Meet The Professor
Immunotherapy and Novel Agents in Gynecologic Cancers

Krishnansu S Tewari, MD
Professor and Division Director
Division of Gynecologic Oncology
University of California, Irvine
Irvine, California

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 Tewari — Disclosures

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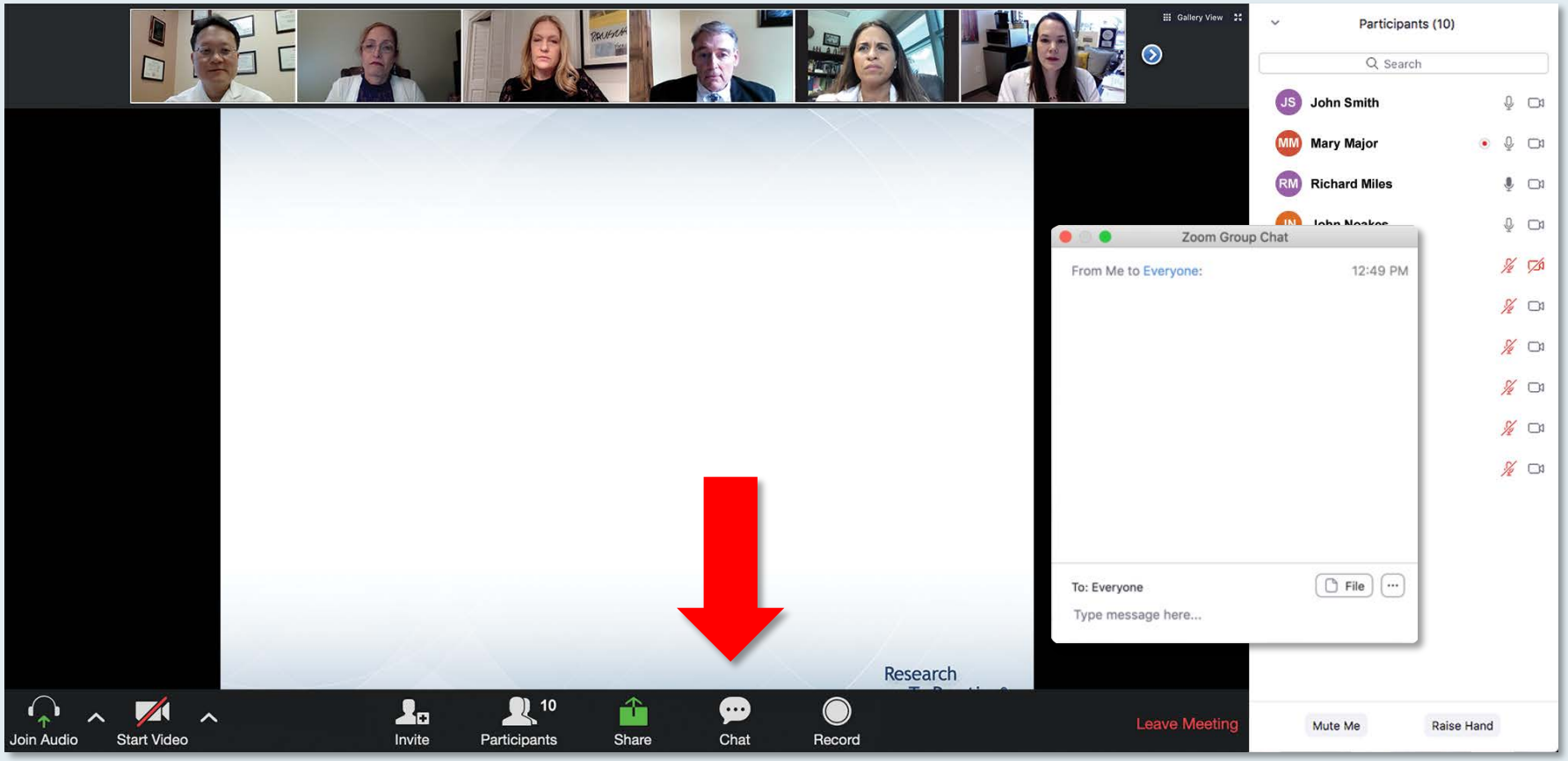
We Encourage Clinicians in Practice to Submit Questions



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

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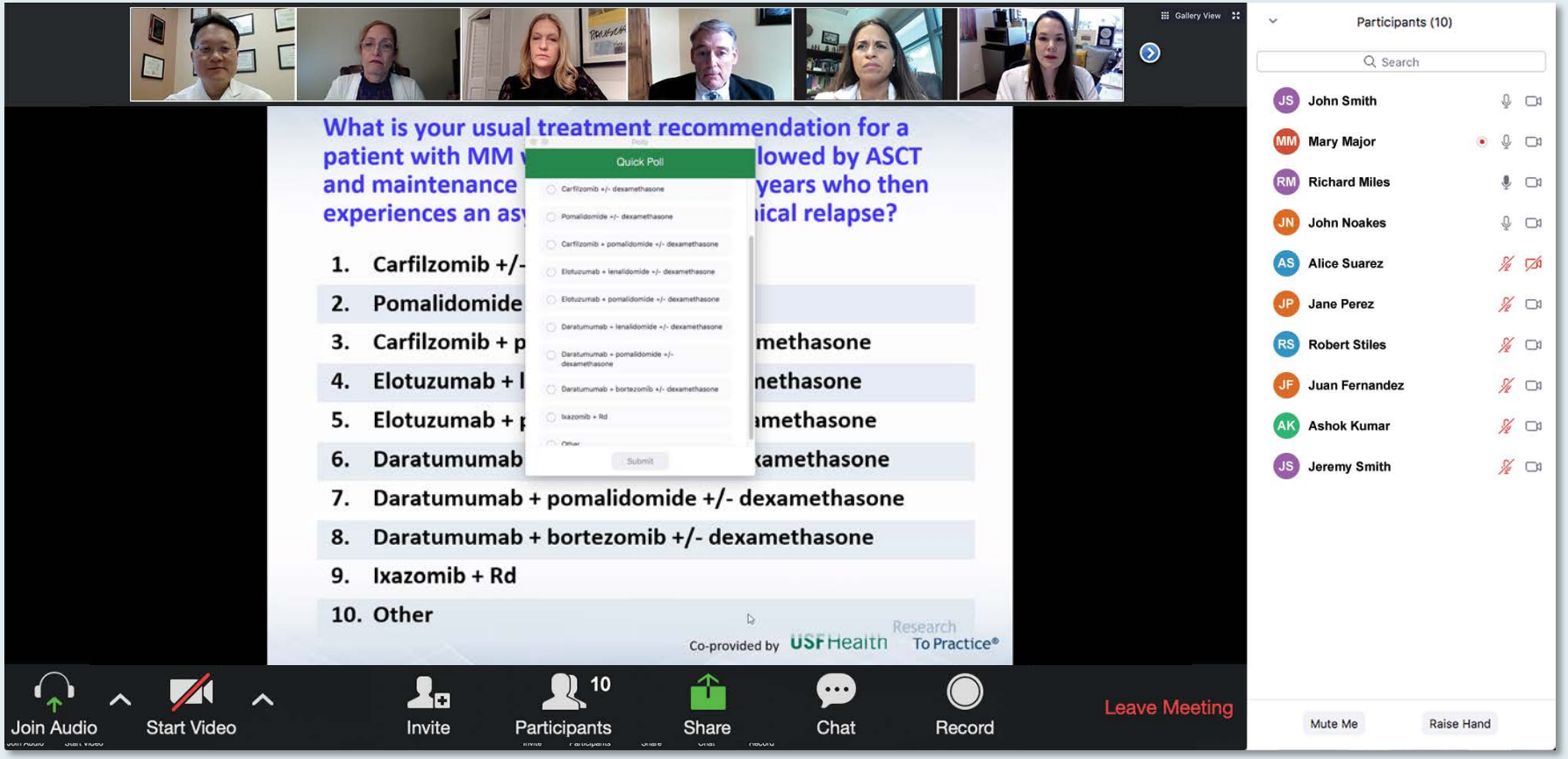
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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Upcoming Webinars

Thursday, November 19, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Multiple Myeloma

Faculty
Kenneth C Anderson, MD

Moderator
Neil Love, MD

Friday, November 20, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Chronic Lymphocytic Leukemia

Faculty
Prof John G Gribben, MD, DSc, FMedSci

Moderator
Neil Love, MD

Upcoming Webinars

Monday, November 23, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Ovarian Cancer

Faculty
Deborah K Armstrong, 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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ONCOLOGY TODAY

COMMENTS ON THE MANAGEMENT OF OVARIAN CANCER DURING THE COVID-19 PANDEMIC

WITH DR NEIL LOVE

DR KATHLEEN MOORE
UNIVERSITY OF OKLAHOMA
HEALTH SCIENCES CENTER

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Meet The Professor
Immunotherapy and Novel Agents in Gynecologic Cancers

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Professor and Division Director
Division of Gynecologic Oncology
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Irvine, California

Meet The Professor Program Participating Faculty

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Director, Winthrop P Rockefeller Cancer Institute
Director, Cancer Service Line
University of Arkansas for Medical Sciences
Little Rock, Arkansas

Ana Oaknin, MD, PhD
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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Chief Scientific Officer
US Oncology Research
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McKesson
The Woodlands, Texas

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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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Miami, Florida

Project Chair
Neil Love, MD
Research To Practice
Miami, Florida

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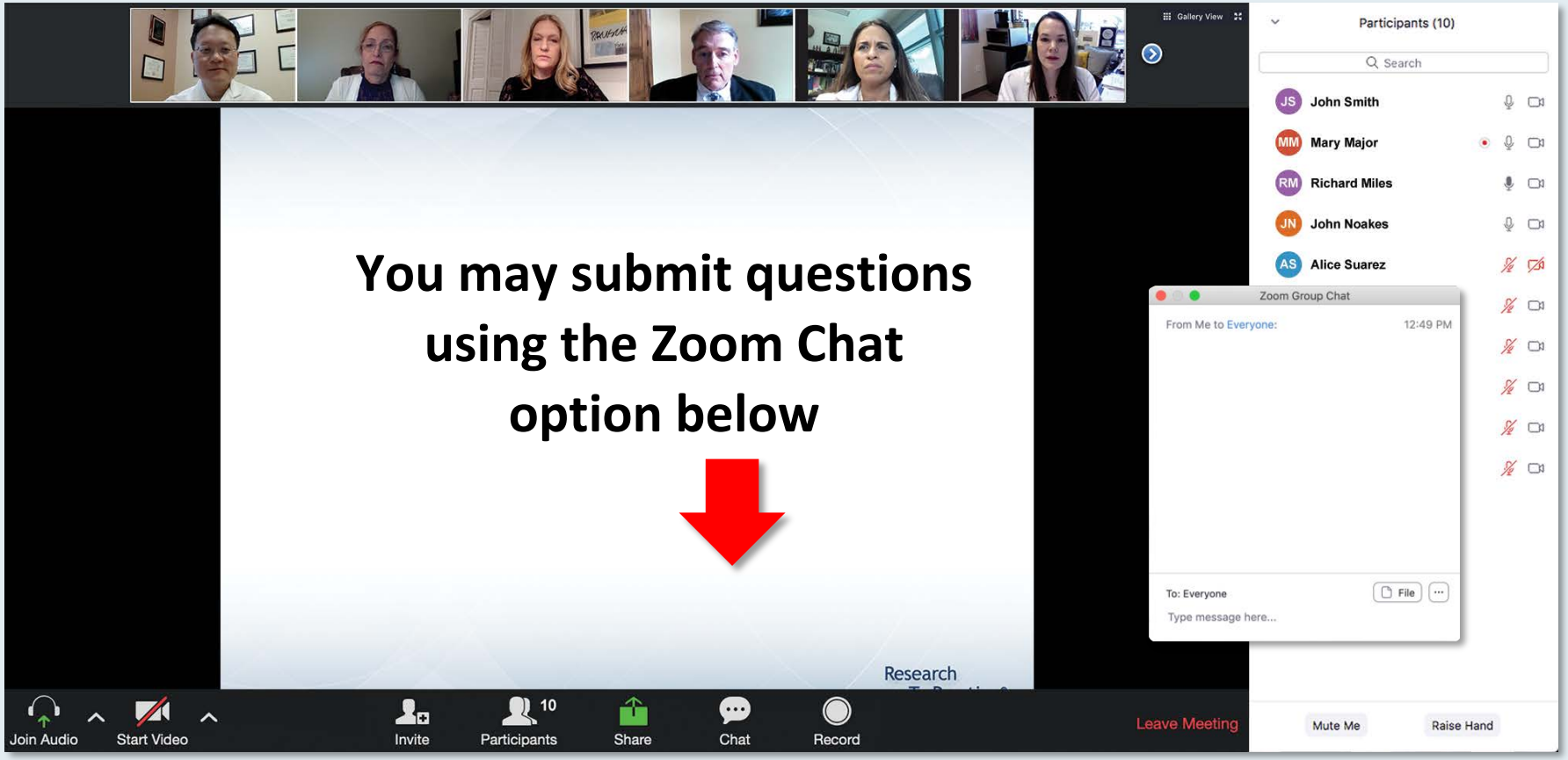
We Encourage Clinicians in Practice to Submit Questions



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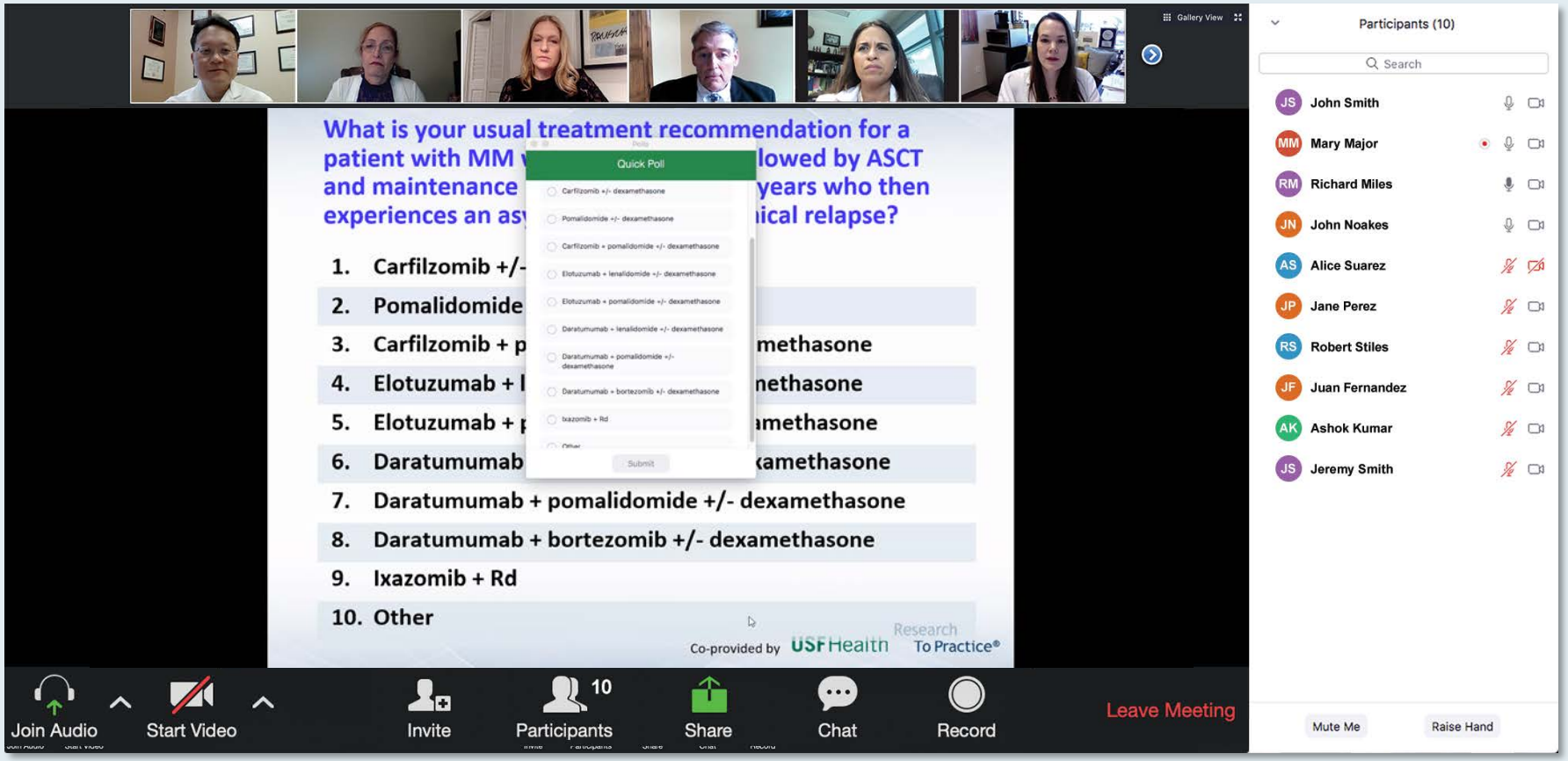

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ONCOLOGY TODAY

COMMENTS ON THE MANAGEMENT OF OVARIAN CANCER DURING THE COVID-19 PANDEMIC

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Division of Gynecologic Oncology
University of California, Irvine
Irvine, California

Allan Freedman, MD
Physician with Suburban Hematology-Oncology Associates
Snellville, Georgia

Neil Morganstein, MD
Hematology Oncology
Atlantic Health System
Summit, New Jersey

Brian M Slomovitz, MD
Professor, Department of Obstetrics and Gynecology
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Miami, Florida

Meet The Professor with Dr Tewari

MODULE 1: Cases and Questions from Drs Freedman, Morganstein and Slomovitz

- Dr Slomovitz: A 34-year-old woman with cervical cancer
  - Part 1: Robotic radical hysterectomy
  - Part 2: GOG-240 regimen at disease progression
  - Part 3: Management of second disease progression
- Dr Freedman: A 75-year-old woman with endometrial cancer and metastatic recurrence in the scalp
- Dr Morganstein: A 64-year-old woman with metastatic endometrial cancer and MLH1 and PMS2 somatic mutations

MODULE 2: Gynecologic Oncology Journal Club with Dr Tewari

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 Slomovitz: A 34-year-old woman with cervical cancer – 1. Robotic radical hysterectomy

Dr Brian Slomovitz

- A 34 year-old woman who has not had a pap smear in 10 years presented to her gynecologist for abnormal bleeding
- A 2-cm cervical mass is found
  - Biopsy: invasive squamous cell carcinoma, +LVSI
- Patient underwent a robotic radical hysterectomy and staging
- Pathology revealed a 3-cm, LVSI+, deeply invasive squamous cell cancer
- Patient refused post-operative radiotherapy

Question

- Should robotic radical hysterectomies still be done based on the data published in the *New England Journal of Medicine* (Ramirez et al. 2018)?

Case Presentation – Dr Slomovitz: A 34-year-old woman with cervical cancer – 2. GOG-240 regimen at disease progression

Dr Brian Slomovitz

- A 34 year-old woman with a 3-cm cervical mass (deeply invasive squamous cell carcinoma, +LVSI) undergoes robotic radical hysterectomy
- Patient refused post-operative radiotherapy
- **Patient presents to ER 6 months later with right flank pain, ARF**
  - **CT scan shows pelvic and para-aortic disease with right hydronephrosis**
  - **PET scan and CT-guided biopsy confirms disease**
- **Cisplatin/paclitaxel/bevacizumab x 6 cycles → CR**
- **PET scan 3 months after treatment shows lung metastases**
- **NGS performed on biopsy: PD-L1 CPS>1**

Question

- Could the robotic procedure have increased her risk of recurrence? What treatment would you offer this patient at this point?

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Case Presentation – Dr Slomovitz: A 34-year-old woman with cervical cancer – 3. Management of second disease progression

Dr Brian Slomovitz

- A 34 year-old woman with a 3-cm cervical mass (deeply invasive squamous cell carcinoma, +LVSI) undergoes robotic radical hysterectomy
- Patient refused post-operative radiotherapy
- Disease recurrence 6 months later
- Cisplatin/paclitaxel/bevacizumab x 6 cycles → CR
- PET scan 3 months after treatment shows lung metastases
- NGS performed on biopsy: PD-L1 CPS>1
- **Considering pembrolizumab or enrollment in clinical trial**

Question

- Should I consider chemotherapy at this point for her? Is pembrolizumab the best treatment option I can offer to her? Are there any newer agents, such as TIL therapy or tisotumab vedotin, that could make a difference for her?

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Case Presentation – Dr Freedman: A 75-year-old woman with endometrial cancer and metastatic recurrence in the scalp

Dr Allan Freedman

- Fall 2018: Initial diagnosis of adenocarcinoma of endometrium
  - Pathology: Stage IB, T1bN0M0, FIGO 3
  - Mismatch repair (MMR) deficient
- Cytoreductive surgery → paclitaxel + carboplatin x 6 cycles; no XRT
- 2020: Relapse developed in calvarium → resection showing moderately differentiated adenocarcinoma
  - PAX 8 +, absent MLH1 and PMS2
  - CT scan showed multiple pulmonary nodules
- XRT to scalp → pembrolizumab for 5 cycles → progression in lungs and bone
- Megestrol alternating with tamoxifen

Questions

- How often do you see MMR deficient endometrial cancer?
- How common is it to observe a treatment failure with immunotherapy in a patient who is MMR deficient? Would there have been an advantage to adding another agent such as lenvatinib to the pembrolizumab in order to see if a response could be obtained?

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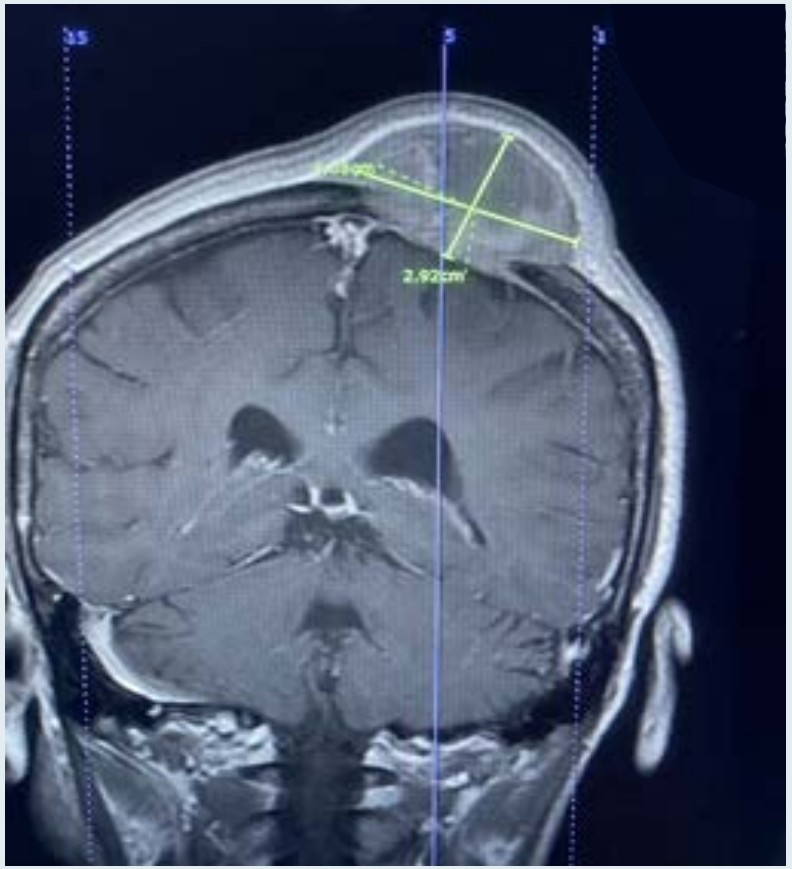
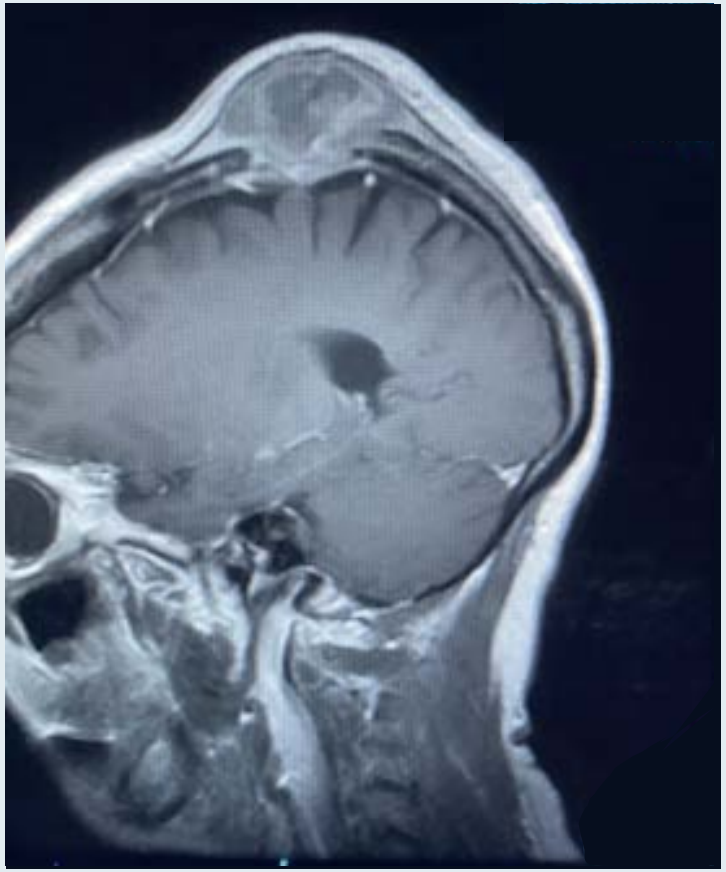
Case Presentation – Dr Freedman: A 75-year-old woman with endometrial cancer and metastatic recurrence in the scalp

Dr Allan Freedman





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Case Presentation – Dr Morganstein: A 64-year-old woman with metastatic endometrial cancer and MLH1 and PMS2 somatic mutations

Dr Neil Morganstein

- Presented with significant vaginal bleeding and pain and initial workup reveals a large endometrial mass and a single bone metastasis
- Upfront surgery due to vaginal bleeding and discomfort
- Biopsy: Loss of MHL1, PMS2, BRAF wildtype
  - MLH1 methylated status, suggesting sporadic (somatic) mutation and microsatellite instability (MSI)
- Offered chemotherapy or immunotherapy as treatment options – patient chose chemotherapy due to its defined duration

Questions

- What duration would you administer immunotherapy in the first-line setting?
- How should one interpret MSI results? Is there any difference in the efficacy of immunotherapy in patients with germline versus somatic mutations?

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Meet The Professor with Dr Tewari

MODULE 1: Cases and Questions from Drs Freedman, Morganstein and Slomovitz

MODULE 2: Gynecologic Oncology Journal Club with Dr Tewari

- Philip John DiSaia, MD
- Robotic surgery for gynecologic cancers
- Evidence-based treatment paradigms for the management of cervical carcinoma
- GOG-240: Circulating tumor cells in advanced cervical cancer
- Education, screening and current challenges in the management of cervical cancer in Tanzania
- Fertility-preserving treatment for and pregnancy with gynecologic cancers
- Review of endometrial cancer in the morbidly obese
- OVAL: VB-111 combined with paclitaxel for platinum-resistant ovarian cancer
- NRG Oncology/GOG-0209: Carboplatin and paclitaxel for advanced endometrial cancer

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

MODULE 4: Key Recent Data Sets

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THE JOURNAL OF
Obstetrics and Gynaecology Research

The official Journal of Asia and Oceania Federation of Obstetrics and Gynaecology
Japan Society of Obstetrics and Gynecology

doi:10.1111/jog.14277

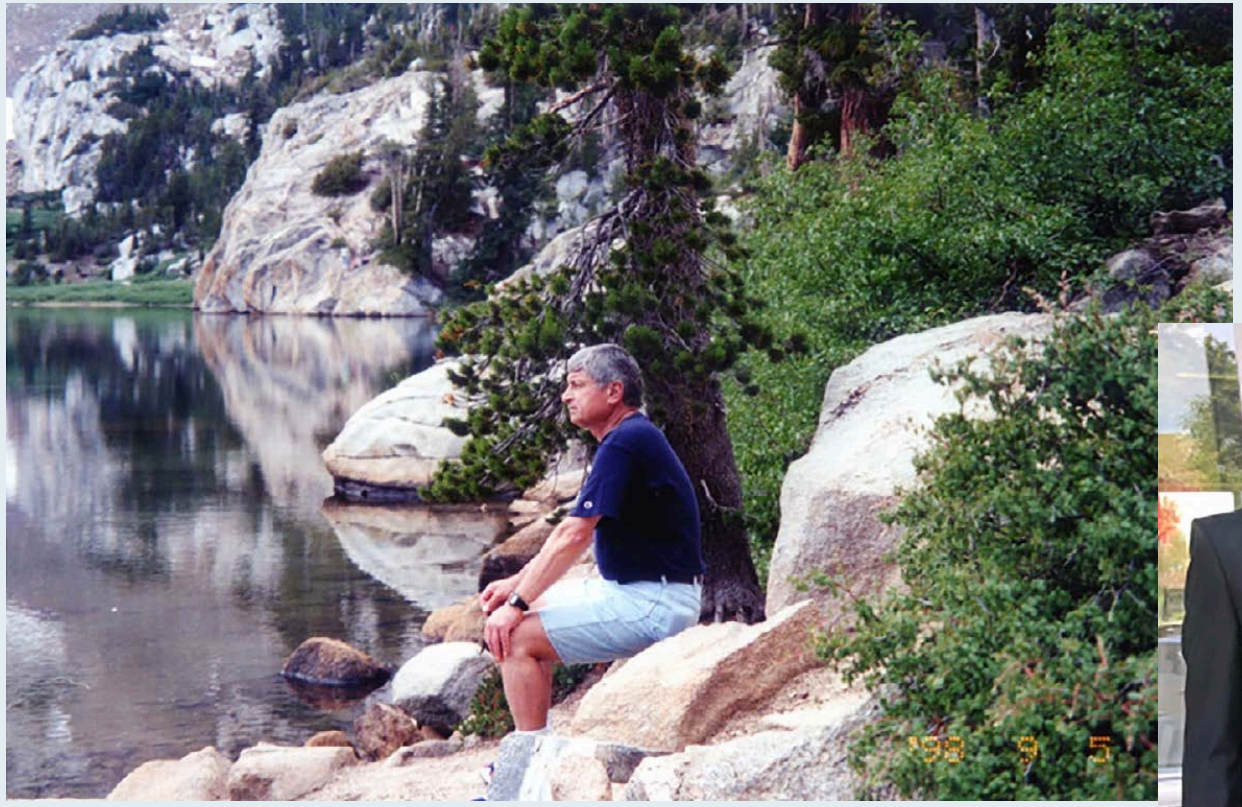
J. Obstet. Gynaecol. Res. Vol. 46, No. 7: 959–988, July 2020

Philip John DiSaia, MD: Available Light & The Origin of Storms

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

***J Obstet Gynaecol Res* 2020;46(7):959-88.**

Philip John DiSaia, MD (August 14, 1937 – September 27, 2018)



Tewari KS, Monk BJ. *J Obstet Gynaecol Res* 2020;46(7):959-88.

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Philip John DiSaia, MD (August 14, 1937 – September 27, 2018)

The Orange County Register B3
Thursday, October 29, 1987

Dr. Philip DiSaia
Prominent cancer surgeon

Special post at UCI created for surgeon

He'll develop, promote medical services

By Susan Peterson
The Register

IRVINE — The University of California has appointed Philip J. DiSaia, a prominent cancer surgeon, to promote and develop new medical services at the college's Irvine campus and its hospital in Orange.

DiSaia, 50, of North Tustin, is a member of the national board of directors of the American Cancer Society and a leading surgeon in gynecological cancers. He has been chairman of the department of obstetrics and gynecology for 10 years.

He will begin his duties Sunday.

The post of associate vice chancellor for health sciences was created for DiSaia, UCI Chancellor Jack Peltason said.

His appointment fills a need for a second administrator, in addition to Dean Edward J. Quilligan, to bring about "the next phase of development for the college of medicine," Peltason said.

"As the facilities in Orange and in Irvine become more adequate for a modern medical school, the proper use ... of those facilities requires more attention," he said.

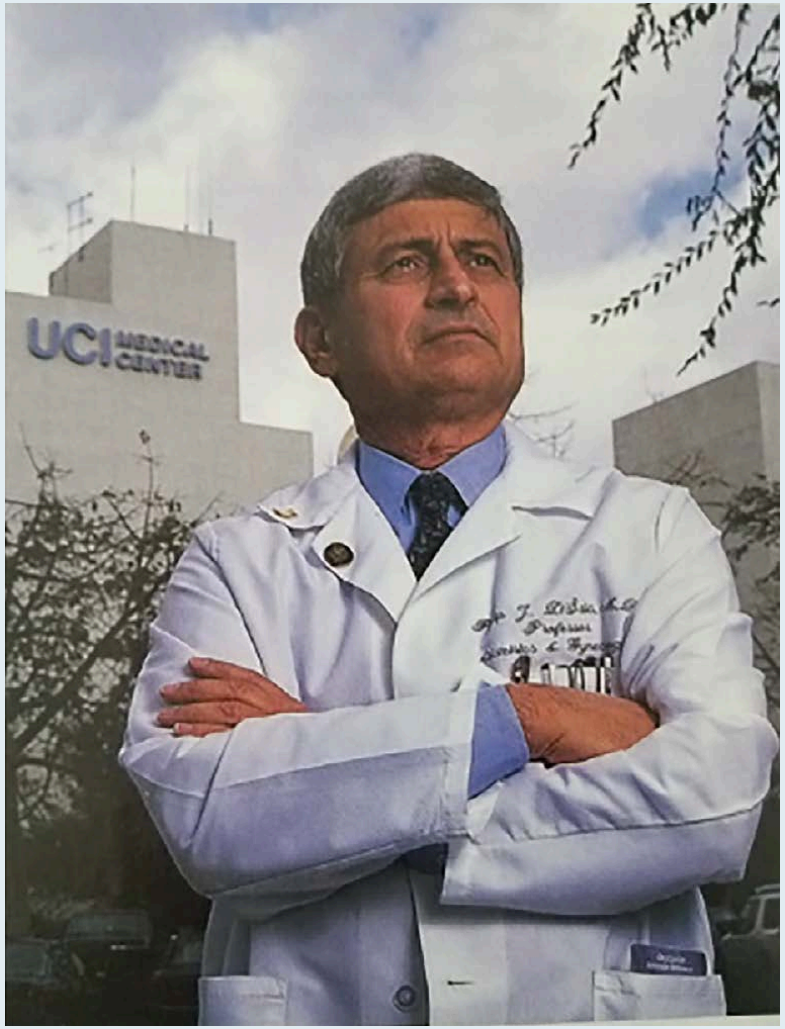
The university is building an outpatient treatment center and medical-office building at the Irvine campus, and it is expanding services at its hospital in Orange.

Quilligan said DiSaia, who was a resident under his direction at Yale University, will oversee planning, marketing and fund raising for UCI's new facilities. He is expected to be paid $160,000 a year in the new position, based on a salary of $72,900 plus a share in the faculty pool — a fund that provides bonuses to doctors who take state jobs.

DiSaia said he wants to create and promote new services that the university can offer to patients, a role critical in the institution's development.

"What we have to do is take this school out of its adolescence and see what we can do about bringing it into adulthood," he said.

The university began developing outpatient medical services on its Irvine campus after it lost a 15-year battle with a coalition of Ir-



Tewari KS, Monk BJ. *J Obstet Gynaecol Res* 2020;46(7):959-88.

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THE JOURNAL OF
Obstetrics and Gynaecology Research

The official Journal of Asia and Oceania Federation of Obstetrics and Gynaecology
Japan Society of Obstetrics and Gynecology

doi:10.1111/jog.14228

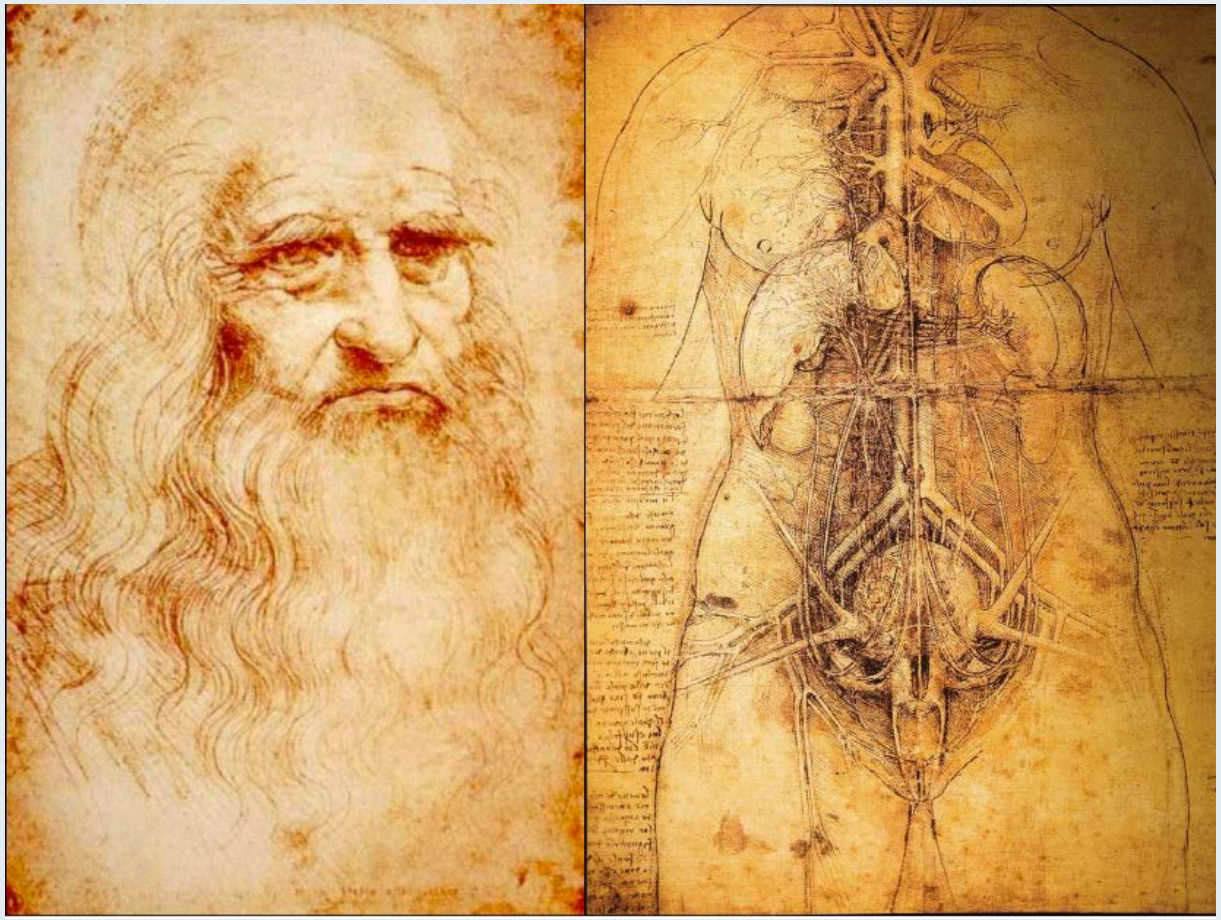
J. Obstet. Gynaecol. Res. Vol. 46, No. 6: 828–843, June 2020

Robotic surgery for gynecologic cancers: indications, techniques and controversies

Kiran H. Clair and Krishnansu S. Tewari

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of California, Irvine, Orange, California, USA

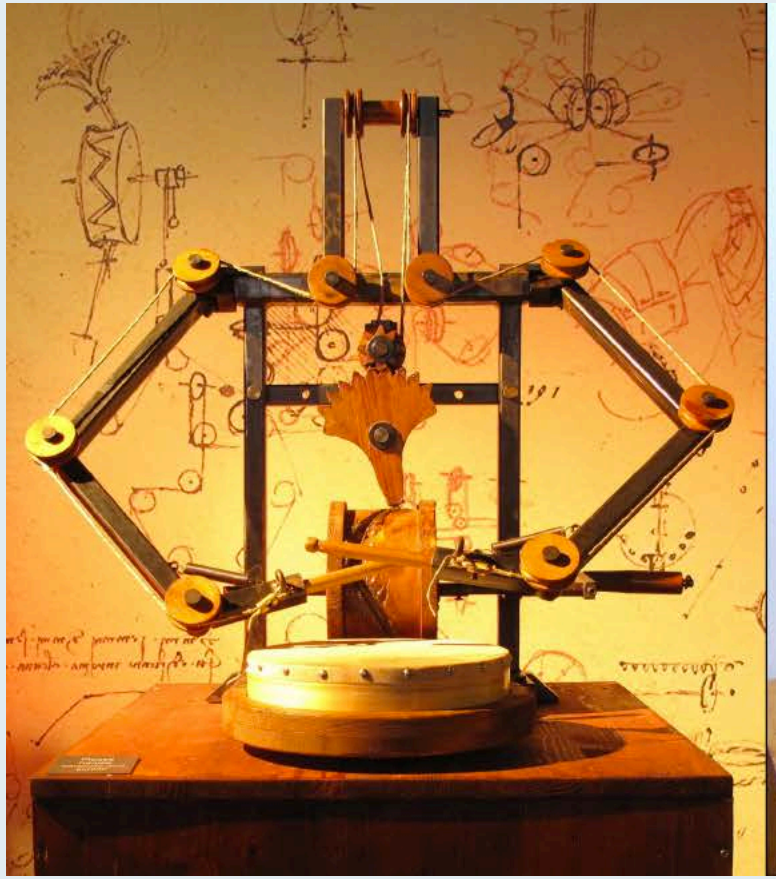
Robotic Surgery: Leonardo da Vinci



Self portrait of da Vinci and his detailed sketch of female anatomy

Clair KH, Tewari KS. *J Obstet Gynaecol Res* 2020;46(6):828-43.

Construction of da Vinci's Robotic Drummer and Robotic Knight



Clair KH, Tewari KS. *J Obstet Gynaecol Res* 2020;46(6):828-43.

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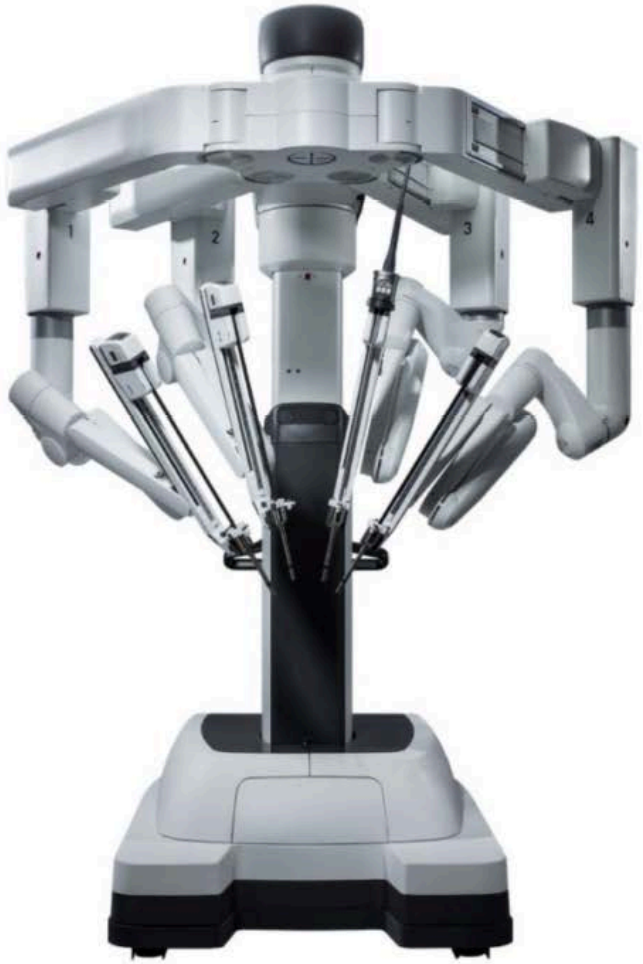
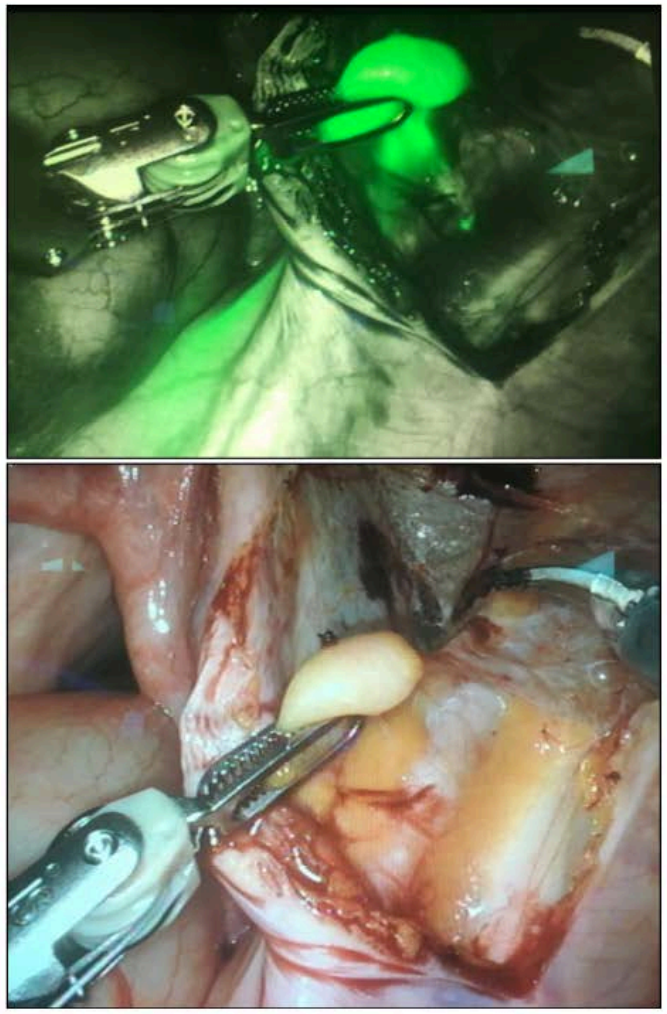
DaVinci Surgical Robot and DaVinci Robot Firefly™ Technology





Clair KH, Tewari KS. *J Obstet Gynaecol Res* 2020;46(6):828-43.

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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.

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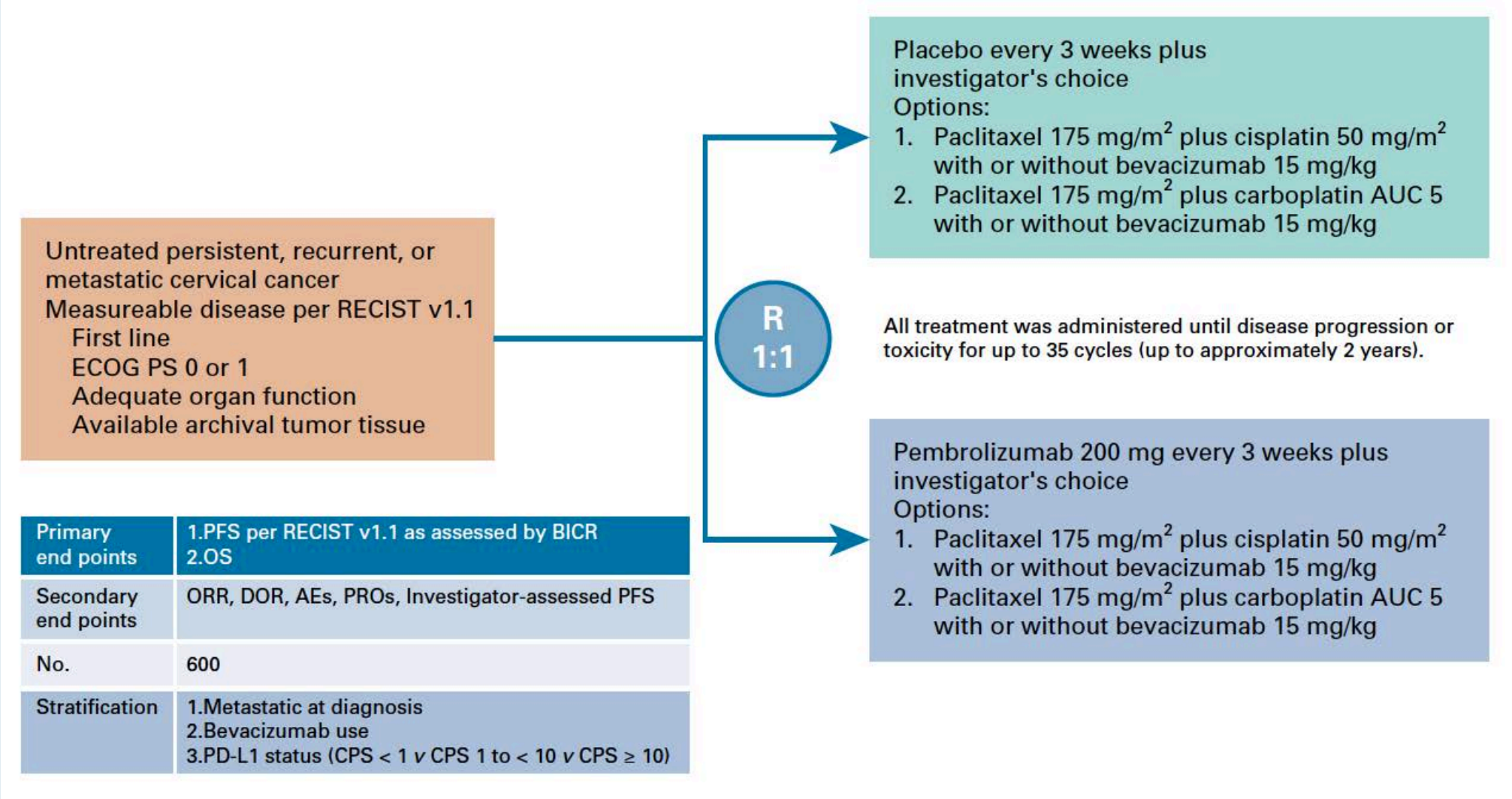
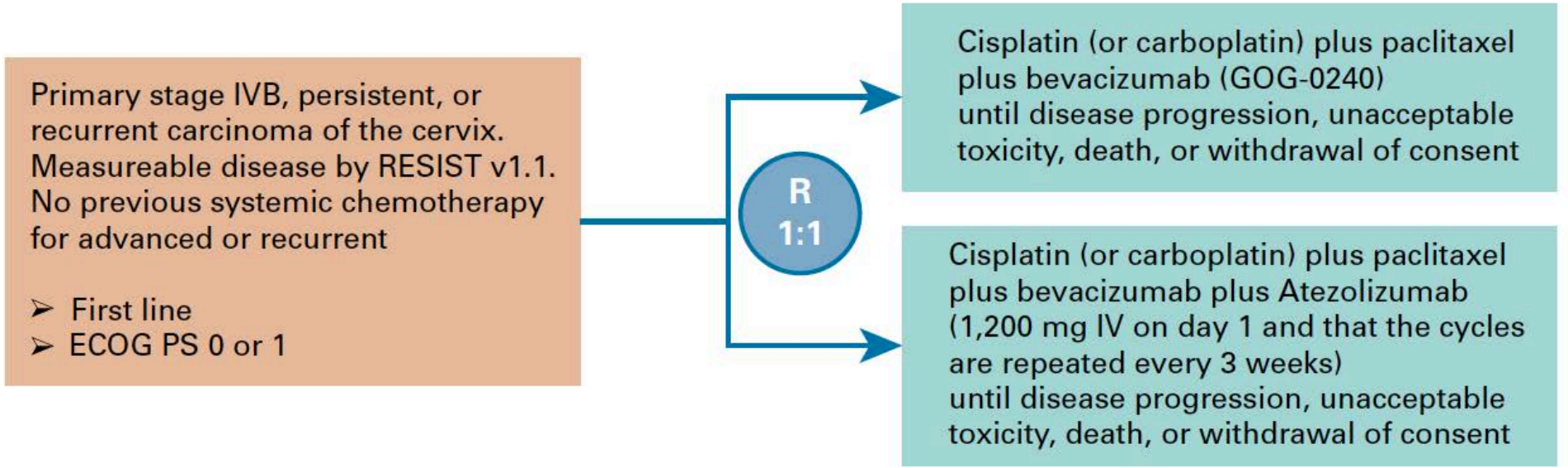
KEYNOTE-826 Trial (NCT03635567)



Primary end points	1.PFS per RECIST v1.1 as assessed by BICR 2.OS
Secondary end points	ORR, DOR, AEs, PROs, Investigator-assessed PFS
No.	600
Stratification	1.Metastatic at diagnosis 2.Bevacizumab use 3.PD-L1 status (CPS < 1 *v* CPS 1 to < 10 *v* CPS ≥ 10)

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

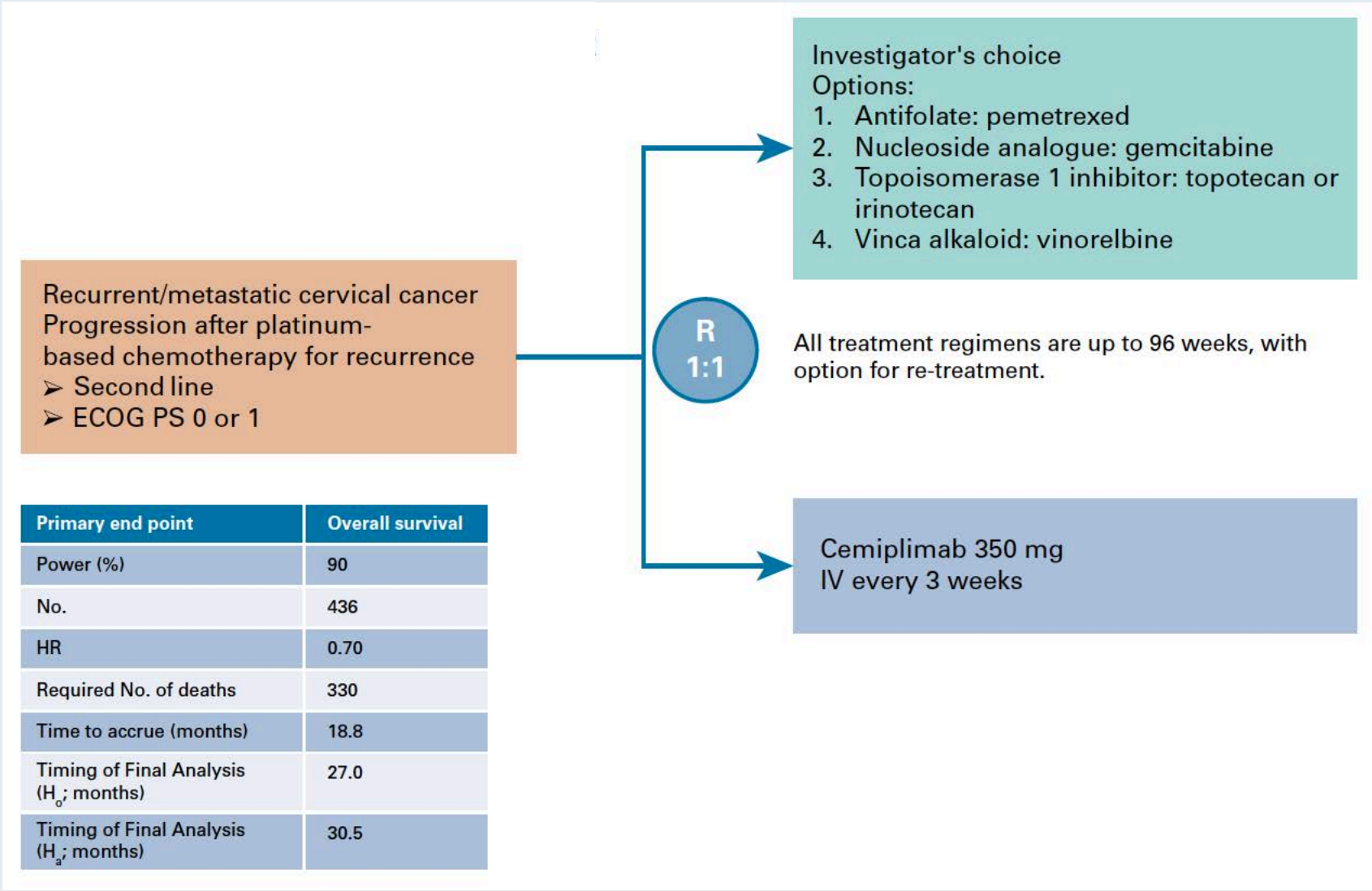
BEATcc Trial (NCT03556839)



Primary end point	OS
Secondary end points	PFS, ORR, DOR, safety, HR-QoL
No.	404
Stratification factors	1.Prior concurrent cisplatin-based chemoradiation 2.Histology: SCCA versus adenocarcinoma (includes adenosquamous) 3.Chemotherapy backbone (cisplatin *v* carboplatin)

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

GOG-3016 (ENGOT Cx9/EMPOWER Cervical-1) Trial (NCT03257267)



Primary end point	Overall survival
Power (%)	90
No.	436
HR	0.70
Required No. of deaths	330
Time to accrue (months)	18.8
Timing of Final Analysis (H_o; months)	27.0
Timing of Final Analysis (H_a; months)	30.5

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

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].

Gynecologic Oncology Reports 29 (2019) 40–47

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

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

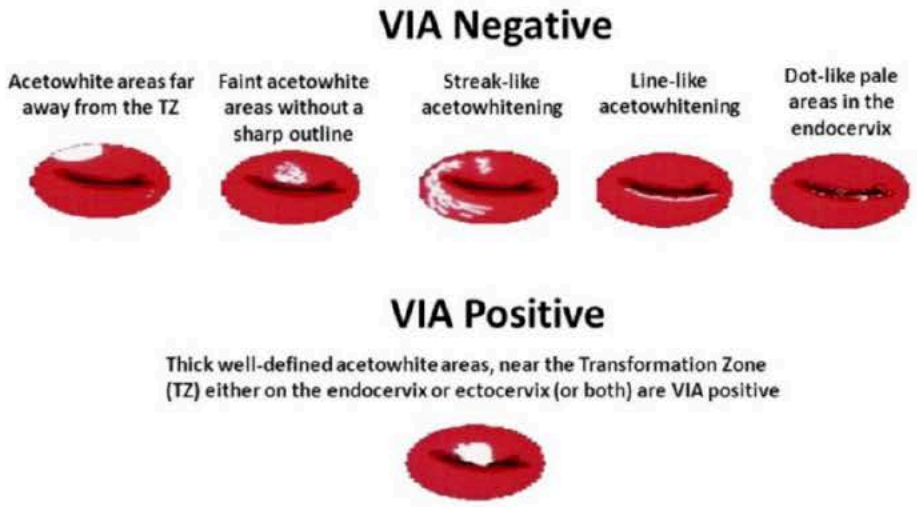
Review article

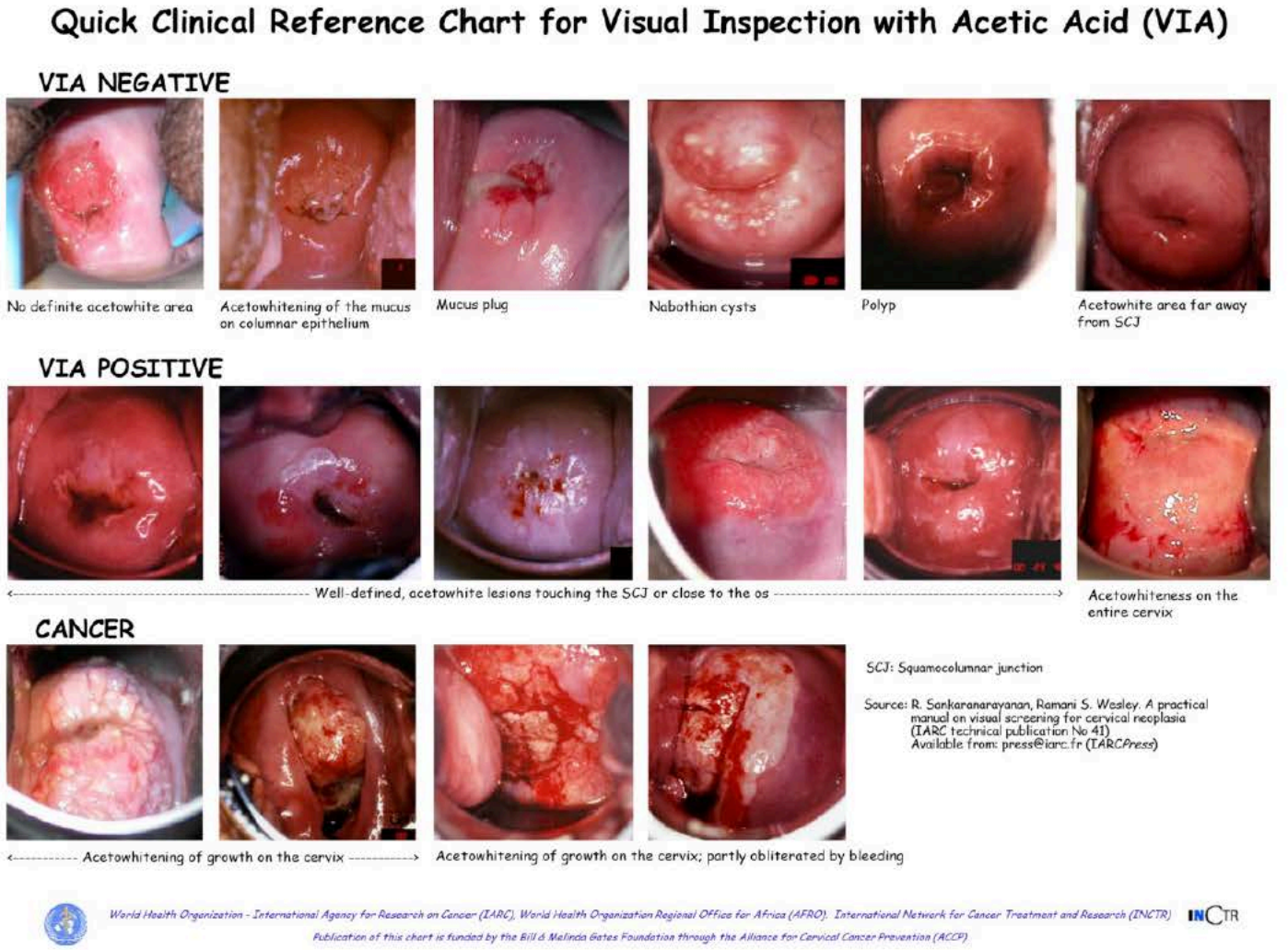
Cervical cancer in Tanzania: A systematic review of current challenges in six domains

Ava S. Runge[a,*], Megan E. Bernstein[a], Alexa N. Lucas[a], Krishnansu S. Tewari[b]

Gynecol Oncol Rep 2019;29:40-47.

Visual Inspection with Acetic Acid Charts for Healthcare Provider Training





Runge AS et al. *Gynecol Oncol Rep* 2019;29:40-47.

Cervical Cancer Screen-and-Treat in Northern Tanzania

Runge AS et al. *Gynecol Oncol Rep* 2019;29:40-47.

RTP RESEARCH TO PRACTICE

Recipients of HPV Vaccine During Campaign Launch in Tanzania (April 2018)

Runge AS et al. *Gynecol Oncol Rep* 2019;29:40-47.

RTP
RESEARCH
TO PRACTICE

REVIEW

CURRENT OPINION

Fertility preserving treatment for gynecologic malignancies: a review of recent literature

Katherine Coakley, Juliet Wolford, and Krishnansu S. Tewari

***Curr Opin Obstet Gynecol* 2020;32(1):51-56.**

RTP RESEARCH TO PRACTICE

Original Research ajog.org

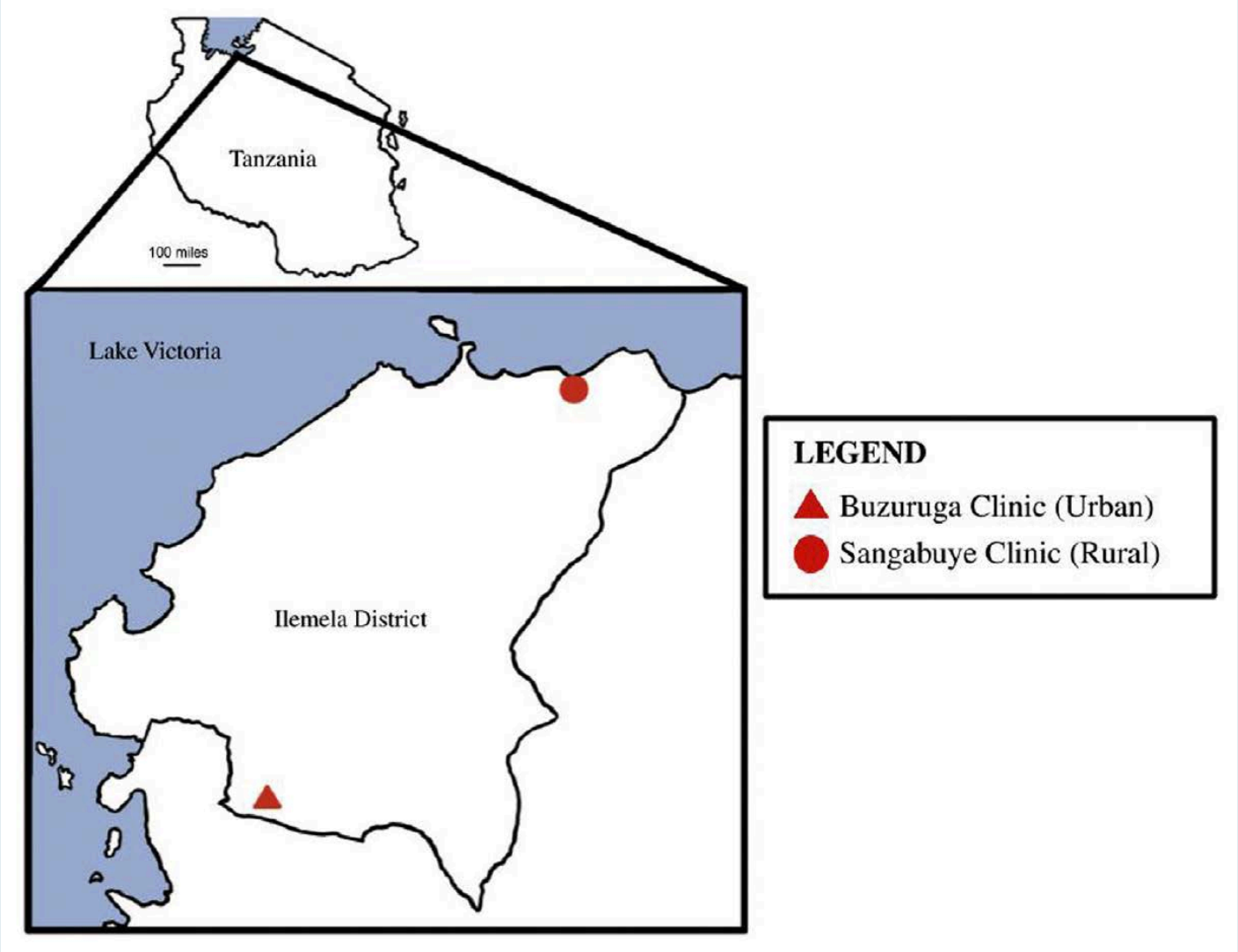
EDUCATION

Implementation of human papillomavirus video education for women participating in mass cervical cancer screening in Tanzania

Emma C. Cooper, BS; Justine A. Maher, BA, MPH; Ariana Naaseh, BA; Elizabeth W. Crawford, BA, BS; Justine O. Chinn, BS; Ava S. Runge, BS; Alexa N. Lucas, BS; Danielle C. Zezoff, BS; Kevin R. Bera, BS; Andreea I. Dinicu, BS; Kayla M. White, BS; Sujata E. Tewari, HSD; Anjali Hari, MD; Megan Bernstein, MD; Jenny Chang, PhD; Argyrios Ziogas, PhD; Diana C. Pearre, MD; Krishnansu S. Tewari, MD, FACOG, FACS, FRSM

Am J Obstet Gynecol 2020:S0002-9378(20)30739-0.

Map of Ilemela District Depicting 2 Study Sites: Urban Buzuruga and Rural Sangabuye)



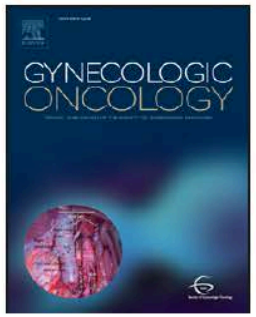
Cooper EC et al. *Am J Obstet Gynecol* 2020:S0002-9378(20)30739-0.

Gynecologic Oncology 157 (2020) 799–809

Contents lists available at ScienceDirect

Gynecologic Oncology

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



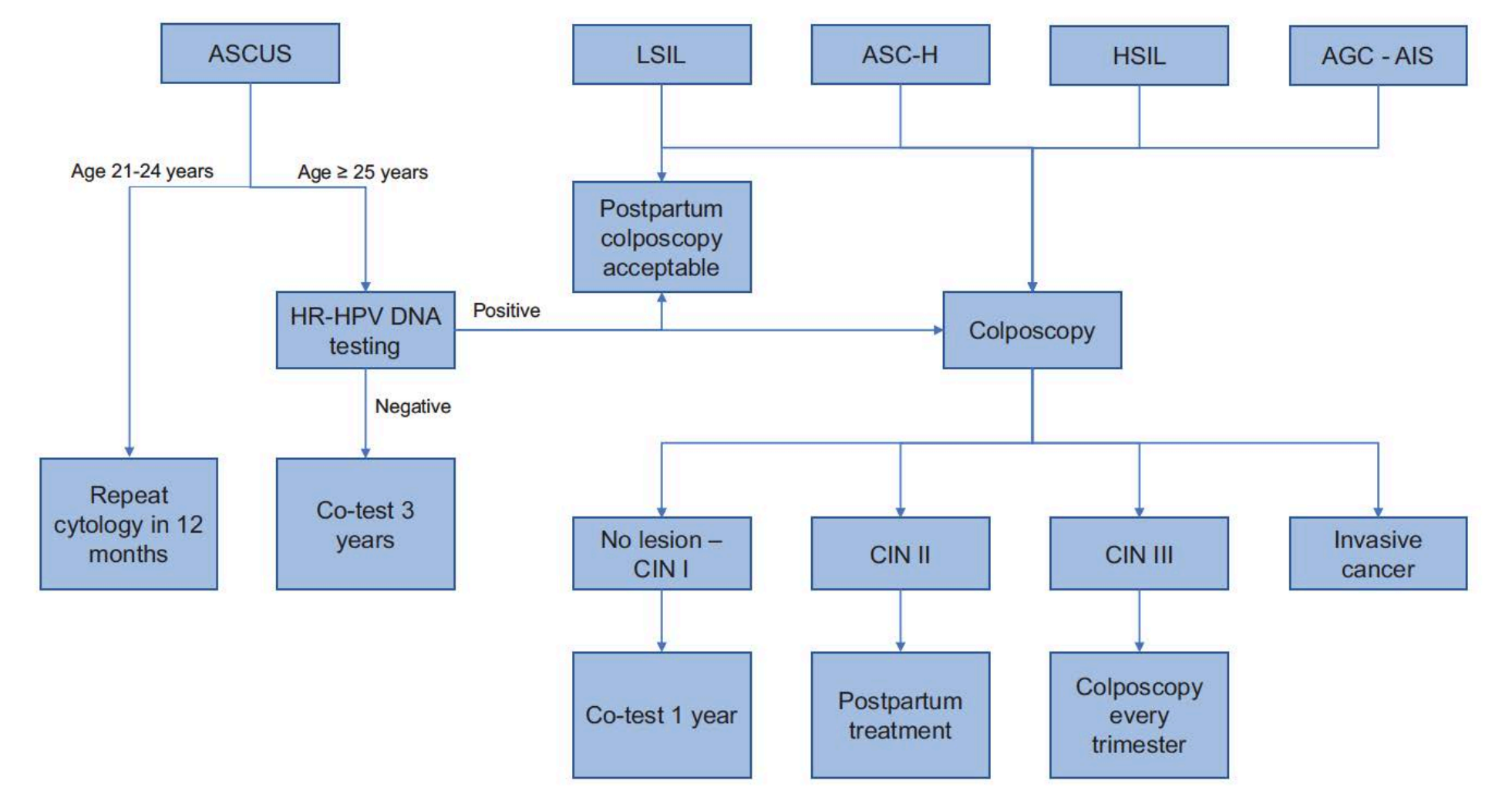
Review Article

Gynecologic cancer in pregnancy

Travis-Riley K. Korenaga, Krishnansu S. Tewari, MD *

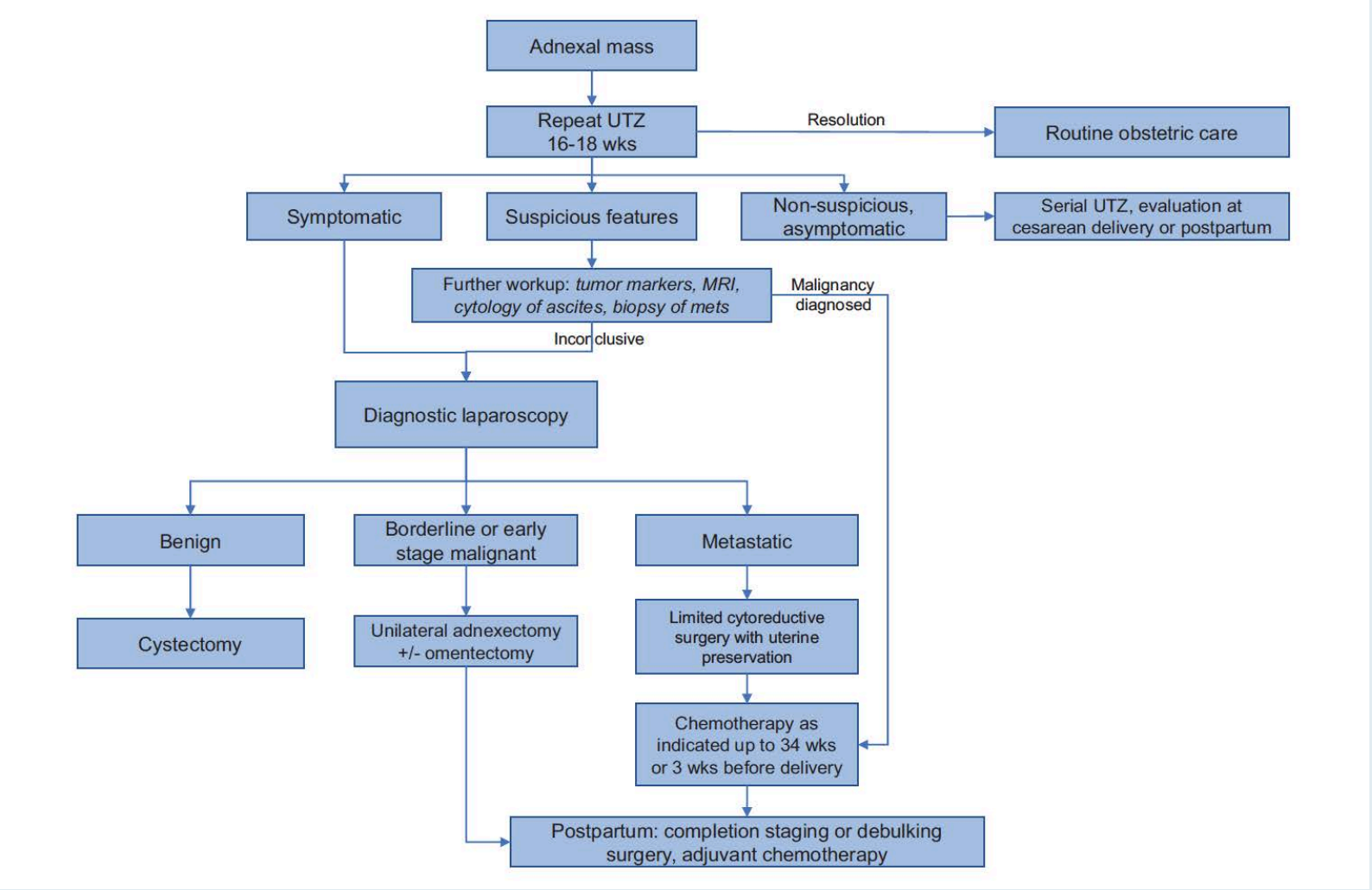
Gynecol Oncol 2020;157(3):799-809.

Algorithm for the Management of Abnormal Cervical Cytology and Cervical Dysplasia in Pregnancy



Korenaga TK, Tewari KS. *Gynecol Oncol* 2020;157(3):799-809.

Algorithm for the Management of the Adnexal Mass and Ovarian Cancer in Pregnancy



Korenaga TK, Tewari KS. *Gynecol Oncol* 2020;157(3):799-809.

RTP RESEARCH TO PRACTICE

REVIEW

CURRENT OPINION

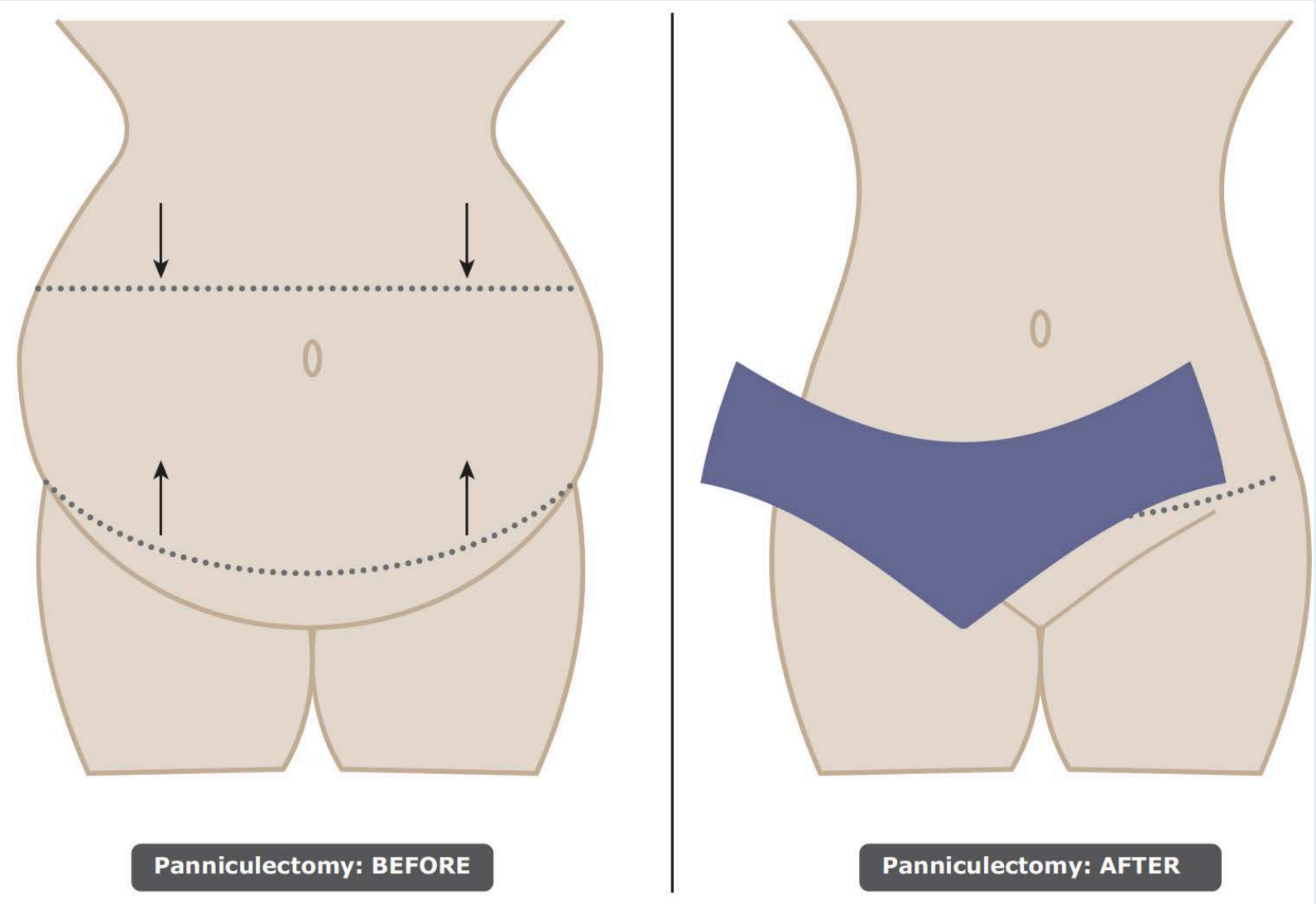
Endometrial cancer in the morbidly obese: a review

Marisa C. Liu, Austin B. Gardner, Juliet E. Wolford, and Krishnansu S. Tewari

***Curr Opin Obstet Gynecol* 2020;32(1):42-50.**

RTP RESEARCH TO PRACTICE

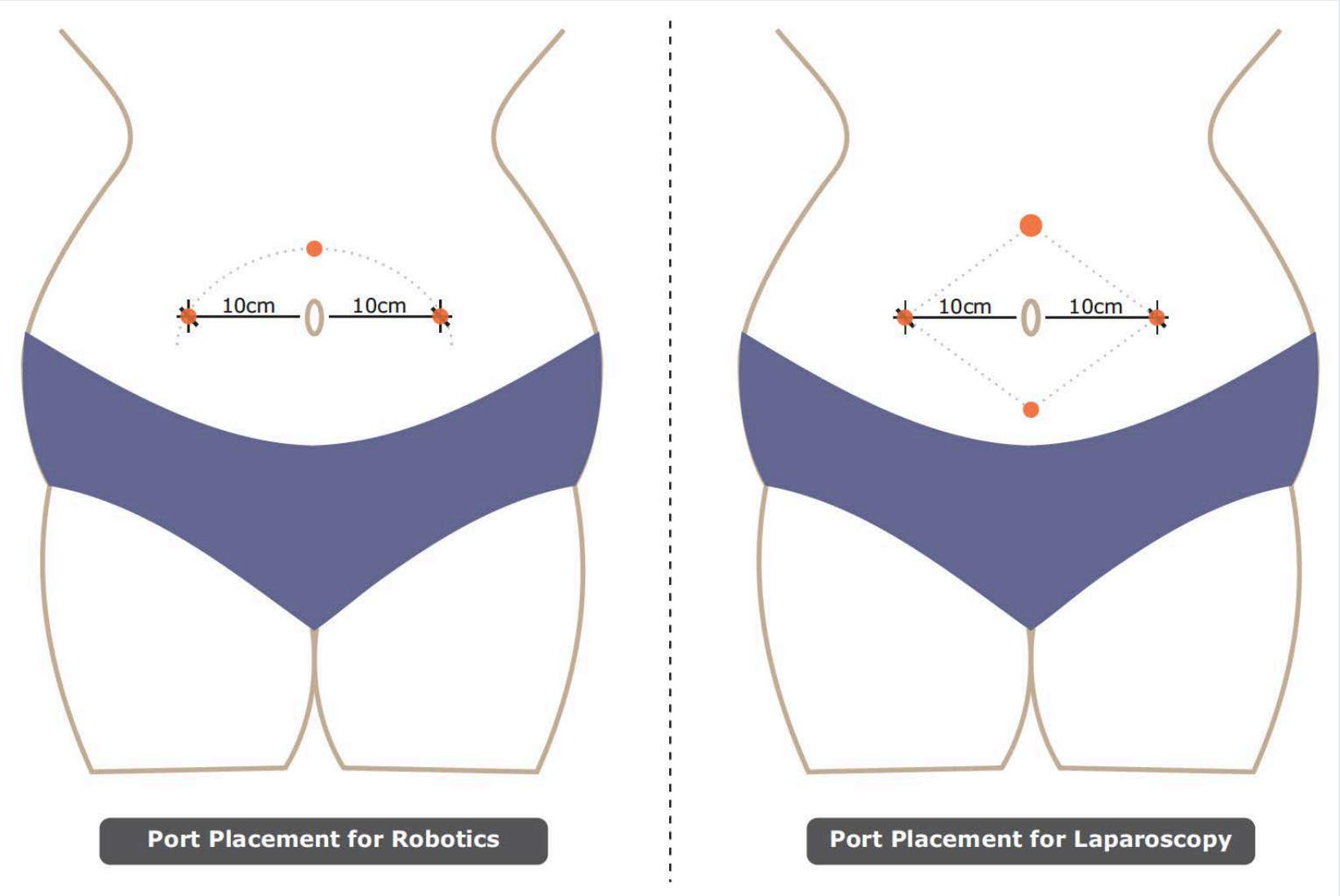
Panniculectomy



Liu MC et al. *Curr Opin Obstet Gynecol* 2020;32(1):42-50.

RTP RESEARCH TO PRACTICE

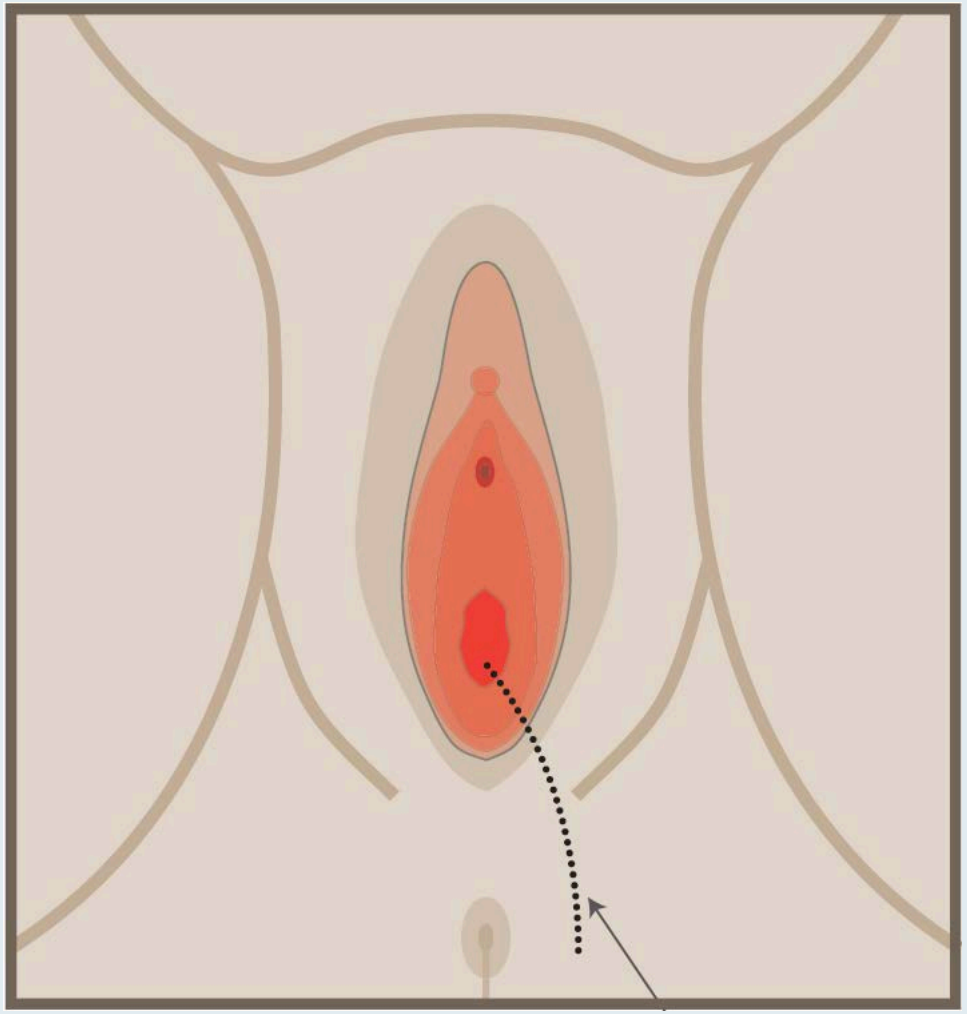
Port Placement



Liu MC et al. *Curr Opin Obstet Gynecol* 2020;32(1):42-50.

RTP RESEARCH TO PRACTICE

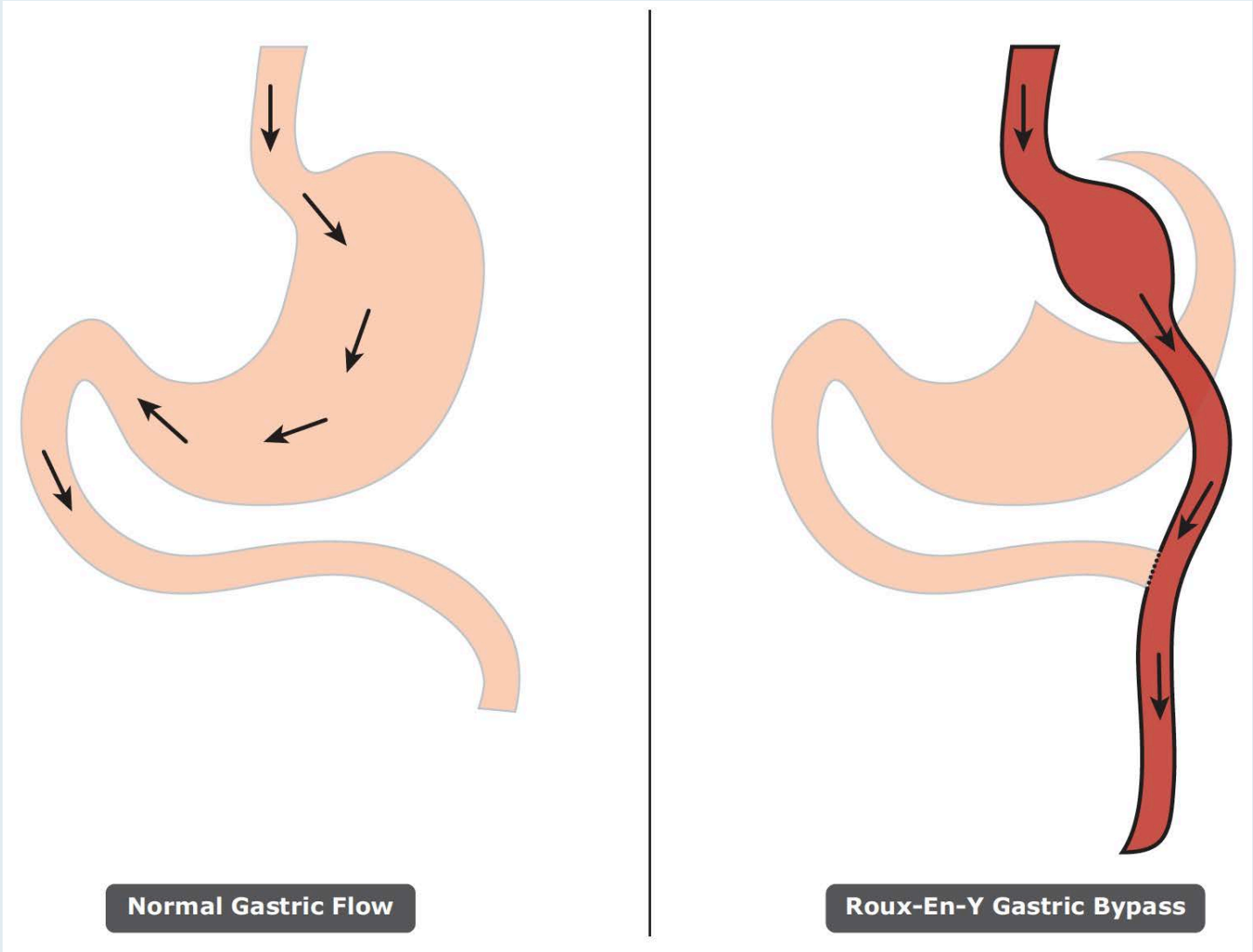
Schuchart Incision



Liu MC et al. *Curr Opin Obstet Gynecol* 2020;32(1):42-50.

RTP RESEARCH TO PRACTICE

Roux-En-Y



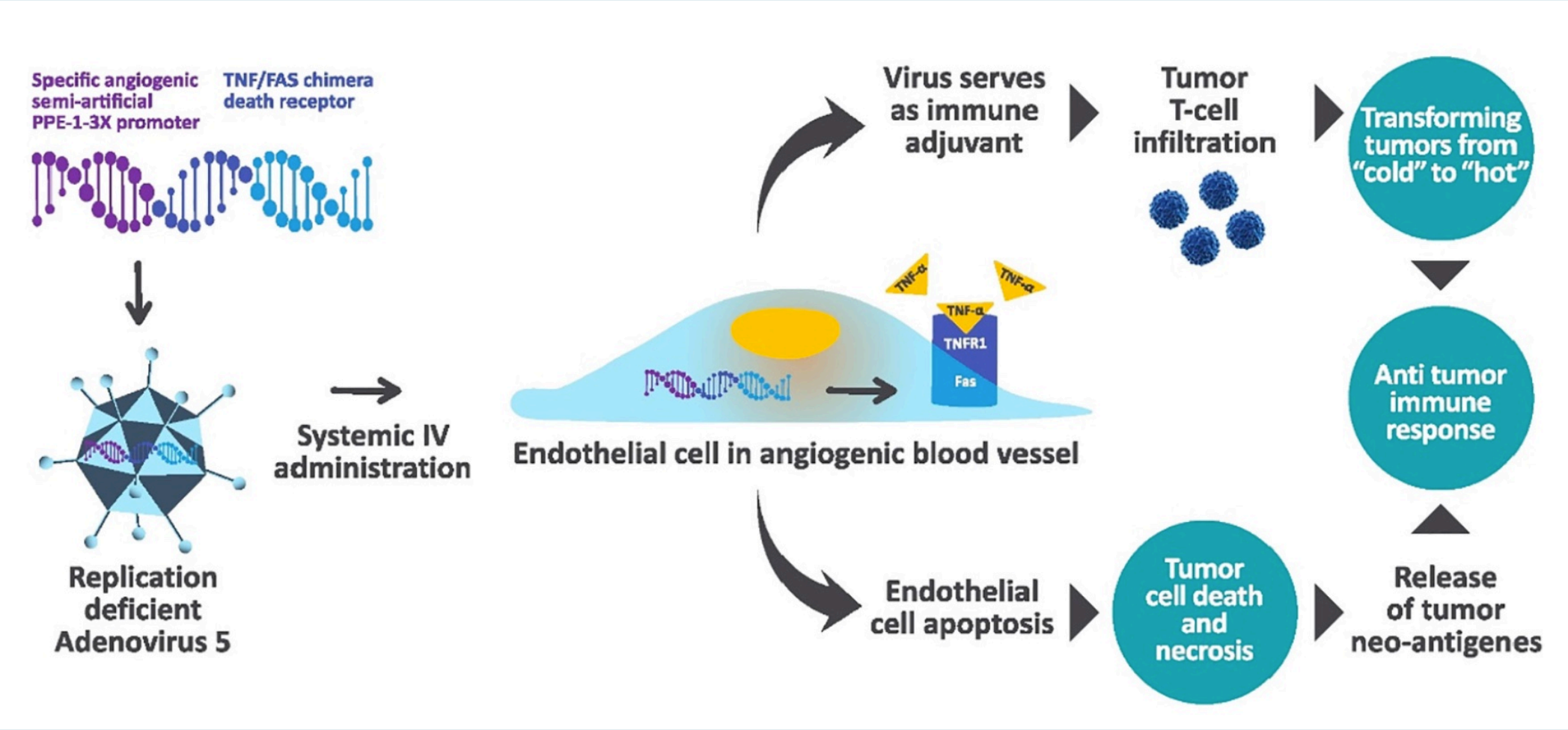
Liu MC et al. *Curr Opin Obstet Gynecol* 2020;32(1):42-50.

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.

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



Arend RC et al. ASCO 2019;Abstract TPS6097.

rapid communications

Carboplatin and Paclitaxel for Advanced Endometrial Cancer: Final Overall Survival and Adverse Event Analysis of a Phase III Trial (NRG Oncology/GOG0209)

David S. Miller, MD[1]; Virginia L. Filiaci, PhD[2]; Robert S. Mannel, MD[3]; David E. Cohn, MD[4]; Takashi Matsumoto, MD[5]; Krishnansu S. Tewari, MD[6]; Paul DiSilvestro, MD[7]; Michael L. Pearl, MD[8]; Peter A. Argenta, MD[9]; Matthew A. Powell, MD[10]; Susan L. Zweizig, MD[11]; David P. Warshal, MD[12]; Parviz Hanjani, MD[13]; Michael E. Carney, MD[14]; Helen Huang, MS[2]; David Cella, PhD[15]; Richard Zaino, MD[16]; and Gini F. Fleming, MD[17]

J Clin Oncol 2020;Sep 29;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Tewari

MODULE 1: Cases and Questions from Drs Freedman, Morganstein and Slomovitz

MODULE 2: Gynecologic Oncology Journal Club with Dr Tewari

- Philip John DiSaia, MD
- Robotic surgery for gynecologic cancers
- Evidence-based treatment paradigms for the management of cervical carcinoma
- GOG-240: Circulating tumor cells in advanced cervical cancer
- Education, screening and current challenges in the management of cervical cancer in Tanzania
- Fertility-preserving treatment for and pregnancy with gynecologic cancers
- Review of endometrial cancer in the morbidly obese
- OVAL: VB-111 combined with paclitaxel for platinum-resistant ovarian cancer
- NRG Oncology/GOG-0209: Carboplatin and paclitaxel for advanced endometrial cancer

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

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 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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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?

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

Meet The Professor with Dr Tewari

MODULE 1: Cases and Questions from Drs Freedman, Morganstein and Slomovitz

MODULE 2: Gynecologic Oncology Journal Club with Dr Tewari

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

MODULE 4: Key Recent Data Sets

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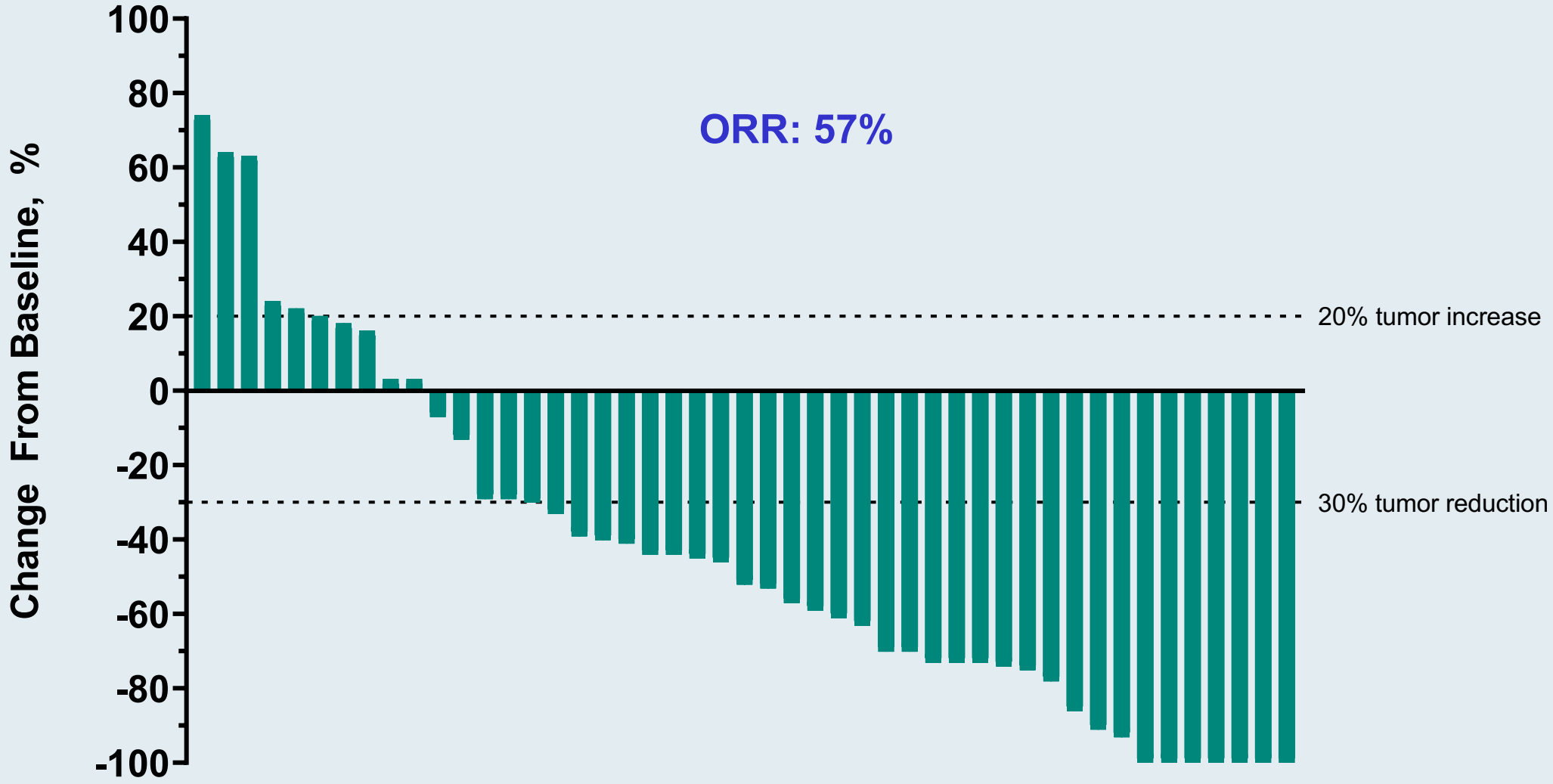
TO PRACTICE

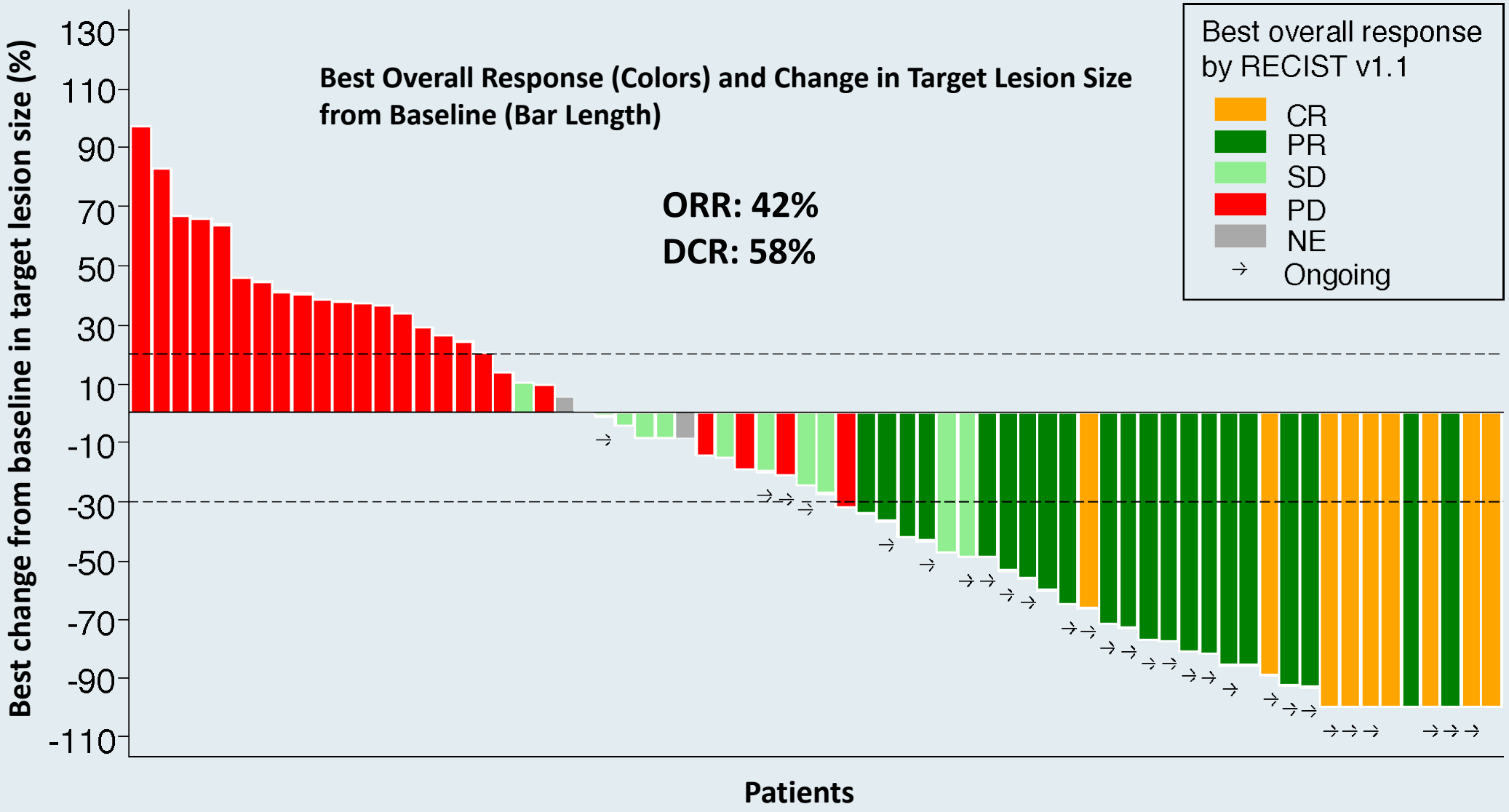
KEYNOTE-158: Best Percentage Change from Baseline in Target Lesion Size with Pembrolizumab Monotherapy in MSI-H Endometrial Cancer



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

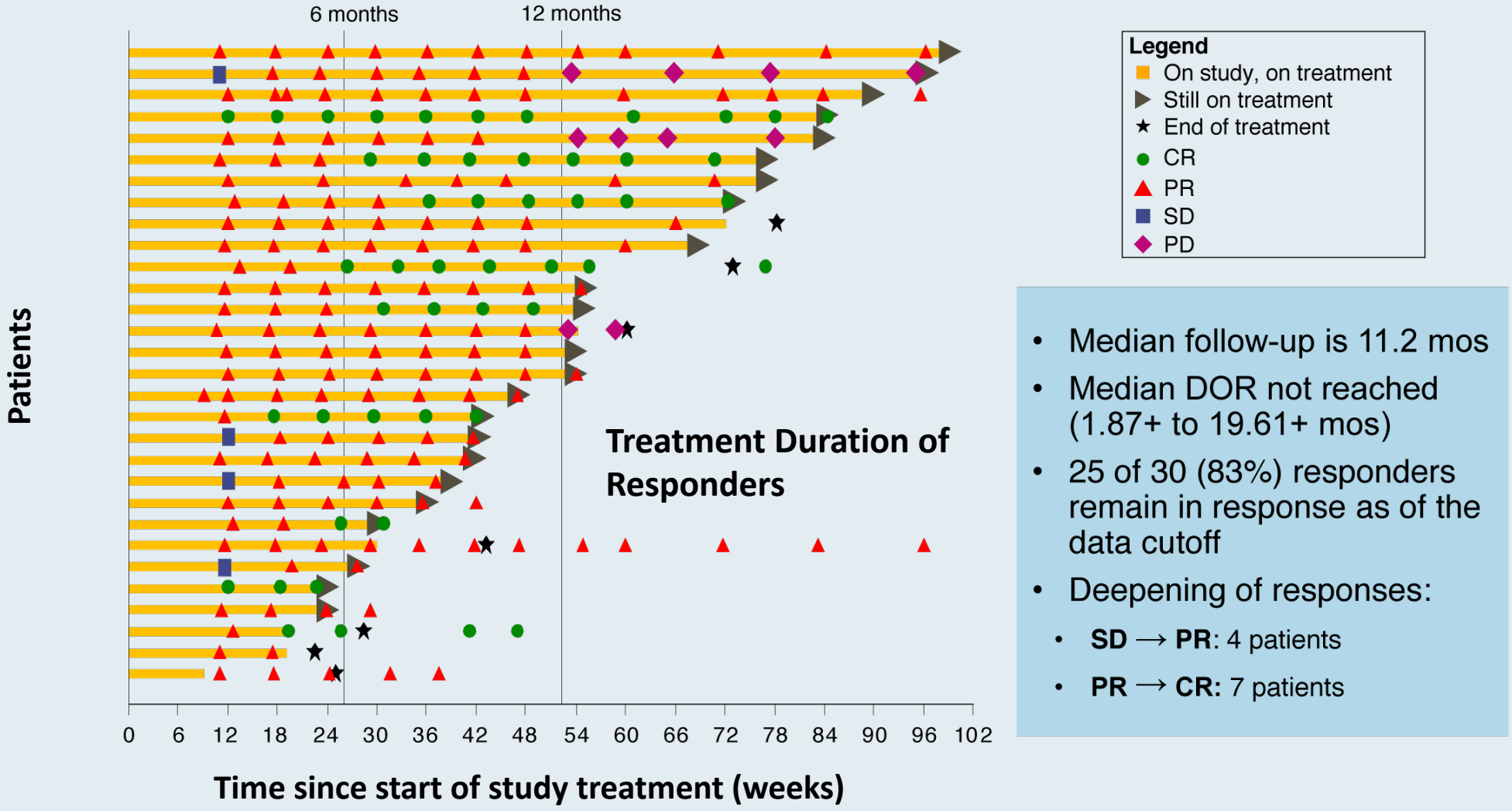
RTP RESEARCH TO PRACTICE

GARNET: Dostarlimab in Recurrent or Advanced dMMR Endometrial Cancer



Oaknin A et al. SGO 2020;Abstract LBA9.

GARNET: Dostarlimab in Recurrent or Advanced dMMR Endometrial Cancer

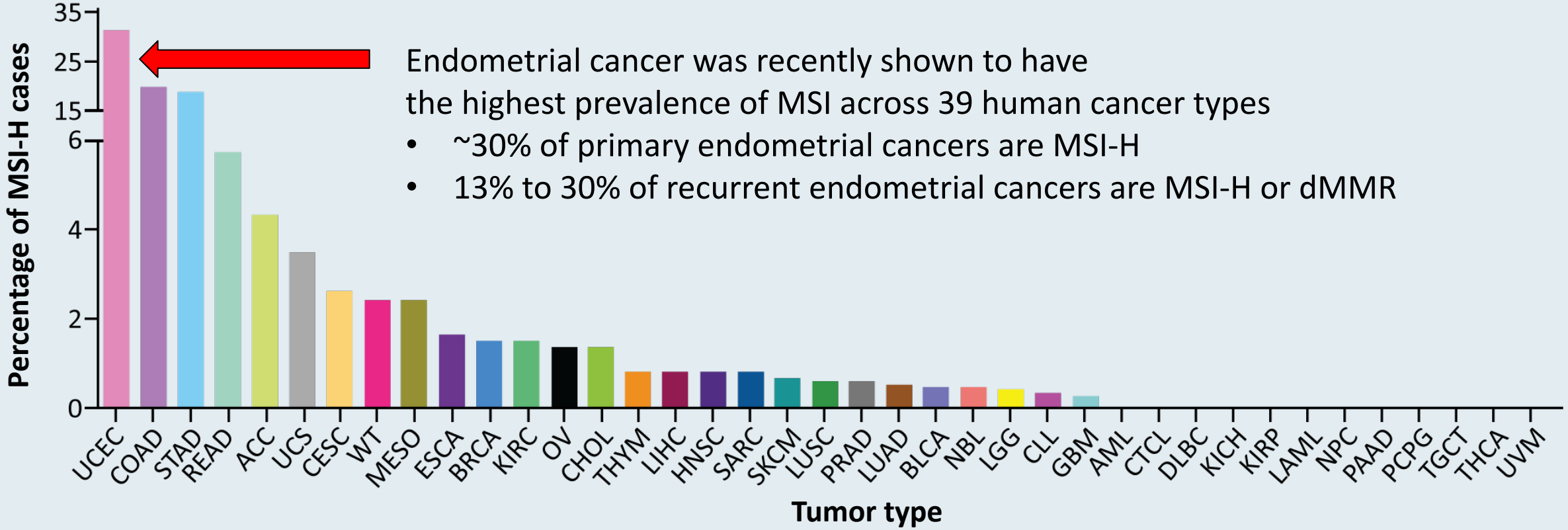


- Median follow-up is 11.2 mos
- Median DOR not reached (1.87+ to 19.61+ mos)
- 25 of 30 (83%) responders remain in response as of the data cutoff
- Deepening of responses:
  - **SD → PR**: 4 patients
  - **PR → CR:** 7 patients

Oaknin A et al. SGO 2020;Abstract LBA9.

MSI-High Across 39 Cancer Types

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



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

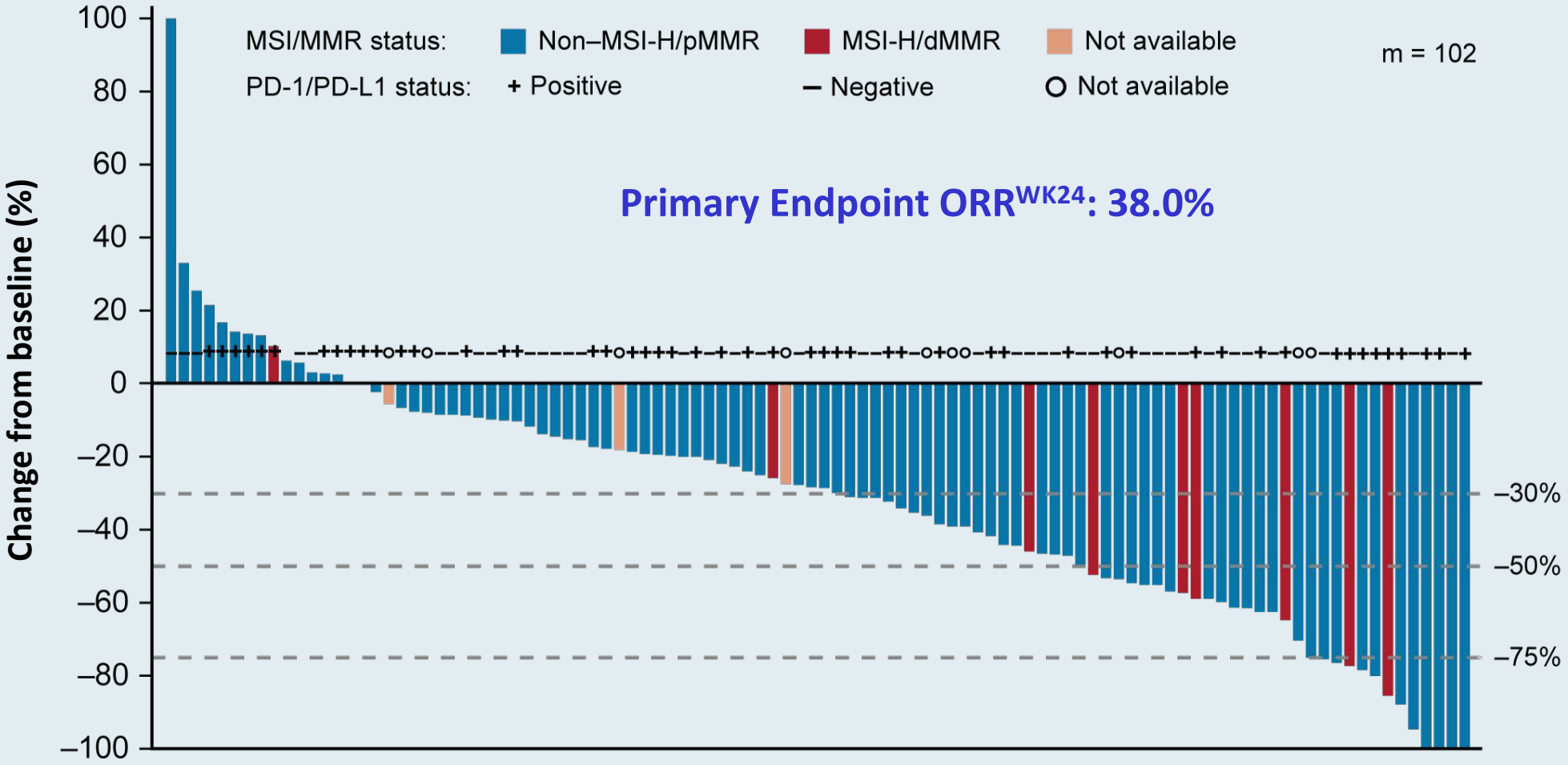
- ~30% of primary endometrial cancers are MSI-H
- 13% to 30% of recurrent endometrial cancers are MSI-H or dMMR

UCEC = uterine corpus endometrial carcinoma

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

RTP RESEARCH TO PRACTICE

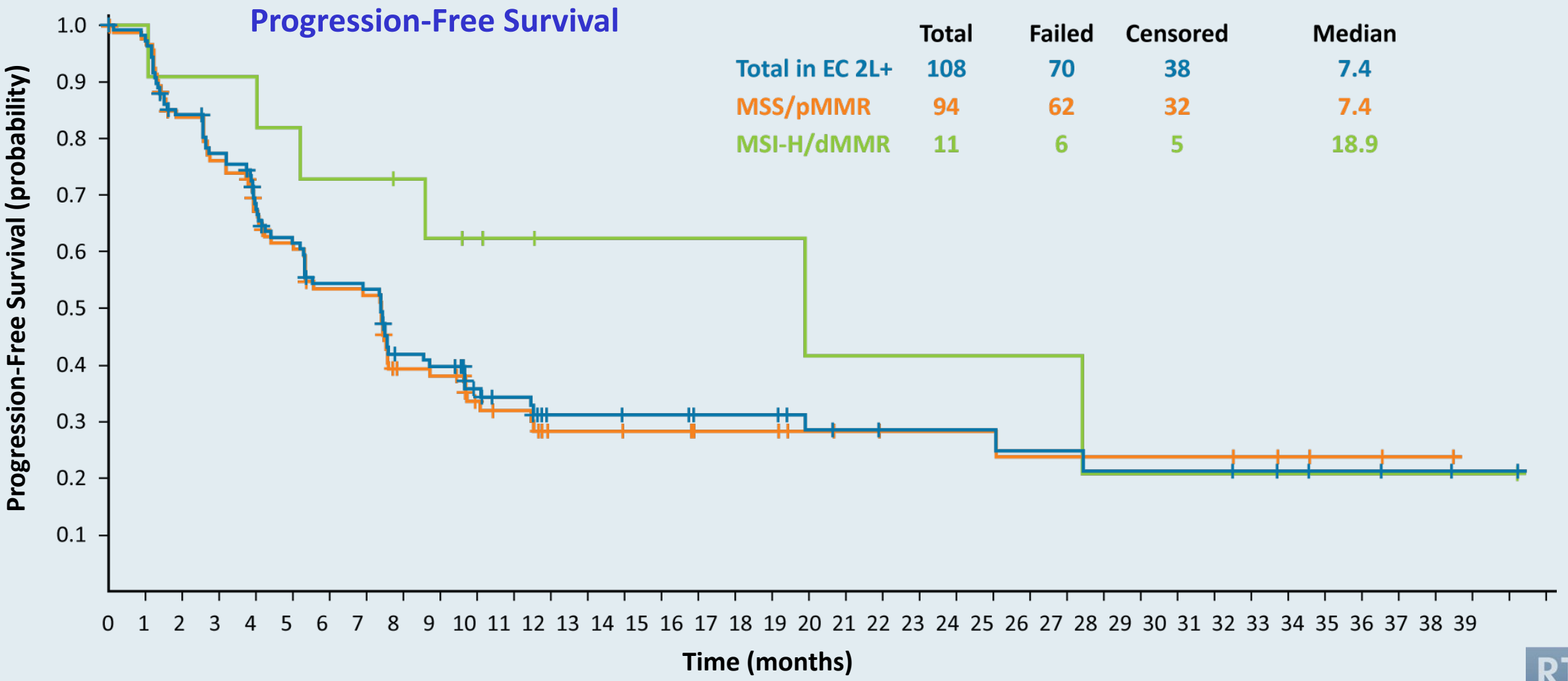
KEYNOTE-146: Pembrolizumab/Lenvatinib in Advanced Endometrial Cancer That Is *Not* MSI-H or dMMR After Disease Progression on Prior Systemic Therapy



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

RTP RESEARCH TO PRACTICE

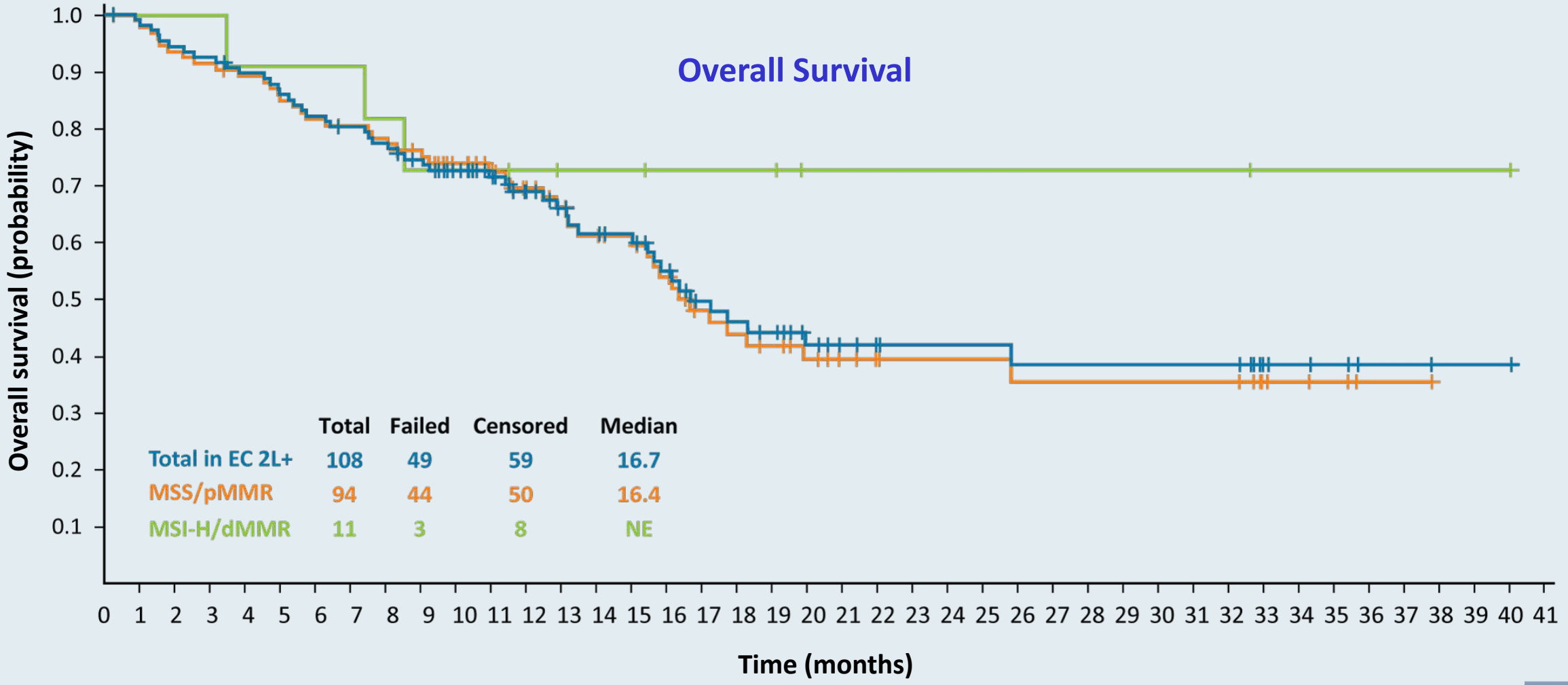
KEYNOTE-146: Pembrolizumab/Lenvatinib in Advanced Endometrial Cancer That Is *Not* MSI-H or dMMR After Progression on Prior Systemic Therapy



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

RTP RESEARCH TO PRACTICE

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



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

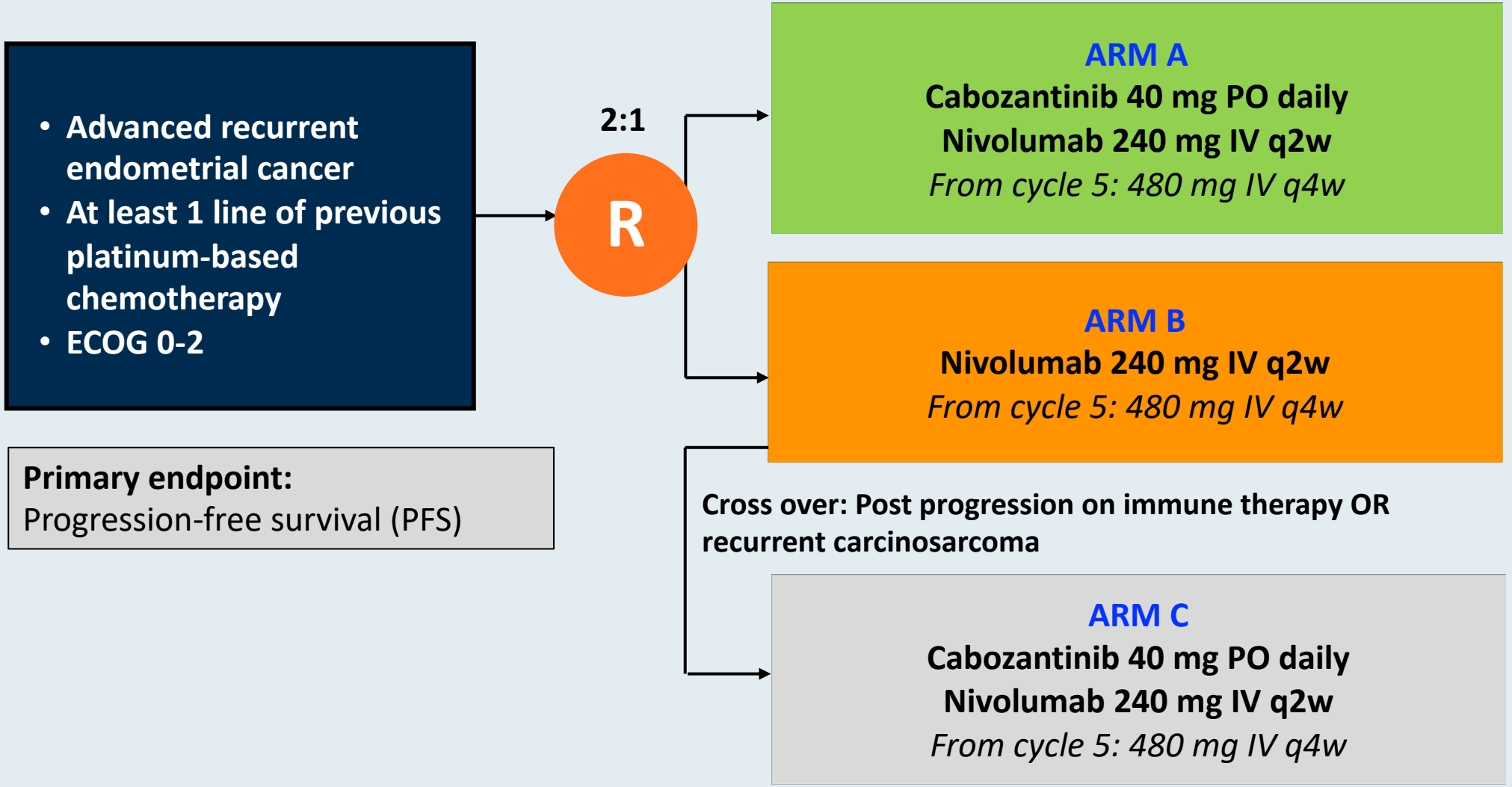
RTP RESEARCH TO PRACTICE

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

Lheureux S et al.

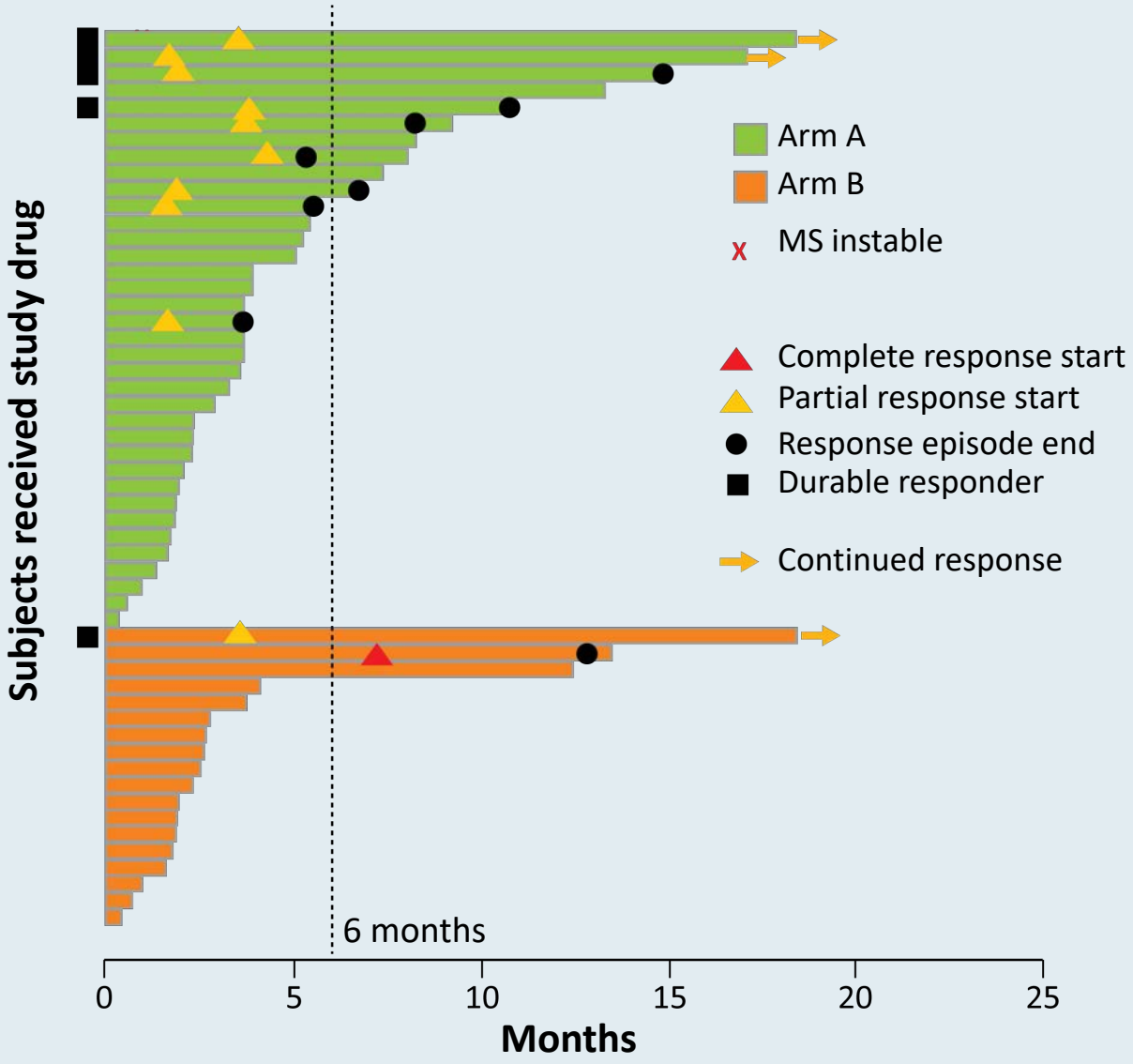
ASCO 2020;Abstract 6010.

NCI 10104 Phase II Study Schema



Lheureux S et al. ASCO 2020;Abstract 6010.

NCI 10104: Response Rate and Duration and Survival Analyses



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

* HR: 0.59, significant

† Immature, 55% events

Lheureux S et al. ASCO 2020;Abstract 6010.

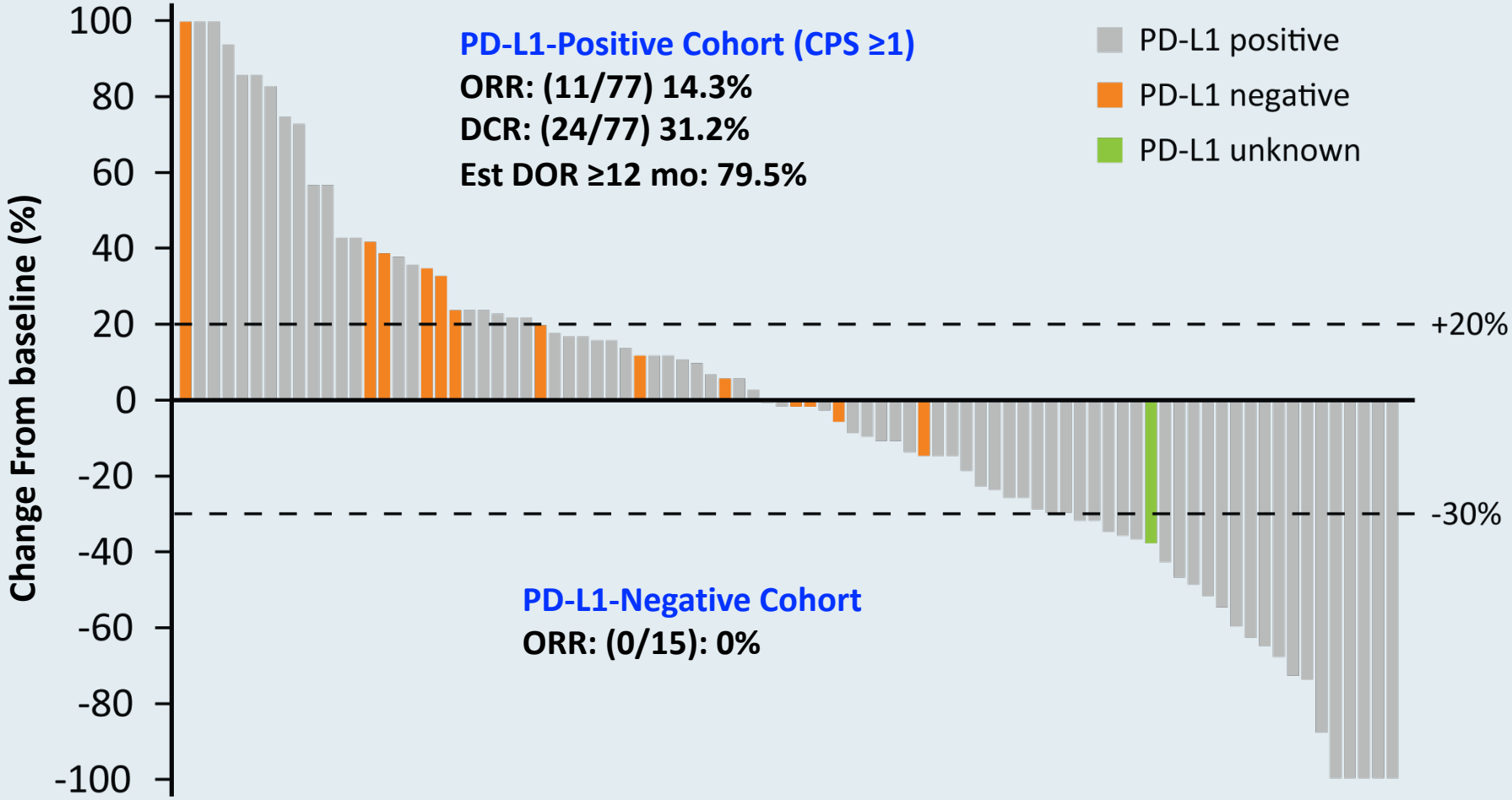
Select Ongoing Phase III Immune Checkpoint Inhibitor Combination Studies

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

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

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

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

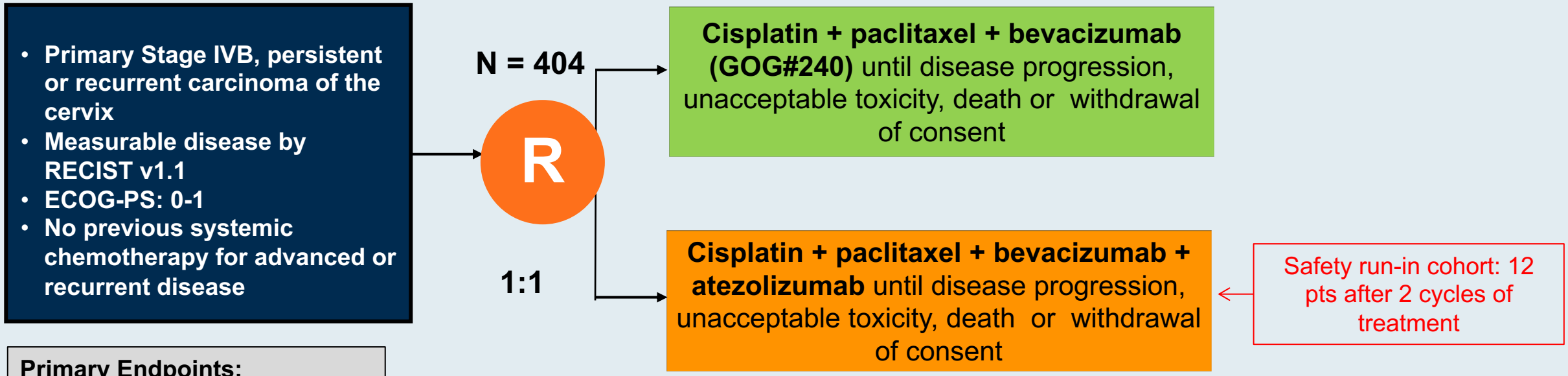


Combined Positive Score (CPS) = PD-L1+ cells (tumor cells, lymphocytes, macrophages) / Total number of tumor cells x 100

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

RTP RESEARCH TO PRACTICE

BEATcc Phase III Randomized Front-Line Trial of Atezolizumab



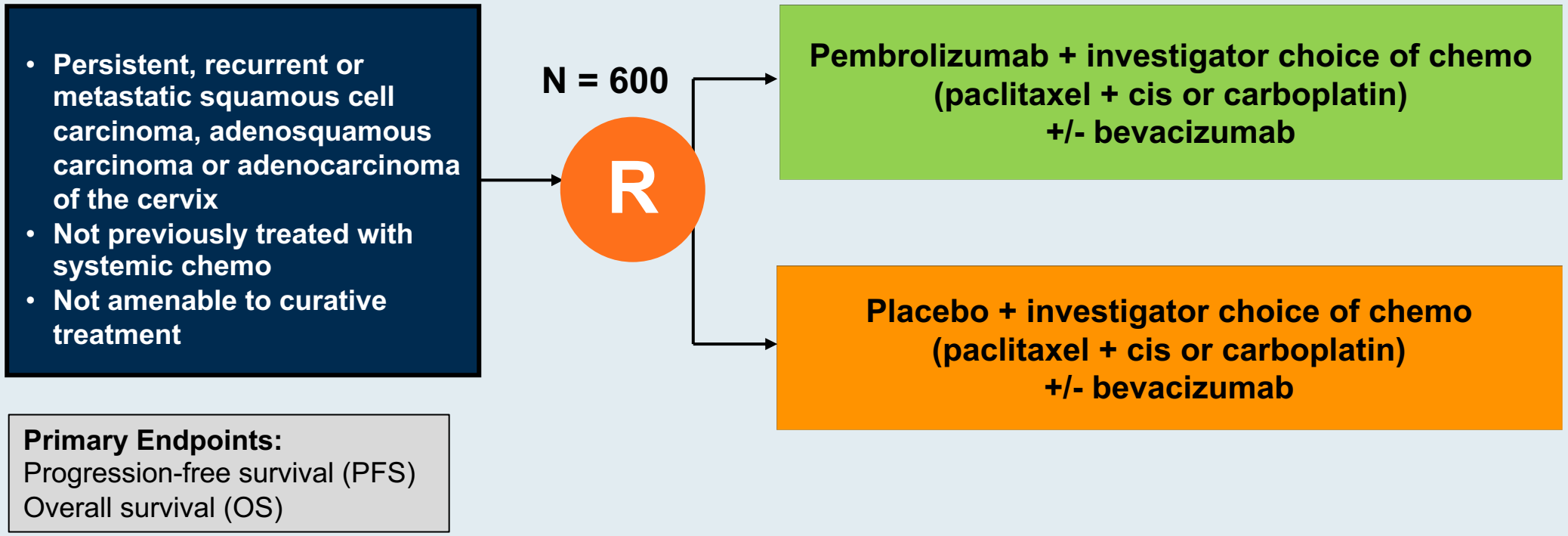
Primary Endpoints:
Overall survival (OS)
Secondary Endpoints:
- PFS
- ORR
- DOR
- Safety
- HR-QOL

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

ClinicalTrials.gov Identifier: NCT03556839

Courtesy of Krishnansu S Tewari, MD

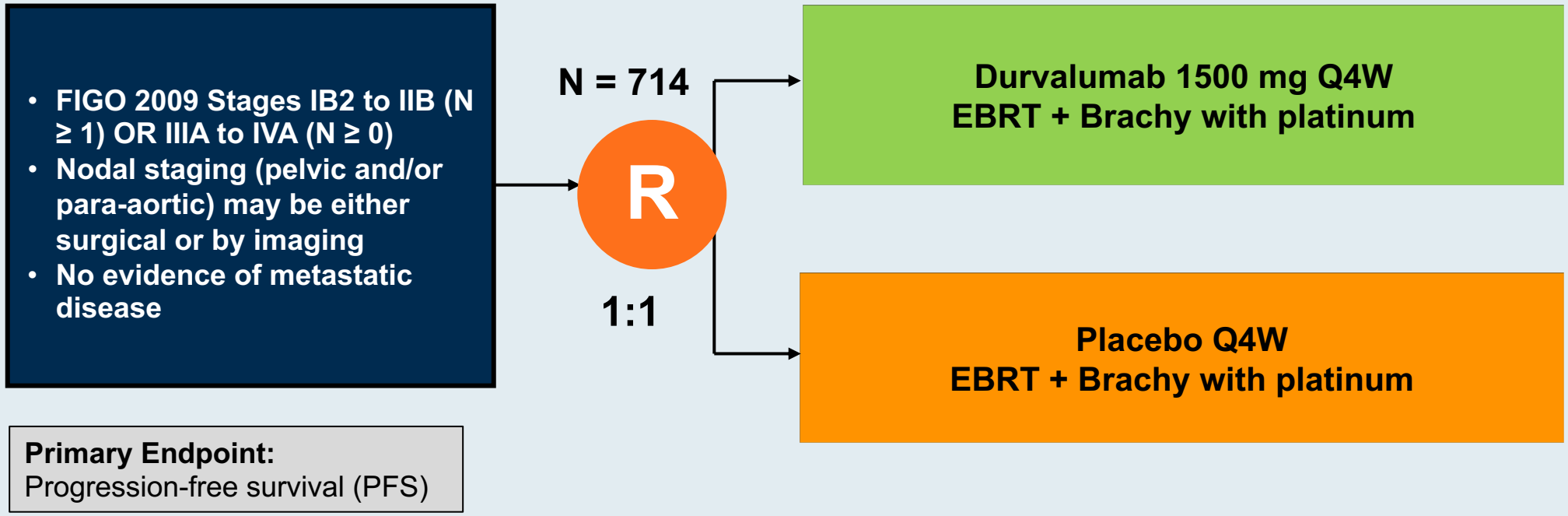
KEYNOTE-826 Phase III Schema



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

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

CALLA Phase III Schema



Primary Endpoint:
Progression-free survival (PFS)

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

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

FDA-Approved Indications for Immunotherapy in Ovarian Cancer

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

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

2020 ASCO ovarian cancer genetics guidelines re MMR testing:

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

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

Courtesy of Ursula Matulonis, MD

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

Matulonis UA et al.

ASCO 2020;Abstract 6005.

KEYNOTE-100 Phase II, 2-Cohort Study Schema

Patients (N = 376)

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

Key exclusion criteria

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

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

Total enrollment: n = 285

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

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

Total enrollment: n = 91

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

Matulonis UA et al. ASCO 2020;Abstract 6005.

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

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

Matulonis UA et al. ASCO 2020;Abstract 6005.

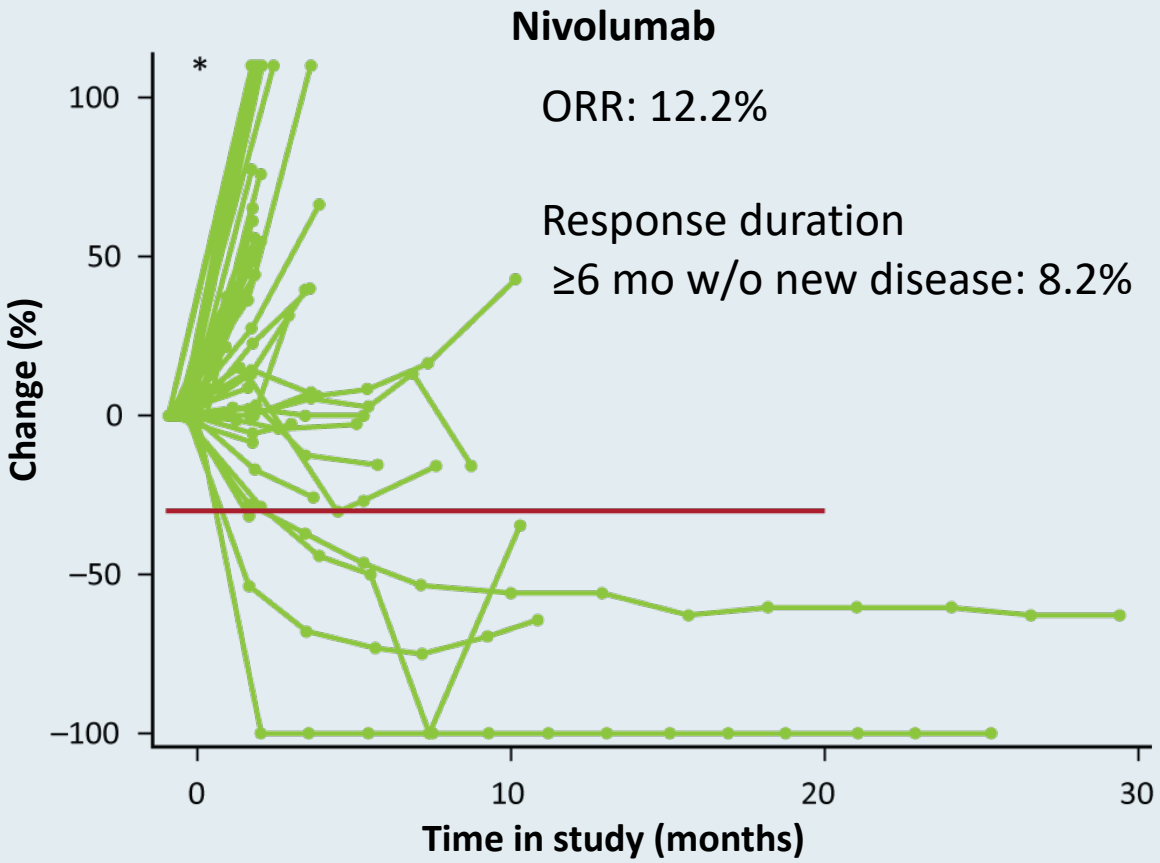
JAVELIN Ovarian 200: Avelumab Alone or in Combination with Pegylated Liposomal Doxorubicin (PLD) versus PLD Alone in Platinum-Resistant or Refractory OC

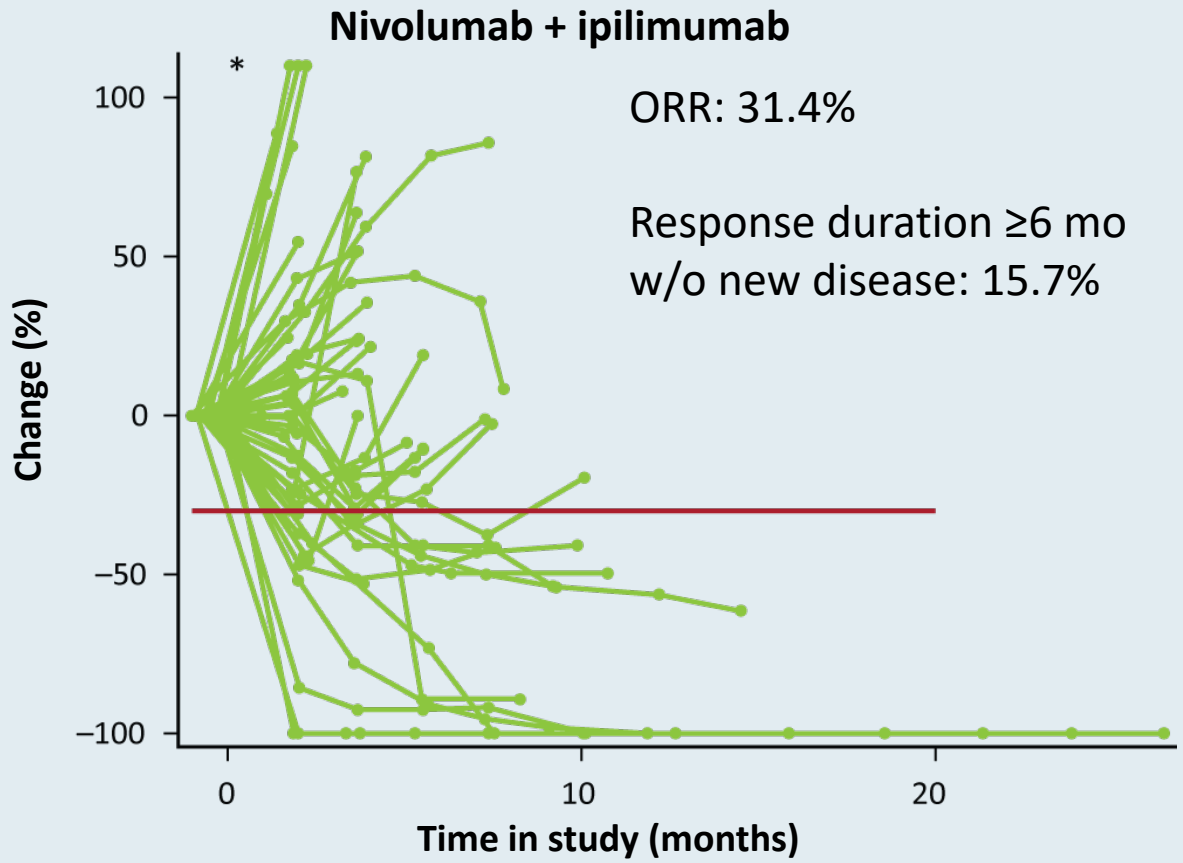
	Avelumab (n = 188)		Avelumab + PLD (n = 188)		PLD (n = 190)	
All patients						
Median OS	11.8 mo		15.7 mo		13.1 mo	
	HR: 1.14, *p* = 0.83		HR: 0.80, *p* = 0.21		Reference	
Median PFS	1.9 mo		3.7 mo		3.5 mo	
	HR: 1.68, *p* > 0.99		HR: 0.78, *p* = 0.03		Reference	
PD-L1 evaluable	**PD-L1+ (n = 91)**	**PD-L1-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

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

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

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

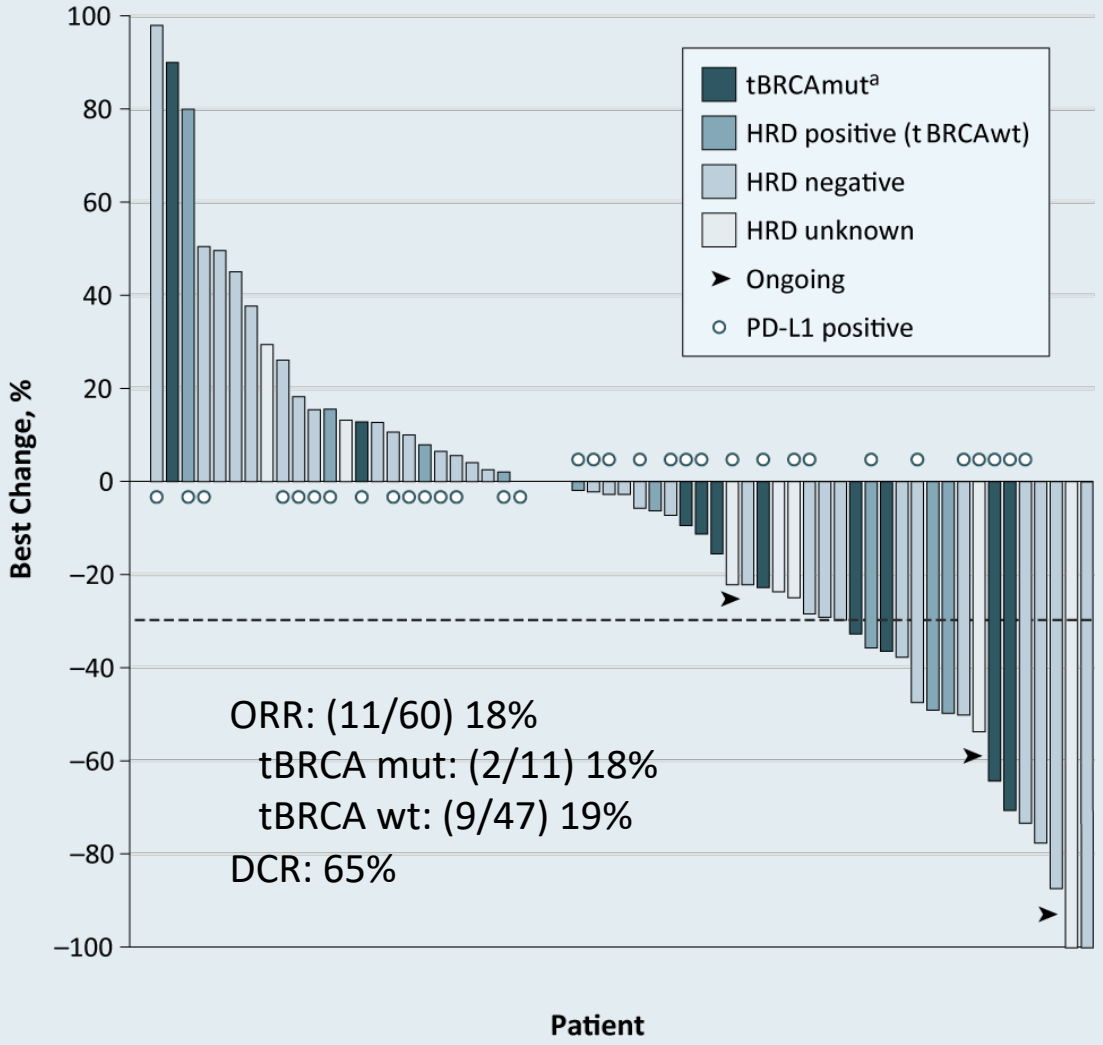


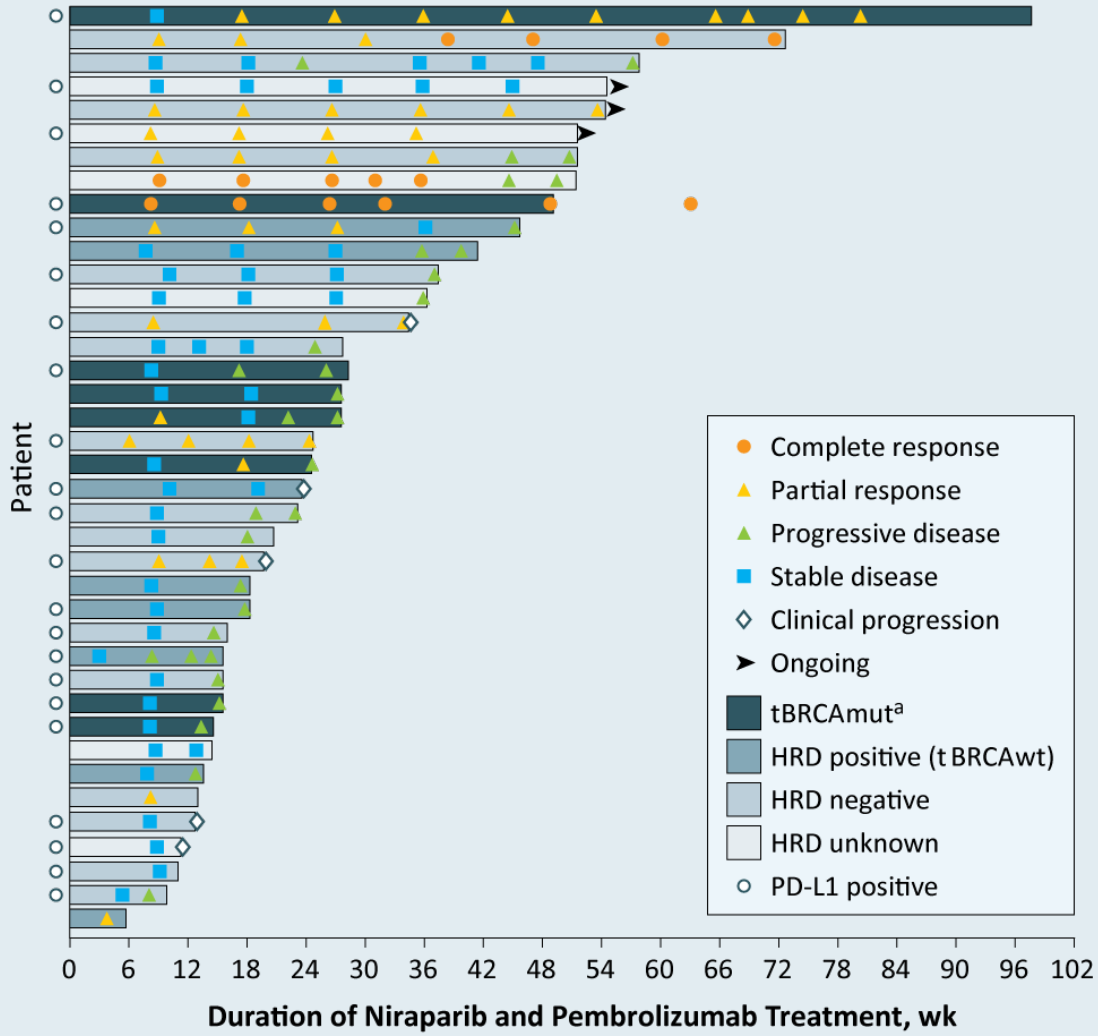


PD-L1 expression was not significantly associated with response in either treatment group

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

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

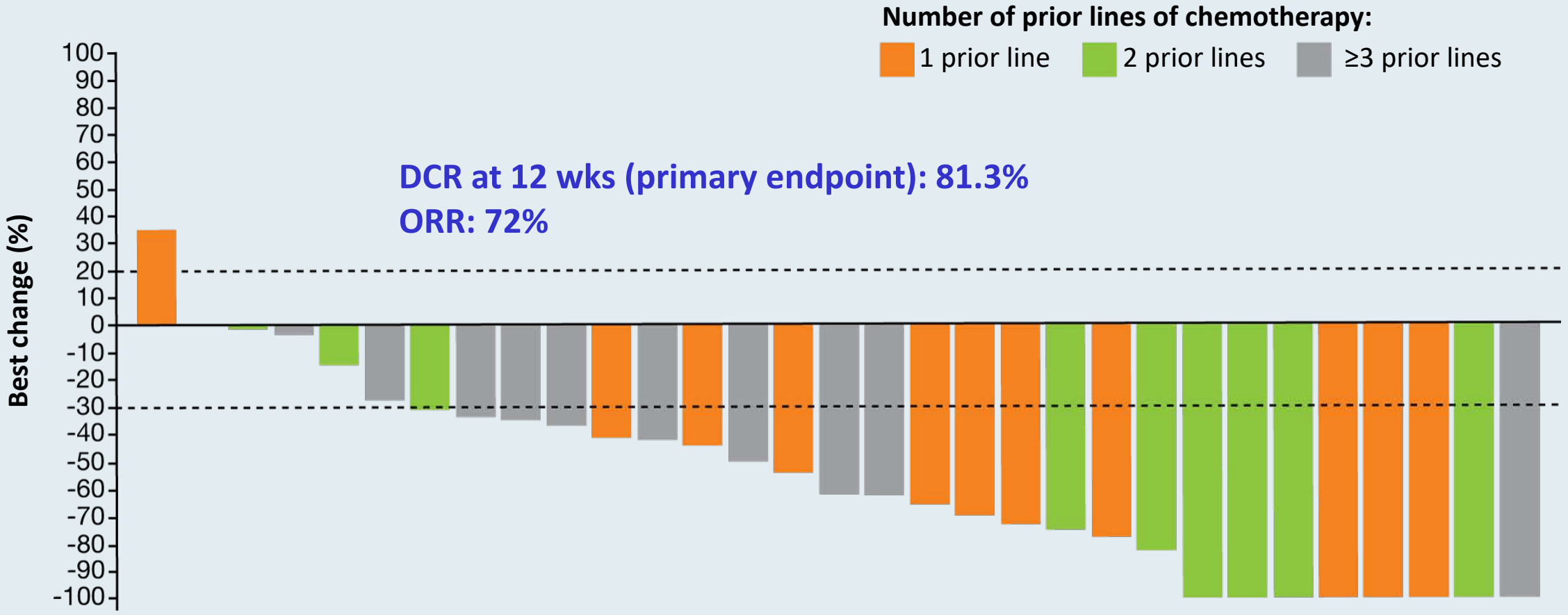




Konstantinopoulos PA, et al. *JAMA Oncol* 2019;5(8):1141-9.

RTP RESEARCH TO PRACTICE

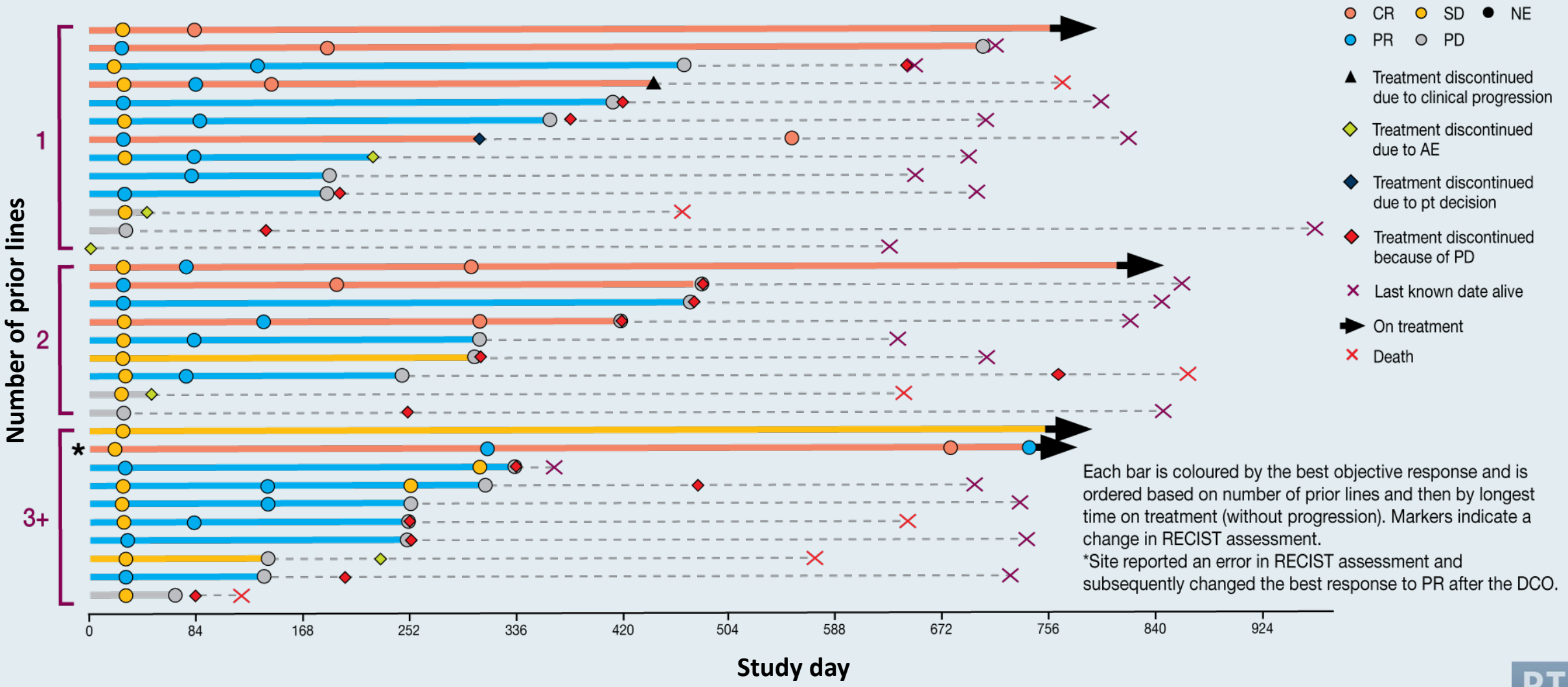
MEDIOLA: A Phase II Study of Olaparib and Durvalumab in gBRCA-Mutated Platinum-Sensitive Relapsed OC



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

RTP RESEARCH TO PRACTICE

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



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

RTP RESEARCH TO PRACTICE

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.

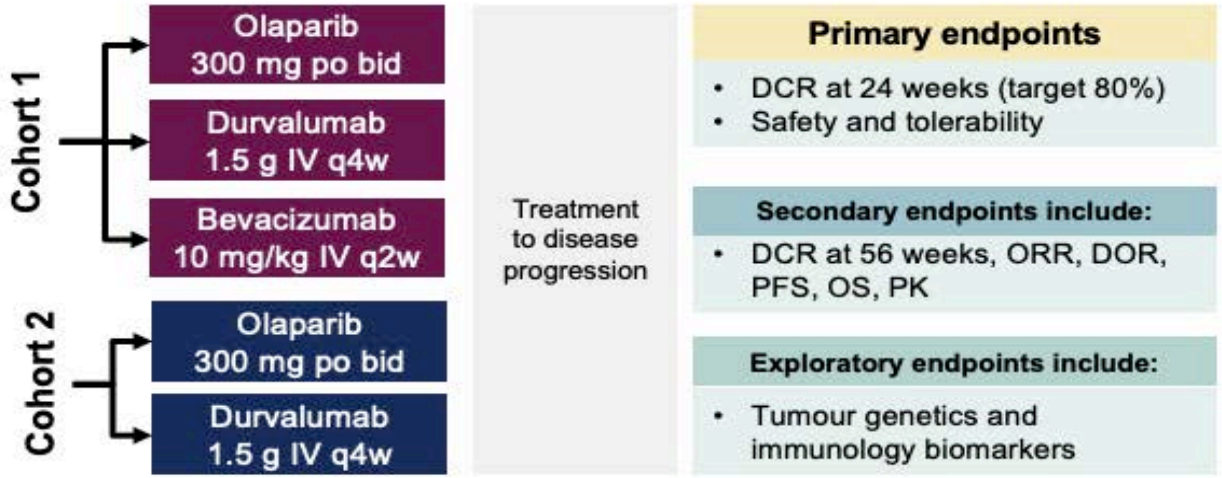
ESMO 2020;Abstract 814MO.

MEDIOLA: gBRCAwt Cohorts

Study Design

Patient population

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



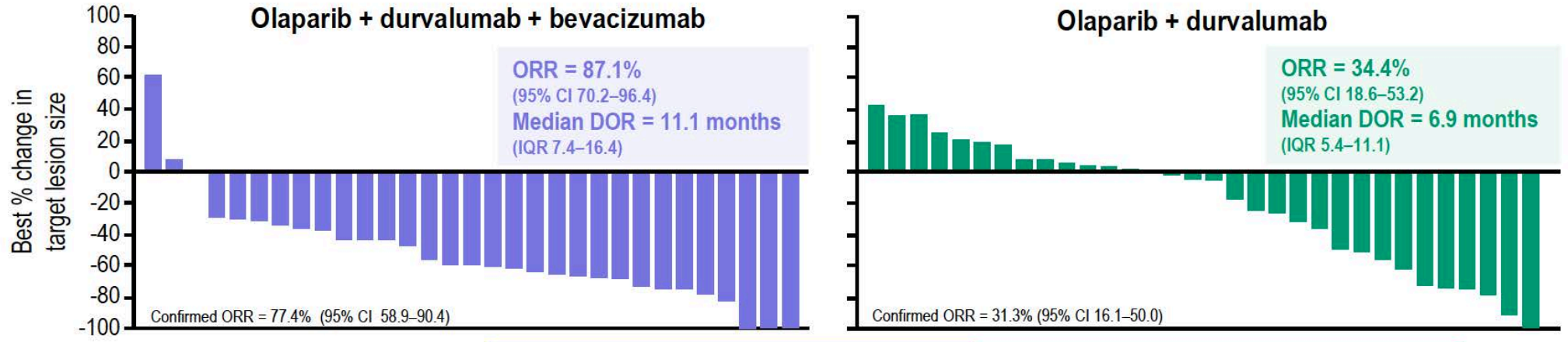
Patient Characteristics

	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

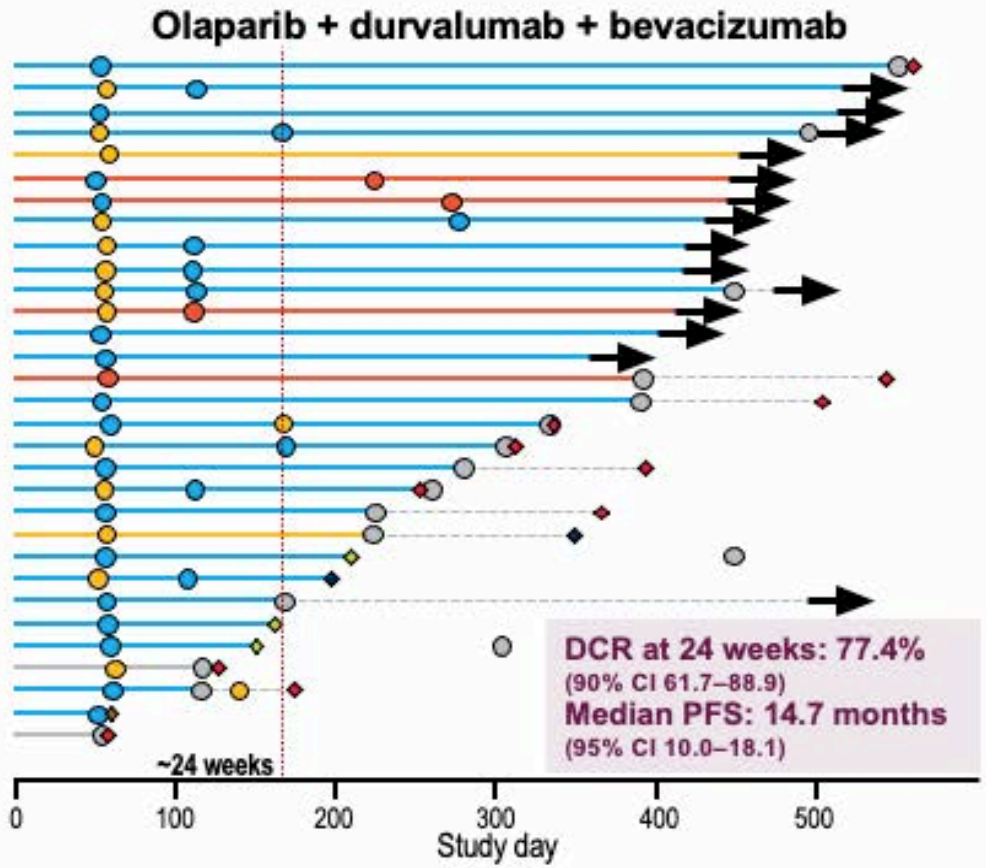
Exploratory analysis suggests ORR with triplet cohort is not dependent on genomic instability status (GIS)

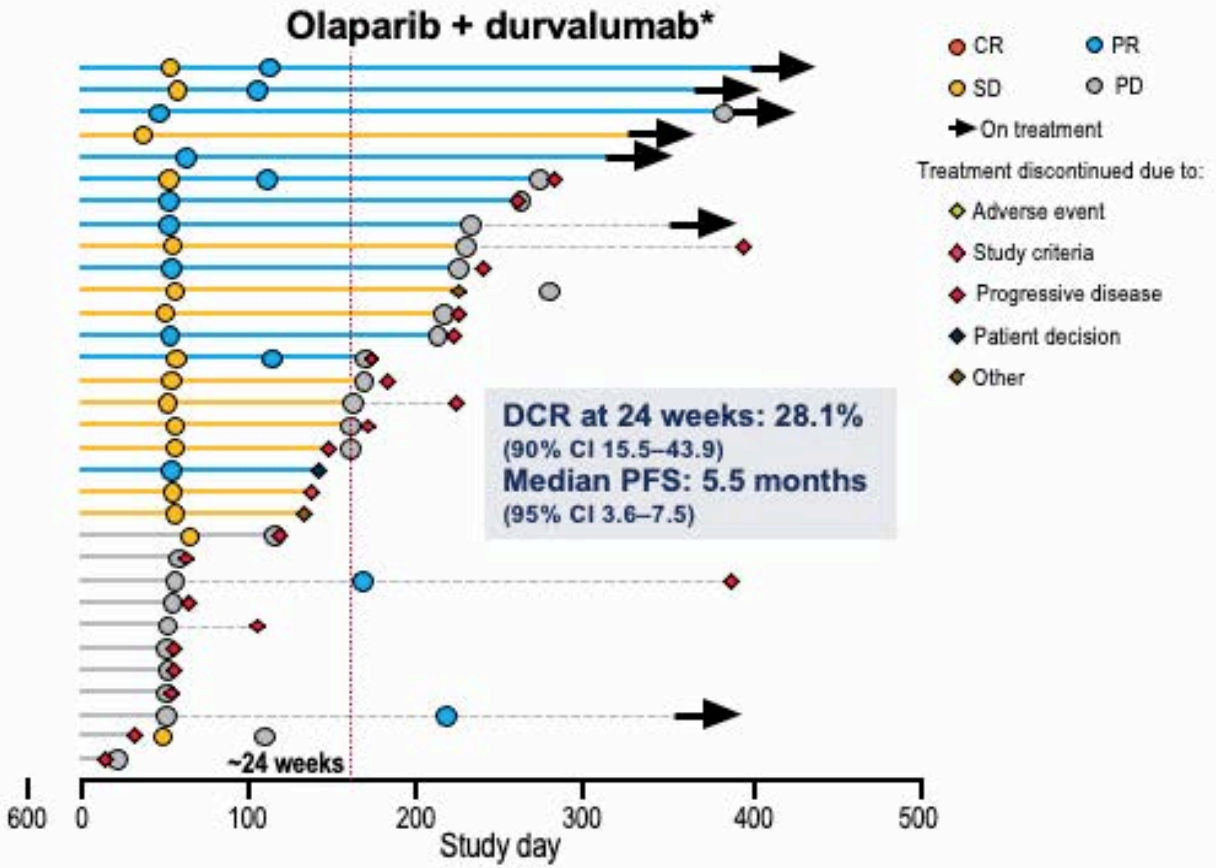


Genomic instability status* subgroup	Olaparib + durvalumab + bevacizumab		Olaparib + durvalumab	
	ORR (95% CI), %	n/N patients	ORR (95% CI), %	n/N patients
GIS-positive	100.0 (69.2–100.0)	10/10	50.0 (18.7–81.3)	5/10
GIS-negative	75.0 (34.9–96.8)	6/8	16.7 (0.4–64.1)	1/6
GIS-unknown	84.6 (54.6–98.1)	11/13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

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

MEDIOLA: TTP or Treatment Discontinuation

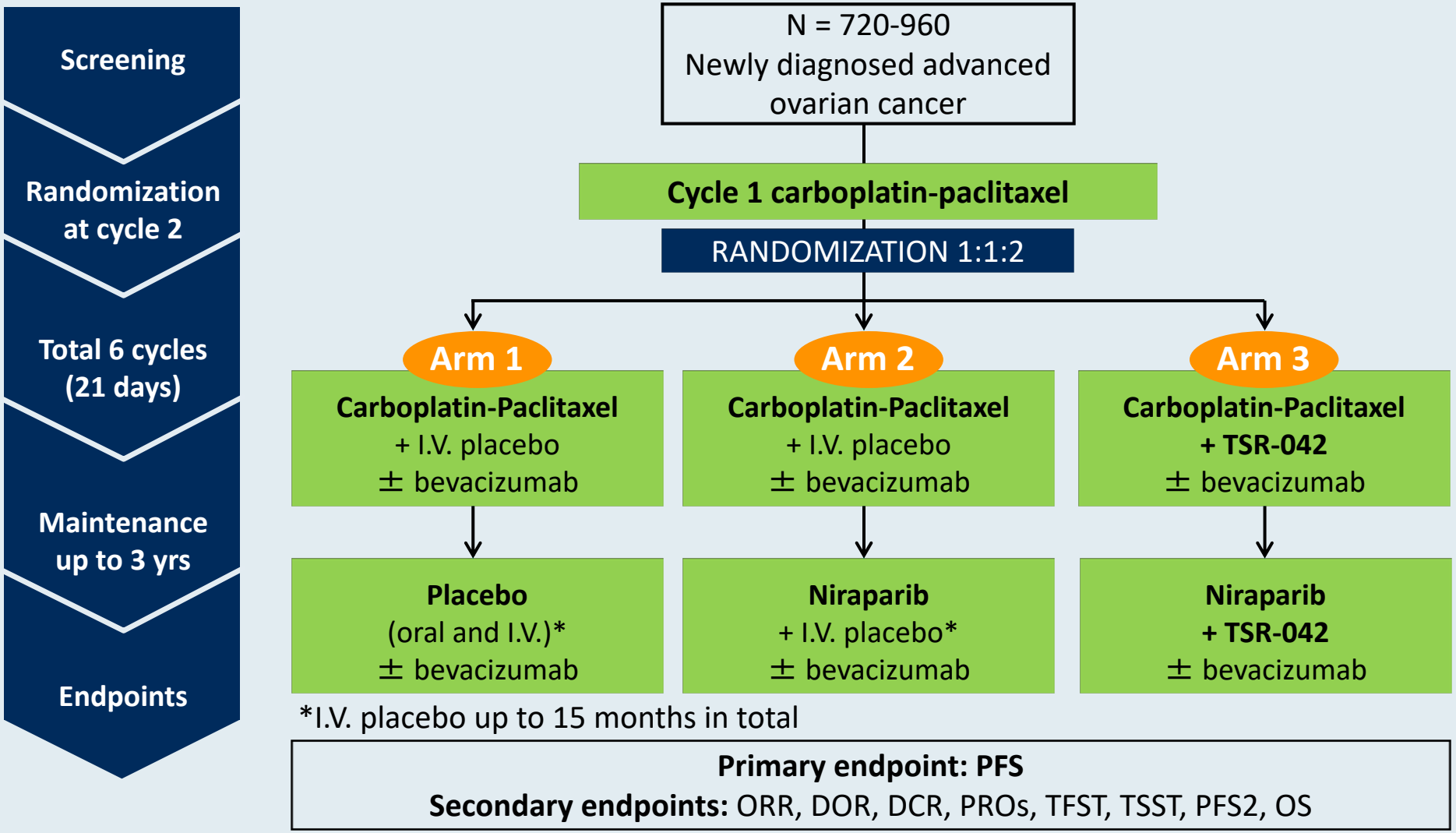




- **Triplet cohort showed high DCT at 24 weeks and a long median PFS**

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

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

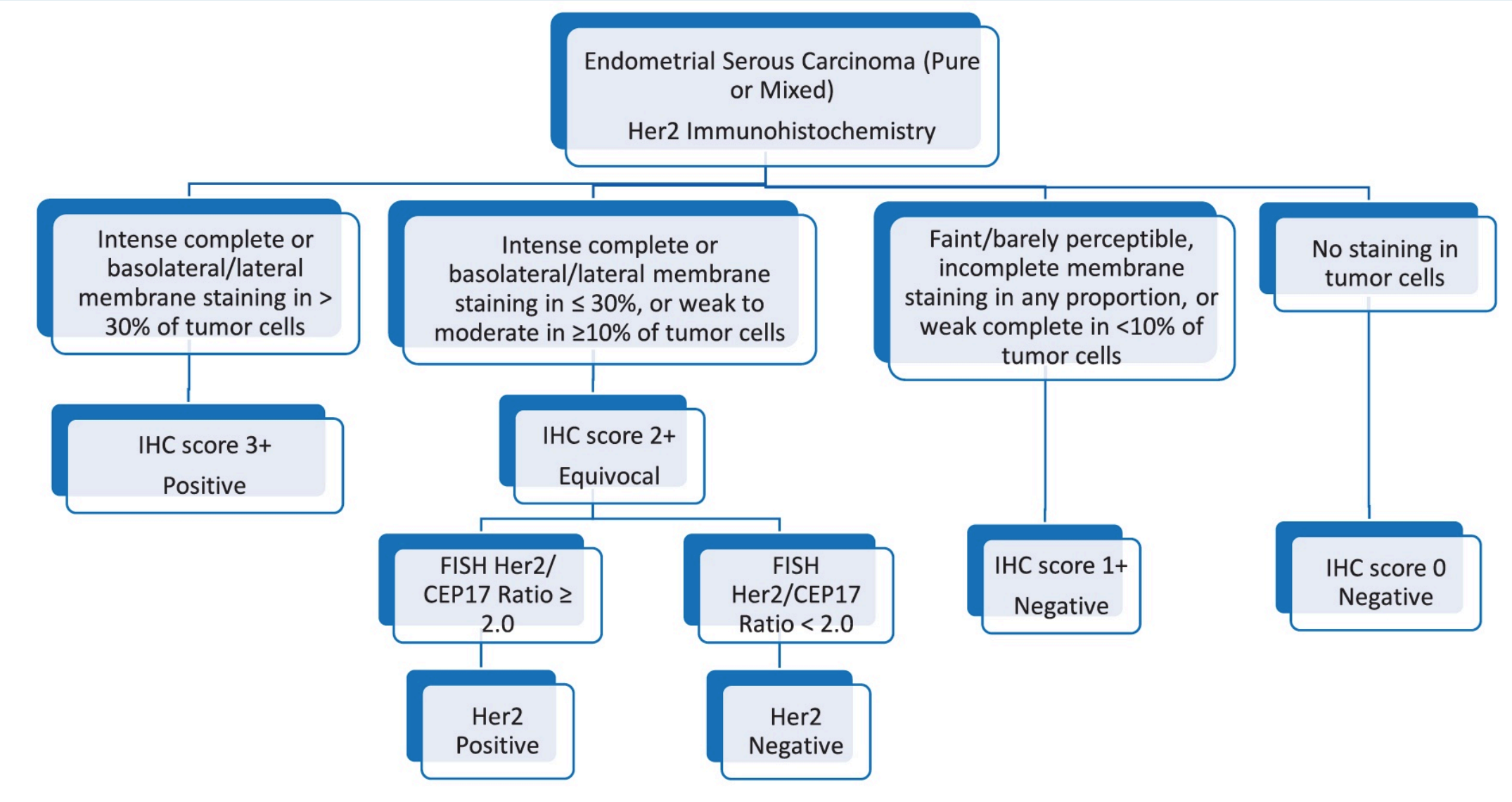
	Breast (ASCO/CAP 2018)[23]	Gastric (ASCO/CAP 2016)[36]	Colorectal (HERACLES Trial)[39]	Endometrial Serous (Fader et al Clinical Trial)[21]
HER2 IHC 3+	>10% circumferential, strong, complete	≥10%, strong complete, or basolateral/lateral	≥50% strong complete, or basolateral/lateral	>30% strong complete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



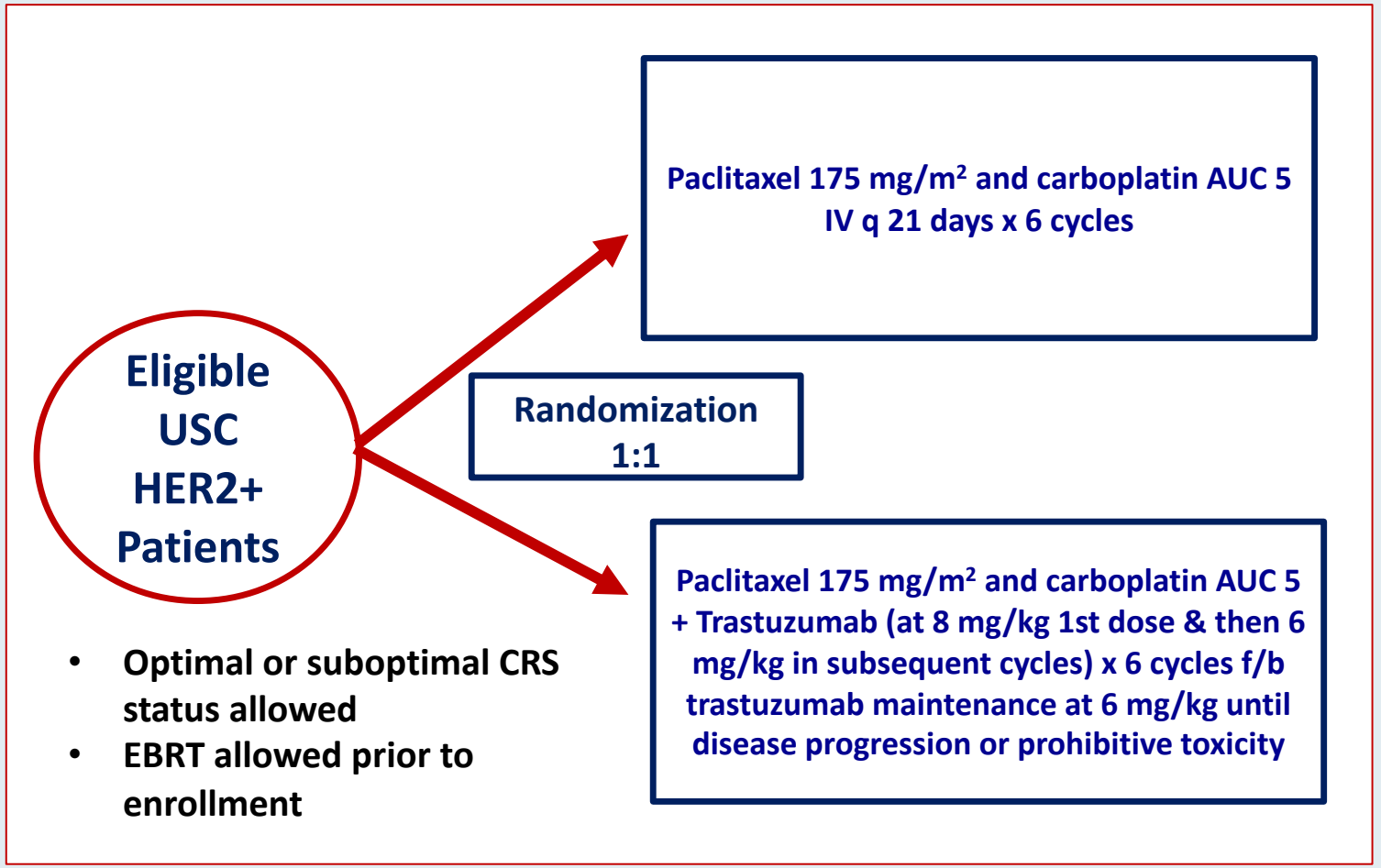
Buza N. *Arch Pathol Lab Med* 2020;[Online ahead of print].

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

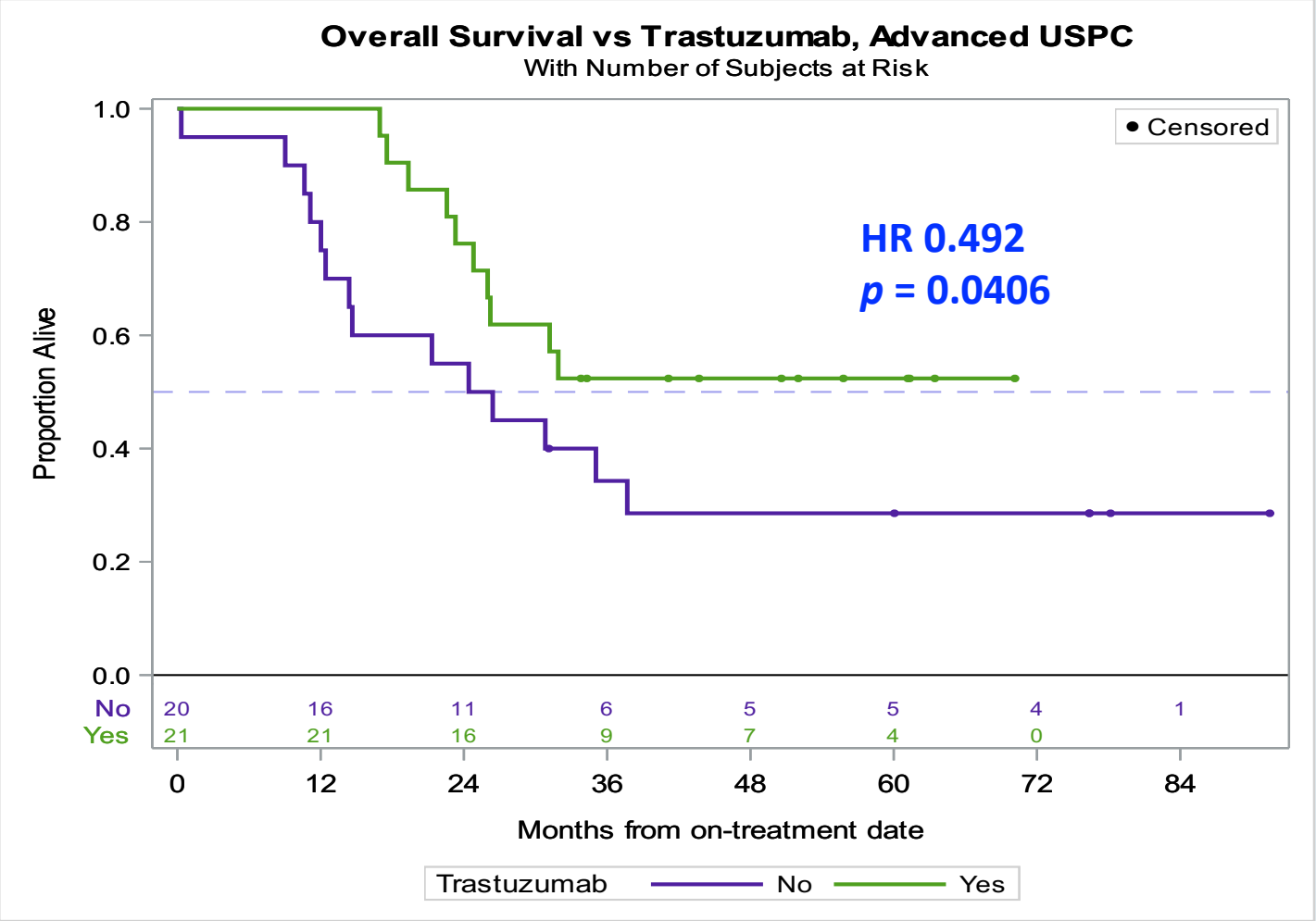


Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

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)



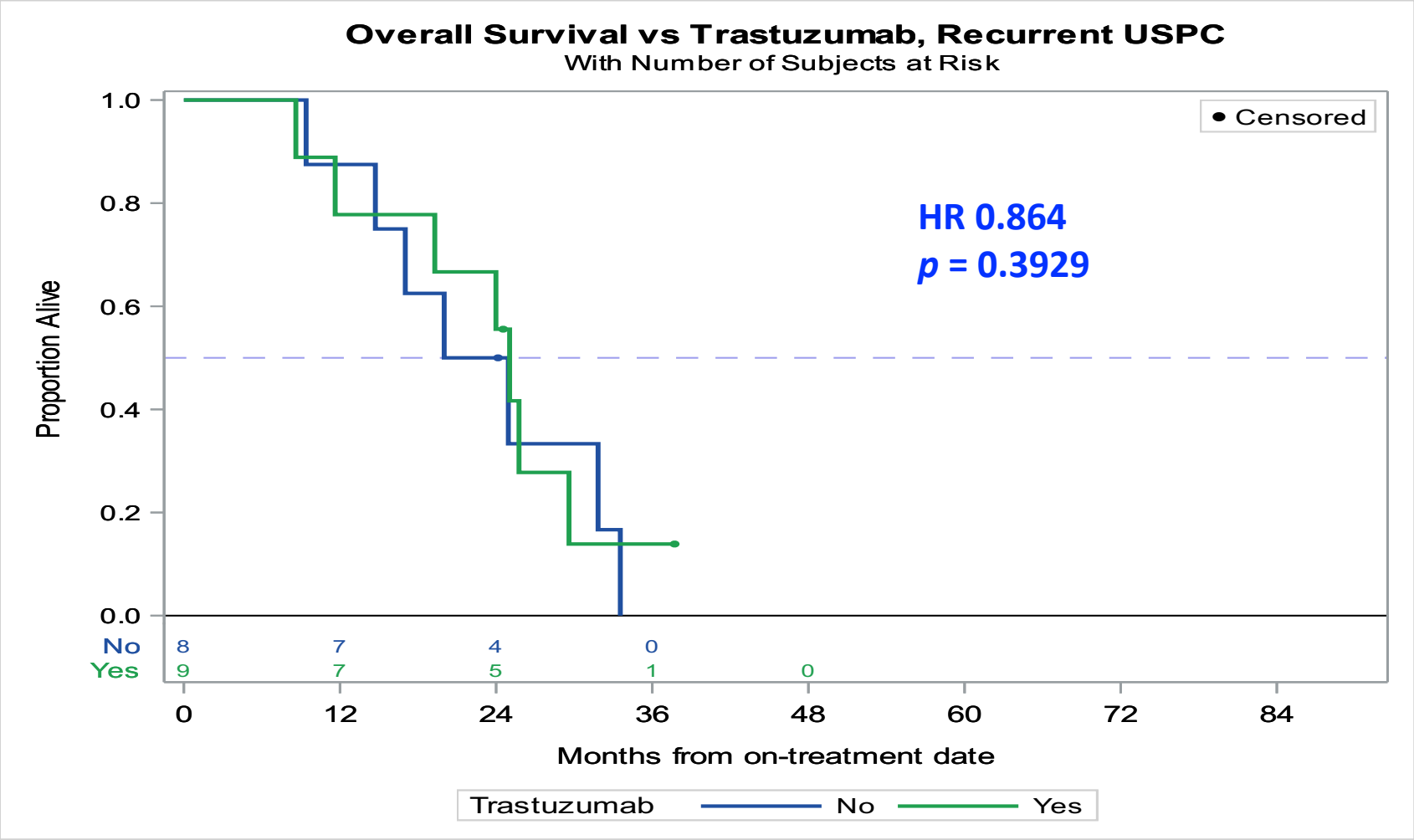
Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

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

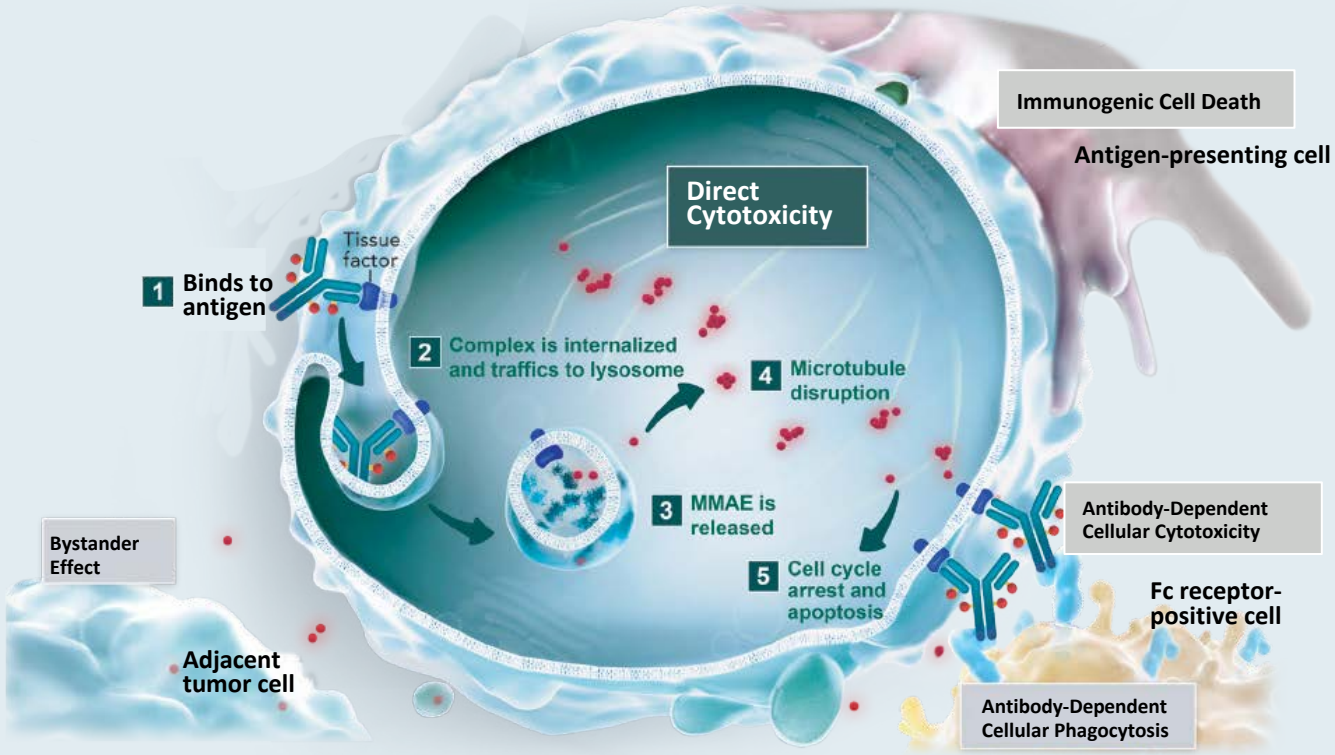
Primary endpoint: ORR
Secondary endpoints include DOR, PFS, OS, DCR

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

Tisotumab Vedotin and Other Novel Agents in Gynecologic Cancers

Mechanism of Action of Tisotumab Vedotin

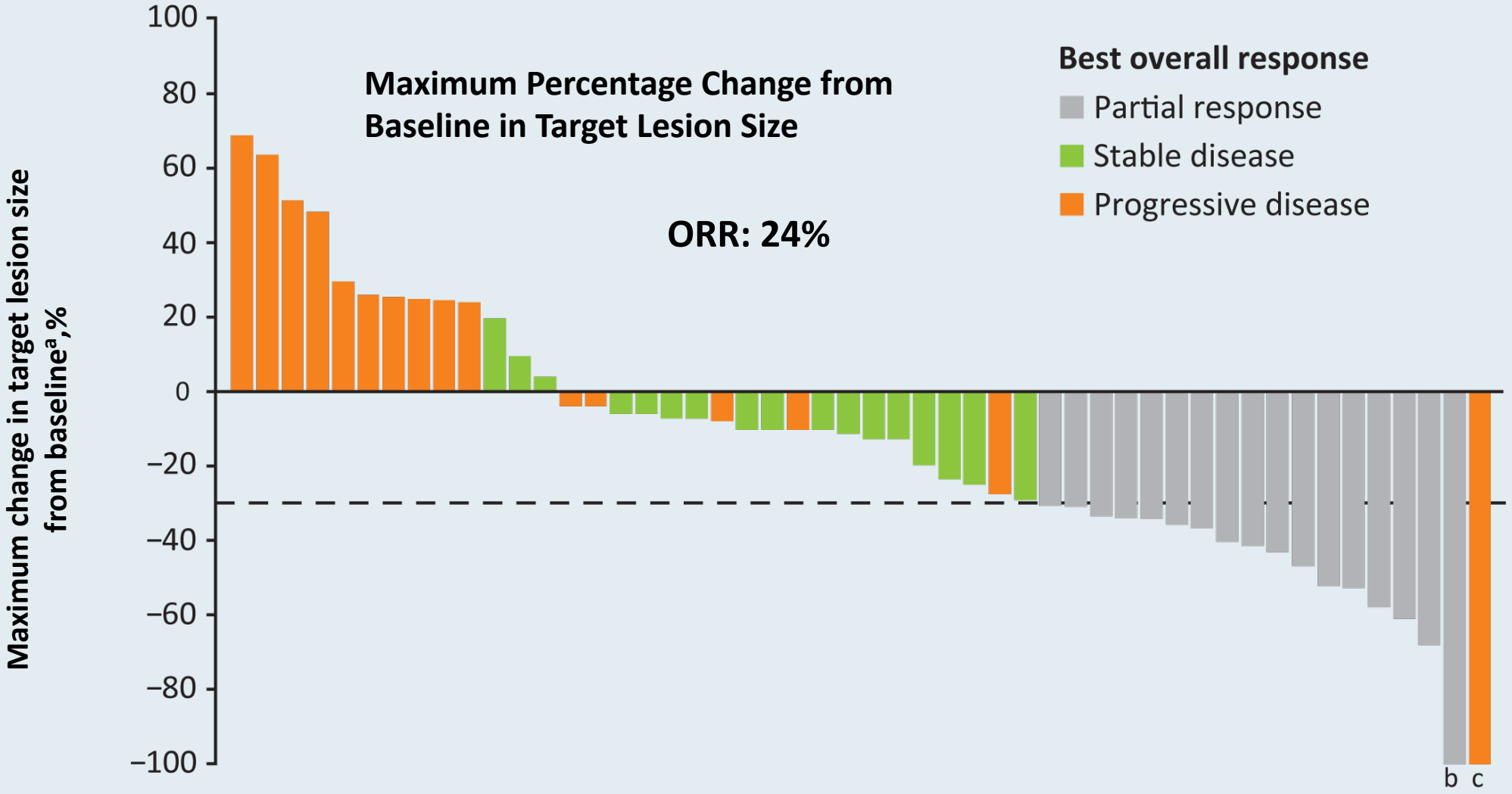
- Tissue factor (TF) is aberrantly expressed in a broad range of solid tumours, including cervical cancer,[1,2] and TF expression has been associated with higher tumour stage and grade, higher metastatic burden and poor prognosis[2]
- TF expression in cervical cancer makes TF a novel target for patients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

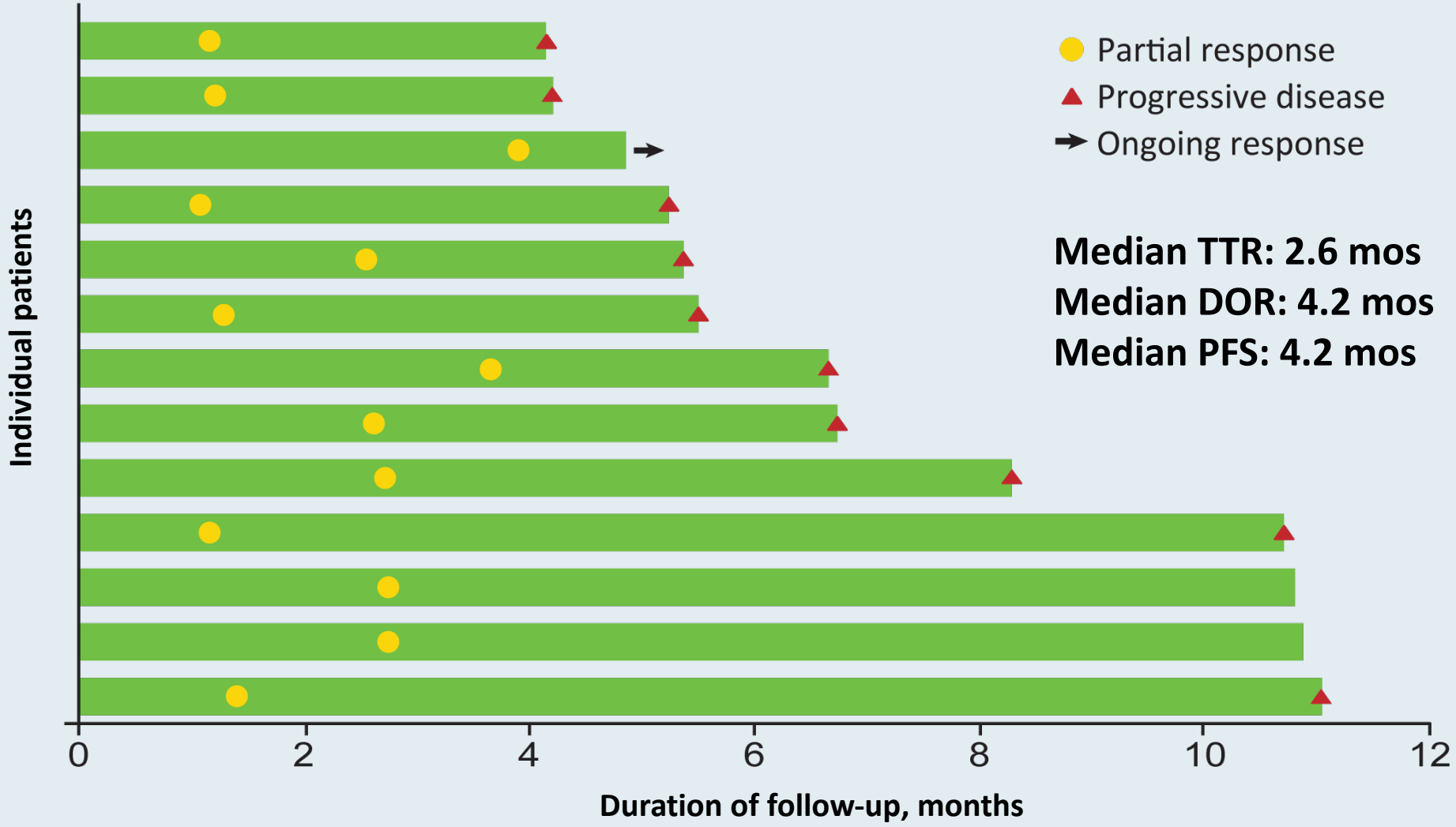
Courtesy of David M O'Malley, MD

innovaTV 201: Best Overall Response to TV



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

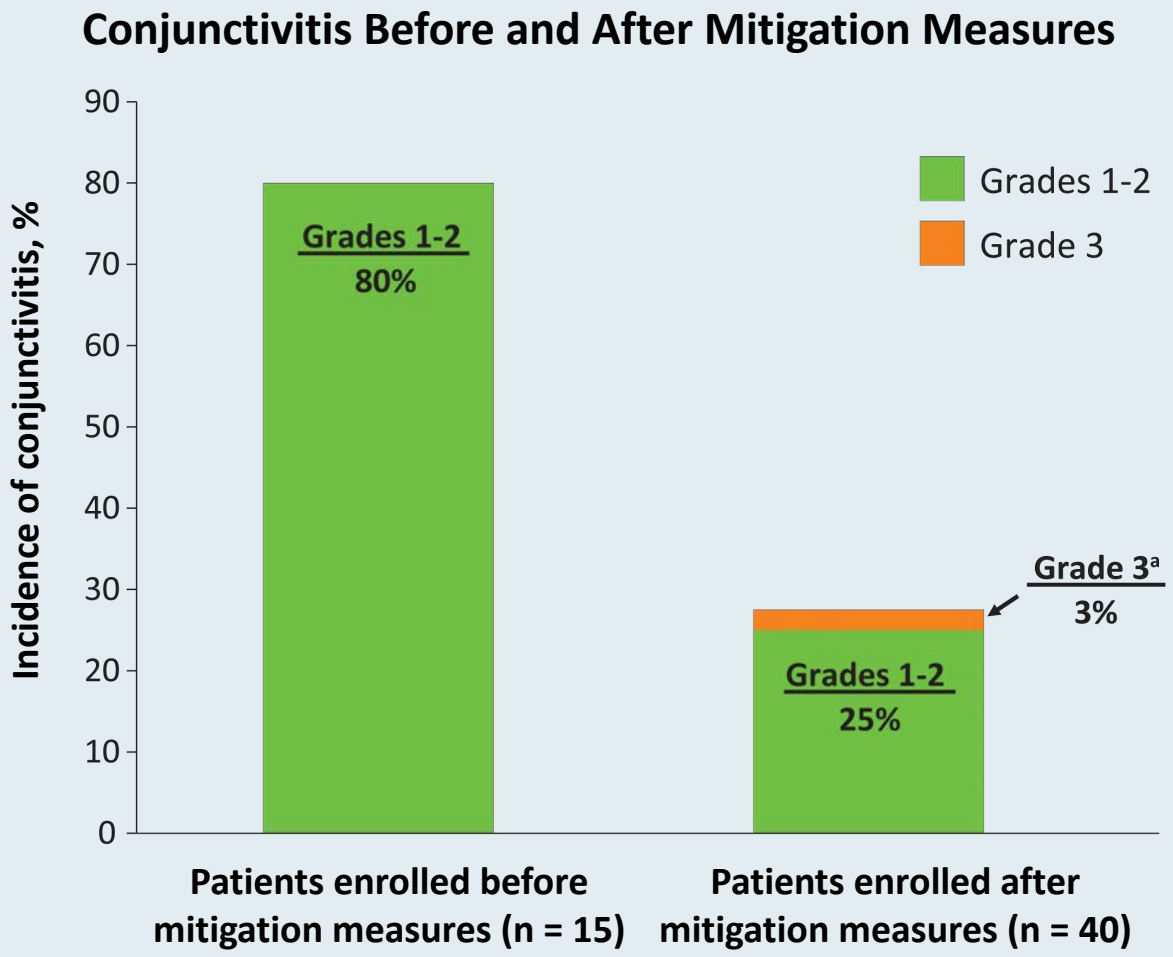
innovaTV 201: Time to Response and Duration of Response in Patients with a Confirmed PR to TV



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

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

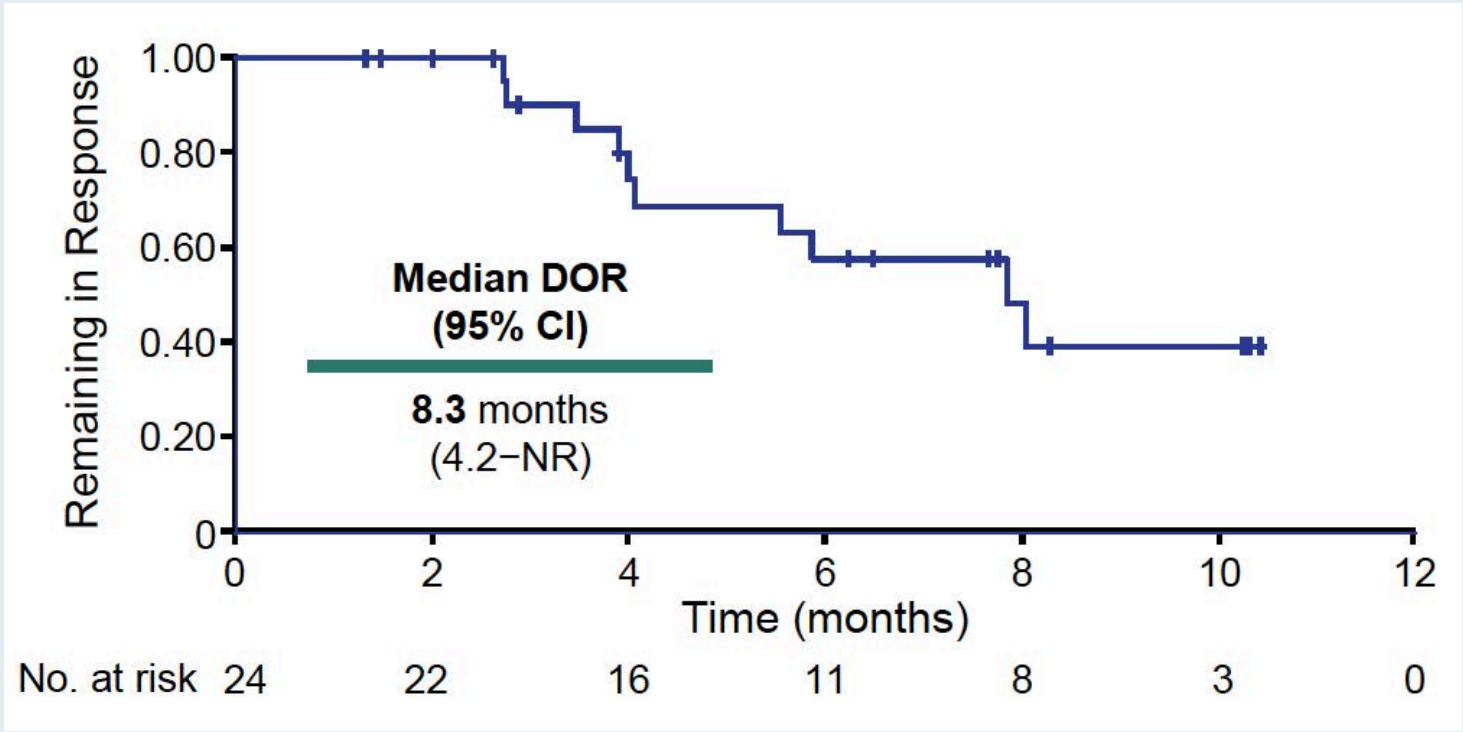
Coleman RL et al.

ESMO 2020;Abstract LBA32.

innovaTV 204: Antitumor Activity by IRC Assessment

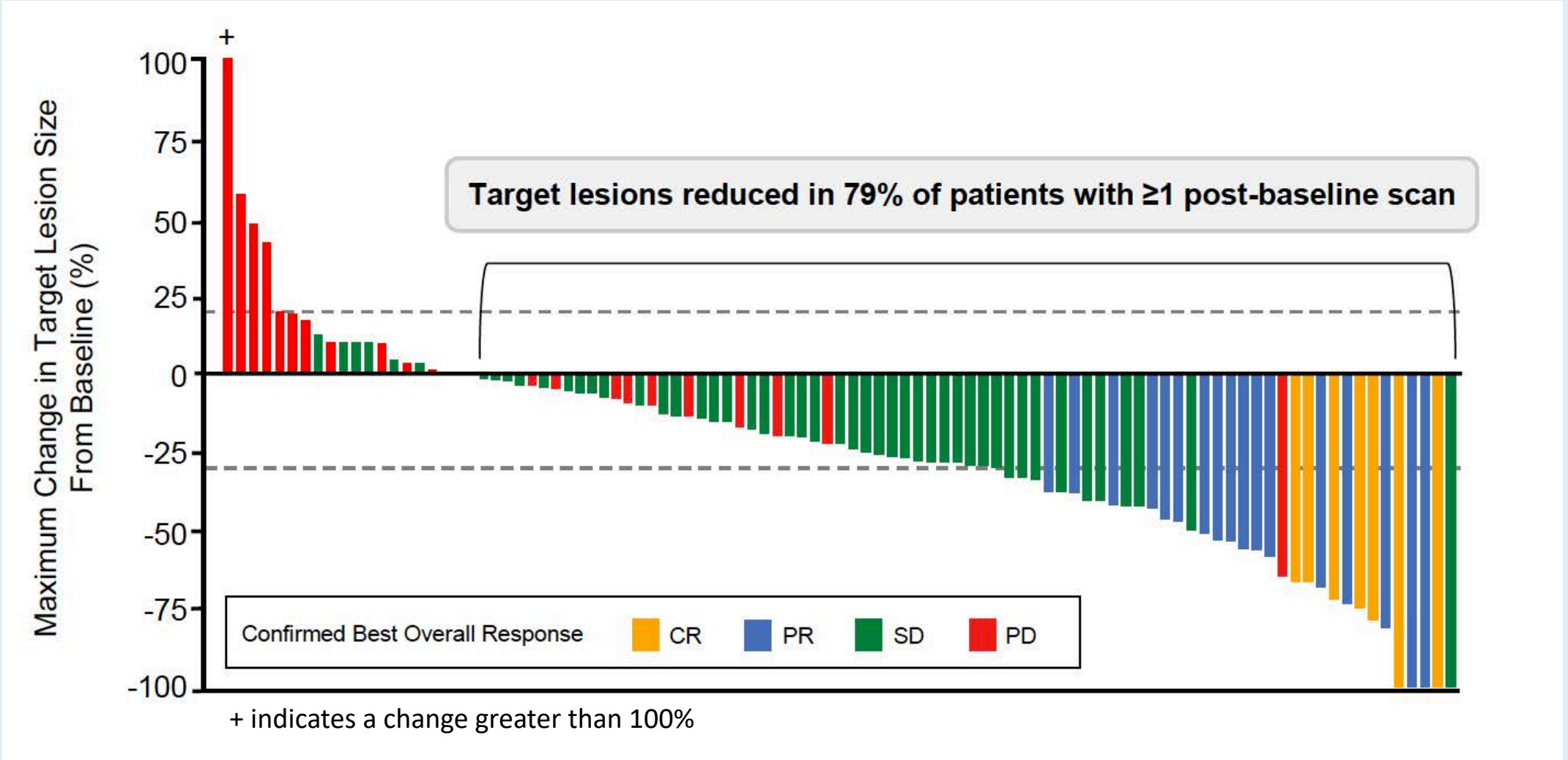
Clinical Variable	N = 101
Confirmed ORR	24%
CR	7%
PR	17%
SD	49%
PD	24%
Not evaluable	4%

Duration of Response



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

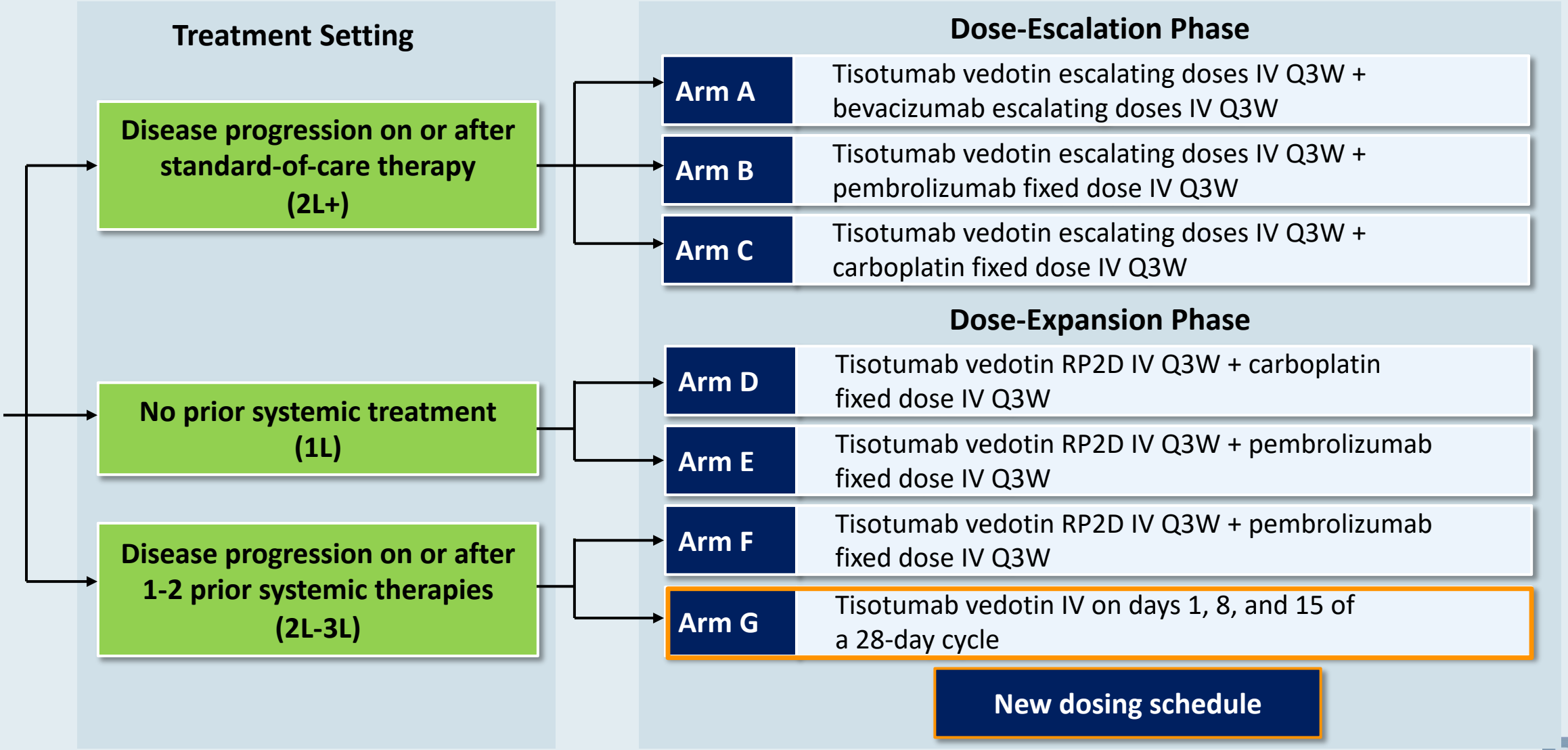
innovaTV 204: Maximum Change in Target Lesion Size by IRC Assessment



+ 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

Meet The Professor
Management of Multiple Myeloma

Thursday, November 19, 2020
12:00 PM – 1:00 PM ET

Faculty

Kenneth C Anderson, 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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