Meet The Professor
Immunotherapy and Novel Agents in Gynecologic Cancers

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Commercial Support

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Dr Love — Disclosures

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Dr Penson — Disclosures

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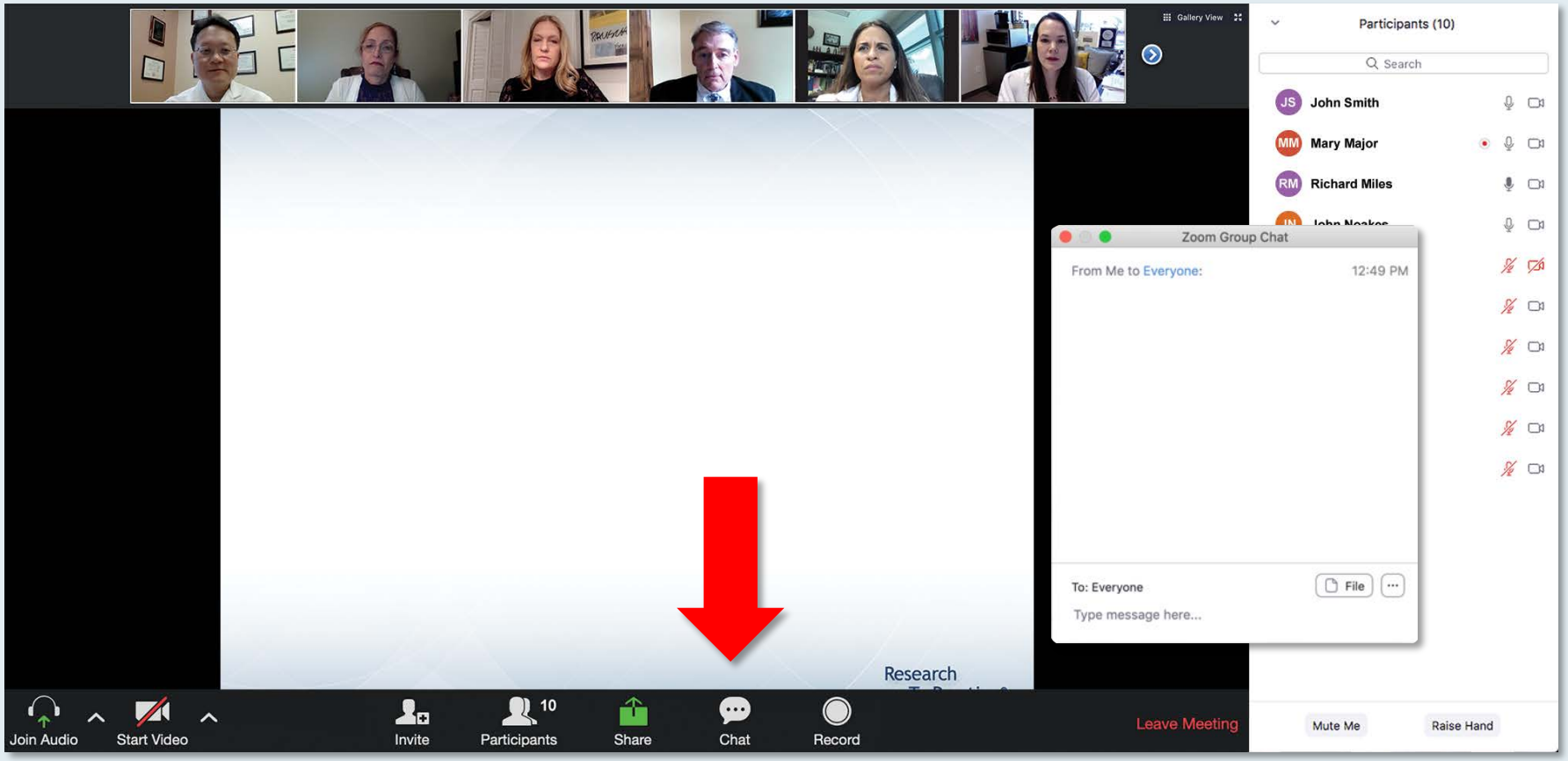
We Encourage Clinicians in Practice to Submit Questions



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

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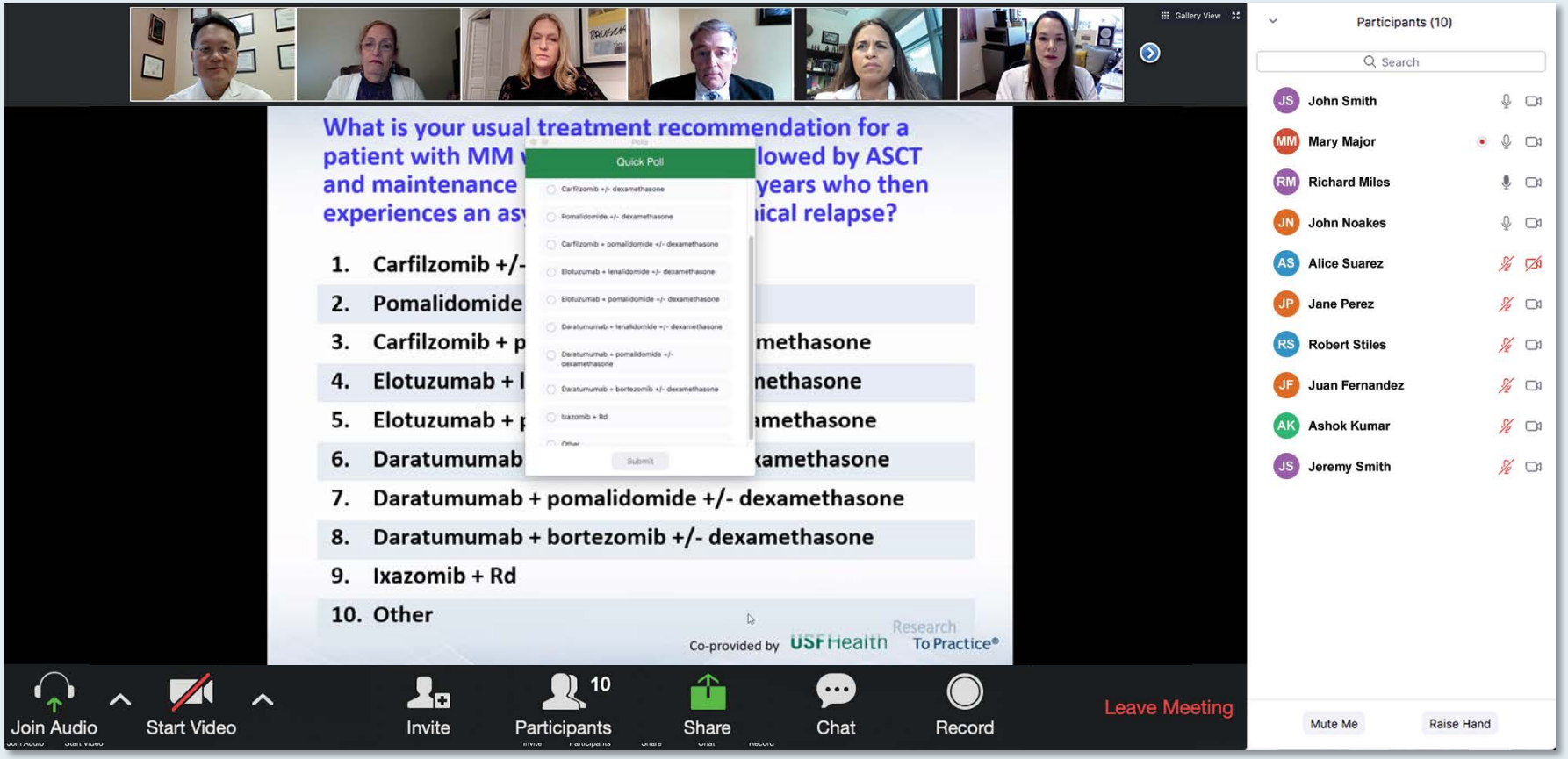
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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Upcoming Webinars

Wednesday, November 4, 2020
12:30 PM – 1:30 PM ET

Meet The Professor: Management of Multiple Myeloma

Faculty
Irene M Ghobrial, MD

Moderator
Neil Love, MD

Friday, November 6, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Ovarian Cancer

Faculty
Mansoor Raza Mirza, MD

Moderator
Neil Love, MD

Thank you for joining us!

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

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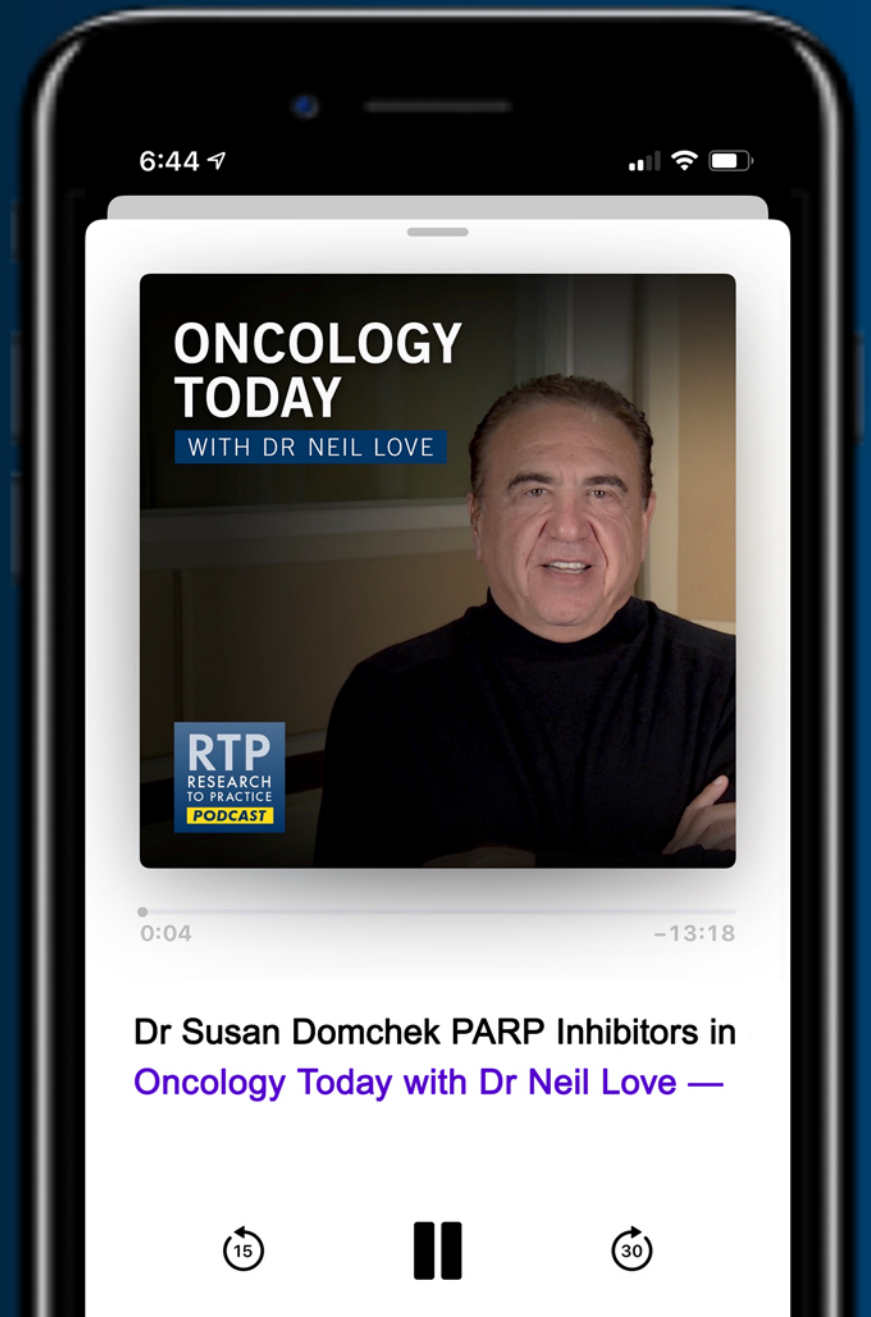

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Meet The Professor Program Participating Faculty

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University of Arkansas for Medical Sciences
Little Rock, Arkansas

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Head of Gynaecologic Cancer Programme
Vall d'Hebron Institute of Oncology
Hospital Universitari Vall d'Hebron
Vall d'Hebron Barcelona Hospital Campus
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US Oncology Research
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Professor
Division Director, Gynecologic Oncology
Co-Director, Gyn Oncology Phase I Program
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Meet The Professor Program Participating Faculty

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Clinical Director, Medical Gynecologic Oncology
Massachusetts General Hospital
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Krishnansu S Tewari, MD
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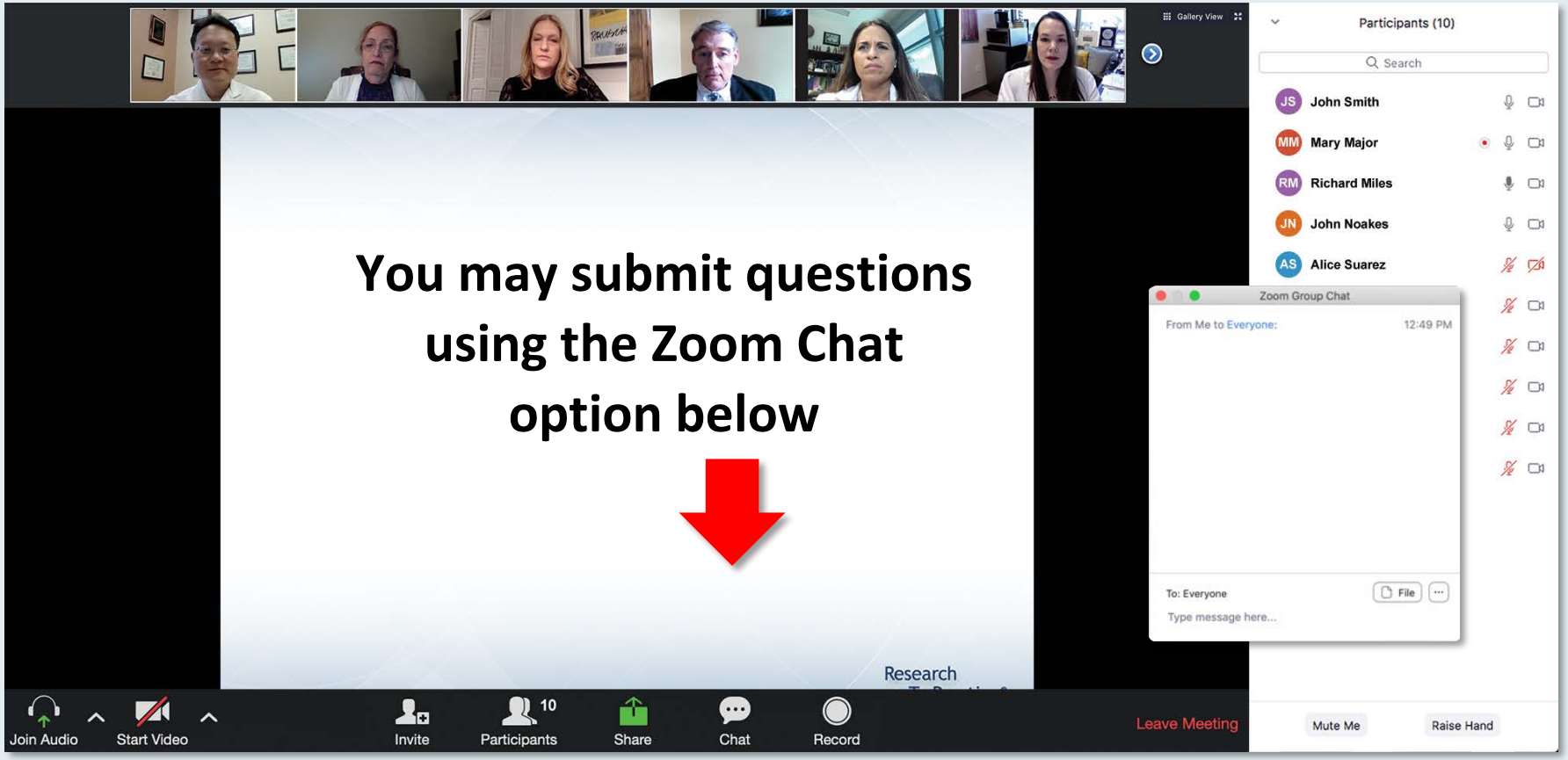

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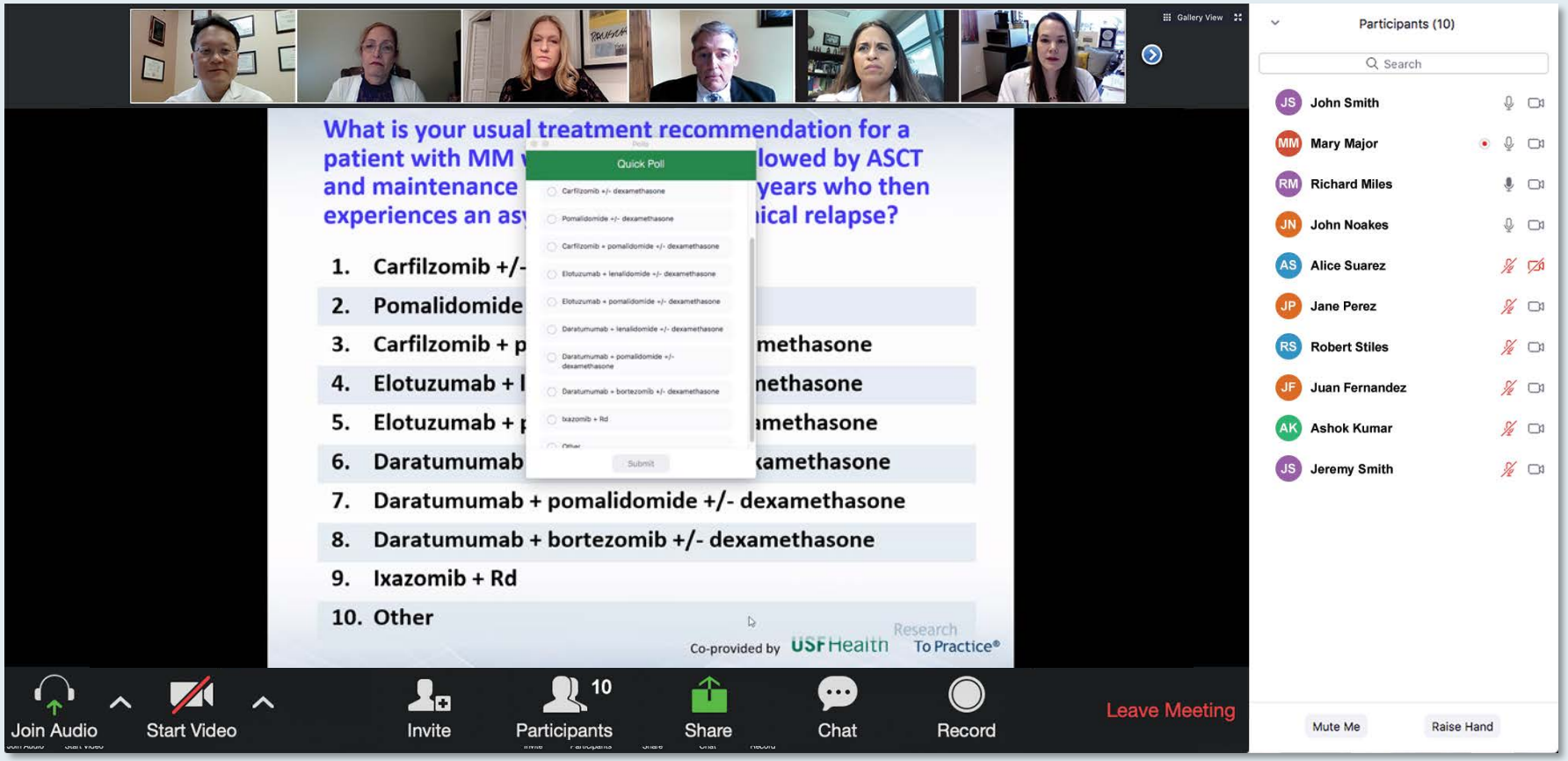

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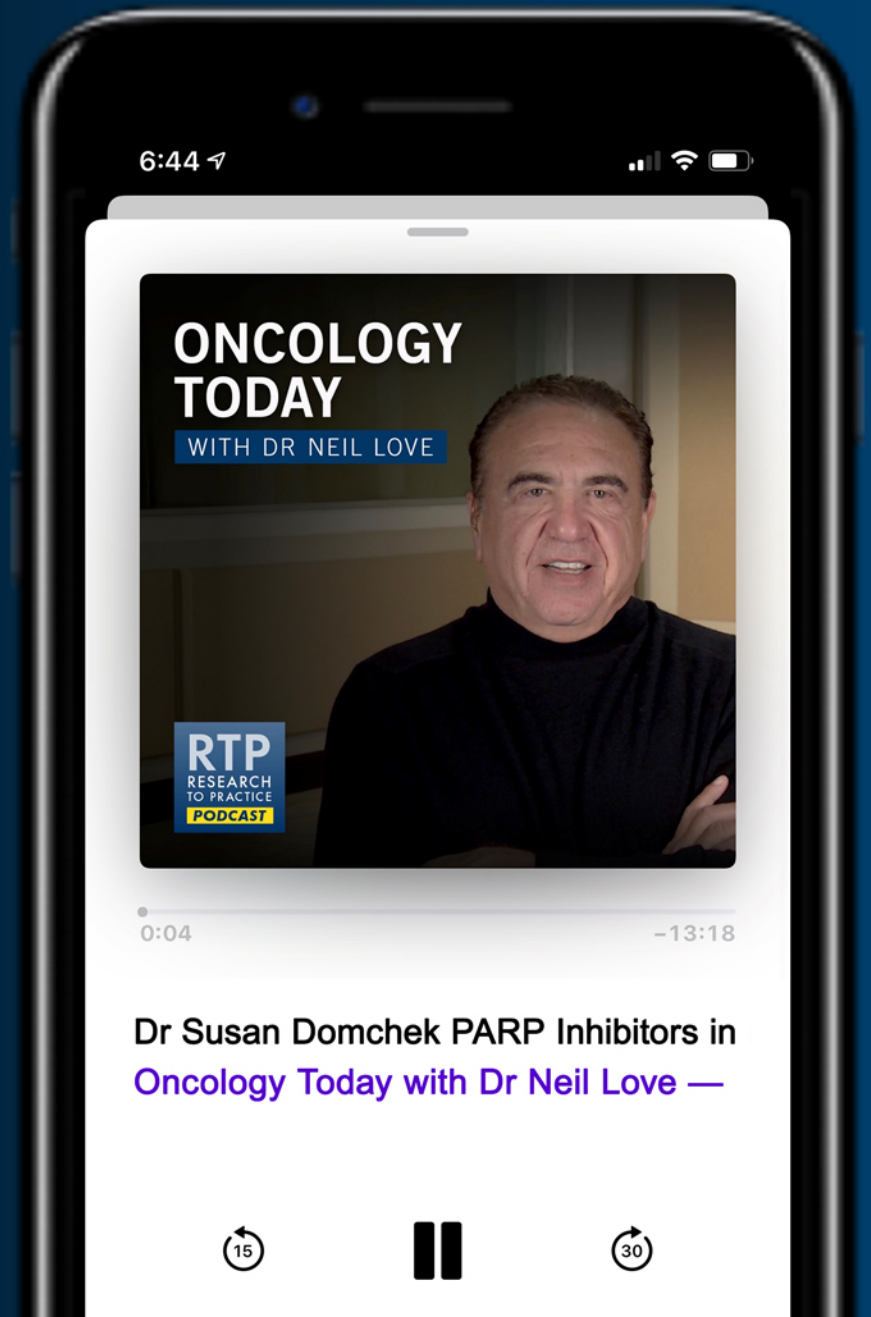

Meet The Professor
Management of Multiple Myeloma

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Irene M Ghobrial, MD

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Meet The Professor
Management of Ovarian Cancer

Friday, November 6, 2020
12:00 PM – 1:00 PM ET

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Dana M Chase, MD
Gynecologic Oncologist, Arizona Oncology (US Oncology Network)
Associate Professor, Creighton University School of Medicine
Assistant Professor, University of Arizona College of Medicine
Phoenix, Arizona

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Meet The Professor with Dr Penson

MODULE 1: Cases from Dr Chase

- A 53-year-old woman with recurrent endometrial cancer – Mismatch repair proficient
- A 60-year-old morbidly obese woman with recurrent endometrial cancer – MMR proficient
- A 70-year-old woman with recurrent endometrial cancer – MMR proficient
- A 29-year-old woman with metastatic squamous cell carcinoma of the cervix
- A 39-year-old woman with Stage IV cervical cancer
- Questions and Comments: Checkpoint inhibitors in ovarian cancer
- A 35-year-old woman with recurrent cervical cancer at a single site

MODULE 2: Gynecologic Oncology Journal Club with Dr Penson

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

MODULE 4: Key Recent Data Sets

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Case Presentation – Dr Chase: A 53-year-old woman with recurrent endometrial cancer – Mismatch repair (MMR) proficient

Dr Dana Chase

- 11/2019: Stage IA Grade 2 endometrial cancer s/p TAH-BSO, pelvic and para-aortic LND
  - Node-negative, no LVI, <50% invasion, MMR intact
  - Positive pelvic washing
- 4/2020: Bilateral hydronephrosis, right intraabdominal mass

Question

- Do you do pelvic washing for endometrial cancer? If yes, and it comes back abnormal, how do you manage the patient?

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Case Presentation – Dr Chase: A 53-year-old woman with recurrent endometrial cancer – MMR proficient (continued)

Dr Dana Chase

- 11/2019: Stage IA Grade 2 endometrial cancer s/p TAH-BSO, pelvic and para-aortic LND
  - Node-negative, no LVI, <50% invasion, MMR intact
  - Positive pelvic washing
- 4/2020: Bilateral hydronephrosis, right intraabdominal mass
- Enrolled on RUBY trial of carboplatin/paclitaxel +/- dostarlimab, with PD after cycle 6
- Pembrolizumab/lenvatinib

Questions

- What is your approach to dosing lenvatinib?
- How do you counsel patients about and manage toxicity from checkpoint inhibitors?
- Is there any reason to use every 6 weeks versus every 3 weeks for the checkpoint inhibitors?

Case Presentation – Dr Chase: A 60-year-old morbidly obese woman with recurrent endometrial cancer – MMR proficient

Dr Dana Chase

- 3/2016: Presents with postmenopausal bleeding and diagnosed with endometrial cancer
  - BMI > 70; Diagnostic laparoscopy unsuccessful, exploratory laparotomy avoided
  - Radiation therapy with EBRT
- 1/2019: Recurrence in endometrium/vagina → Carboplatin/paclitaxel x 6, with residual disease
- 1/2020: BMI 45; TRH/BSO, with residual tumor
- Significant recurrence in the pelvis
- Pembrolizumab/lenvatinib, with CR

Questions

- What is your "real world" experience with patients who are MMR intact in terms of response rates? How do you counsel patients about what to expect in terms of pembrolizumab/lenvatinib efficacy?
- What do you recommend in terms of testing?

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Case Presentation – Dr Chase: A 70-year-old woman with recurrent endometrial cancer – MMR proficient

Dr Dana Chase

- 3/2019: Stage IIIA, Grade 2 endometrial cancer s/p TRH-BSO, PSLND
- Carboplatin/paclitaxel x 6
- 3/2020: Abdominal wall mass and sclerotic bone lesion
- Pembrolizumab/lenvatinib, with CR
  - Progressive development of nephritis and colitis, both resolved with high-dose steroids

Questions

- How do you manage the toxicities associated with checkpoint inhibitor therapy?
- If we are able to control the nephritis and colitis, could we re-treat with pembrolizumab/lenvatinib? Have you ever re-treated after resolution of Grade III-IV toxicity from checkpoint inhibitors?

Case Presentation – Dr Chase: A 29-year-old woman with metastatic squamous cell carcinoma of the cervix

Dr Dana Chase

- 7/2019: Stage IB1 squamous cell carcinoma of the cervix
  - Radical hysterectomy, with positive nodes
- Adjuvant cisplatin with concurrent RT and vaginal brachytherapy
- 1/2020: Abdominal mass → Radical resection with negative margins and RT → Incisional recurrence and PD in the lung
- Enrolled on a clinical trial of tisotumab vedotin (discontinued after 1 dose due to ocular toxicity)
- 6/2020: Carboplatin/paclitaxel/bevacizumab (GOG-240 regimen)

Questions

- What is your experience with the toxicities from tisotumab vedotin? How frequently do patients develop these ocular toxicities and how do you manage them?
- Where do you sequence tisotumab vedotin in terms of lines of therapy? Would you use it after the GOG-240 regimen? Would you put it in before GOG-240 in a patient who already received cisplatin with radiation therapy?

Case Presentation – Dr Chase: A 39-year-old woman with Stage IV cervical cancer

Dr Dana Chase

- 2017: Stage IV cervical cancer
- Platinum/paclitaxel/bevacizumab (GOG-240 regimen) x 1 year → *Nab* paclitaxel/bevacizumab → bevacizumab
- 8/2019 CT: Metastatic progression in the lungs

Questions

- What is your acceptable response rate in toxicity for GOG-240 failures?
- In a patient receiving the GOG-240 regimen and responding, do you "peel" anything off, or do you continue with all 3 drugs?

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Questions and Comments: Checkpoint inhibitors in ovarian cancer

Dr Dana Chase

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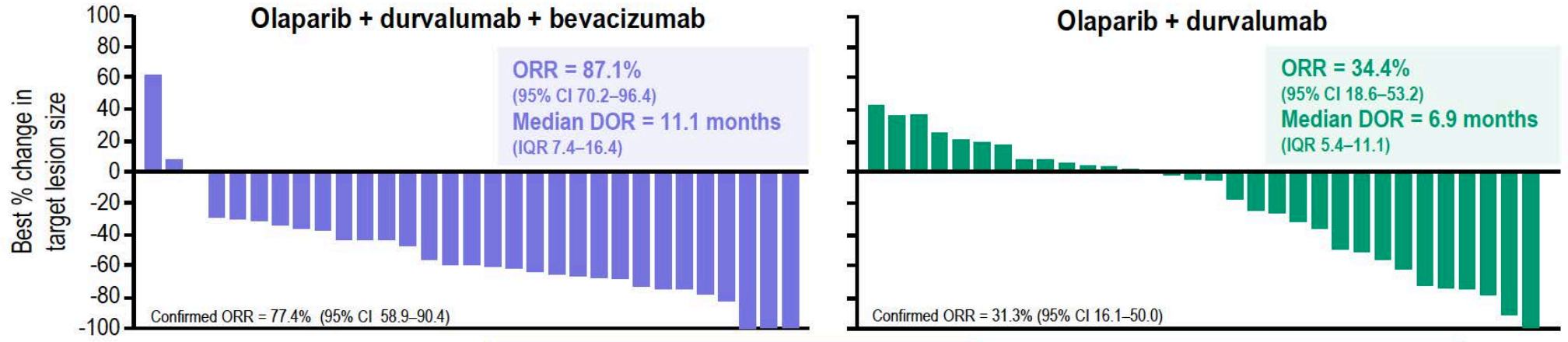
MEDIOLA: A Phase II Study of Olaparib and Durvalumab with or without Bevacizumab for Platinum-Sensitive Relapsed OC: No Germline BRCA Mutation Cohort

Exploratory analysis suggests ORR with triplet cohort is not dependent on genomic instability status (GIS)



Genomic instability status* subgroup	Olaparib + durvalumab + bevacizumab		Olaparib + durvalumab	
	ORR (95% CI), %	n/N patients	ORR (95% CI), %	n/N patients
GIS-positive	100.0 (69.2–100.0)	10/10	50.0 (18.7–81.3)	5/10
GIS-negative	75.0 (34.9–96.8)	6/8	16.7 (0.4–64.1)	1/6
GIS-unknown	84.6 (54.6–98.1)	11/13	31.3 (11.0–58.7)	5/16

Drew Y et al. ESMO 2020;Abstract 814MO.

Case Presentation – Dr Chase: A 35-year-old woman with recurrent cervical cancer at a single site

Dr Dana M Chase

- Stage IIB cervical cancer
- Cisplatin with concurrent RT, brachytherapy
- Three-month scan: Suspicious lymph node in the radiated field (unable to do needle biopsy)
  → Observation
- Six weeks later: Increased size of para-aortic node → Needle biopsy: Consistent with recurrent disease

Questions

- How do you decide to resect a lymph node in a patient with recurrent cervical cancer where it's a single site of recurrence?
- Do you only do it if it's outside of the radiated field? Do you do it even if it's in the radiated field?
- What role would a lymphadenectomy play in a patient like her?

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Meet The Professor with Dr Penson

MODULE 1: Cases from Dr Chase

MODULE 2: Gynecologic Oncology Journal Club with Dr Penson

- Second-line lenvatinib for recurrent endometrial cancer
- GOG-240: Circulating tumor cells in advanced cervical cancer
- Clinical trial participation and aggressive care at the end of life for patients with ovarian cancer (OC)
- Ofranergene obadenovec (VB-111) alone or combined with paclitaxel for platinum-resistant OC
- Pembrolizumab with pegylated liposomal doxorubicin for platinum-resistant OC
- Berzosertib with gemcitabine for platinum-resistant high-grade serous OC
- Avelumab in MMR-deficient and proficient recurrent or persistent endometrial cancer
- Nivolumab/bevacizumab for relapsed OC
- Mirvetuximab soravtansine with bevacizumab for platinum-resistant OC
- First-in-human study of STRO-002, an anti-folate receptor alpha antibody-drug conjugate, for platinum-resistant/refractory OC

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

MODULE 4: Key Recent Data Sets

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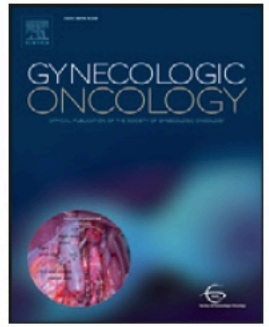
Gynecologic Oncology 156 (2020) 575–582

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

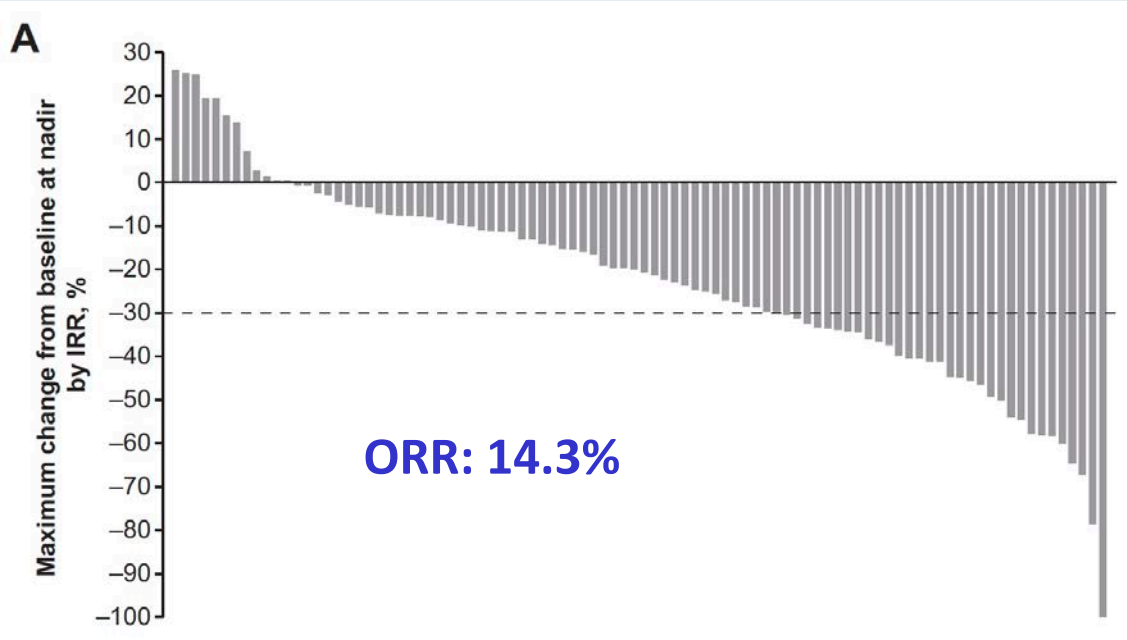


Second-line lenvatinib in patients with recurrent endometrial cancer☆,☆☆

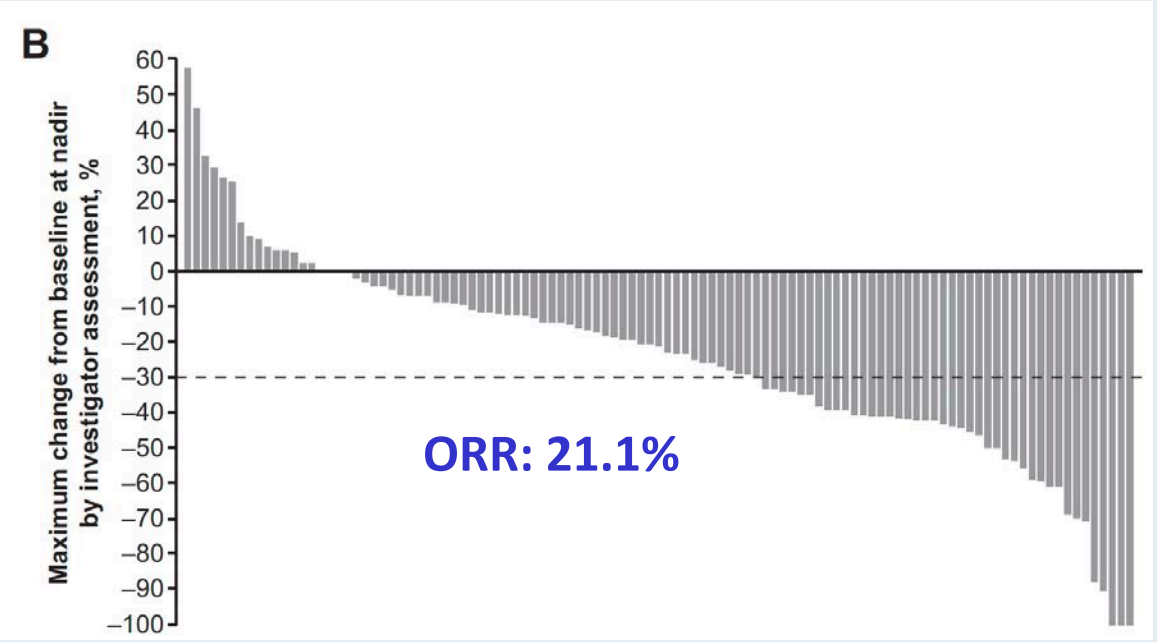
Ignace Vergote [a,*], Matthew A. Powell [b], Michael G. Teneriello [c], David S. Miller [d], Agustin A. Garcia [e], Olga N. Mikheeva [f], Mariusz Bidzinski [g], Cristina Ligia Cebotaru [h], Corina E. Dutcus [i], Min Ren [i], Tadashi Kadowaki [j,1], Yasuhiro Funahashi [j], Richard T. Penson [k]

Second-Line Lenvatinib: Maximum Percentage Change from Baseline to Nadir in Sum Diameter of Target Lesions in the ITT Population

Independent Radiologic Review



Investigator Assessment



Vergote I et al. *Gynecol Oncol* 2020;156(3):575-82.

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MOLECULAR CANCER THERAPEUTICS | CANCER BIOLOGY AND TRANSLATIONAL STUDIES

Circulating Tumor Cells In Advanced Cervical Cancer: NRG Oncology—Gynecologic Oncology Group Study 240 (NCT 00803062)

Krishnansu S. Tewari[1], Michael W. Sill[2,3,4], Bradley J. Monk[5], Richard T. Penson[6], David H. Moore[7], Heather A. Lankes[2,3,4], Lois M. Ramondetta[8], Lisa M. Landrum[9], Leslie M. Randall[1], Ana Oaknin[10], Mario M. Leitao[11], Eric L. Eisenhauer[12], Paul DiSilvestro[13], Linda Van Le[14], Michael L. Pearl[15], James J. Burke[16,17], Ritu Salani[18], Debra L. Richardson[19], Helen E. Michael[20], David W. Kindelberger[21], and Michael J. Birrer[6]

Mol Cancer Ther 2020;[Online ahead of print].

Original research

INTERNATIONAL JOURNAL OF GYNECOLOGICAL CANCER

Clinical trial participation and aggressive care at the end of life in patients with ovarian cancer

Roni Nitecki ,[1,2] Alexandra S Bercow,[1,2] Allison A Gockley,[3] Hang Lee,[4] Richard T Penson,[5] Whitfield B Growdon[6]

Int J Gynecol Cancer 2020;30(2):201-6.

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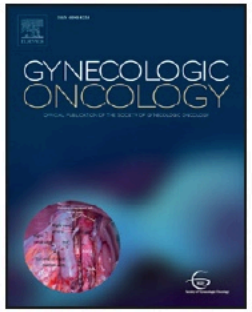
Gynecologic Oncology 157 (2020) 578–584

Contents lists available at ScienceDirect

Gynecologic Oncology

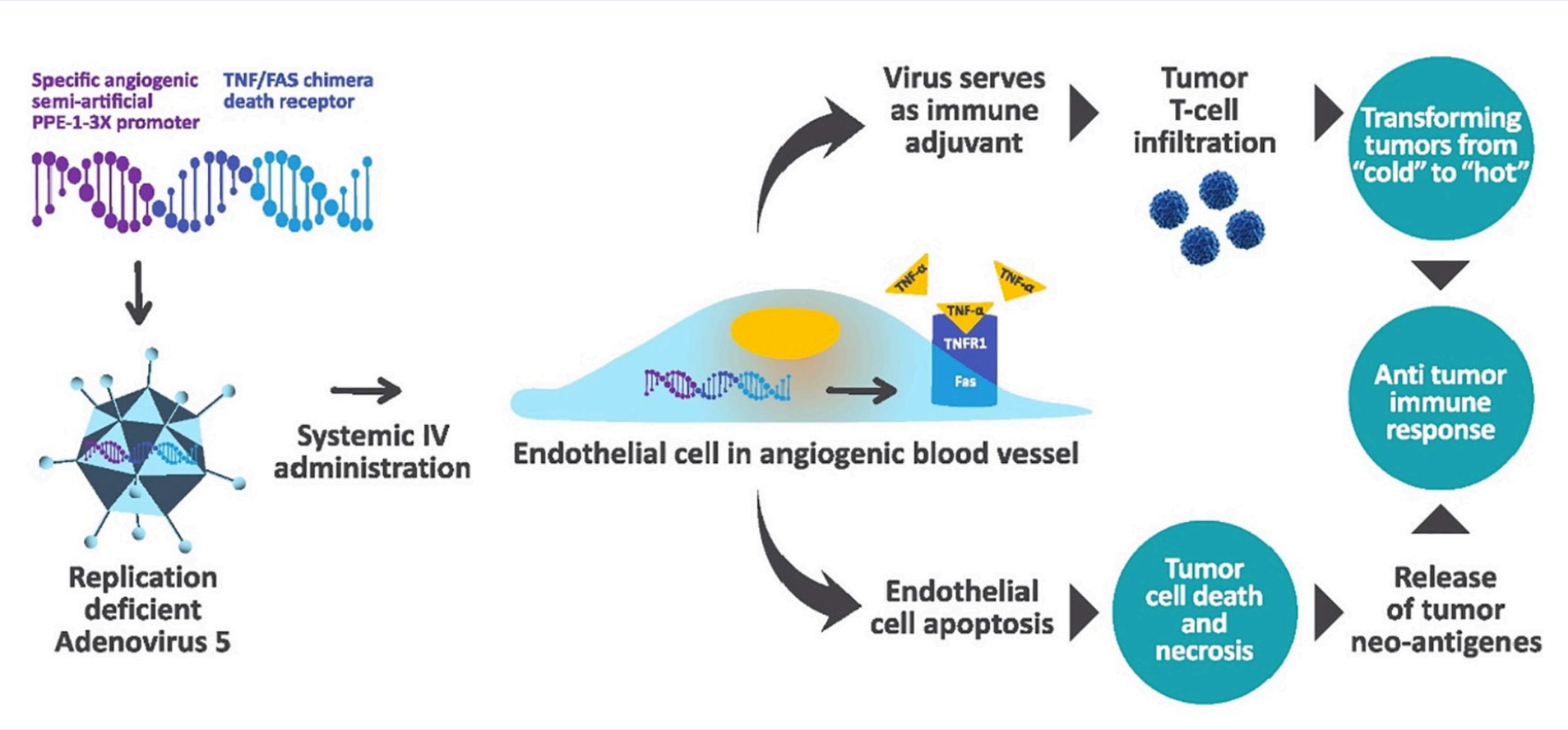
journal homepage: www.elsevier.com/locate/ygyno



Ofranergene obadenovec (VB-111) in platinum-resistant ovarian cancer; favorable response rates in a phase I/II study are associated with an immunotherapeutic effect

Rebecca C. Arend [a], Hannah M. Beer [a], Yael C. Cohen [d], Suzanne Berlin [c], Michael J. Birrer [e], Susana M. Campos [c], Tamar Rachmilewitz Minei [d], Dror Harats [d], Jaclyn A. Wall [a], McKenzie E. Foxall [a], Richard T. Penson [b,*]

VB-111: Novel, Dual Mechanism for Targeting Solid Tumors



Three main components of VB-111: (i) a vector, (ii) a tissue- and condition-specific promoter (DNA regulatory sequence) and (iii) a functional transgene which encodes the therapeutic protein. The dual mechanism of action of VB-111 promotes anti-angiogenesis/vascular disruption and induces tumor directed intra-tumor immune response.

Arend RC et al. *Gynecol Oncol* 2020;157(3):578-84.

Clinical Trial in Progress: Pivotal Study of VB-111 Combined with Paclitaxel versus Paclitaxel for Treatment of Platinum-Resistant Ovarian Cancer (OVAL, VB-111-701/GOG-3018)

Arend RC et al.

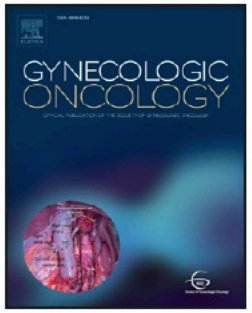
ASCO 2019;Abstract TPS6097.

Gynecologic Oncology 159 (2020) 72–78

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno



Combined pembrolizumab and pegylated liposomal doxorubicin in platinum resistant ovarian cancer: A phase 2 clinical trial

Elizabeth K. Lee [a], Niya Xiong [b], Su-Chun Cheng [b], William T. Barry [b], Richard T. Penson [c], Panagiotis A. Konstantinopoulos [a,d], Mark A. Hoffman [e], Neil Horowitz [d,f], Don S. Dizon [g], Elizabeth H. Stover [a,d], Alexi A. Wright [a,d], Susana M. Campos [a,d], Carolyn Krasner [c,1], Stephanie Morrissey [d], Christin Whalen [d], Roxanne Quinn [d], Ursula A. Matulonis [a,d,*,2], Joyce F. Liu [a,d,*,2]

Lancet Oncol 2020;21(7):957-68.

Berzosertib plus gemcitabine versus gemcitabine alone in platinum-resistant high-grade serous ovarian cancer: a multicentre, open-label, randomised, phase 2 trial

Panagiotis A Konstantinopoulos, Su-Chun Cheng, Andrea E Wahner Hendrickson, Richard T Penson, Susan T Schumer, L Austin Doyle, Elizabeth K Lee, Elise C Kohn, Linda R Duska, Marta A Crispens, Alexander B Olawaiye, Ira S Winer, Lisa M Barroilhet, Siqing Fu, Michael T McHale, Russell J Schilder, Anniina Färkkilä, Dipanjan Chowdhury, Jennifer Curtis, Roxanne S Quinn, Brittany Bowes, Alan D D'Andrea, Geoffrey I Shapiro, Ursula A Matulonis**

original report

Phase II Study of Avelumab in Patients With Mismatch Repair Deficient and Mismatch Repair Proficient Recurrent/Persistent Endometrial Cancer

Panagiotis A. Konstantinopoulos, MD, PhD[1]; Weixiu Luo, MS[1]; Joyce F. Liu, MD[1]; Doga C. Gulhan, PhD[2]; Carolyn Krasner, MD[1]; Jeffrey J. Ishizuka, MD, DPhil[1]; Allison A. Gockley, MD[3]; Mary Buss, MD, MPH[4]; Whitfield B. Growdon, MD[5]; Heather Crowe[5]; Susana Campos, MD, MPH[1]; Neal I. Lindeman, MD[3]; Sarah Hill, MD, PhD[3]; Elizabeth Stover, MD, PhD[1]; Susan Schumer, MD[1]; Alexi A. Wright, MD, MPH[1]; Jennifer Curtis, MS[1]; Roxanne Quinn[1]; Christin Whalen, RN[1]; Kathryn P. Gray, PhD[1]; Richard T. Penson, MD[5]; Stephen A. Cannistra, MD[4]; Gini F. Fleming, MD[6]; and Ursula A. Matulonis, MD[1]

J Clin Oncol 2019;37(30):2786-94.

Research

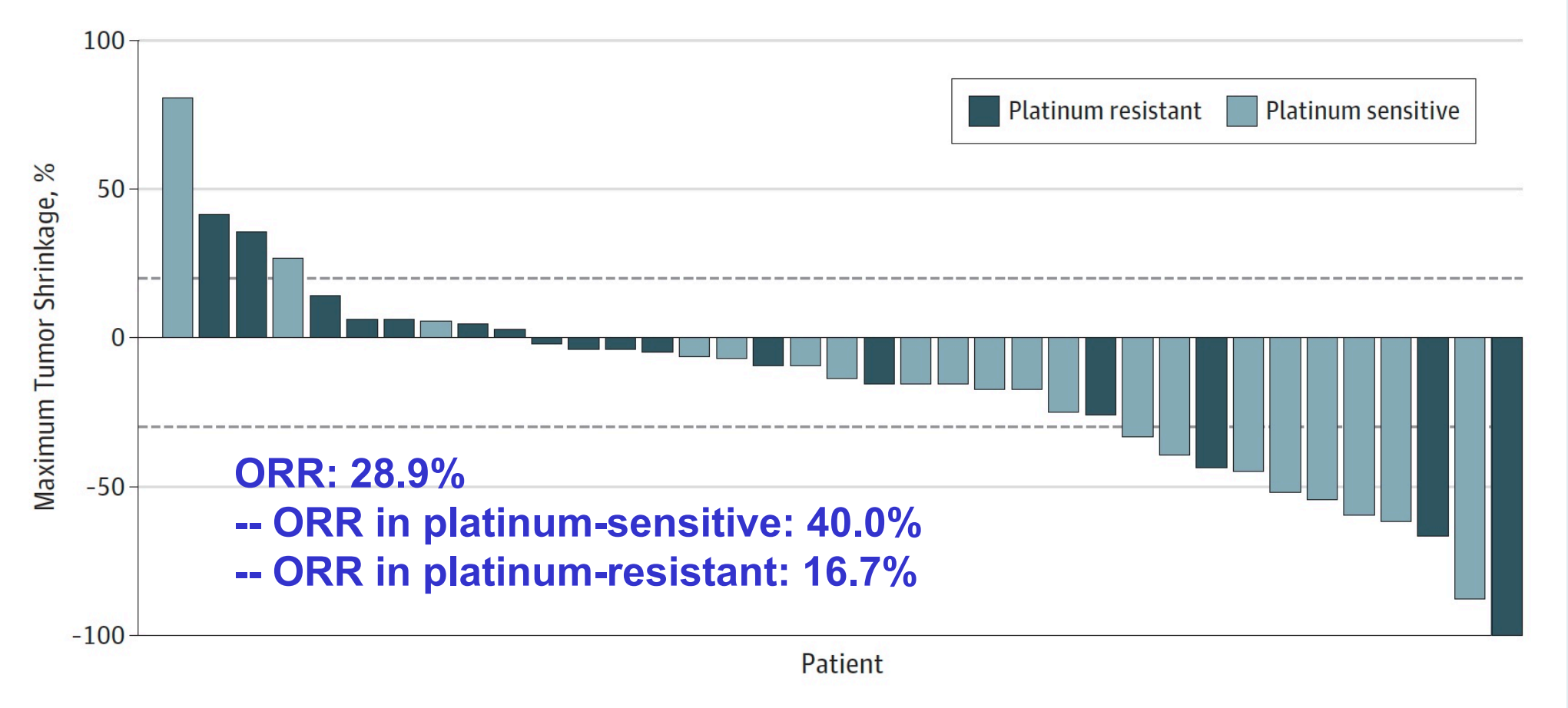
JAMA Oncol 2019;5(12):1731-8.

JAMA Oncology | Original Investigation

Assessment of Combined Nivolumab and Bevacizumab in Relapsed Ovarian Cancer
A Phase 2 Clinical Trial

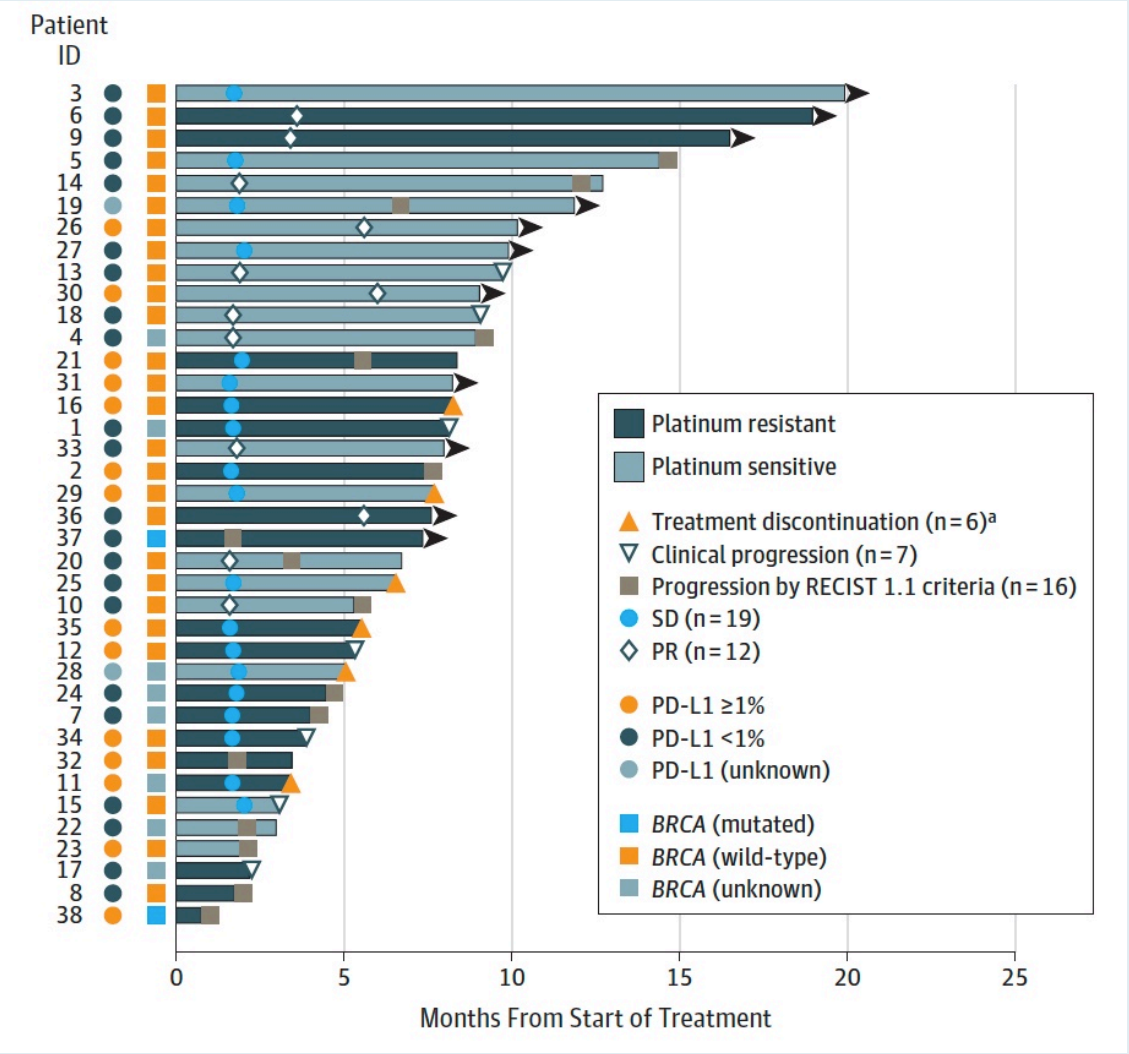
Joyce F. Liu, MD, MPH; Christina Herold, MD; Kathryn P. Gray, PhD; Richard T. Penson, MD; Neil Horowitz, MD; Panagiotis A. Konstantinopoulos, MD; Cesar M. Castro, MD; Sarah J. Hill, MD, PhD; Jennifer Curtis, MS; Weixiu Luo, MS; Ursula A. Matulonis, MD; Stephen A. Cannistra, MD; Don S. Dizon, MD

Nivolumab/Bevacizumab for Relapsed Ovarian Cancer: Best Responses in Evaluable Patients



Liu JF et al. *JAMA Oncol* 2019;5(12):1731-8.

Nivolumab/Bevacizumab in Relapsed Ovarian Cancer: Time Receiving Treatment



ID indicates identification; PD-L1, programmed death ligand 1; PR, partial response; SD, stable disease.

[a] Six patients discontinued treatment for the following reasons: withdrawal of consent (n = 3); recurrent, grade 2 treatment-related pneumonitis (n = 1); grade 3 treatment-related transaminitis (n = 1); and increase in disease during treatment for treatment-related pneumonitis (n = 1).

Liu JF et al. *JAMA Oncol* 2019;5(12):1731-8.

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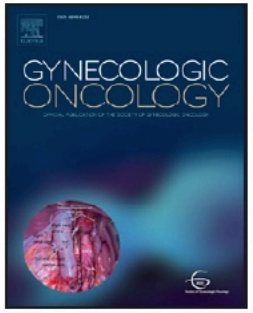
Gynecologic Oncology 157 (2020) 379–385

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno



Phase Ib study of mirvetuximab soravtansine, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), in combination with bevacizumab in patients with platinum-resistant ovarian cancer

David M. O'Malley [a,*], Ursula A. Matulonis [b], Michael J. Birrer [c], Cesar M. Castro [d], Lucy Gilbert [e], Ignace Vergote [f], Lainie P. Martin [g], Gina M. Mantia-Smaldone [h], Antonio González Martin [i], Raquel Bratos [j], Richard T. Penson [d], Karim Malek [k], Kathleen N. Moore [l,m]

STRO-002-GM1, a First in Human, Phase 1 Study of STRO-002, an Anti-Folate Receptor Alpha (FRα) Antibody Drug Conjugate (ADC), in Patients with Advanced Platinum-Resistant/Refractory Epithelial Ovarian Cancer (OC), Including Fallopian Tube or Primary Peritoneal Cancers

Naumann RW et al.

AACR 2020;Abstract CT125.

Meet The Professor with Dr Penson

MODULE 1: Cases from Dr Chase

MODULE 2: Gynecologic Oncology Journal Club with Dr Penson

- Second-line lenvatinib for recurrent endometrial cancer
- GOG-240: Circulating tumor cells in advanced cervical cancer
- Clinical trial participation and aggressive care at the end of life for patients with ovarian cancer (OC)
- Ofranergene obadenovec (VB-111) alone or combined with paclitaxel for platinum-resistant OC
- Pembrolizumab with pegylated liposomal doxorubicin for platinum-resistant OC
- Berzosertib with gemcitabine for platinum-resistant high-grade serous OC
- Avelumab in MMR-deficient and proficient recurrent or persistent endometrial cancer
- Nivolumab/bevacizumab for relapsed OC
- Mirvetuximab soravtansine with bevacizumab for platinum-resistant OC
- First-in-human study of STRO-002, an anti-folate receptor alpha antibody-drug conjugate, for platinum-resistant/refractory OC

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

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RTP RESEARCH TO PRACTICE

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

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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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

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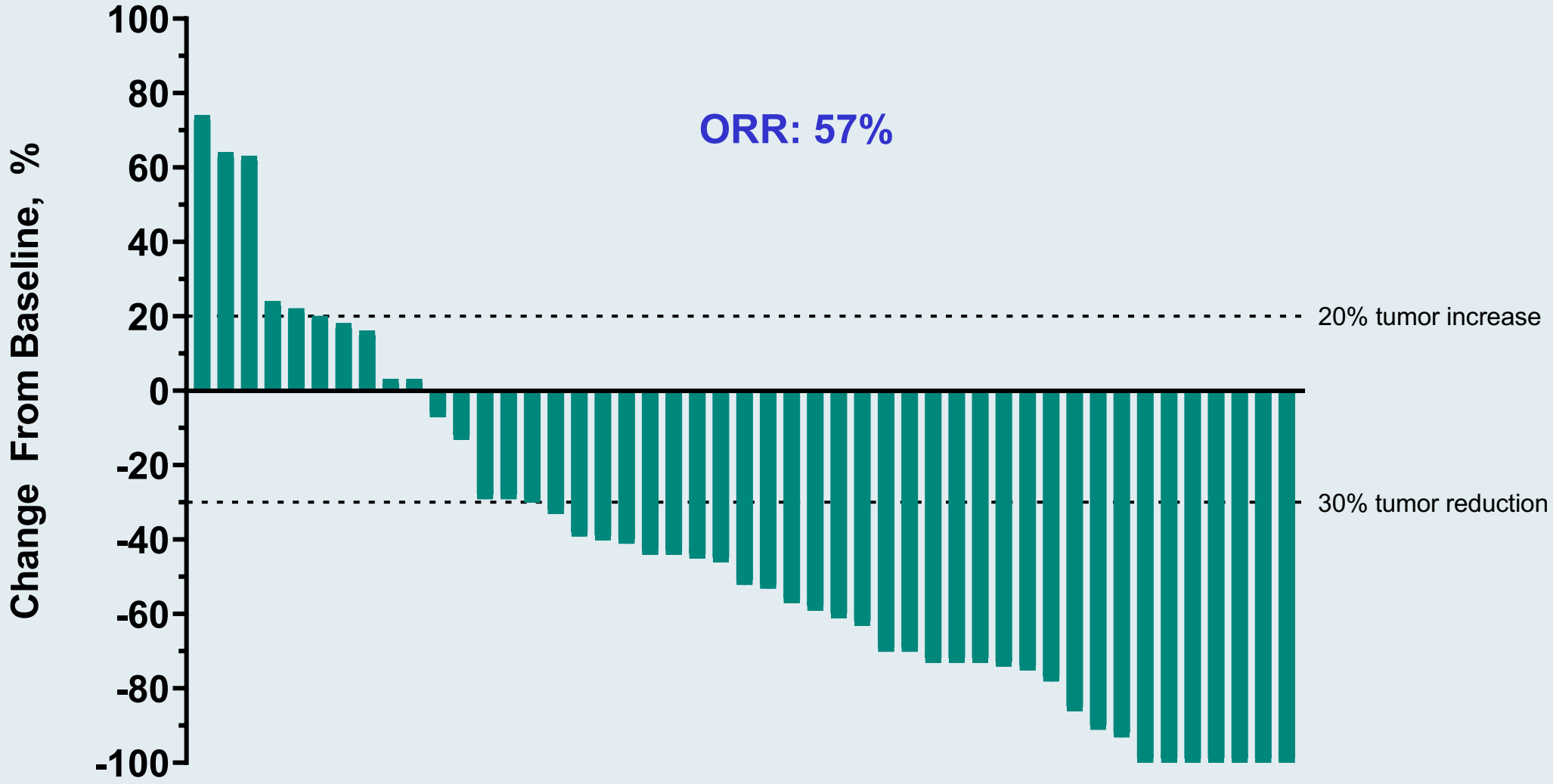
KEYNOTE-158: Best Percentage Change from Baseline in Target Lesion Size with Pembrolizumab Monotherapy in MSI-H Endometrial Cancer



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

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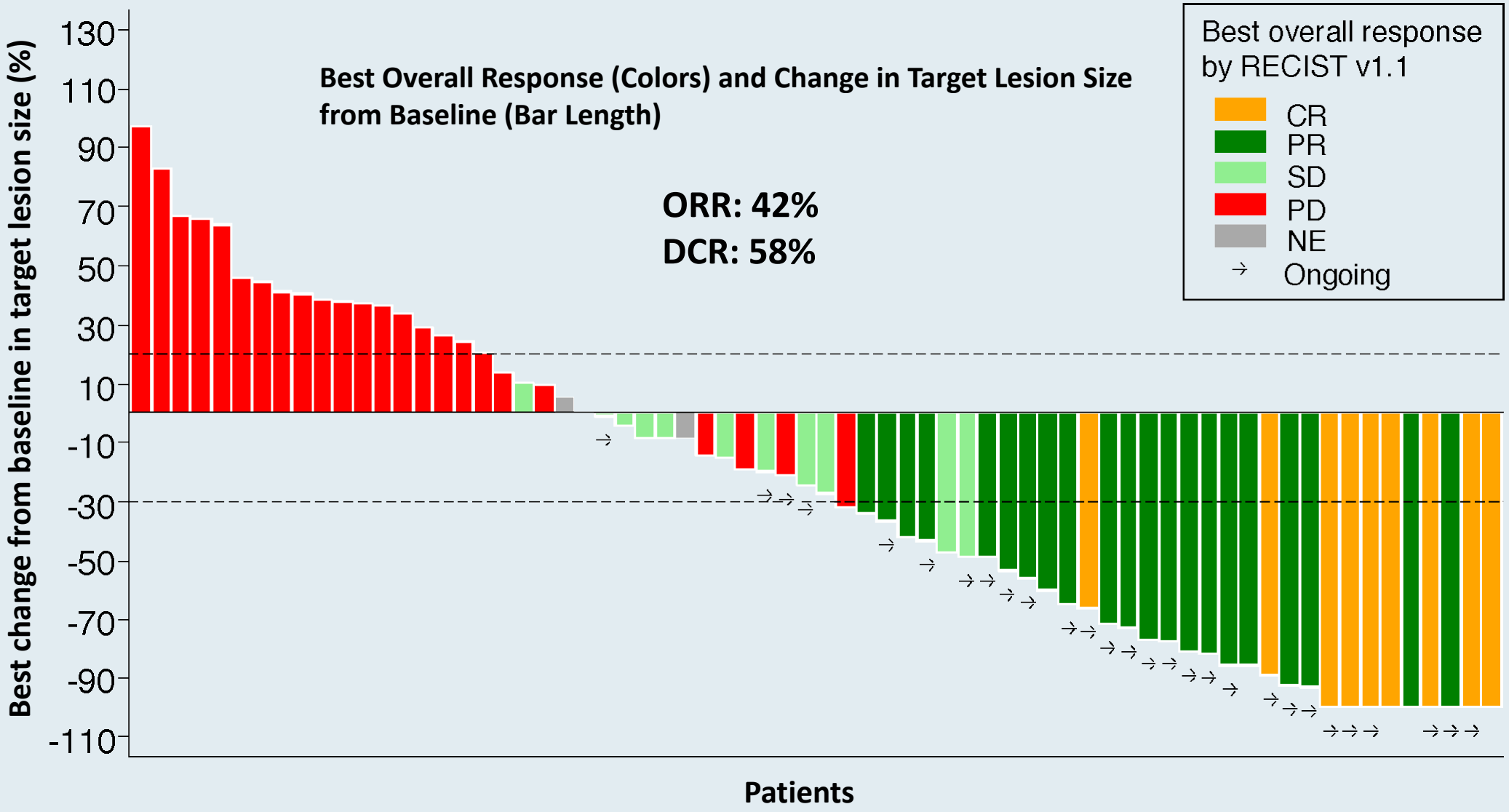
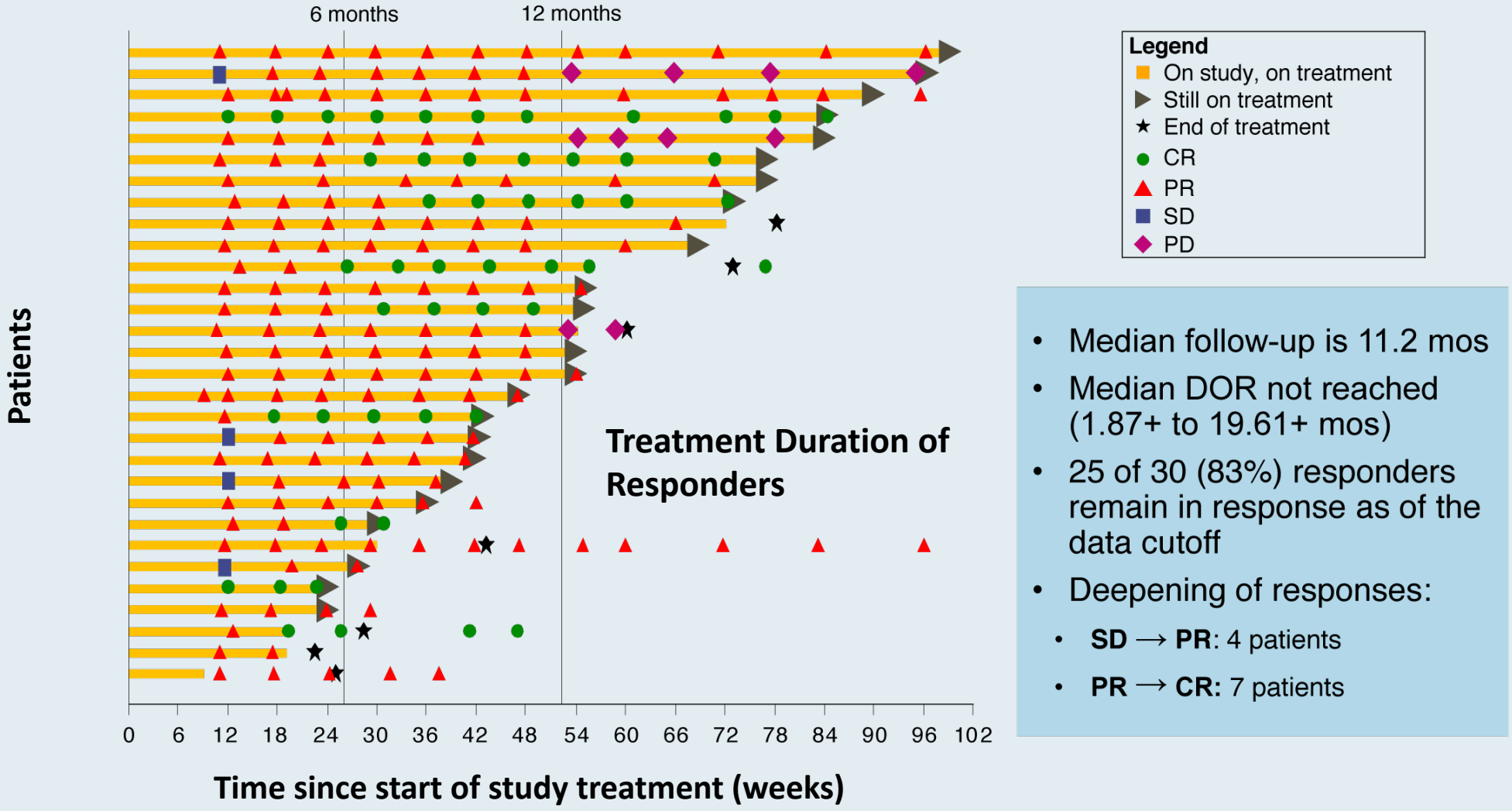
GARNET: Dostarlimab in Recurrent or Advanced dMMR Endometrial Cancer



Oaknin A et al. SGO 2020;Abstract LBA9.

GARNET: Dostarlimab in Recurrent or Advanced dMMR Endometrial Cancer

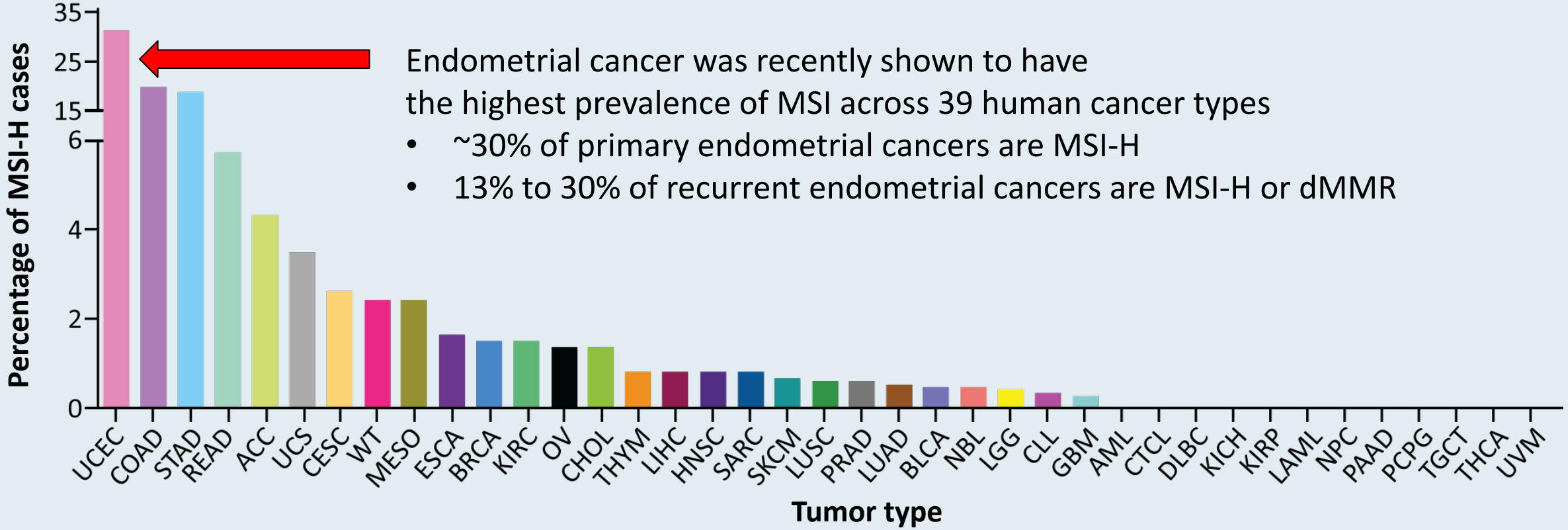


- Median follow-up is 11.2 mos
- Median DOR not reached (1.87+ to 19.61+ mos)
- 25 of 30 (83%) responders remain in response as of the data cutoff
- Deepening of responses:
  - **SD → PR**: 4 patients
  - **PR → CR:** 7 patients

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

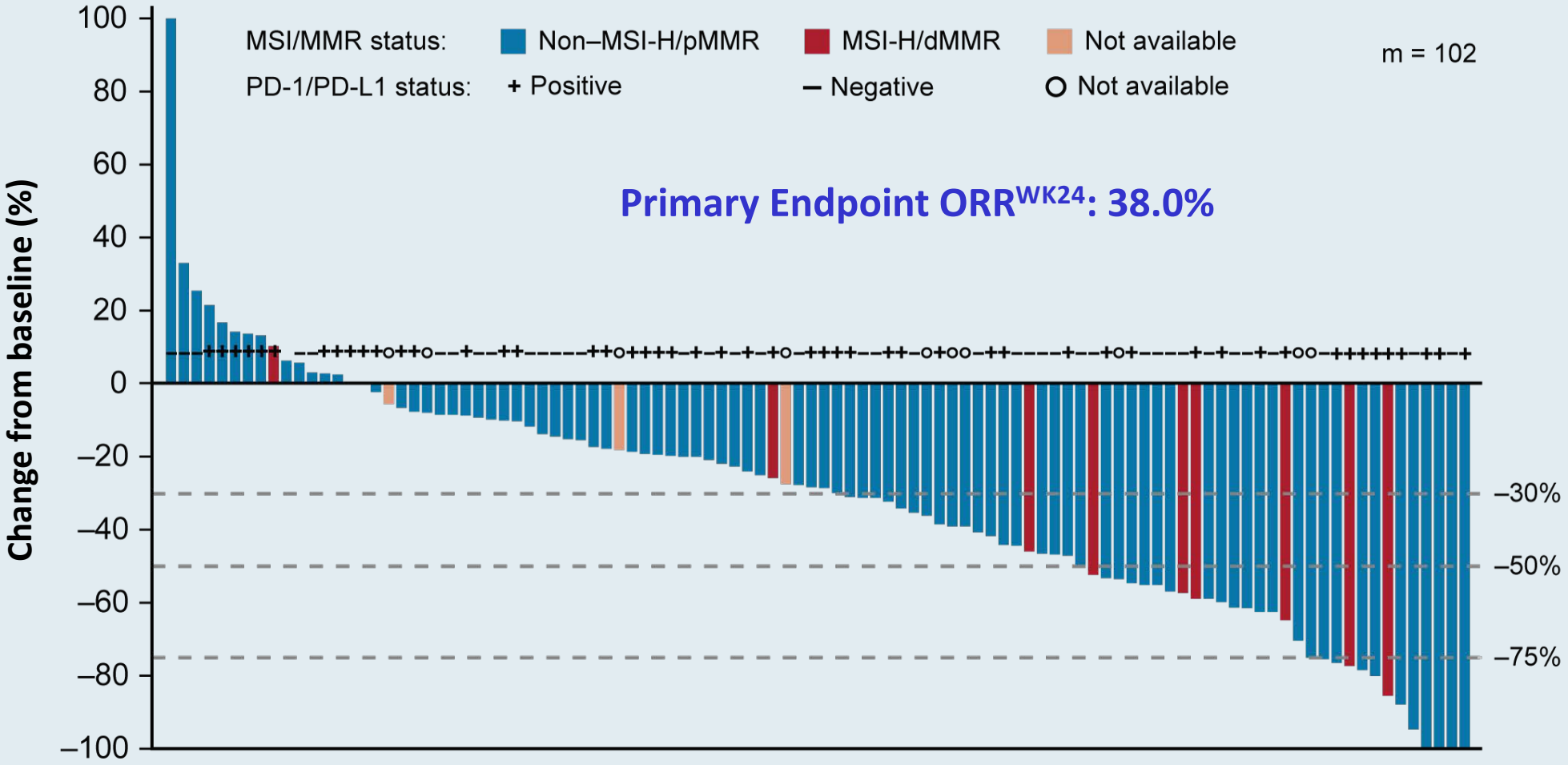
- ~30% of primary endometrial cancers are MSI-H
- 13% to 30% of recurrent endometrial cancers are MSI-H or dMMR

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

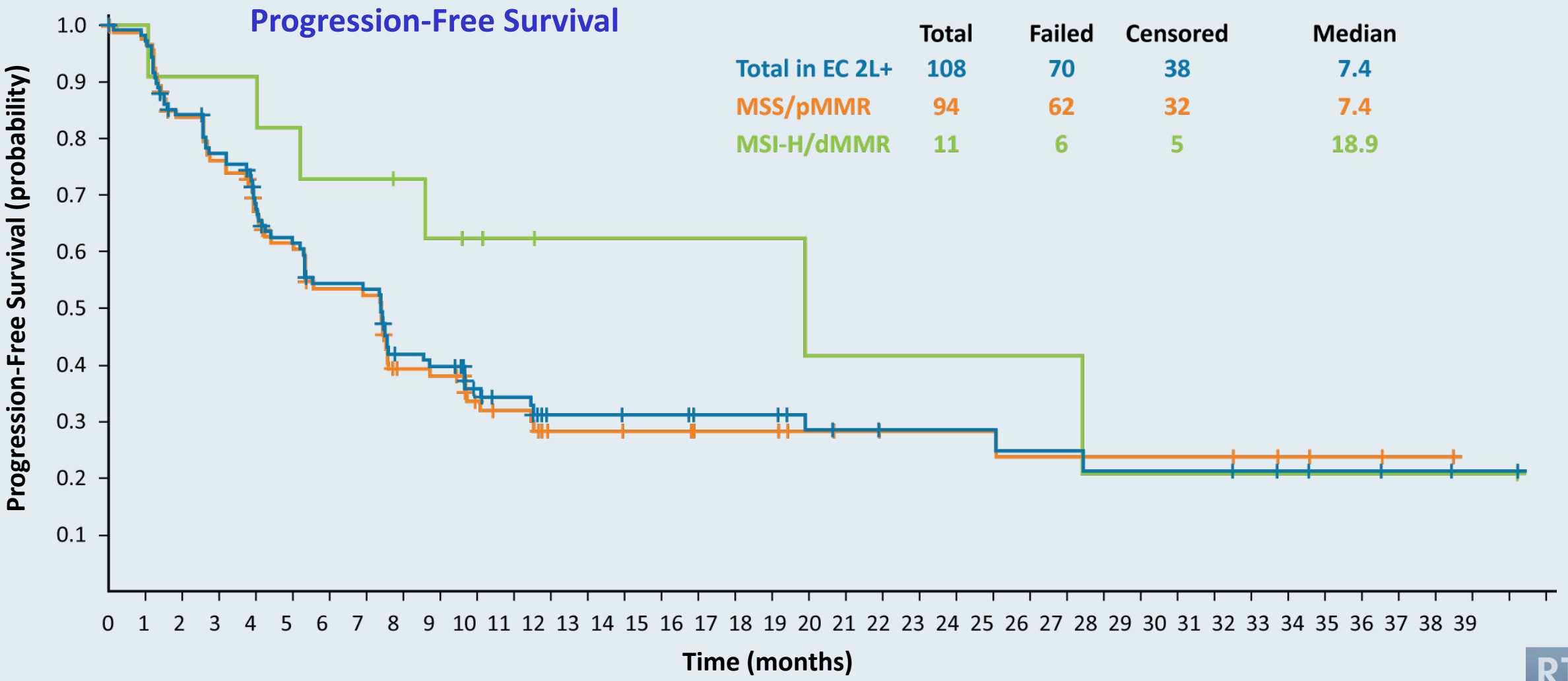
KEYNOTE-146: Pembrolizumab/Lenvatinib in Advanced Endometrial Cancer That Is *Not* MSI-H or dMMR After Disease Progression on Prior Systemic Therapy



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

RTP RESEARCH TO PRACTICE

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

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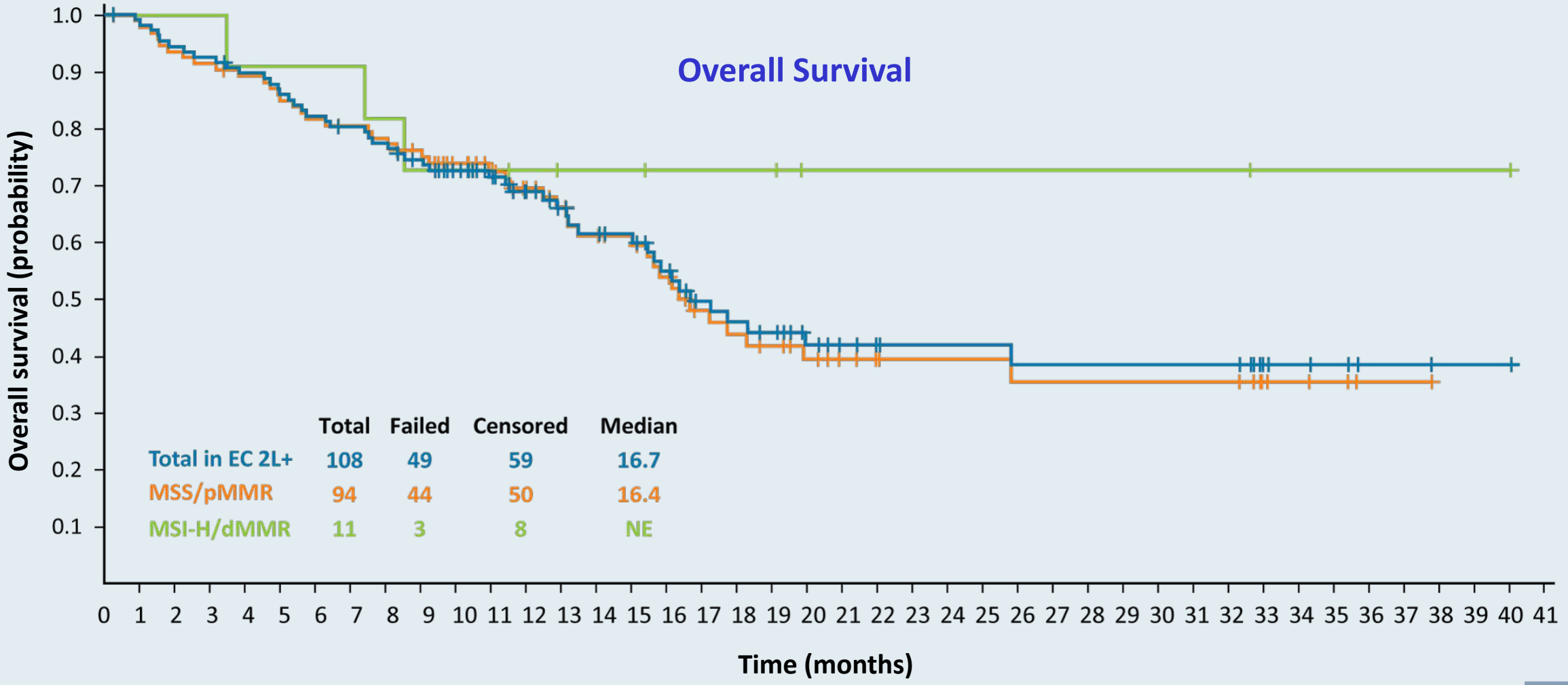

Makker V et al. *J Clin Oncol* 2020;[Online ahead of print].

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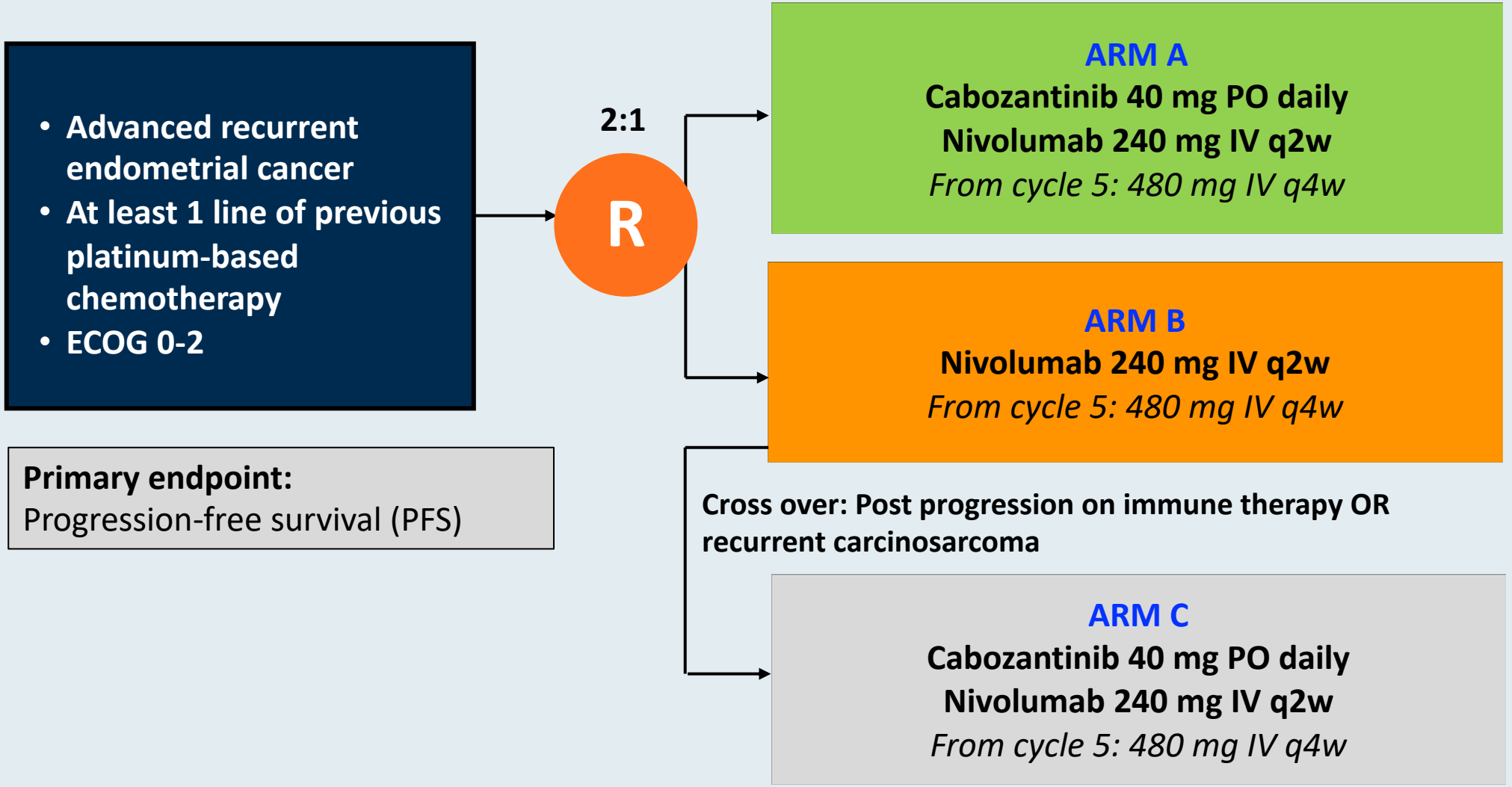
NCI 10104: A Randomized Phase 2 Study of Cabozantinib in Combination with Nivolumab in Advanced, Recurrent Metastatic Endometrial Cancer

Lheureux S et al.

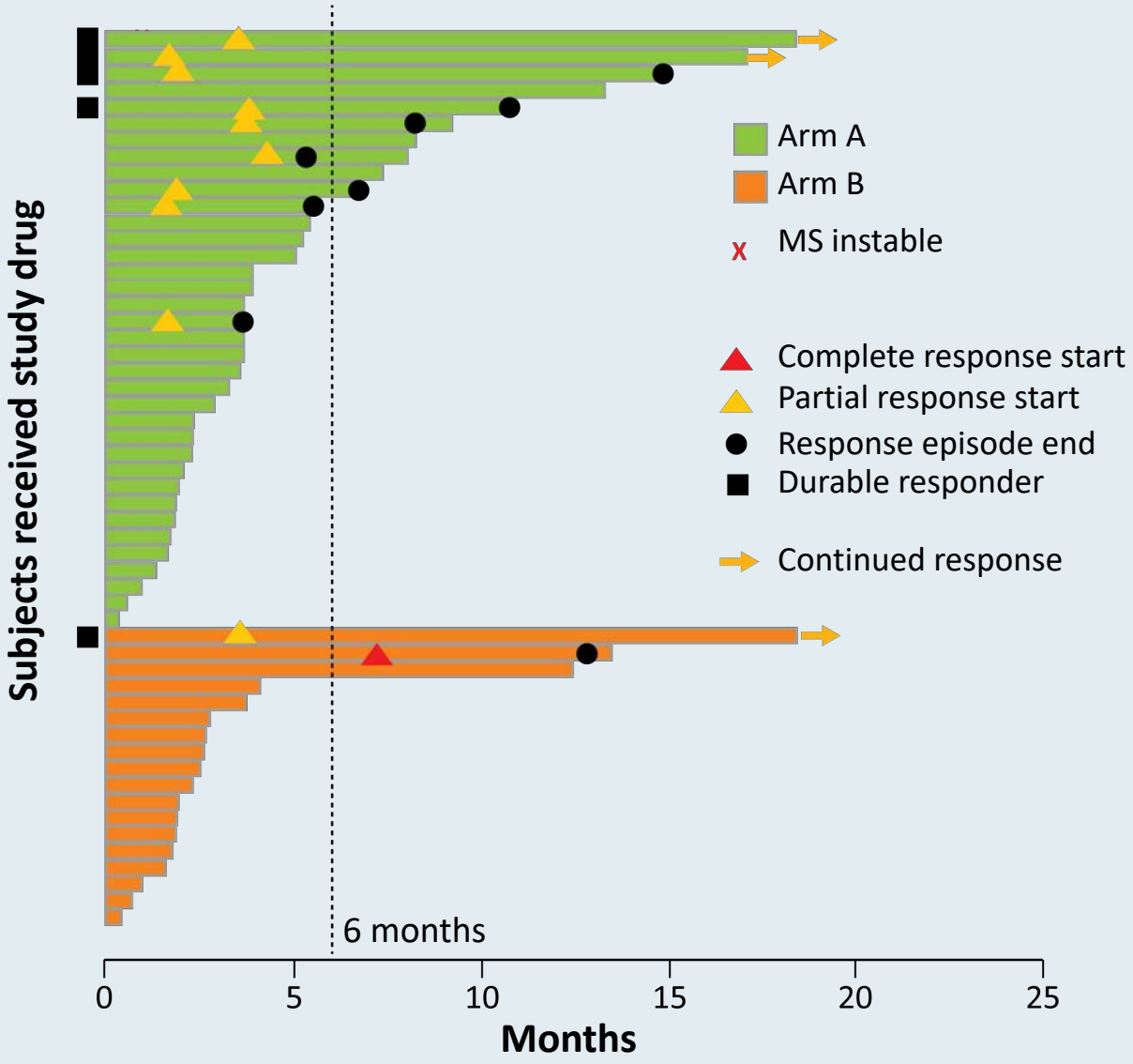
ASCO 2020;Abstract 6010.

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.

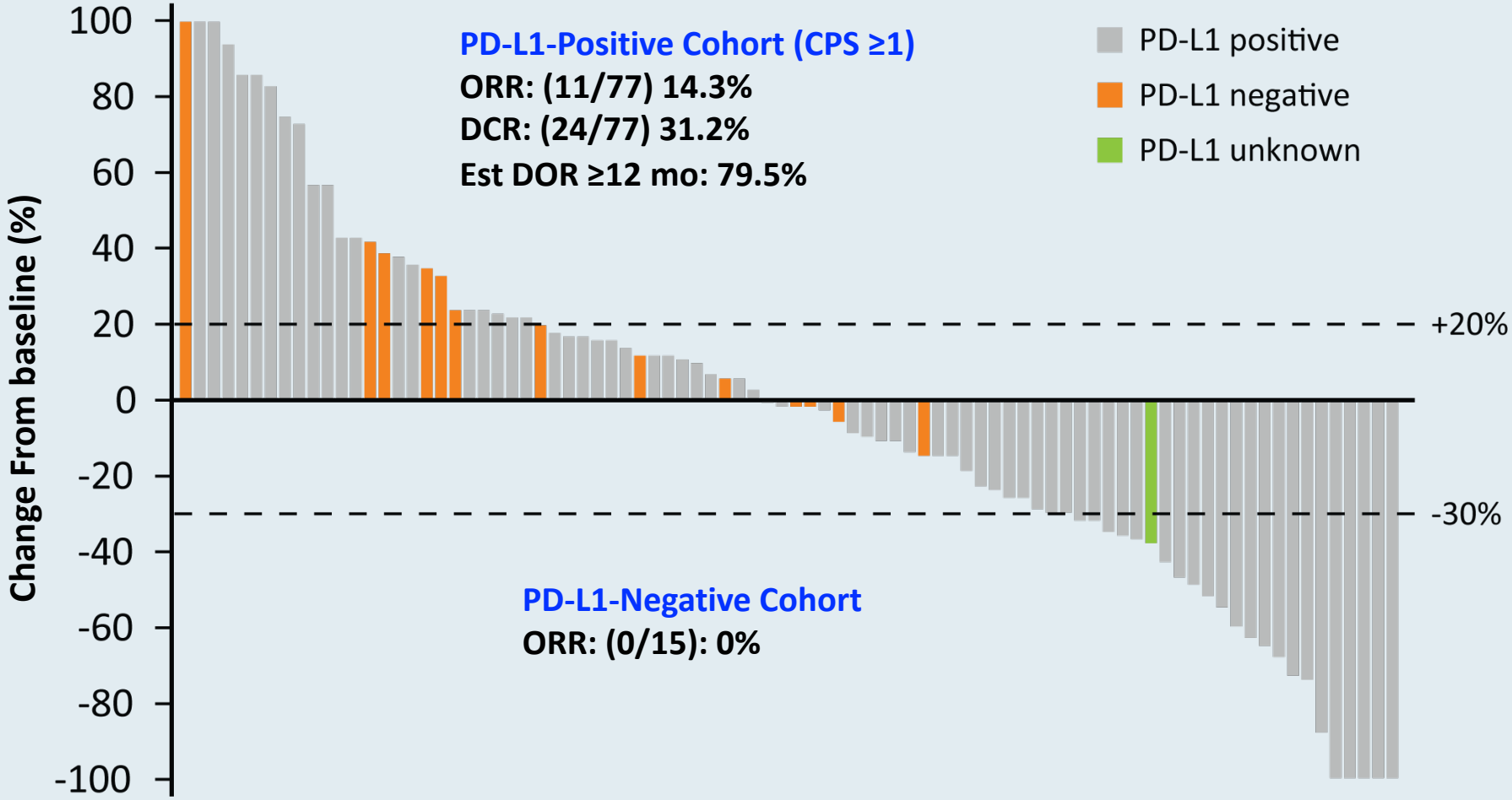
Select Ongoing Phase III Immune Checkpoint Inhibitor Combination Studies

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.

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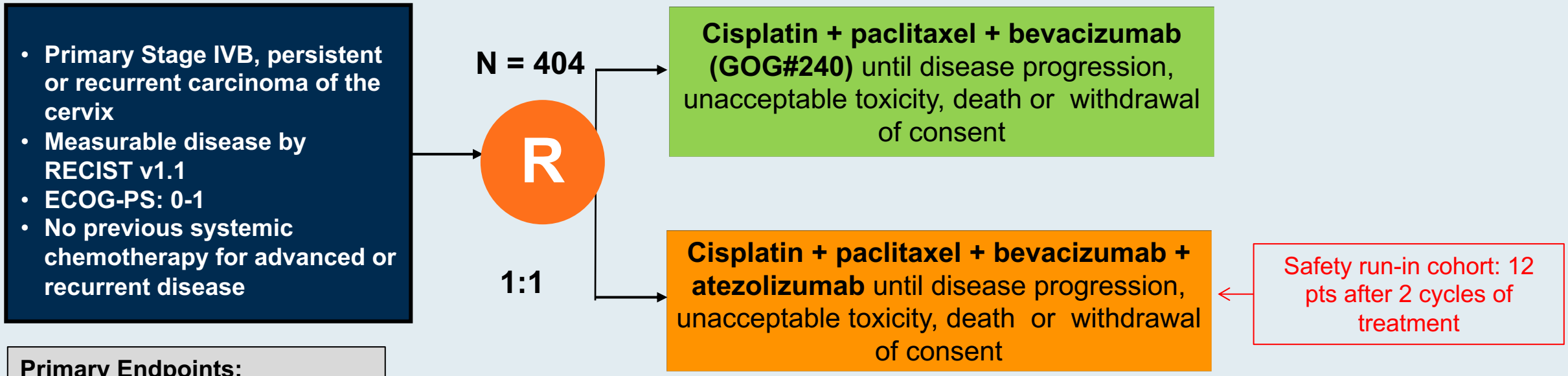
BEATcc Phase III Randomized Front-Line Trial of Atezolizumab



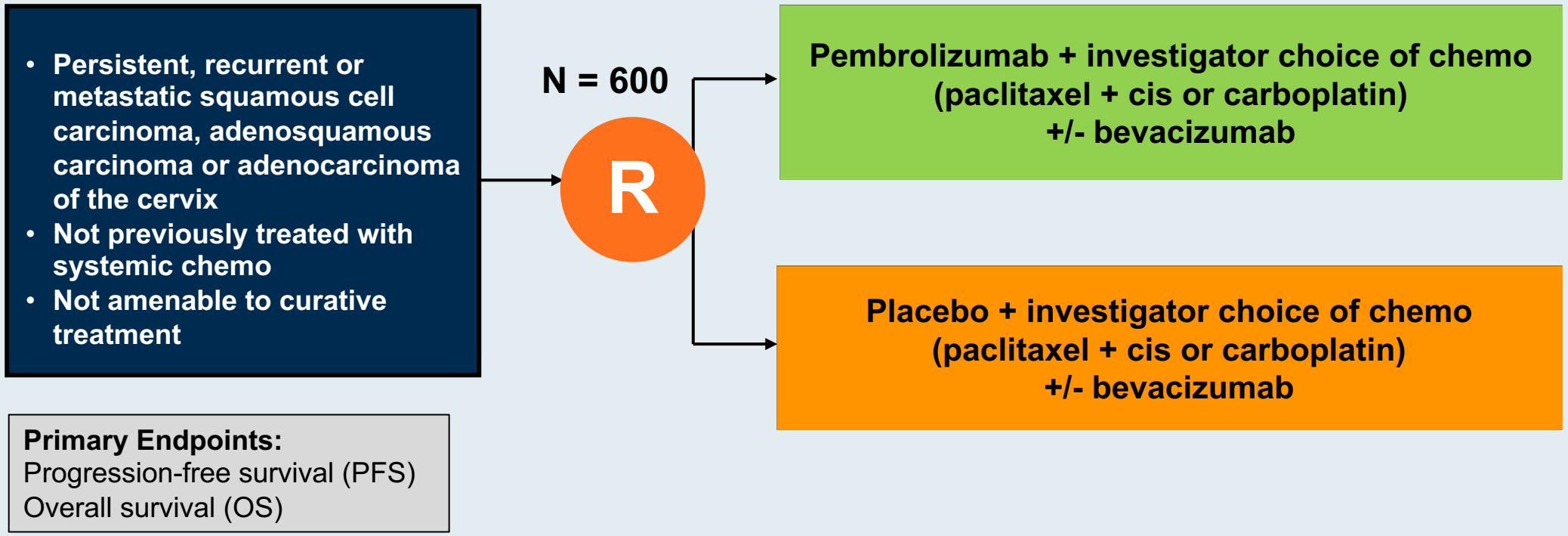
Primary Endpoints:
Overall survival (OS)
Secondary Endpoints:
- PFS
- ORR
- DOR
- Safety
- HR-QOL

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

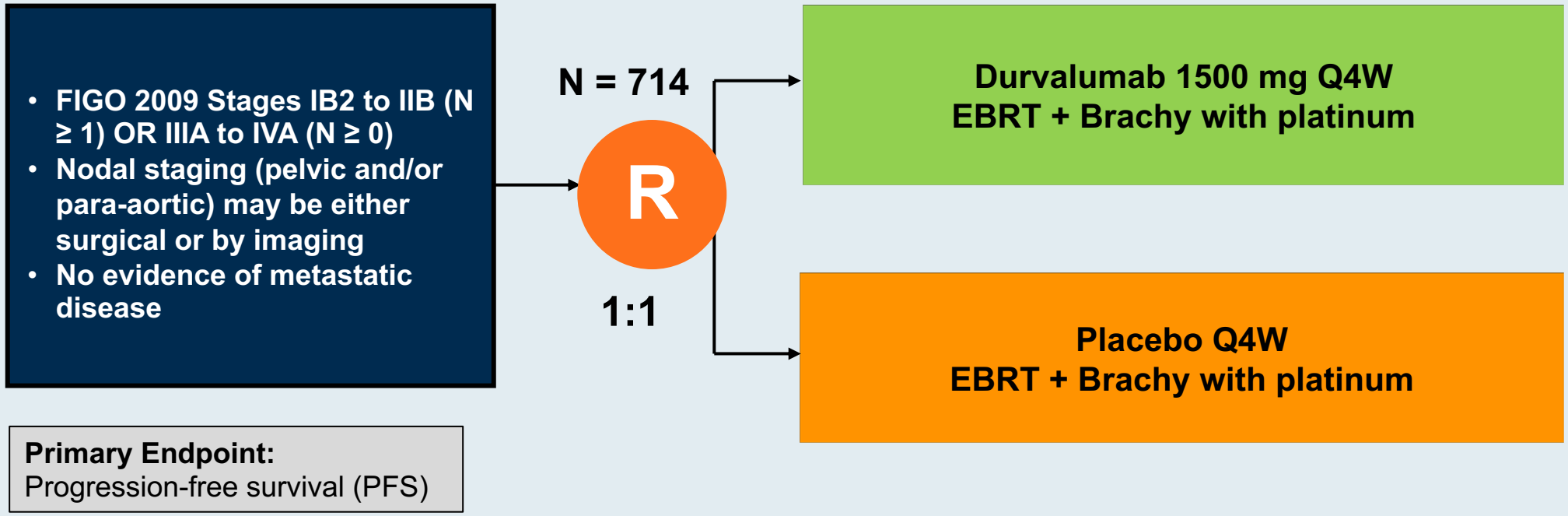
KEYNOTE-826 Phase III Schema



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.

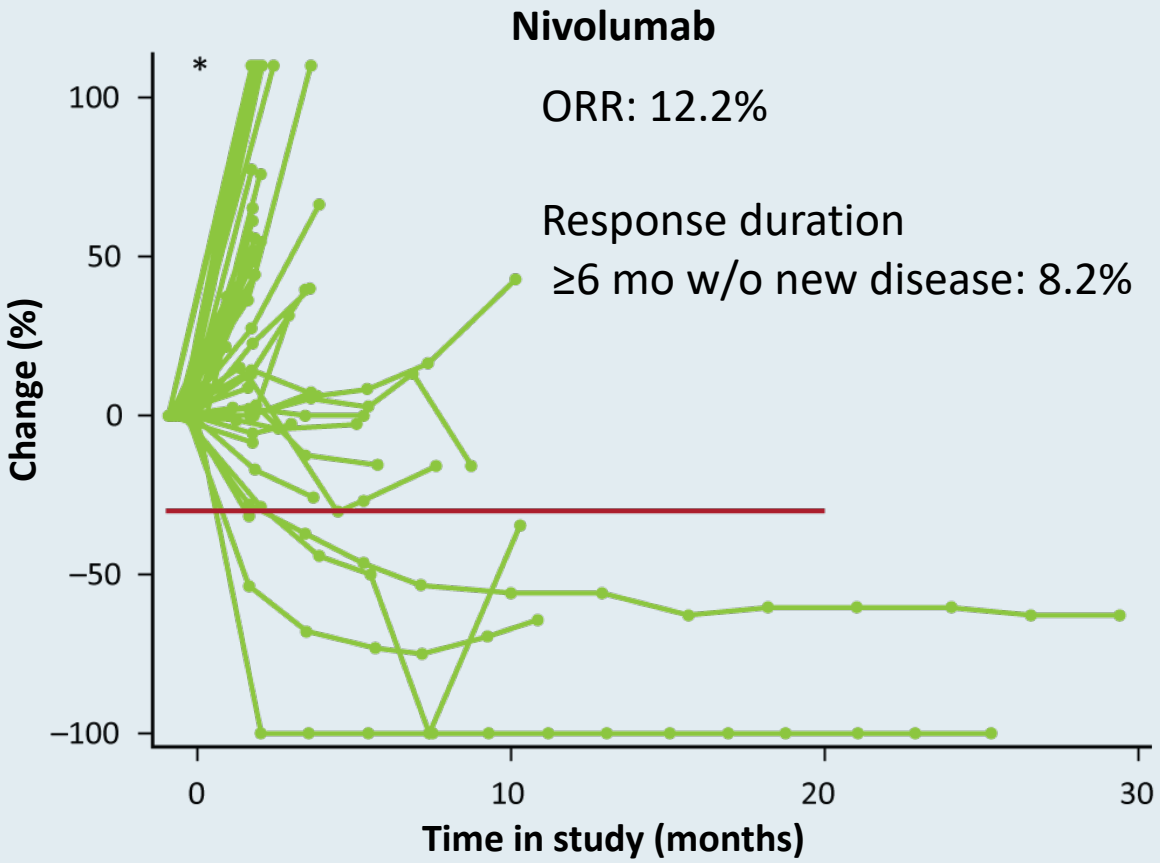
JAVELIN Ovarian 200: Avelumab Alone or in Combination with Pegylated Liposomal Doxorubicin (PLD) versus PLD Alone in Platinum-Resistant or Refractory OC

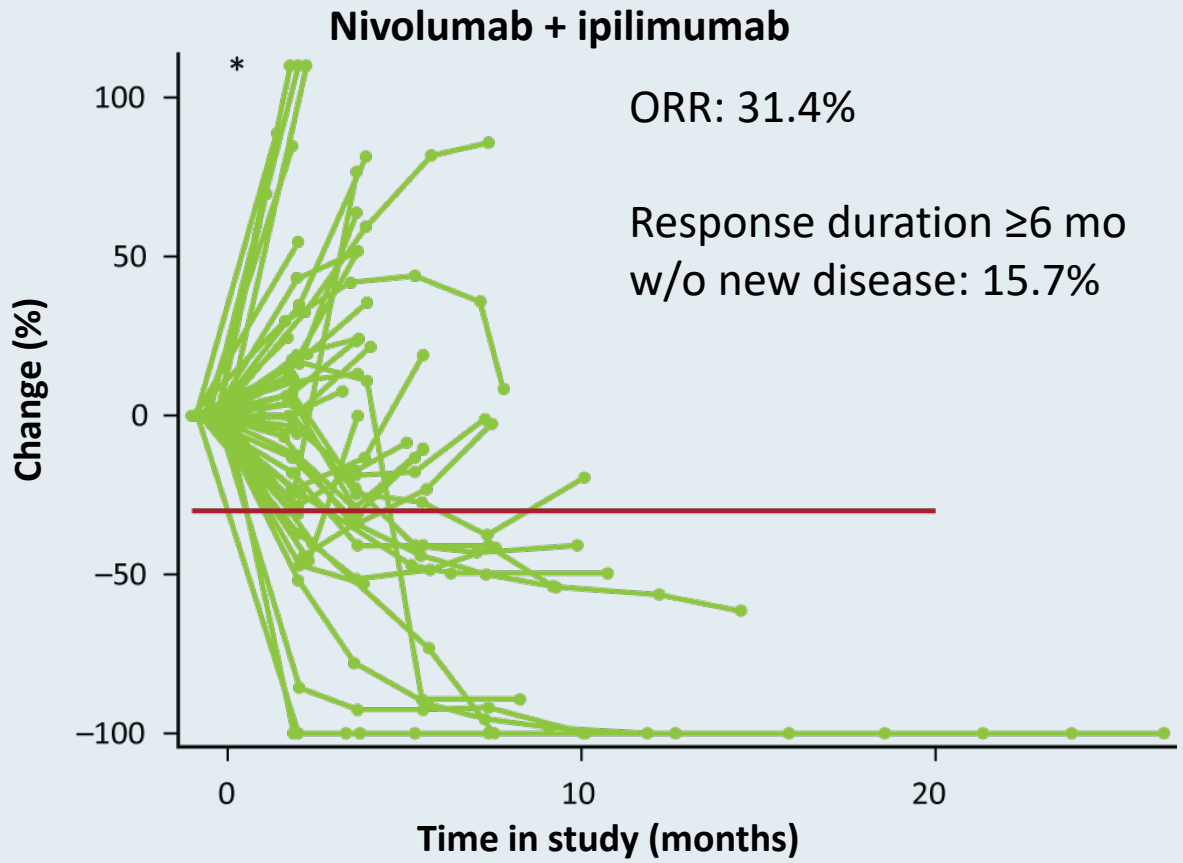
	Avelumab (n = 188)		Avelumab + PLD (n = 188)		PLD (n = 190)	
All patients						
Median OS	11.8 mo		15.7 mo		13.1 mo	
	HR: 1.14, *p* = 0.83		HR: 0.80, *p* = 0.21		Reference	
Median PFS	1.9 mo		3.7 mo		3.5 mo	
	HR: 1.68, *p* > 0.99		HR: 0.78, *p* = 0.03		Reference	
PD-L1 evaluable	**PD-L1+ (n = 91)**	**PD-L1- (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)

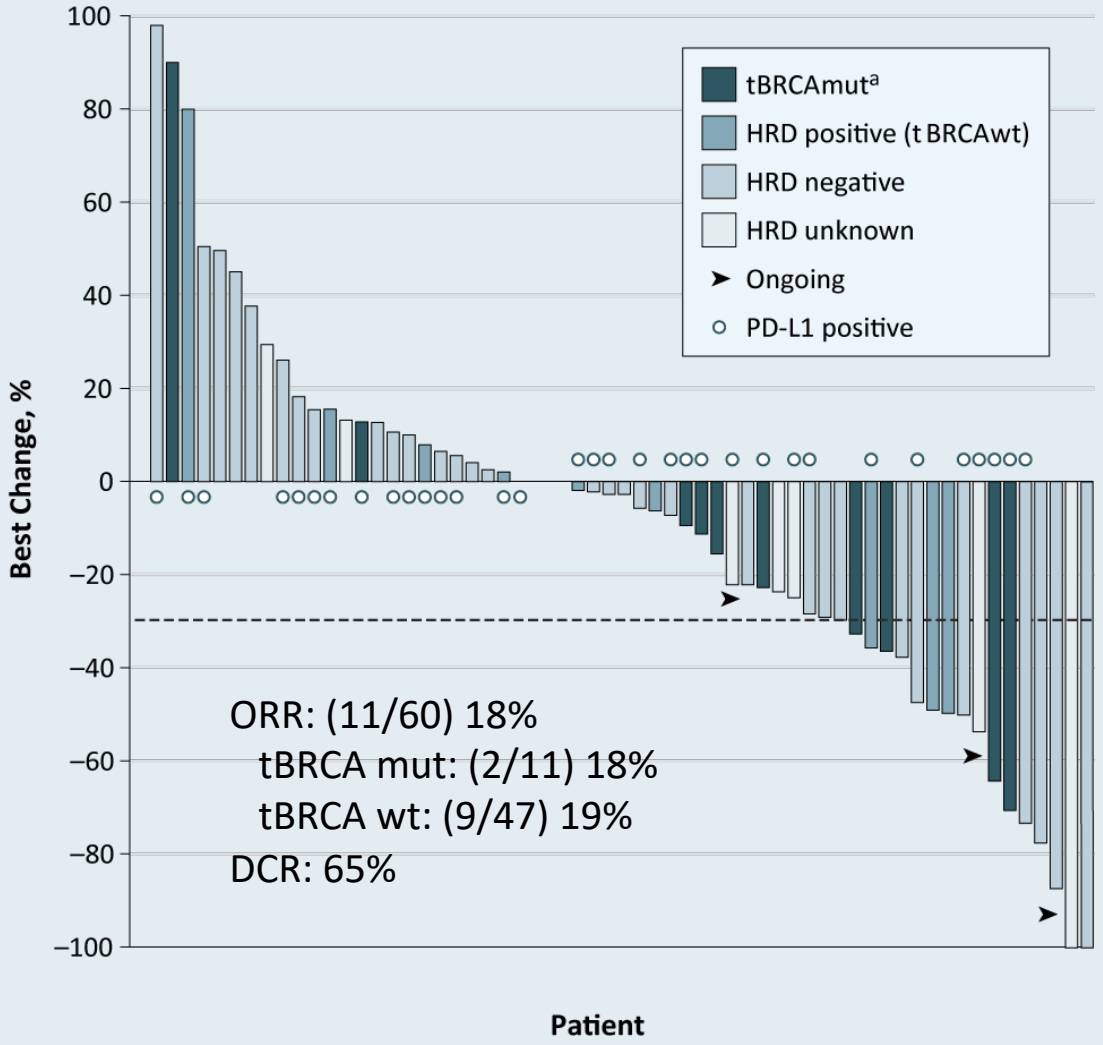


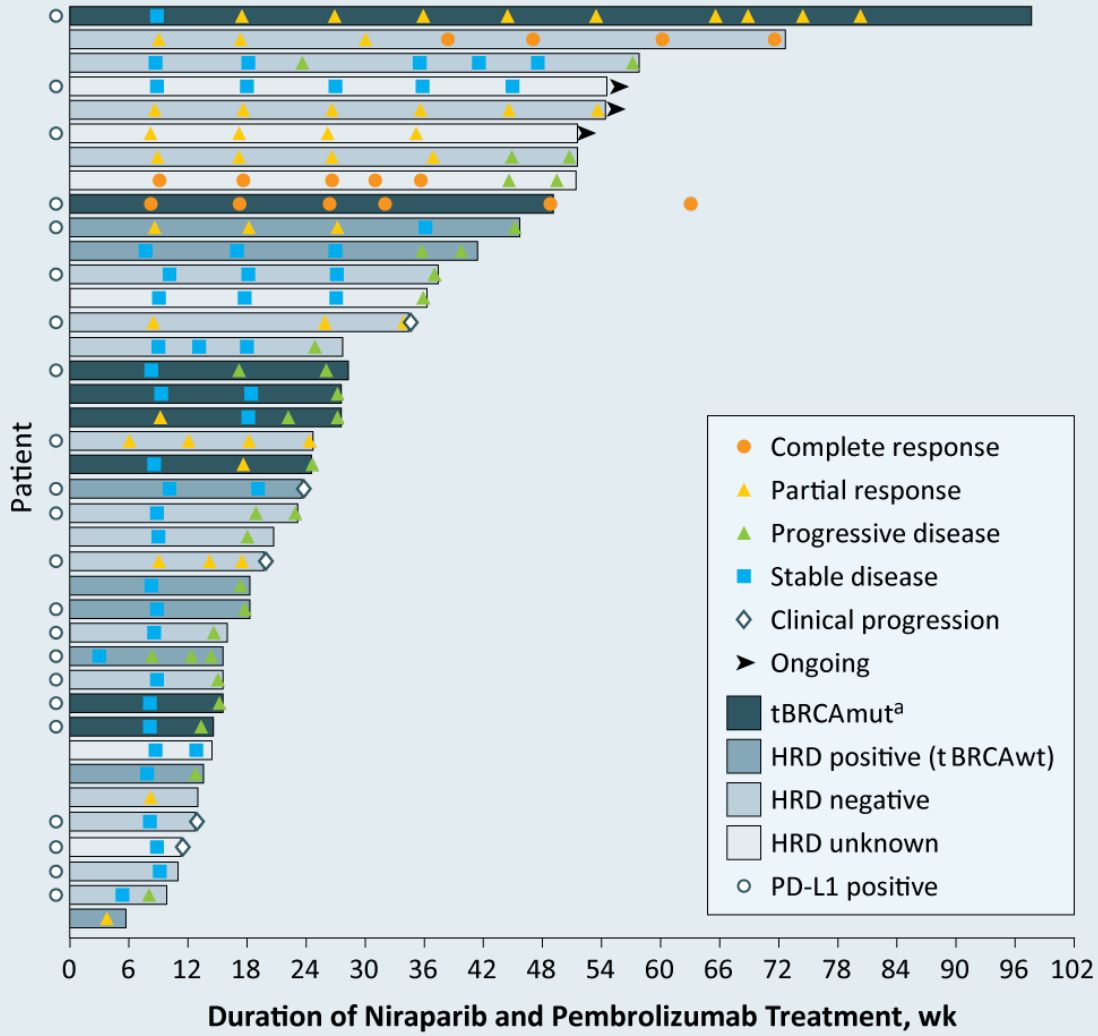


PD-L1 expression was not significantly associated with response in either treatment group

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

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

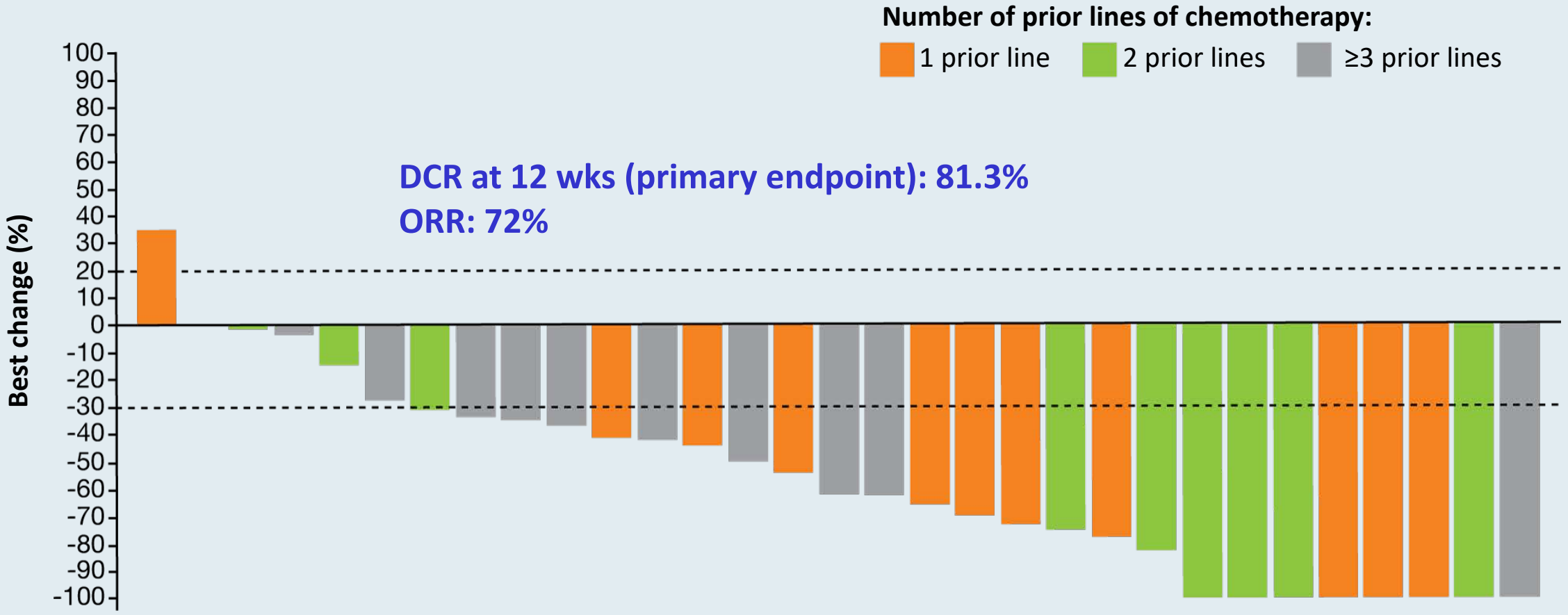




Konstantinopoulos PA, et al. *JAMA Oncol* 2019;5(8):1141-9.

RTP RESEARCH TO PRACTICE

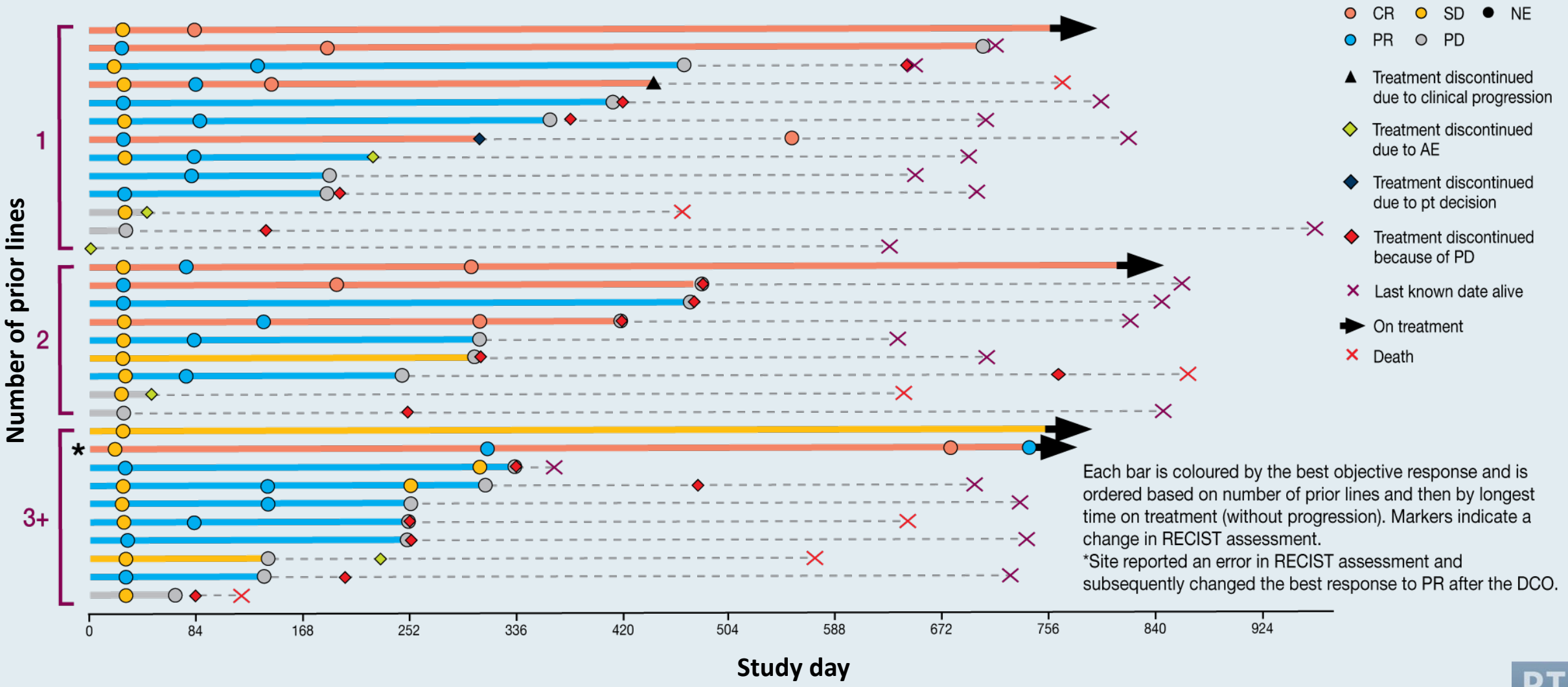
MEDIOLA: A Phase II Study of Olaparib and Durvalumab in gBRCA-Mutated Platinum-Sensitive Relapsed OC



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

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.

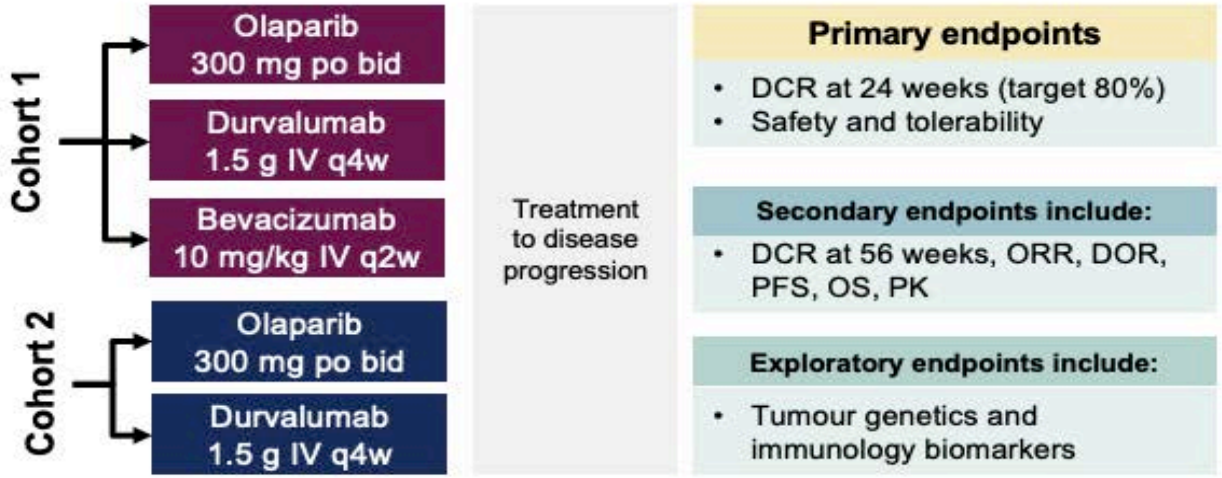
ESMO 2020;Abstract 814MO.

MEDIOLA: gBRCAwt Cohorts

Study Design

Patient population

- gBRCAwt
- PSR ovarian cancer
- ≤2 prior lines of chemotherapy
- PARP inhibitor and IO agent naïve

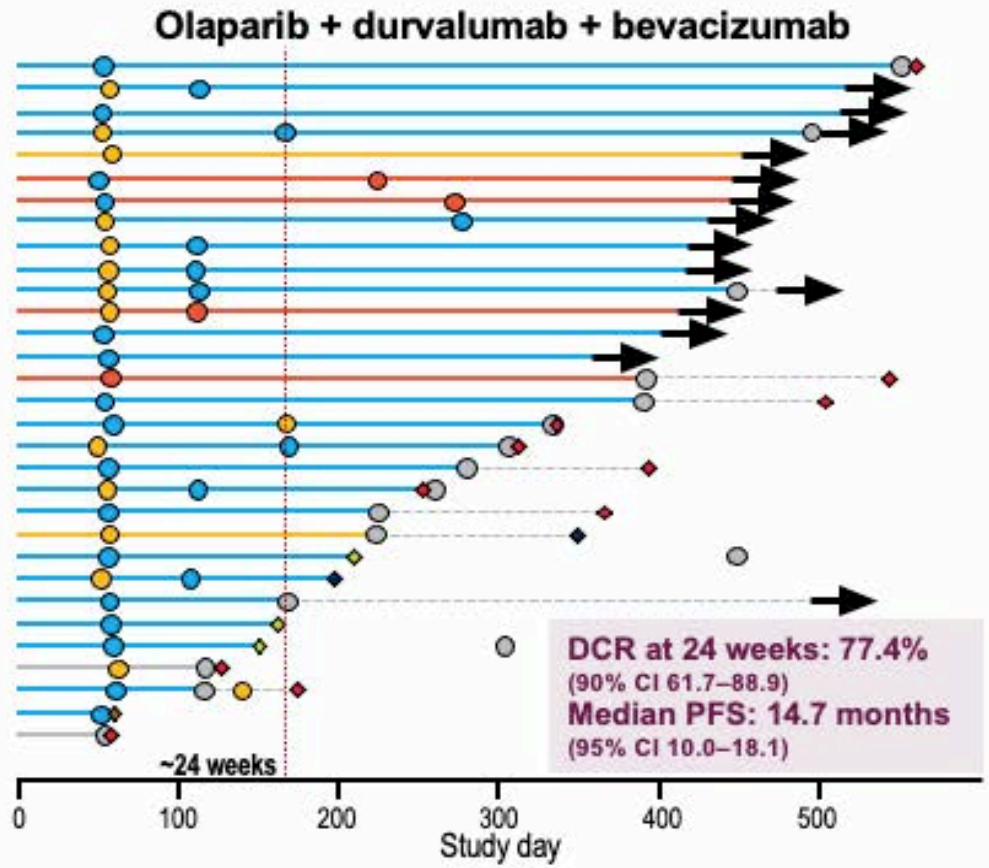


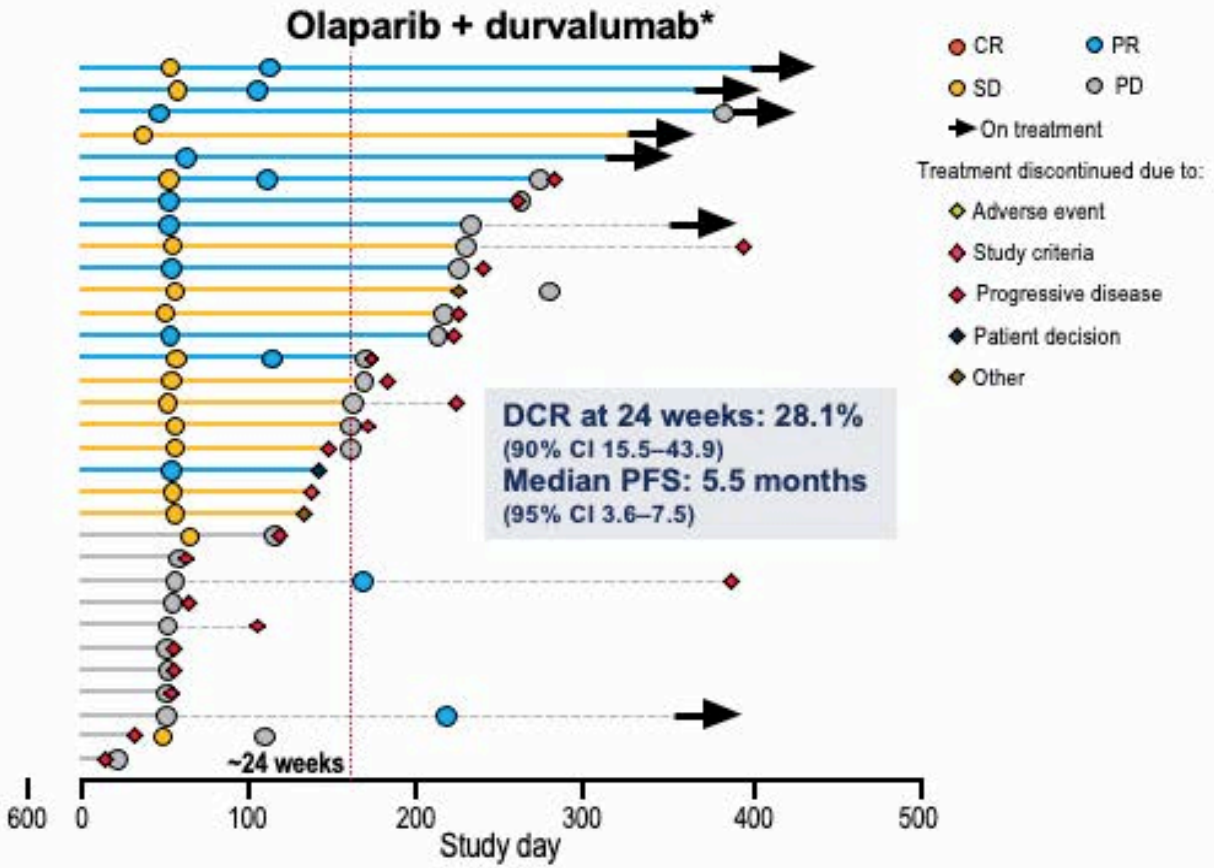
Patient Characteristics

	Olap + durva + bev (N=31)	Olap + durva (N=32)
Median age, years	64.0	68.5
Age group (years), n (%)		
<50	3 (9.7)	4 (12.5)
≥50–<65	14 (45.2)	8 (25.0)
≥65	14 (45.2)	20 (62.5)
Race, n (%)		
White	20 (64.5)	24 (75.0)
Asian	10 (32.3)	3 (9.4)
Other	1 (3.2)	5 (15.6)
Platinum sensitivity, n (%)		
>6–12 months	18 (58.1)	14 (43.8)
>12 months	13 (41.9)	18 (56.3)
Number of prior lines of chemotherapy, n (%)		
1 prior line	20 (64.5)	23 (71.9)
2 prior lines	11 (35.5)	9 (28.1)
Enrolment completed	January 2019	February 2019
Patients on study treatment at DCO, n (%) (13 February 2020)		
Olap; durva; bev	13 (41.9); 13 (41.9); 12 (38.7)	7 (21.9); 6 (18.8); NA

Drew Y et al. ESMO 2020;Abstract 814MO.

MEDIOLA: TTP or Treatment Discontinuation

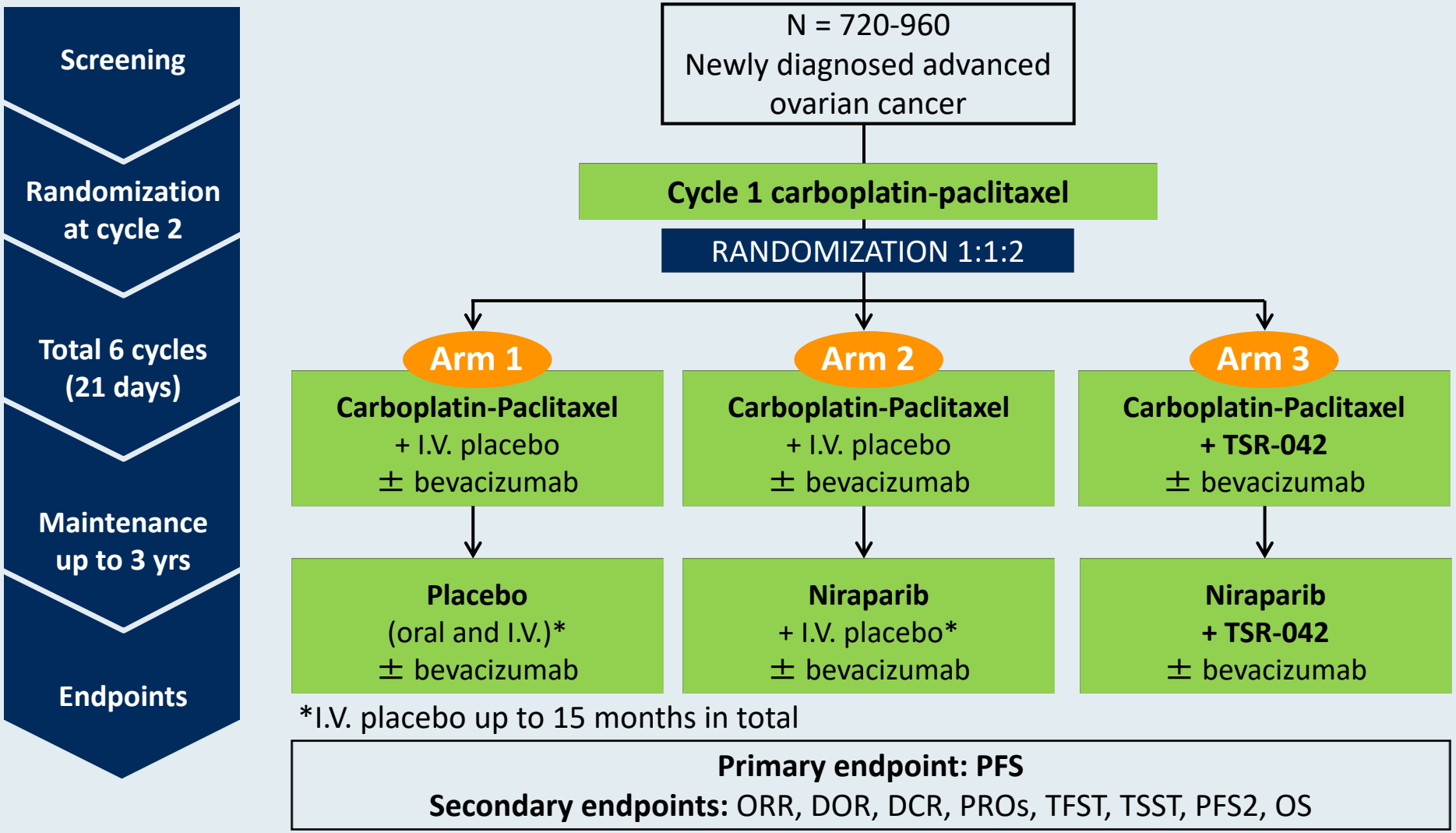




- **Triplet cohort showed high DCT at 24 weeks and a long median PFS**

Drew Y et al. ESMO 2020;Abstract 814MO.

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

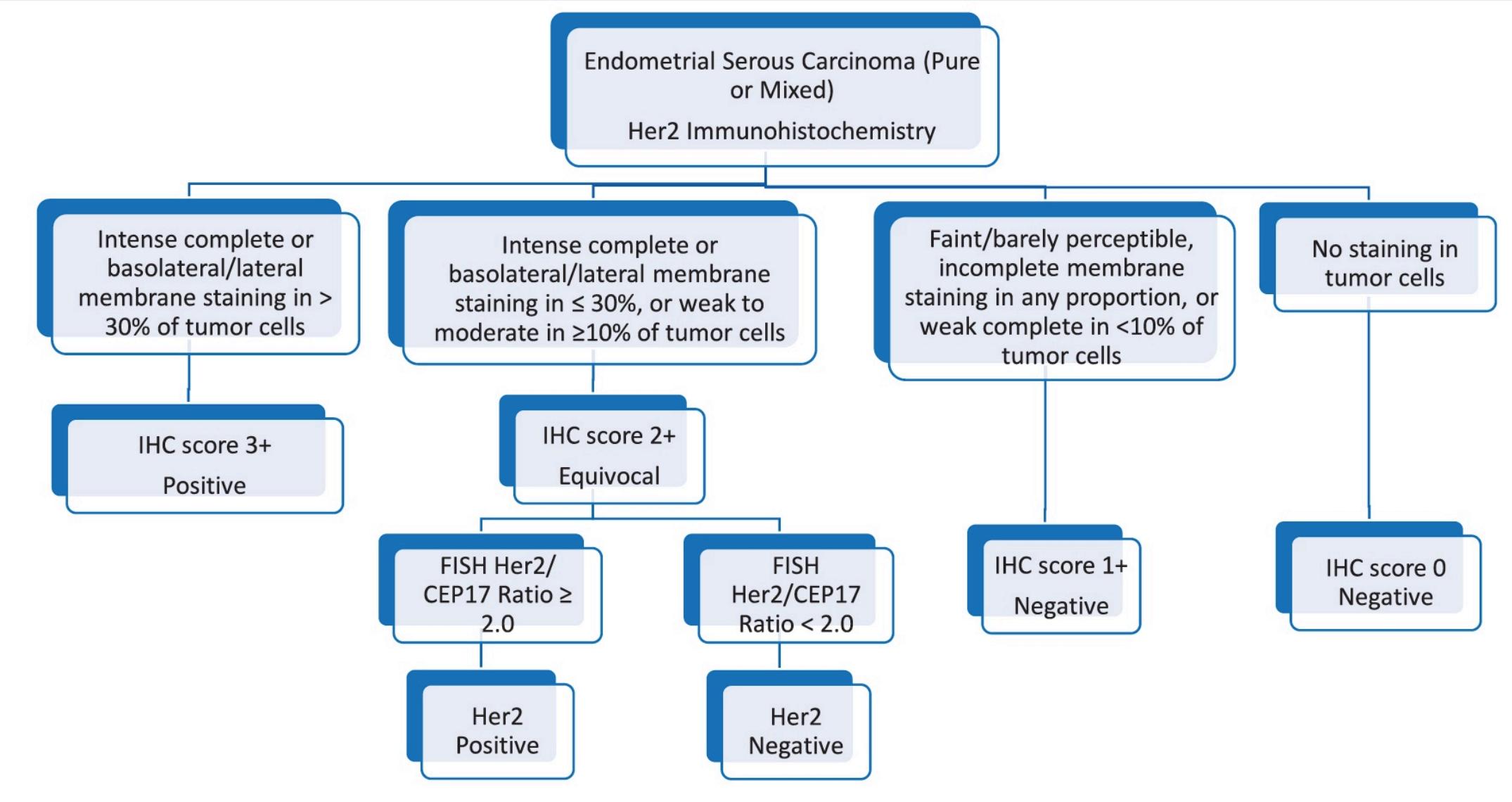
	Breast (ASCO/CAP 2018)[23]	Gastric (ASCO/CAP 2016)[36]	Colorectal (HERACLES Trial)[39]	Endometrial Serous (Fader et al Clinical Trial)[21]
HER2 IHC 3+	>10% circumferential, strong, complete	≥10%, strong complete, or basolateral/lateral	≥50% strong complete, or basolateral/lateral	>30% strong complete 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



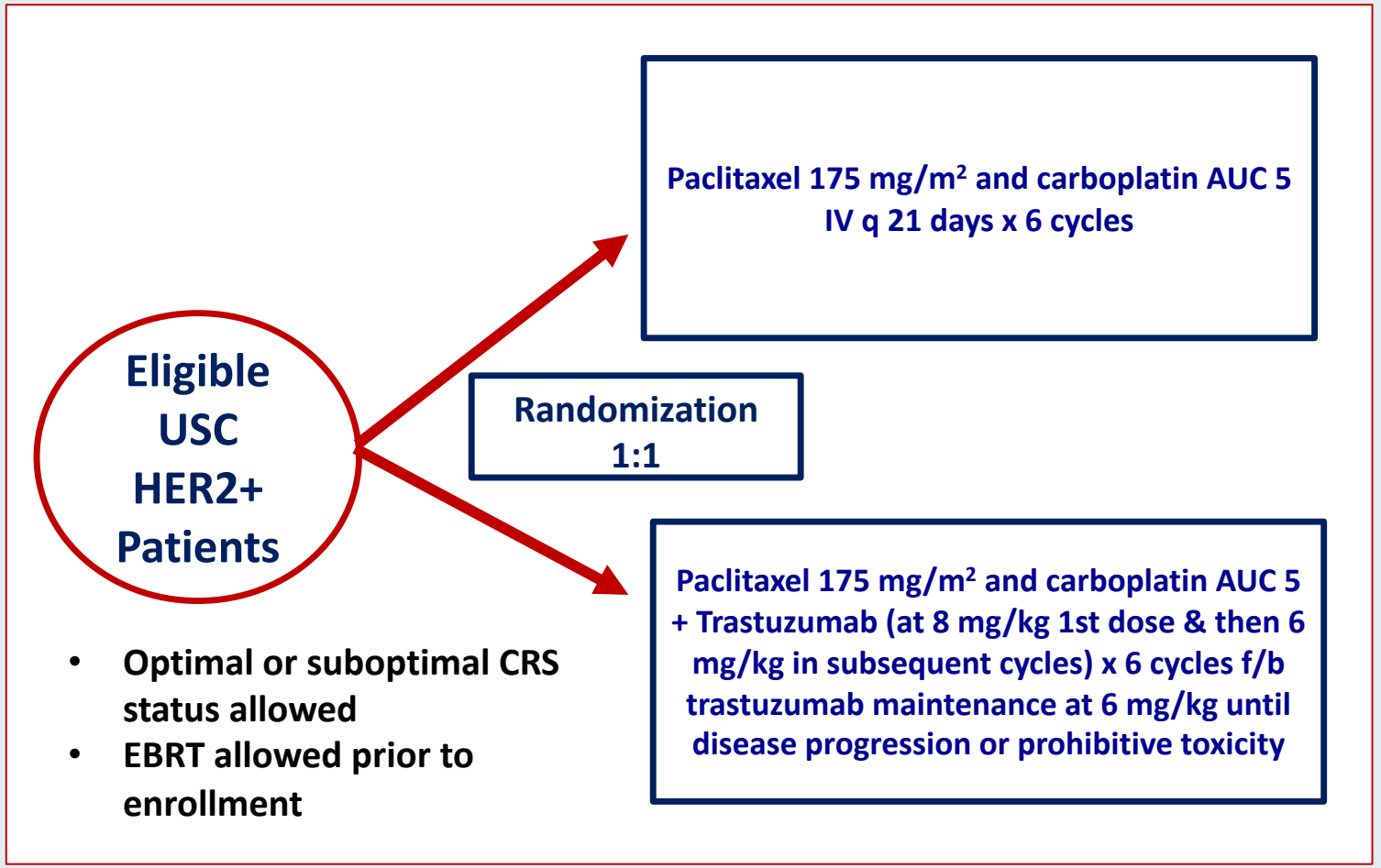
Buza N. *Arch Pathol Lab Med* 2020;[Online ahead of print].

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

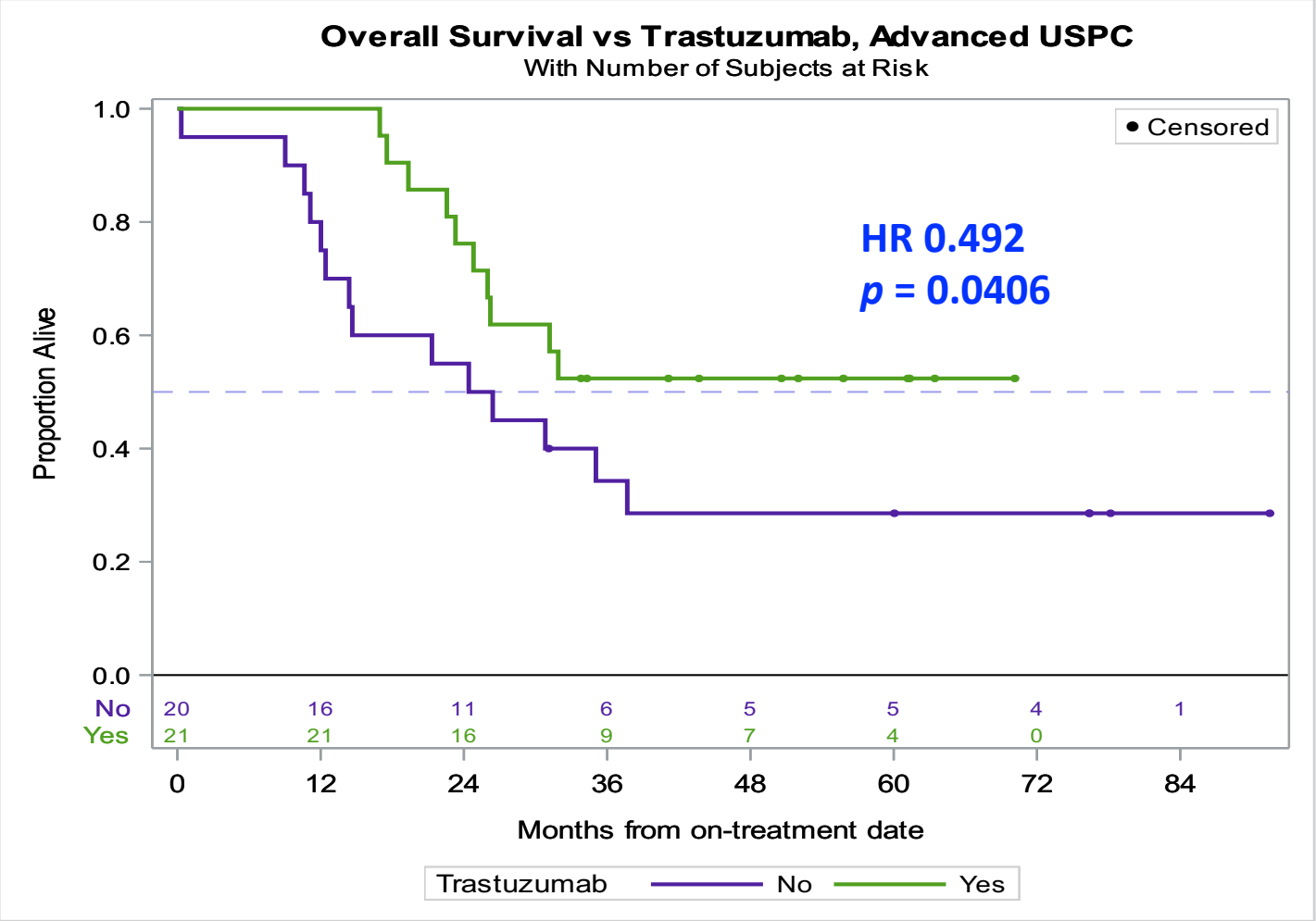


Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

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)



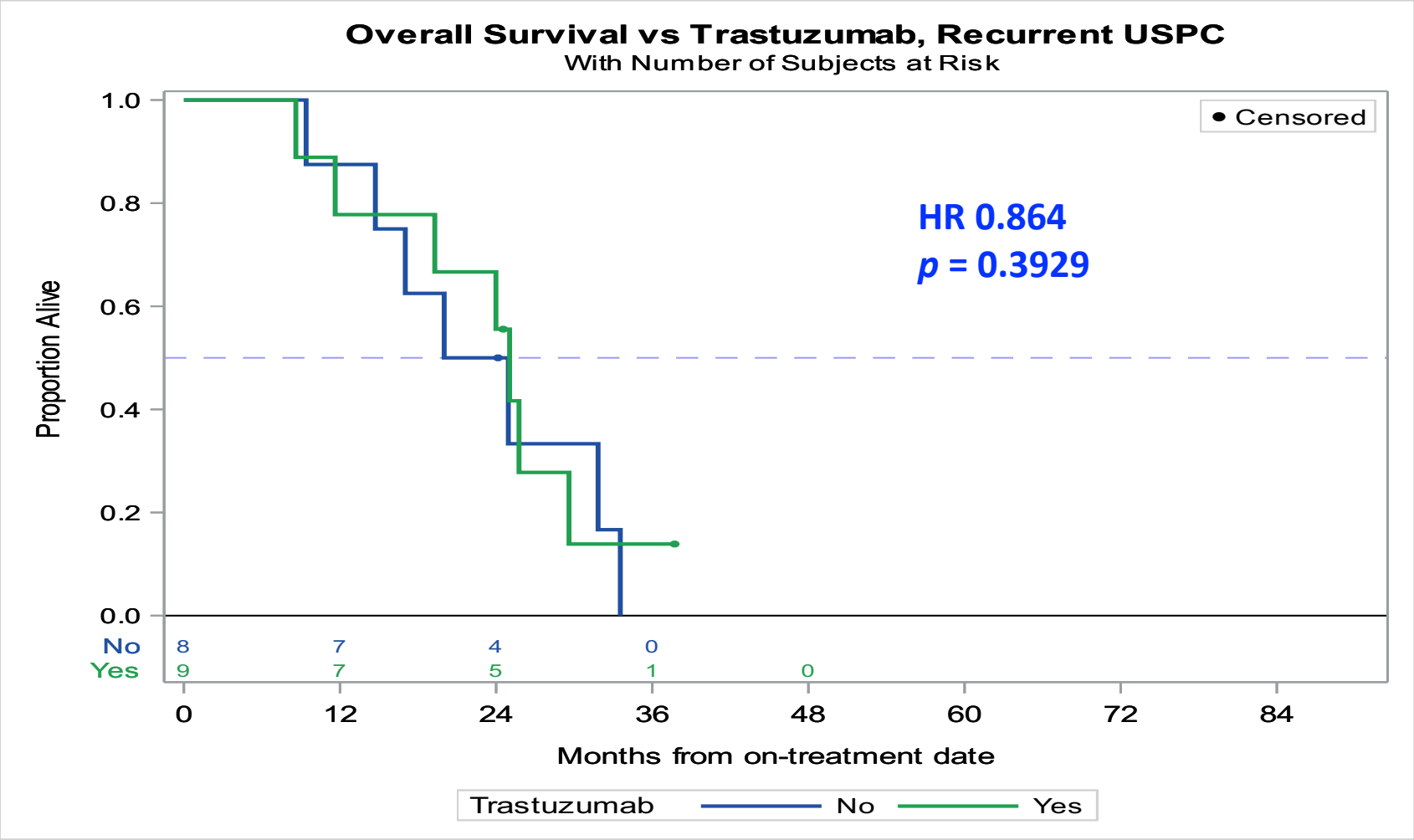
Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

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

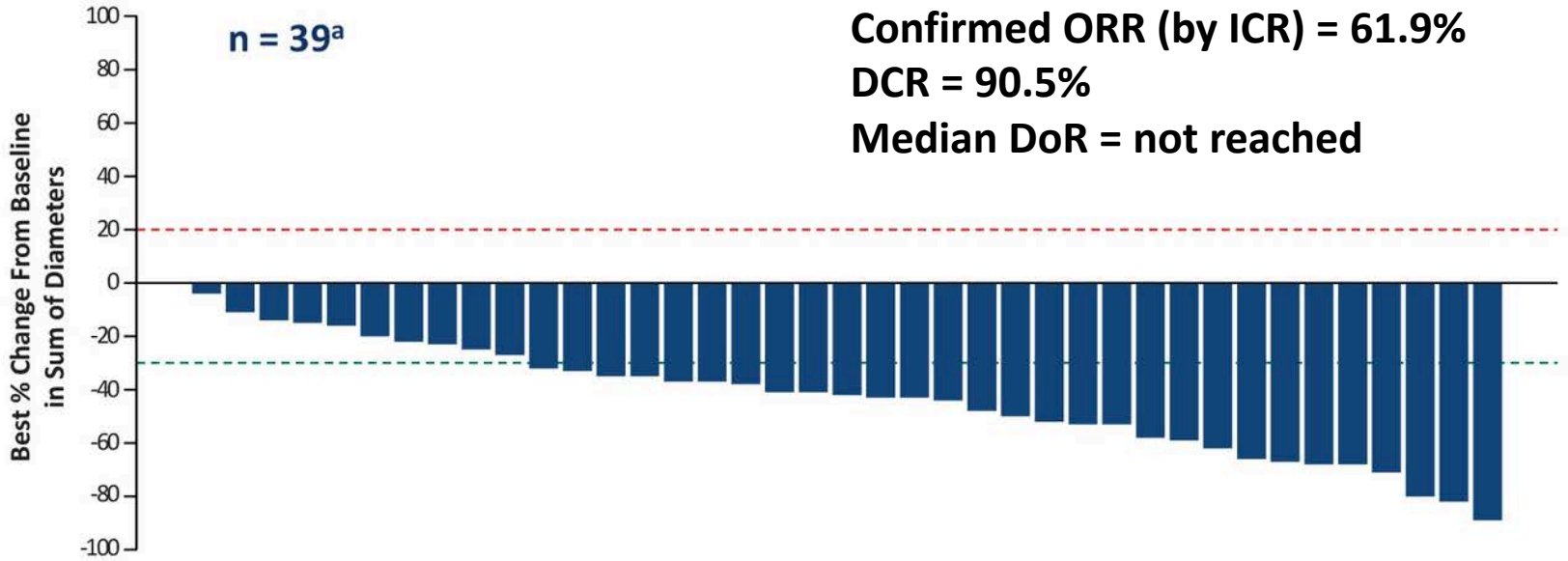
7 cohorts will be evaluated:
Endometrial cancer, cervical cancer, ovarian cancer, bladder cancer, biliary tract cancer, pancreatic cancer and rare tumors

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.

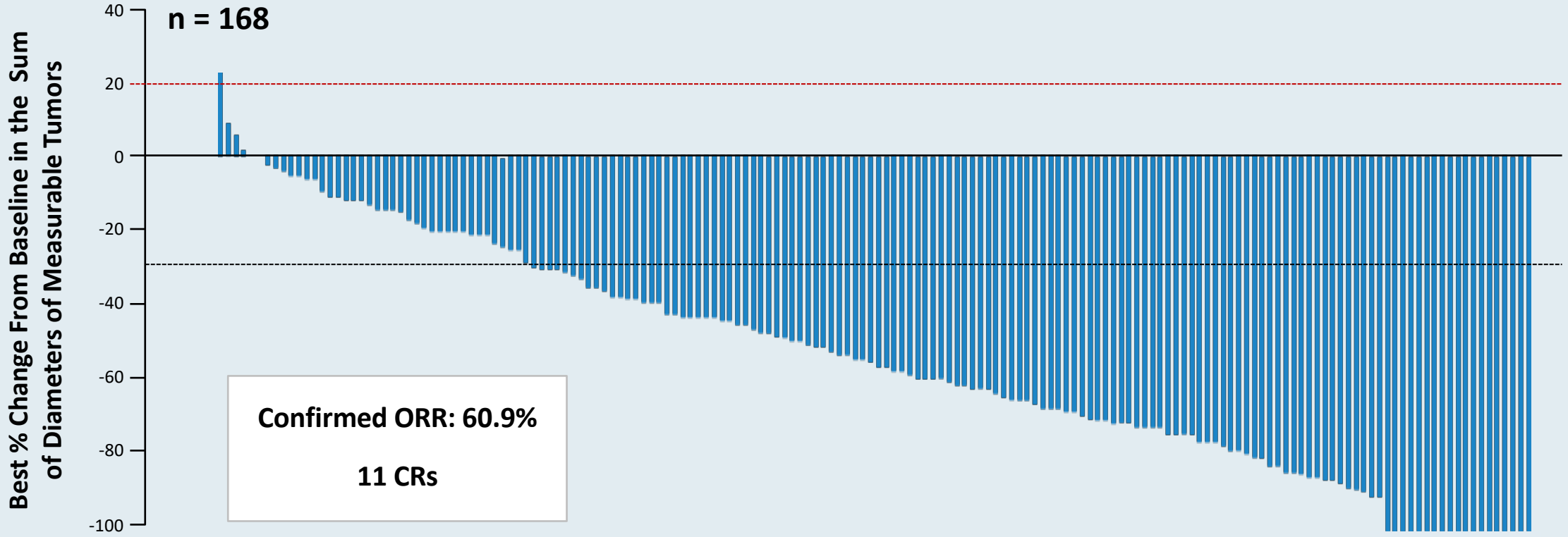
Median PFS = 14.0 months

Smit EF et al. ASCO 2020;Abstract 9504.

RTP RESEARCH TO PRACTICE

DESTINY-Breast01: Best Change in Tumor Size

Trastuzumab Deruxtecan in Breast Cancer

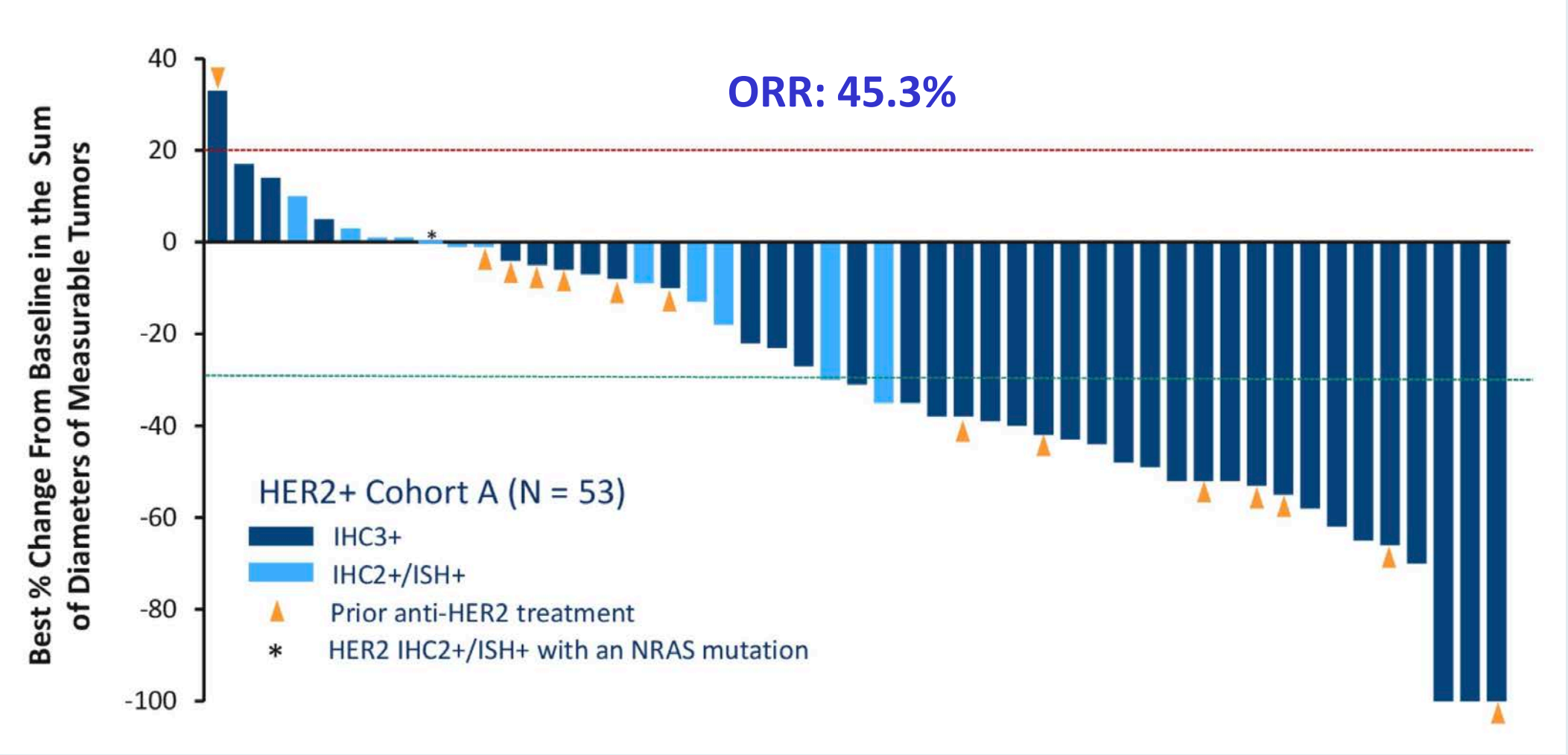


By independent central review.
The line at 20% indicates progressive disease; the line at −30% indicates partial response.
Includes all patients who received T-DXd 5.4 mg/kg (intent-to-treat analysis; N=184).

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

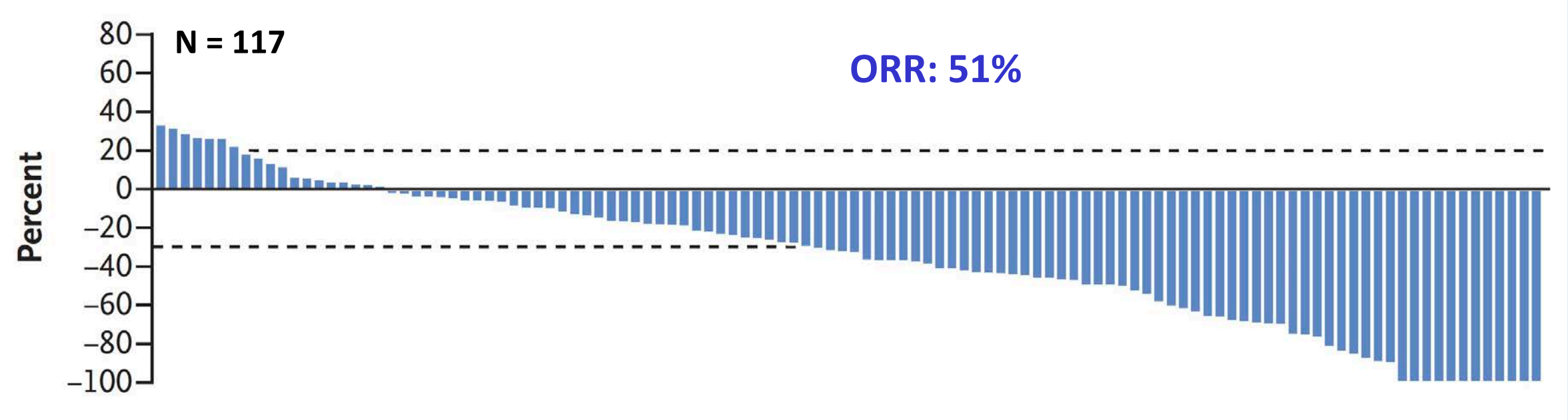


Siena S et al. ASCO 2020;Abstract 4000.

RTP RESEARCH TO PRACTICE

DESTINY-Gastric01: Best Change in Tumor Size

Trastuzumab Deruxtecan in Gastric Cancer



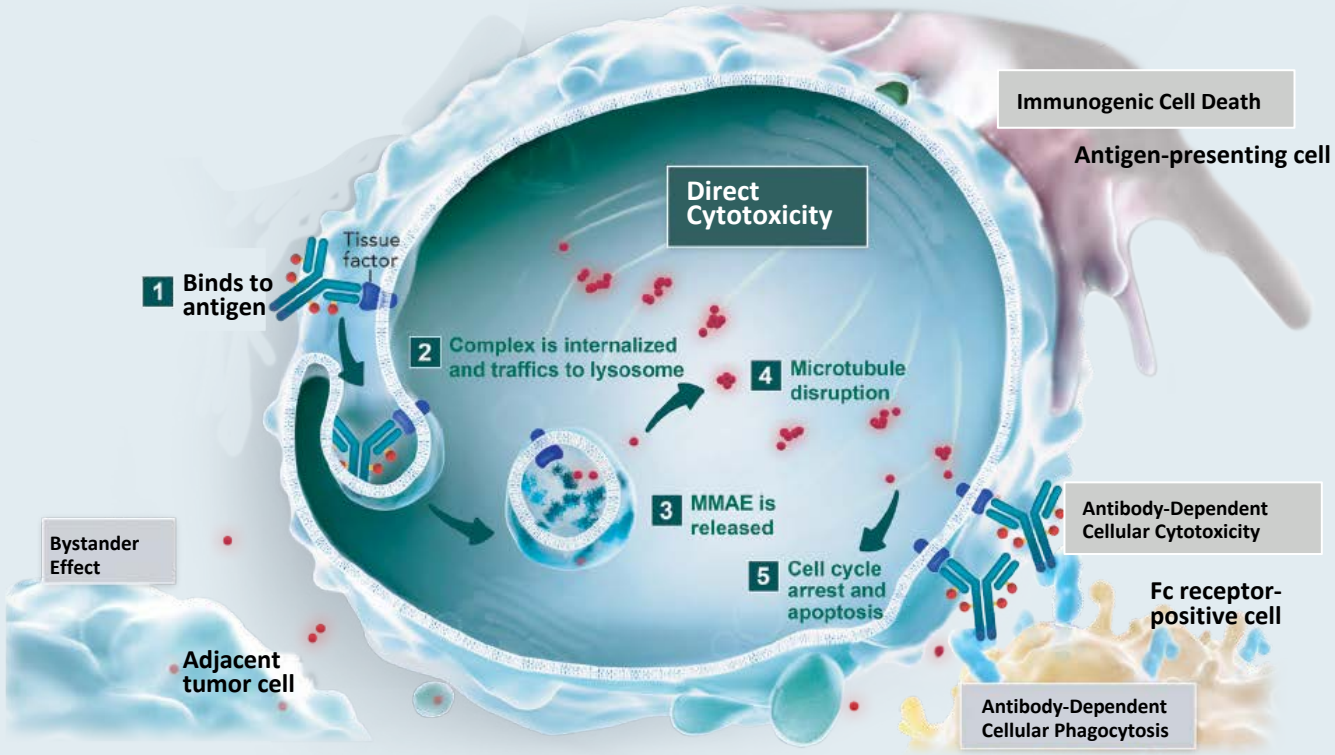
Shitara K et al. N Engl J Med 2020;382:2419-30.

RTP RESEARCH TO PRACTICE

Tisotumab Vedotin and Other Novel Agents in Gynecologic Cancers

Mechanism of Action of Tisotumab Vedotin

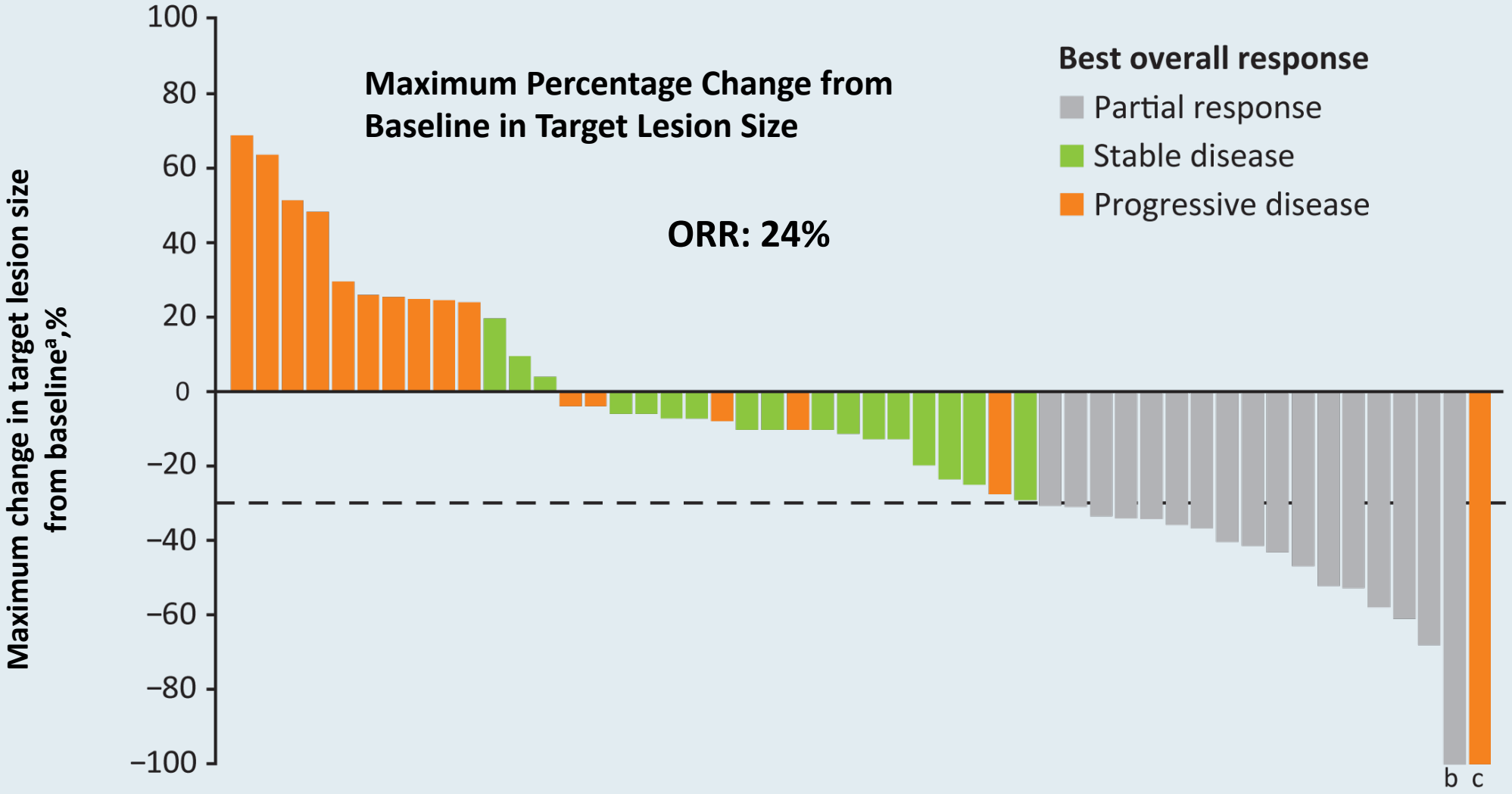
- Tissue factor (TF) is aberrantly expressed in a broad range of solid tumours, including cervical cancer,[1,2] and TF expression has been associated with higher tumour stage and grade, higher metastatic burden and poor prognosis[2]
- TF expression in cervical cancer makes TF a novel target for patients 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.

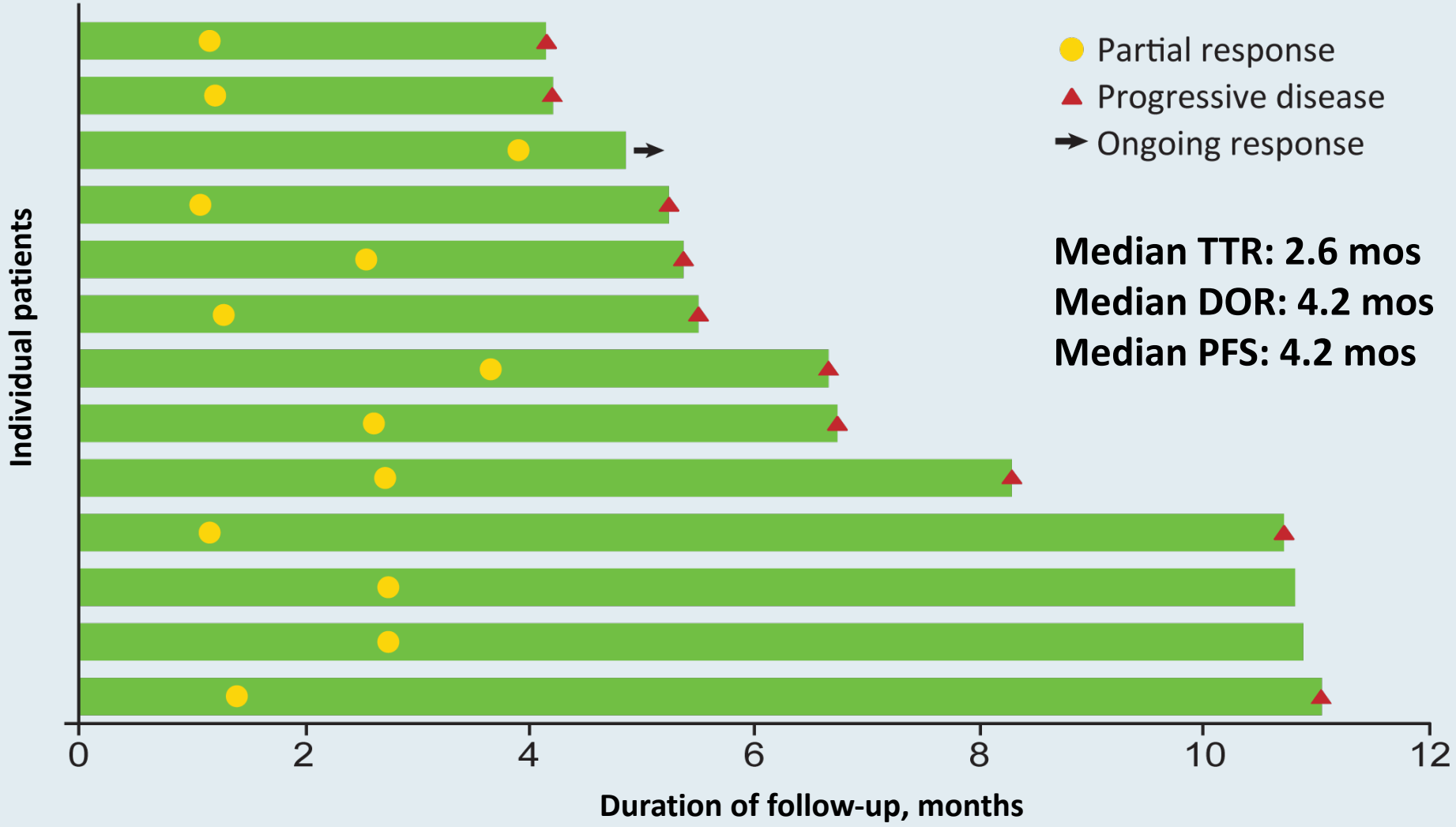
Courtesy of David M O'Malley, MD

innovaTV 201: Best Overall Response to TV



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

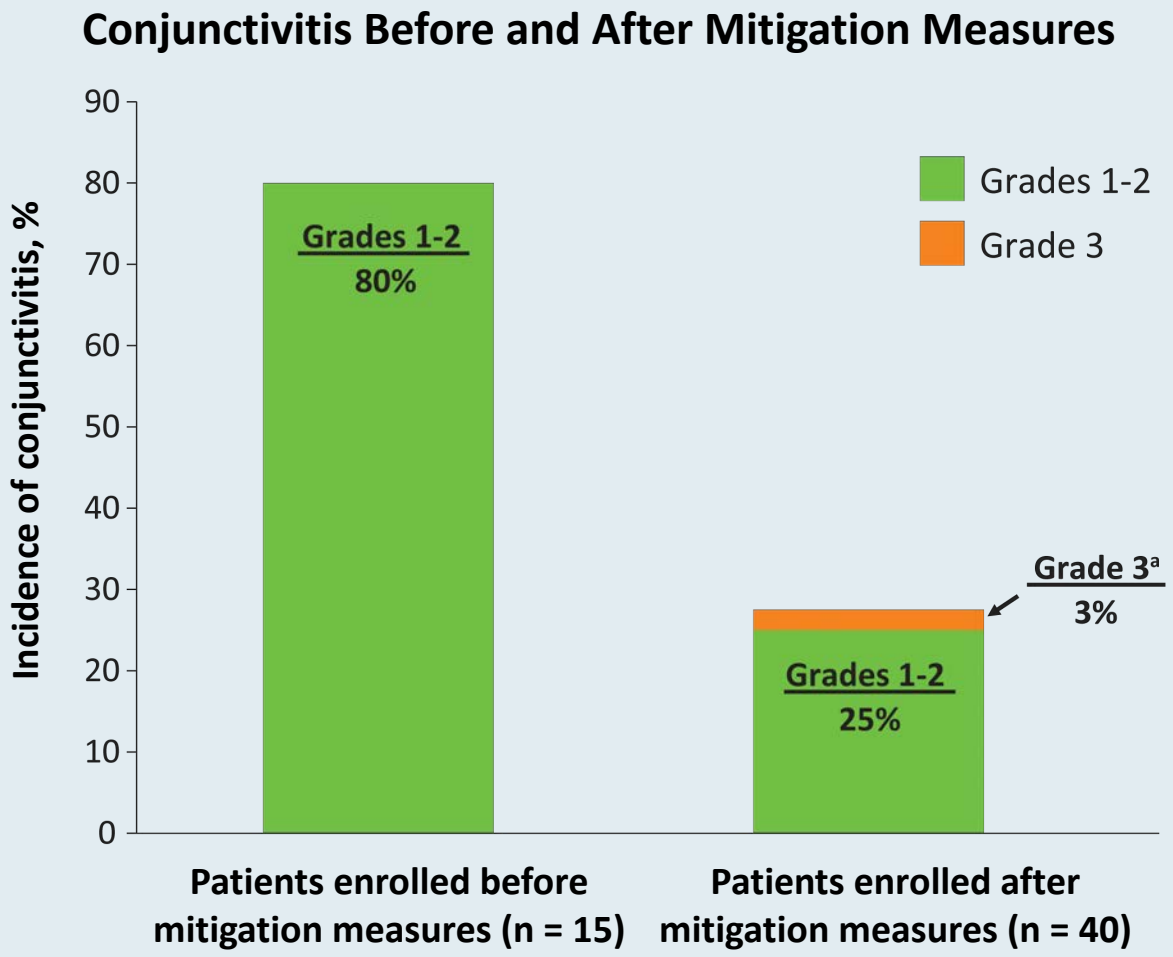
innovaTV 201: Time to Response and Duration of Response in Patients with a Confirmed PR to TV



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.

RTP RESEARCH TO PRACTICE

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

Press Release – June 30, 2020

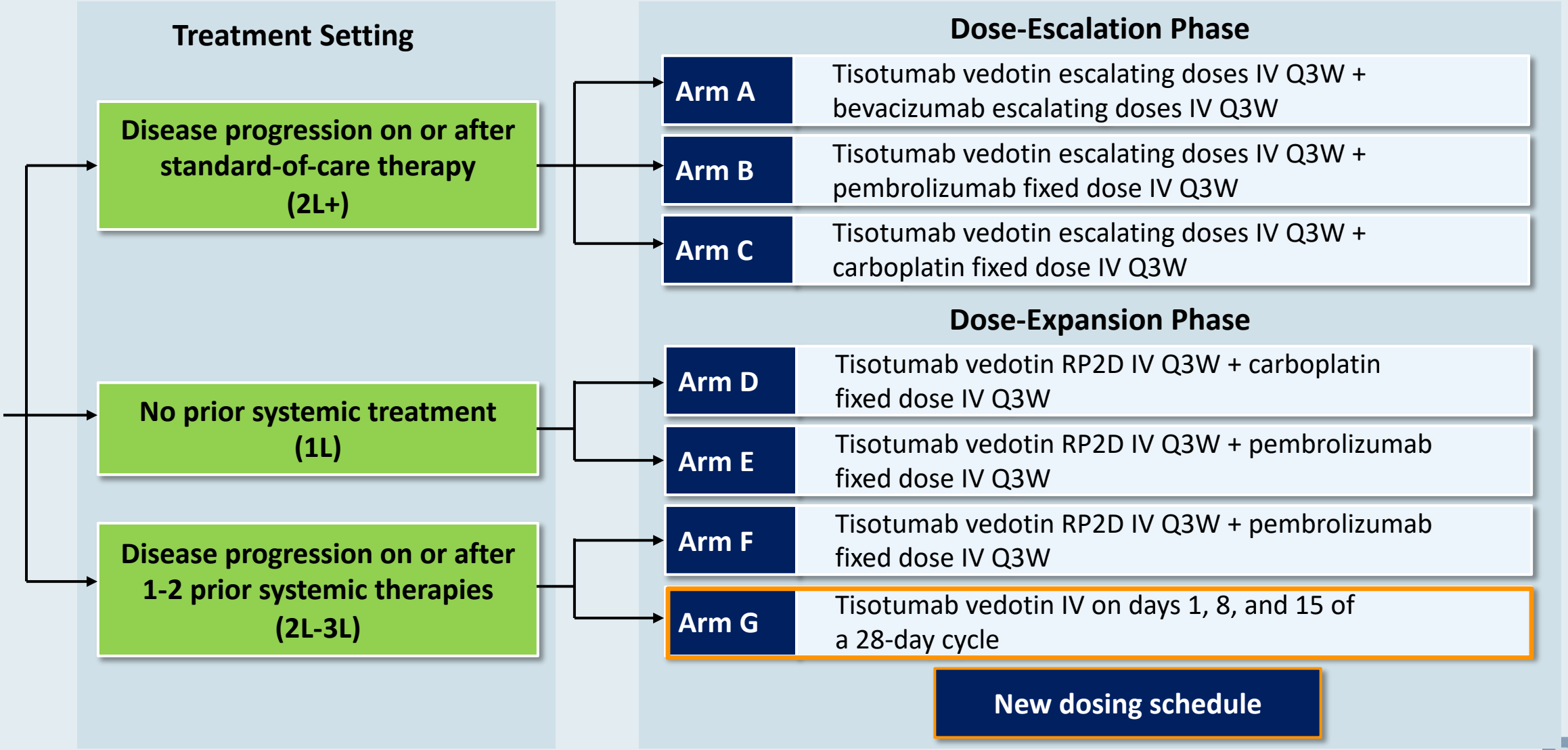
"Positive topline results [were announced] from the single-arm, phase 2 innovaTV 204 trial evaluating tisotumab vedotin administered every 3 weeks for the treatment of patients who have relapsed or progressed on or after prior treatment for recurrent or metastatic cervical cancer.

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

Meet The Professor
Management of Multiple Myeloma

Wednesday, November 4, 2020
12:30 PM – 1:30 PM ET

Faculty

Irene M Ghobrial, 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 business days.

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