Meet The Professor
Immunotherapy and Novel Agents in Gynecologic Cancers

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Arizona Oncology (US Oncology Network)
University of Arizona College of Medicine
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Medical Director, US Oncology Network (McKesson) Gynecologic Program
Co-Director, GOG Partners
Member, Board of Directors, GOG Foundation
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Commercial Support

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

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Dr Love — Disclosures

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Dr Monk — Disclosures

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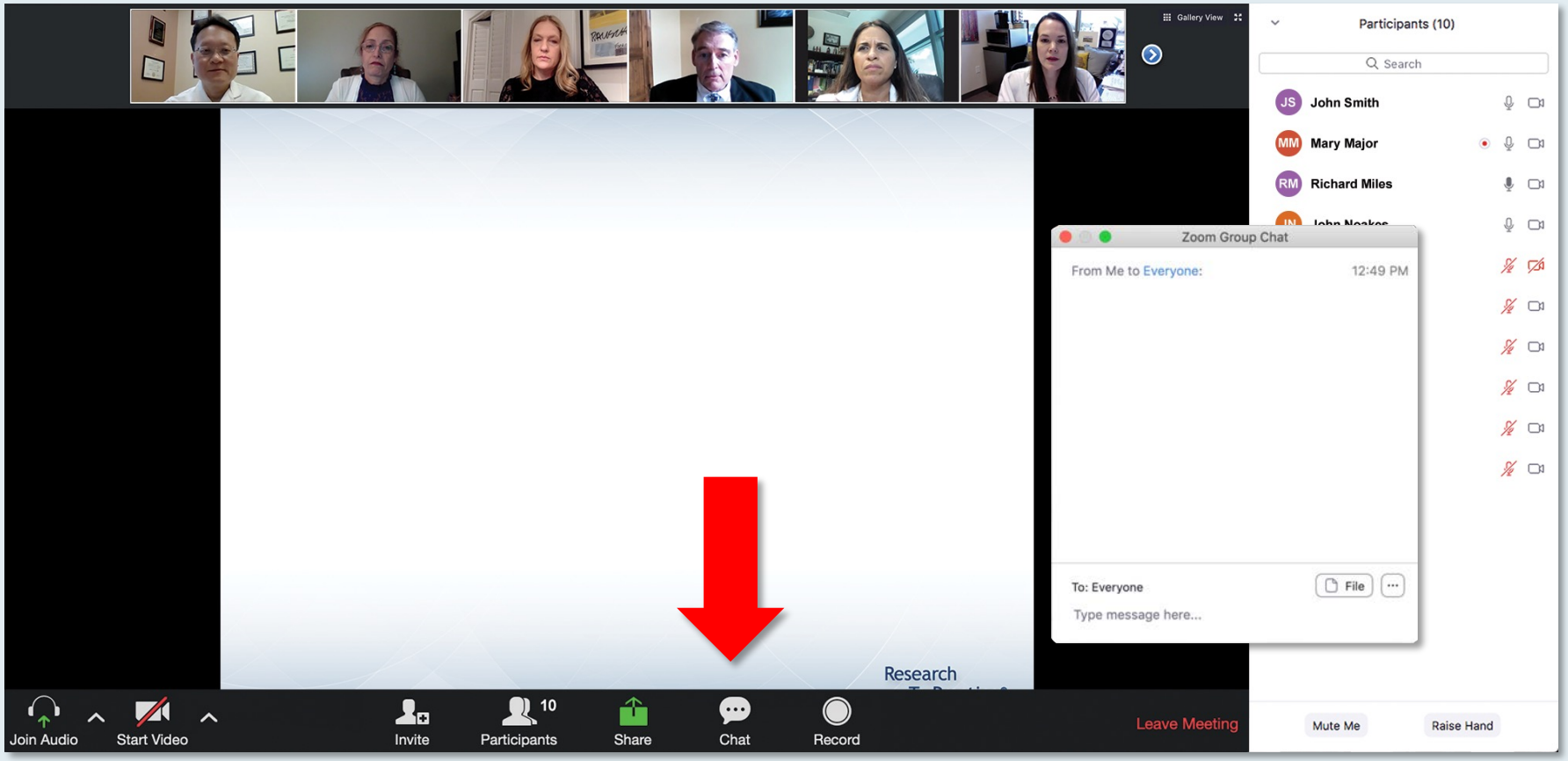

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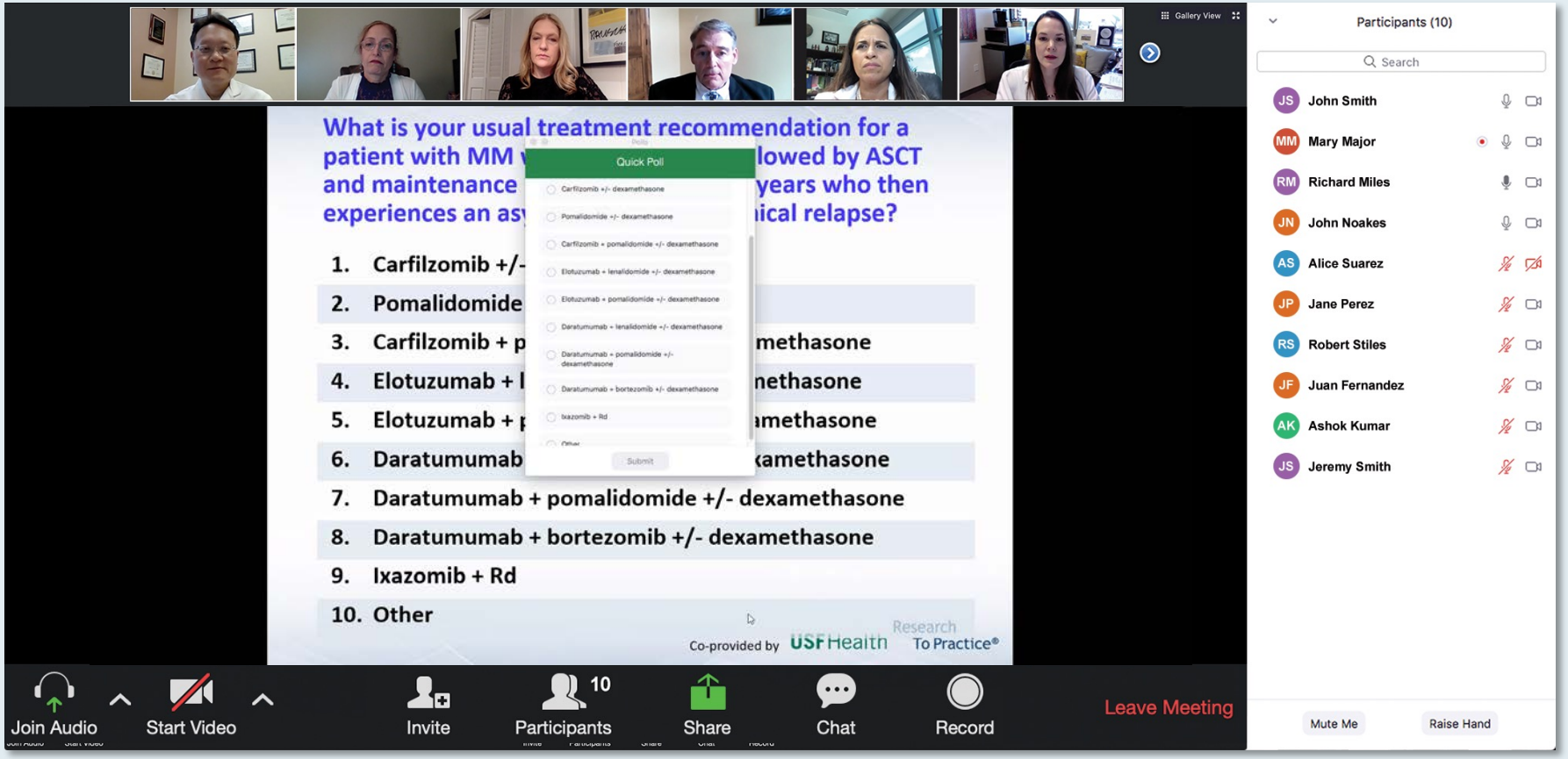
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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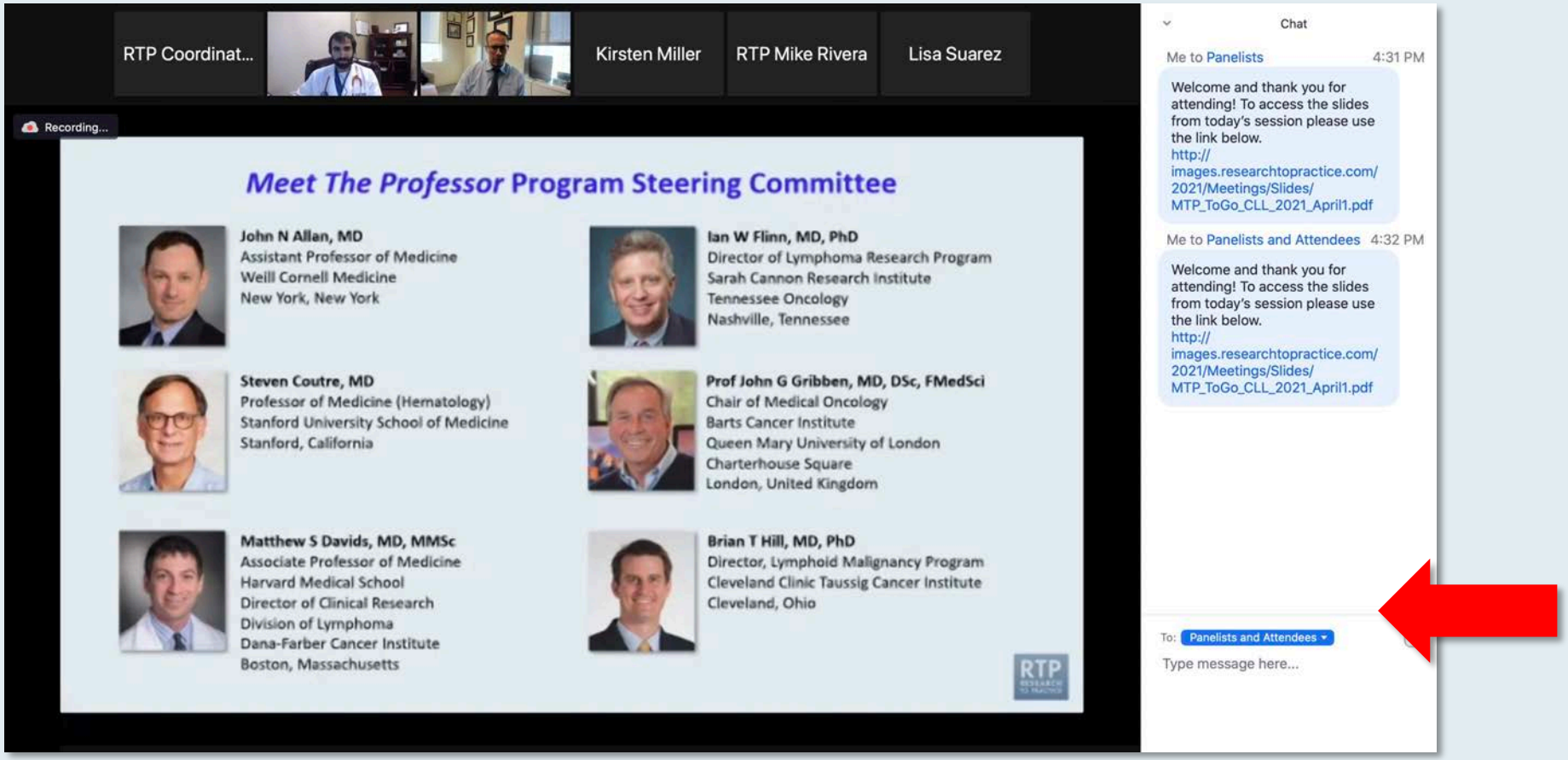

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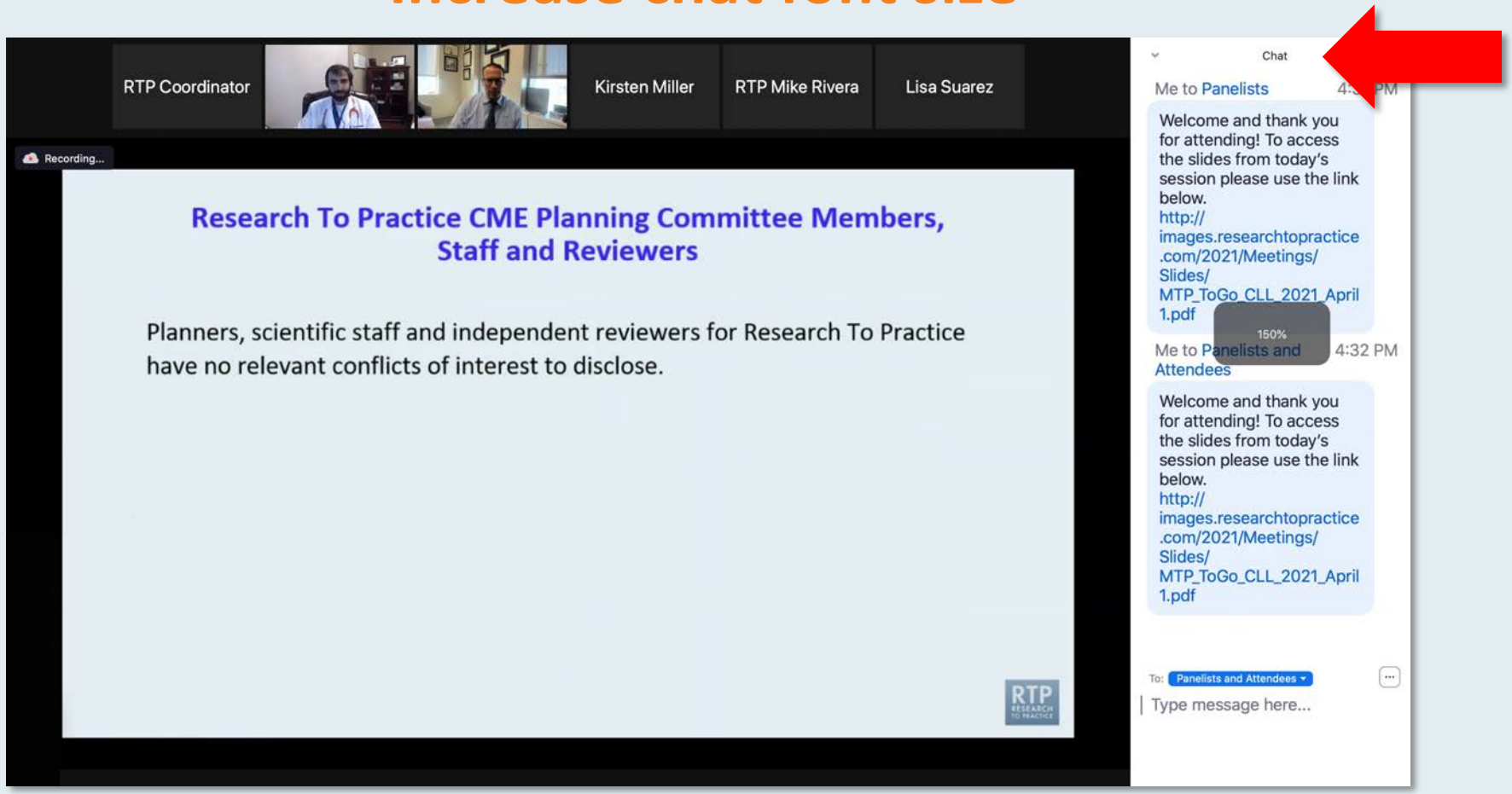

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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WITH DR NEIL LOVE

PARP Inhibitors in Ovarian Cancer

DR ANTONIO GONZÁLEZ-MARTÍN
CLÍNICA UNIVERSIDAD DE NAVARRA

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Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

Tuesday, April 6, 2021
12:00 PM – 1:00 PM ET

Faculty

Sumanta K Pal, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Thursday, April 8, 2021
5:00 PM – 6:00 PM ET

Faculty

Dirk Arnold, MD, PhD

Moderator

Neil Love, MD

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Ask the Investigators: Applying Emerging Clinical Research to the Care of Patients with Gastroesophageal Cancers

Monday, April 12, 2021
6:30 PM – 7:30 PM ET

Faculty

Joseph Chao, MD
Yelena Y Janjigian, MD

Moderator

Neil Love, MD

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Meet The Professor

Management of Chronic Lymphocytic Leukemia

Thursday, April 15, 2021
5:00 PM – 6:00 PM ET

Faculty

John N Allan, MD

Moderator

Neil Love, MD

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Dissecting the Decision: Investigator Perspectives on Key Issues in the Management of Common Cancers

Independent Satellite Symposia (ISS) Hosted in Conjunction with the 2021 Oncology Nursing Society (ONS) Annual Congress

Breast Cancer
Tuesday, April 20, 2021
8:30 AM – 10:00 AM ET

Non-Small Cell Lung Cancer
Tuesday, April 20, 2021
5:00 PM – 6:30 PM ET

Acute Myeloid Leukemia
Wednesday, April 21, 2021
12:00 PM – 1:00 PM ET

Colorectal and Gastroesophageal Cancers
Wednesday, April 21, 2021
4:45 PM – 5:45 PM ET

Prostate Cancer
Thursday, April 22, 2021
8:30 AM – 10:00 AM ET

Hodgkin and Non-Hodgkin Lymphomas
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Multiple Myeloma
Tuesday, April 27, 2021
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Gynecologic Cancers
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Urothelial Bladder Carcinoma
Wednesday, April 28, 2021
12:00 PM – 1:00 PM ET

Chronic Lymphocytic Lymphoma
Thursday, April 29, 2021
8:30 AM – 10:00 AM ET

Chimeric Antigen Receptor T-Cell Therapy
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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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Meet The Professor Program Participating Faculty

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Vice Chancellor, UAMS
Director, Winthrop P Rockefeller Cancer Institute
Director, Cancer Service Line
University of Arkansas for Medical Sciences
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Chief Scientific Officer
US Oncology Research
Gynecologic Oncology
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UCLA Medical Center
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Hospital Universitari Vall d'Hebron
Vall d'Hebron Barcelona Hospital Campus
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Meet The Professor Program Participating Faculty

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Gynaecological Oncologist
Leuven Cancer Institute
University Hospital Leuven
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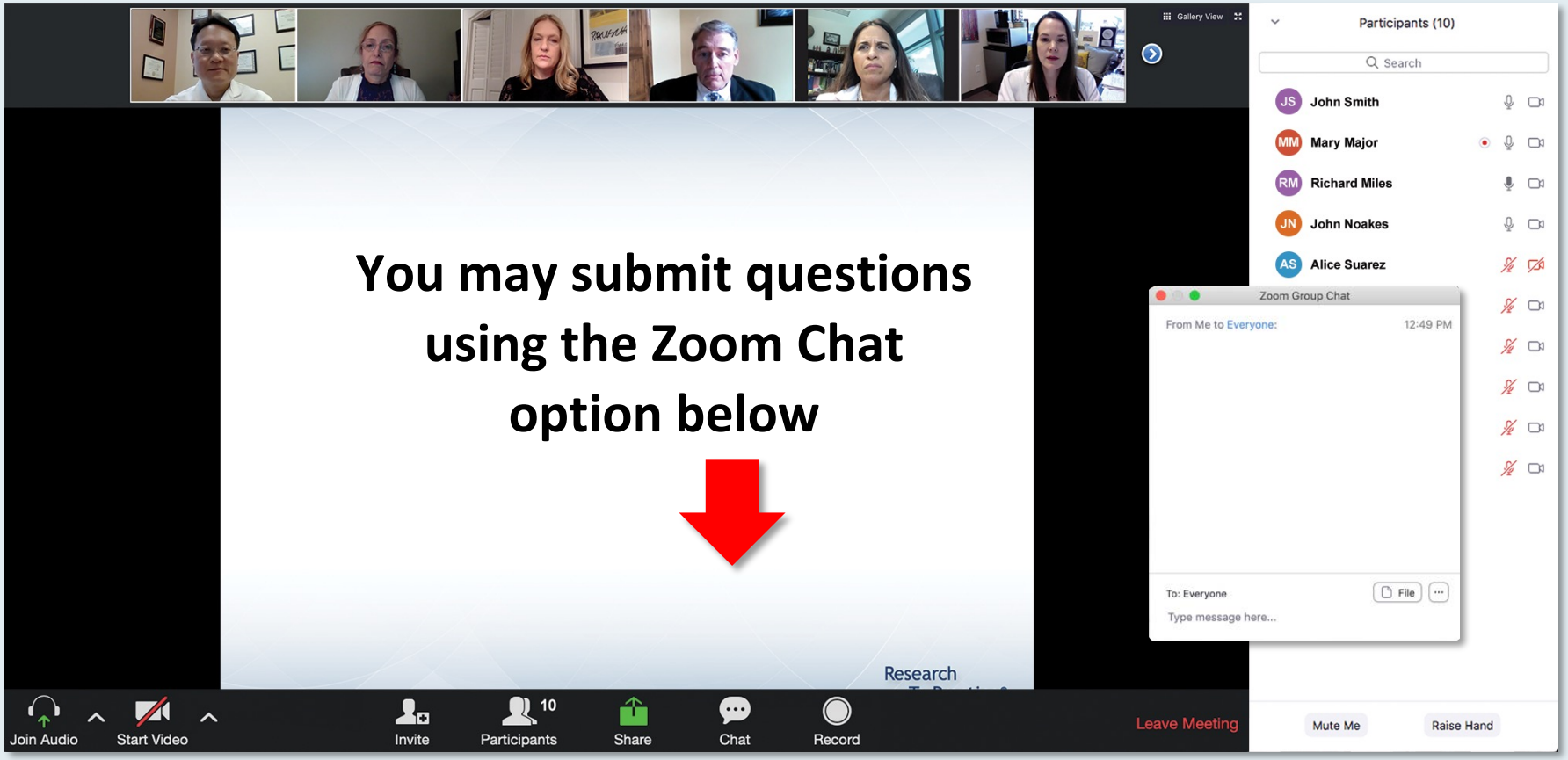

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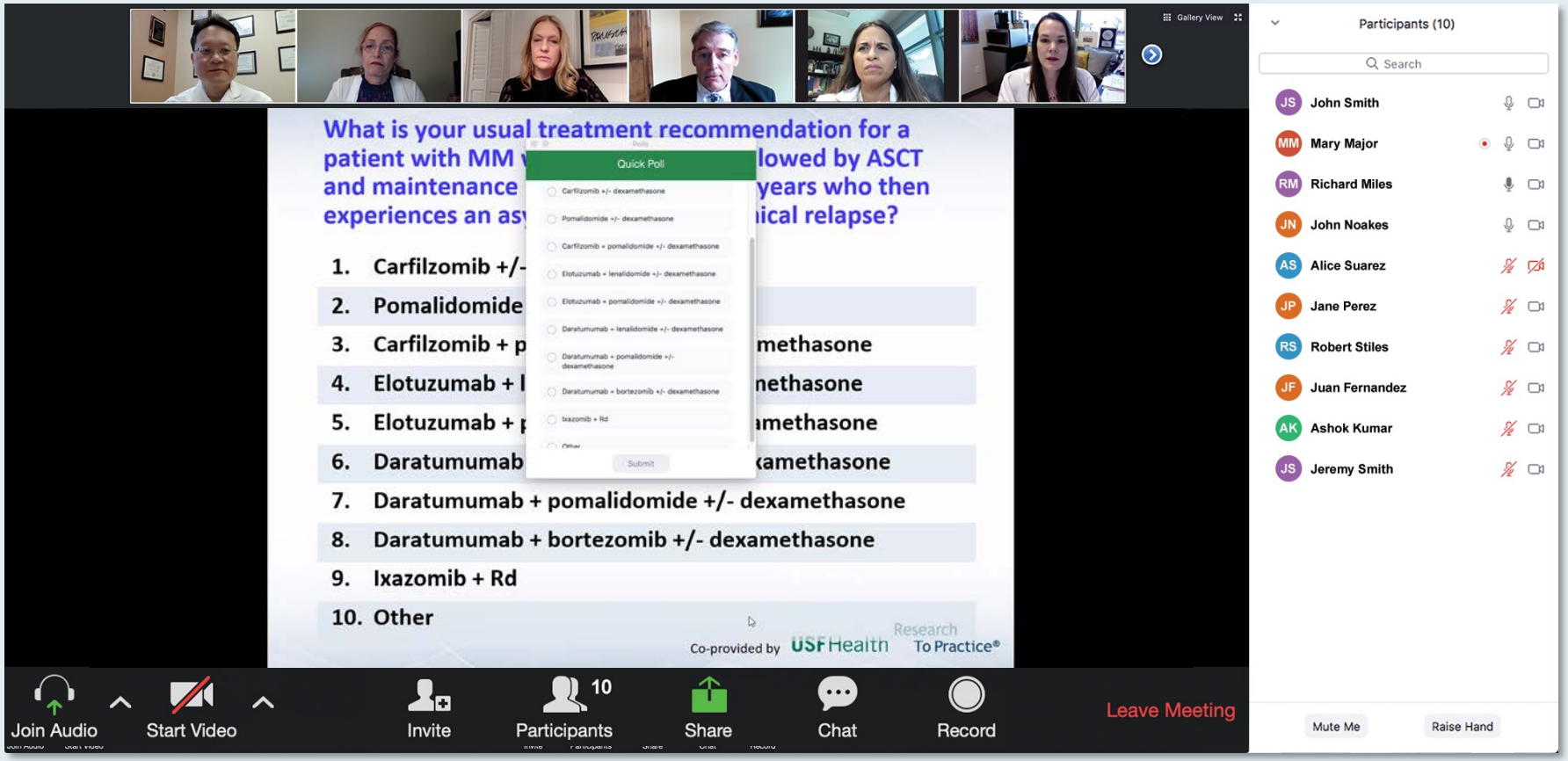

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Spencer Henick Bachow, MD
Hematologist/Oncologist at Lynn Cancer Institute
Affiliate Assistant Professor of Medicine at FAU
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Linda R Duska, MD, MPH
Professor of Obstetrics and Gynecology
Division of Gynecologic Oncology
University of Virginia School of Medicine
Charlottesville, Virginia

John Yang, MD
Chief of Hematology/Oncology
Steward/St Anne's Hospital
Westwood, Massachusetts

Meet The Professor with Dr Monk

MODULE 1: Cases from General Medical Oncology Practices

- Dr Duska: A 46-year-old woman with recurrent endometrioid adenocarcinoma
- Dr Bachow: A 56-year-old woman with metastatic carcinosarcoma — No targetable mutations, PD-L1 0, TMB low
- Dr Yang: A 70-year-old woman with MSS, ER-positive metastatic endometrial cancer
- Dr Duska: A 48-year-old woman with metastatic cervical cancer (Parts 1 and 2)
- Dr Duska: A 52-year-old woman with metastatic cervical cancer (Parts 1 and 2)

MODULE 2: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 3: Gynecologic Oncology Journal Club with Dr Monk

MODULE 4: Key Recent Data Sets

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Phase III Trial of Cemiplimab Monotherapy in Advanced Cervical Cancer Stopped Early for Positive Result on Overall Survival

Press Release – March 15, 2021

"Regeneron Pharmaceuticals, Inc. and Sanofi today announced positive results demonstrating an overall survival (OS) benefit from the Phase 3 trial investigating the PD-1 inhibitor cemiplimab monotherapy compared to chemotherapy, in patients previously treated with chemotherapy whose cervical cancer is recurrent or metastatic. The trial will be stopped early based on a unanimous recommendation by the Independent Data Monitoring Committee (IDMC), and the data will form the basis of regulatory submissions in 2021 ...

"This is the largest Phase 3 randomized clinical trial in advanced cervical cancer and included women (median age: 51 years) with either squamous cell carcinoma or adenocarcinoma. Patients were randomized to receive cemiplimab monotherapy (350 mg every 3 weeks) or an investigator's choice of commonly used chemotherapy (pemetrexed, vinorelbine, topotecan, irinotecan or gemcitabine). Compared to chemotherapy, patients receiving cemiplimab experienced: Total population: 31% reduced risk of death; Squamous cell carcinoma: 27% reduced risk of death; Adenocarcinoma: 44% reduced risk of death. The primary endpoint for the trial was OS, analyzed first among patients with squamous cell carcinoma, then in the total population…

"Detailed results will be presented at an upcoming medical meeting."

https://finance.yahoo.com/news/phase-3-trial-libtayo-cemiplimab-060000401.html?guccounter=1

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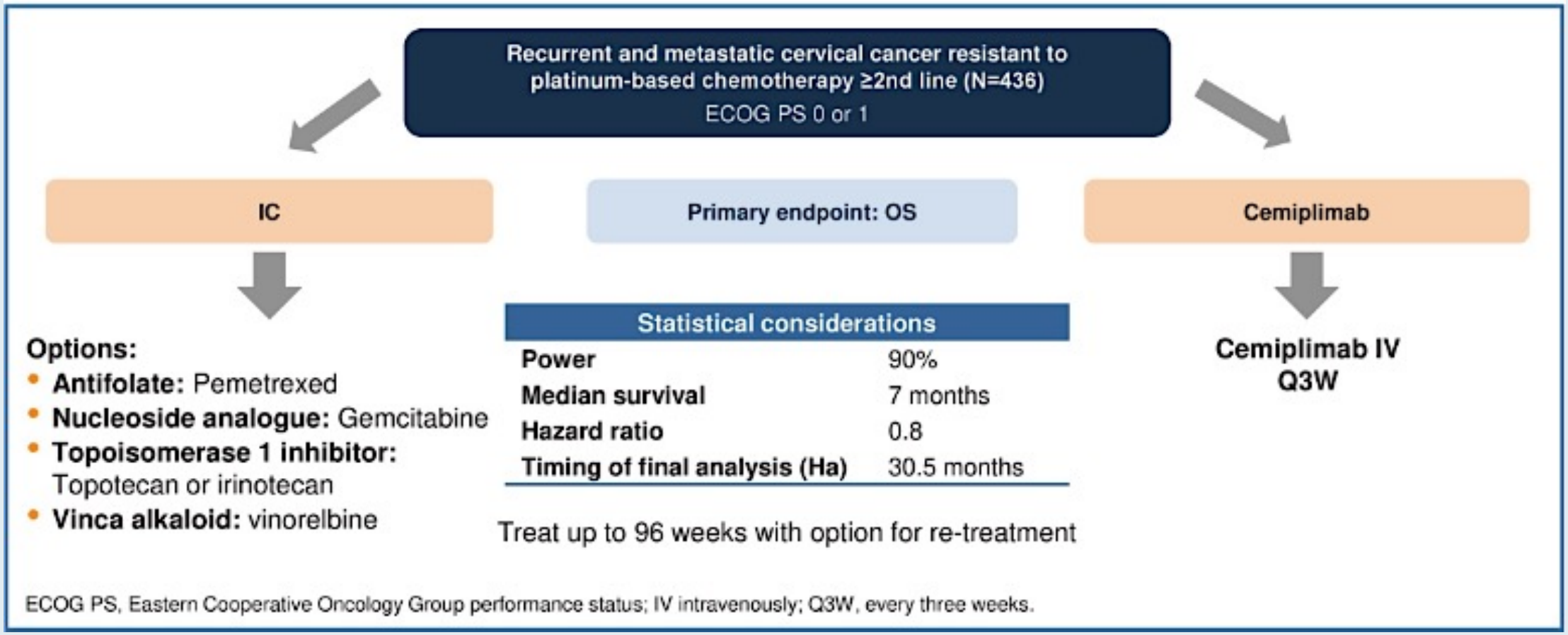
Phase III Trial of Cemiplimab Monotherapy in Advanced Cervical Cancer: Study Design



IC = investigator's choice

Tewari KS et al. ASCO 2018;Abstract TPS5600.

Meet The Professor with Dr Monk

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Case Presentation – Dr Duska: A 46-year-old woman with recurrent endometrioid adenocarcinoma

Dr Linda Duska

- PMH: Asthma, dyslipidemia, GERD, HTN, diabetes, obesity (BMI 48)
- Abnormal uterine bleeding → Endometrial biopsy: FIGO Grade 1 endometrioid adenocarcinoma
- ELAP TAHBSO, with bilateral pelvic lymph node dissection
  - Pathology: Grade 2 endometrioid adenocarcinoma, 22 negative lymph nodes
  - Loss of expression of MLH1 and PMS2
- Post-operative vaginal cuff RT
- 10 months later: New RLE edema and right hydroureter
- CT: Bilateral pelvic masses, right inguinal lymphadenopathy → US-guided biopsy: recurrent disease
- Carboplatin/paclitaxel x 7, with PR but subsequent PD
- Dostarlimab on the GARNET trial x 2 years, with PR as best response
  - Q3 weeks for first 4 cycles, then Q6 weeks thereafter

Case Presentation – Dr Bachow: A 56-year-old woman with metastatic carcinosarcoma with no targetable mutations – PD-L1: 0, TMB low

Dr Spencer Bachow

- 10/2019: Cytoreductive TAHBSO, with peritoneal biopsies
  - Carcinosarcoma mixed Mullerian tumor (pT3a N2a MX)
- CT chest/abdomen/pelvis: Lung nodules and pelvic lymph nodes
- Carboplatin/paclitaxel x 6 (Uninsured, unable to obtain bevacizumab), with PR
- Consolidative RT to pelvis
- 6 months later PET CT: Diffuse metastatic disease above and below diaphragm
- NGS: No targetable mutations, PD-L1 0, TMB low; Germline testing: Negative
- Lenvatinib/pembrolizumab, with hypothyroidism (levothyroxine)

Questions

- Is lenvatinib/pembrolizumab an option in relapsed carcinosarcoma of the uterus? How many of these patients were included in the original trials? What is your experience with response and toxicity of these agents in patients with carcinosarcomas of the uterus?
- For lenvatinib/pembrolizumab, do you start at the highest dose or a lower dose of lenvatinib? What side effects do you look for? How quickly do you see responses in these patients?

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Case Presentation – Dr Yang: A 70-year-old woman with microsatellite-stable, ER-positive metastatic endometrial cancer

Dr John Yang

- PMH: Morbid obesity (BMI 46), O2-dependent chronic hypoxia
- Heavily pretreated for metastatic endometrial cancer past 6 years
  - Carboplatin/paclitaxel, gemcitabine, liposomal doxorubicin, *nab*-paclitaxel, with response to each drug
- Currently, on bevacizumab with stable disease
  - ECOG PS: 2-3

Questions

- Once her disease progresses, what is the potential role for lenvatinib/pembrolizumab? How well tolerated is the combination?
- Can either drug be given as a single agent for a patient with compromised performance status?

Case Presentation – Dr Duska: A 48-year-old woman with metastatic cervical cancer – Part 1

Dr Linda Duska

- Heavy post-coital bleeding → Pelvic exam: Exophytic 4-cm cervical mass, with no palpable extra-cervical disease
- Biopsies: Squamous cell carcinoma
- Radical abdominal hysterectomy with BSO, BPLND
- Final Pathology: Invasive squamous cell carcinoma, poorly differentiated with 1 positive parametrial node, 32 negative pelvic nodes (FIGO Stage IIIC2)

Case Presentation – Dr Duska: A 48-year-old woman with metastatic cervical cancer – Part 2

Dr Linda Duska

- Heavy post-coital bleeding → Pelvic exam: Exophytic 4-cm cervical mass, with no palpable extra-cervical disease
- Biopsies: Squamous cell carcinoma
- Radical abdominal hysterectomy with BSO, BPLND
- Final Pathology: Invasive squamous cell carcinoma, poorly differentiated with 1 positive parametrial node, 32 negative pelvic nodes (FIGO Stage IIIC2)
- ***Whole pelvic RT 5040 cGy with weekly cisplatin***
- ***2 months later: Presents to ER with right flank pain***
  - ***CT and PET: Peritoneal disease***
- ***Enrolled on BEATcc Phase III study: Receives platinum chemo + paclitaxel/bevacizumab + atezolizumab***
  - ***Good response after 4 cycles***

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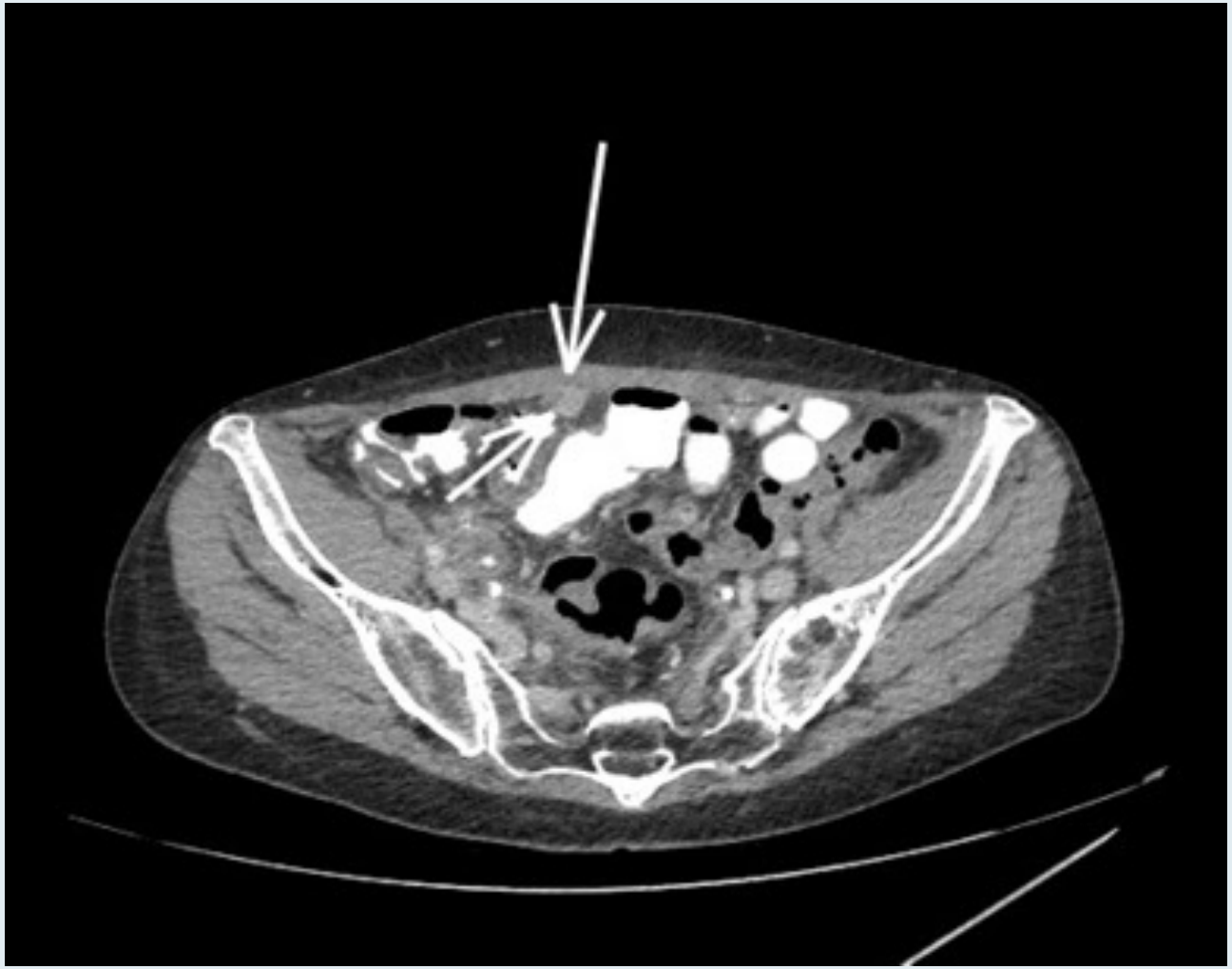
Case Presentation – Dr Duska: A 48-year-old woman with metastatic cervical cancer

Dr Linda Duska



Case Presentation – Dr Duska: A 52-year-old woman with metastatic cervical cancer – Part 1

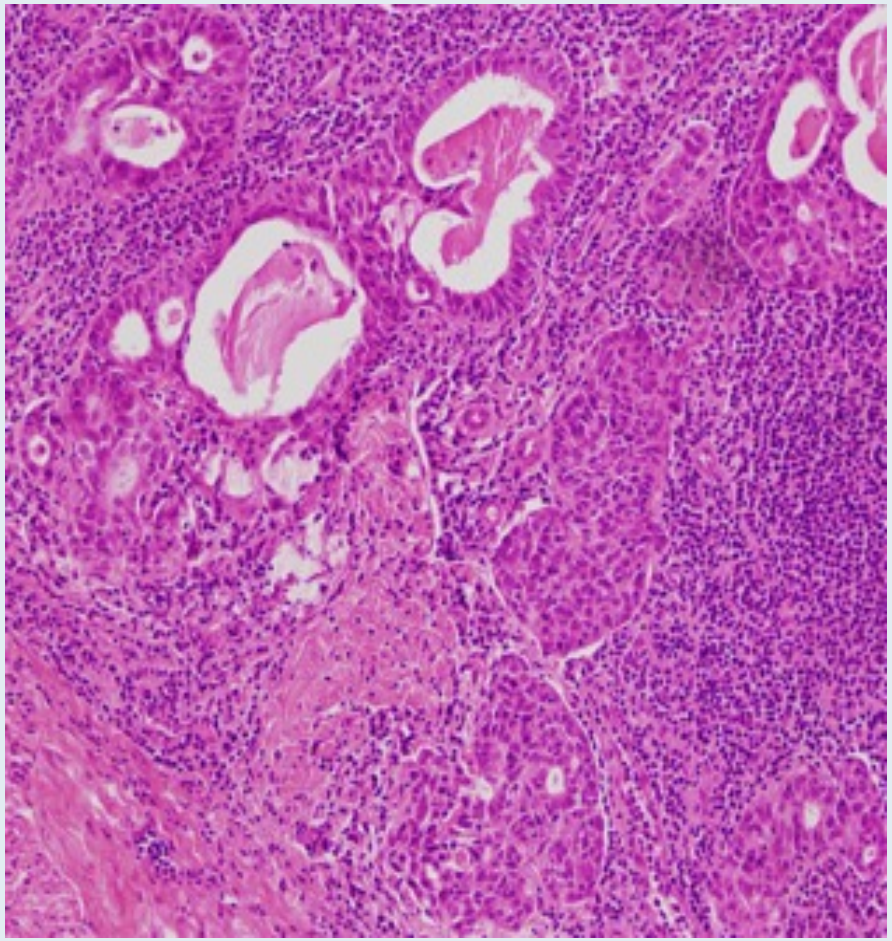
Dr Linda Duska

- PMH: Insomnia, vertigo, arthritis, sleep apnea, HTN, obesity (BMI 40)
- Postmenopausal uterine bleeding → Evaluation: Cervical mass
- PET/CT, MRI and biopsy: Adenosquamous carcinoma consistent with cervical primary
- Chemoradiation with cisplatin x 5 plus HDR brachytherapy, with good response
- 10 months later: CT/PET/biopsy confirms recurrent disease in right pelvic node
- Carboplatin/paclitaxel/bevacizumab x 6 → RT, with no residual disease
- 4 months later during routine surveillance: Multiple pulmonary nodules staining positive for PD-L1
- Pembrolizumab x 6, with CT showing increase in size of pulmonary nodules

Case Presentation – Dr Duska: A 52-year-old woman with metastatic cervical cancer

Dr Linda Duska

Adenosquamous carcinoma of the primary



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Case Presentation – Dr Duska: A 52-year-old woman with metastatic cervical cancer – Part 2

Dr Linda Duska

- PMH: Insomnia, vertigo, arthritis, sleep apnea, HTN, obesity (BMI: 40)
- Postmenopausal uterine bleeding → Evaluation: Cervical mass
- PET/CT, MRI and biopsy: Adenosquamous carcinoma consistent with cervical primary
- Chemoradiation with cisplatin x 5 plus HDR brachytherapy, with good response
- 10 months later: CT/PET/biopsy confirms recurrent disease in right pelvic node
- Carboplatin/paclitaxel/bevacizumab x 6 → RT, with no residual disease
- 4 months later during routine surveillance: Multiple pulmonary nodules staining positive for PD-L1
- Pembrolizumab x 6, with CT showing increase in size of pulmonary nodules

Questions

- ***What do you anticipate the community-based side effect rate for eye toxicity is with tisotumab vedotin compared to what was observed on the clinical trial?***
- ***Do you expect the response rate to tisotumab vedotin observed in the study to be reproducible in the community?***

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Meet The Professor with Dr Monk

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MODULE 3: Gynecologic Oncology Journal Club with Dr Monk

- Evidence-based treatment paradigm for invasive cervical carcinoma (CC)
- Patient characteristics, treatment patterns and clinical outcomes with previously treated recurrent or metastatic CC
- innovaTV 204 trial: Tisotumab vedotin for previously treated recurrent or metastatic CC
- innovaTV 205 trial: Tisotumab vedotin ± bevacizumab, pembrolizumab or carboplatin for recurrent or metastatic CC
- CALLA trial results: Concurrent and adjuvant durvalumab with chemoRT versus chemoRT alone for locally advanced CC
- Anti-PD-1 balstilimab alone or in combination with anti-CTLA-4 zalifrelimab for recurrent or metastatic CC
- Phase II SUMMIT basket trial: Neratinib for patients with metastatic CC with HER2 mutation
- Immune checkpoint inhibitors as switch or continuation maintenance therapy for solid tumors
- Incorporation of whole pelvic radiation into treatment of Stage IVB CC
- Sequential chemotherapy for early-stage, post-radical hysterectomy CC: Are the STARS aligned?

MODULE 4: Key Recent Data Sets

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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 metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel if their disease was microsatellite stable (MSS)?

 Dr Birrer	Lenvatinib/ pembrolizumab	 Dr Penson	Lenvatinib/ pembrolizumab
 Dr Coleman	Lenvatinib/ pembrolizumab	 Dr Powell	Lenvatinib/ pembrolizumab
 Dr Oaknin	Lenvatinib/ pembrolizumab	 Dr Slomovitz	Lenvatinib/ pembrolizumab
 Dr O'Malley	Lenvatinib/ pembrolizumab	 Dr Tewari	Lenvatinib/ pembrolizumab

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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 MSI high?

 Dr Birrer	Pembrolizumab	 Dr Penson	Pembrolizumab
 Dr Coleman	Pembrolizumab	 Dr Powell	Pembrolizumab
 Dr Oaknin	Dostarlimab	 Dr Slomovitz	Pembrolizumab
 Dr O'Malley	Pembrolizumab	 Dr Tewari	Pembrolizumab

RTP RESEARCH TO PRACTICE

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?

 Dr Birrer	Second line	 Dr Penson	First line
 Dr Coleman	Second line	 Dr Powell	Second line
 Dr Oaknin	Second line	 Dr Slomovitz	Second line
 Dr O'Malley	First line	 Dr Tewari	Second line

RTP RESEARCH TO PRACTICE

For a patient with MSI-high metastatic endometrial cancer for whom you are going to initiate an anti-PD-1/PD-L1 antibody, which regimen do you generally use?

 Dr Birrer	Pembrolizumab	 Dr Penson	Pembrolizumab
 Dr Coleman	Pembrolizumab	 Dr Powell	Pembrolizumab
 Dr Oaknin	Dostarlimab	 Dr Slomovitz	Pembrolizumab
 Dr O'Malley	Pembrolizumab	 Dr Tewari	Pembrolizumab

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, 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. Cemiplimab
5. 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?

 Dr Birrer	Pembrolizumab	 Dr Penson	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 Dr Coleman	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher	 Dr Powell	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 Dr Oaknin	Anti-PD-1/PD-L1 antibody in general	 Dr Slomovitz	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 Dr O'Malley	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher	 Dr Tewari	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher

RTP RESEARCH TO PRACTICE

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 and cemiplimab were accessible, what would likely be your next line of treatment?

1. Pembrolizumab
2. Cemiplimab
3. Tisotumab vedotin
4. Other

RTP
RESEARCH
TO PRACTICE

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?

 Dr Birrer	Well tolerated except for epistasis	 Dr Penson	Excited by it
 Dr Coleman	Similar to other single-agent chemotherapy	 Dr Powell	Reasonable toxicity
 Dr Oaknin	Moderate toxicity	 Dr Slomovitz	Well tolerated; ocular side effects
 Dr O'Malley	Reasonable toxicity	 Dr Tewari	Relatively well tolerated so far

RTP RESEARCH TO PRACTICE

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?

 Dr Birrer	Yes	 Dr Penson	Yes
 Dr Coleman	Yes	 Dr Powell	Yes
 Dr Oaknin	No	 Dr Slomovitz	No
 Dr O'Malley	Yes	 Dr Tewari	No

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Monk

MODULE 1: Cases from General Medical Oncology Practices

MODULE 2: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 3: Gynecologic Oncology Journal Club with Dr Monk

- Evidence-based treatment paradigm for invasive cervical carcinoma (CC)
- Patient characteristics, treatment patterns and clinical outcomes with previously treated recurrent or metastatic CC
- innovaTV 204 trial: Tisotumab vedotin for previously treated recurrent or metastatic CC
- innovaTV 205 trial: Tisotumab vedotin ± bevacizumab, pembrolizumab or carboplatin for recurrent or metastatic CC
- CALLA trial results: Concurrent and adjuvant durvalumab with chemoRT versus chemoRT alone for locally advanced CC
- Anti-PD-1 balstilimab alone or in combination with anti-CTLA-4 zalifrelimab for recurrent or metastatic CC
- Phase II SUMMIT basket trial: Neratinib for patients with metastatic CC with HER2 mutation
- Immune checkpoint inhibitors as switch or continuation maintenance therapy for solid tumors
- Incorporation of whole pelvic radiation into treatment of Stage IVB CC
- Sequential chemotherapy for early-stage, post-radical hysterectomy CC: Are the STARS aligned?

MODULE 4: Key Recent Data Sets

RTP
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TO PRACTICE

SPECIAL SERIES: ADVANCES IN THE MANAGEMENT OF GYNECOLOGIC CANCERS

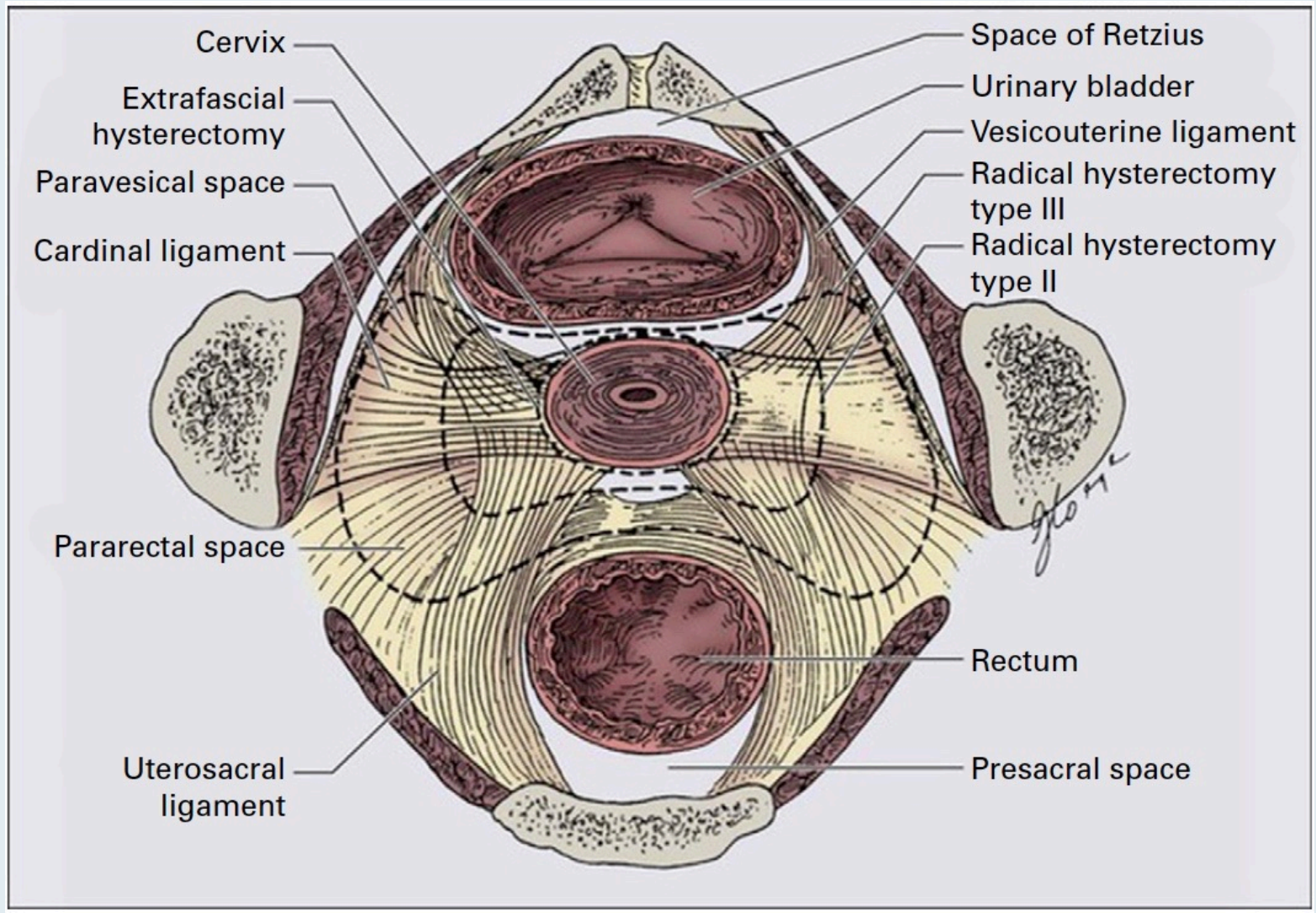
review article

Evidence-Based Treatment Paradigms for Management of Invasive Cervical Carcinoma

Krishnansu S. Tewari, MD[1] and Bradley J. Monk, MD[2,3]

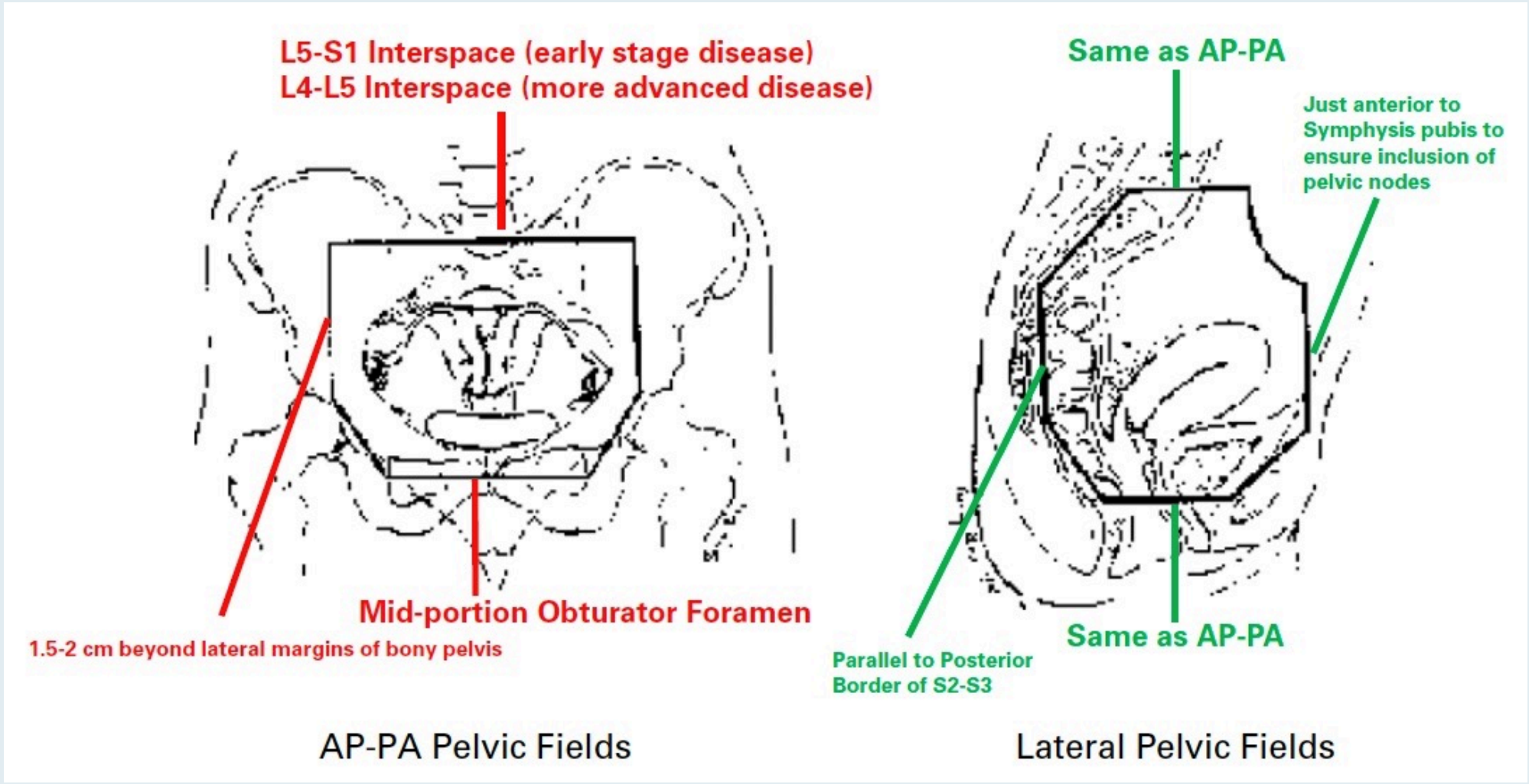
J Clin Oncol 2019;37(27):2472-89.

Pelvic Anatomy and Types of Hysterectomy



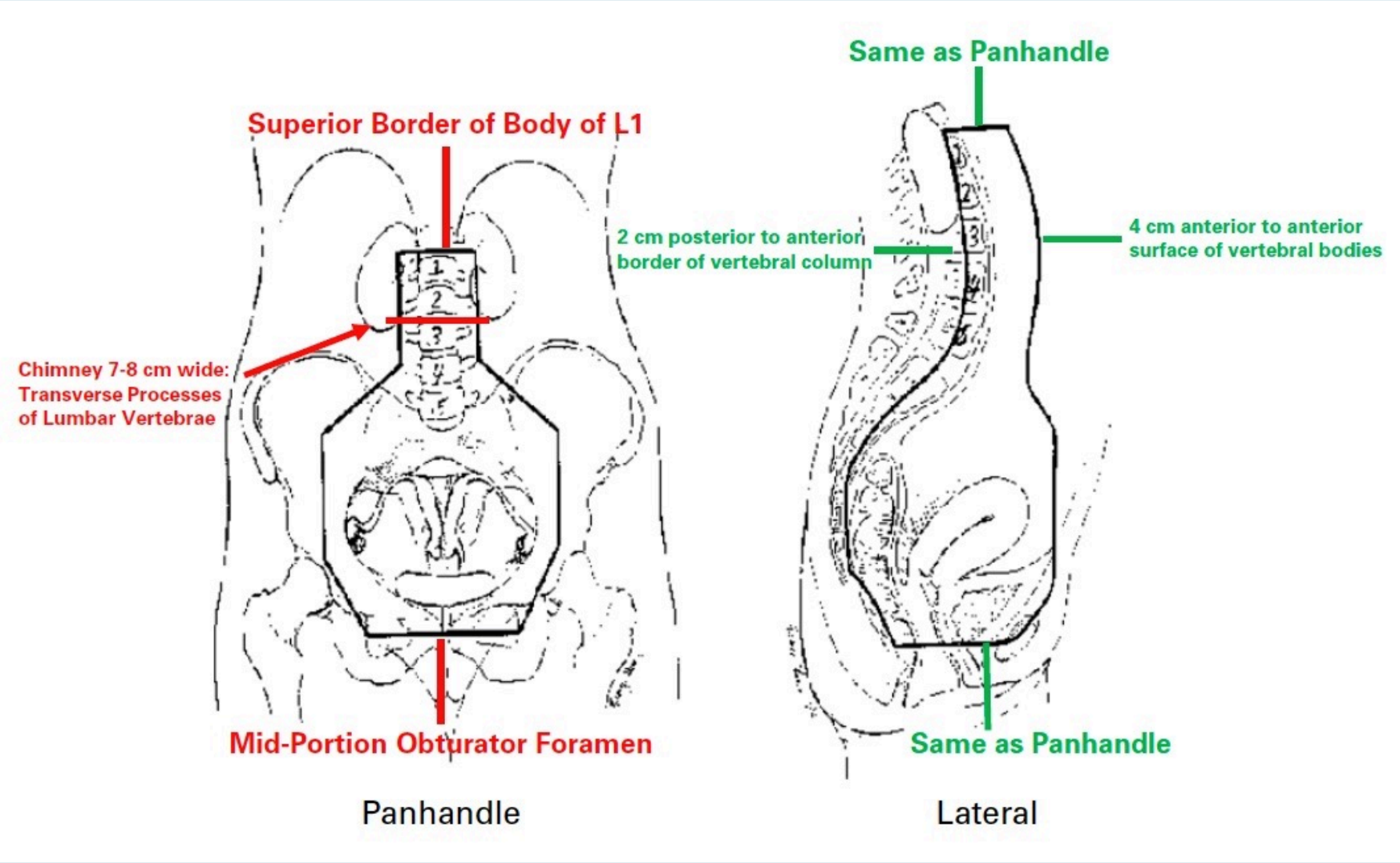
Tewari KS, Monk BJ. *J Clin Oncol* 2019;37(27):2472-89.

Whole Pelvic Radiation



Tewari KS, Monk BJ. *J Clin Oncol* 2019;37(27):2472-89.

Extended Field (Para-aortic) Radiation



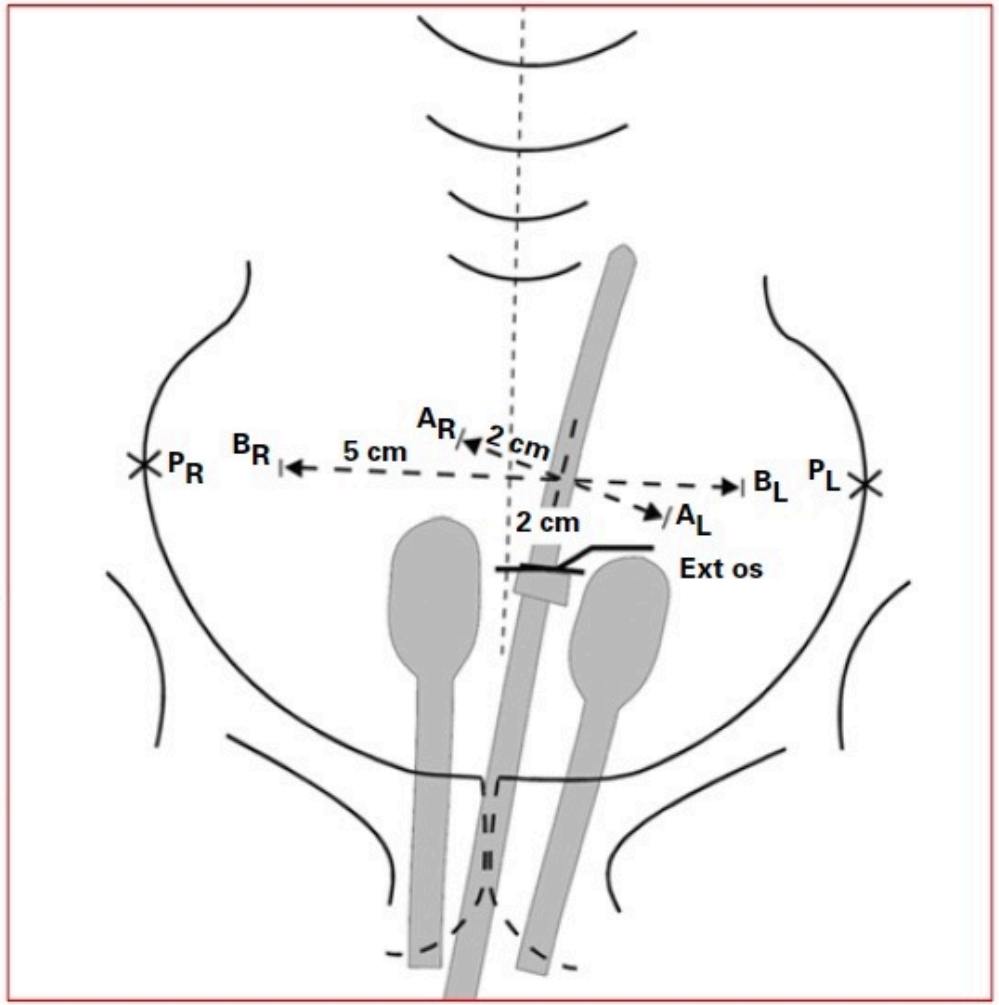
Tewari KS, Monk BJ. *J Clin Oncol* 2019;37(27):2472-89.

Brachytherapy

POINT A:
Referenced to the uterus.
Points A Right and Left are located 2 cm lateral to the internal os measured perpendicular to the inter-uterine canal. The internal os is 2 cm superior to the external os. Therefore Point A represents the parametria.

POINT B:
Referenced to the pelvic bone.
Points B Right and Left are 5 cm lateral to the patient midline on a line perpendicular to the midline passing through the internal os.
Therefore Point B represents the pelvic lymph nodes..

POINT P:
Points P Right and Left are located on the pelvic brim at the widest extent of the bony pelvis.



Tewari KS, Monk BJ. *J Clin Oncol* 2019;37(27):2472-89.

RTP RESEARCH TO PRACTICE

***Gynecol Oncol* 2021;[Online ahead of print].**

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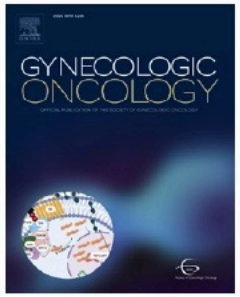
journal homepage: www.elsevier.com/locate/ygyno



Patient characteristics, treatment patterns, and clinical outcomes among patients with previously treated recurrent or metastatic cervical cancer: A community oncology-based analysis

Zachary Alholm [a], Bradley J. Monk [b,*], Jie Ting [c], Sonia Pulgar [c], Marley Boyd [d], Lavanya Sudharshan [d], Savreet Bains [e], Leonardo Nicacio [c], Robert L. Coleman [f]

VIRTUAL 2020 ESMO congress

Tisotumab Vedotin in Previously Treated Recurrent or Metastatic Cervical Cancer: Results From the Phase 2 innovaTV 204/ GOG-3023/ENGOT-cx6 Study

Robert L. Coleman,[1] Domenica Lorusso,[2] Christine Gennigens,[3] Antonio González-Martín,[4] Leslie Randall,[5] David Cibula,[6] Bente Lund,[7] Linn Woelber,[8] Sandro Pignata,[9] Frederic Forget,[10] Andrés Redondo,[11] Reshma Rangwala,[12] Signe Diness Vindeløv,[13] Menghui Chen,[12] Jeffrey R. Harris,[12] Leonardo Viana Nicacio,[14] Melinda S. L. Teng,[14] Margaret Smith,[12] Bradley J. Monk,[15] Ignace Vergote[16]

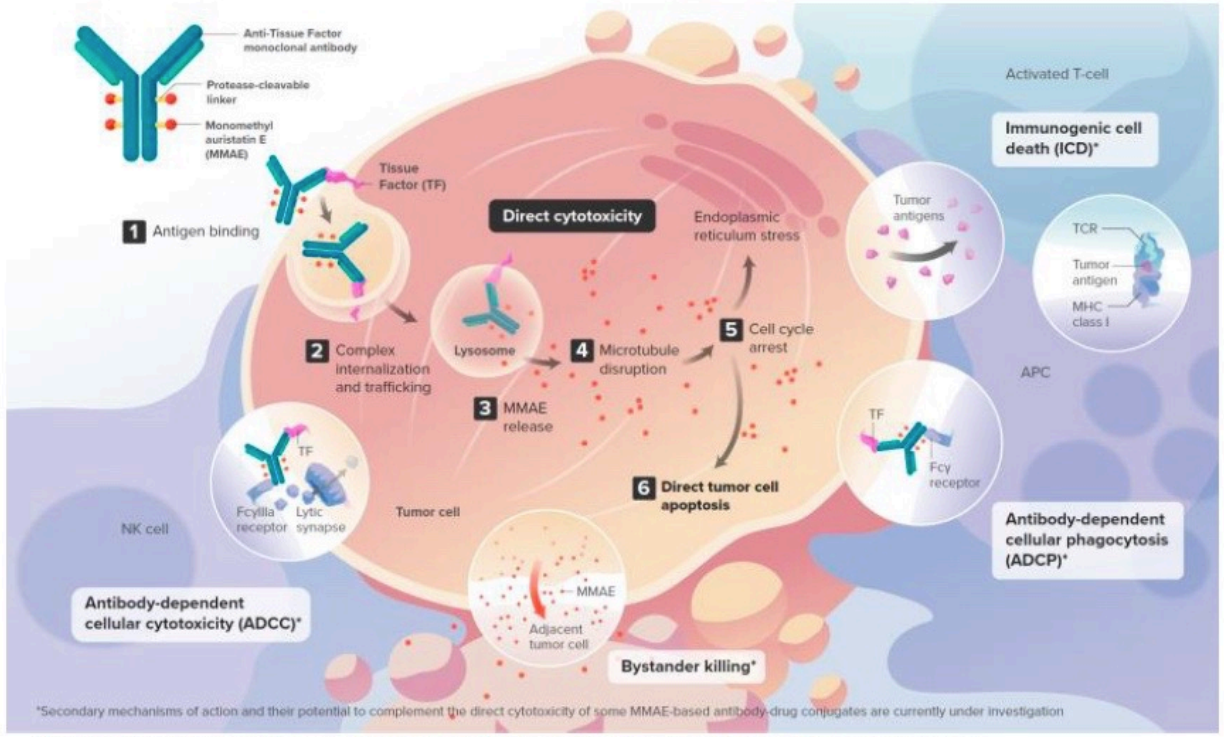
[1]US Oncology, The Woodlands Houston, TX, USA; [2]Multicentre Italian Trials in Ovarian Cancer and Gynaecological Malignancies Group (MITO) and Scientific Directorate and Department of Women and Child Health, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; [3]Department of Medical Oncology, Centre Hospitalier Universitaire de Liège, Liège, Belgium; [4]Grupo Español de Investigación en Cáncer de Ovario (GEICO) and Department of Medical Oncology, Clínica Universidad de Navarra, Madrid, Spain; [5]Massey Cancer Center, Virginia Commonwealth University, Richmond, VA, USA; [6]Central and Eastern European Gynecologic Oncology Group (CEEGOG) and Department of Obstetrics and Gynecology, First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic; [7]Aalborg University Hospital, Aalborg, Denmark; [8]Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) study group and University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [9]MITO and Istituto Nazionale per lo Studio e la Cura dei Tumori, "Fondazione G. Pascale" IRCCS, Naples, Italy; [10]Centre Hospitalier de l'Ardenne, Libramont, Belgium; [11]Grupo Español de Investigación en Cáncer de Ovario (GEICO) and Hospital Universitario La Paz-IdiPAZ, Madrid, Spain; [12]Genmab US, Inc., Princeton, NJ, USA; [13]Genmab, Copenhagen, Denmark; [14]Seattle Genetics, Inc., Bothell, WA, USA; [15]Arizona Oncology (US Oncology Network), University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA; [16]Belgium and Luxembourg Gynaecological Oncology Group, University of Leuven, Leuven Cancer Institute, Leuven, Belgium.

ESMO 2020;Abstract LBA32

RTP RESEARCH TO PRACTICE

Proposed MOA of Tisotumab Vedotin

- Tisotumab vedotin is an investigational antibody-drug conjugate directed to tissue factor (TF) and covalently linked to the microtubule-disrupting agent MMAE via a protease-cleavable linker[1,2]
- TF is highly prevalent in cervical cancer and other solid tumors and is associated with cancer pathophysiology and poor prognosis[3-5]
  - TF is co-opted by tumor cells to promote tumor growth, angiogenesis, and metastasis[6]
  - In normal physiology, TF's primary role is to initiate the coagulation cascade after vascular injury[6]
- Tisotumab vedotin has multiple anti-tumor effects[1,2,7]



Tisotumab vedotin is an investigational agent, and its safety and efficacy have not been established.

1. Breij EC et al. *Cancer Res.* 2014;74(4):1214-1226. 2. De Goeij BE et al. *Mol Cancer Ther.* 2015;14(5):1130-1140. 3. Pan L et al. *Mol Med Rep.* 2019;19:2077-2086. 4. Cocco E et al. *BMC Cancer.* 2011;11:263. 5. Zhao X et al. *Exp Ther Med.* 2018;16:4075-4081. 6. Forster Y et al. *Clin Chim Acta.* 2006;364:12-21 7. Alley SC et al. American Association for Cancer Research Annual Meeting; March 29 – April 3, 2019; Atlanta, GA, USA; Abstract #221.
ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; MMAE, monomethyl auristatin E; MOA, mechanism of action; TF, tissue factor.

Coleman RL et al. ESMO 2020;Abstract LBA32.

innovaTV 204 Study Design

innovaTV 204 (NCT03438396) is a pivotal phase 2 single-arm, multicenter (United States and Europe) study evaluating tisotumab vedotin in patients with previously treated recurrent and/or metastatic cervical cancer

Key Eligibility Criteria

- Recurrent or extrapelvic metastatic cervical cancer
- Progressed during or after doublet chemotherapy[a] with bevacizumab (if eligible)
- Received ≤2 prior systemic regimens[b]
- ECOG PS 0-1

Enrolled: 102[c]
Treated: 101*

Tisotumab vedotin
2.0 mg/kg IV Q3W

Until PD or unacceptable toxicity

Tumor responses assessed using CT or MRI at baseline, every 6 weeks for the first 30 weeks, and every 12 weeks thereafter

*Study sample size calculated assuming a confirmed ORR of 21% to 25% with tisotumab vedotin and to provide ≥80% power to exclude an ORR of ≤11%[e]

Primary Endpoint
- ORR[d] per RECIST v1.1, by independent imaging review committee (IRC)

Secondary Endpoints
- ORR[d] per RECIST v1.1, by investigator
- DOR, TTR, and PFS by IRC and investigator
- OS
- Safety

Exploratory Endpoints
- Biomarkers
- HRQoL

[a]Paclitaxel plus platinum (cisplatin or carboplatin) or paclitaxel plus topotecan. [b]Adjuvant or neoadjuvant chemotherapy or if administered with radiation therapy, was not counted as a prior systemic regimen. [c]June 2018 to April 2019. [d]Responses were confirmed by subsequent repeat imaging performed ≥4 weeks after initial response assessment. [e]Using one-sided exact binomial test at 0.025 significance level.
CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IRC, independent review committee; IV, intravenous; MRI, magnetic resonance imaging; OS, overall survival; PD, progressive disease; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; TTR, time to response.

Coleman RL et al. ESMO 2020;Abstract LBA32.

Baseline Demographics & Disease Characteristics

	N=101
Age, median (range), years	50 (31–78)
Race, (n %)	
White	96 (95)
Asian	2 (2)
Black or African American	1 (1)
Other	2 (2)
ECOG PS, n (%)	
0	59 (58)
1	42 (42)
Histology, n (%)	
Squamous cell carcinoma	69 (68)
Adenocarcinoma	27 (27)
Adenosquamous carcinoma	5 (5)
Extrapelvic metastatic disease at baseline, n (%)	95 (94)

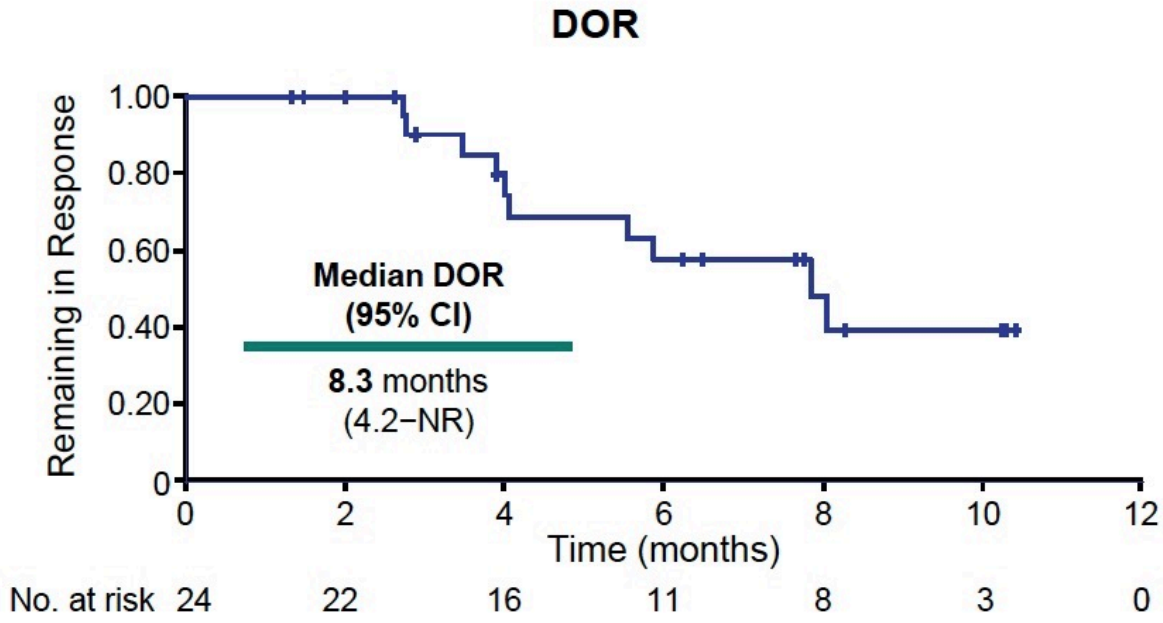
	N=101
Prior cisplatin plus radiation, n (%)	
Yes	55 (54)
No	46 (46)
Prior lines of systemic regimen for recurrent/metastatic disease,[a] n (%)	
1	71 (70)
2	30 (30)
Prior bevacizumab plus doublet chemotherapy as 1L therapy,[b] n (%)	64 (63)
Response to last systemic regimen,[a] n (%)	
Yes	38 (38)
No	57 (56)
Unknown	6 (6)
Biopsy evaluable, n (%)	80 (79)
Positive membrane TF expression,[c] n (%)	77 (96)

Data cutoff: February 06, 2020.
[a]Systemic regimen administered in the metastatic or recurrent setting. [b]Doublet chemotherapy defined as paclitaxel-platinum or paclitaxel-topotecan. [c]Positive TF expression defined as any positive membrane staining on tumor cells out of biopsy-evaluable population (n=80).
1L, first-line; ECOG PS, Eastern Cooperative Group performance status; TF, tissue factor.

Coleman RL et al. ESMO 2020;Abstract LBA32.

Antitumor Activity by IRC Assessment

	N=101
Confirmed ORR (95% CI),[a] %	**24 (15.9−33.3)**
CR, n (%)	7 (7)
PR, n (%)	17 (17)
SD, n (%)	49 (49)
PD, n (%)	24 (24)
Not evaluable, n (%)	4 (4)



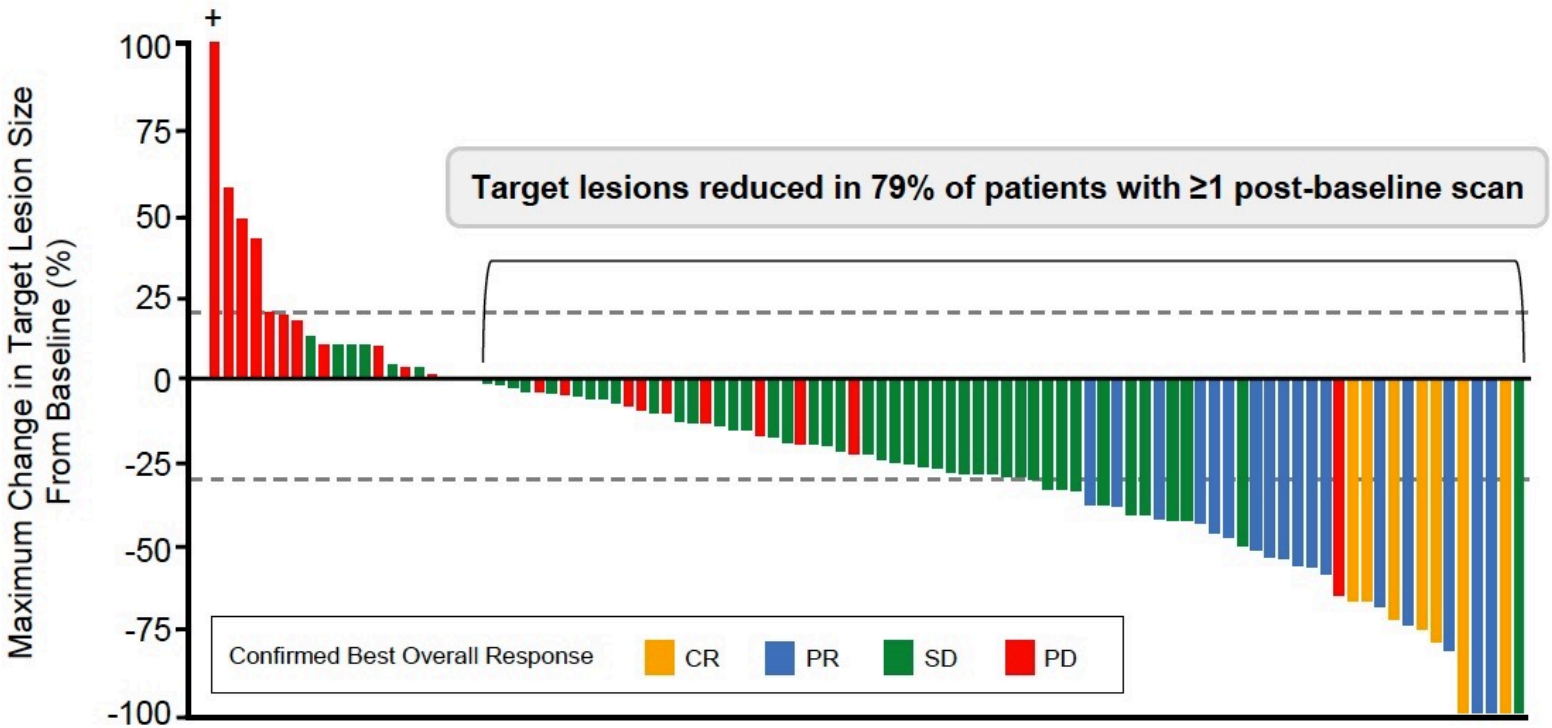
Clinically meaningful and durable responses were observed

Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months.
[a]Based on the Clopper-Pearson method.
CI, confidence interval; CR, complete response; DOR, duration of response; IRC, independent review committee; NR, not reached; ORR, objective response rate; PD, disease progression; PR, partial response; SD, stable disease.

Coleman RL et al. ESMO 2020;Abstract LBA32.

VIRTUAL 2020 ESMO congress

Maximum Change in Target Lesion Size by IRC Assessment

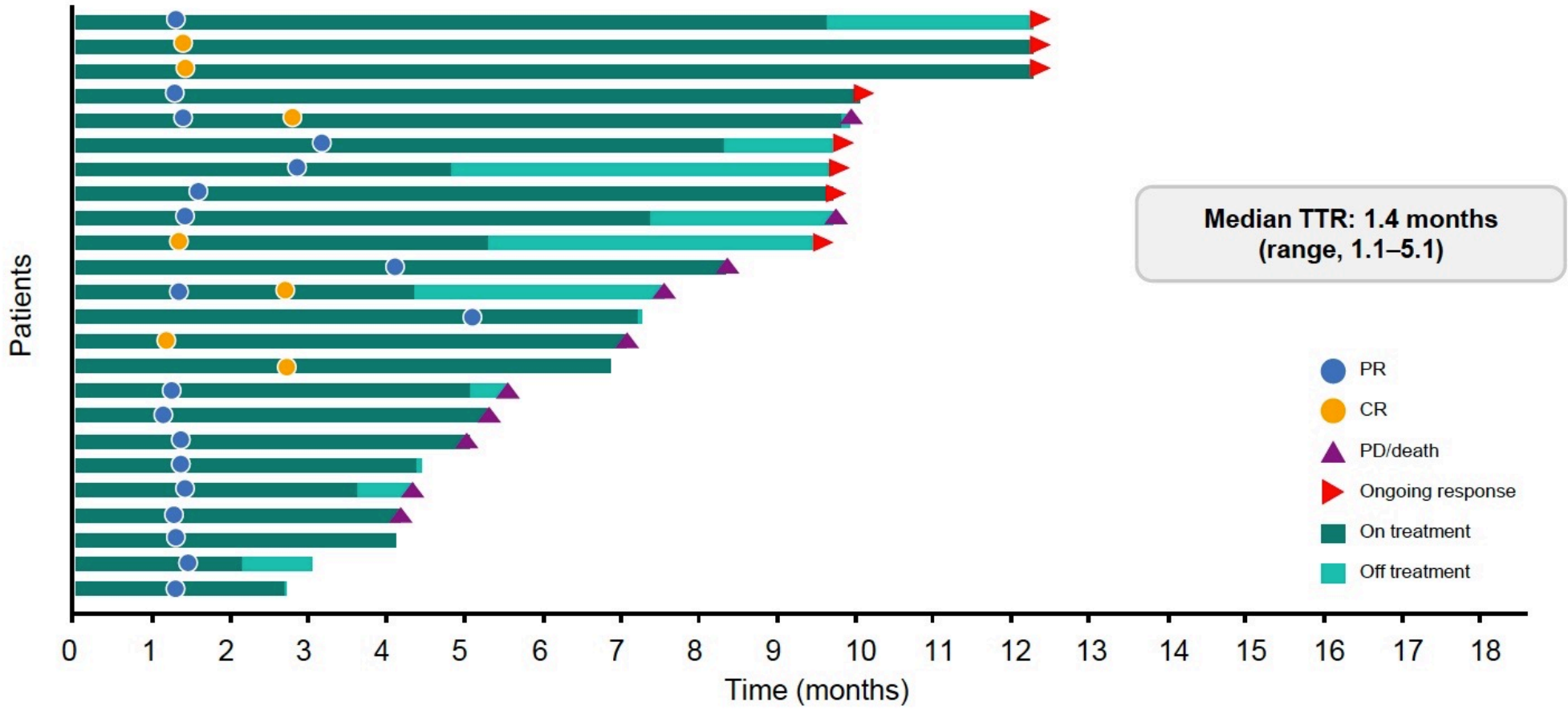


Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months. + indicates a change greater than 100%. Horizontal dashed lines indicate 20% increase and 30% decrease in target lesion diameters from baseline for RECIST v1.1 assessment. Colored bars represent the best overall confirmed response. CR, PR, SD, and PD were based on RECIST v1.1 as evaluated by IRC.
CR, complete response; IRC, independent review committee; PD, disease progression; PR, partial response; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; SD, stable disease.

Coleman RL et al. ESMO 2020;Abstract LBA32.

RTP RESEARCH TO PRACTICE

Confirmed Responders by IRC Assessment



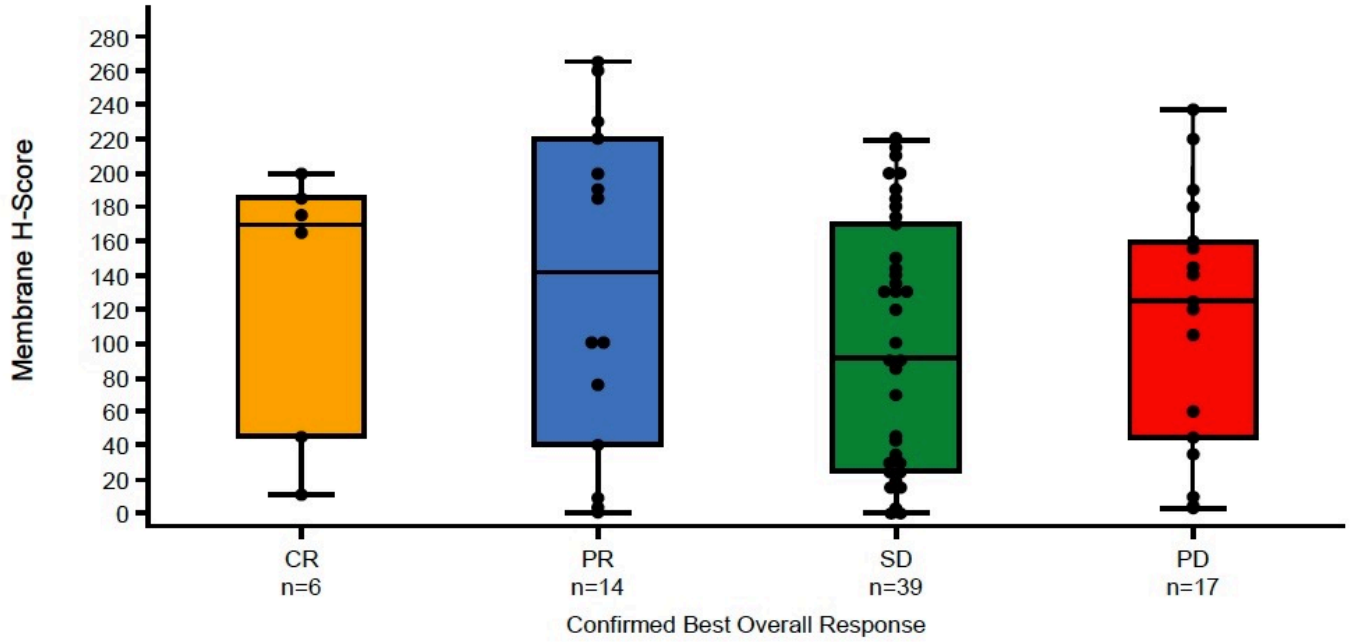
Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months.
Symbols closest to the Y-axis indicate the first response. A second symbol on a lane indicates a response that improved from a PR to a CR.
CR, complete response; IRC, independent review committee; PD, disease progression; PR, partial response; TTR, time to response.

Coleman RL et al. ESMO 2020;Abstract LBA32.

Tissue Factor Expression Analyses

- Response to tisotumab vedotin was observed regardless of membrane TF expression level
- Of the 80 patients for whom TF expression data were available, 76 (95%) were also evaluable for response
- Similar distribution of TF expression was observed between the different response groups

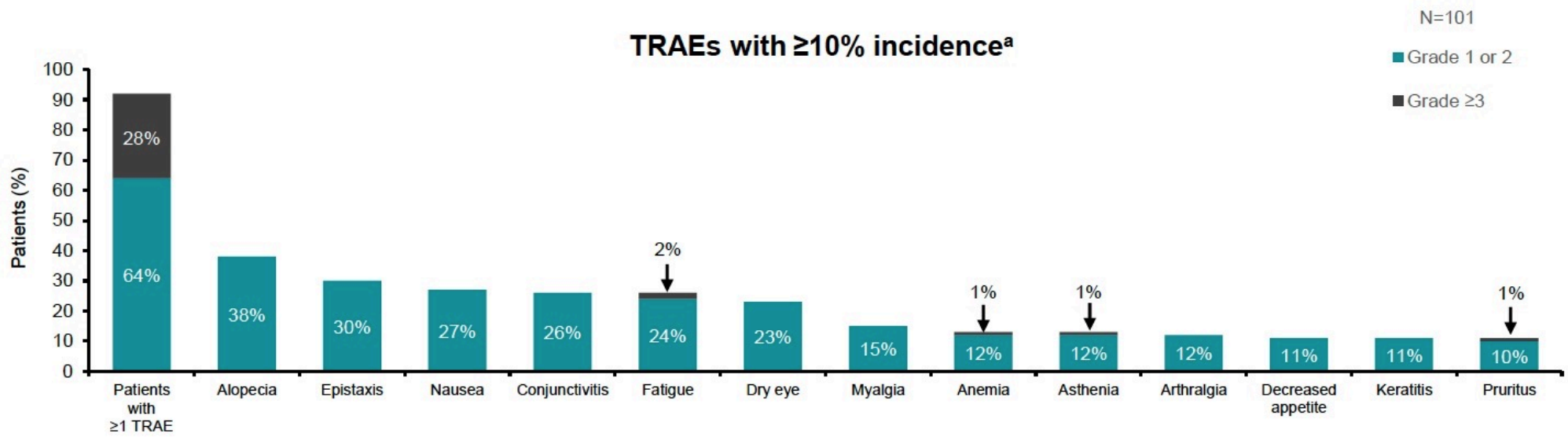
Tumor Membrane H-Score at Baseline by Confirmed Best Overall Response by IRC Assessment



Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months.
CR, complete response; IRC, independent review committee; PD, disease progression; PR, partial response; SD, stable disease; TF, tissue factor.

Coleman RL et al. ESMO 2020;Abstract LBA32.

Most Common TRAEs with Tisotumab Vedotin



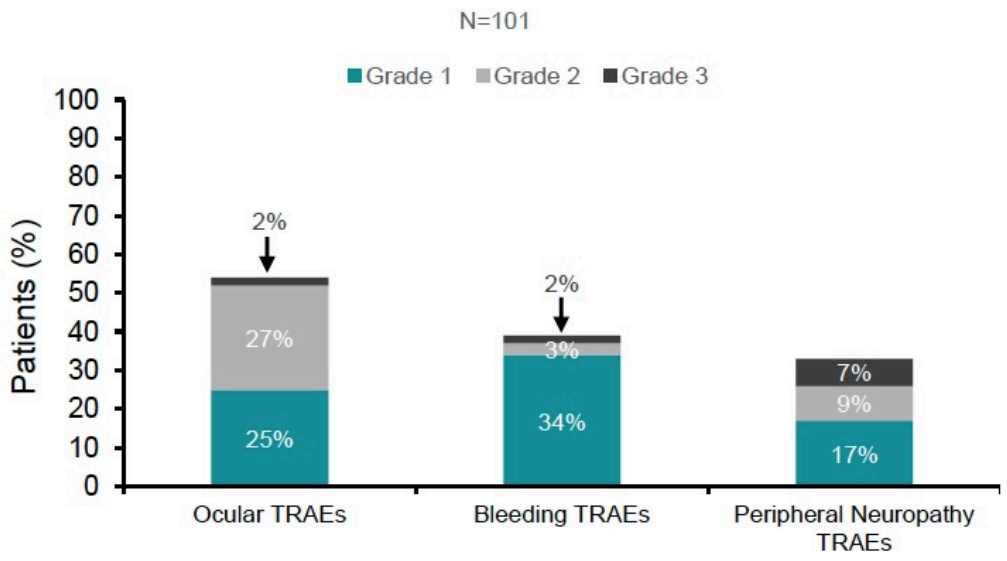
- **Most TRAEs were grade 1 or 2 and no new safety signals were reported**
- **One death due to septic shock was considered by the investigator to be related to therapy[b]**

Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months. Median duration of treatment: 4.2 months (range, 1–16).
[a]Any-grade AEs included if ≥10%. [b]Three treatment-emergent deaths unrelated to therapy included one case of ileus and two with unknown causes.
TRAE, treatment-related adverse event.

Coleman RL et al. ESMO 2020;Abstract LBA32.

Prespecified AEs of Interest of Tisotumab Vedotin

Ocular,[a] bleeding,[b] and peripheral neuropathy[c] TRAEs



	Ocular	Bleeding	Peripheral Neuropathy
Time to onset (median, months)	1.4	0.3	3.1
Events resolved, %	86	90	21
Time to resolution[d] (median, months)	0.7	0.5	0.6

- **Ocular AEs were mostly mild to moderate, resolved, and were manageable with an eye care plan**
- **Most bleeding events were grade 1 epistaxis (28%) of which majority resolved**
- **Most peripheral neuropathy events (known MMAE-related toxicity) were grade 1 and manageable with dose modifications; resolution was limited by follow-up period**

Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months.
[a]Any ocular SMQ (conjunctival disorders SMQ, corneal disorders SMQ, scleral disorders SMQ, retinal disorders SMQ, periorbital and eyelid disorders SMQ, ocular infections SMQ, optic nerve disorders SMQ, glaucoma SMQ, lacrimal disorders SMQ, and eye disorders SMQ). [b]Hemorrhage SMQ. [c]Peripheral neuropathy SMQ. [d]Assessment limited by the protocol-defined follow-up period for AE of only 30 days after the last dose.
AE, adverse event; MMAE, monomethyl auristatin E; SMQ, standardized MedDRA queries; TRAE, treatment-related adverse events.

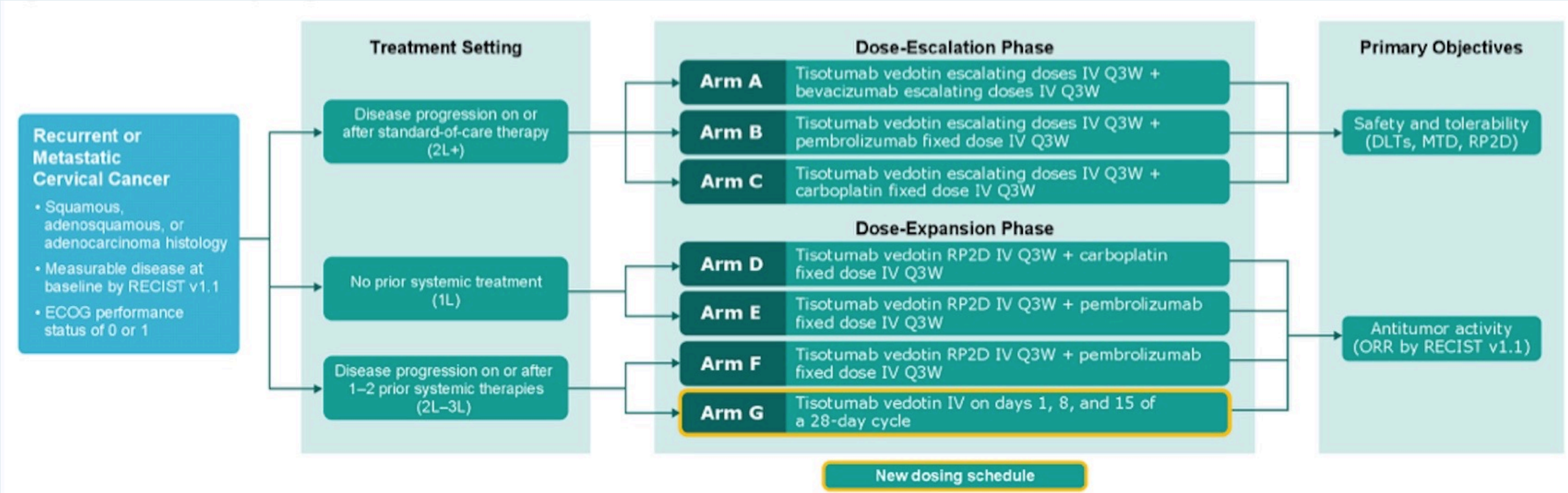
Coleman RL et al. ESMO 2020;Abstract LBA32.

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.

innovaTV 205 Study Design



2L, second-line; 3L, third-line; DLTs, dose-limiting toxicities; ECOG, Eastern Cooperative Oncology Group; IV, intravenously; MTD, maximum tolerated dose; ORR, objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; RP2D, recommended phase 2 dose.

Vergote I et al. ASCO 2020;Abstract TPS6095.

Int J Gynecol Cancer 2020;30(7):1065-70

Clinical trial

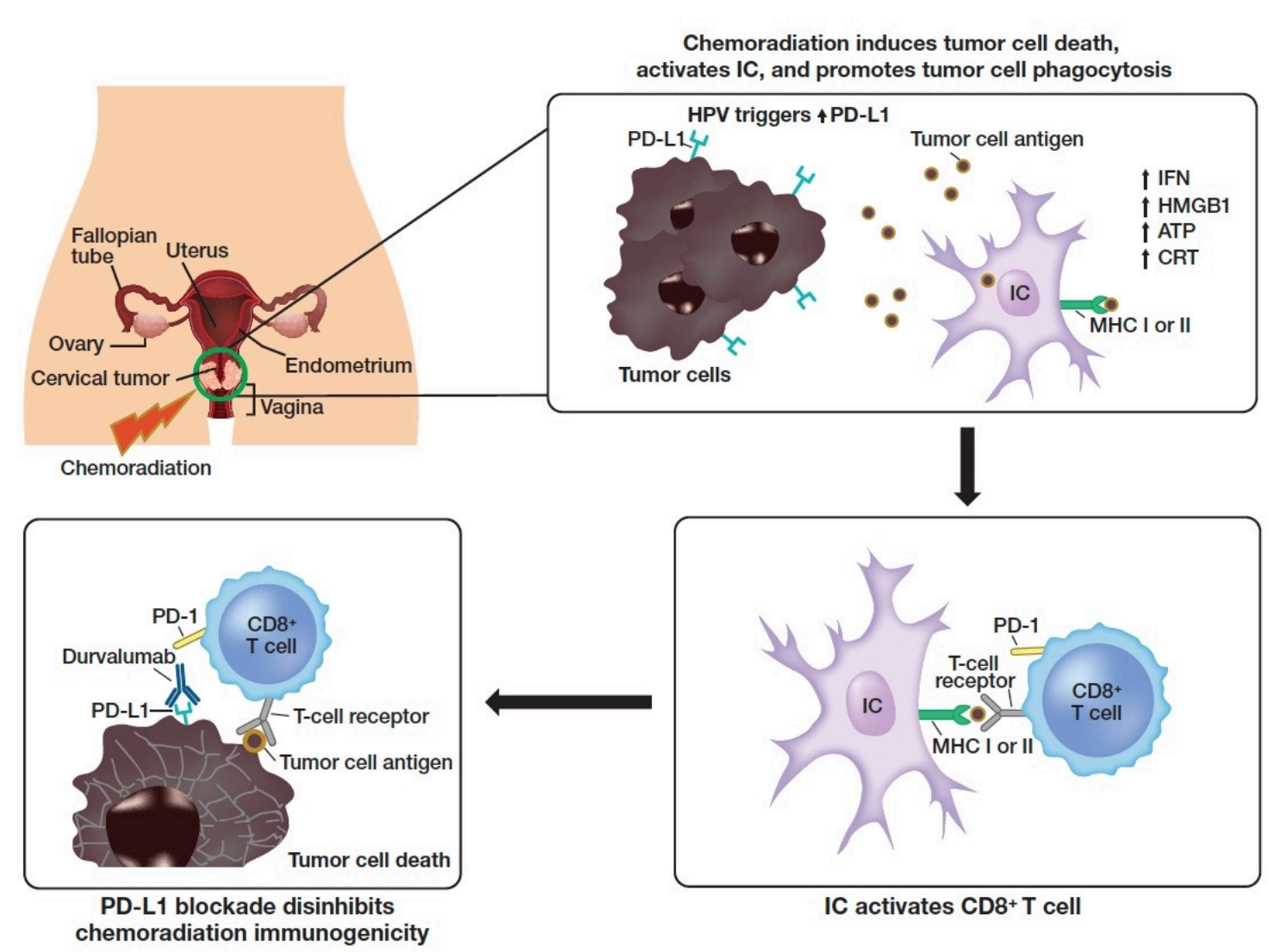
INTERNATIONAL JOURNAL OF GYNECOLOGICAL CANCER

OPEN ACCESS

CALLA: Efficacy and safety of concurrent and adjuvant durvalumab with chemoradiotherapy versus chemoradiotherapy alone in women with locally advanced cervical cancer: a phase III, randomized, double-blind, multicenter study

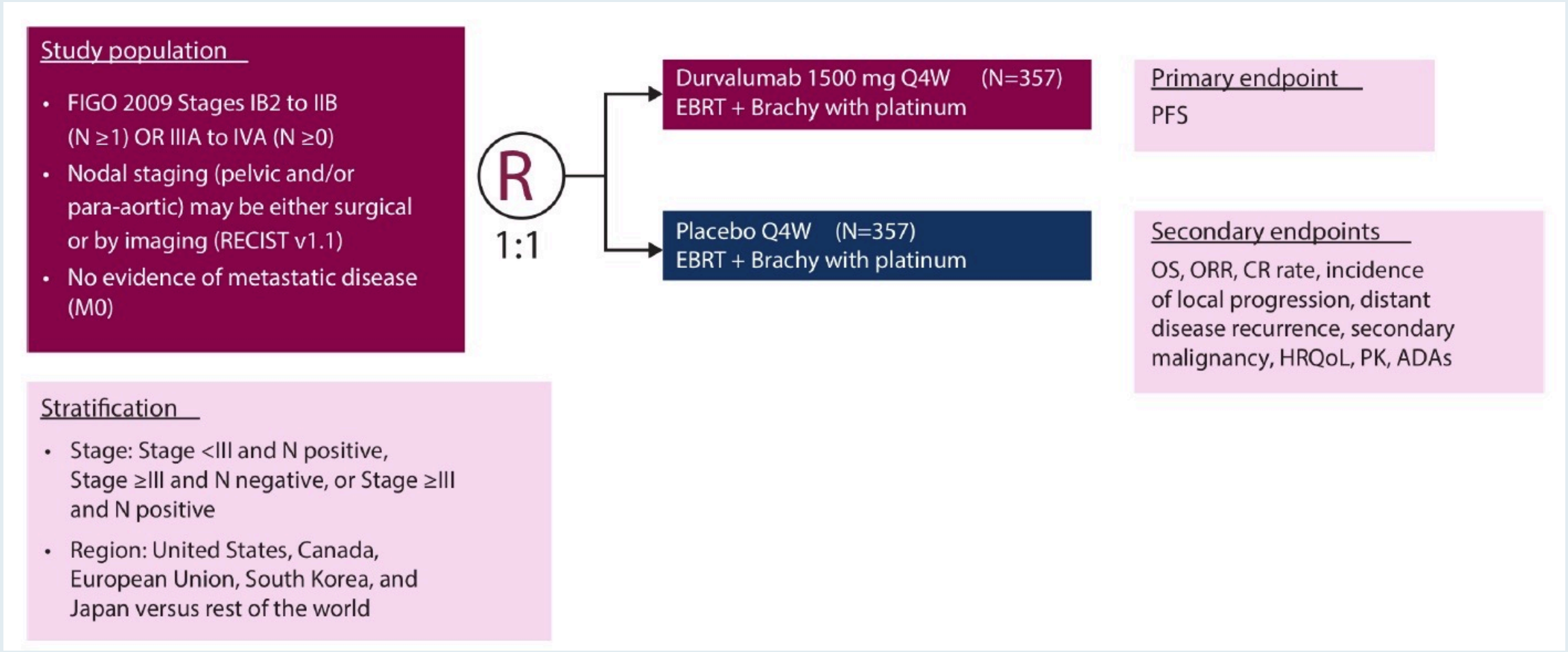
Jyoti Mayadev,[1] Ana T Nunes,[2] Mary Li,[2] Michelle Marcovitz,[2] Mark C Lanasa,[2] Bradley J Monk[3]

Concurrent Chemoradiation Therapy + Anti-PD-1/PD-L1 Therapies



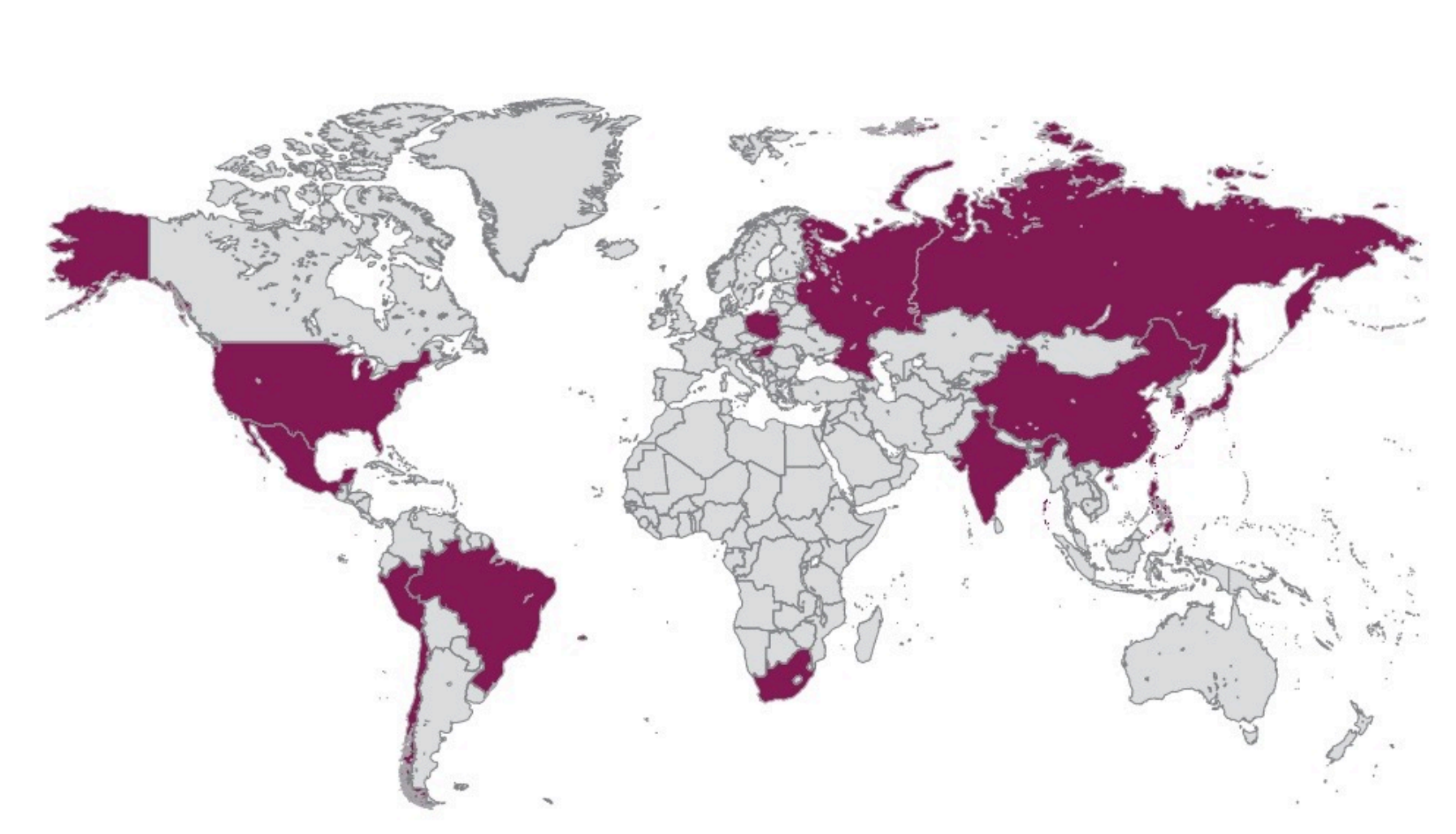
Mayadev J et al. *Int J Gynecol Cancer* 2020;30(7):1065-70.

CALLA Study Design



Mayadev J et al. *Int J Gynecol Cancer* 2020;30(7):1065-70.

CALLA Planned Study Sites: Approximately 131 Sites Including 114 Sites Outside the United States



Mayadev J et al. *Int J Gynecol Cancer* 2020;30(7):1065-70.

RTP RESEARCH TO PRACTICE

VIRTUAL 2020 ESMO congress

ESMO 2020;Abstract LBA34

Balstilimab (anti-PD-1) Alone and in Combination with Zalifrelimab (anti-CTLA-4) for Recurrent/Metastatic (R/M) Cervical Cancer (CC) Preliminary Results of Two Independent Ph2 Trials (NCT03104699 and NCT03495882)

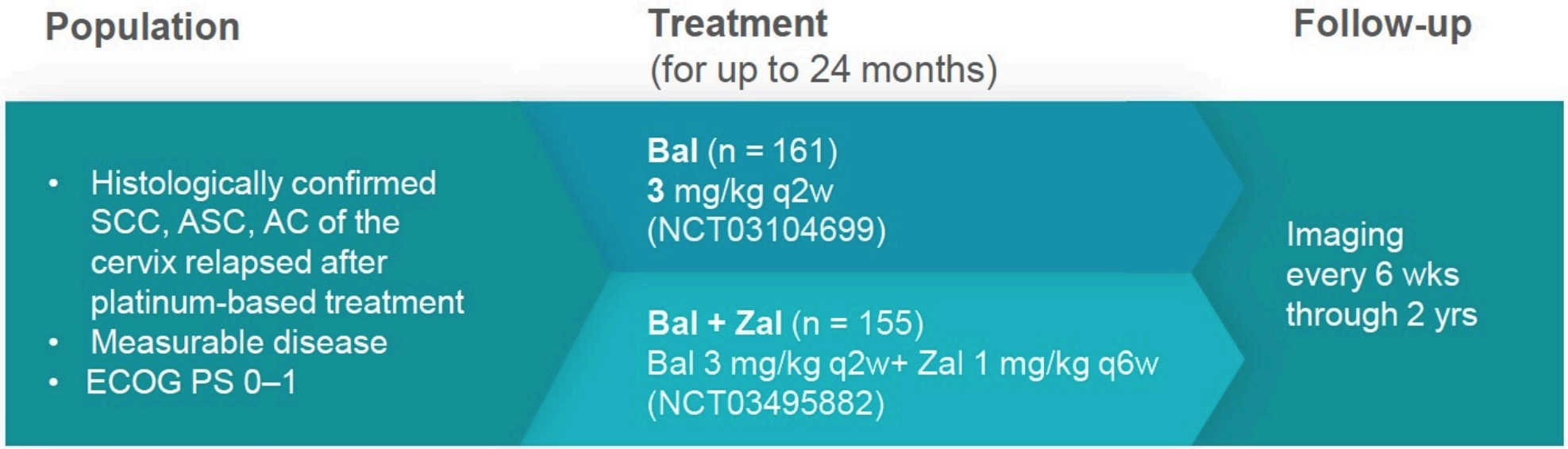
O'Malley DM[1]; Oaknin A[2]; Monk B[3]; Leary A[4]; Selle F[5]; Alexandre J[6]; Randall L[6]; Rojas C[7]; Neffa M[8]; Kryzhanivska A[9]; Gladieff L[10]; Berton D[11]; Meniawy T[12]; Lugowska I[13]; Bondarenko I[14]; Moore K[15]; Ortuzar Feliu W[16]; Ancukiewicz M[16]; Shapiro I[16]; Ray-Coquard I[17]

[1]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [2]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [3]University of Arizona College of Medicine, Creighton University School of Medicine at St. Joseph's Hospital Phoenix, AZ, USA; [4]Institut de Cancérologie Gustave Roussy, Villejuif, France; [5]APHP Centre - Université de Paris, Hôpital Cochin, Paris, France; [6]Massey Cancer Center, Virginia Commonwealth University, Richmond, VA, USA; [7]Centro de Investigaciones Clinicas, Bradford Hill, Chile; [8]CI of Healthcare Regional Clinical Specialized Dispensary of the Radiation Protection, Department of Surgery, Kharkiv, Ukraine; [9]CI Transcarpathian Cl Onc Center Dep of Surgery#1 SHEI Ivano-Frankivsk NMU, Ivano-Frankivsk, Ukraine; [10]Le Centre René Gauducheau, Saint-Herblain, France; [11]Institut Claudius Regaud, IUCT Oncopole, Toulouse, France; [12]Linear Clinical Research, Perth, Australia; [13]Centrum Onkologii-Instytut im.M.Sklodowskiej Curie, Warsaw, Poland; [14]CI Dnipropetrovsk CMCH #4 of Dnipropetrovsk RC Dept of Chemotherapy SI Dnipropetrovsk MA of MOHU, Dniepro, Ukraine; [15]Stephenson Cancer Center at the University of Oklahoma, Oklahoma City, OK, USA ; [16]Agenus Inc., Lexington, MA, USA; [17]Centre Léon Bérard, Lyon, France

RTP RESEARCH TO PRACTICE

Study Design

Two Parallel, Single-arm Trials Testing Balstilimab Alone and with Zalifrelimab in Recurrent/Metastatic Cervical Cancer



- **Primary endpoint:** Independent Review Committee (IRC) ORR by RECIST 1.1
- **Secondary endpoints:** DOR,PFS, OS,

SCC – Squamous-cell cancer; ASC – Adenosquamous cancer; AC – Adenocarcinoma

VIRTUAL 2020 ESMO congress

O'Malley DM et al. ESMO 2020;Abstract LBA34.

RTP RESEARCH TO PRACTICE

Primary Endpoint: Tumor Response

Responses in all patients	Balstilimab Only		Balstilimab + Zalifrelimab	
	mITT (n=160)	≥1 Prior chemotherapy (n=138)	mITT (N=143)	≥1 Prior chemotherapy (n=119)
Best Overall Response %, (95% CI)	**23 (14%) [10, 21]**	**18 (13%) [8, 20]**	**31 (22%) [16, 29]**	**24 (20%) [14, 28]**
Complete Response	3 (2%)	3 (2%)	8 (6%)	6 (5%)
Partial Response	20 (12%)	15 (11%)	23 (16%)	18 (15%)
Duration (mon) of Response, median [range obs]	15.4 [1.1+,15.4]	15.4 [1.3+,15.4]	NR [1.3+,16.6+]	NR [1.3+,15.4+]
ORR by tumor histology				
SCC # responders/# treated (%)	18/100 (18%)	13/83 (16%)	29/106 (27%)	22/82 (27%)
AdenoCa/AdnoSq # responders/# treated (%)	5/59 (8%)	5/55 (9%)	2/37 (5%)	2/37 (5%)

Data cut-off: 7/31/2020

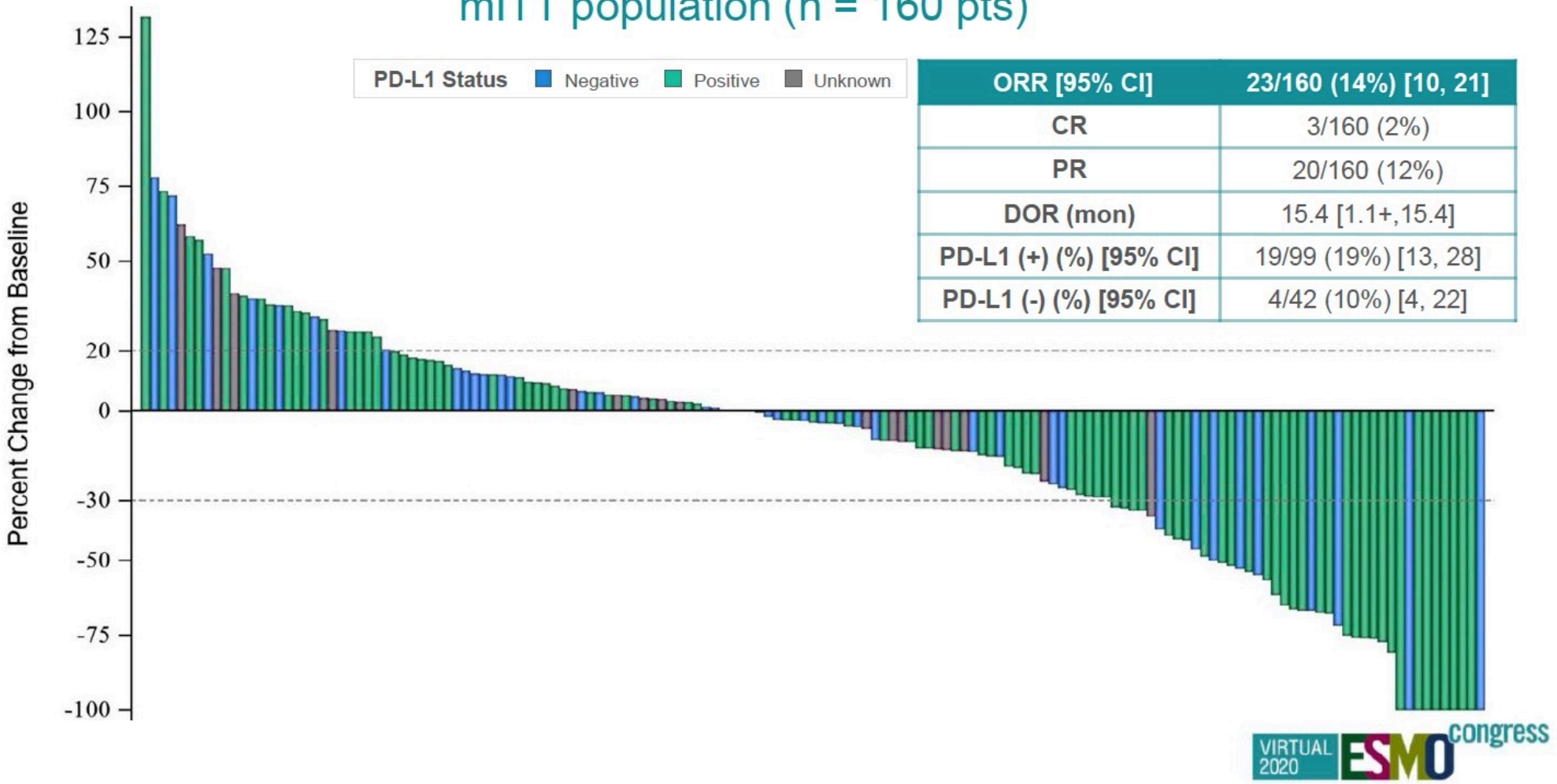
VIRTUAL 2020 ESMO congress

O'Malley DM et al. ESMO 2020;Abstract LBA34.

RTP RESEARCH TO PRACTICE

Tumor Response with Balstilimab Monotherapy

mITT population (n = 160 pts)



ORR [95% CI]	23/160 (14%) [10, 21]
CR	3/160 (2%)
PR	20/160 (12%)
DOR (mon)	15.4 [1.1+,15.4]
PD-L1 (+) (%) [95% CI]	19/99 (19%) [13, 28]
PD-L1 (-) (%) [95% CI]	4/42 (10%) [4, 22]

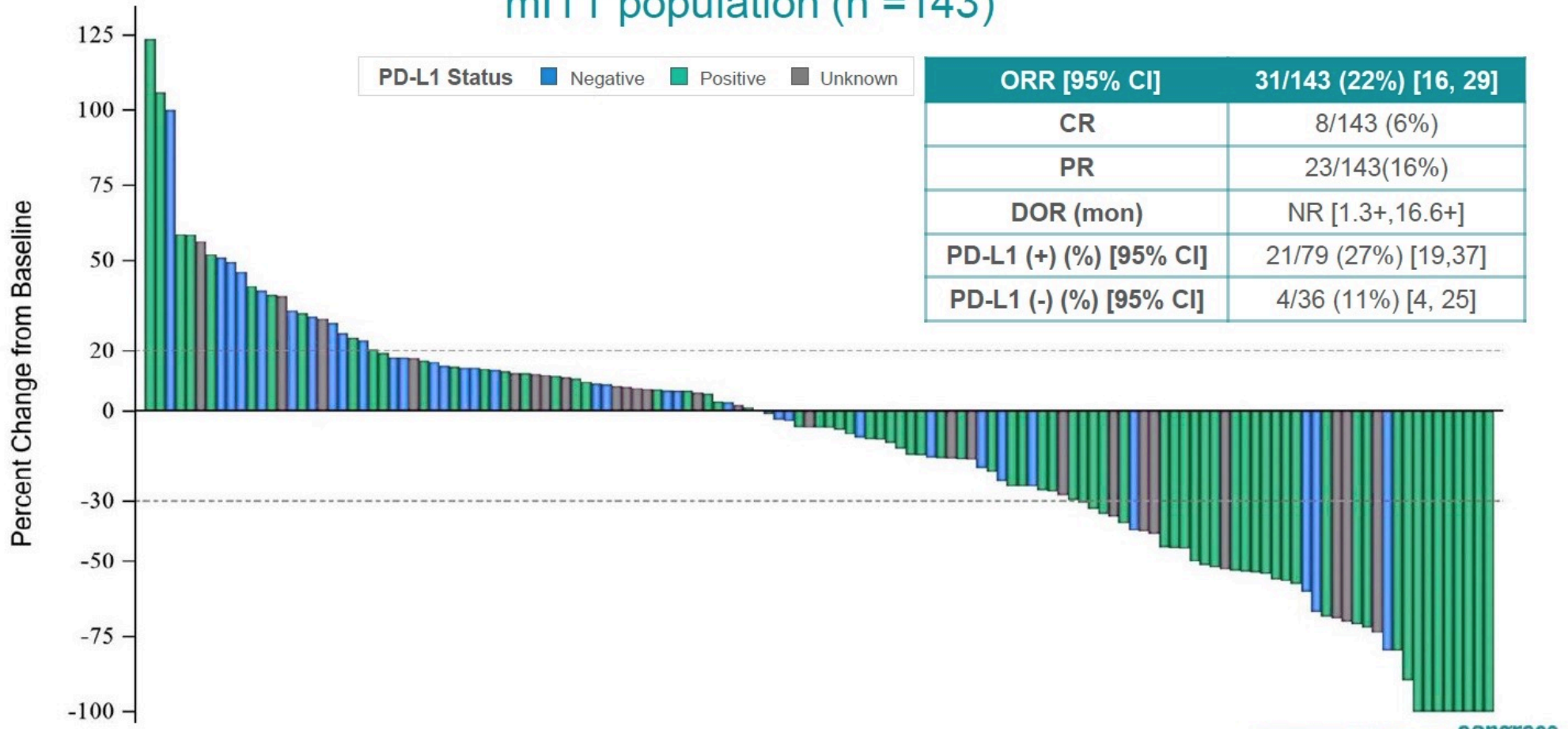
VIRTUAL 2020 ESMO congress

O'Malley DM et al. ESMO 2020;Abstract LBA34.

RTP RESEARCH TO PRACTICE

Tumor Response with Balstilimab plus Zalifrelimab

mITT population (n =143)



ORR [95% CI]	31/143 (22%) [16, 29]
CR	8/143 (6%)
PR	23/143(16%)
DOR (mon)	NR [1.3+,16.6+]
PD-L1 (+) (%) [95% CI]	21/79 (27%) [19,37]
PD-L1 (-) (%) [95% CI]	4/36 (11%) [4, 25]

VIRTUAL 2020 ESMO congress

O'Malley DM et al. ESMO 2020;Abstract LBA34.

RTP RESEARCH TO PRACTICE

Immune-Related Adverse Events*

Safety Population

Any grade irTRAEs, n (%)	Bal N= 161	Bal/Zal N=155
Gastrointestinal disorders	9 (5.6)	**13 (8.4)**
Laboratory abnormalities**	9 (5.6)	**18 (11.6)**
Endocrine disorders	8 (5.0)	**29 (18.7)**
Grade ≥3 irTRAEs, n (%)		
Gastrointestinal disorders	5 (3.1)	4 (2.6)
Laboratory abnormalities**	2 (1.2)	6 (3.9)
Skin and sc. tissue disorders	1 (0.6)	3 (1.9)

* Investigator reported events
** Lab. abnormalities observed in creatinine, lipase, aminotransferases, electrolytes and thyroid stimulating hormone levels

VIRTUAL 2020 ESMO congress

O'Malley DM et al. ESMO 2020;Abstract LBA34.

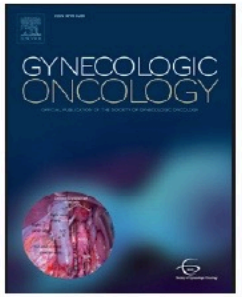
RTP RESEARCH TO PRACTICE

Gynecologic Oncology 159 (2020) 150–156

Contents lists available at ScienceDirect

Gynecologic Oncology

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

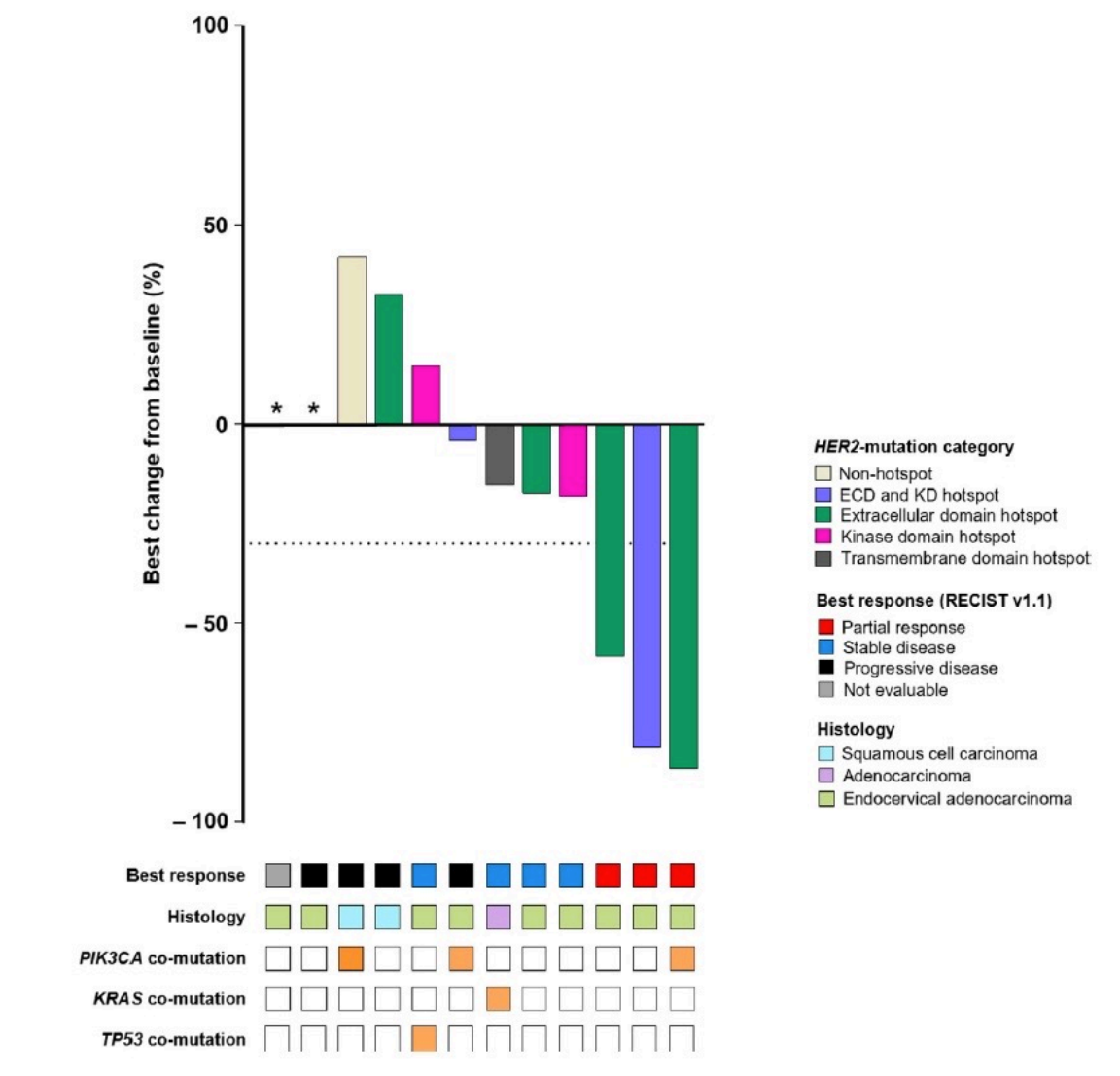


Research paper

Neratinib in patients with *HER2*-mutant, metastatic cervical cancer: Findings from the phase 2 SUMMIT basket trial

Ana Oaknin [a,1], Claire F. Friedman [b,1], Lynda D. Roman [c], Anishka D'Souza [c], Irene Brana [a], François-Clement Bidard [d], Jonathan Goldman [e], Edwin A. Alvarez [f], Valentina Boni [g], Adam C. ElNaggar [h], Rodolfo Passalacqua [i], Khanh T.M. Do [j], Alessandro D. Santin [k], Kiana Keyvanjah [l], Feng Xu [l], Lisa D. Eli [l], Alshad S. Lalani [l], Richard P. Bryce [l], David M. Hyman [b,2], Funda Meric-Bernstam [m], David B. Solit [b], Bradley J. Monk [n,*,3]

Best Change in Tumor Size and Characteristics in RECIST Efficacy Evaluable Patients (N=12)



Oaknin A et al. *Gynecol Oncol* 2020;159(1):150-6.

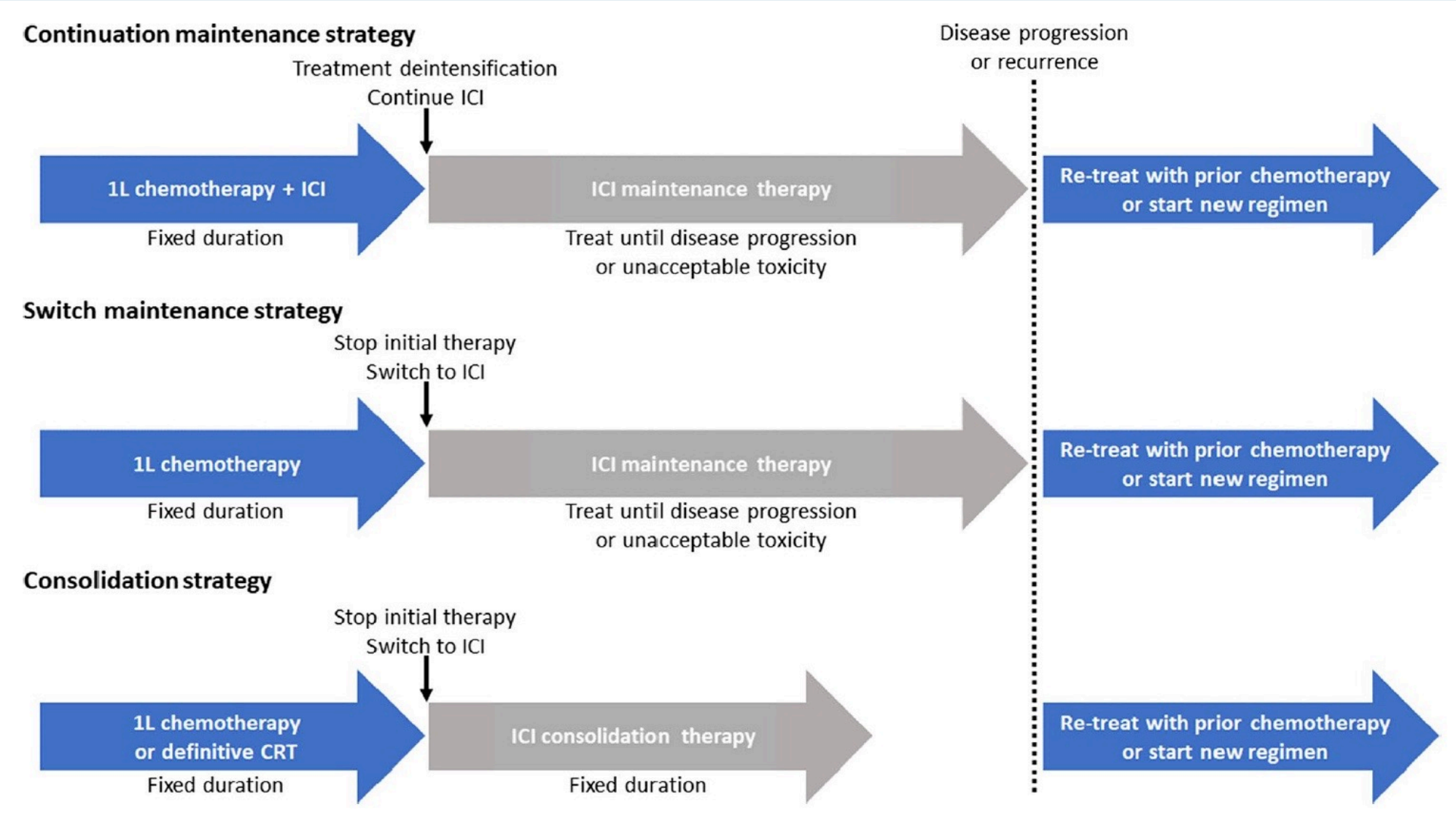
Targeted Oncology (2019) 14:505–525
https://doi.org/10.1007/s11523-019-00665-1

REVIEW ARTICLE

Immune Checkpoint Inhibitors as Switch or Continuation Maintenance Therapy in Solid Tumors: Rationale and Current State

Petros Grivas[1] · Bradley J. Monk[2] · Daniel Petrylak[3] · Martin Reck[4] · Grace Foley[5] · Silke Guenther[6] · Dan Hennessy[7] · Constantin Makris[8] · Markus Moehler[9]

Schematic of Immune Checkpoint Inhibitor (ICI)-Based Maintenance Strategies Being Investigated in Clinical Trials



Grivas P et al. *Target Oncol* 2019;14(5):505-25.

RTP RESEARCH TO PRACTICE

Gynecol Oncol. 2020 January ; 156(1): 100–106.

Incorporation of whole pelvic radiation into treatment of stage IVB cervical cancer: A novel treatment strategy

Victoria Perkins[a], Kathleen Moore[a], Sara Vesely[e], Koji Matsuo[b], Sayedamin Mostofizadeh[b], Travis T. Sims[c], Jayanthi Lea[c], Dominique Barnes[d], Sixia Chen[e], Matthew Carlson[c], Lynda Roman[b], Bradley J. Monk[d], Laura L. Holman[a,*]

EDITORIAL

Sequential Chemotherapy for Early-Stage, Post-Radical Hysterectomy Cervical Cancer

Are the STARS Aligned?

Leslie M. Randall, MD; Jyoti Mayadev, MD; Bradley J. Monk, MD

JAMA Oncol 2021;7(3):353-4.

Meet The Professor with Dr Monk

MODULE 1: Cases from General Medical Oncology Practices

MODULE 2: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 3: Gynecologic Oncology Journal Club with Dr Monk

- Evidence-based treatment paradigm for invasive cervical carcinoma (CC)
- Patient characteristics, treatment patterns and clinical outcomes with previously treated recurrent or metastatic CC
- innovaTV 204 trial: Tisotumab vedotin for previously treated recurrent or metastatic CC
- innovaTV 205 trial: Tisotumab vedotin ± bevacizumab, pembrolizumab or carboplatin for recurrent or metastatic CC
- CALLA trial results: Concurrent and adjuvant durvalumab with chemoRT versus chemoRT alone for locally advanced CC
- Anti-PD-1 balstilimab alone or in combination with anti-CTLA-4 zalifrelimab for recurrent or metastatic CC
- Phase II SUMMIT basket trial: Neratinib for patients with metastatic CC with HER2 mutation
- Immune checkpoint inhibitors as switch or continuation maintenance therapy for solid tumors
- Incorporation of whole pelvic radiation into treatment of Stage IVB CC
- Sequential chemotherapy for early-stage, post-radical hysterectomy CC: Are the STARS aligned?

MODULE 4: Key Recent Data Sets

RTP RESEARCH TO PRACTICE

Anti-PD-1/PD-L1 Checkpoint Inhibitors in Endometrial Cancer

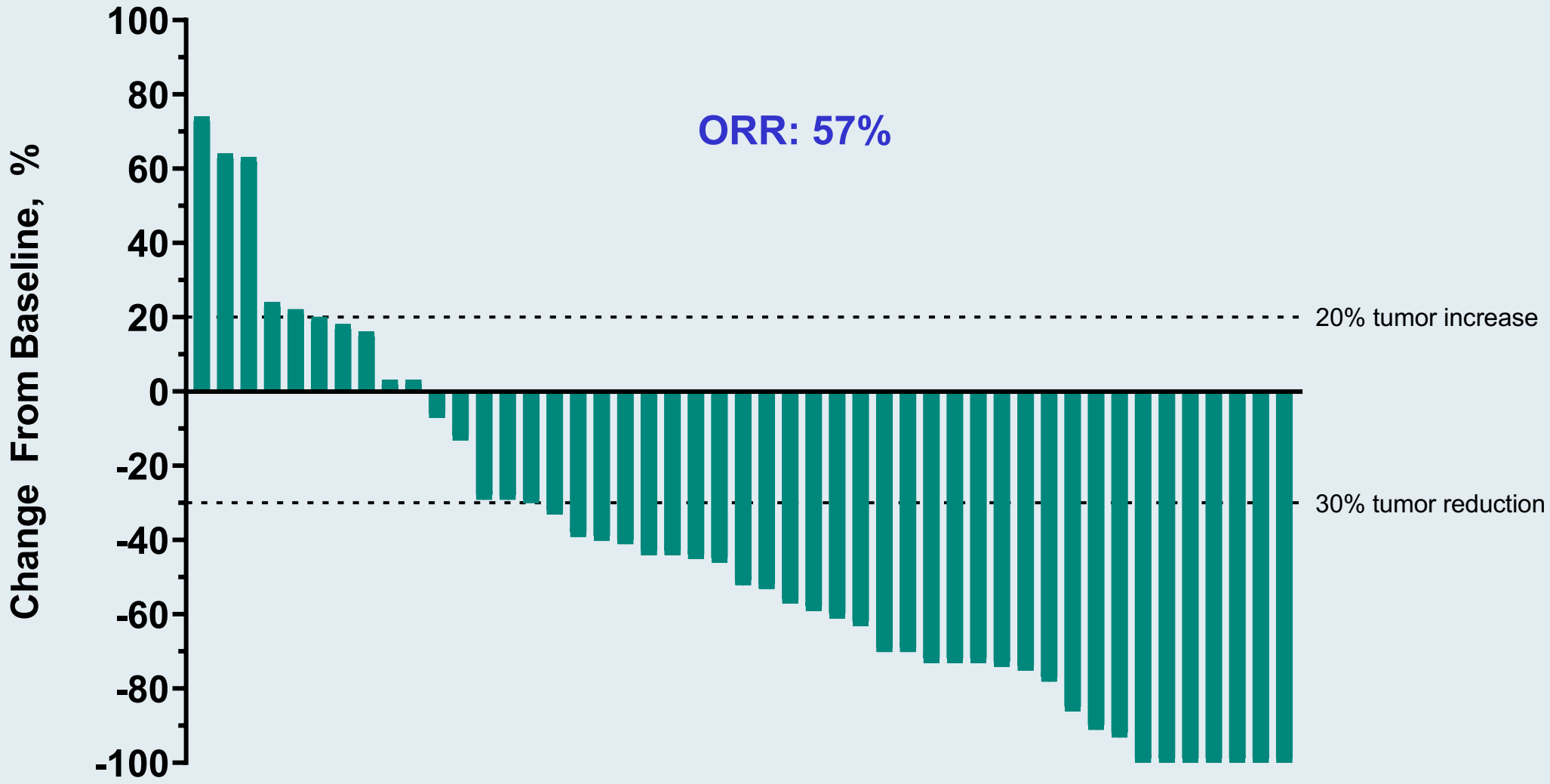
RTP
RESEARCH
TO PRACTICE

Pembrolizumab in Patients with MSI-H Advanced Endometrial Cancer from the KEYNOTE-158 Study

O’Malley D et al.

ESMO 2019;Abstract 1044P.

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



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

RTP RESEARCH TO PRACTICE

Research

JAMA Oncol 2020;6(11):1766-72

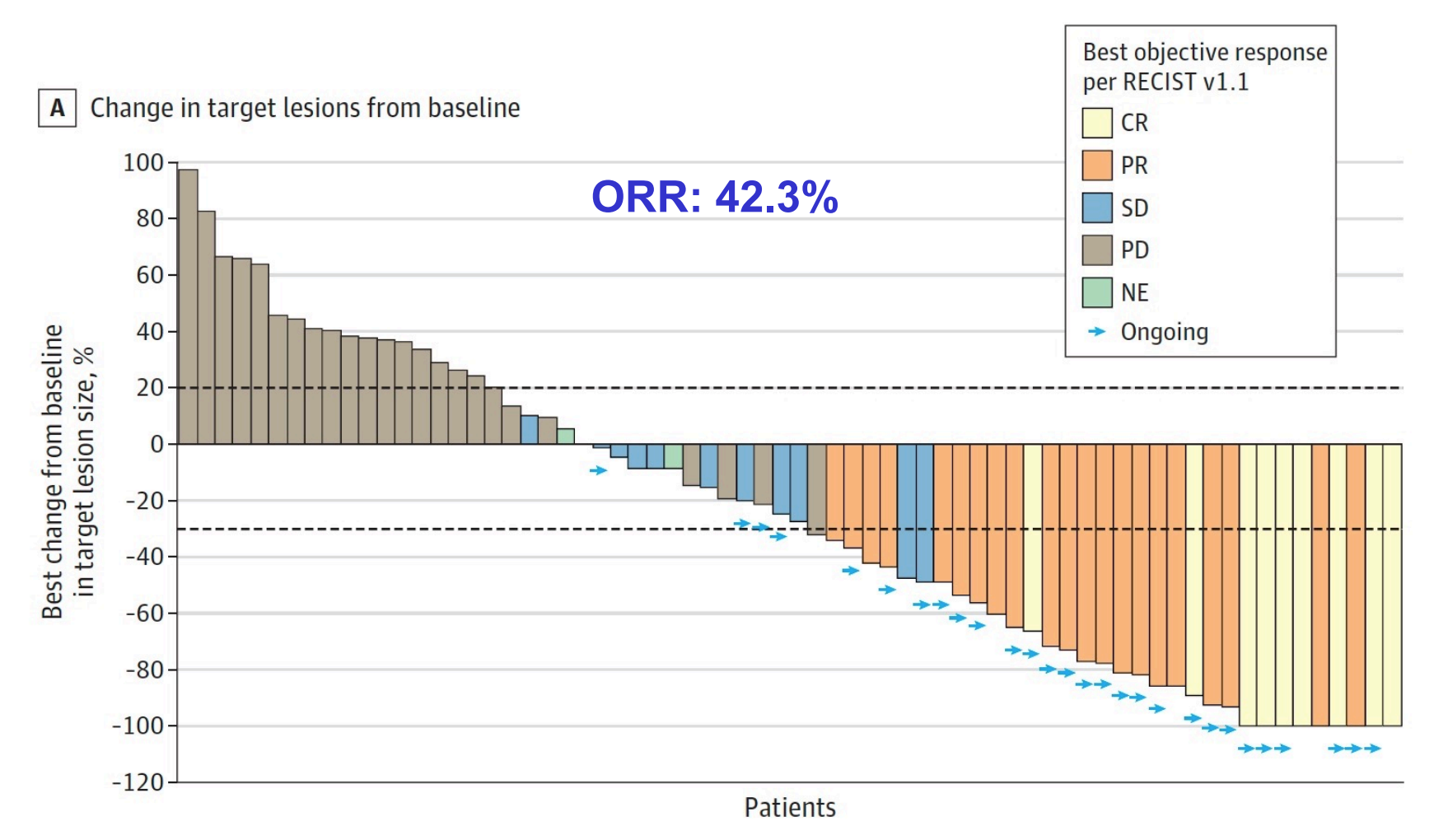
JAMA Oncology | Original Investigation

Clinical Activity and Safety of the Anti–Programmed Death 1 Monoclonal Antibody Dostarlimab for Patients With Recurrent or Advanced Mismatch Repair–Deficient Endometrial Cancer

A Nonrandomized Phase 1 Clinical Trial

Ana Oaknin, MD, PhD; Anna V. Tinker, MD; Lucy Gilbert, MD; Vanessa Samouëlian, MD; Cara Mathews, MD; Jubilee Brown, MD; Maria-Pilar Barretina-Ginesta, MD; Victor Moreno, MD; Adriano Gravina, MD; Cyril Abdeddaim, MD; Susana Banerjee, MD; Wei Guo, PhD; Hadi Danaee, ScD; Ellie Im, MD; Renaud Sabatier, MD

GARNET: Dostarlimab for Recurrent or Advanced dMMR Endometrial Cancer — Best Percentage Change in Lesion Size



Oaknin A et al. *JAMA Oncol* 2020;6(11):1766-72.

RTP RESEARCH TO PRACTICE

Interim Analysis of the Immune-Related Endpoints of the Mismatch Repair Deficient (dMMR) and Proficient (MMRp) Endometrial Cancer Cohorts from the GARNET Study

Pothuri B et al.

SGO 2021;Abstract 10417.

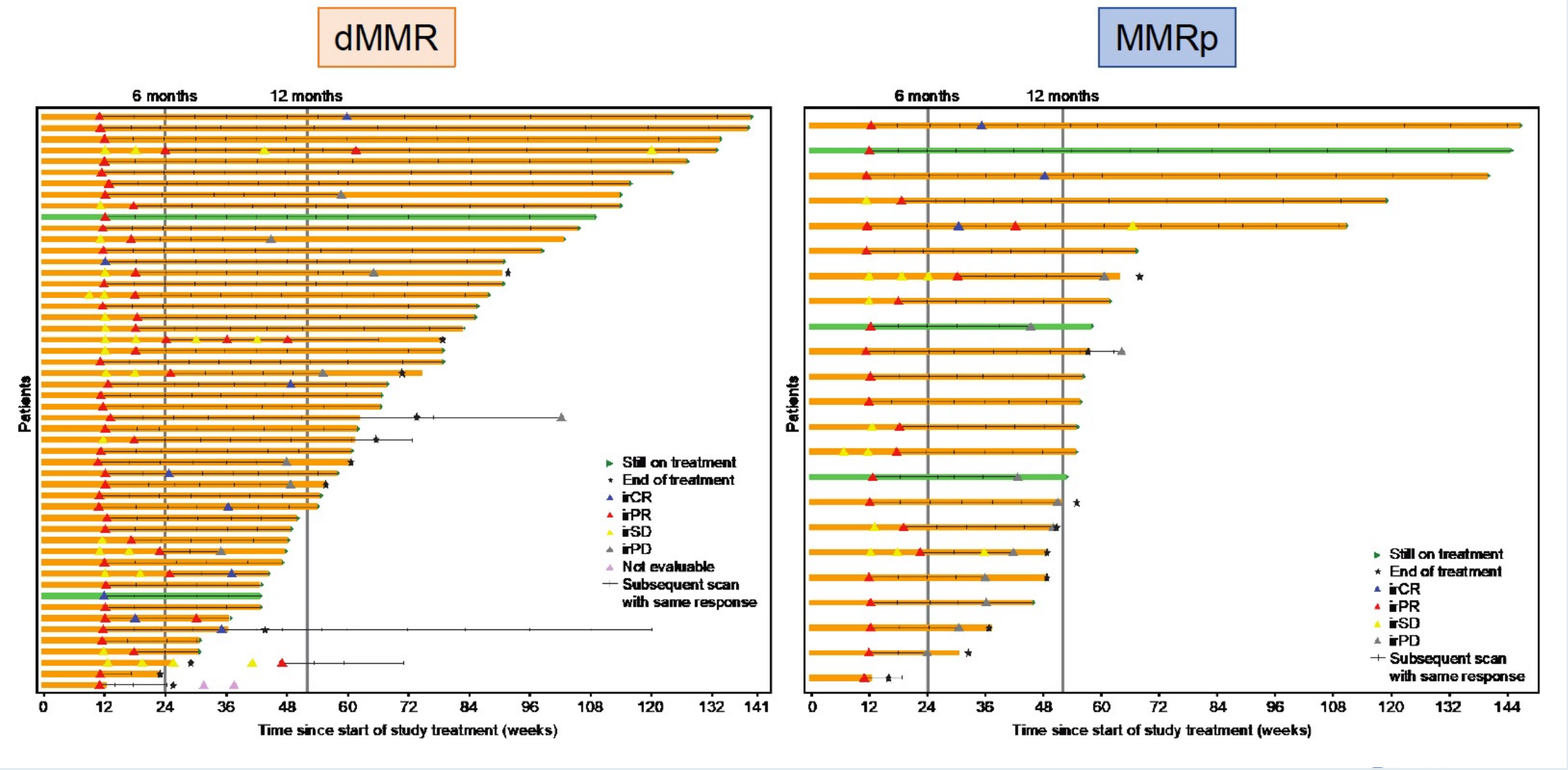
GARNET: Immune-Related Secondary Endpoints

(irRECIST by investigator assessment)		
Variable	dMMR N=110	MMRp N=144
Follow-up, median (range), months	16.5 (0.03–30.6)	13.7 (0.03–33.1)
irORR, n (%)	50 (45.5)	20 (13.9)
irCR	7 (6.4)	3 (2.1)
irPR	43 (39.1)	17 (11.8)
irSD	20 (18.2)	41 (28.5)
irPD	36 (32.7)	63 (43.8)
NE	4 (3.6)	20 (13.9)
irDCR,[a] n (%)	70 (63.6)	61 (42.4)
irDOR,[b] months	NR	12.2

[a]Includes CR, PR, and SD ≥12 weeks; [b]Only includes responders.

Pothuri B et al. SGO 2021;Abstract 10417.

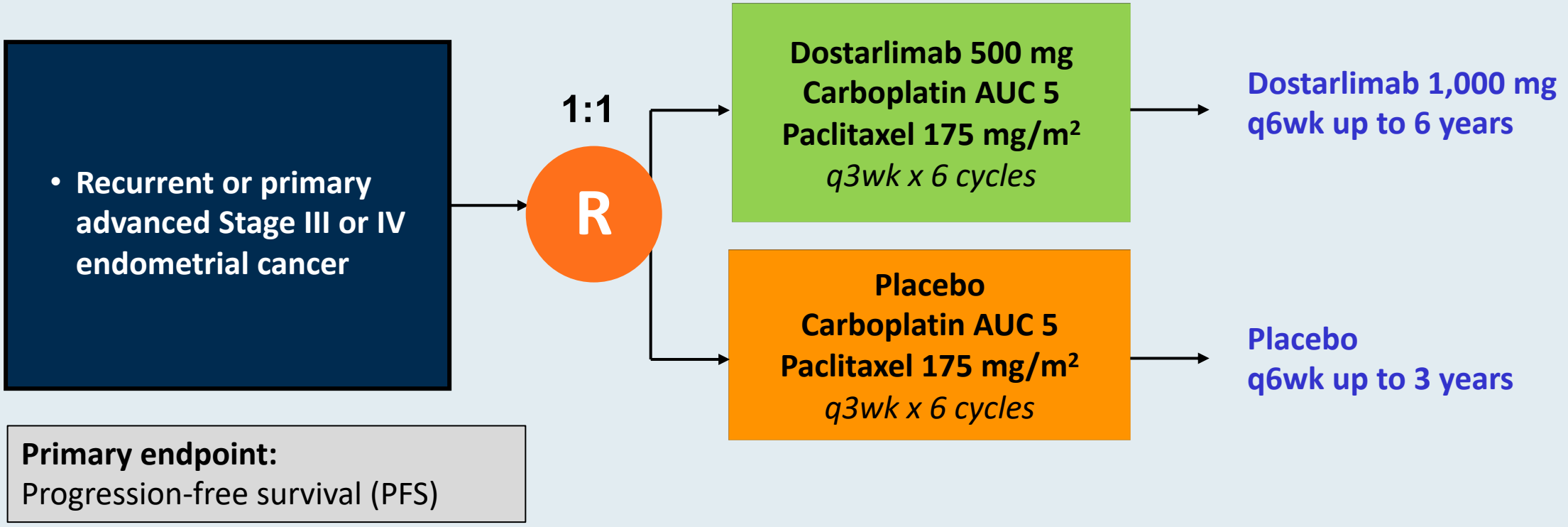
GARNET: Duration of Response



Pothuri B et al. SGO 2021;Abstract 10417.

RTP RESEARCH TO PRACTICE

ENGOT-EN6/NSGO-RUBY Phase III Schema



Mirza MR et al. ASCO 2020;Abstract TPS6107.

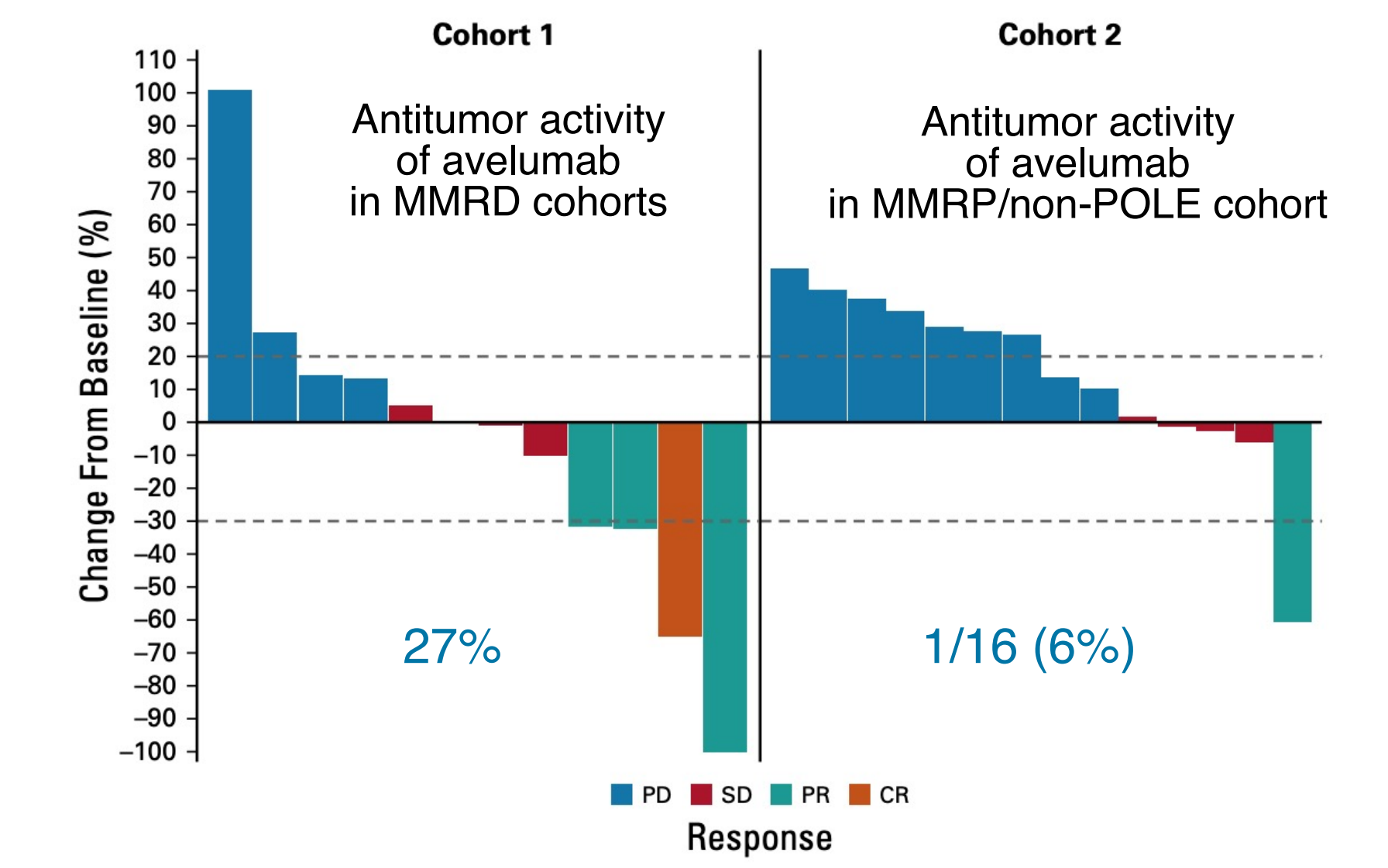
original report

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

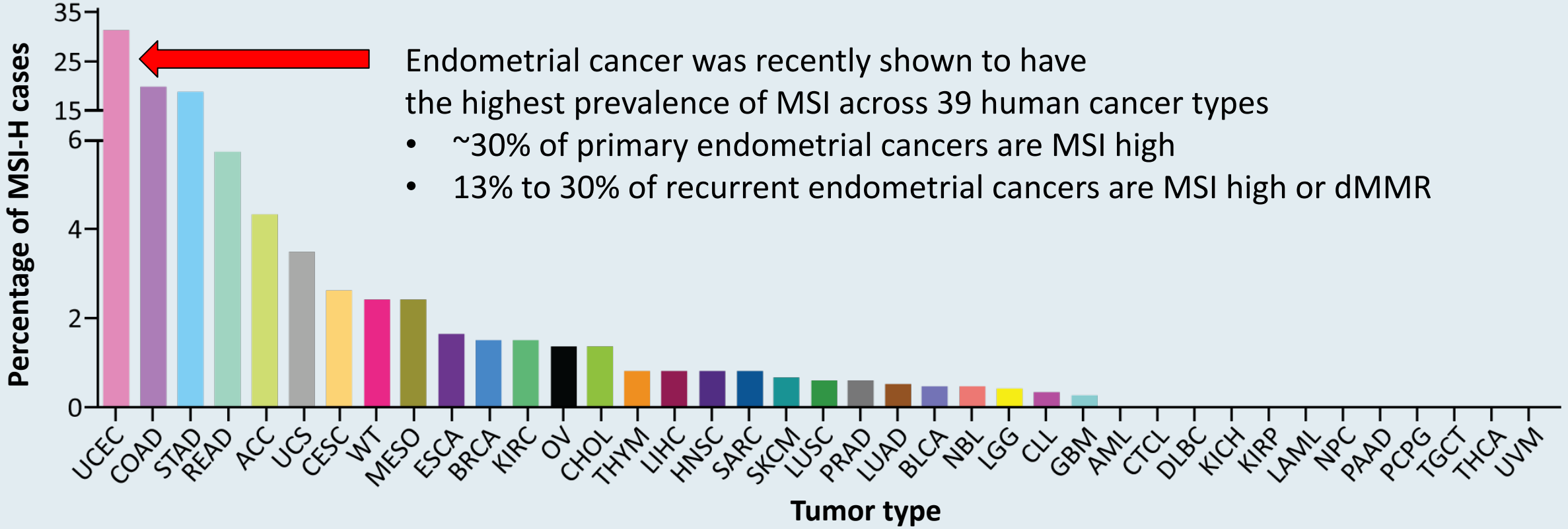
Objective Response Rate: Avelumab



Konstantinopoulos PA, et al. *J Clin Oncol* 2019;37(30):2786-94.

High MSI 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 high
- 13% to 30% of recurrent endometrial cancers are MSI high 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

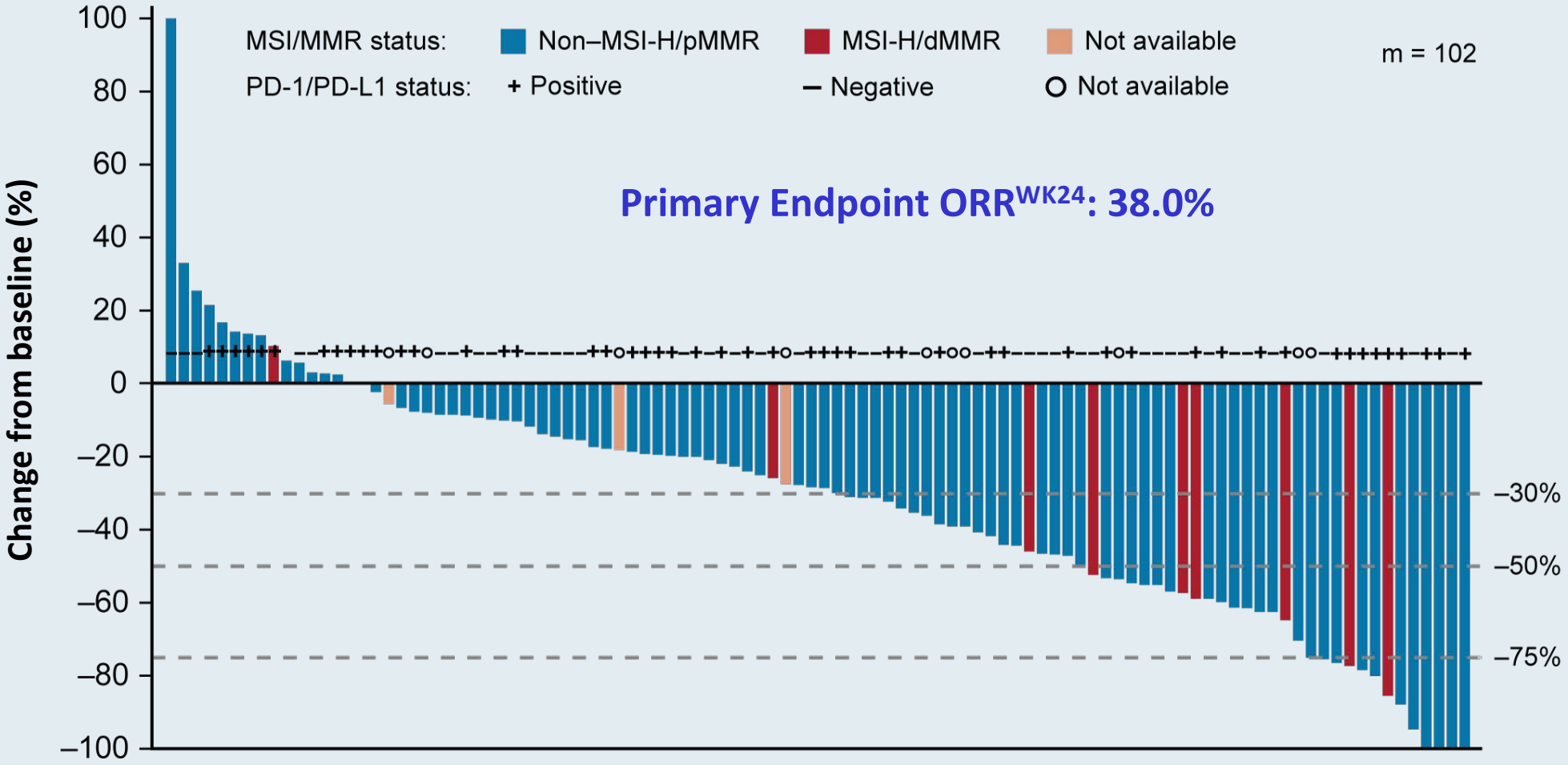
original reports

Lenvatinib Plus Pembrolizumab in Patients With Advanced Endometrial Cancer

Vicky Makker, MD[1]; Matthew H. Taylor, MD[2]; Carol Aghajanian, MD[1]; Ana Oaknin, MD, PhD[3]; James Mier, MD[4]; Allen L. Cohn, MD[5]; Margarita Romeo, MD, PhD[6]; Raquel Bratos, MD[7]; Marcia S. Brose, MD, PhD[8]; Christopher DiSimone, MD[9]; Mark Messing, MD[10]; Daniel E. Stepan, MD[11]; Corina E. Dutcus, MD[12]; Jane Wu, PhD[12]; Emmett V. Schmidt, MD, PhD[13]; Robert Orlowski, MD[13]; Pallavi Sachdev, PhD[12]; Robert Shumaker, PhD[11]; and Antonio Casado Herraez, MD, PhD[14]

J Clin Oncol 2020;38(26):2981-92

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



Makker V et al. *J Clin Oncol* 2020;38(26):2981-92.

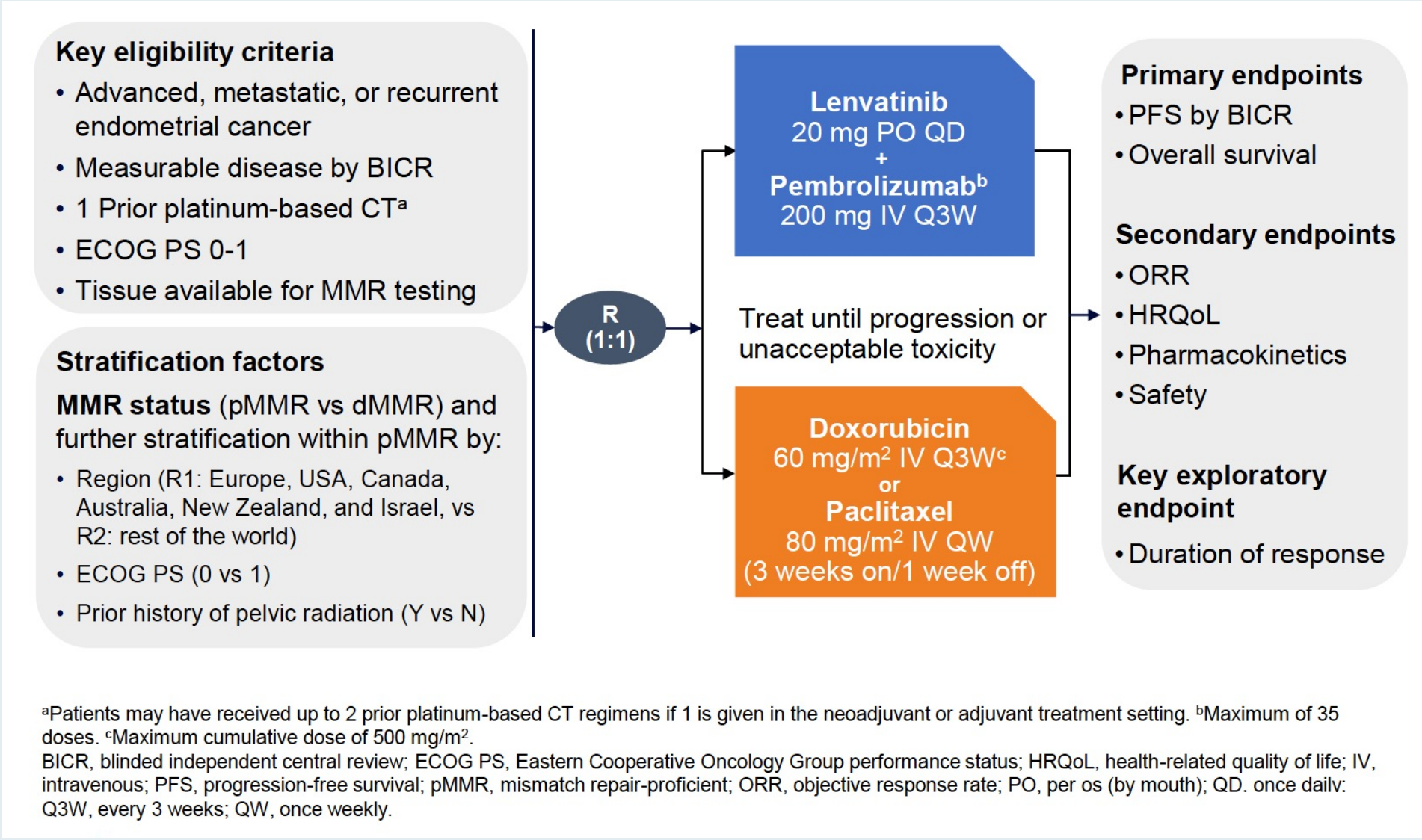
RTP RESEARCH TO PRACTICE

A Multicenter, Open-Label, Randomized, Phase III Study to Compare the Efficacy and Safety of Lenvatinib in Combination with Pembrolizumab versus Treatment of Physician's Choice in Patients with Advanced Endometrial Cancer: Study 309/KEYNOTE-775

Makker V et al.

SGO 2021;Abstract 11512.

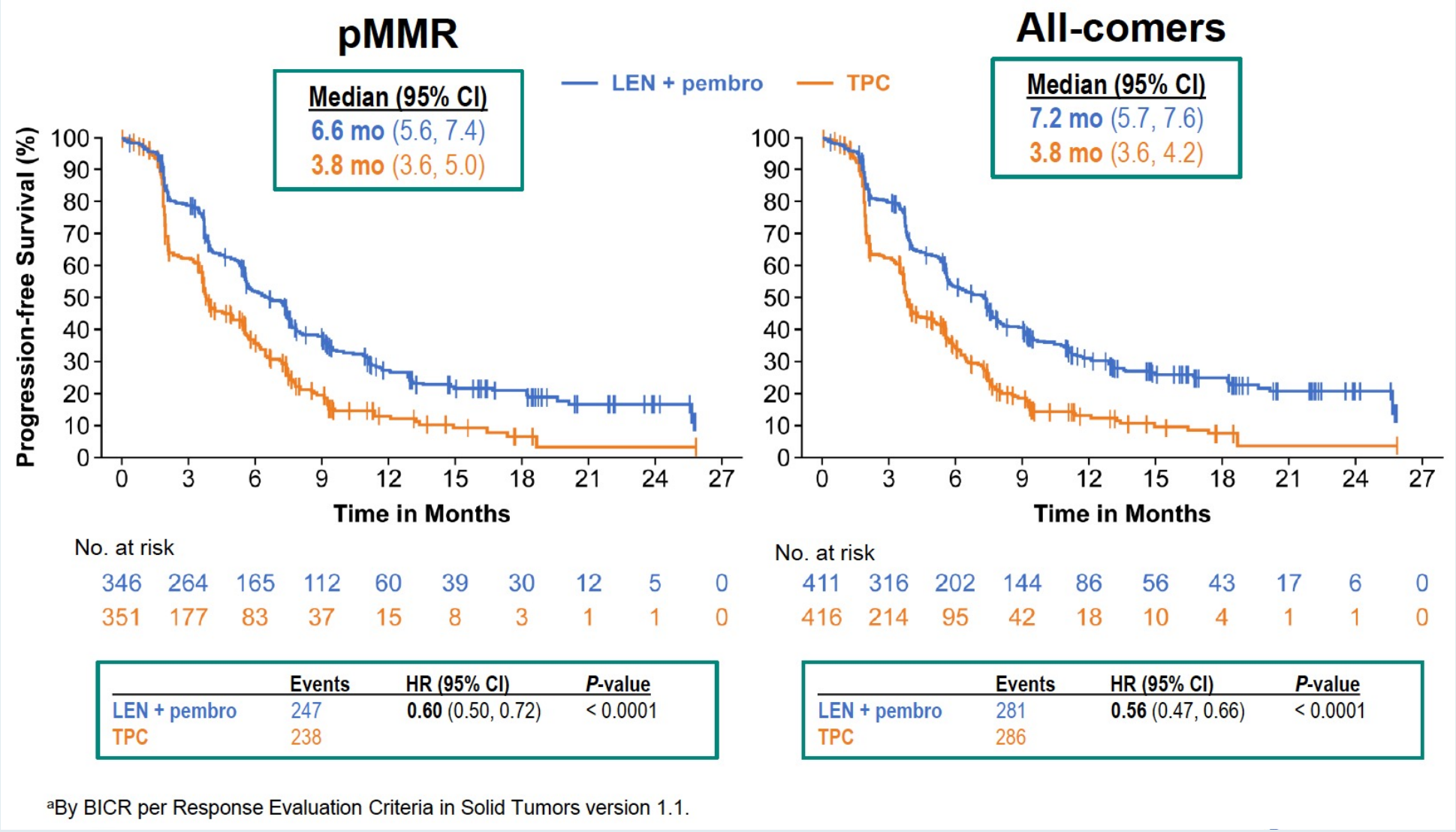
Study 309/KEYNOTE-775: Phase III Trial Schema



[a]Patients may have received up to 2 prior platinum-based CT regimens if 1 is given in the neoadjuvant or adjuvant treatment setting. [b]Maximum of 35 doses. [c]Maximum cumulative dose of 500 mg/m².
BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IV, intravenous; PFS, progression-free survival; pMMR, mismatch repair-proficient; ORR, objective response rate; PO, per os (by mouth); QD. once dailv: Q3W, every 3 weeks; QW, once weekly.

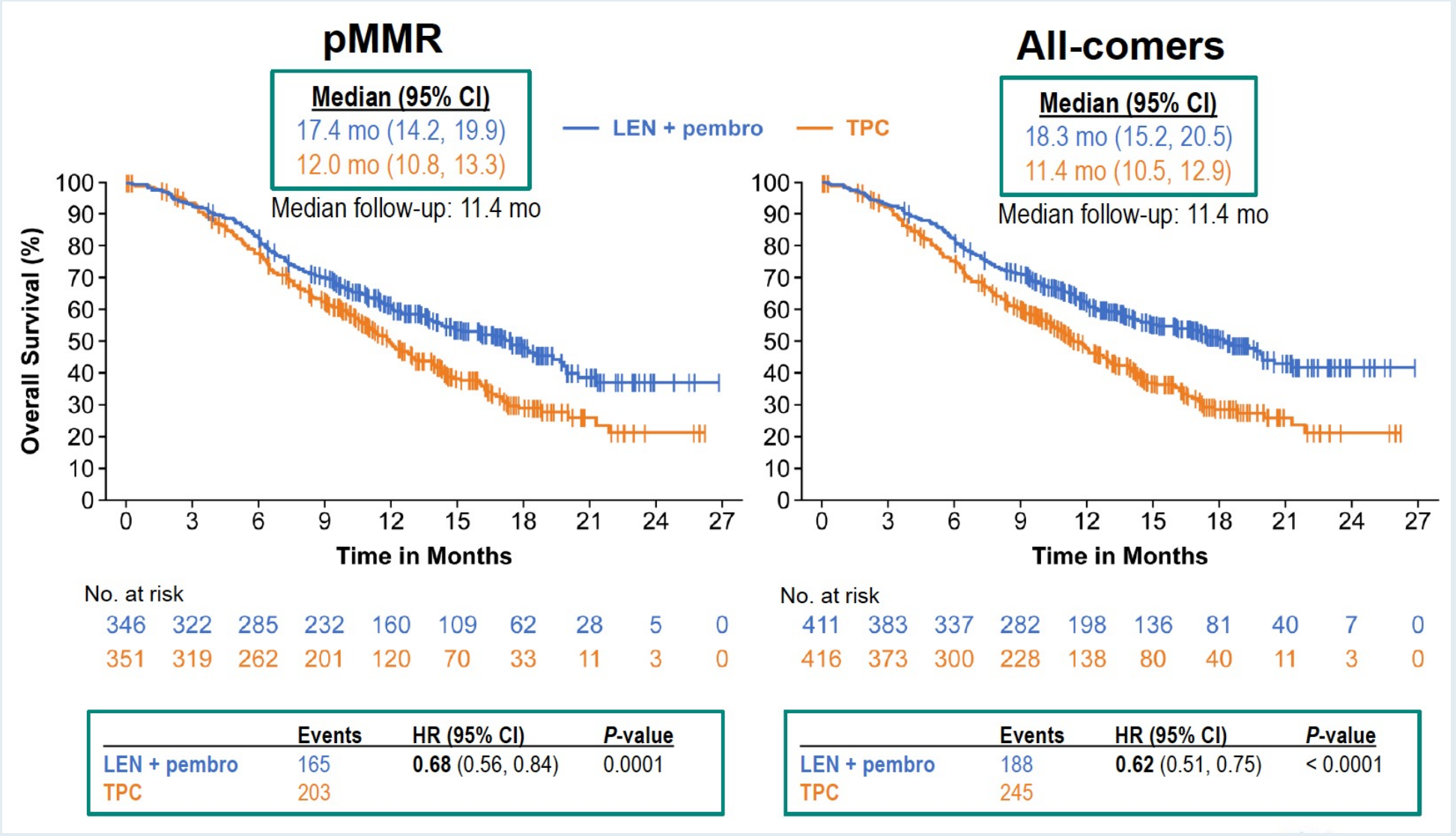
Makker V et al. SGO 2021;Abstract 11512.

Study 309/KEYNOTE-775: Progression-Free Survival



Makker V et al. SGO 2021;Abstract 11512.

Study 309/KEYNOTE-775: Overall Survival



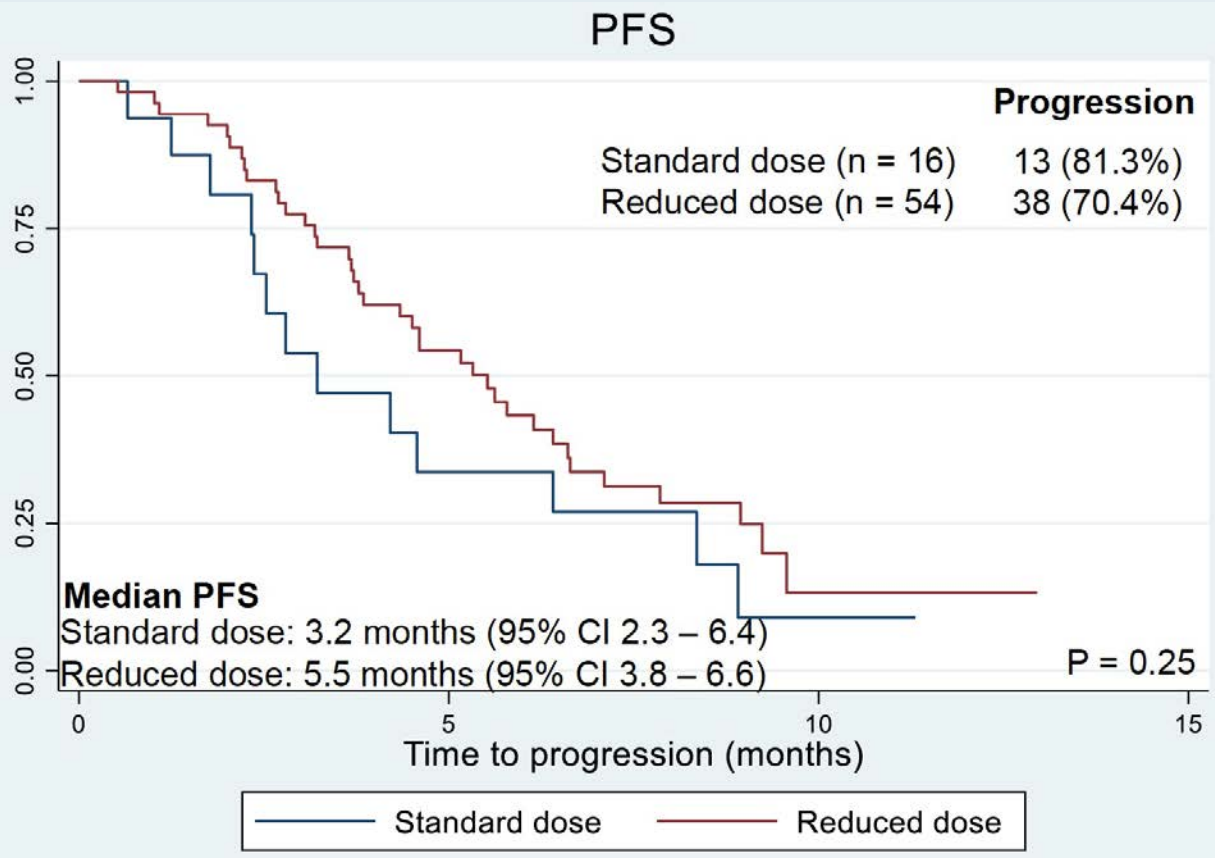
Makker V et al. SGO 2021;Abstract 11512.

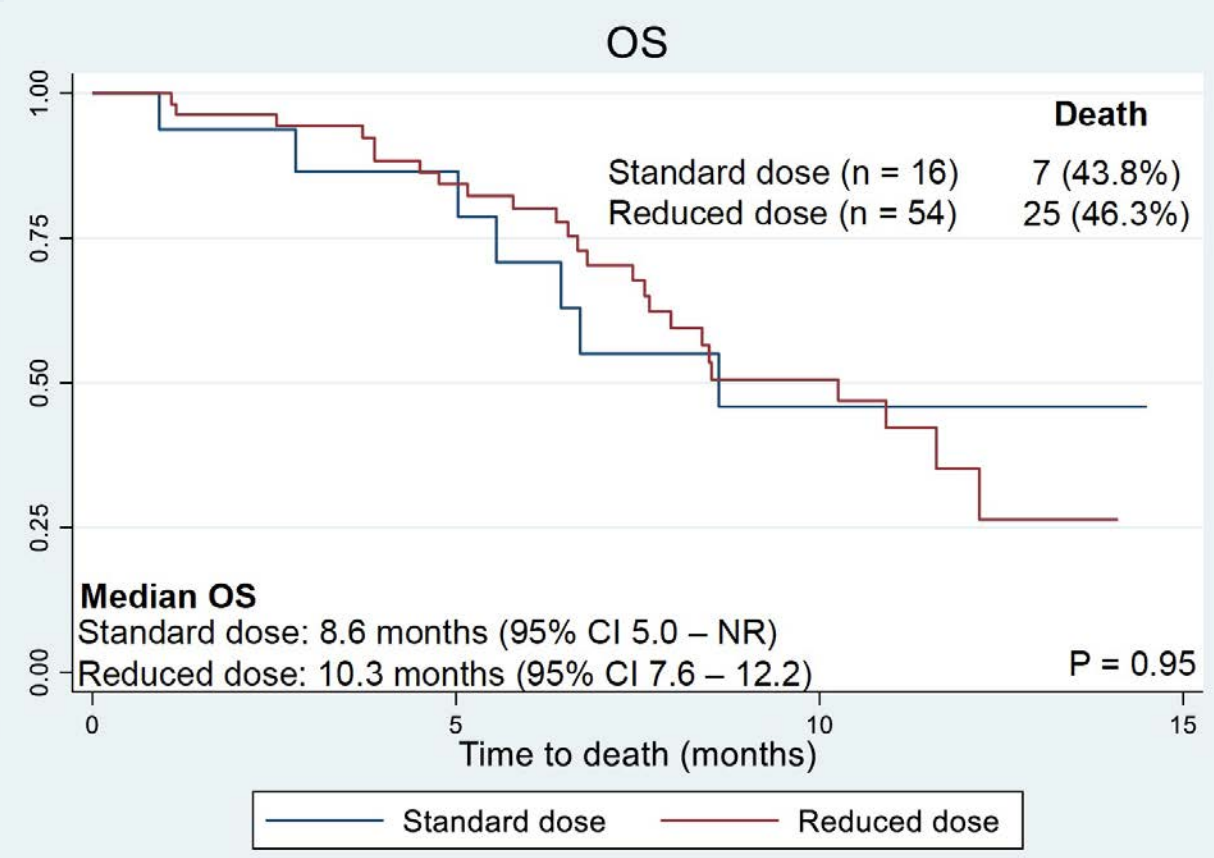
The Use of Pembrolizumab and Lenvatinib Combination Therapy in Endometrial Cancer: An Examination of Toxicity and Treatment Efficacy in Clinical Practice

How JA et al.

SGO 2021;Abstract 10775.

Retrospective Analysis of Reduced-Dose Lenvatinib (<20 mg) with Pembrolizumab at MD Anderson Cancer Center





- Reduced starting dose of lenvatinib was associated with longer time to treatment toxicity and fewer dose de-escalations.
- "Published studies and these results may support using lenvatinib at a starting dose of 14 mg daily in clinical practice."

How JA et al. SGO 2021;Abstract 10775.

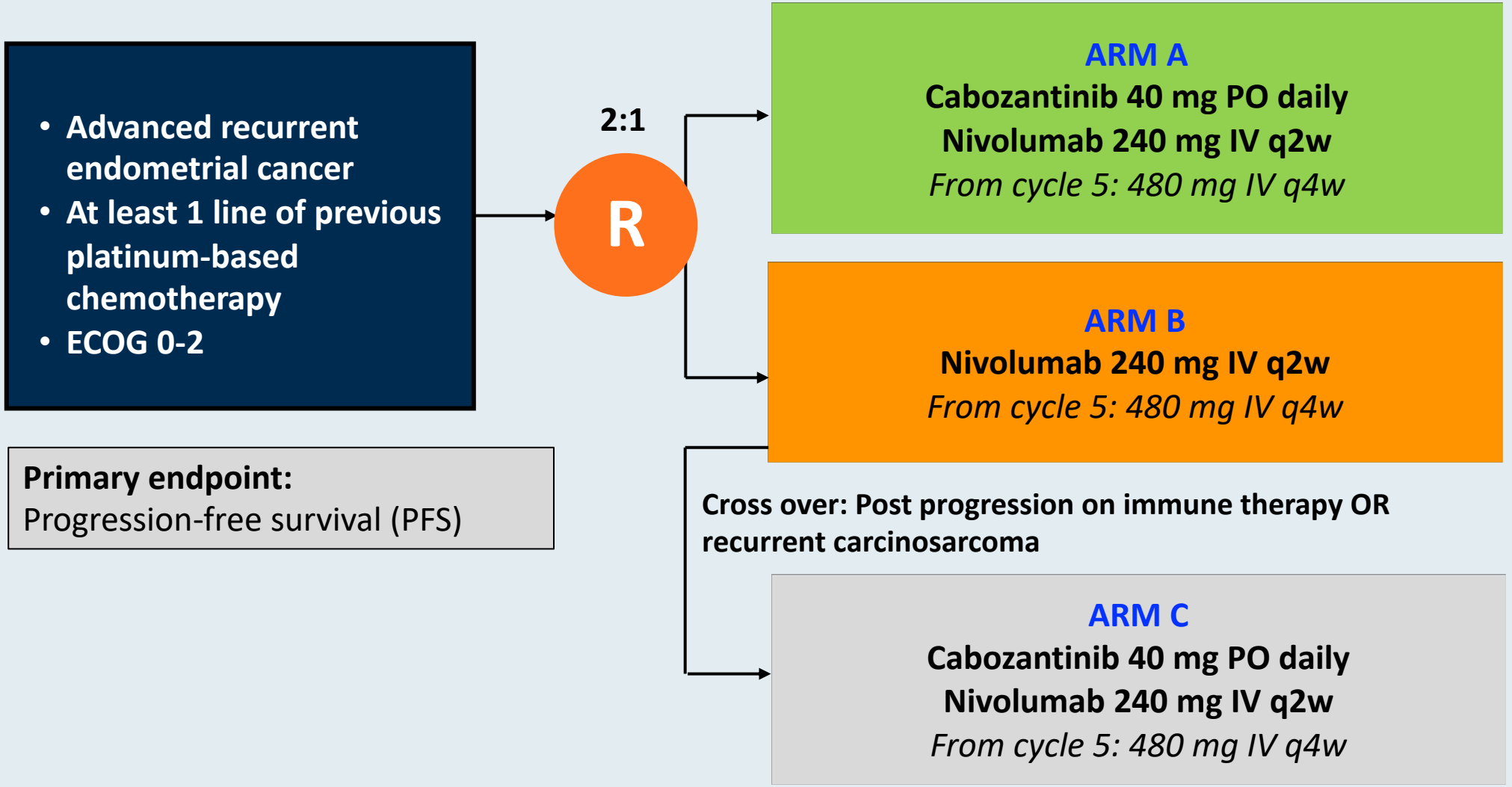
RTP RESEARCH TO PRACTICE

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

Lheureux S et al.

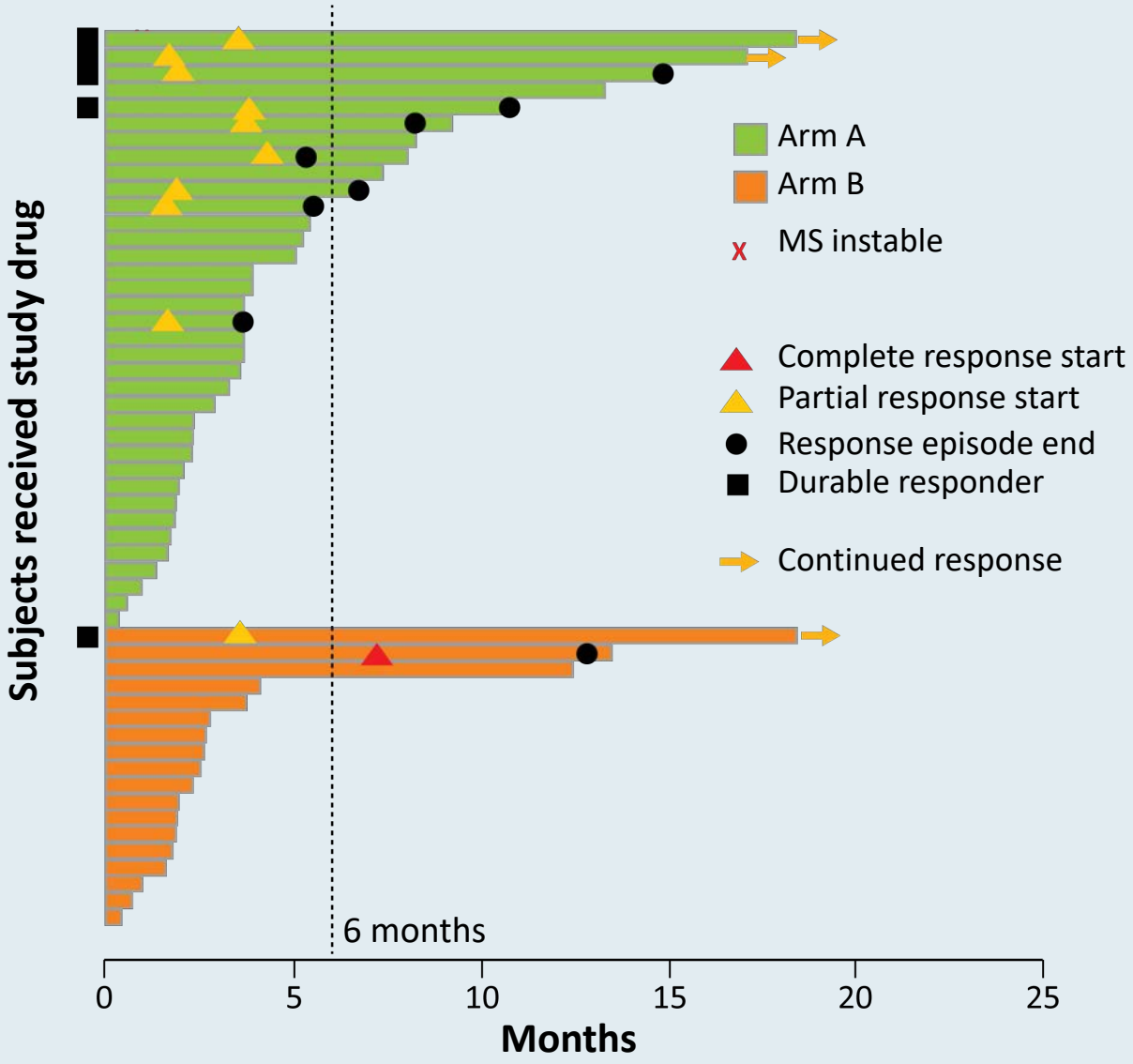
ASCO 2020;Abstract 6010.

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.

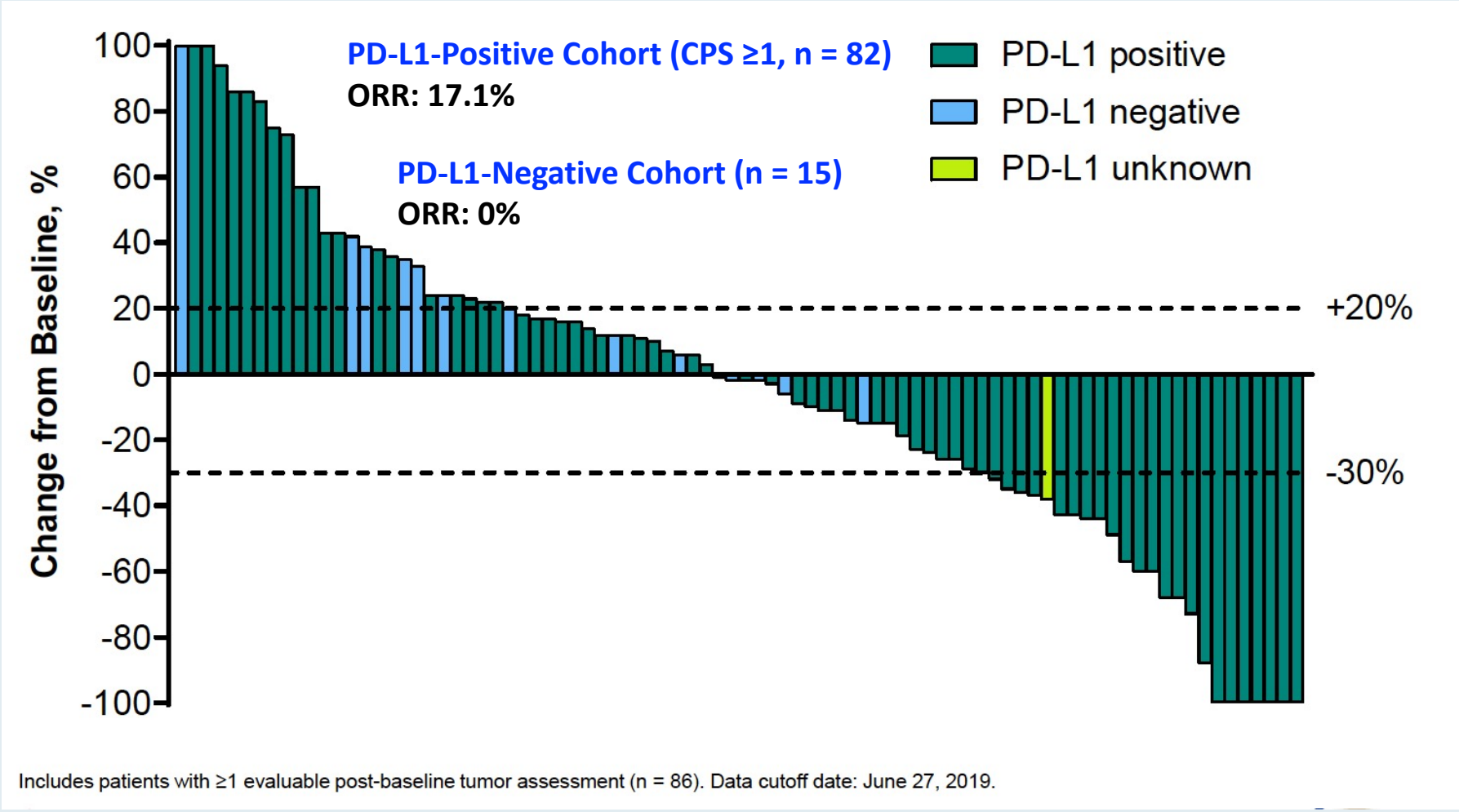
Anti-PD-1/PD-L1 Antibodies in Cervical Cancer

Pembrolizumab Treatment of Advanced Cervical Cancer: Updated Results from the Phase II KEYNOTE-158 Study

Chung HC et al.

SGO 2021;Abstract 10440.

Phase II KEYNOTE-158: Updated Results with Pembrolizumab for Previously Treated Advanced Cervical Cancer



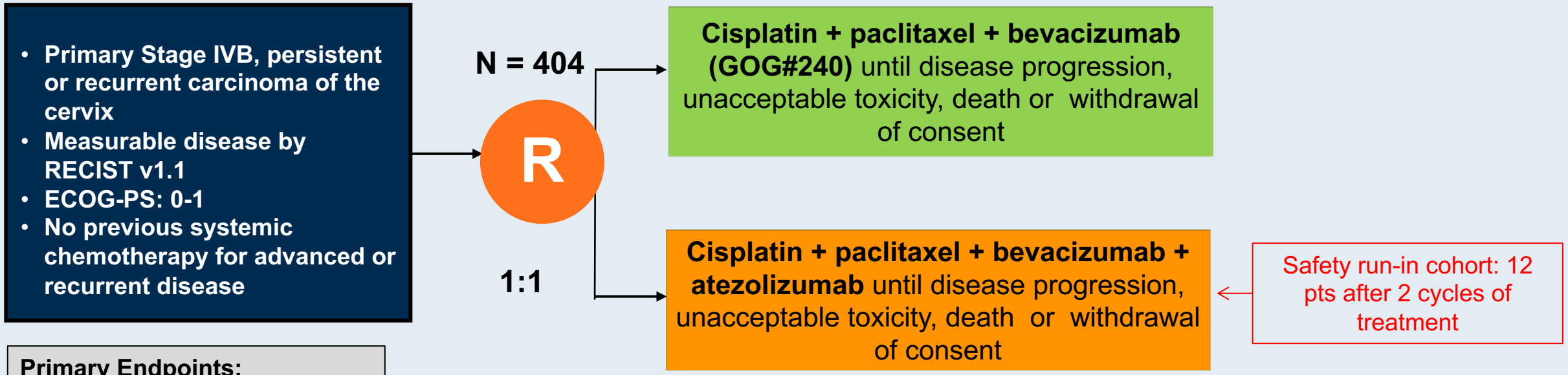
Includes patients with ≥1 evaluable post-baseline tumor assessment (n = 86). Data cutoff date: June 27, 2019.

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

Chung HC et al. SGO 2021;Abstract 10440.

RTP RESEARCH TO PRACTICE

BEATcc Phase III Randomized Front-Line Trial of Atezolizumab



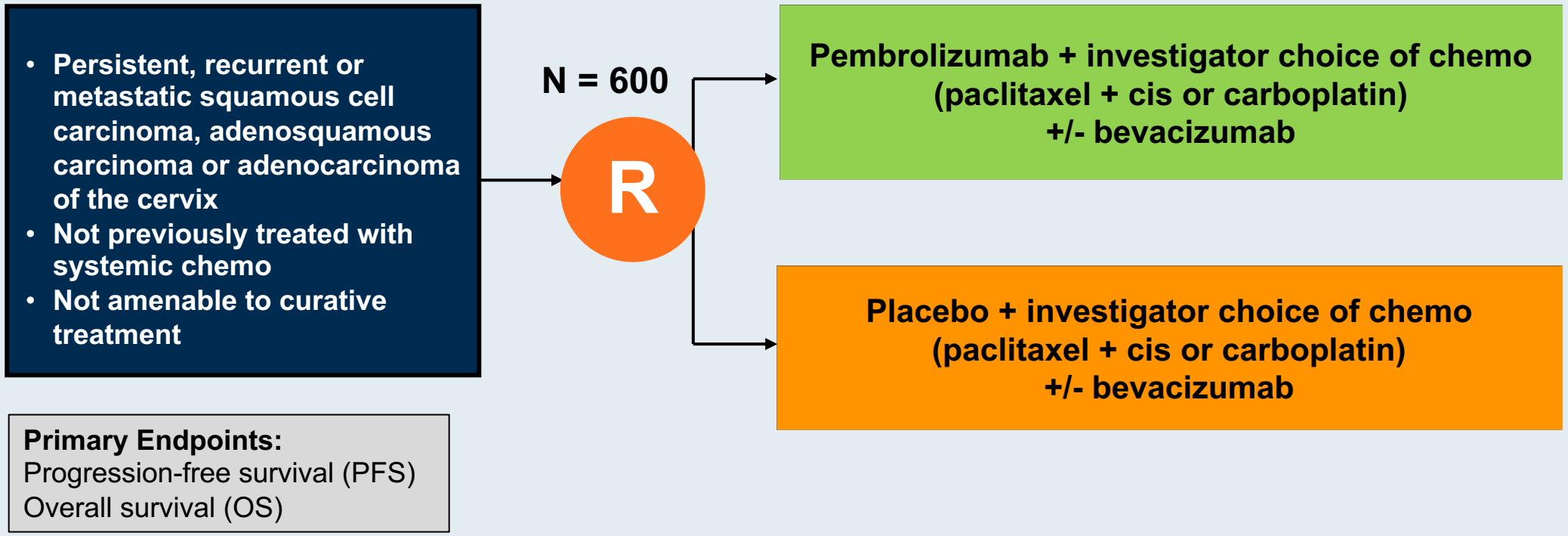
Primary Endpoints:
Overall survival (OS)
Secondary Endpoints:
- PFS
- ORR
- DOR
- Safety
- HR-QOL

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

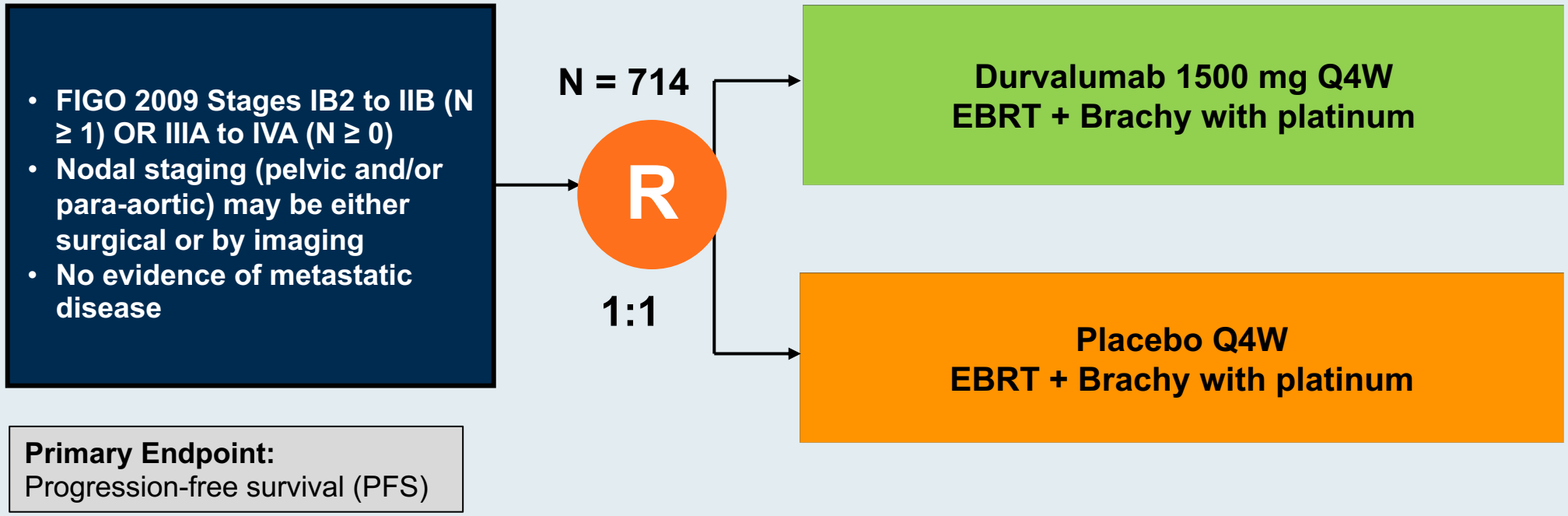
KEYNOTE-826 Phase III Schema



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.

Avelumab Alone or in Combination with Pegylated Liposomal Doxorubicin versus Pegylated Liposomal Doxorubicin Alone in Platinum-Resistant or Refractory Epithelial Ovarian Cancer: Primary and Biomarker Analysis of the Phase III JAVELIN Ovarian 200 Trial

Pujade-Lauraine E et al.

SGO 2019;Abstract LBA1.

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.

original reports

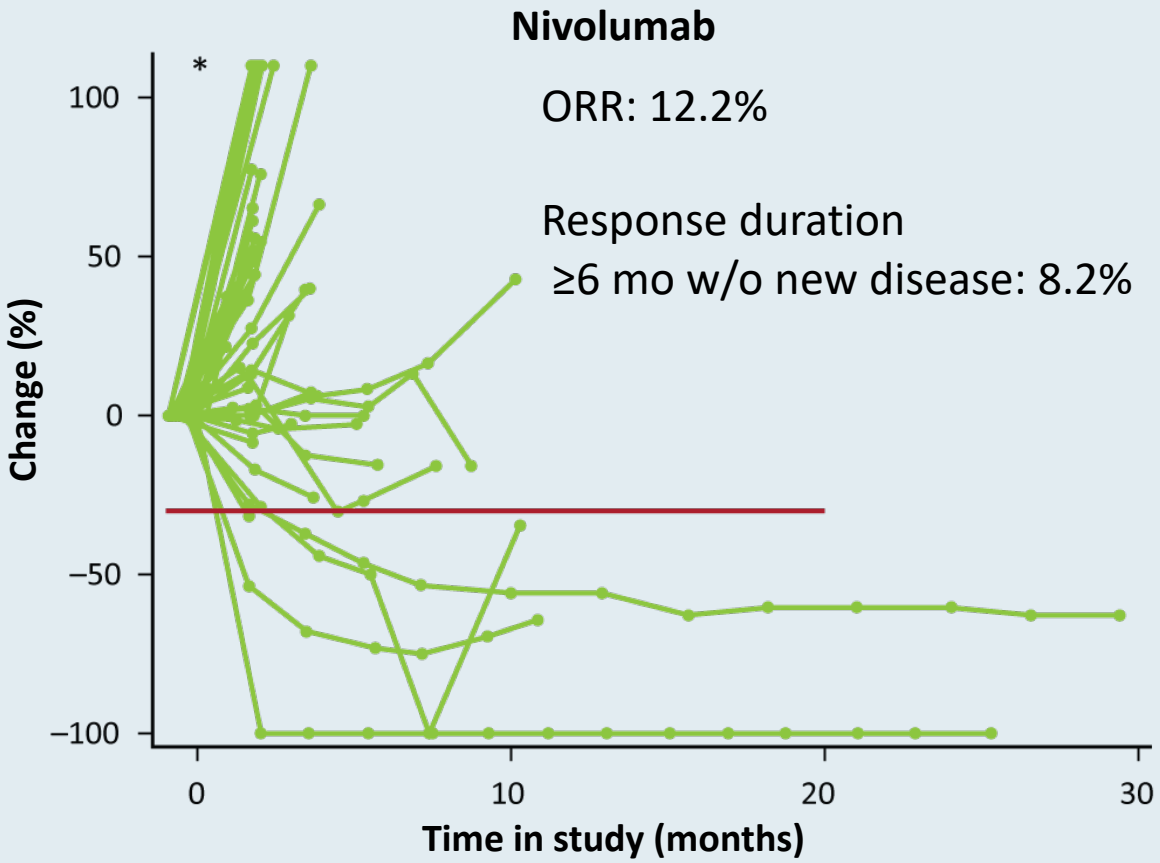
Randomized Phase II Trial of Nivolumab Versus Nivolumab and Ipilimumab for Recurrent or Persistent Ovarian Cancer: An NRG Oncology Study

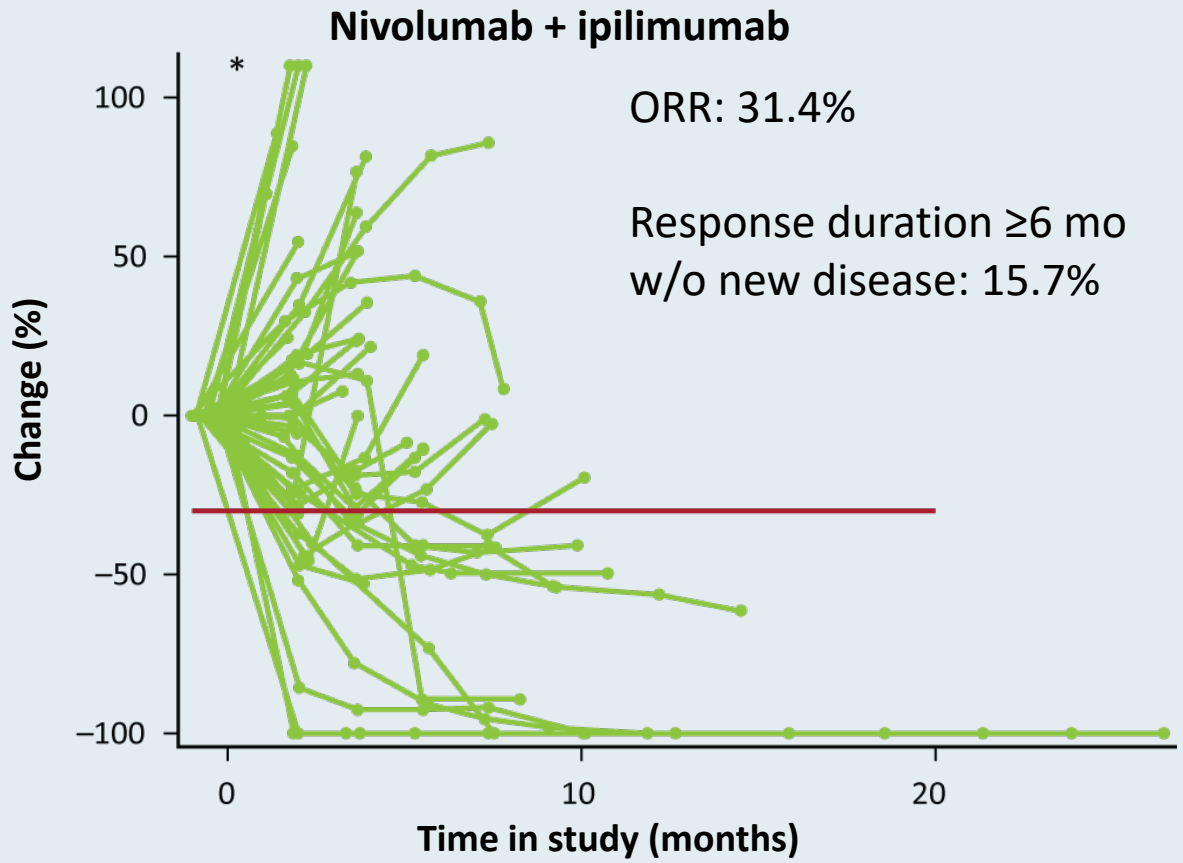
Dmitriy Zamarin, MD, PhD[1]; Robert A. Burger, MD[2]; Michael W. Sill, PhD[3]; Daniel J. Powell Jr, PhD[4]; Heather A. Lankes, PhD, MPH[5]; Michael D. Feldman, MD, PhD[4]; Oliver Zivanovic, MD, PhD[1]; Camille Gunderson, MD[6]; Emily Ko, MD, MSCR[2]; Cara Mathews, MD[7]; Sudarshan Sharma, MD[8]; Andrea R. Hagemann, MD[9]; Samir Khleif, MD[10]; and Carol Aghajanian, MD[1]

J Clin Oncol 2020;38:1814-23

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.

Research

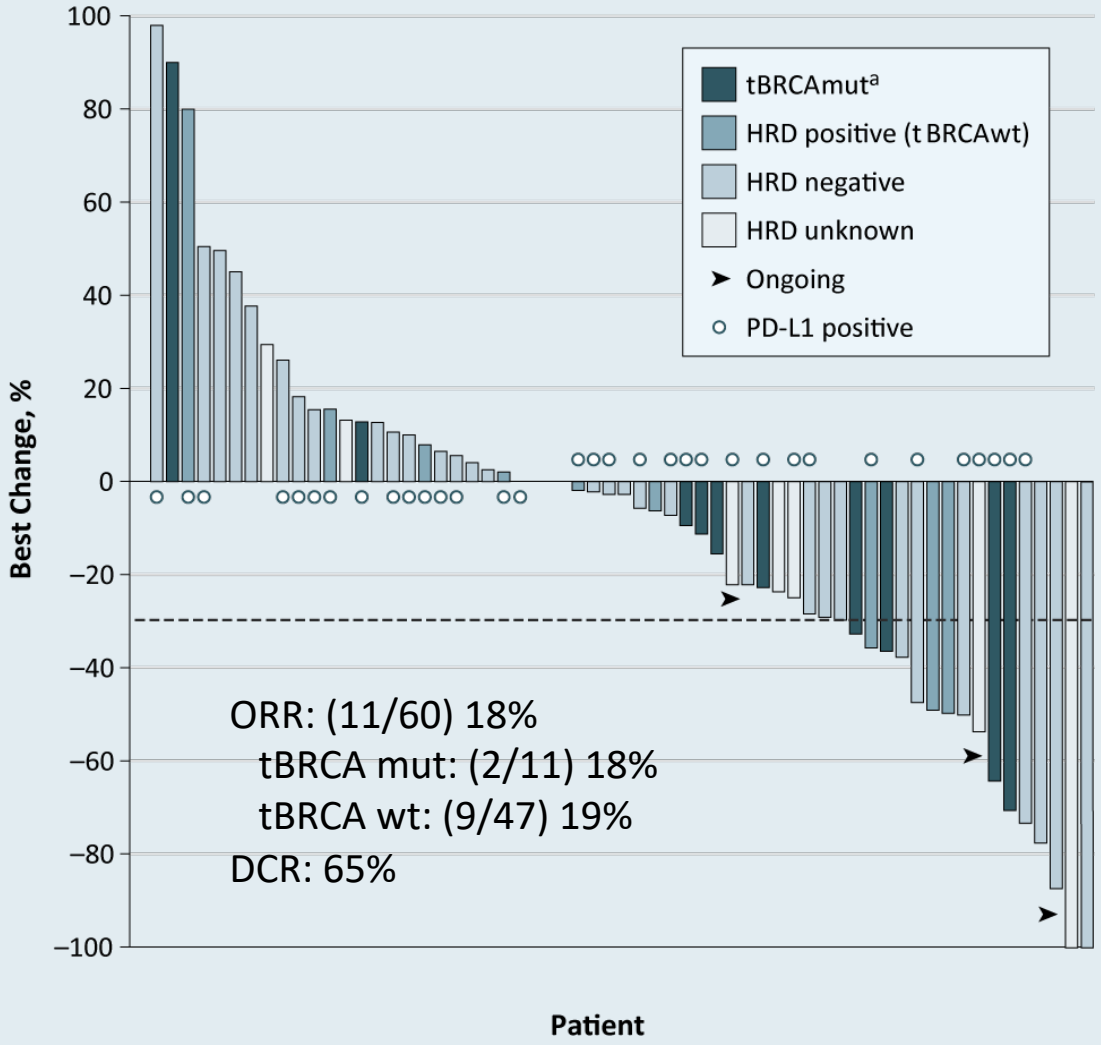
JAMA Oncol 2019;5(8):1141-9

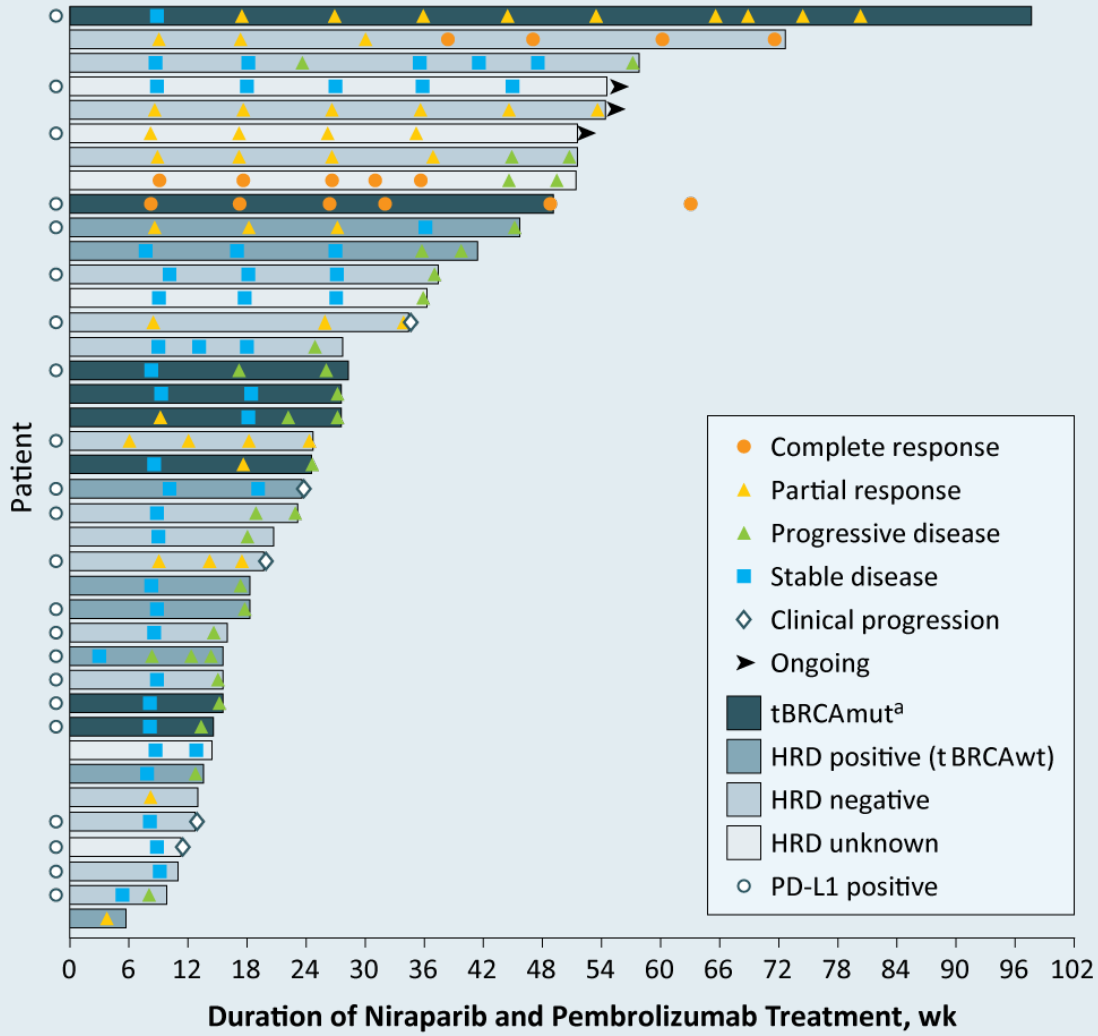
JAMA Oncology | Original Investigation

Single-Arm Phases 1 and 2 Trial of Niraparib in Combination With Pembrolizumab in Patients With Recurrent Platinum-Resistant Ovarian Carcinoma

Panagiotis A. Konstantinopoulos, MD, PhD; Steven Waggoner, MD; Gregory A. Vidal, MD; Monica Mita, MD; John W. Moroney, MD; Robert Holloway, MD; Linda Van Le, MD; Jasgit C. Sachdev, MD; Eloise Chapman-Davis, MD; Gerardo Colon-Otero, MD; Richard T. Penson, MD; Ursula A. Matulonis, MD; Young Bae Kim, MD; Kathleen N. Moore, MD; Elizabeth M. Swisher, MD; Anniina Färkkilä, MD; Alan D'Andrea, MD; Erica Stringer-Reasor, MD; Jing Wang, PhD; Nathan Buerstatte, MPH; Sujata Arora, MS; Julie R. Graham, PhD; Dmitri Bobilev, MD; Bruce J. Dezube, MD; Pamela Munster, MD

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

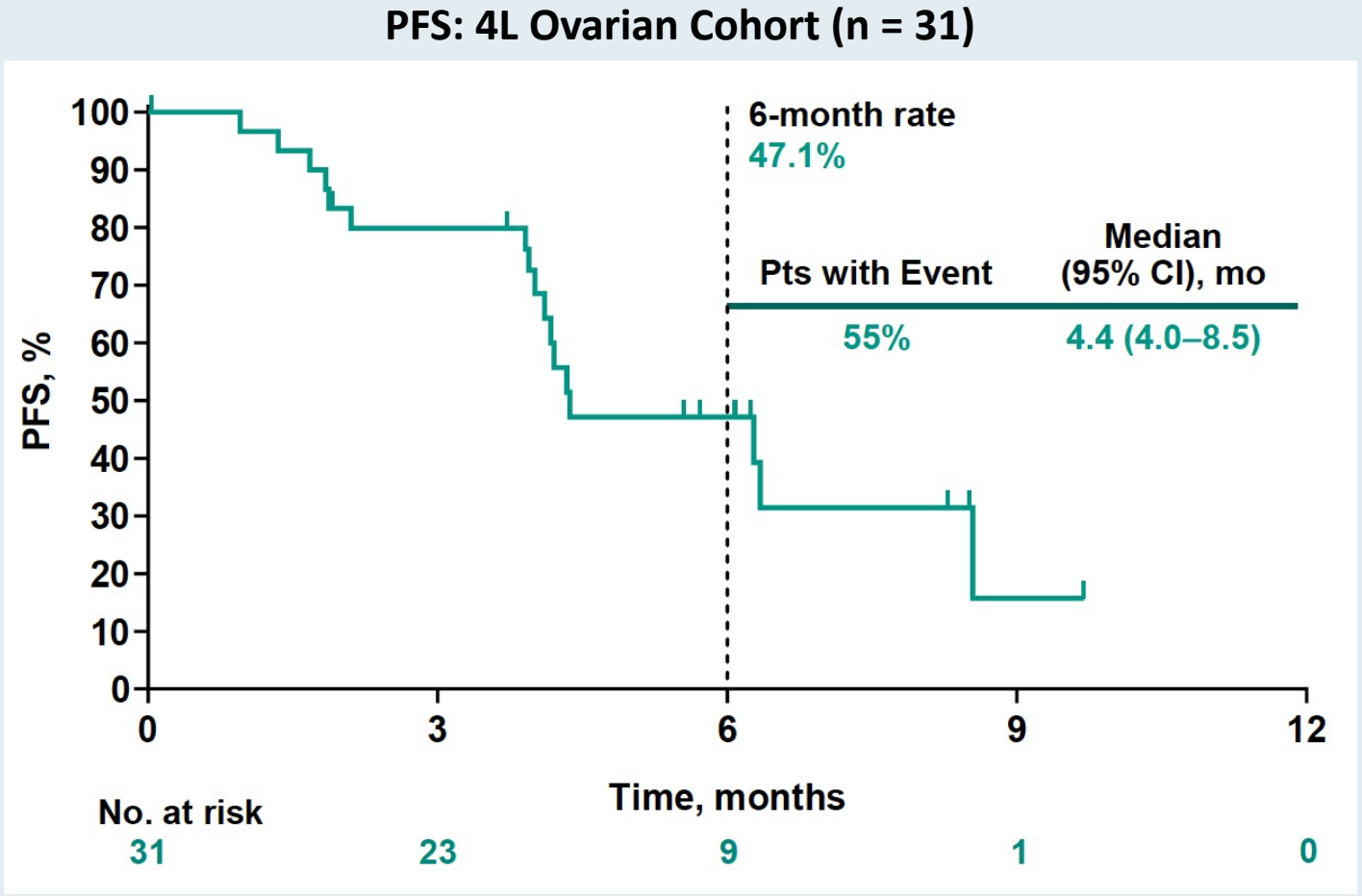
LEAP-005: Phase II Study of Lenvatinib (Len) plus Pembrolizumab (Pembro) in Patients (Pts) with Previously Treated Advanced Solid Tumours

Lwin Z et al.

ESMO 2020;Abstract LBA41.

LEAP-005: Antitumor Activity in Ovarian Cancer Cohort

	4L Ovarian Cohort (n = 31)
ORR	32.3%
CR	3%
PR	29%
DCR	74.2%
DoR (median, mo)	NR



Lwin Z et al. *ESMO* 2020;Abstract LBA41.

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.

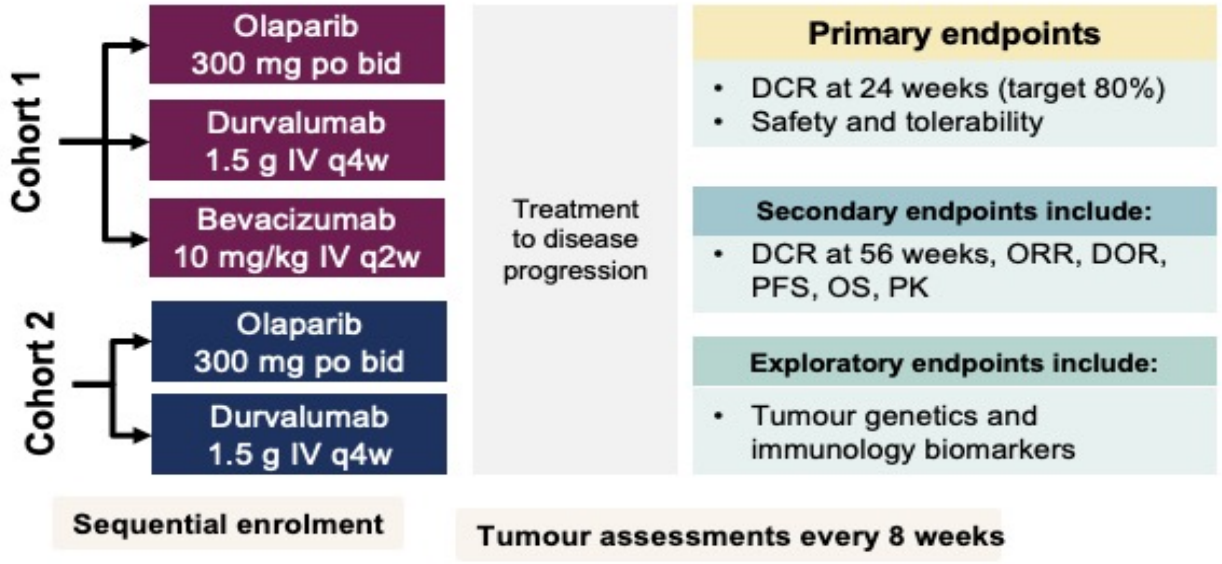
ESMO 2020;Abstract 814MO.

MEDIOLA: gBRCAwt Cohorts

Study Design

Patient population

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



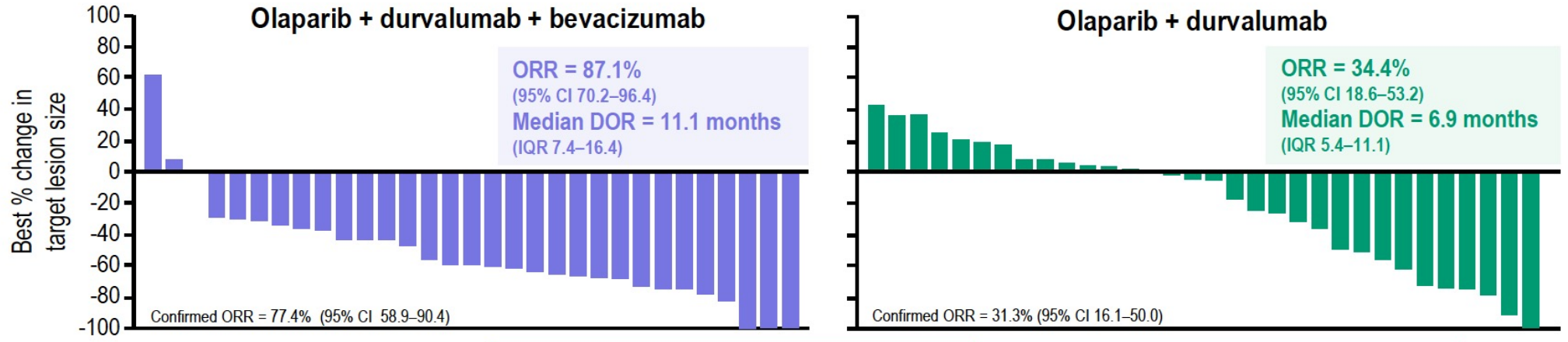
Patient Characteristics

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

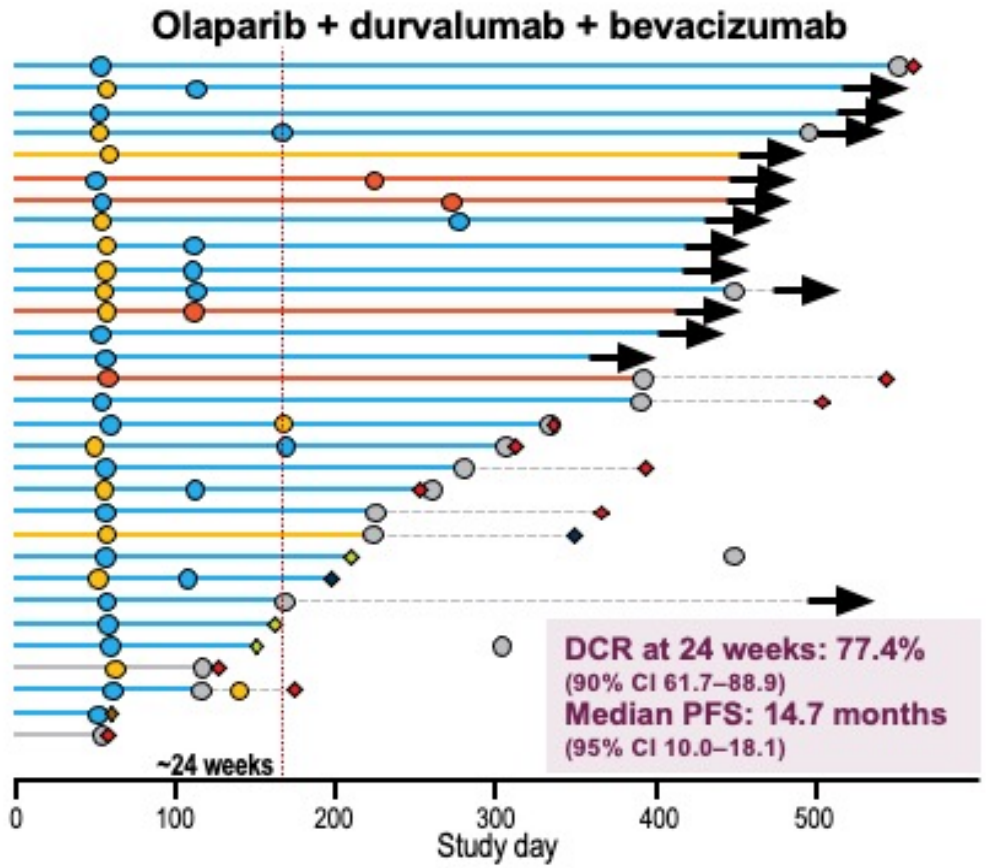
Exploratory analysis suggests ORR with triplet cohort is not dependent on genomic instability status (GIS)

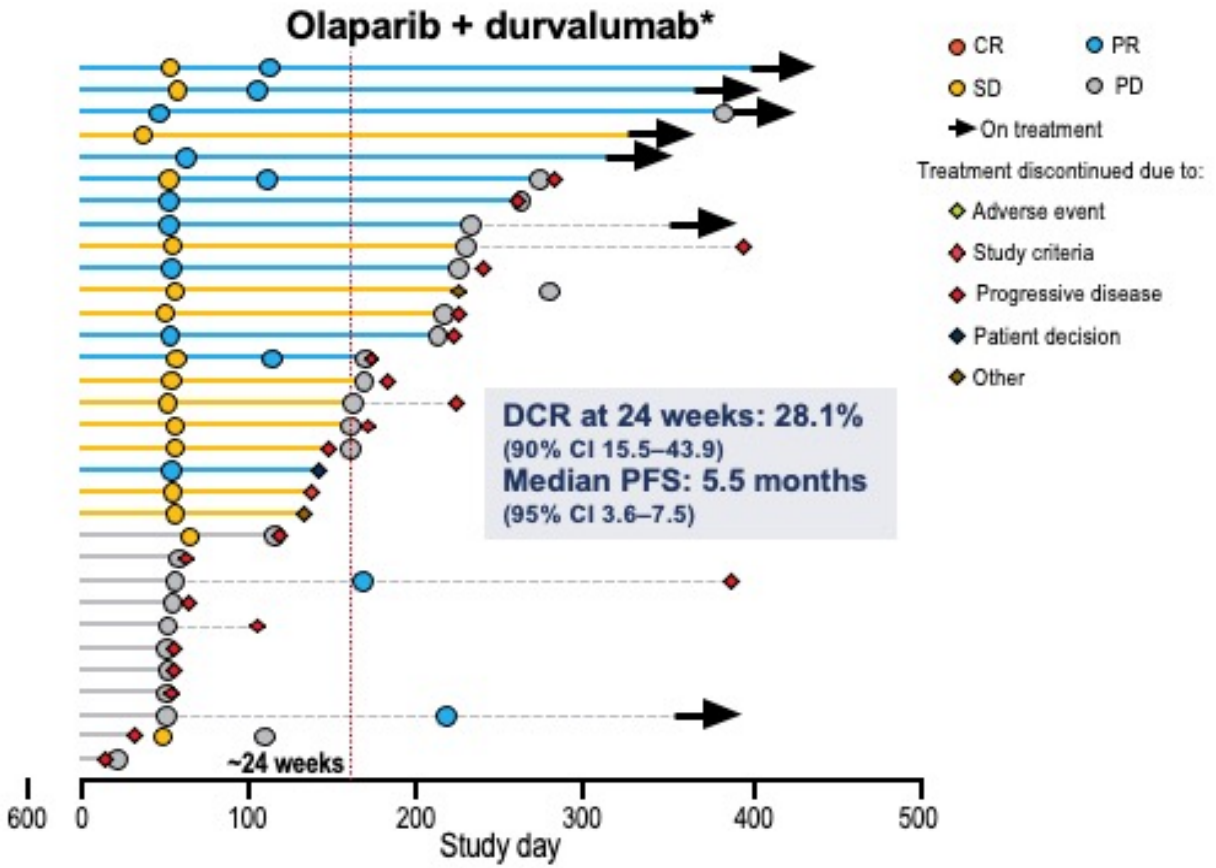


Genomic instability status* subgroup	Olaparib + durvalumab + bevacizumab		Olaparib + durvalumab	
	ORR (95% CI), %	n/N patients	ORR (95% CI), %	n/N patients
GIS-positive	100.0 (69.2–100.0)	10/10	50.0 (18.7–81.3)	5/10
GIS-negative	75.0 (34.9–96.8)	6/8	16.7 (0.4–64.1)	1/6
GIS-unknown	84.6 (54.6–98.1)	11/13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

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

MEDIOLA: TTP or Treatment Discontinuation



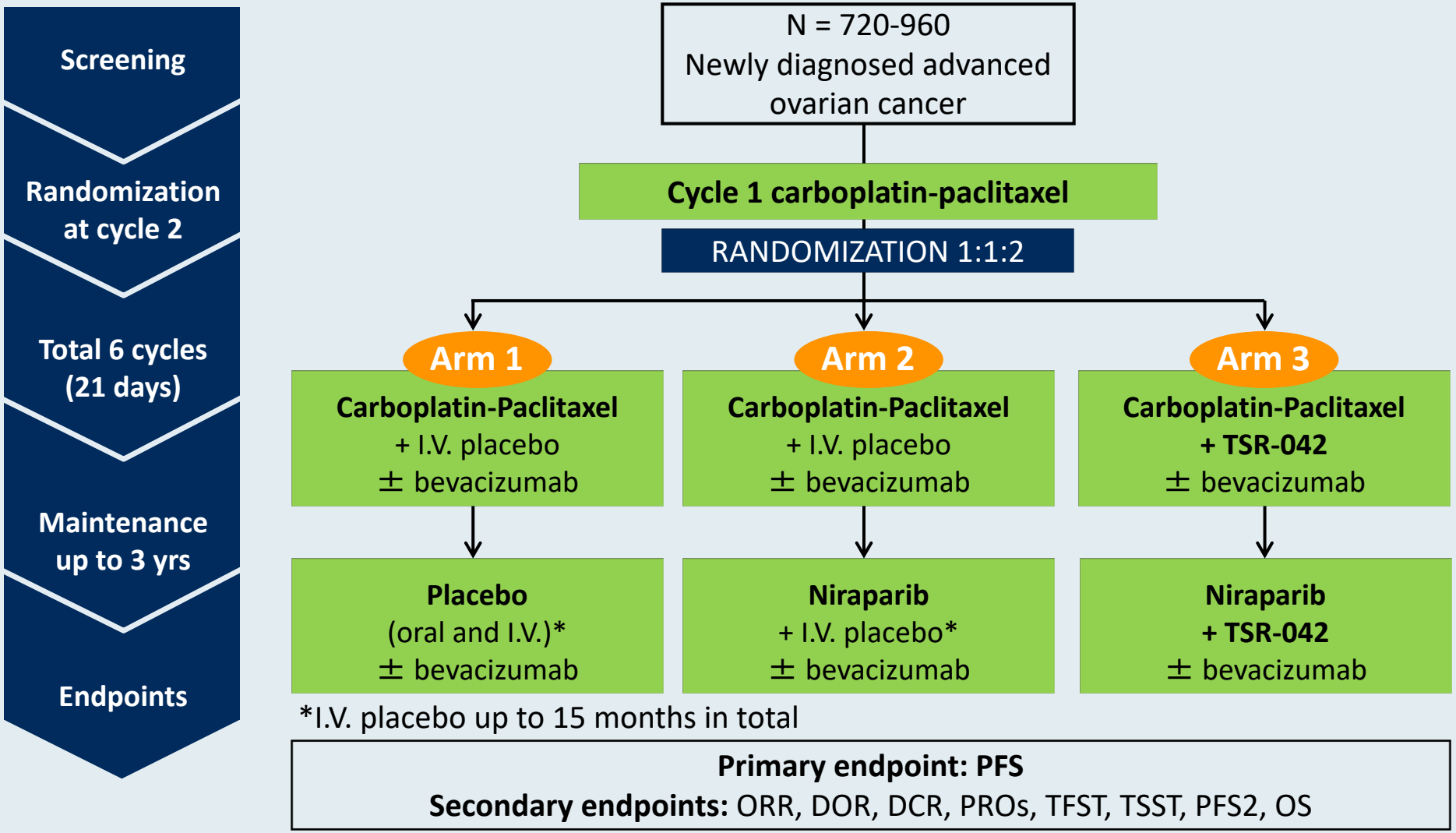


- **Triplet cohort showed high DCT at 24 weeks and a long median PFS**

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

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

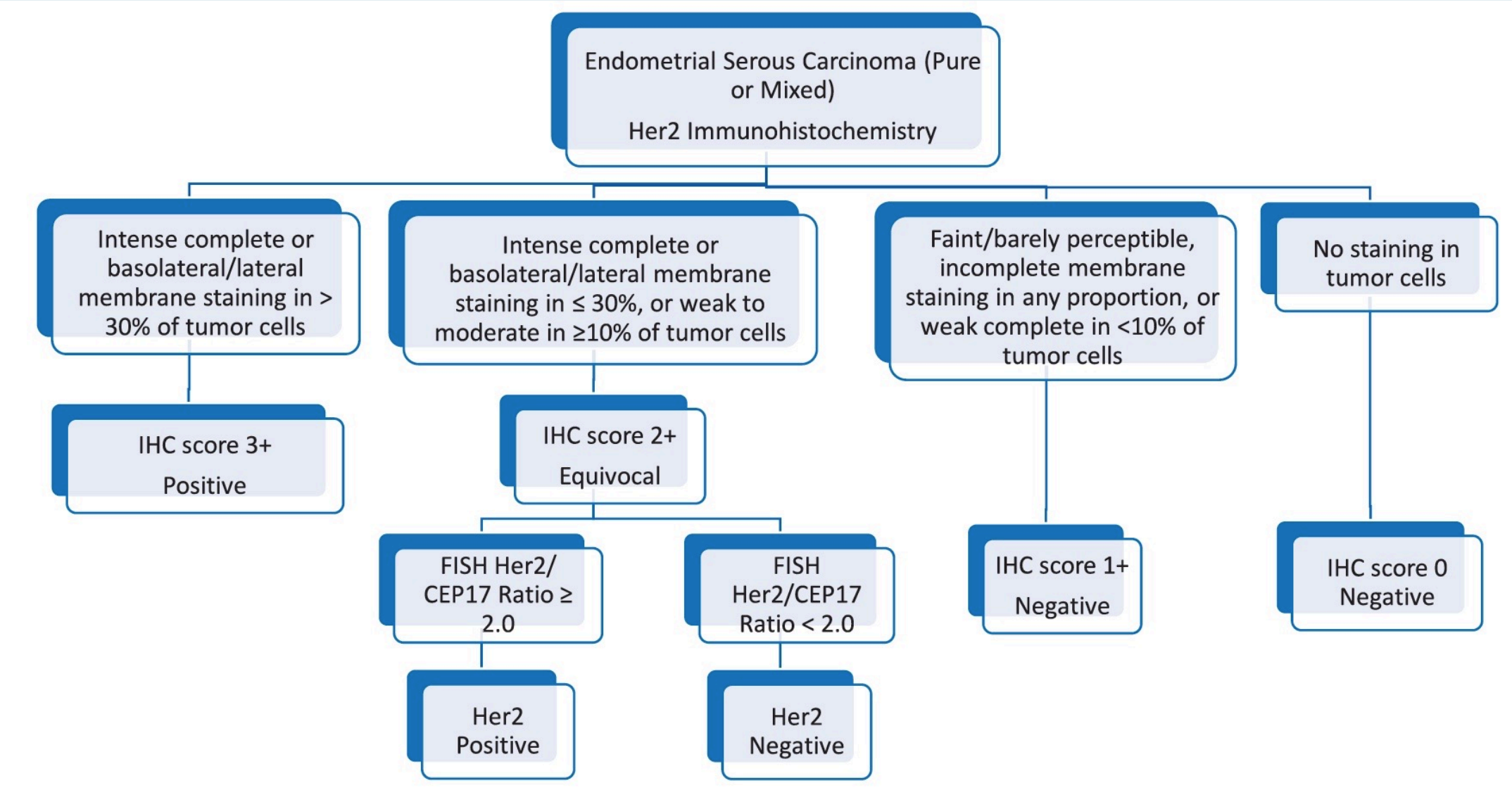
	Breast (ASCO/CAP 2018)[23]	Gastric (ASCO/CAP 2016)[36]	Colorectal (HERACLES Trial)[39]	Endometrial Serous (Fader et al Clinical Trial)[21]
HER2 IHC 3+	>10% circumferential, strong, complete	≥10%, strong complete, or basolateral/lateral	≥50% strong complete, or basolateral/lateral	>30% strong complete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



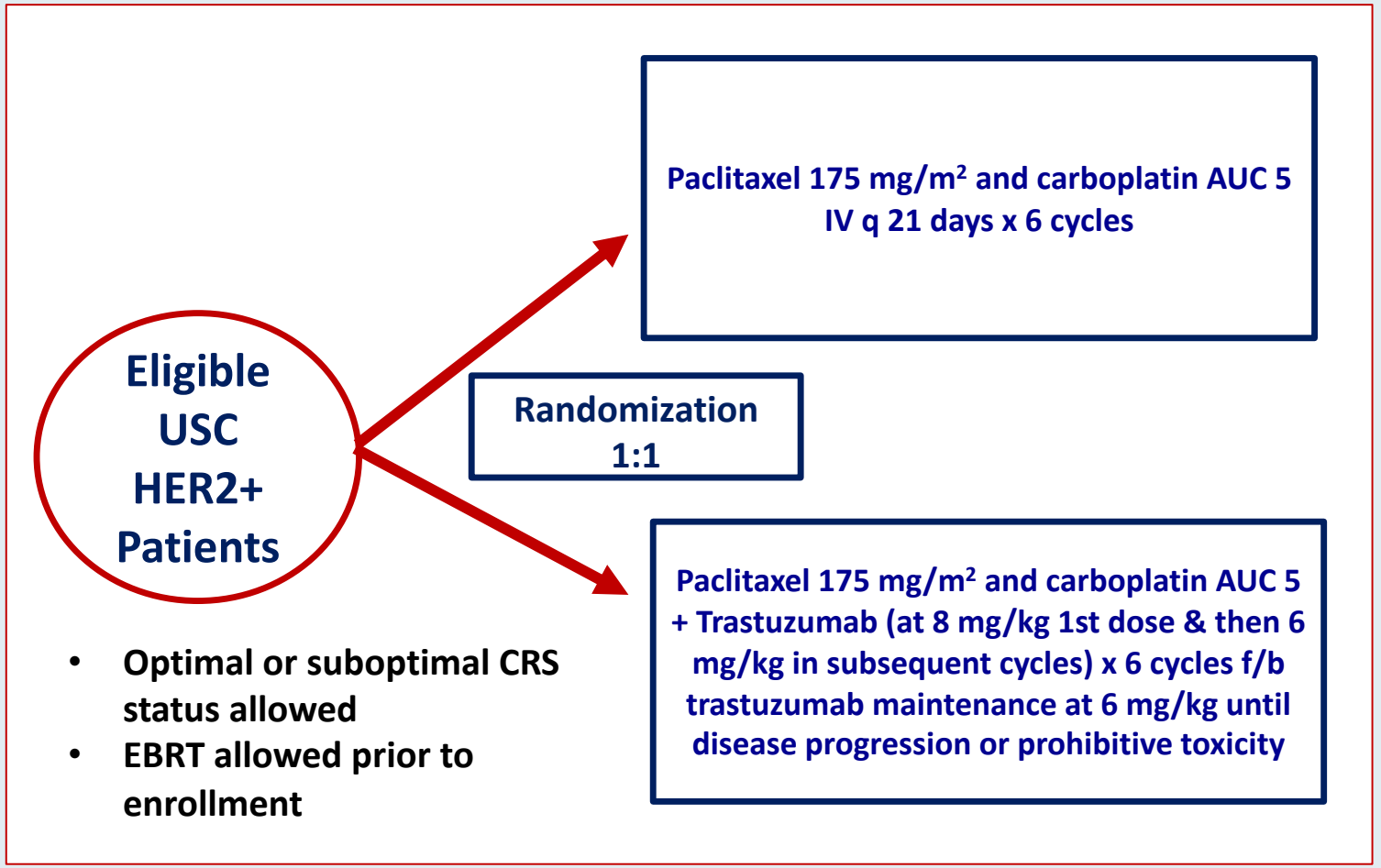
Buza N. *Arch Pathol Lab Med* 2020;[Online ahead of print].

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

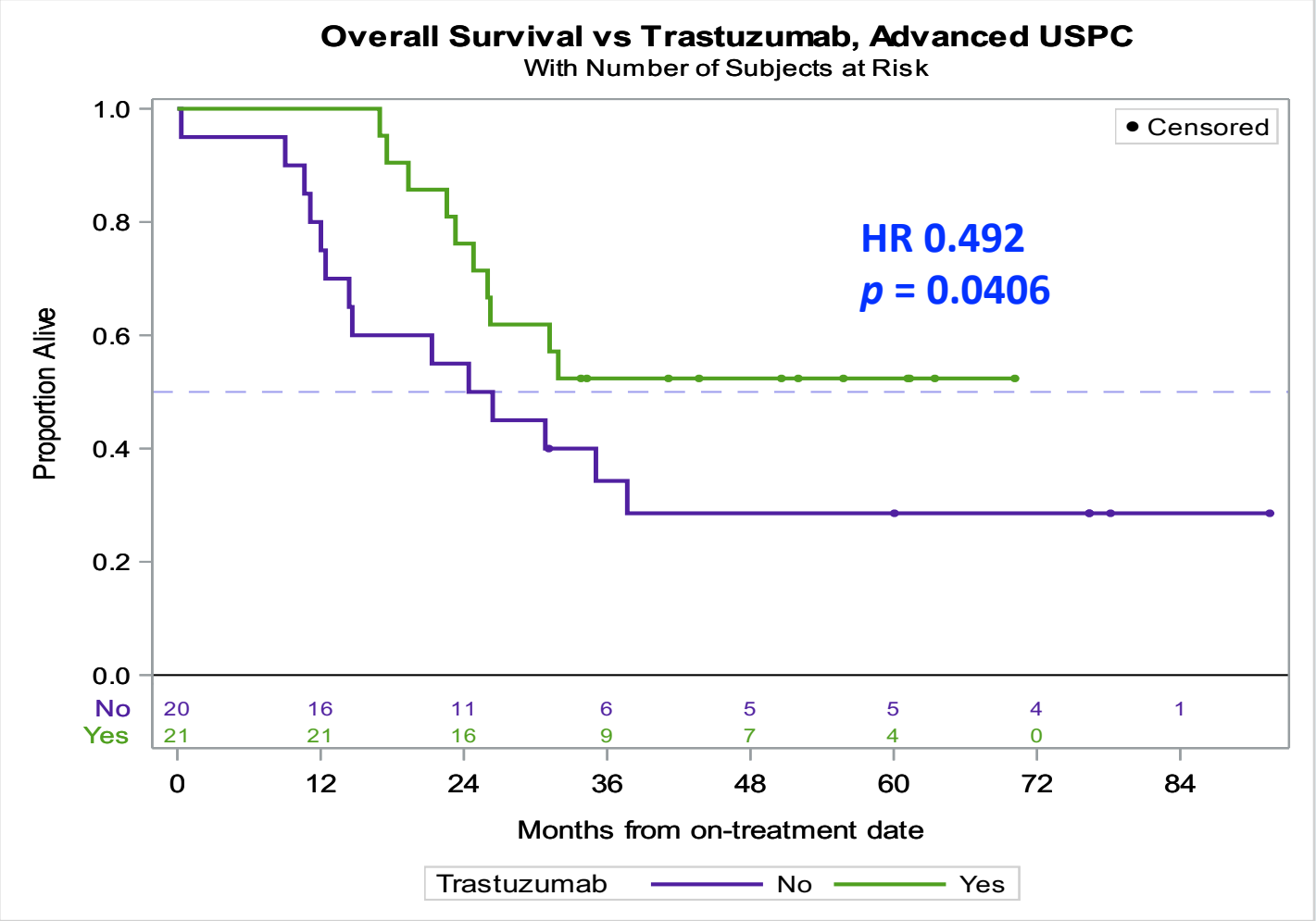


Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

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)



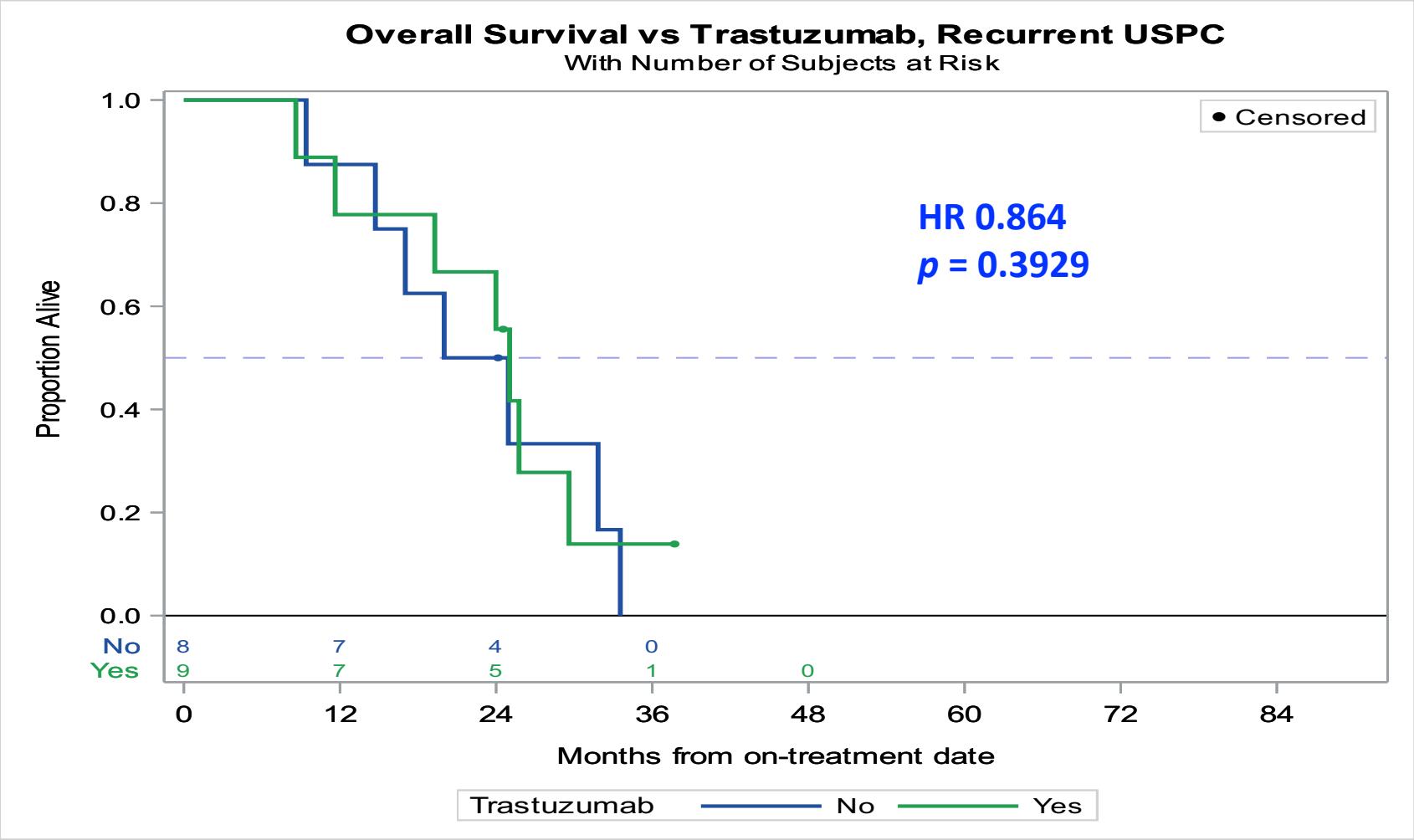
Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

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

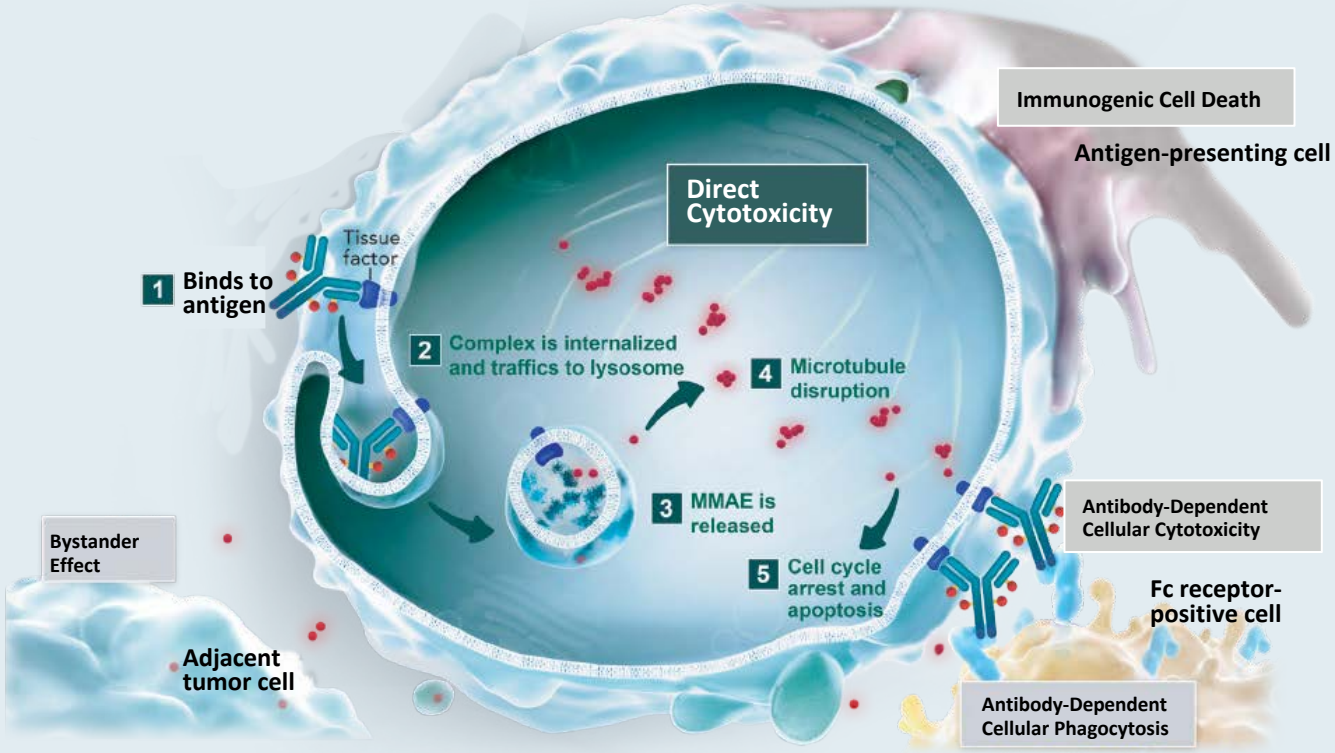
https://www.clinicaltrials.gov/ct2/show/NCT04482309.

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]

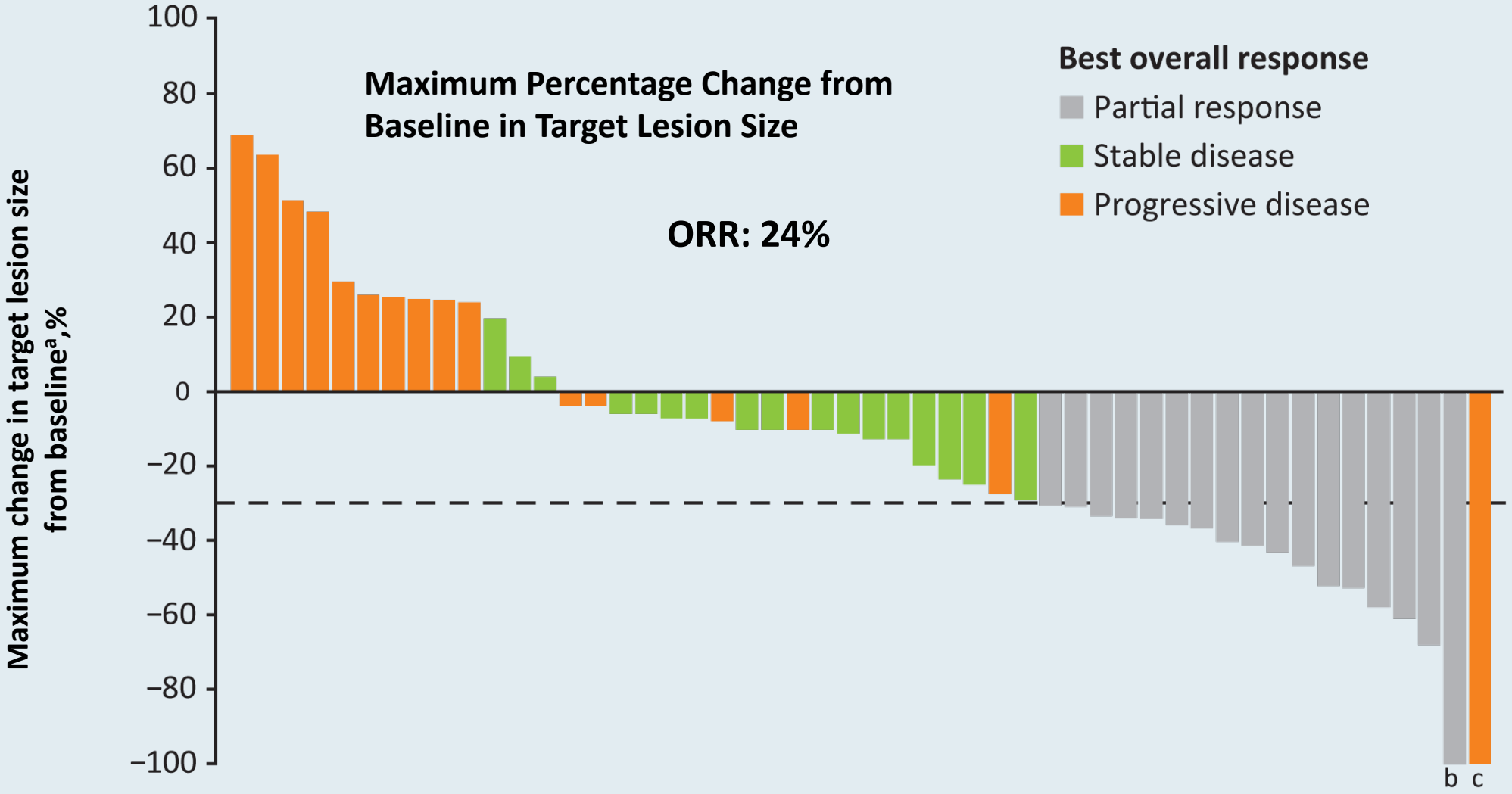


1. Förster Y, et al. *Clin Chim Acta,* 2006. 2. Cocco E, et al. *BMC Cancer,* 2011.
3. Breij EC, et al. *Cancer Res,* 2014. 4. De Goeij BE, et al. *Mol Cancer Ther,* 2015.

Courtesy of David M O'Malley, MD

RTP RESEARCH TO PRACTICE

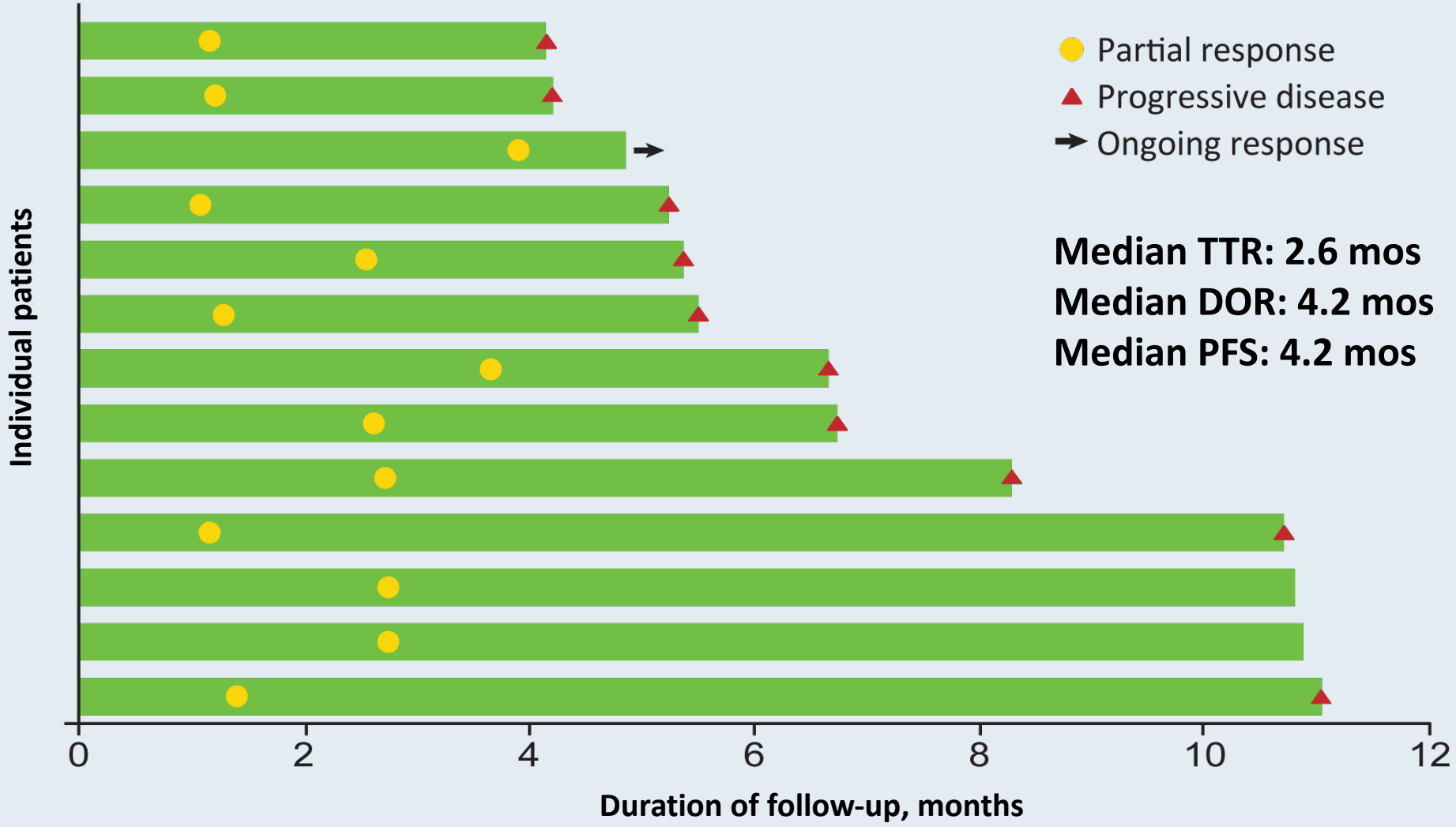
innovaTV 201: Best Overall Response to TV



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

RTP RESEARCH TO PRACTICE

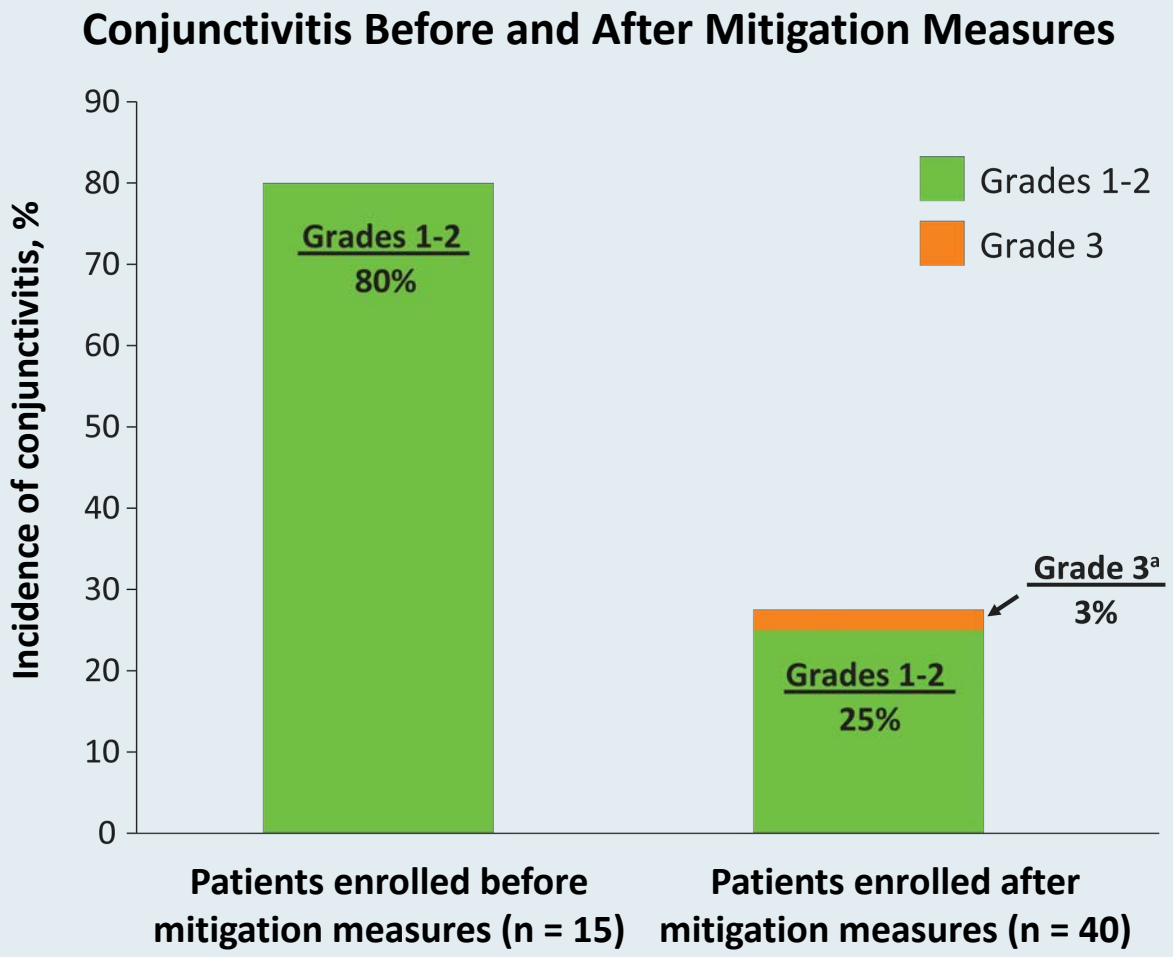
innovaTV 201: Time to Response and Duration of Response in Patients with a Confirmed PR to TV



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

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

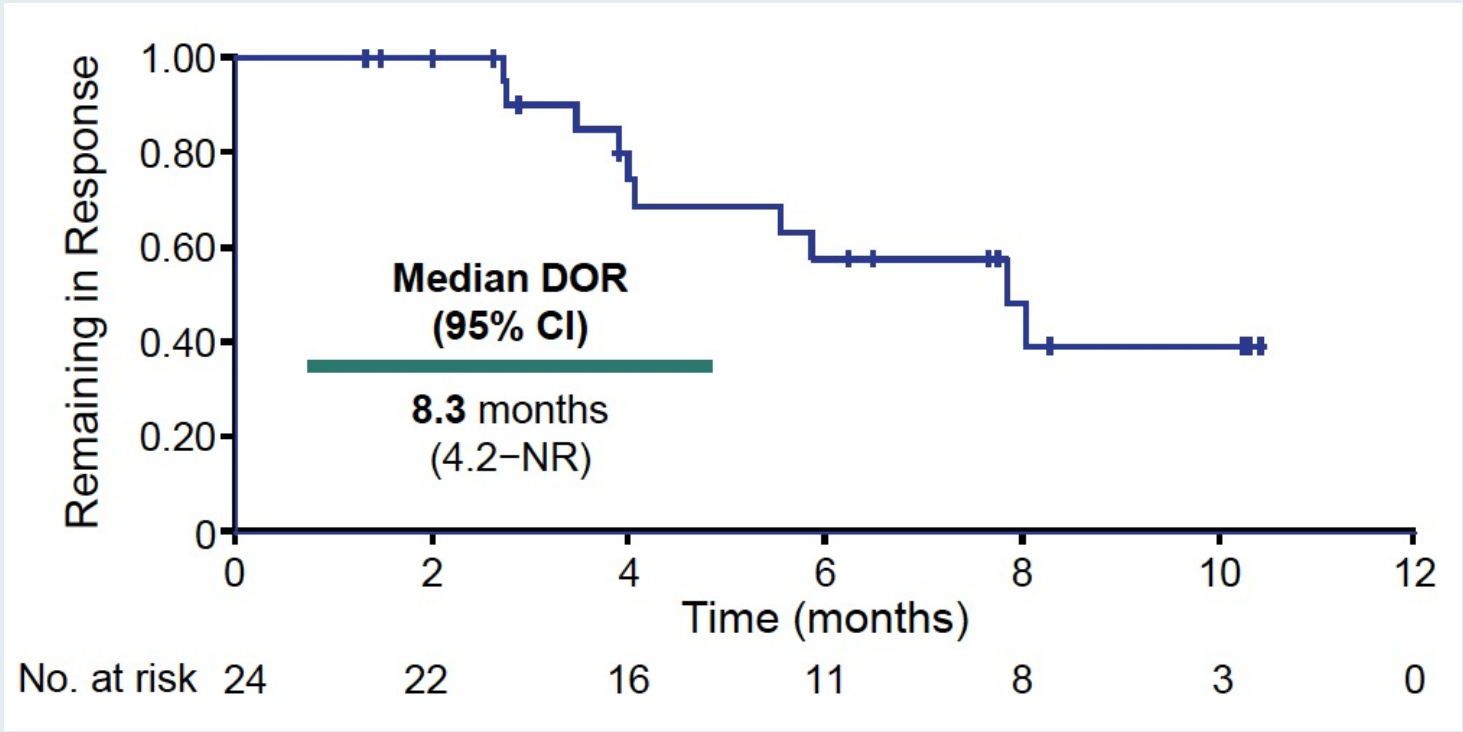
Coleman RL et al.

ESMO 2020;Abstract LBA32.

innovaTV 204: Antitumor Activity by IRC Assessment

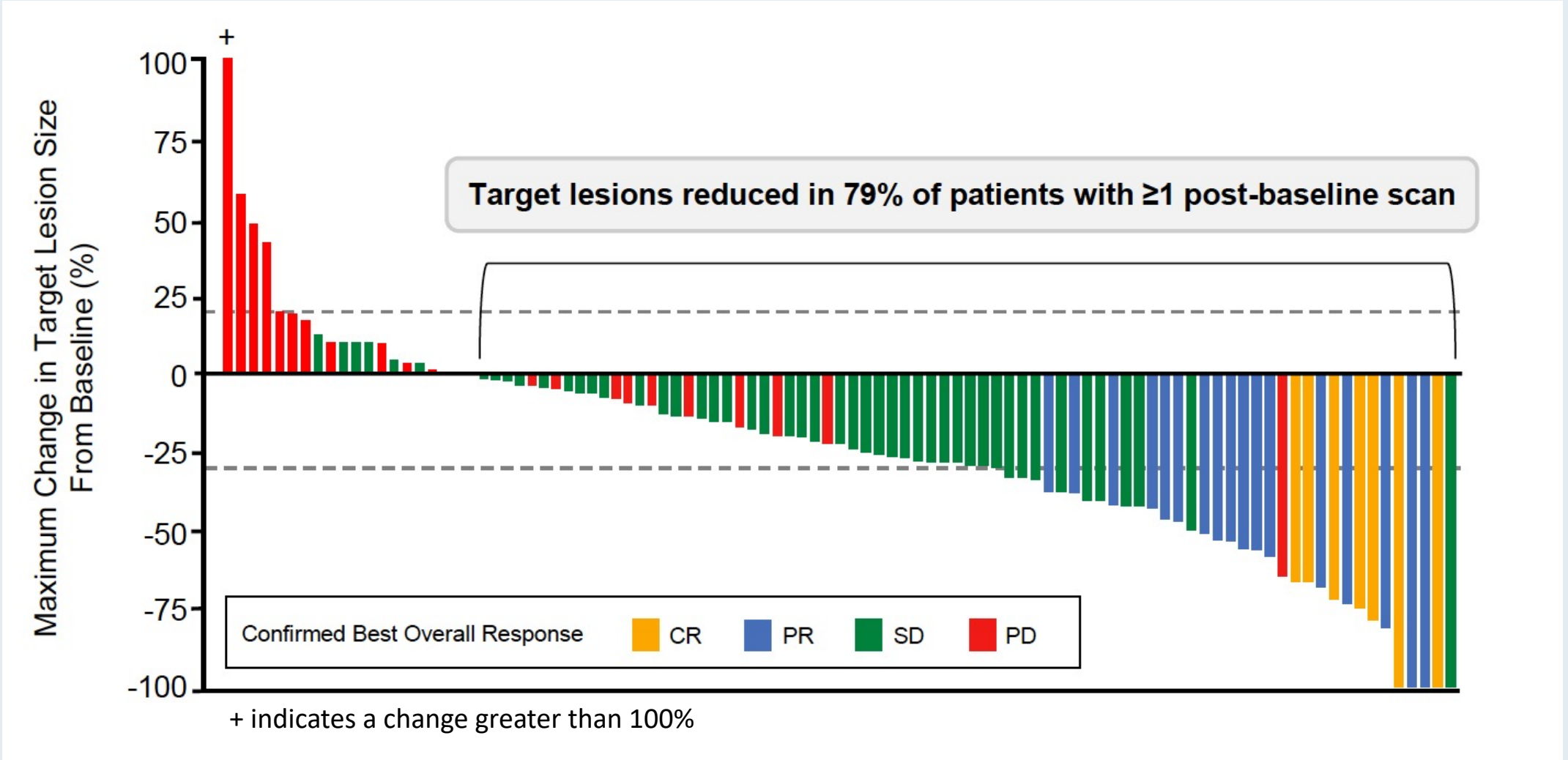
Clinical Variable	N = 101
Confirmed ORR	24%
CR	7%
PR	17%
SD	49%
PD	24%
Not evaluable	4%

Duration of Response



Coleman RL et al. *ESMO* 2020;Abstract LBA32.

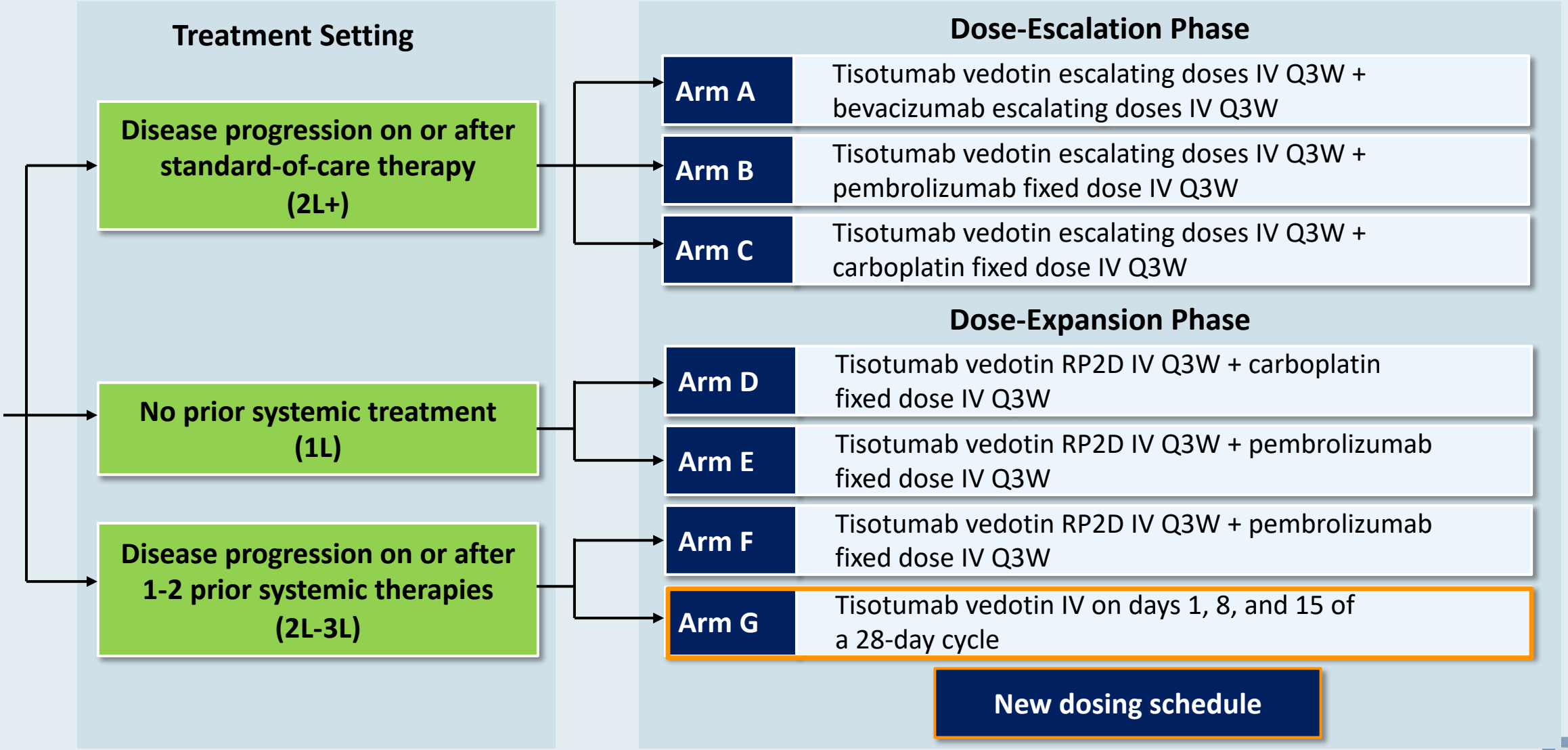
innovaTV 204: Maximum Change in Target Lesion Size by IRC Assessment



+ indicates a change greater than 100%

Coleman RL et al. *ESMO* 2020;Abstract LBA32.

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



Courtesy of David M O'Malley, MD

Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

Tuesday, April 6, 2021
12:00 PM – 1:00 PM ET

Faculty

Sumanta K Pal, 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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