastatic disease
- Disease progression after prior treatment or no satisfactory alternative treatment option
- Prior HER2-targeted therapy allowed
- HER2 expression may be based on local or central assessment

Trastuzumab deruxtecan

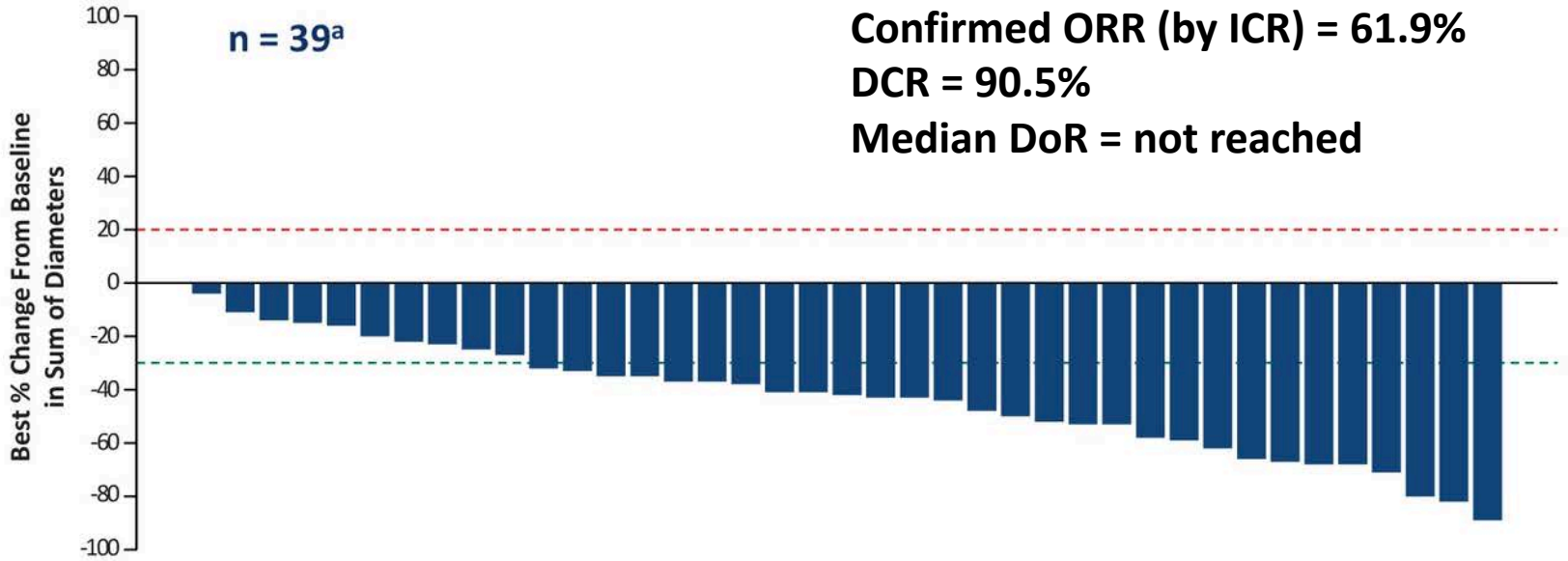
7 cohorts will be evaluated:
Endometrial cancer, cervical cancer, ovarian cancer, bladder cancer, biliary tract cancer, pancreatic cancer and rare tumors

Primary endpoint: ORR
Secondary endpoints include DOR, PFS, OS, DCR

https://www.clinicaltrials.gov/ct2/show/NCT04482309.

DESTINY-Lung01: Best Change in Tumor Size

Trastuzumab Deruxtecan in Lung Cancer



Based on independent central review. Baseline is last measurement taken before enrollment. Shown is best (minimum) percent change from baseline in the sum of diameters for all target lesions.

[a] One patient was missing a baseline assessment and 2 additional patients were missing post-baseline assessments.

Median PFS = 14.0 months

Smit EF et al. ASCO 2020;Abstract 9504.

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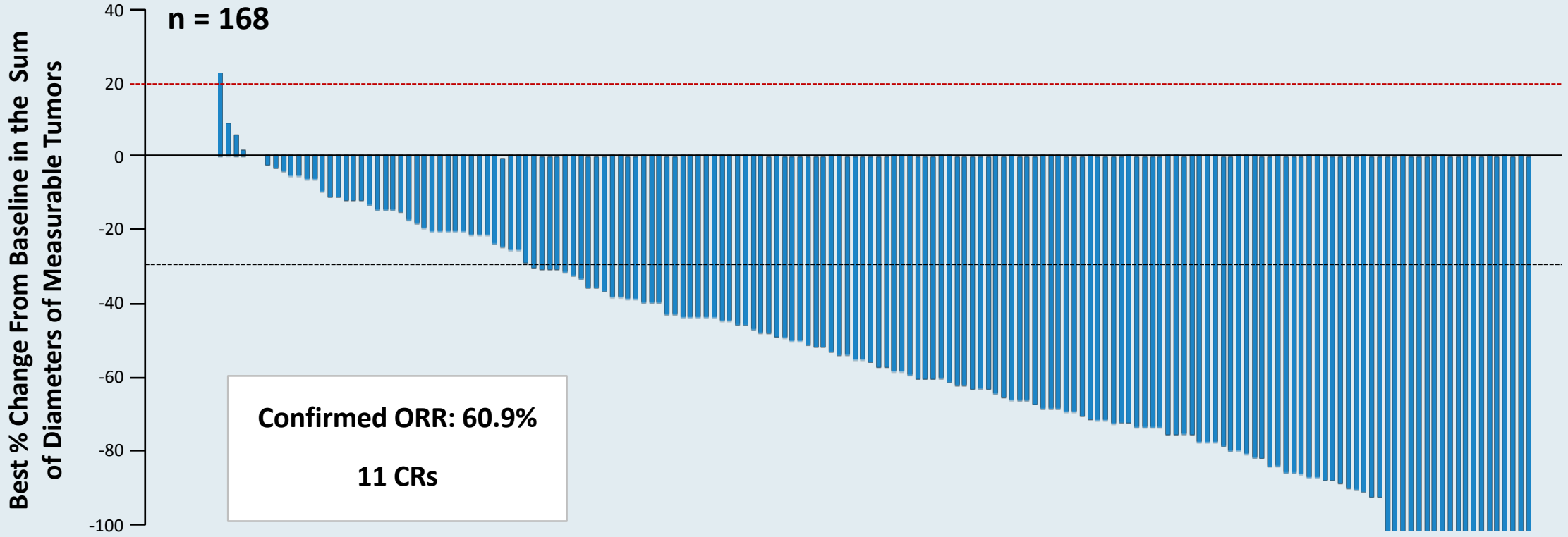
DESTINY-Breast01: Best Change in Tumor Size

Trastuzumab Deruxtecan in Breast Cancer

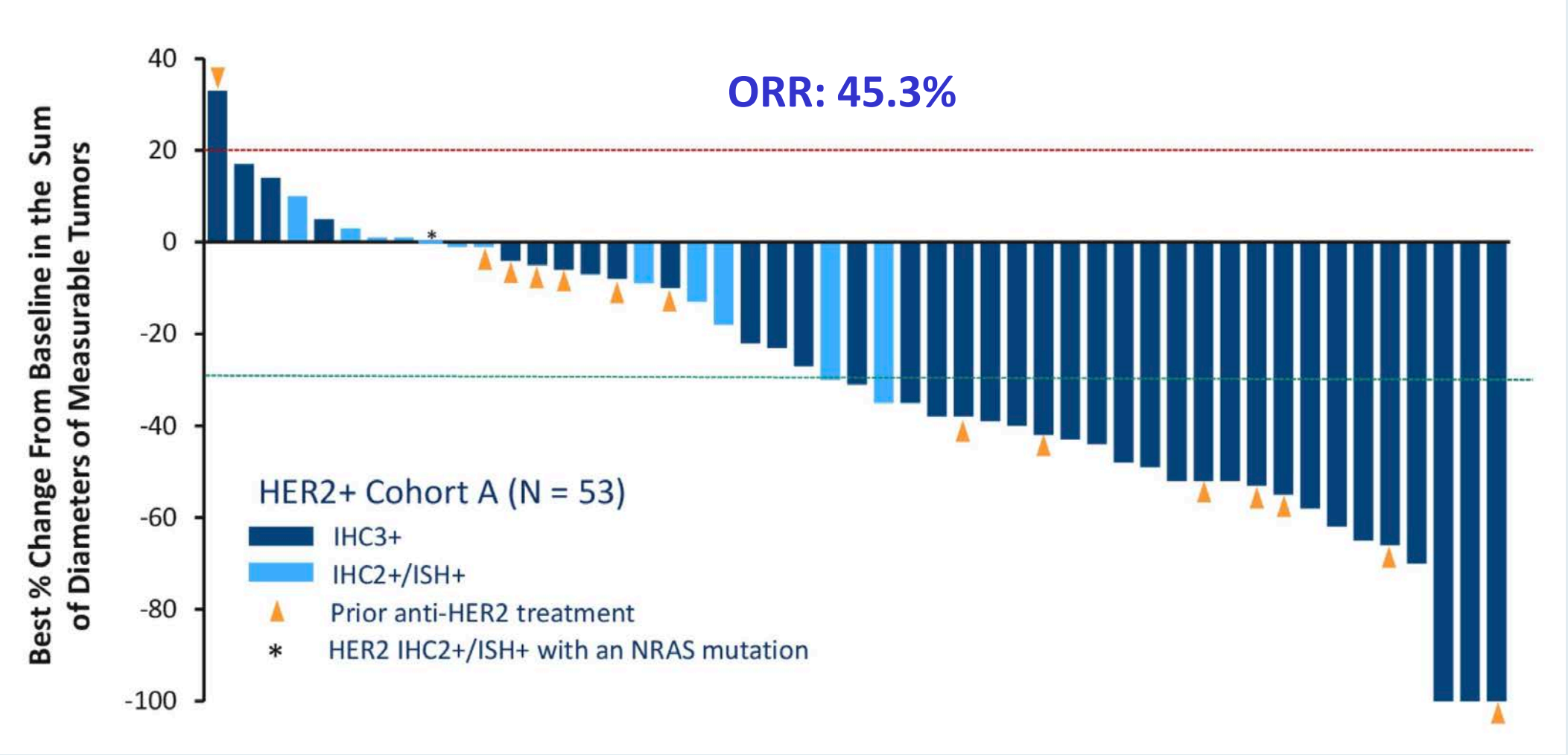


By independent central review.
The line at 20% indicates progressive disease; the line at −30% indicates partial response.
Includes all patients who received T-DXd 5.4 mg/kg (intent-to-treat analysis; N=184).

Krop IE et al. San Antonio Breast Cancer Symposium 2019;Abstract GS1-03.

DESTINY-CRC01: Best Change in Tumor Size

Trastuzumab Deruxtecan in Colorectal Cancer

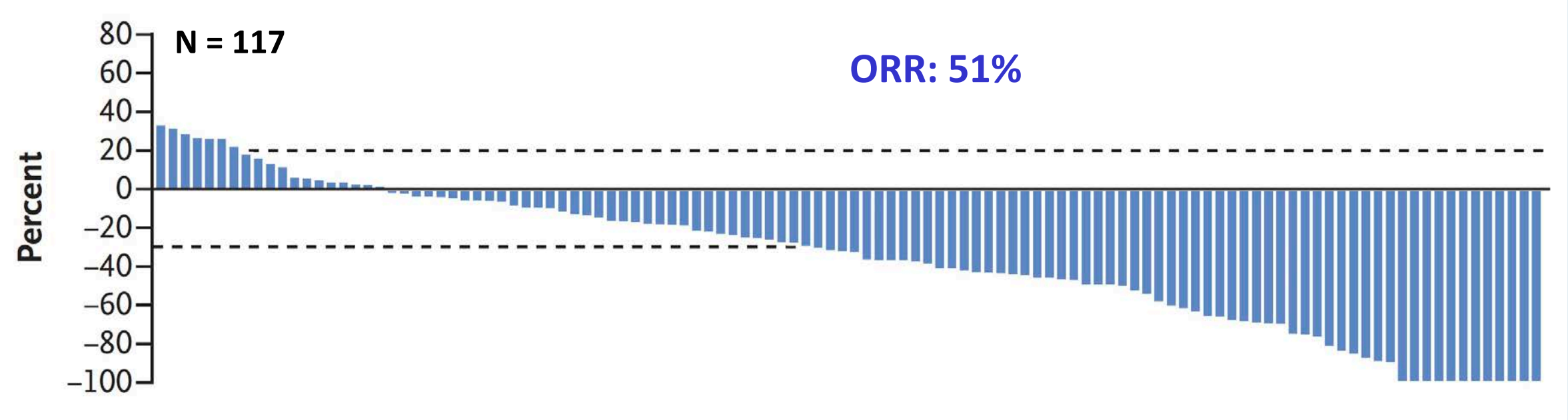


Siena S et al. ASCO 2020;Abstract 4000.

RTP RESEARCH TO PRACTICE

DESTINY-Gastric01: Best Change in Tumor Size

Trastuzumab Deruxtecan in Gastric Cancer



Shitara K et al. N Engl J Med 2020;382:2419-30.

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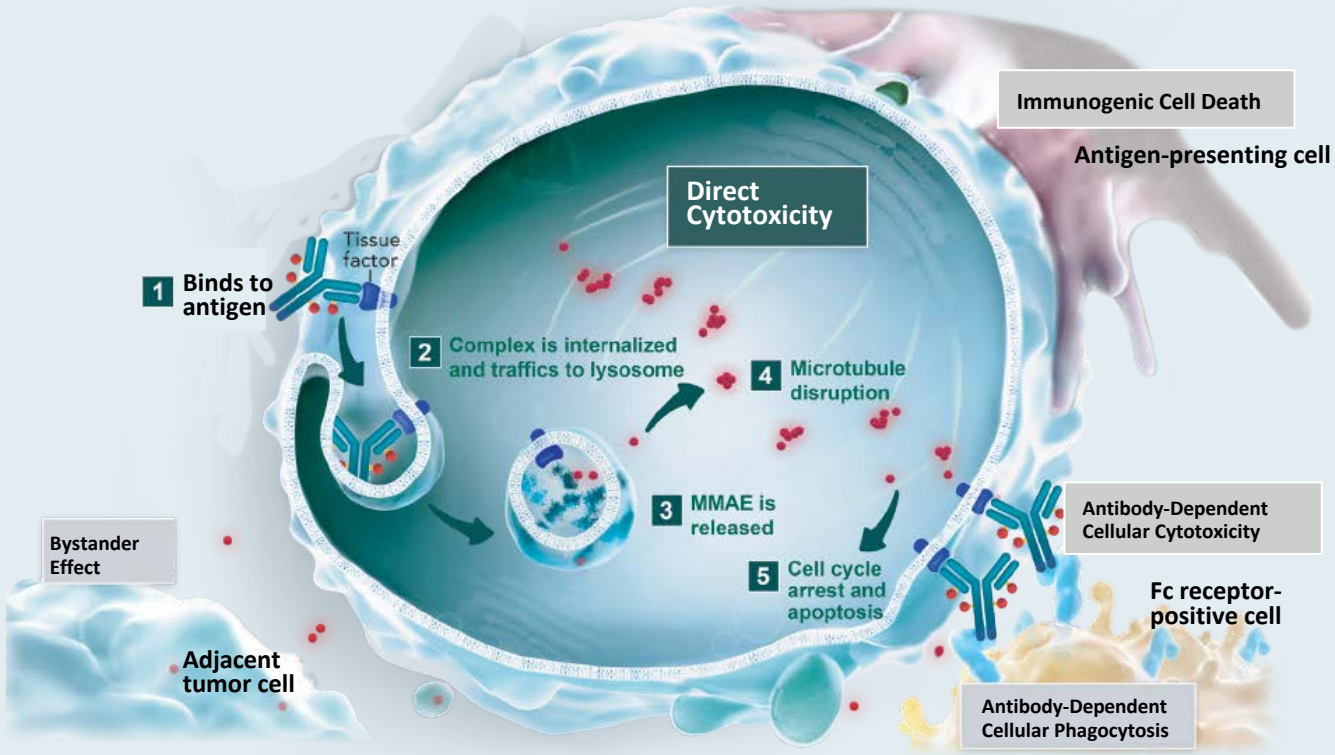
Tisotumab Vedotin and Other Novel Agents in Gynecologic Cancers

Mechanism of Action of Tisotumab Vedotin

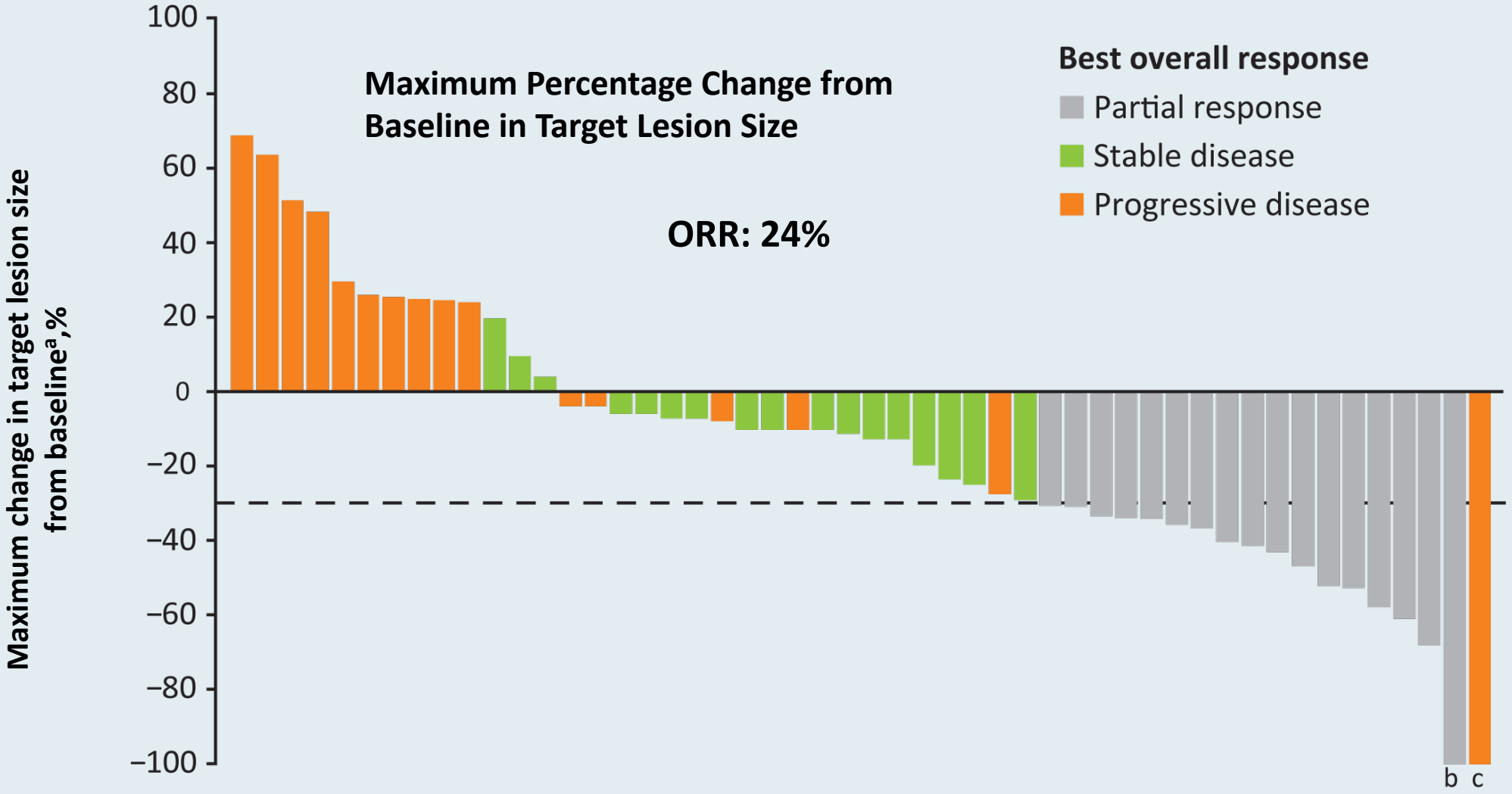
- Tissue factor (TF) is aberrantly expressed in a broad range of solid tumours, including cervical cancer,[1,2] and TF expression has been associated with higher tumour stage and grade, higher metastatic burden and poor prognosis[2]
- TF expression in cervical cancer makes TF a novel target for patients with cervical cancer
- ADC targets TF
  - Monoclonal Antibody targets TF
  - Payload: Microtubule disrupting MMAE
- Allowing for direct cytotoxicity and bystander killing, as well as antibody-dependent cellular cytotoxicity[3,4]



1. Förster Y, et al. *Clin Chim Acta,* 2006. 2. Cocco E, et al. *BMC Cancer,* 2011.
3. Breij EC, et al. *Cancer Res,* 2014. 4. De Goeij BE, et al. *Mol Cancer Ther,* 2015.

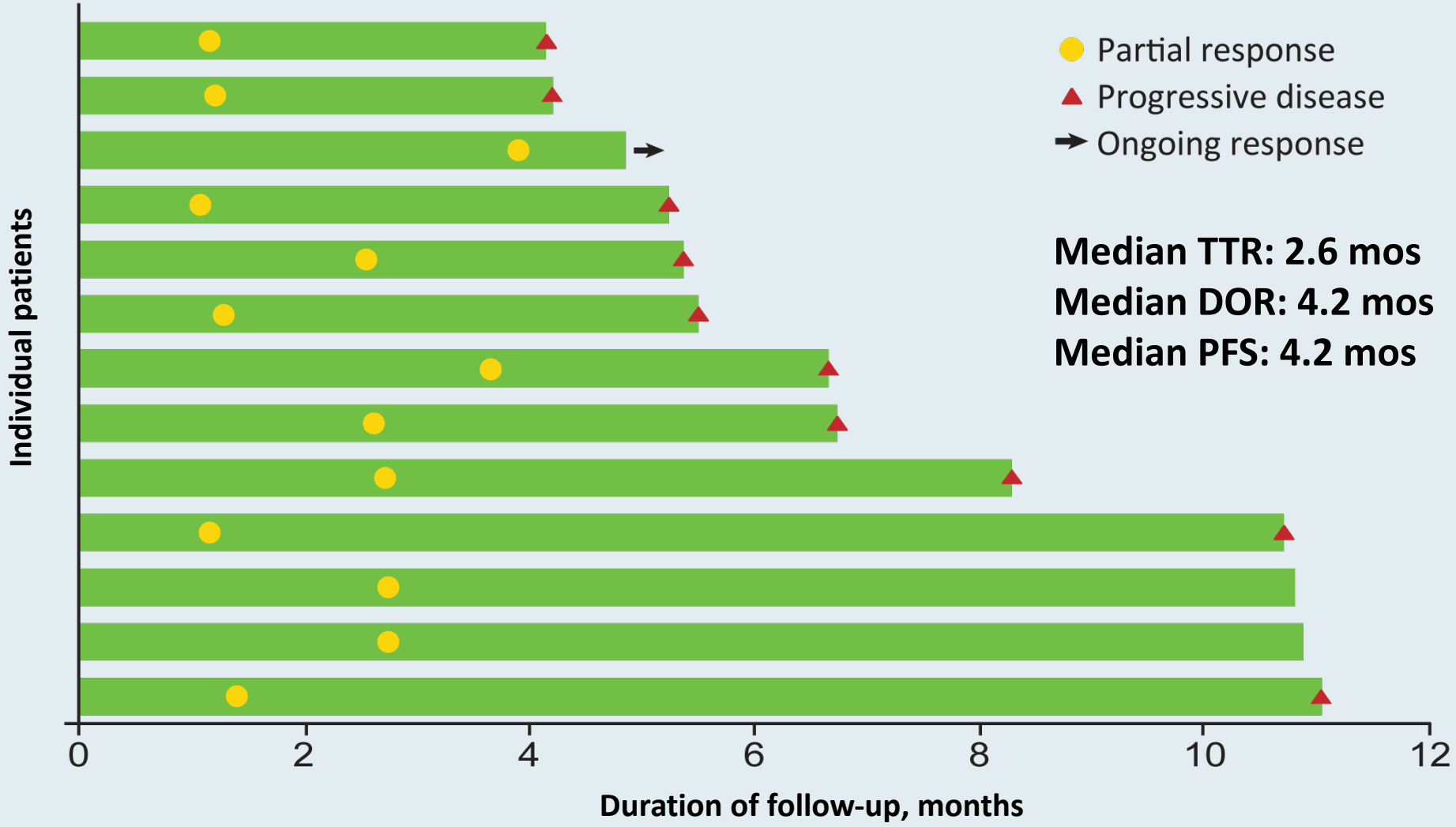
Courtesy of David M O'Malley, MD

innovaTV 201: Best Overall Response to TV



Hong DS et al. *Clin Cancer Res* 2020;26:1220-8.

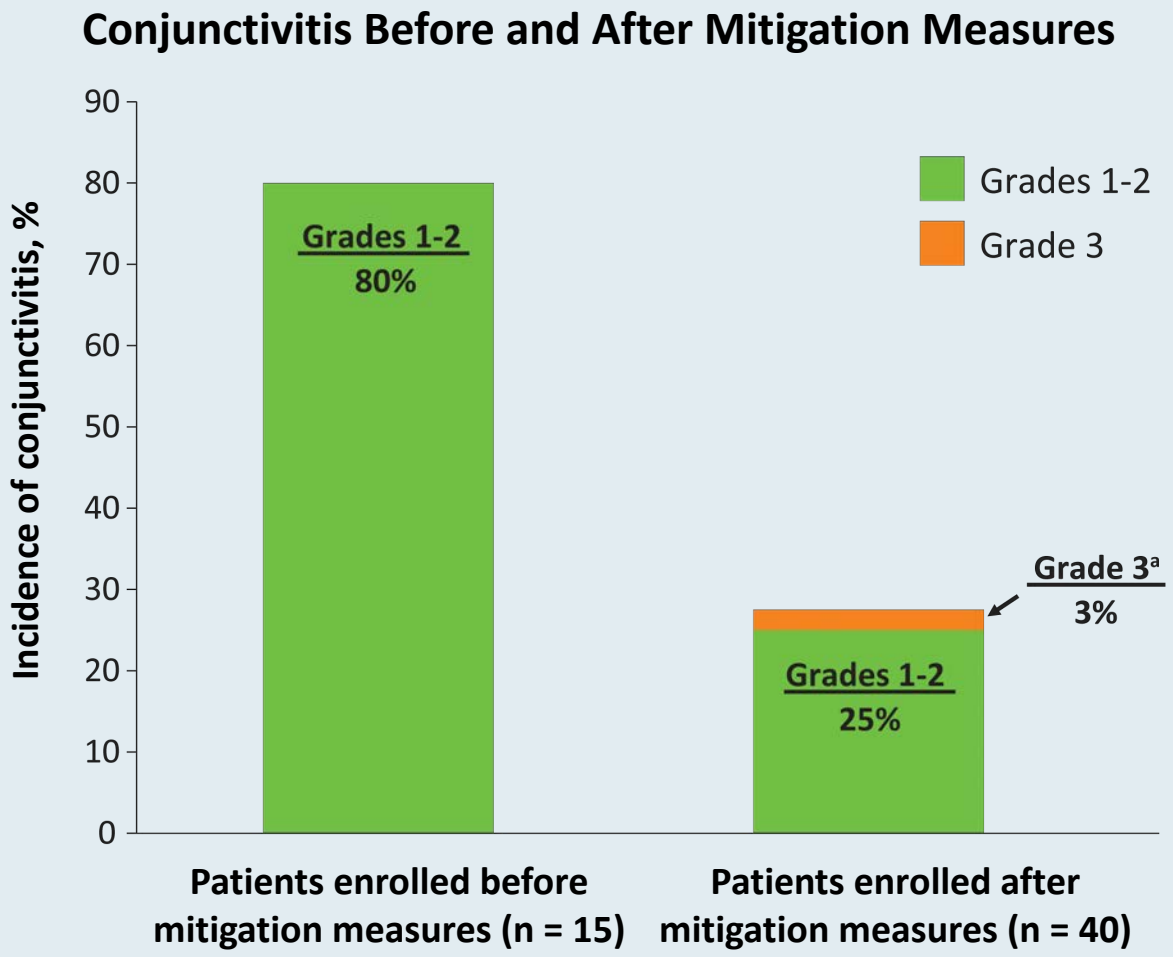
innovaTV 201: Time to Response and Duration of Response in Patients with a Confirmed PR to TV



Hong DS et al. *Clin Cancer Res* 2020;26:1220-8.

innovaTV 201: Treatment-Emergent Adverse Events

Adverse events	N = 55	
	All grade	Grade ≥3
Fatigue	51%	9%
Nausea	49%	5%
Neuropathy	55%	11%
Bleeding-related AEs	73%	5%
Ocular AEs	65%	2%
Conjunctivitis	42%	2%
Dry eye	24%	0
Ulcerative keratitis	7%	0
Blepharitis	5%	0
Keratitis	5%	0



Hong DS et al. *Clin Cancer Res* 2020;26:1220-8.

[a] One patient with grade 3 conjunctivitis after mitigation measures were implemented. No grade 3 events were observed before mitigation measures were implemented.

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Positive Topline Results with Tisotumab Vedotin in the Phase II InnovaTV 204 Trial

Press Release – June 30, 2020

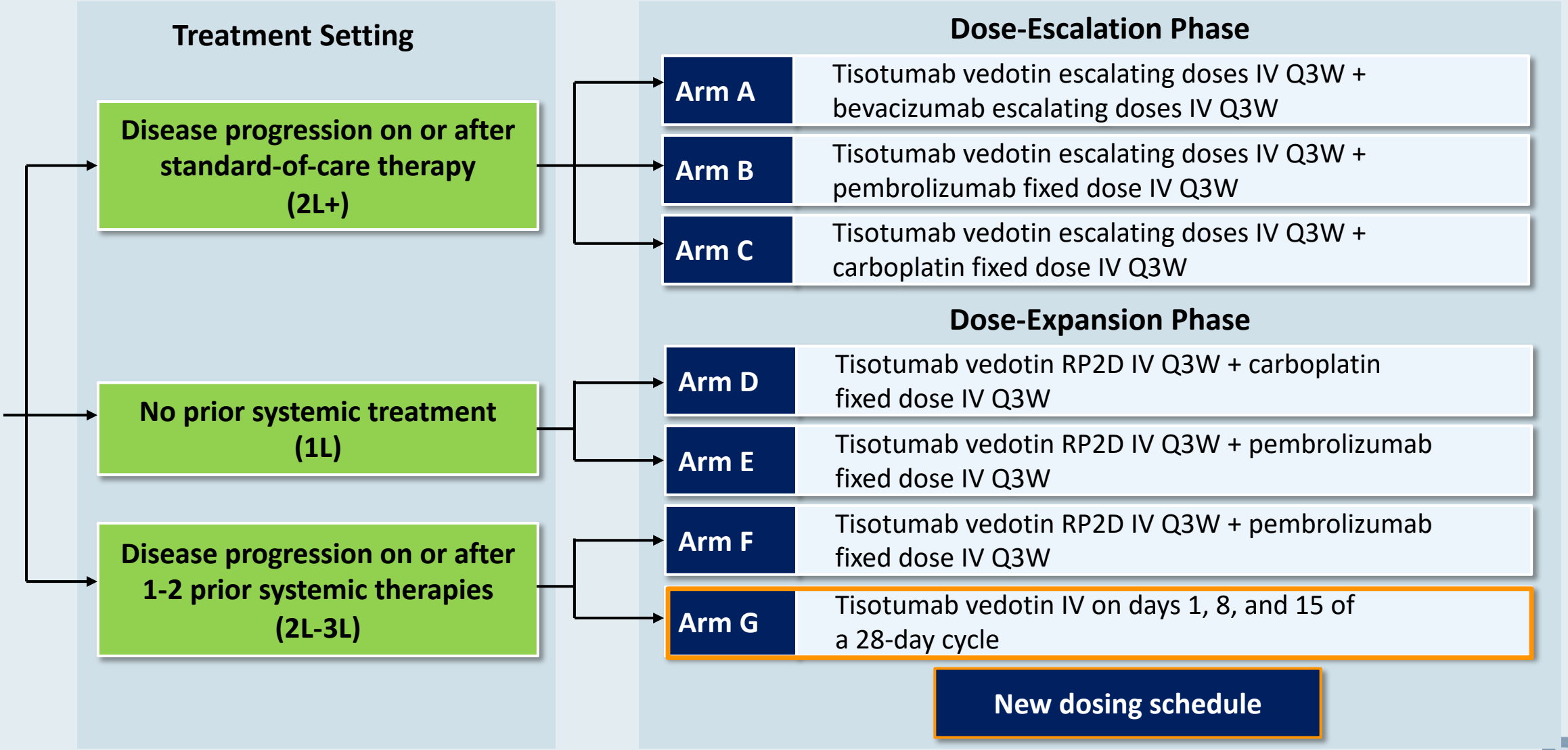
"Positive topline results [were announced] from the single-arm, phase 2 innovaTV 204 trial evaluating tisotumab vedotin administered every 3 weeks for the treatment of patients who have relapsed or progressed on or after prior treatment for recurrent or metastatic cervical cancer.

Overall, 101 patients were treated with tisotumab vedotin at multiple centers across the US and Europe. Results from the trial demonstrated a 24% confirmed ORR by independent central review with a median DOR of 8.3 months. The most common treatment-related adverse events included alopecia, epistaxis, nausea, conjunctivitis, fatigue, and dry eye."

https://www.cancernetwork.com/view/tisotumab-vedotin-sees-positive-topline-results-in-the-phase-2-innovatv-204-trial

RTP RESEARCH TO PRACTICE

innovaTV 205 (GOG 3024): Recurrent or Metastatic Cervical Cancer



Courtesy of David M O'Malley, MD

Current Questions and Controversies in the Management of Lung Cancer

A Meet The Professor Series

Tuesday, September 29, 2020
12:00 PM – 1:00 PM ET

Faculty
Benjamin Levy, MD

Moderator
Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 days.

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