

Meet The Professor
**Immunotherapy and Novel Agents in
Gynecologic Cancers**

Gottfried E Konecny, MD

Professor-in-Residence

Division of Hematology-Oncology

Department of Medicine, David Geffen School of Medicine

UCLA Medical Center

Los Angeles, California

Commercial Support

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

Dr Love — Disclosures

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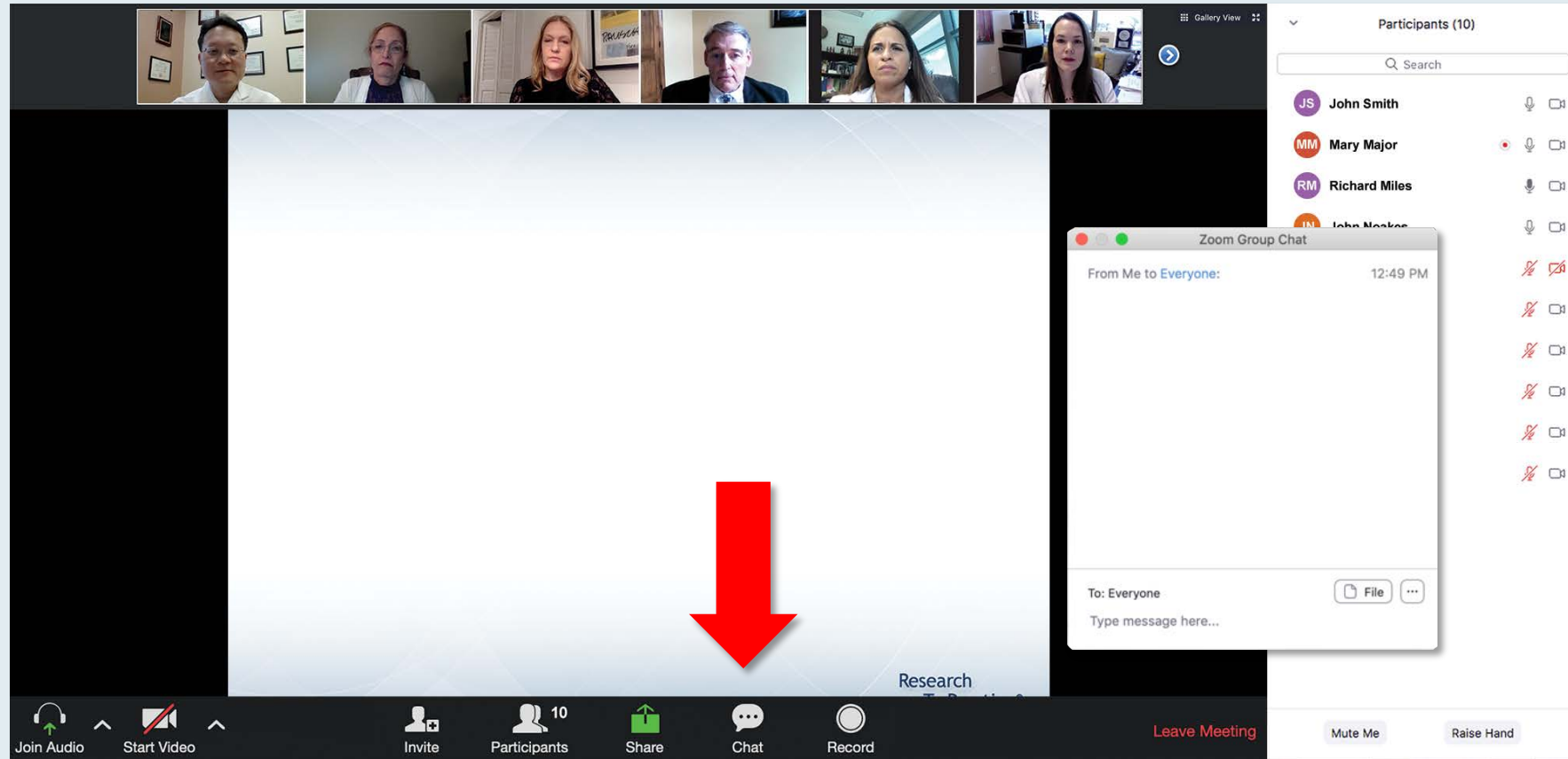
Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Konecny — Disclosures

Dr Konecny has no financial interests or affiliations to disclose.

We Encourage Clinicians in Practice to Submit Questions



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

Familiarizing Yourself with the Zoom Interface

How to answer poll questions

The screenshot shows a Zoom meeting interface. At the top, there are six video thumbnails of participants. Below them is a large slide with a poll question: "What is your usual treatment recommendation for a patient with MM followed by ASCT and maintenance experiences an asymptomatic relapse?". The slide lists ten options, including combinations of Carfilzomib, Pomalidomide, Elotuzumab, Daratumumab, and Ixazomib with or without dexamethasone. A "Quick Poll" window is overlaid on the slide, showing the same options with radio buttons for selection. The Zoom control bar at the bottom includes icons for Join Audio, Start Video, Invite, Participants (10), Share, Chat, Record, and Leave Meeting. On the right side, there is a "Participants (10)" list with names and status icons (mute, video off).

Participants (10)

Search

- JS John Smith
- MM Mary Major
- RM Richard Miles
- JN John Noakes
- AS Alice Suarez
- JP Jane Perez
- RS Robert Stiles
- JF Juan Fernandez
- AK Ashok Kumar
- JS Jeremy Smith

What is your usual treatment recommendation for a patient with MM followed by ASCT and maintenance experiences an asymptomatic relapse?

Quick Poll

- Carfilzomib +/- dexamethasone
- Pomalidomide +/- dexamethasone
- Carfilzomib + pomalidomide +/- dexamethasone
- Elotuzumab + lenalidomide +/- dexamethasone
- Elotuzumab + pomalidomide +/- dexamethasone
- Daratumumab + lenalidomide +/- dexamethasone
- Daratumumab + pomalidomide +/- dexamethasone
- Daratumumab + bortezomib +/- dexamethasone
- Ixazomib + Rd
- Other

Submit

Co-provided by USF Health Research To Practice®

Join Audio Start Video Invite Participants 10 Share Chat Record Leave Meeting Mute Me Raise Hand

When a poll question pops up, click your answer choice from the available options.
Results will be shown after everyone has answered.

Upcoming Webinars

**Thursday, December 10, 2020
8:30 PM – 10:00 PM ET**

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

Faculty

Carey K Anders, MD
Erika Hamilton, MD
Sara Hurvitz, MD
Mark D Pegram, MD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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

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Upcoming Webinars

Tuesday, December 15, 2020
5:00 PM – 6:00 PM ET

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

**Hepatobiliary and Pancreatic
Cancers**

Faculty

Tanios Bekaii-Saab, MD
Lipika Goyal, MD, MPhil

Moderator

Neil Love, MD

Wednesday, December 16, 2020
12:00 PM – 1:00 PM ET

**Meet The Professor:
Management of Multiple
Myeloma**

Faculty

Peter Voorhees, MD

Moderator

Neil Love, MD

Upcoming Webinars

**Wednesday, December 16, 2020
2:00 PM – 3:00 PM ET**

**Meet The Professor: Management
of Chronic Lymphocytic
Leukemia**

Faculty

Nitin Jain, 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.

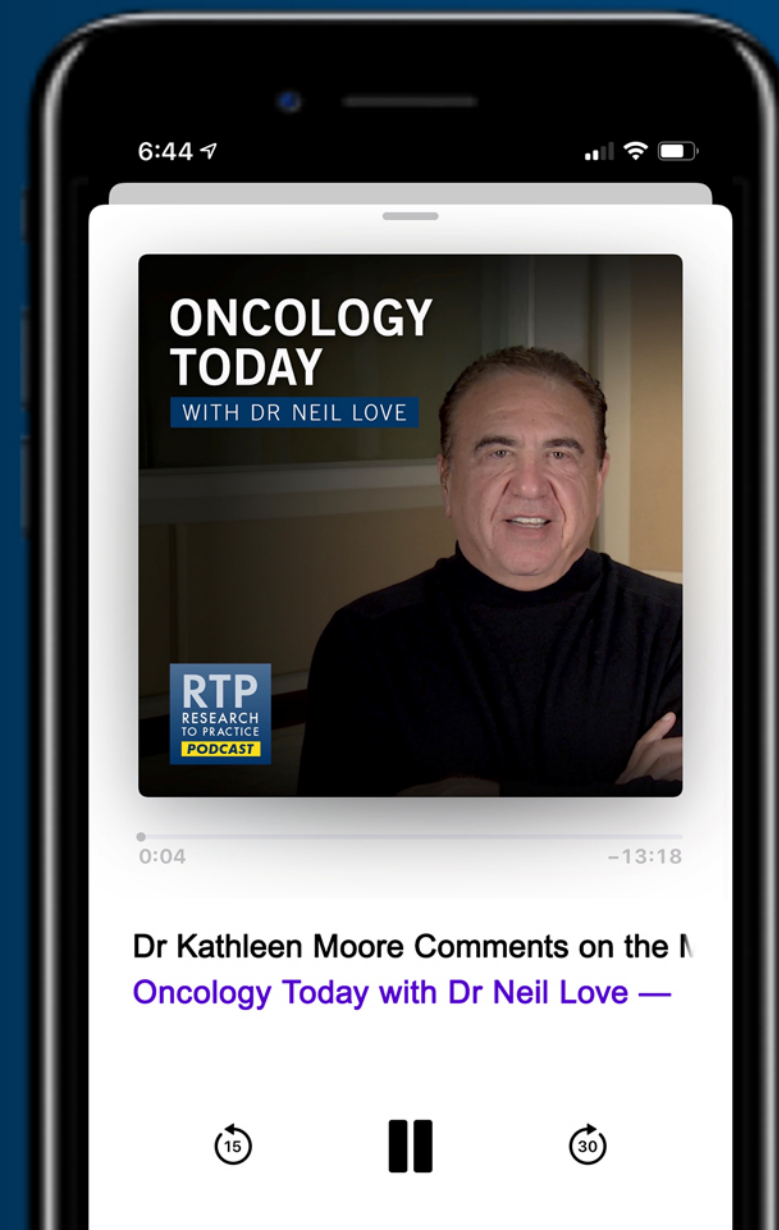
ONCOLOGY TODAY

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 Program Participating Faculty



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Director, Winthrop P Rockefeller Cancer Institute
Director, Cancer Service Line
University of Arkansas for Medical Sciences
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Meet The Professor Program Participating Faculty



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Project Chair
Neil Love, MD
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Miami, Florida

We Encourage Clinicians in Practice to Submit Questions

The image shows a Zoom meeting interface. At the top, there is a gallery view of six participants. The main area displays a presentation slide with the text: "You may submit questions using the Zoom Chat option below". A large red arrow points downwards from this text. On the right side, there is a "Participants (10)" list with names and icons for audio and video. Below the participants list, a "Zoom Group Chat" window is open, showing a message from "Me to Everyone" at 12:49 PM. The chat window has a text input field and a "File" button. At the bottom of the Zoom interface, there is a toolbar with icons for "Join Audio", "Start Video", "Invite", "Participants", "Share", "Chat", and "Record". A "Leave Meeting" button is also visible on the right side of the toolbar.

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What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

1. Carfilzomib +/- dexamethasone
2. Pomalidomide +/- dexamethasone
3. Carfilzomib + pomalidomide +/- dexamethasone
4. Elotuzumab + lenalidomide +/- dexamethasone
5. Elotuzumab + pomalidomide +/- dexamethasone
6. Daratumumab + lenalidomide +/- dexamethasone
7. Daratumumab + pomalidomide +/- dexamethasone
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9. Ixazomib + Rd
10. Other

Co-provided by **USF Health** Research To Practice®

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Mute Me Raise Hand

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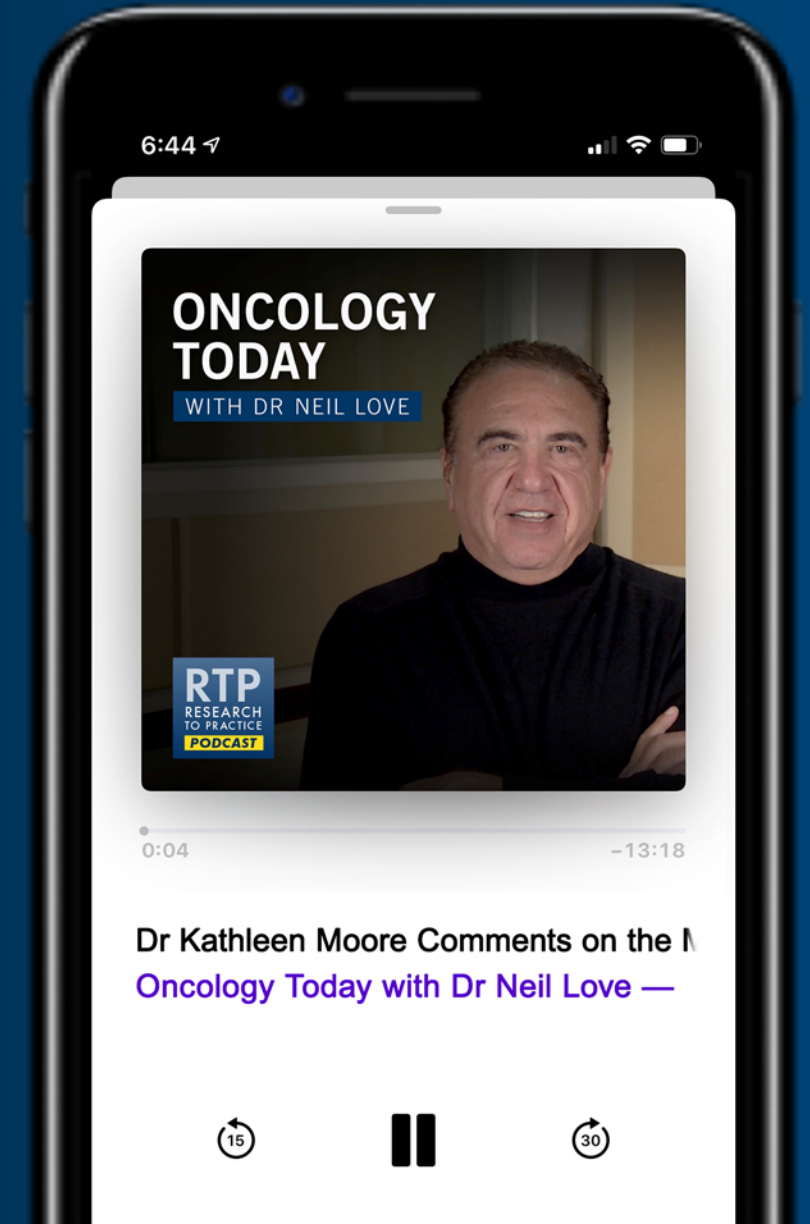
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Mansoor Raza Mirza, MD

Medical Director, Nordic Society of Gynaecological Oncology

Vice-Chairman, Danish Society of Gynaecologic Oncology

Executive Director, Gynecologic Cancer InterGroup

Chief Oncologist, Department of Oncology

Rigshospitalet, Copenhagen University Hospital

Copenhagen, Denmark

Meet The Professor with Dr Konecny

MODULE 1: Clinical Scenarios and Comments from Dr Mirza

- A 68-year-old woman with advanced, recurrent endometrial cancer – MSI high
- A 68-year-old woman with endometrioid adenocarcinoma and lung metastases – ER-positive, MSI high
 - Comment: Preferred treatment option
- A 68-year-old woman with advanced, recurrent endometrial cancer – MSS
- A 68-year-old woman with serous adenocarcinoma of the endometrium and lung metastases – MSS
 - Comment: Preferred treatment option
- Question: Starting dose of lenvatinib
- Question: Preemptive antihypertensive treatment
- A 68-year-old woman with disease relapse after chemoradiation therapy
- A 68-year-old woman with metastatic cervical cancer and disease progression after cisplatin/paclitaxel/bevacizumab
 - Comment: Preferred treatment option

MODULE 2: Gynecologic Oncology Journal Club with Dr Konecny

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

MODULE 4: Key Recent Data Sets

On Dec 8, 2020, at 11:20 PM, Ranju Gupta wrote:

Dear Neil,

I wanted to see if you can help me get expert opinion regarding my patient and colleague with newly diagnosed Uterine Leiomyosarcoma

47yrs old premenopausal woman with history of fibroids and abnormal uterine bleeding. she took OCP's for 3mo and developed worsening bleeding.

10/9/2020: s/o EAU, RA hysterectomy plus bilateral salpingectomy plus pelvic washing.

She later had b/l oophorectomy done

pathology: Uterine leiomyosarcoma

FIGO stage IB, pT1b Nx M0.

11.4 cm(most of this is leiomyoma with areas of leiomyosarcoma), moderate to high-grade leiomyosarcoma with no lymphovascular invasion, epithelioid and spindle type, no serosal involvement

ER 85%, PR 95% positive

Path reviewed at MGH and confirmed.

question:

1. Any role for adjuvant chemo or RT? - I recommended no adjuvant treatment. what is your expert opinion?
2. since her leiomyosarcoma is strongly ER/PR+, any role of adjuvant endocrine treatment like aromatase inhibitor? - i reviewed the literature and found some role in metastatic setting but found no evidence in early stage Leiomyosarcoma?

I appreciate your help and look forward to the expert opinion.

In general, what treatment would you recommend for a 68-year-old woman with Stage IIIC, microsatellite instability-high (MSI-high) endometrial cancer who undergoes R0 resection, completes adjuvant carboplatin/paclitaxel and relapses with lung metastases 4 months later?



Dr Mansoor Raza Mirza

In general, what treatment would you recommend for a 68-year-old woman with Stage IIIC, microsatellite instability-high (MSI-high) endometrial cancer who undergoes R0 resection, completes adjuvant carboplatin/paclitaxel and relapses with lung metastases 4 months later?

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

In general, what treatment would you recommend for a 68-year-old woman with ER-positive, MSI-high endometrioid adenocarcinoma who presents with lung metastases?



Dr Mansoor Raza Mirza

In general, what treatment would you recommend for a 68-year-old woman with ER-positive, MSI-high endometrioid adenocarcinoma who presents with lung metastases?

1. Carboplatin/paclitaxel
2. Endocrine therapy
3. Lenvatinib/pembrolizumab
4. Pembrolizumab
5. Other chemotherapy
6. Other

Comments: Preferred treatment for a 68-year-old woman with ER-positive, MSI-high endometrioid adenocarcinoma who presents with lung metastases



Dr Mansoor Raza Mirza

In general, what treatment would you recommend for a 68-year-old woman with Stage IIIC, microsatellite-stable (MSS) endometrial cancer who undergoes R0 resection, completes adjuvant carboplatin/paclitaxel and experiences relapse with lung metastases 5 months later?



Dr Mansoor Raza Mirza

In general, what treatment would you recommend for a 68-year-old woman with Stage IIIC, microsatellite-stable (MSS) endometrial cancer who undergoes R0 resection, completes adjuvant carboplatin/paclitaxel and experiences relapse with lung metastases 5 months later?

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

In general, what treatment would you recommend for a 68-year-old woman with MSS serous adenocarcinoma of the endometrium who presents with lung metastases?



Dr Mansoor Raza Mirza

In general, what treatment would you recommend for a 68-year-old woman with MSS serous adenocarcinoma of the endometrium who presents with lung metastases?

1. Carboplatin/paclitaxel
2. Lenvatinib/pembrolizumab
3. Pembrolizumab
4. Other chemotherapy
5. Other

Comments: Preferred treatment for a 68-year-old woman with MSS serous adenocarcinoma of the endometrium who presents with lung metastases?



Dr Mansoor Raza Mirza

**When initiating lenvatinib and pembrolizumab for a woman with endometrial cancer, what is your typical starting dose of lenvatinib?
When would you start antihypertensive treatment?**



Dr Mansoor Raza Mirza

When initiating lenvatinib and pembrolizumab for a woman with endometrial cancer, what is your typical starting dose of lenvatinib?

1. 20 mg qd
2. 14 mg qd
3. 10 mg qd
4. 8 mg qd
5. Other

When initiating lenvatinib and pembrolizumab for a woman with endometrial cancer and no history of hypertension, when would you start antihypertensive treatment?

1. Preemptively
2. After symptoms occur
3. Other

In general, what treatment would you recommend for a 68-year-old woman with advanced-stage squamous cell cervical cancer who received chemoradiation therapy and now has metastatic disease relapse?



Dr Mansoor Raza Mirza

In general, what treatment would you recommend for a 68-year-old woman with advanced-stage squamous cell cervical cancer who received chemoradiation therapy and now has metastatic disease relapse?

1. Platinum/paclitaxel
2. Platinum/paclitaxel/bevacizumab
3. Platinum/paclitaxel/bevacizumab/pembrolizumab
4. Pembrolizumab
5. Other chemotherapy
6. Other

In general, what treatment would you recommend for a 68-year-old woman with advanced-stage squamous cell cervical cancer who experienced relapse after chemoradiation therapy, received cisplatin/paclitaxel/bevacizumab and now has progressive disease again?



Dr Mansoor Raza Mirza

In general, what treatment would you recommend for a 68-year-old woman with advanced-stage squamous cell cervical cancer who experienced relapse after chemoradiation therapy, received cisplatin/paclitaxel/bevacizumab and now has progressive disease again?

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

Comment: Preferred second-line treatment for metastatic cervical cancer



Dr Mansoor Raza Mirza

Meet The Professor with Dr Konecny

MODULE 1: Clinical Scenarios and Comments from Dr Mirza

MODULE 2: Gynecologic Oncology Journal Club with Dr Konecny

- *NEJM* review paper: Endometrial cancer
- Comprehensive genomic profiling of recurrent endometrial cancer: Implications for therapy
- Somatic BRCA mutations in endometrial cancer and the clinical implications
- Inhibition of PD-1 (pembrolizumab) and VEGF (lenvatinib) in MSS endometrial cancer
- Potential predictive biomarkers for immunotherapy in ovarian cancer
- Association of PD-L1 expression and gene microarray with molecular subtypes of ovarian cancer
- KANSL1 as a biomarker and target gene for immune response and HDAC inhibition in ovarian cancer
- Targeting ERBB family genomic alterations in gynecologic cancer
- Mirvetuximab soravtansine and gemcitabine for FR α -positive endometrial cancer
- OVARIO trial: Niraparib/bevacizumab after front-line platinum-based chemotherapy/bevacizumab for ovarian cancer
- OPAL trial (cohort A): TSR-042, bevacizumab and niraparib for platinum-resistant ovarian cancer
- Combining PARP and CDK4/6 inhibitors for MYC-driven ovarian cancer
- Mechanisms of PARP inhibitor resistance in ovarian cancer
- PrOTYPE: Development and validation of the gene expression predictor of HGSOC molecular subtype

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

MODULE 4: Key Recent Data Sets

N Engl J Med 2020;383:2053-64

The NEW ENGLAND JOURNAL of MEDICINE

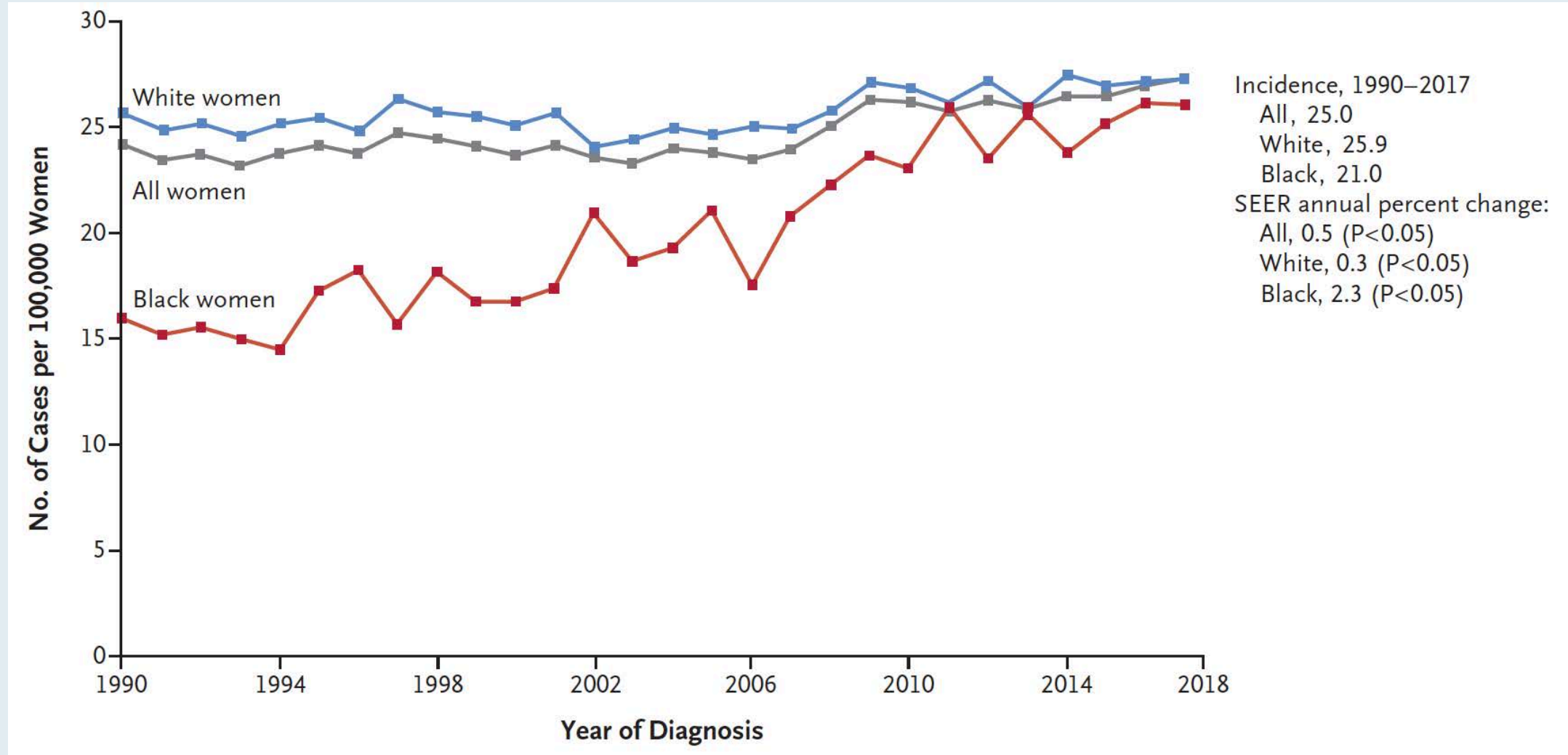
REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

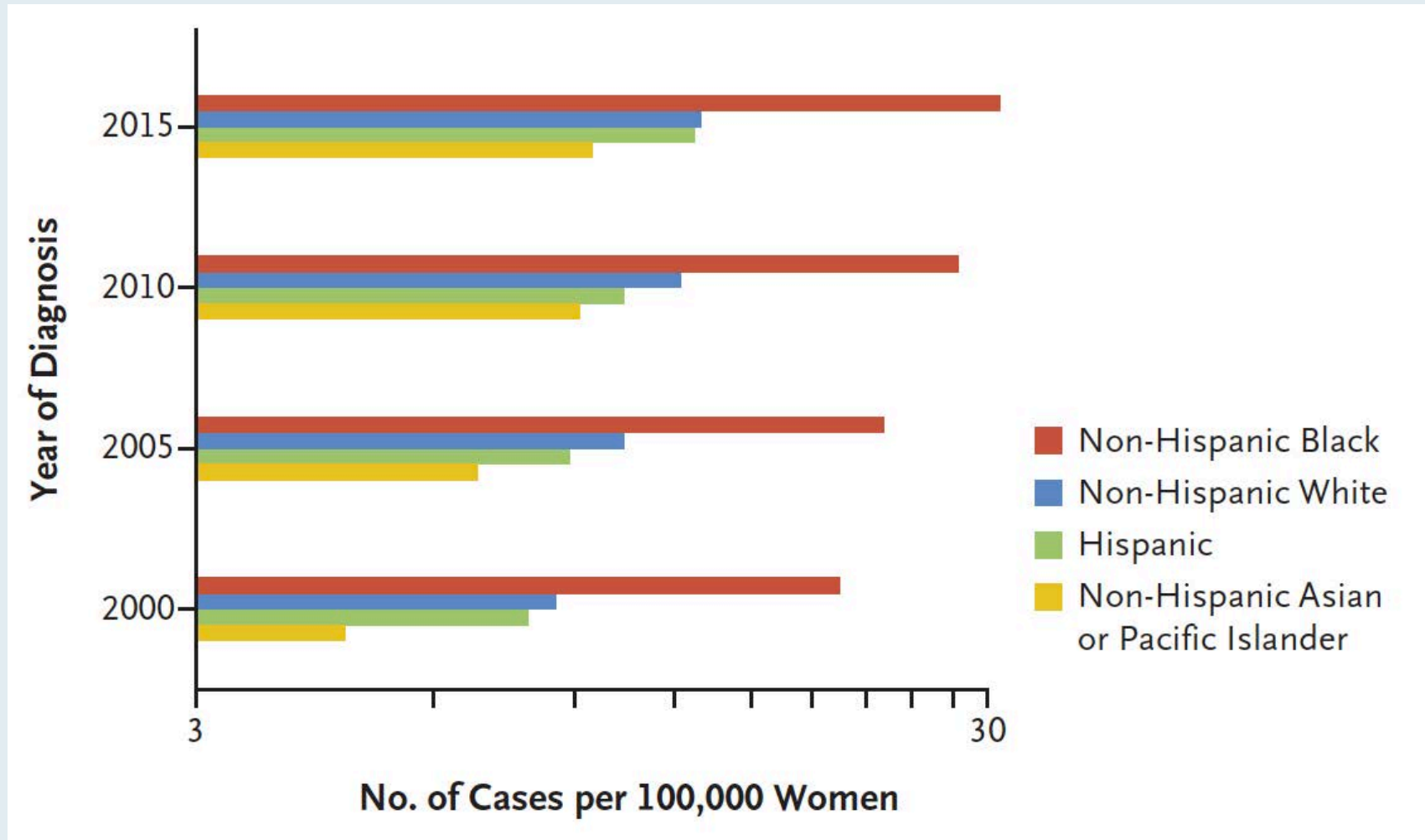
Endometrial Cancer

Karen H. Lu, M.D., and Russell R. Broaddus, M.D., Ph.D.

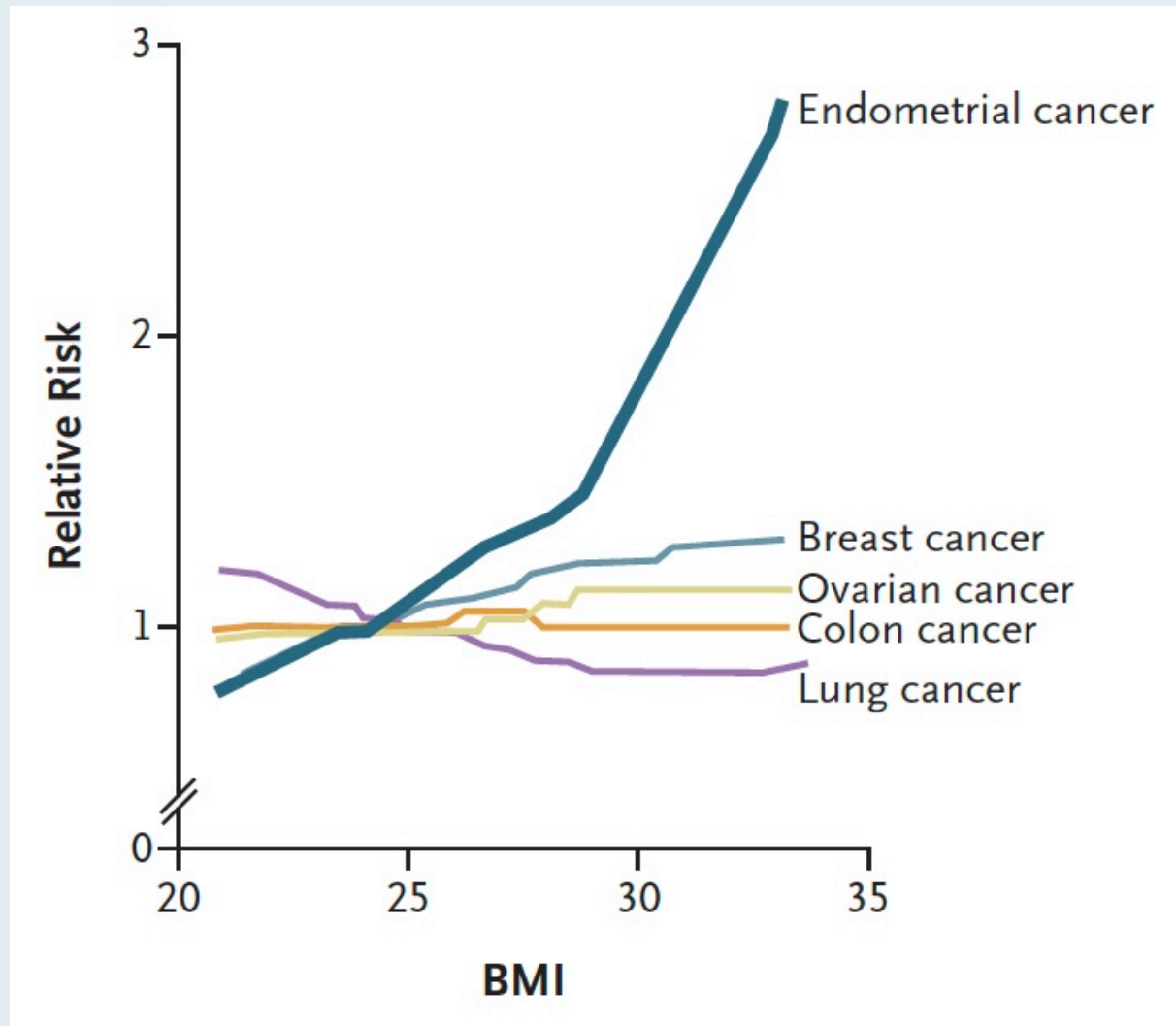
Age-Adjusted Incidence of Endometrial Cancer in White and Black Women



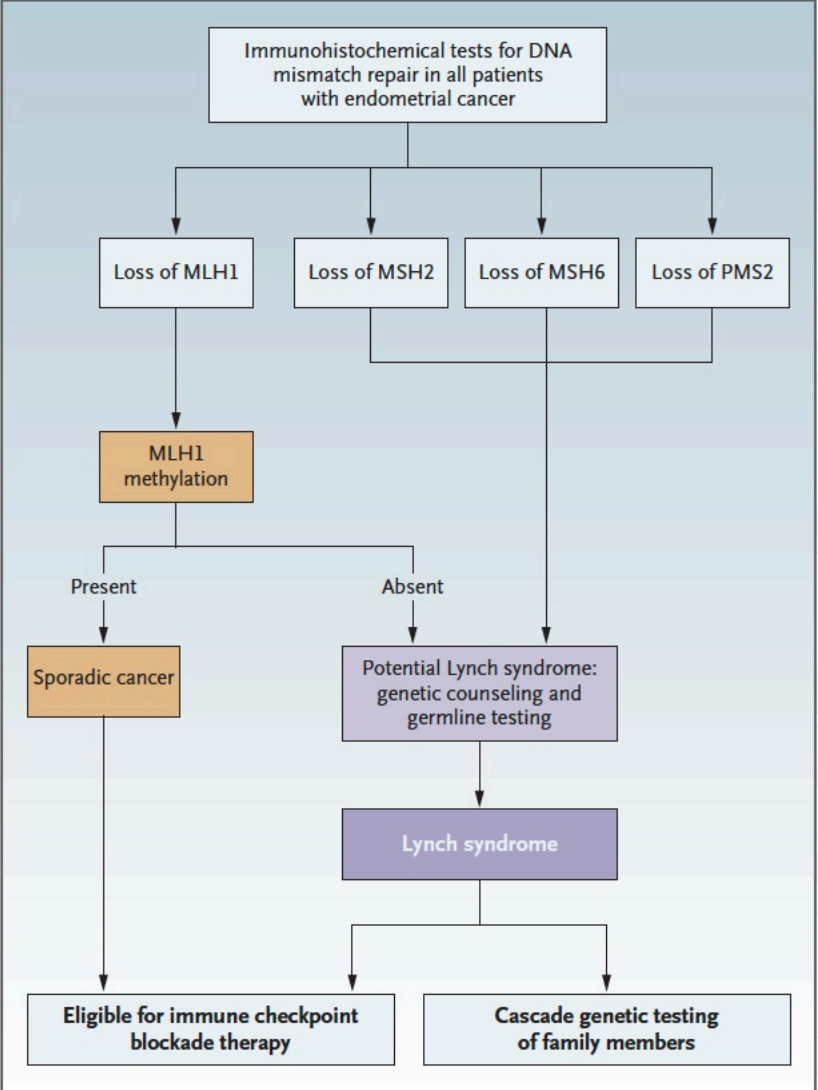
Age-Adjusted and Hysterectomy-Corrected Incidence of Nonendometrioid Endometrial Cancer According to Race



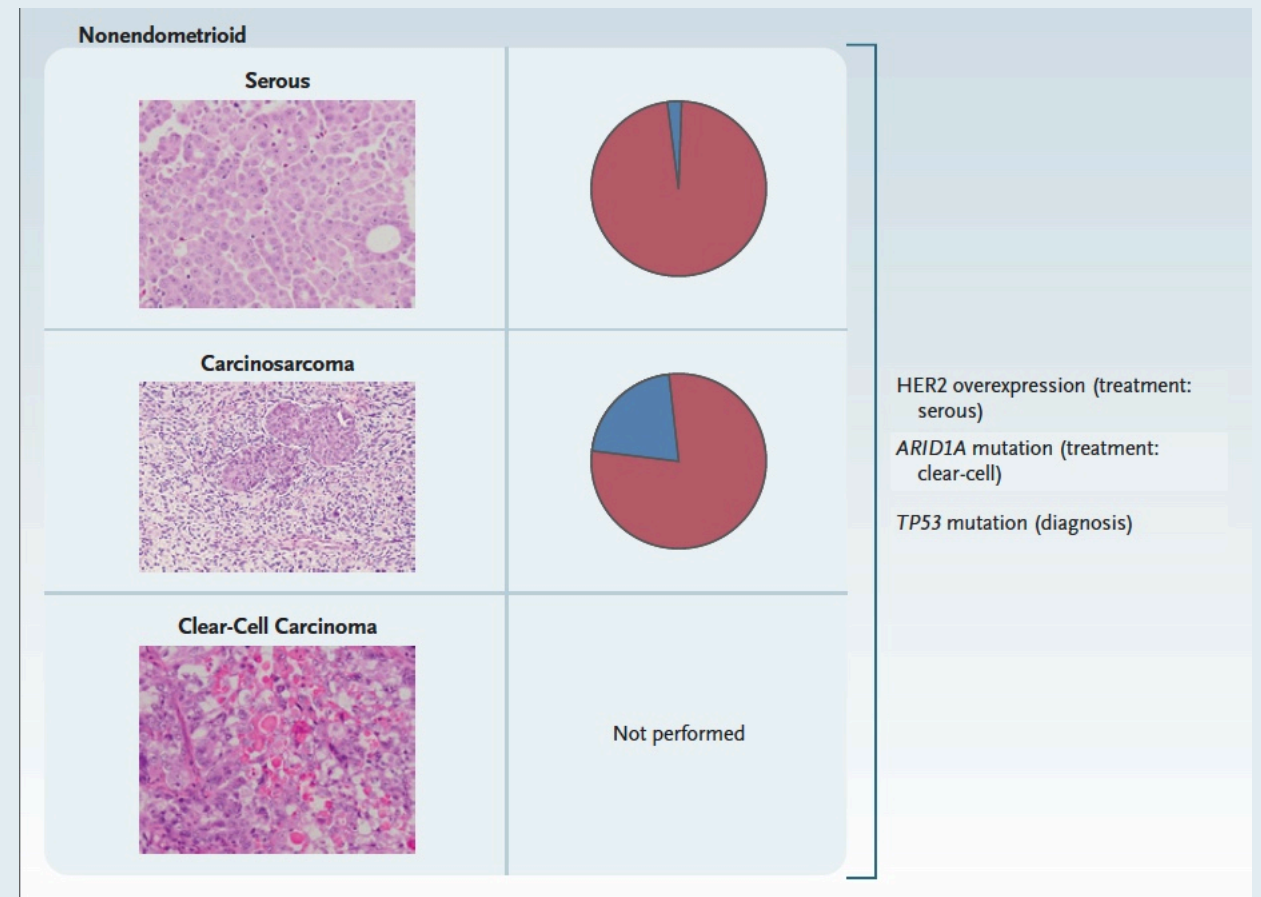
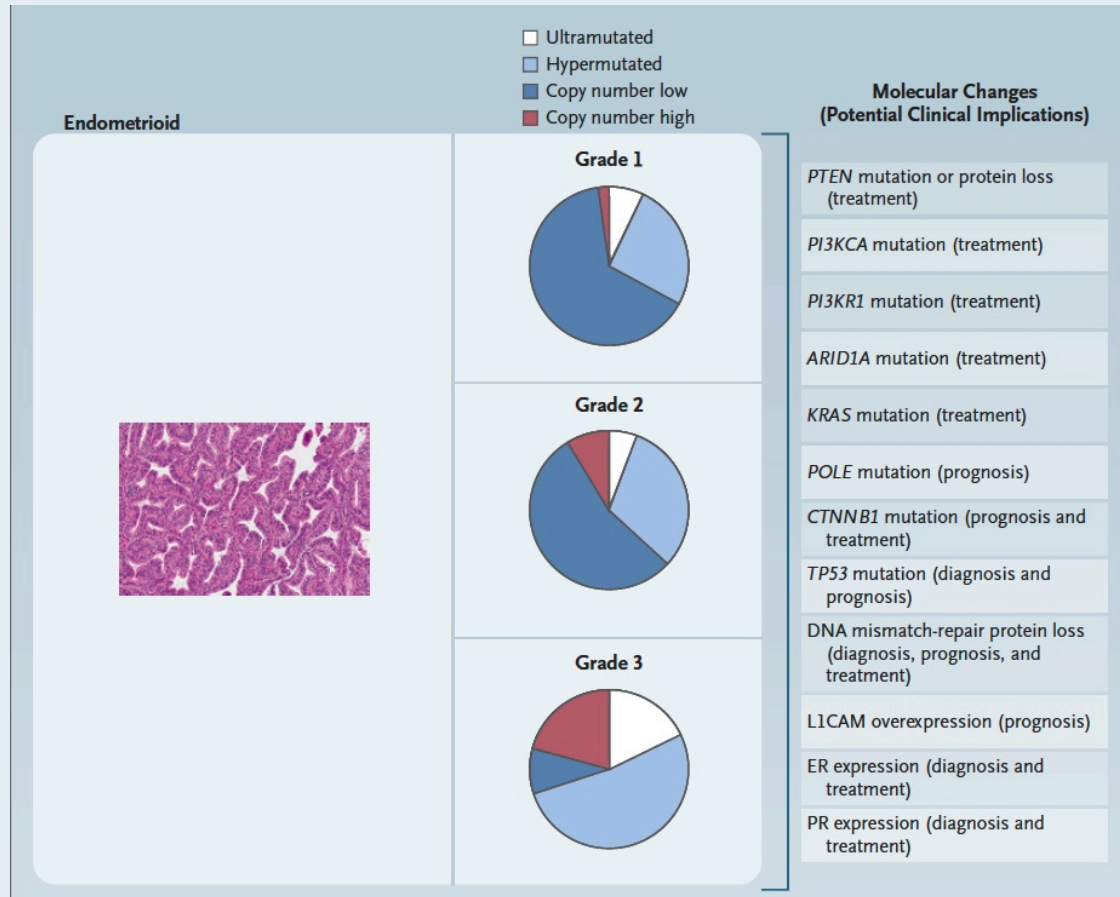
Association of Endometrial Cancer with Body-Mass Index



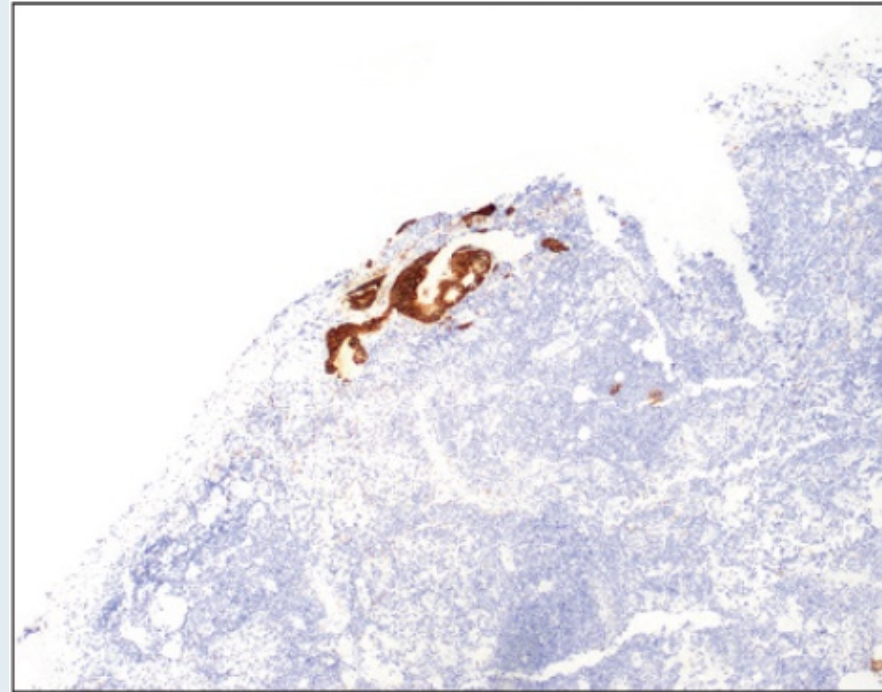
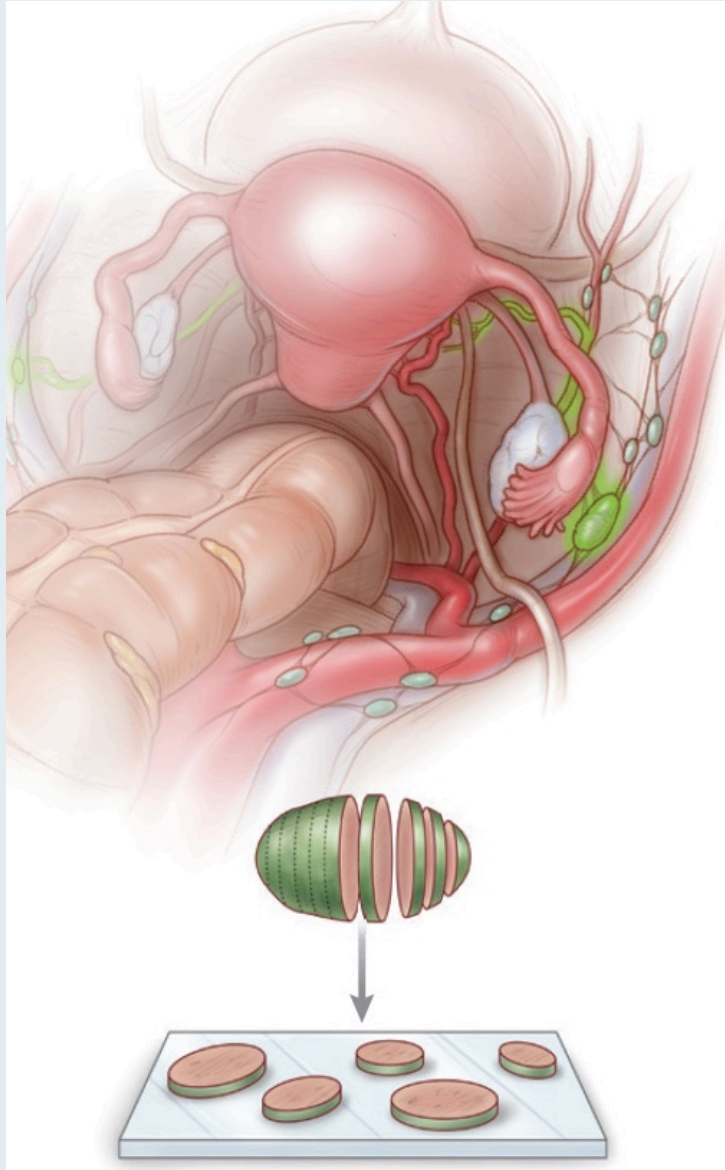
Use of DNA Mismatch-Repair Analysis in Endometrial Cancer to Guide Decisions about Treatment, Prevention and Screening



Complex Interplay among the Type of Endometrial Cancer (Endometrioid or Nonendometrioid), Endometrioid Tumor Grade and Molecular Changes in the Tumor



Sentinel-Node Strategy in Endometrial Cancer



Gynecol Oncol. 2019 September ; 154(3): 461–466. doi:10.1016/j.ygyno.2019.06.016.

Comprehensive genomic profiling of recurrent endometrial cancer: Implications for selection of systemic therapy[☆]

**Emily N. Prendergast^a, Laura L. Holman^c, Annie Y. Liu^a, Tiffany S. Lai^a, Maira P. Campos^b,
Jacqueline N. Fahey^a, Xiaoyan Wang^d, Nabilah Abdelaal^c, Jian Yu Rao^e, Julia A. Elvin^f,
Kathleen M. Moore^c, Gottfried E. Konecny^{a,b,*}, Joshua G. Cohen^a**

Exploratory Analysis of Somatic BRCA Mutations in Endometrial Cancer and Its Clinical Implications

Burkett Jr WC et al.
SGO 2019;Abstract 2453.

Comment



Inhibition of PD-1 and VEGF in microsatellite-stable endometrial cancer

Konecny GE. *Lancet Oncol* 2019;20(5):612-4.

Lancet Oncol 2019;20:711-8

Articles

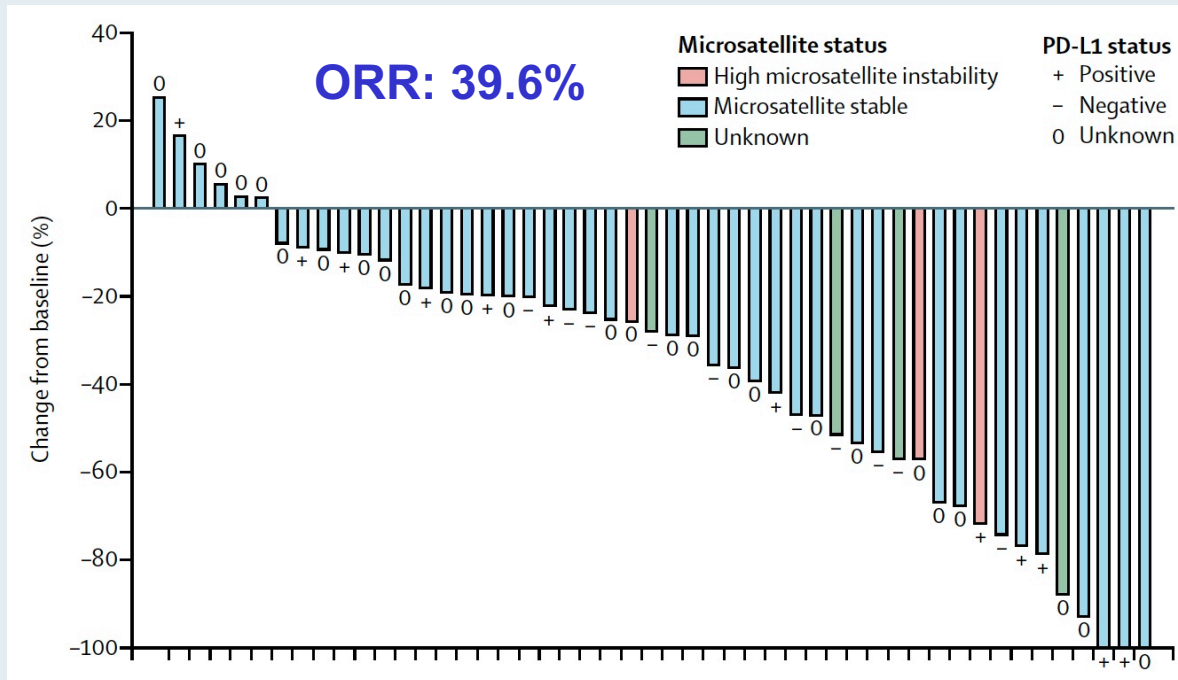
Lenvatinib plus pembrolizumab in patients with advanced endometrial cancer: an interim analysis of a multicentre, open-label, single-arm, phase 2 trial



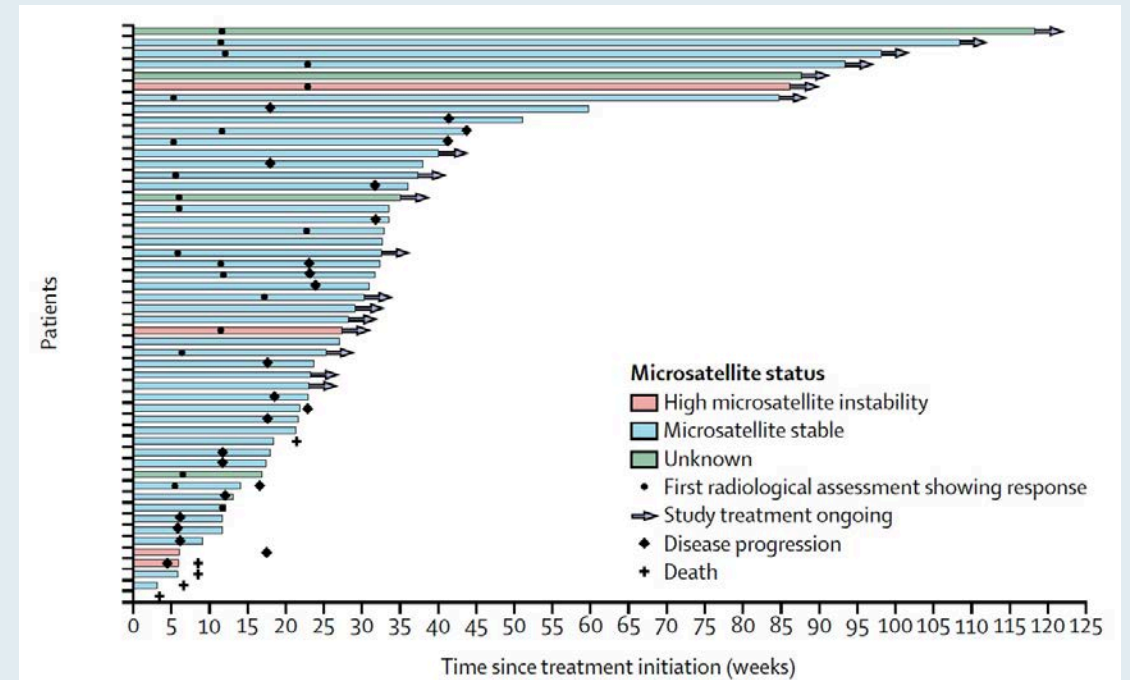
Vicky Makker, Drew Rasco, Nicholas J Vogelzang, Marcia S Brose, Allen L Cohn, James Mier, Christopher Di Simone, David M Hyman, Daniel E Stepan, Corina E Dutcus, Emmett V Schmidt, Matthew Guo, Pallavi Sachdev, Robert Shumaker, Carol Aghajanian, Matthew Taylor

Lenvatinib/Pembrolizumab in Advanced Endometrial Cancer

Maximum percentage change in sum of diameters of target lesions from baseline



Time on treatment



Summary of Select Patient Characteristics and Response

Lenvatinib/Pembrolizumab Group (N = 53)		Investigator Review: Response (N = 53)	
Number of previous therapies		Best overall response	
One	43%	Complete response	1.9%
Two	45%	Partial response	37.7%
Three or more	13%	Stable disease	47.2%
PD-L1 status		Progressive disease	7.5%
Positive	25%	Unknown or not measurable	5.7%
Negative	21%	Median duration of response	
Unknown	55%	Median	NE
Microsatellite status		Range	1.2-23.4 mo
High-MSI	8%	Proportion with responses \geq 6 mos	83.0%
MSS	85%	Proportion with responses \geq 12 mos	64.5%
Unknown	8%	Median time to response	2.7 mo

Summary of Select Adverse Events (AEs)

	Grade 1-2	Grade 3*
Any treatment-related AEs	25%	68%
Fatigue	49%	6%
Hypothyroidism	47%	0
Nausea	38%	0
Arthralgia	26%	0
Palmar-plantar erythrodysesthesia syndrome	26%	6%
Hypertension	25%	34%

* No Grade 4 treatment-related AEs were reported, and 1 Grade 5 event (intracranial haemorrhage) was reported.



Biomarkers that may predict response to immunotherapy in ovarian malignancies

Curtis D. Chin^{a,}, Charlene M. Fares^{b,*}, Gottfried E. Konecny^b,
and Jianyu Rao^a*

Modern Pathology (2020) 33:2001–2010
<https://doi.org/10.1038/s41379-020-0567-3>

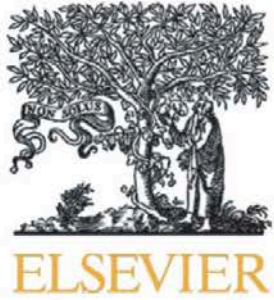


ARTICLE



Association of PD-L1 expression by immunohistochemistry and gene microarray with molecular subtypes of ovarian tumors

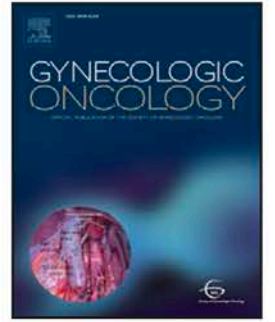
Curtis David Chin¹ · Charlene Marie Fares ² · Maira Campos² · Hsiao-Wang Chen² · Itsushi Peter Shintaku¹ · Gottfried Ewald Konecny² · Jianyu Rao¹



Contents lists available at [ScienceDirect](#)

Gynecologic Oncology

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



Analysis in epithelial ovarian cancer identifies *KANSL1* as a biomarker and target gene for immune response and HDAC inhibition

Marlena S. Fejzo ^{*}, Hsiao-Wang Chen, Lee Anderson, Martina SJ McDermott, Beth Karlan, Gottfried E. Konecny, Dennis J. Slamon

***Gynecol Oncol* 2020;[Online ahead of print].**

Targeting ERBB Family Genomic Alterations in Gynecological Malignancies

Gay L et al.

SGO 2019;Abstract 1319.

A Phase I Study of Mirvetuximab Soravtansine (MIRV) and Gemcitabine (G) in Pts with Selected FR α -Positive Solid Tumours: Results in the Endometrial Cancer (EC) Cohort

Cristea MC et al.

ESMO 2020;Abstract 863P.

Phase II OVARIO Study of Niraparib + Bevacizumab Therapy in Advanced Ovarian Cancer Following Front-Line Platinum-Based Chemotherapy with Bevacizumab

Hardesty MM et al.
SGO 2020;Abstract 4.

An Open-Label Phase II Study of Combination of TSR-042, Bevacizumab, and Niraparib in Patients with Platinum-Resistant Ovarian Cancer (OC): Cohort A of the OPAL Trial

Liu J et al.

AACR 2019;Abstract CT157/1.

EBioMedicine 43 (2019) 9–10



Contents lists available at [ScienceDirect](#)

EBioMedicine

journal homepage: www.ebiomedicine.com

EBioMedicine
Published by [THE LANCET](#)

Commentary

Combining PARP and CDK4/6 inhibitors in MYC driven ovarian cancer



Gottfried E. Konecny

REVIEW

Curr Opin Obstet Gynecol 2020;32(1):36-41.



Mechanisms of PARP inhibitor resistance in ovarian cancer

Kari Kubalanza^a and Gottfried E. Konecny^{a,b}

Development and Validation of the Gene Expression Predictor of High-grade Serous Ovarian Carcinoma Molecular SubTYPE (PrOTYPE)



Aline Talhouk^{1,2}, Joshy George³, Chen Wang⁴, Timothy Budden^{5,6}, Tuan Zea Tan⁷, Derek S. Chiu¹, Stefan Kommoss⁸, Huei San Leong⁹, Stephanie Chen¹⁰, Maria P. Intermaggio⁵, Blake Gilks^{1,11}, Tayyeb M. Nazeran¹, Mila Volchek¹², Wafaa Elatreh¹³, Rex C. Bentley¹⁴, Janine Senz^{1,11}, Amy Lum¹, Veronica Chow¹, Hanwei Sudderuddin¹, Robertson Mackenzie¹, Samuel C.Y. Leong¹, Geyi Liu¹, Dustin Johnson¹, Billy Chen¹, AOCs Group^{9,15,16}, Jennifer Alsop¹⁷, Susana N. Banerjee¹⁸, Sabine Behrens¹⁹, Clara Bodelon²⁰, Alison H. Brand²¹, Louise Brinton²⁰, Michael E. Carney²², Yoke-Eng Chiew^{16,21}, Kara L. Cushing-Haugen²³, Cezary Cybulski²⁴, Darren Ennis^{25,26}, Sian Fereday^{9,27}, Renée T. Fortner¹⁹, Jesús García-Donas²⁸, Aleksandra Gentry-Maharaj²⁹, Rosalind Glasspool³⁰, Teodora Goranova³¹, Casey S. Greene³², Paul Haluska³³, Holly R. Harris^{23,34}, Joy Hendley^{9,27}, Brenda Y. Hernandez³⁵, Esther Herpel³⁶, Mercedes Jimenez-Linan³⁷, Chloe Karpinskyj²⁹, Scott H. Kaufmann^{33,38}, Gary L. Keeney³⁹, Catherine J. Kennedy^{16,21}, Martin Köbel⁴⁰, Jennifer M. Koziak⁴¹, Melissa C. Larson⁴, Jenny Lester^{42,43}, Liz-Anne Lewsley⁴⁴, Jolanta Lissowska⁴⁵, Jan Lubiński²⁴, Hugh Luk³⁵, Geoff Macintyre³¹, Sven Mahner⁴⁶, Iain A. McNeish^{25,26}, Janusz Menkiszak⁴⁷, Nikilyn Nevins⁴⁸, Ana Osorio^{49,50}, Oleg Oszurek²⁴, José Palacios⁵¹, Samantha Hinsley⁴⁴, Celeste L. Pearce^{52,53}, Malcolm C. Pike^{53,54}, Anna M. Piskorz³¹, Isabelle Ray-Coquard⁵⁵, Valerie Rhenius¹⁷, Cristina Rodriguez-Antona^{50,56}, Raghwa Sharma^{57,58}, Mark E. Sherman⁵⁹, Dilrini De Silva³¹, Naveena Singh⁶⁰, Peter Sinn⁶¹, Dennis Slamon⁶², Honglin Song¹⁷, Helen Steed⁶³, Euan A. Stronach²⁵, Pamela J. Thompson⁶⁴, Aleksandra Tołoczko²⁴, Britton Trabert²⁰, Nadia Traficante^{9,27}, Chiu-Chen Tseng⁶⁵, Martin Widschwendter⁶⁶, Lynne R. Wilkens³⁵, Stacey J. Winham⁴, Boris Winterhoff⁶⁷, Alicia Beeghly-Fadiel⁶⁸, Javier Benitez^{49,50}, Andrew Berchuck⁶⁹, James D. Brenton³¹, Robert Brown⁷⁰, Jenny Chang-Claude^{19,71}, Georgia Chenevix-Trench¹⁵, Anna deFazio^{16,21}, Peter A. Fasching^{62,72}, María J. García^{50,56}, Simon A. Gayther⁷³, Marc T. Goodman⁶⁴, Jacek Gronwald²⁴, Michelle J. Henderson⁷⁴, Beth Y. Karlan^{42,43}, Linda E. Kelemen⁷⁵, Usha Menon²⁹, Sandra Orsulic^{42,43}, Paul D.P. Pharoah^{17,76}, Nicolas Wentzensen²⁰, Anna H. Wu⁶⁵, Joellen M. Schildkraut⁷⁷, Mary Anne Rossing^{23,34}, Gottfried E. Konecny⁶², David G. Huntsman^{1,2,11,78}, Ruby Yun-Ju Huang^{7,79}, Ellen L. Goode⁸⁰, Susan J. Ramus^{5,81}, Jennifer A. Doherty⁸², David D. Bowtell^{9,27}, and Michael S. Anglesio^{1,2,11}

Meet The Professor with Dr Konecny

MODULE 1: Clinical Scenarios and Comments from Dr Mirza

MODULE 2: Gynecologic Oncology Journal Club with Dr Konecny

- *NEJM* review paper: Endometrial cancer
- Comprehensive genomic profiling of recurrent endometrial cancer: Implications for therapy
- Somatic BRCA mutations in endometrial cancer and the clinical implications
- Inhibition of PD-1 (pembrolizumab) and VEGF (lenvatinib) in MSS endometrial cancer
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- PrOTYPE: Development and validation of the gene expression predictor of HGSOC molecular subtype

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

MODULE 4: Key Recent Data Sets











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)?

 <p>MICHAEL J BIRRER, MD, PHD</p>	Lenvatinib/pembrolizumab	 <p>RICHARD T PENSON, MD, MRCP</p>	Lenvatinib/pembrolizumab
 <p>ROBERT L COLEMAN, MD</p>	Lenvatinib/pembrolizumab	 <p>MATTHEW A POWELL, MD</p>	Lenvatinib/pembrolizumab
 <p>GOTTFRIED E KONECNY, MD</p>	Lenvatinib/pembrolizumab	 <p>BRIAN M SLOMOVITZ, MD</p>	Lenvatinib/pembrolizumab
 <p>ANA OAKNIN, MD, PHD</p>	Lenvatinib/pembrolizumab	 <p>KRISHNANSU S TEWARI, MD</p>	Lenvatinib/pembrolizumab
 <p>DAVID M O'MALLEY, MD</p>	Lenvatinib/pembrolizumab	 <p>PROFESSOR IGNACE VERGOTE</p>	Lenvatinib/pembrolizumab











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?

 <p>MICHAEL J BIRRER, MD, PHD</p>	Pembrolizumab	 <p>RICHARD T PENSON, MD, MRCP</p>	Pembrolizumab
 <p>ROBERT L COLEMAN, MD</p>	Pembrolizumab	 <p>MATTHEW A POWELL, MD</p>	Pembrolizumab
 <p>GOTTFRIED E KONECNY, MD</p>	Pembrolizumab	 <p>BRIAN M SLOMOVITZ, MD</p>	Pembrolizumab
 <p>ANA OAKNIN, MD, PHD</p>	Dostarlimab	 <p>KRISHNANSU S TEWARI, MD</p>	Pembrolizumab
 <p>DAVID M O'MALLEY, MD</p>	Pembrolizumab	 <p>PROFESSOR IGNACE VERGOTE</p>	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?

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











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?

 <p>MICHAEL J BIRRER, MD, PHD</p>	Pembrolizumab	 <p>RICHARD T PENSON, MD, MRCP</p>	Pembrolizumab
 <p>ROBERT L COLEMAN, MD</p>	Pembrolizumab	 <p>MATTHEW A POWELL, MD</p>	Pembrolizumab
 <p>GOTTFRIED E KONECNY, MD</p>	Pembrolizumab	 <p>BRIAN M SLOMOVITZ, MD</p>	Pembrolizumab
 <p>ANA OAKNIN, MD, PHD</p>	Dostarlimab	 <p>KRISHNANSU S TEWARI, MD</p>	Pembrolizumab
 <p>DAVID M O'MALLEY, MD</p>	Pembrolizumab	 <p>PROFESSOR IGNACE VERGOTE</p>	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?

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

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

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?

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

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

 <p>MICHAEL J BIRRER, MD, PHD</p>	Well tolerated except for epistaxis	 <p>RICHARD T PENSON, MD, MRCP</p>	Excited by it
 <p>ROBERT L COLEMAN, MD</p>	Similar to other single-agent chemotherapy	 <p>MATTHEW A POWELL, MD</p>	Reasonable toxicity
 <p>GOTTFRIED E KONECNY, MD</p>	Acceptable tolerability	 <p>BRIAN M SLOMOVITZ, MD</p>	Well tolerated; ocular side effects
 <p>ANA OAKNIN, MD, PHD</p>	Moderate toxicity	 <p>KRISHNANSU S TEWARI, MD</p>	Relatively well tolerated so far
 <p>DAVID M O'MALLEY, MD</p>	Reasonable toxicity	 <p>PROFESSOR IGNACE VERGOTE</p>	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 tisetumab vedotin were approved, what would likely be your next line of treatment?

1. Pembrolizumab
2. Tisetumab vedotin
3. Other

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?

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

Meet The Professor with Dr Konecny

MODULE 1: Clinical Scenarios and Comments from Dr Mirza

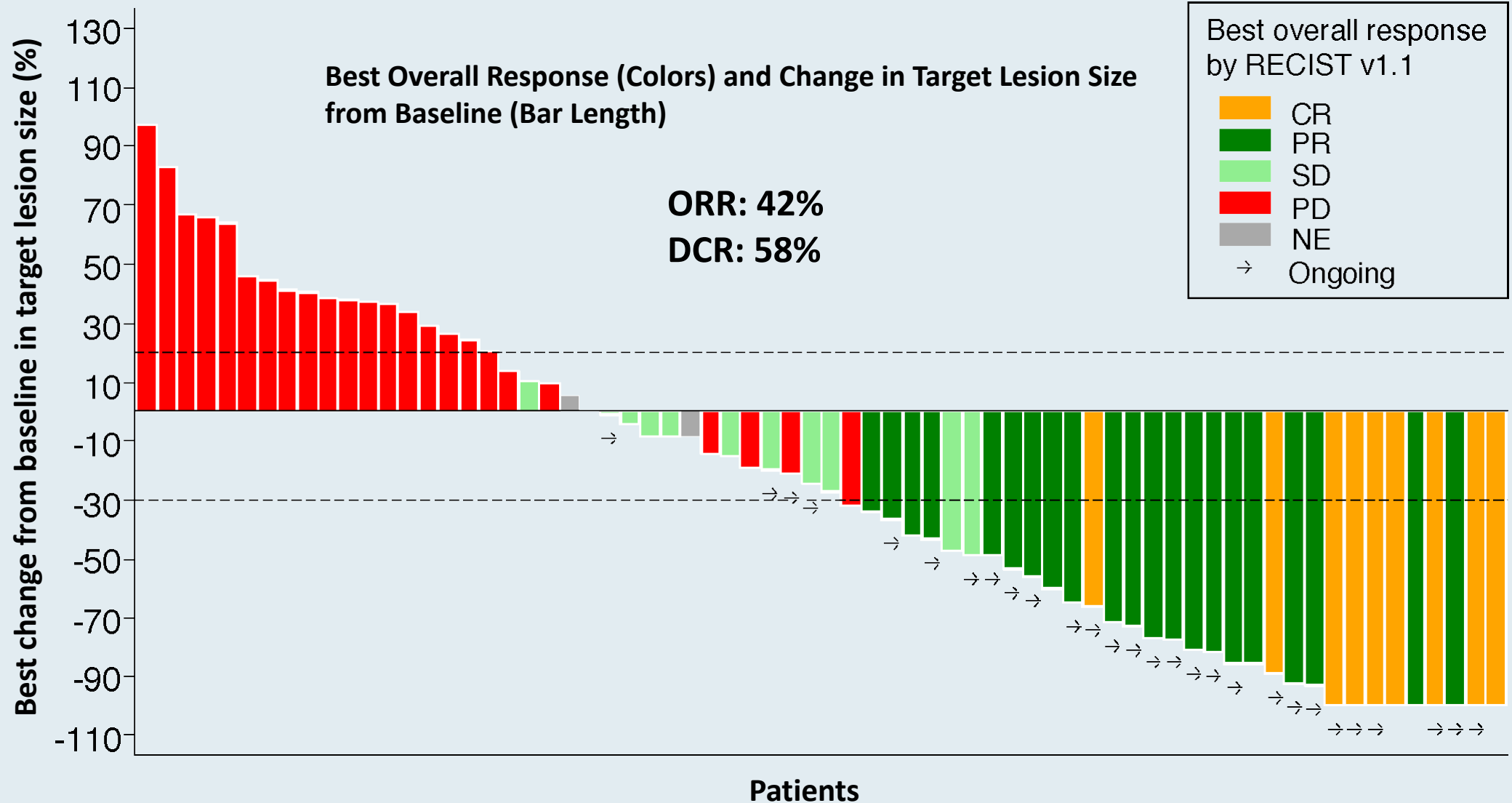
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- PrOTYPE: Development and validation of the gene expression predictor of HGSOC molecular subtype

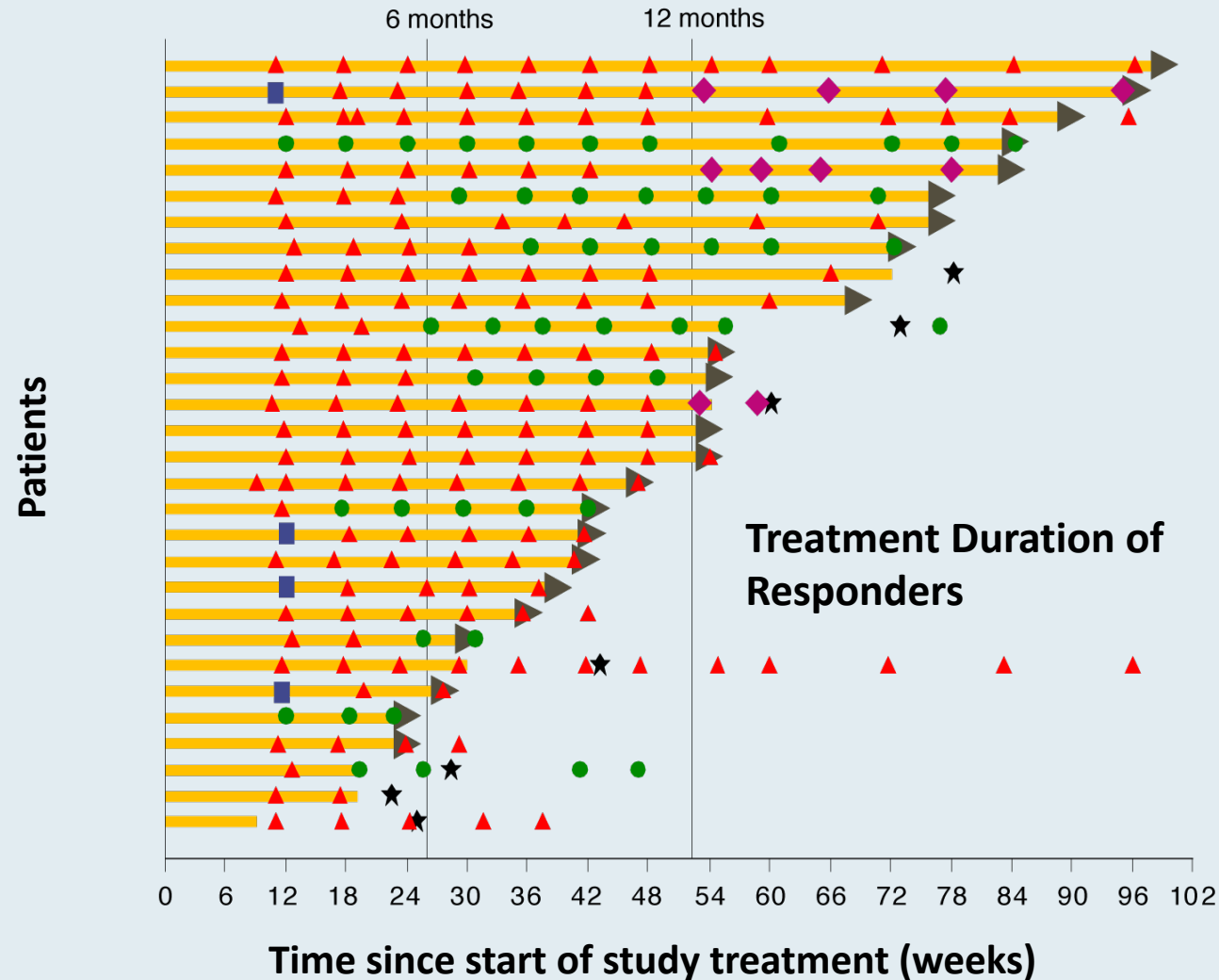
MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Data Sets

GARNET: Dostarlimab in Recurrent or Advanced dMMR Endometrial Cancer



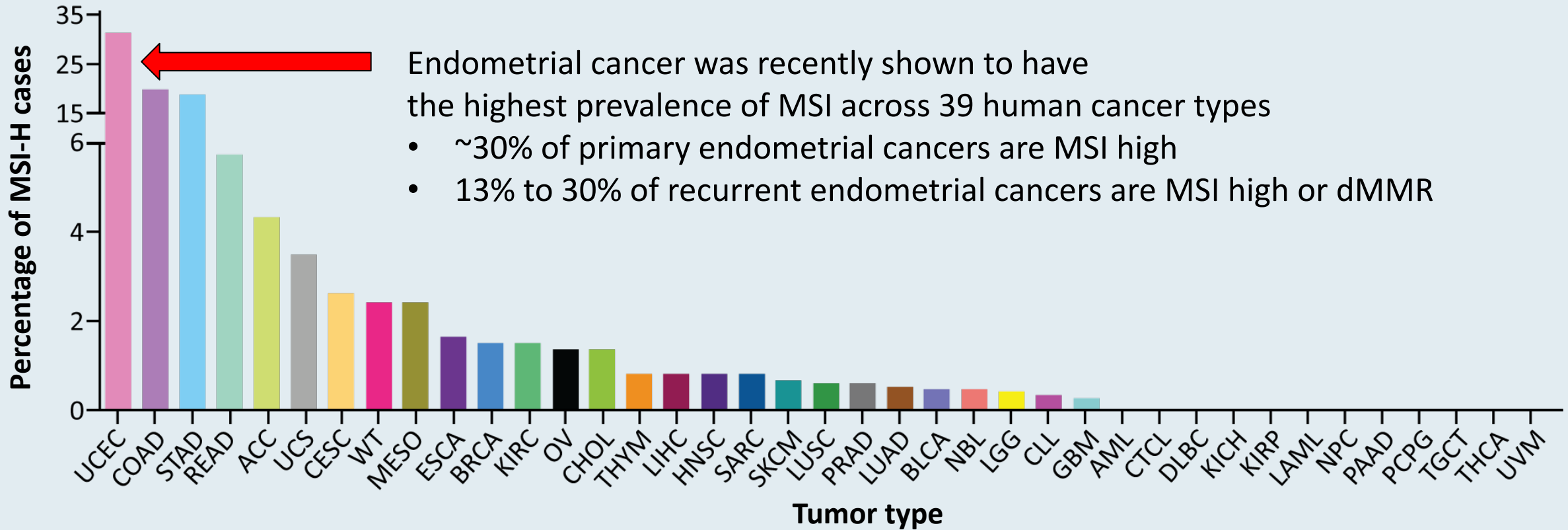
GARNET: Dostarlimab in Recurrent or Advanced dMMR Endometrial Cancer



- 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

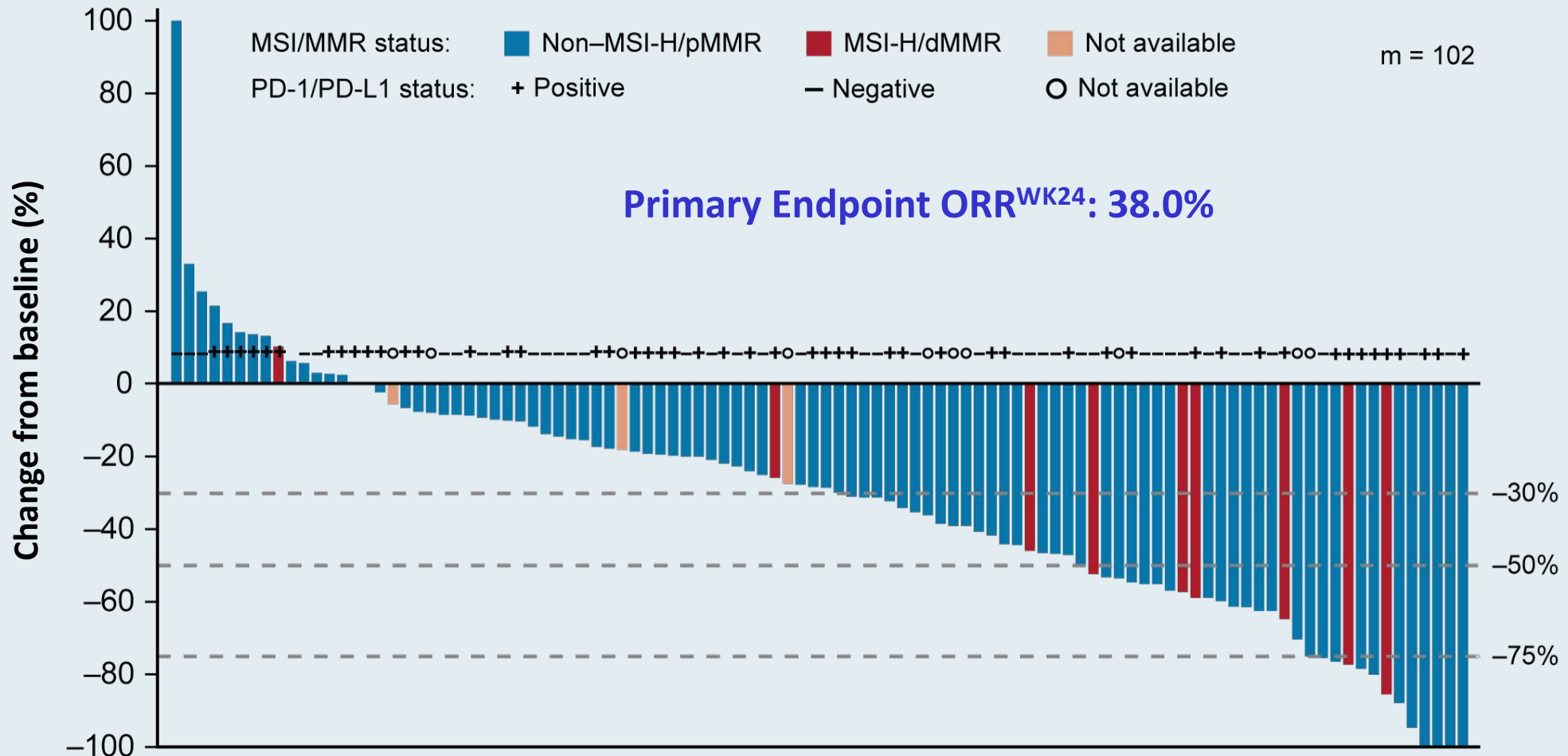
High MSI Across 39 Cancer Types

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

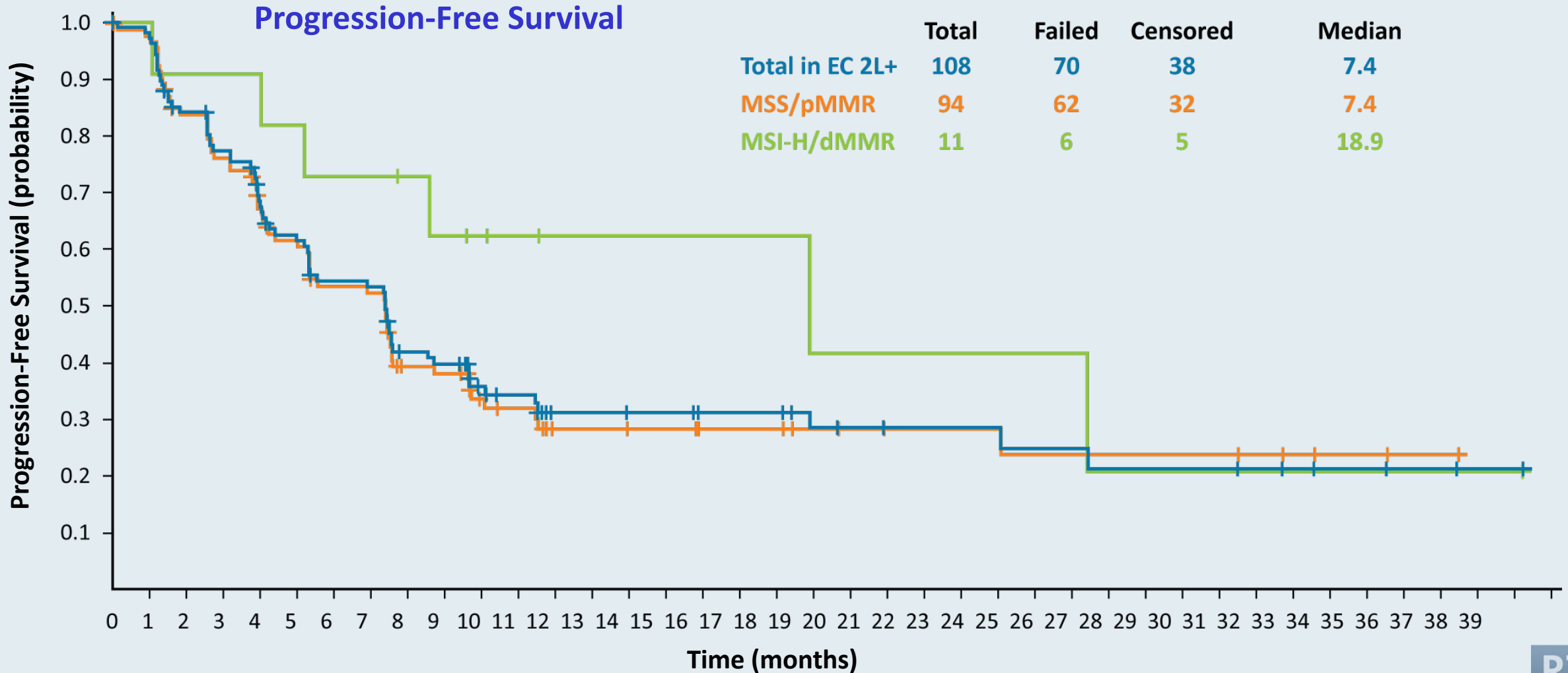


UCEC = uterine corpus endometrial carcinoma

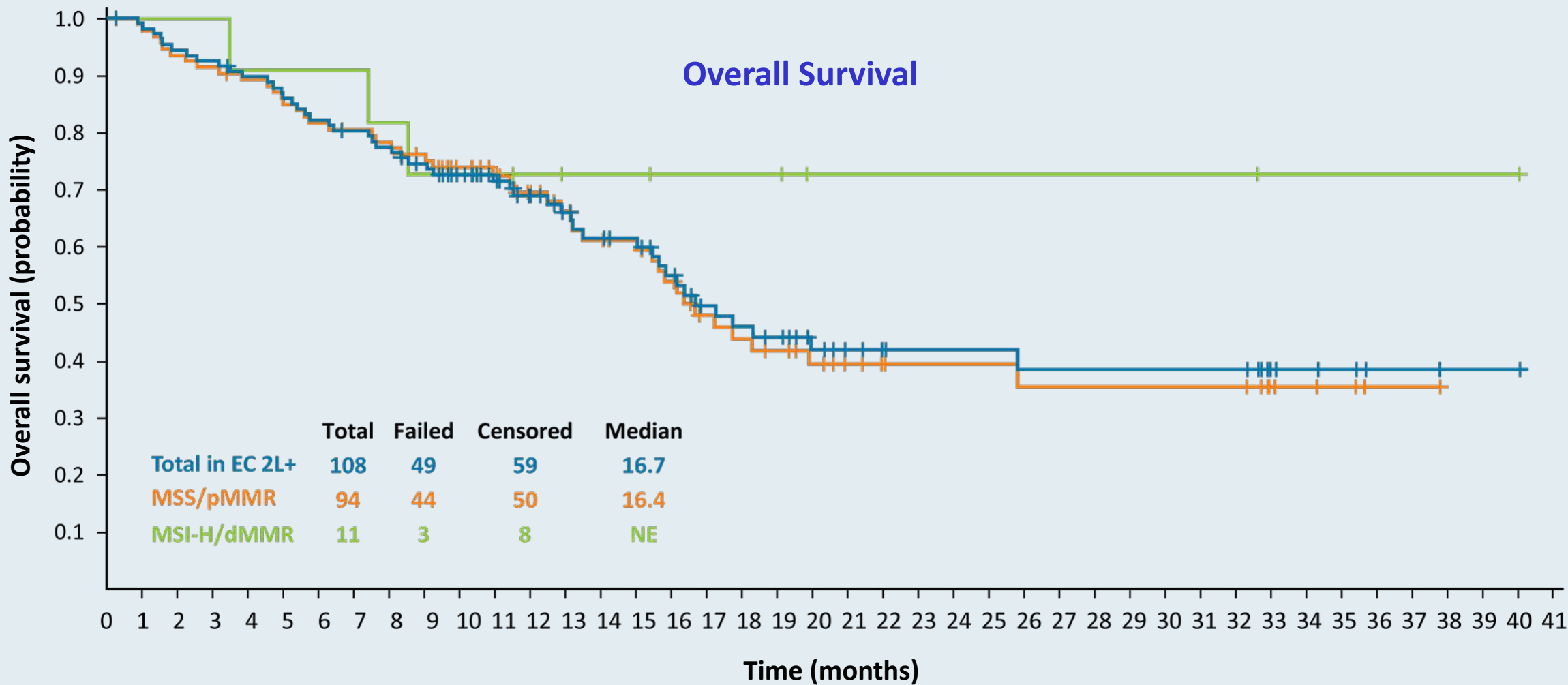
KEYNOTE-146: Pembrolizumab/Lenvatinib in Advanced Endometrial Cancer That Is Not MSI High or dMMR After Disease Progression on Prior Systemic Therapy



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



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

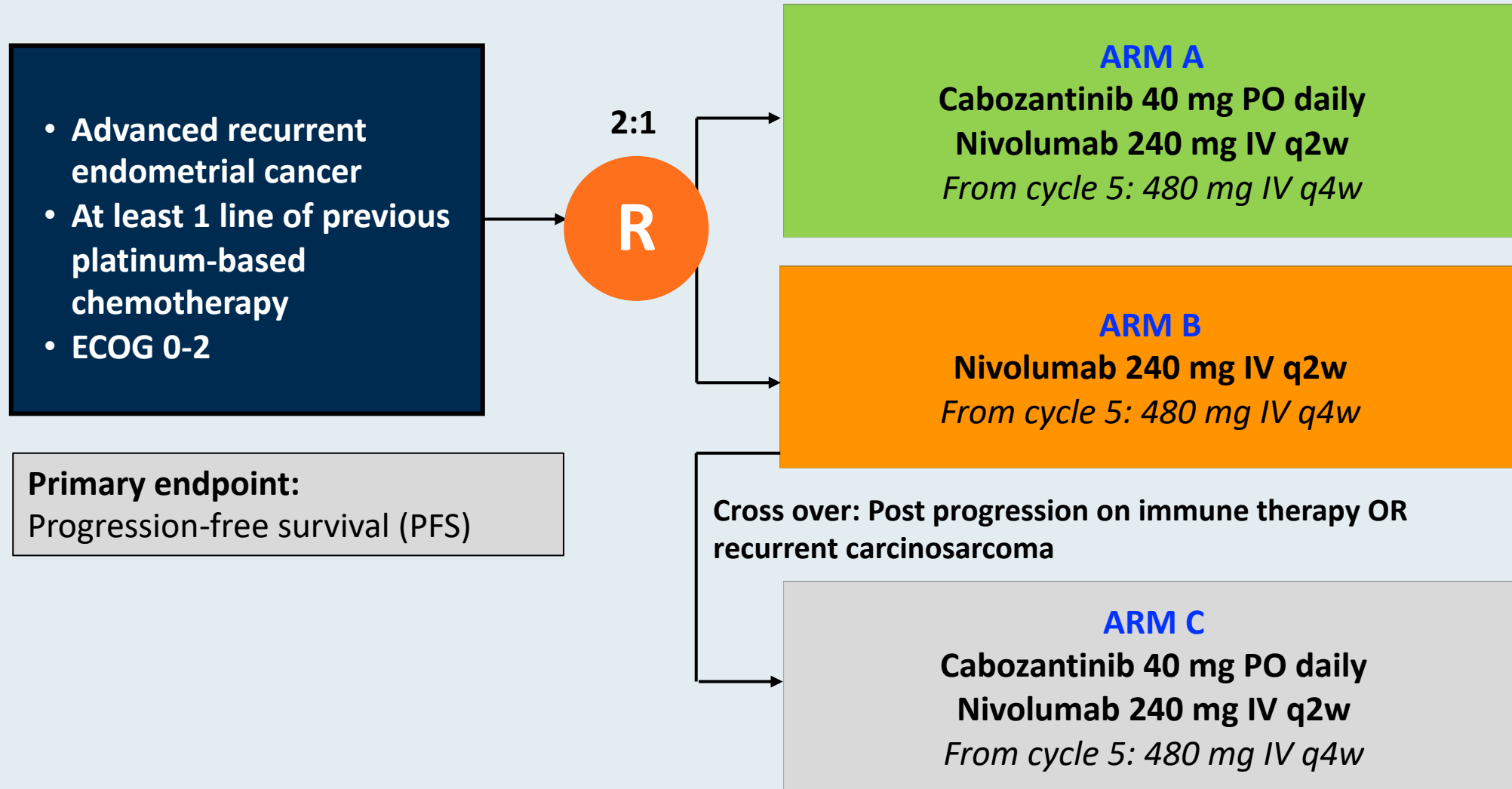


NCI 10104: A Randomized Phase 2 Study of Cabozantinib in Combination with Nivolumab in Advanced, Recurrent Metastatic Endometrial Cancer

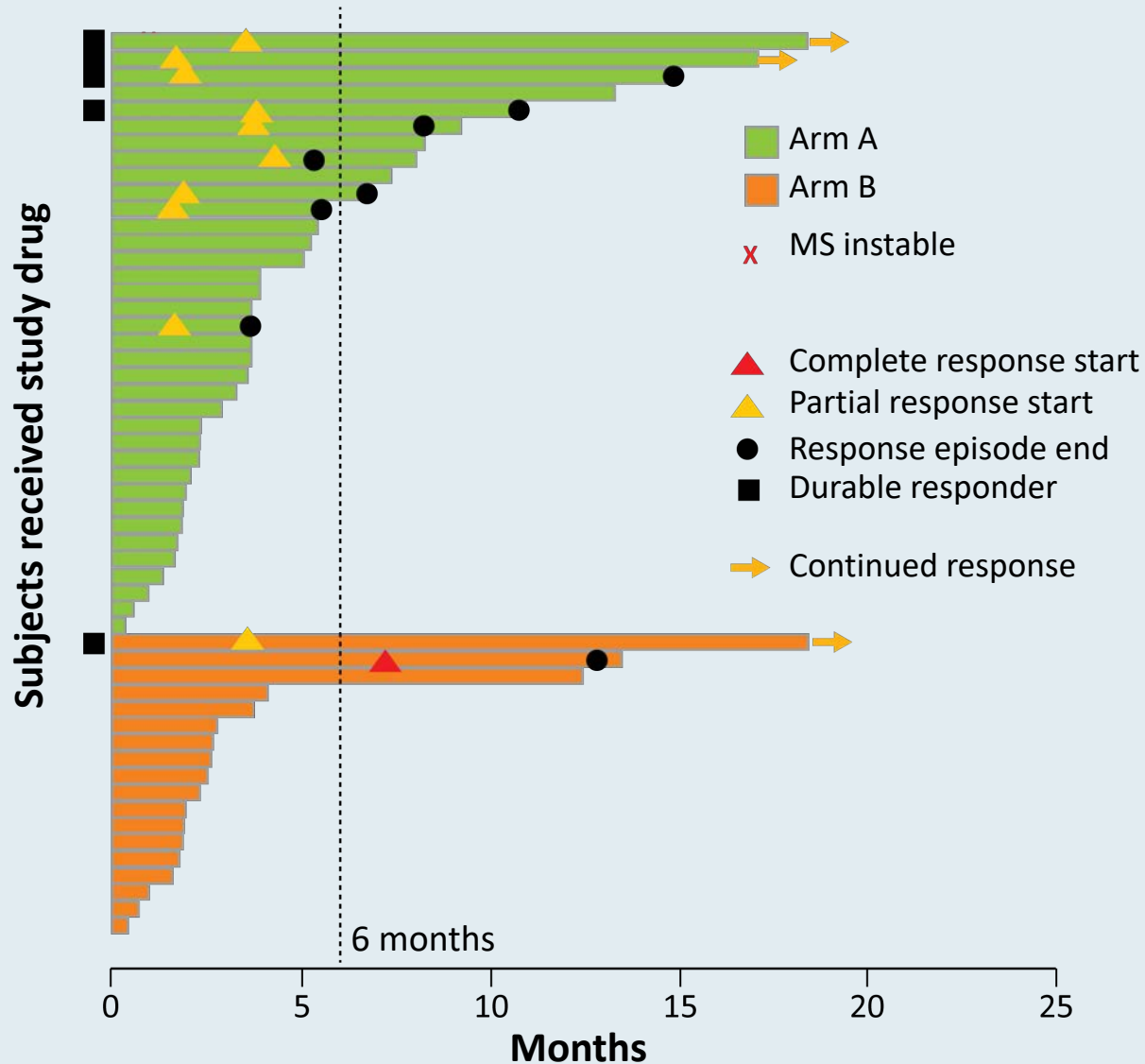
Lheureux S et al.

ASCO 2020;Abstract 6010.

NCI 10104 Phase II Study Schema



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

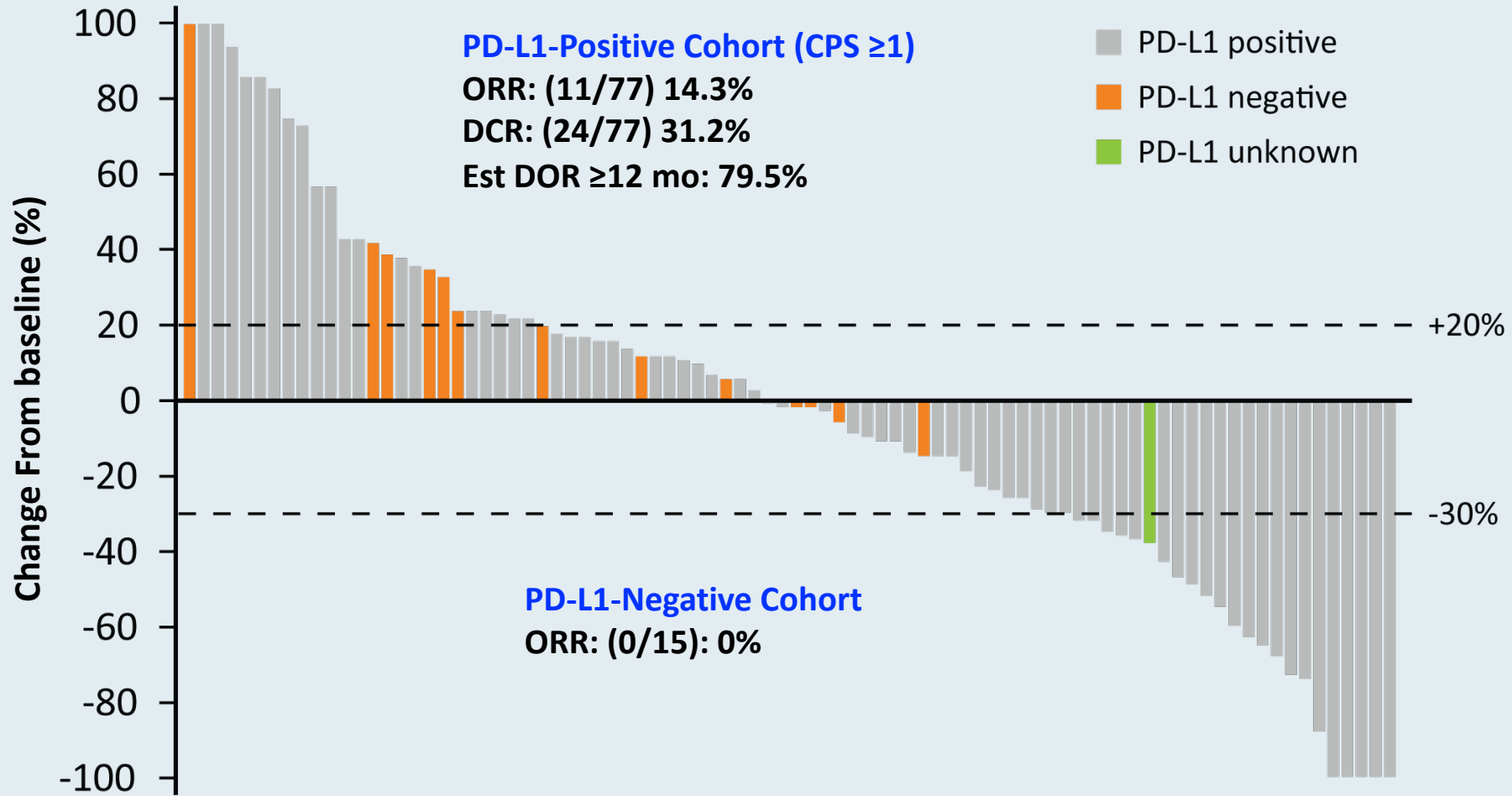
[†] Immature, 55% events

Select Ongoing Phase III Immune Checkpoint Inhibitor Combination Studies

Trial	N	Eligibility	Randomization
KEYNOTE-775	780	<ul style="list-style-type: none"> Advanced, recurrent or metastatic EC PD after 1 prior platinum-based chemo regimen 	<ul style="list-style-type: none"> Pembro + lenvatinib Paclitaxel + carboplatin
LEAP-001	720	<ul style="list-style-type: none"> Stage III, IV or recurrent EC May have received 1 prior line of platinum-based adjuvant or neoadjuvant chemo 	<ul style="list-style-type: none"> Pembro + lenvatinib Paclitaxel + carboplatin
NRG-GY018	810	<ul style="list-style-type: none"> Stage III, IVA or IVB or recurrent EC No prior chemo for EC, except adjuvant 	<ul style="list-style-type: none"> Pembro + paclitaxel + carboplatin → Pembro Placebo + paclitaxel + carboplatin → Placebo
RUBY	470	<ul style="list-style-type: none"> Stage III, IV or first recurrent EC 	<ul style="list-style-type: none"> Dostarlimab + paclitaxel + carboplatin Placebo + paclitaxel + carboplatin
AtTEnd	550	<ul style="list-style-type: none"> Newly dx with residual disease after surgery, OR inoperable Stage III-IV naïve to first-line systemic treatment 	<ul style="list-style-type: none"> Atezolizumab + paclitaxel + carboplatin Placebo + paclitaxel + carboplatin

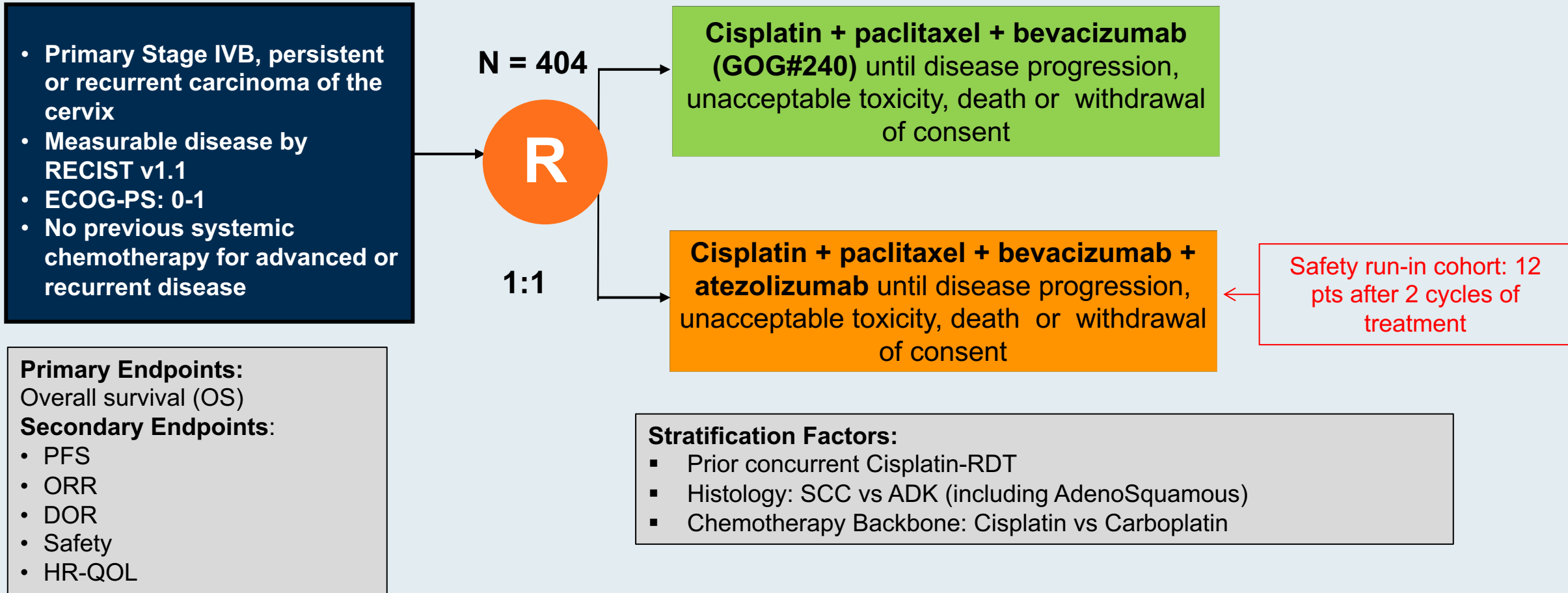
Anti-PD-1/PD-L1 Antibodies in Cervical Cancer

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

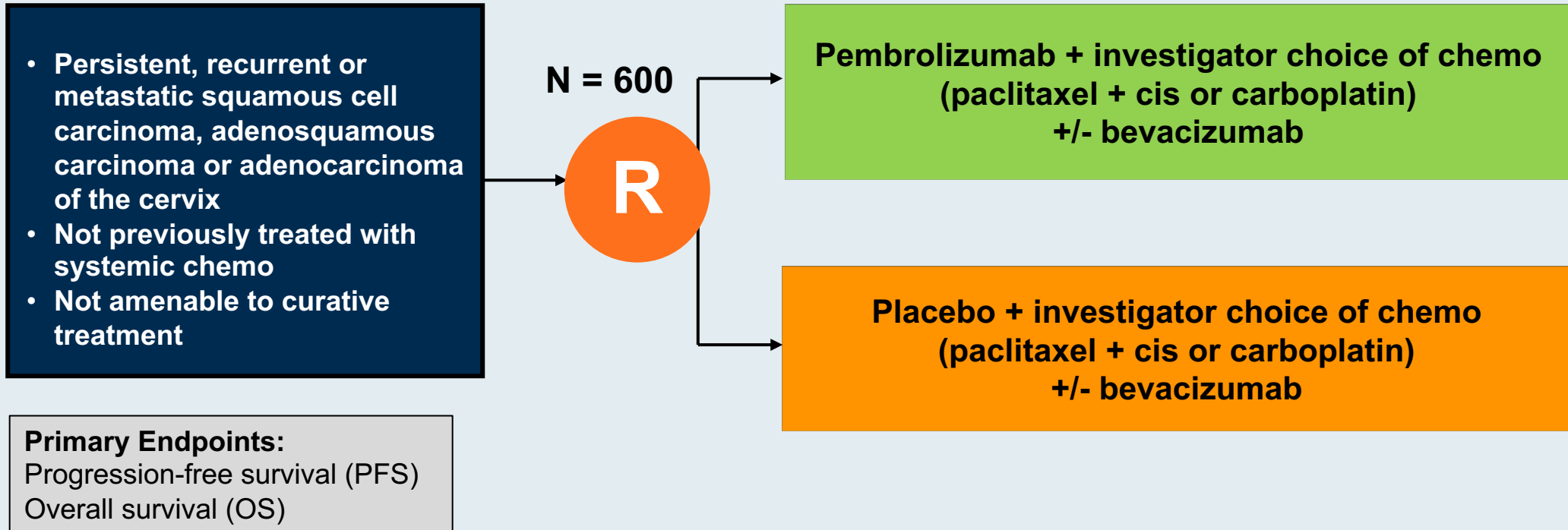


Combined Positive Score (CPS) = PD-L1+ cells (tumor cells, lymphocytes, macrophages) / Total number of tumor cells x 100

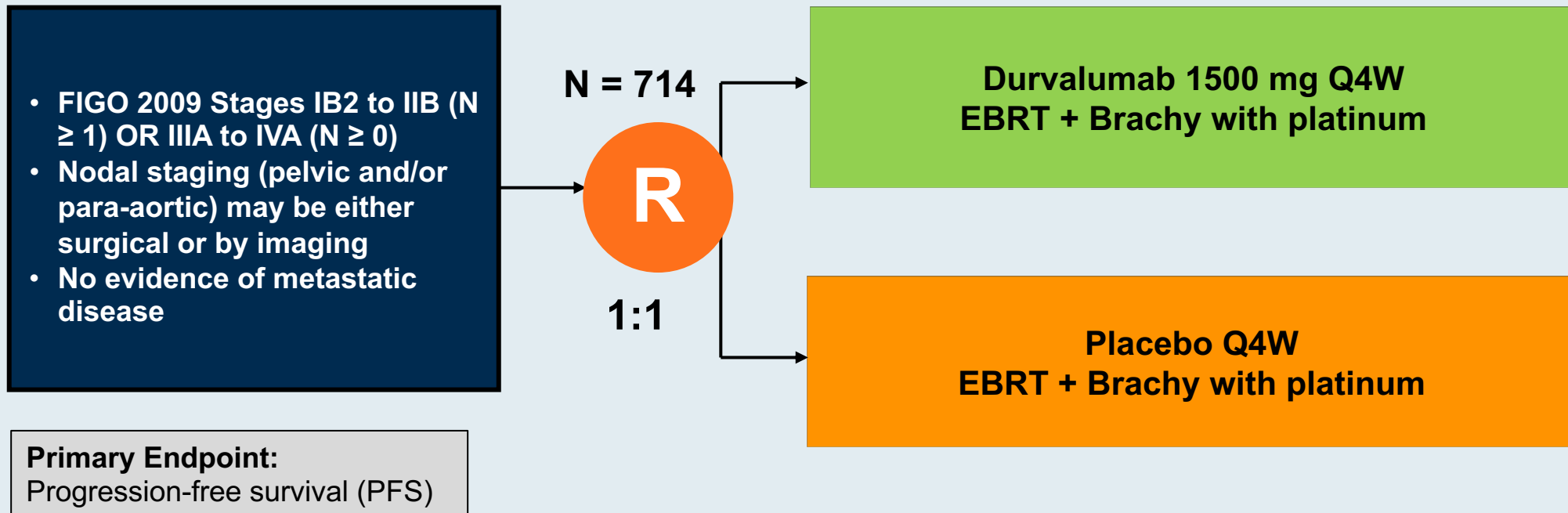
BEATcc Phase III Randomized Front-Line Trial of Atezolizumab



KEYNOTE-826 Phase III Schema



CALLA Phase III Schema



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

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

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

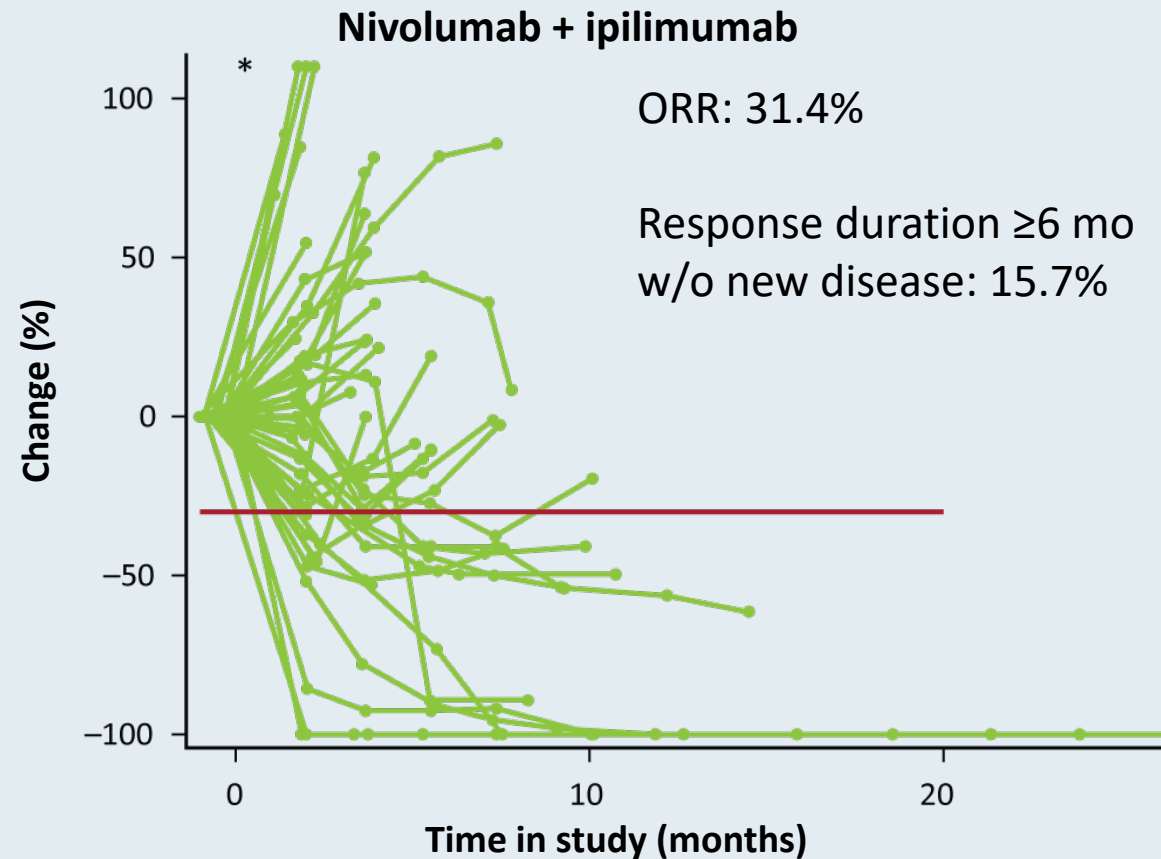
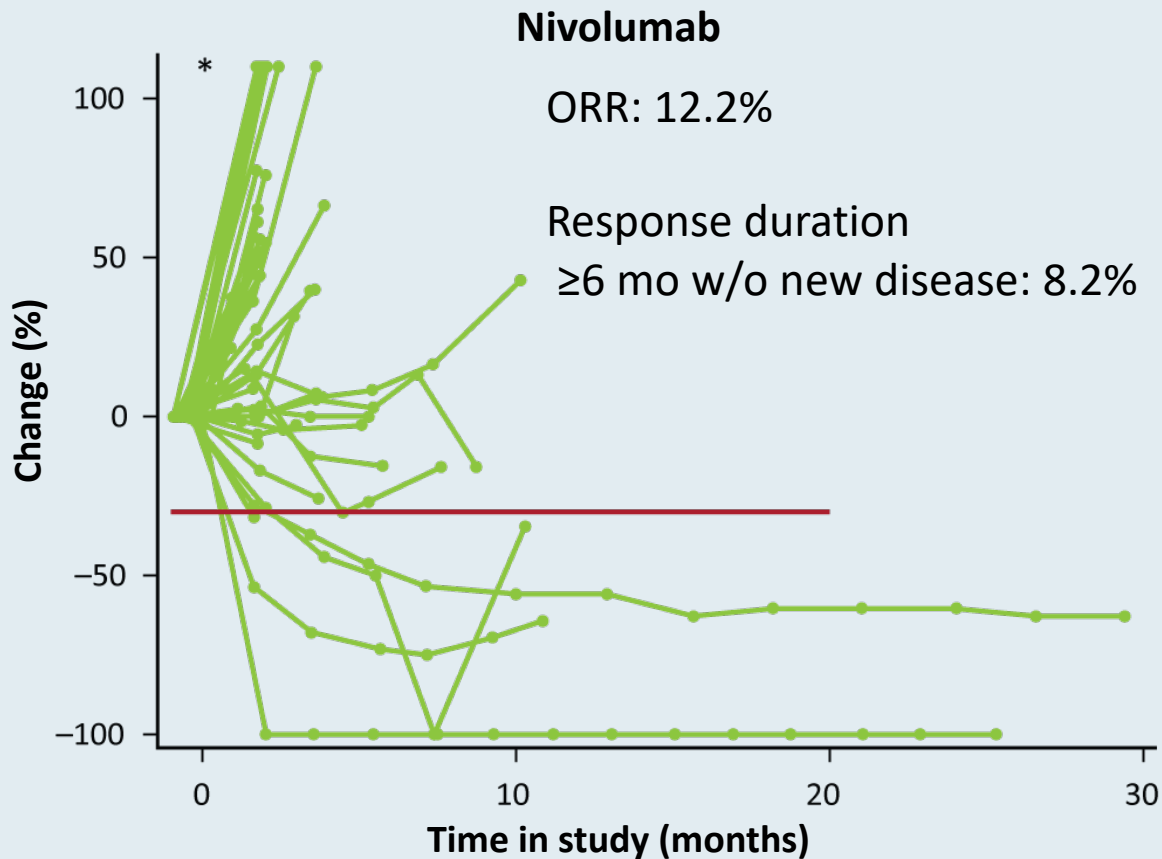
Endpoint	Cohort A 1-3 prior lines PFI/TFI 3-12 months			Cohort B 4-6 prior lines PFI/TFI ≥3 months			Cohorts A + B All comers		
	All n = 285	CPS ≥1 n = 101	CPS ≥10 n =43	All n = 91	CPS ≥1 n = 49	CPS ≥10 n = 22	All n = 376	CPS ≥1 n = 150	CPS ≥10 n = 65
ORR	8.1%	6.9%	11.6%	9.9%	10.2%	18.2%	8.5%	8.0%	13.8%
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

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, <i>p</i> = 0.83		HR: 0.80, <i>p</i> = 0.21		Reference	
Median PFS	1.9 mo		3.7 mo		3.5 mo	
	HR: 1.68, <i>p</i> > 0.99		HR: 0.78, <i>p</i> = 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

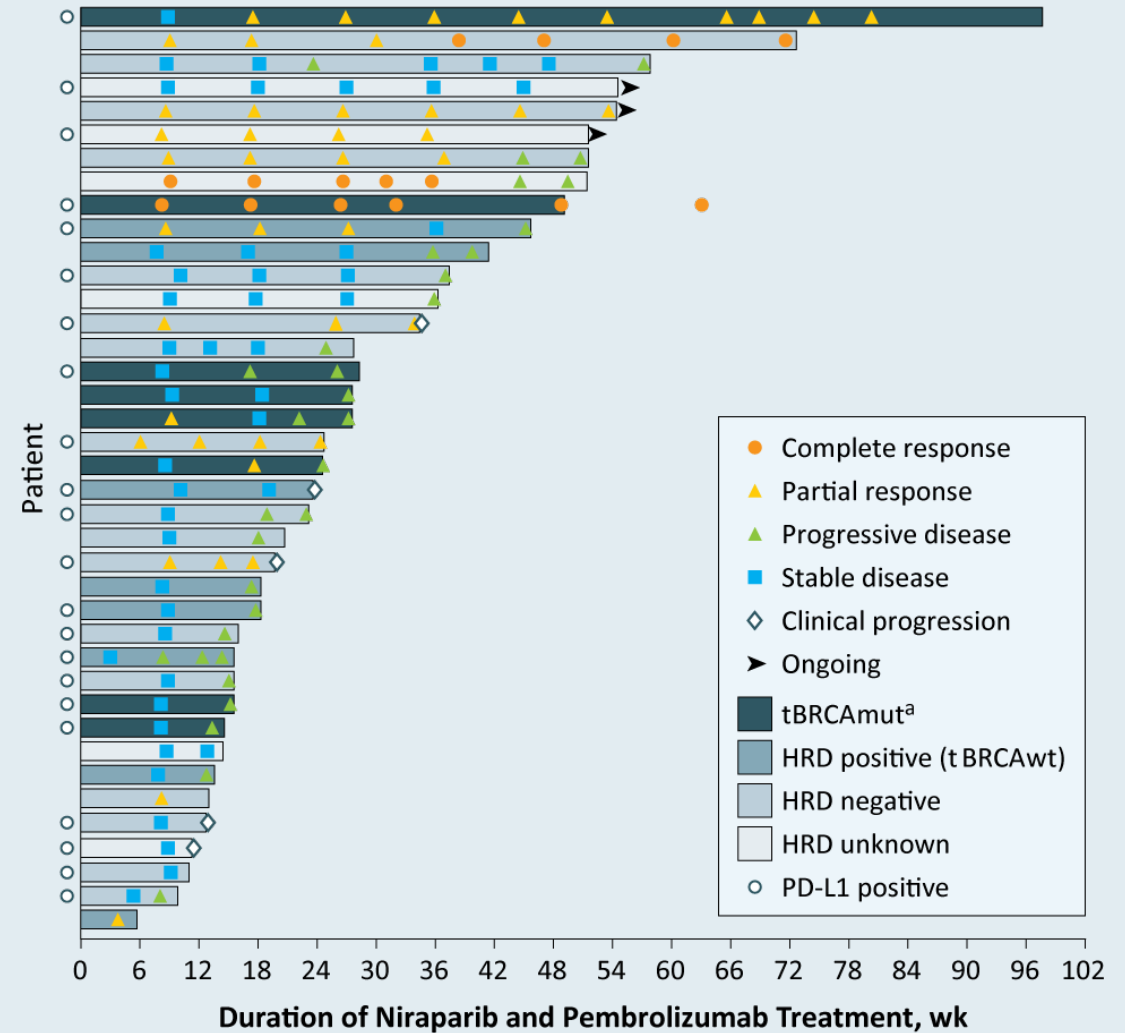
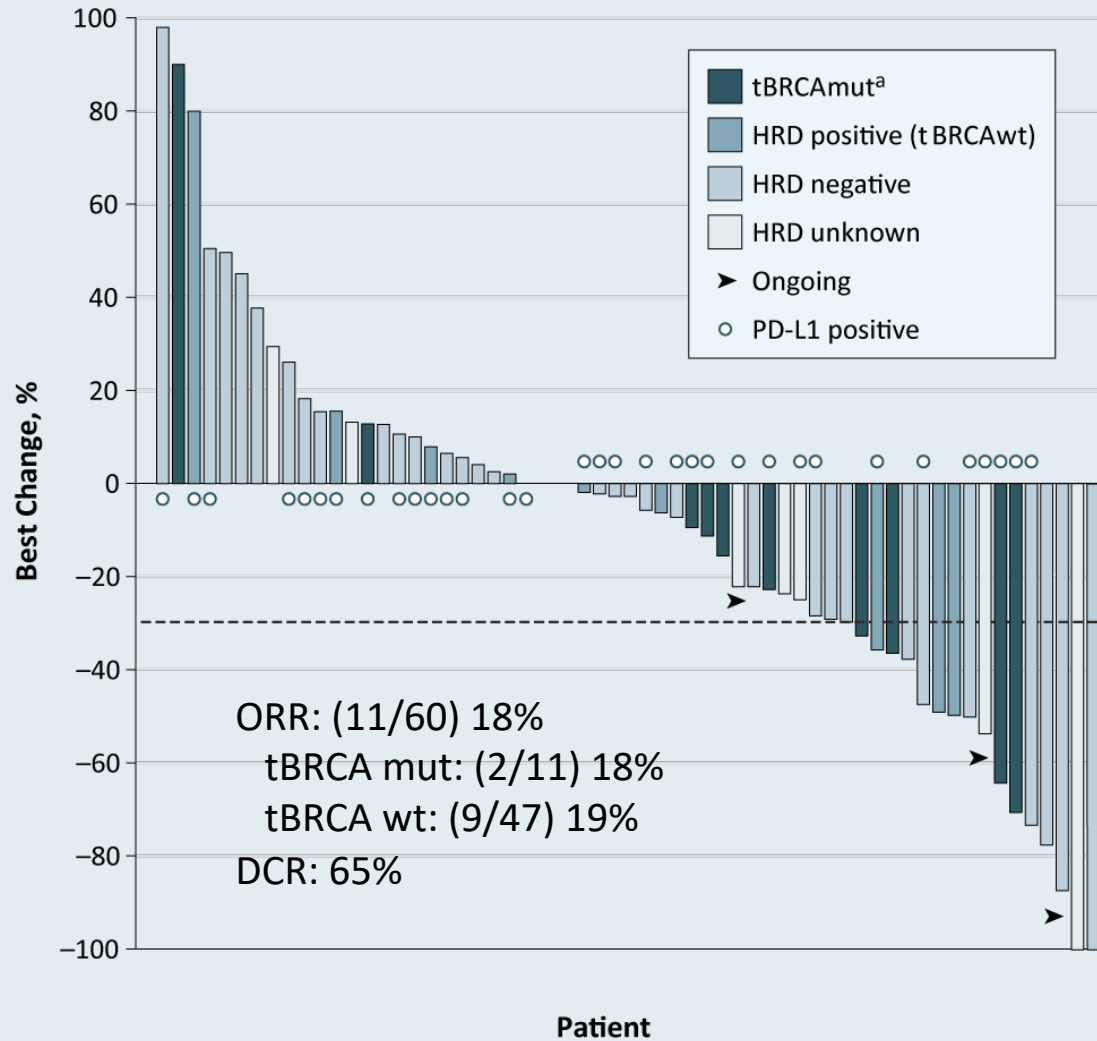
NRG GY003 Phase II Study of Nivolumab with or without Ipilimumab in Recurrent or Persistent OC

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

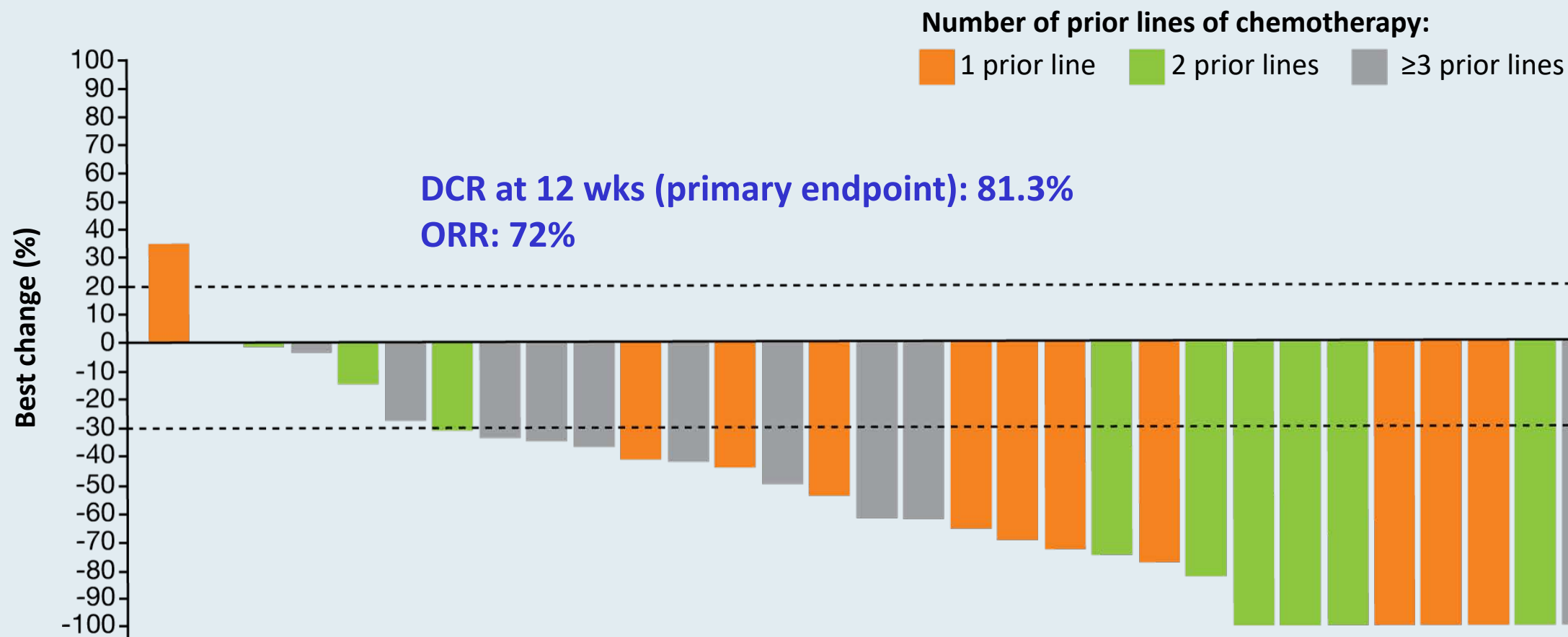


PD-L1 expression was not significantly associated with response in either treatment group

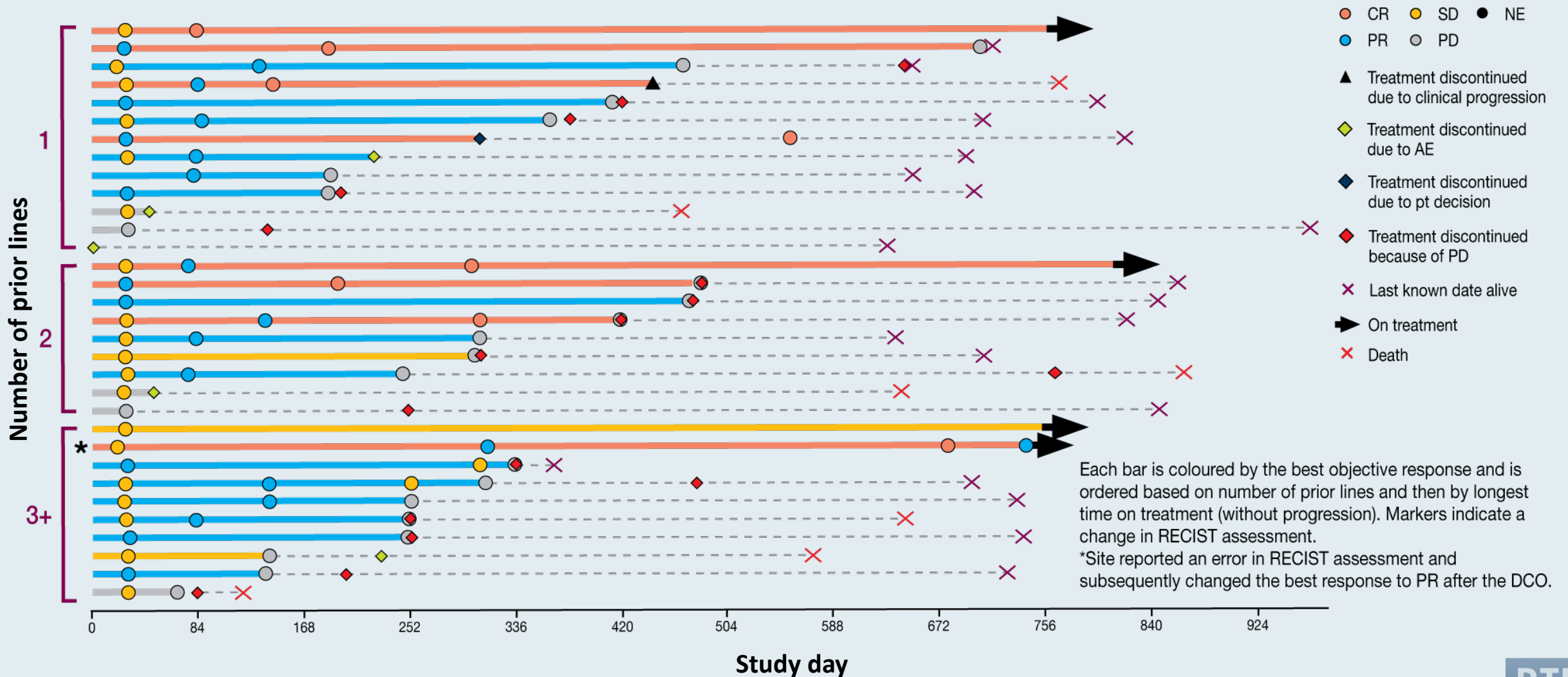
TOPACIO/KEYNOTE-162: Niraparib and Pembrolizumab in Recurrent Platinum-Resistant Ovarian Cancer



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



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



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.

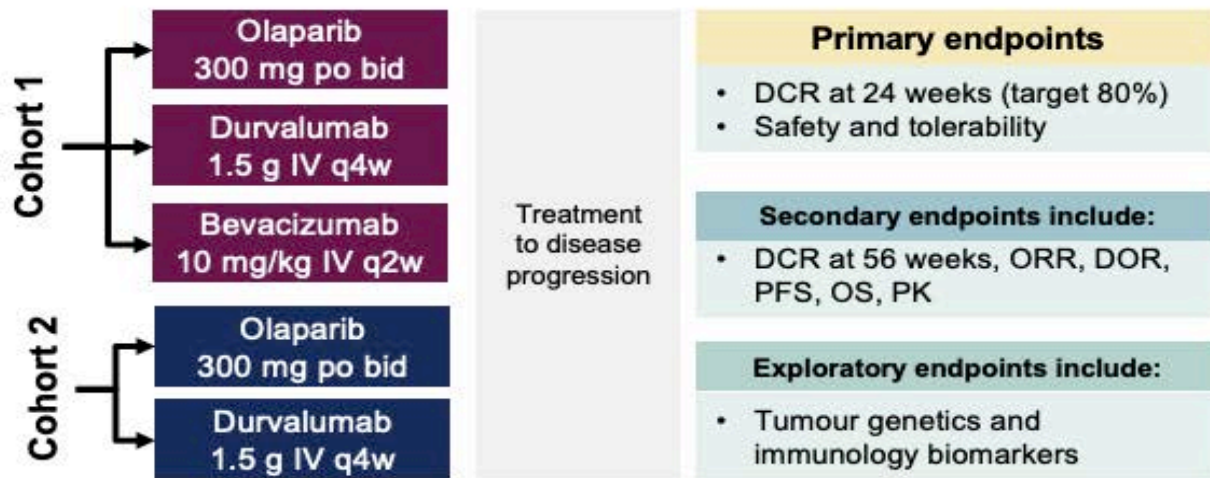
ESMO 2020;Abstract 814MO.

MEDIOLA: gBRCAwt Cohorts

Study Design

Patient population

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



Sequential enrolment

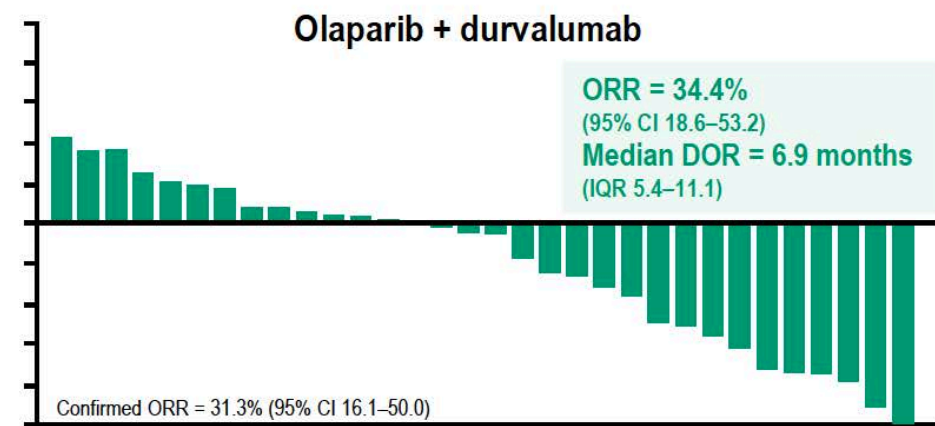
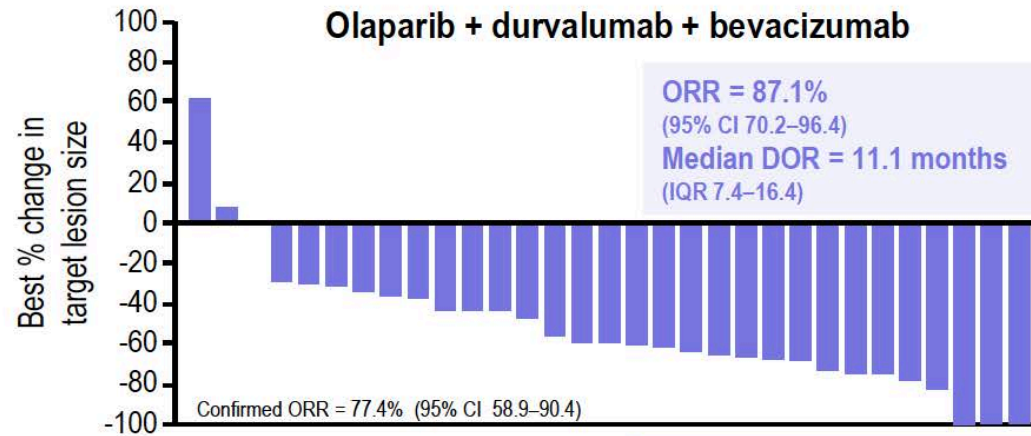
Tumour assessments every 8 weeks

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

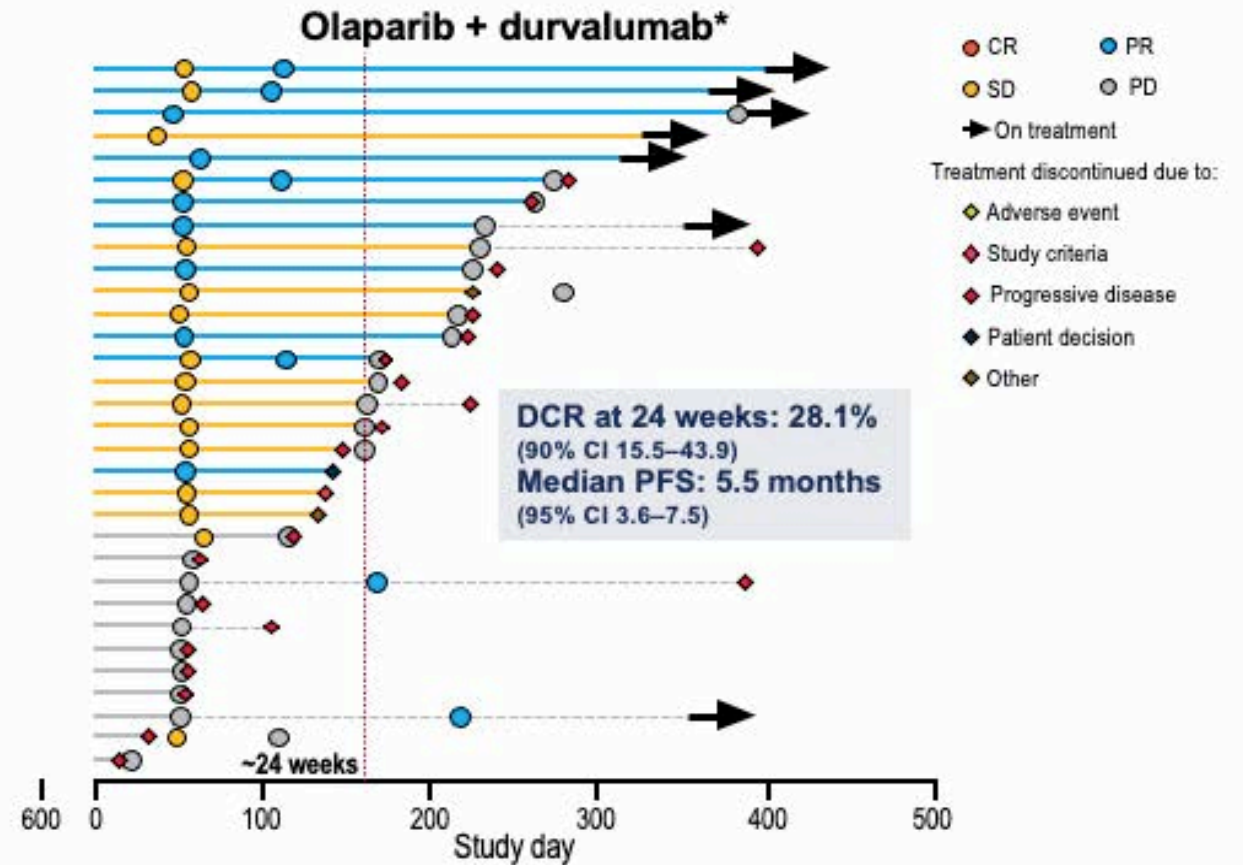
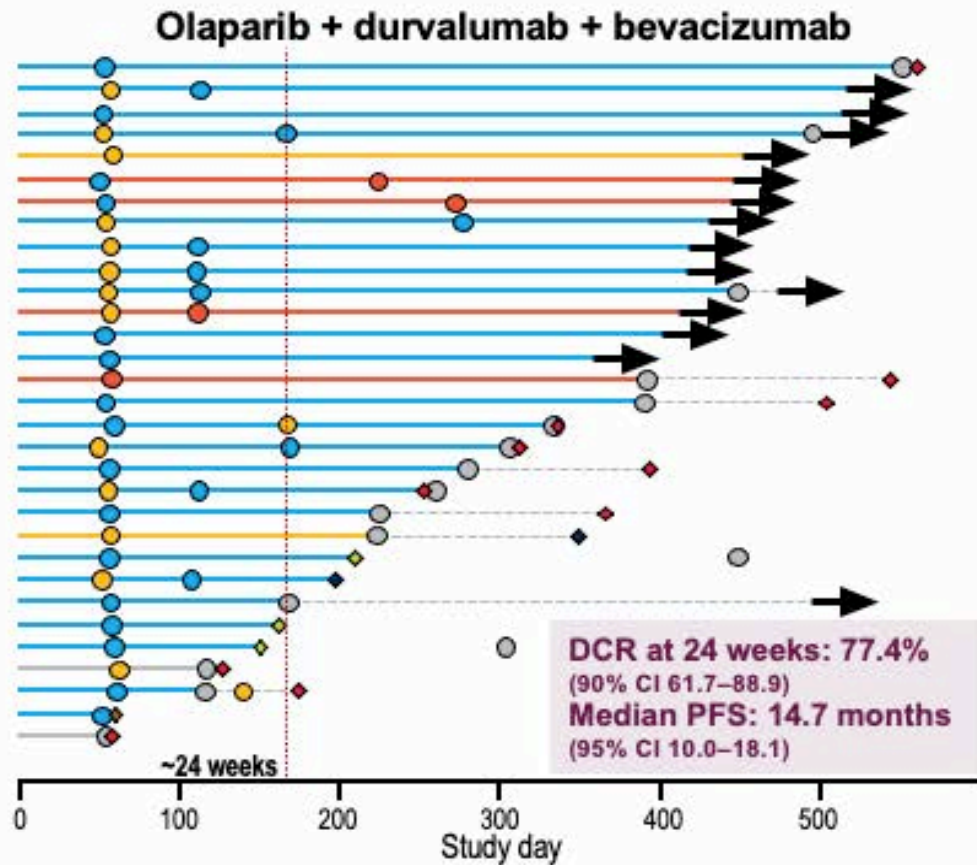
MEDIOLA: A Phase II Study of Olaparib and Durvalumab with or without Bevacizumab for Platinum-Sensitive Relapsed OC: No Germline BRCA Mutation Cohort

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



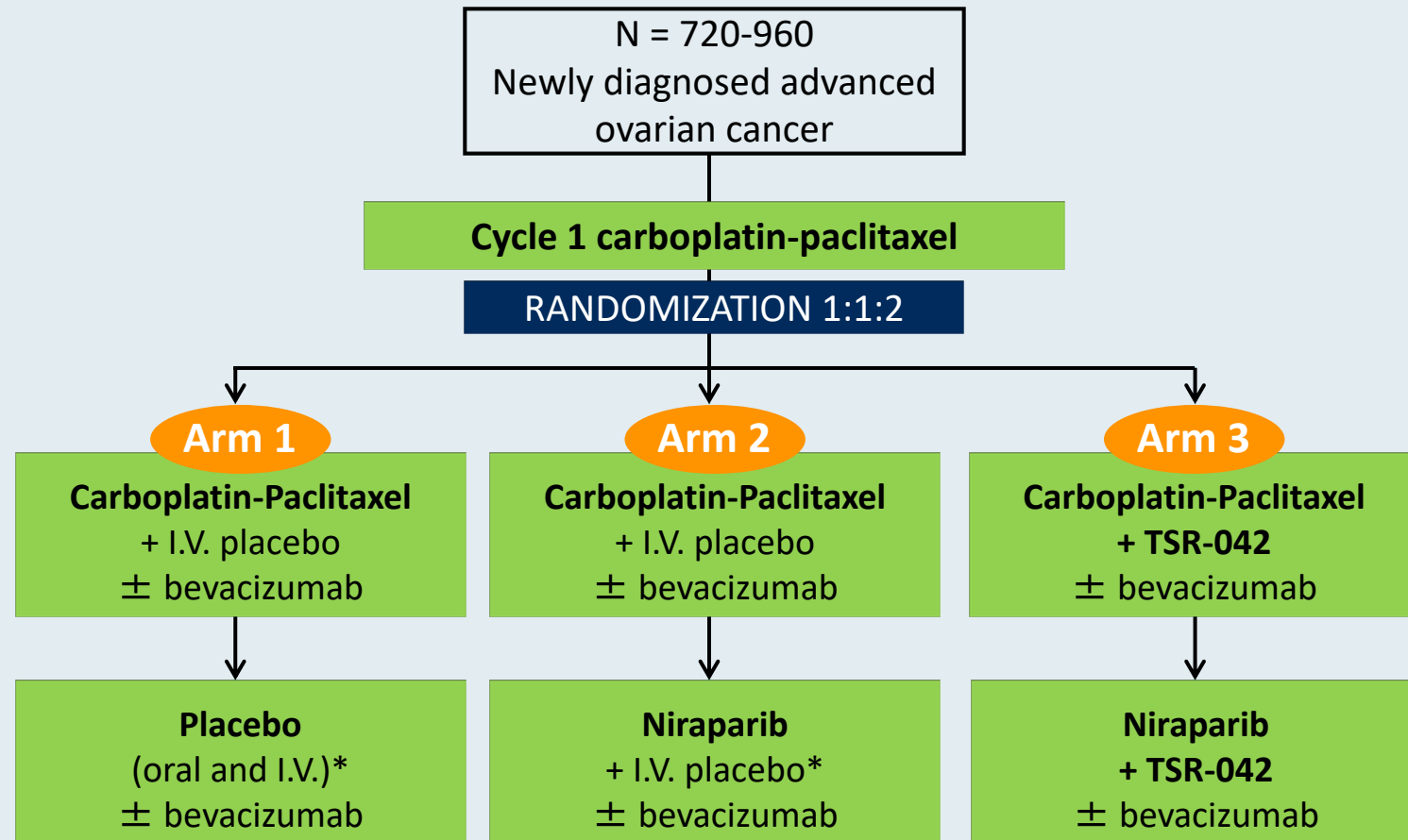
Genomic instability status* subgroup	Olaparib + durvalumab + bevacizumab		Olaparib + durvalumab	
	ORR (95% CI), %	n/N patients	ORR (95% CI), %	n/N patients
GIS-positive	100.0 (69.2–100.0)	10/10	50.0 (18.7–81.3)	5/10
GIS-negative	75.0 (34.9–96.8)	6/8	16.7 (0.4–64.1)	1/6
GIS-unknown	84.6 (54.6–98.1)	11/13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

MEDIOLA: TTP or Treatment Discontinuation



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

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



*I.V. placebo up to 15 months in total

Primary endpoint: PFS
Secondary endpoints: ORR, DOR, DCR, PROs, TFST, TSST, PFS2, OS

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

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	<ul style="list-style-type: none"> • Rucaparib + nivolumab • Rucaparib + placebo • Nivolumab + placebo • Placebo
DUO-O (NCT03737643)	1,056	Maintenance therapy after 1L platinum-based chemo/bev ± durvalumab	<ul style="list-style-type: none"> • Bevacizumab • Bevacizumab + durvalumab • Bevacizumab + durvalumab + olaparib

HER2-Positive Endometrial Cancer

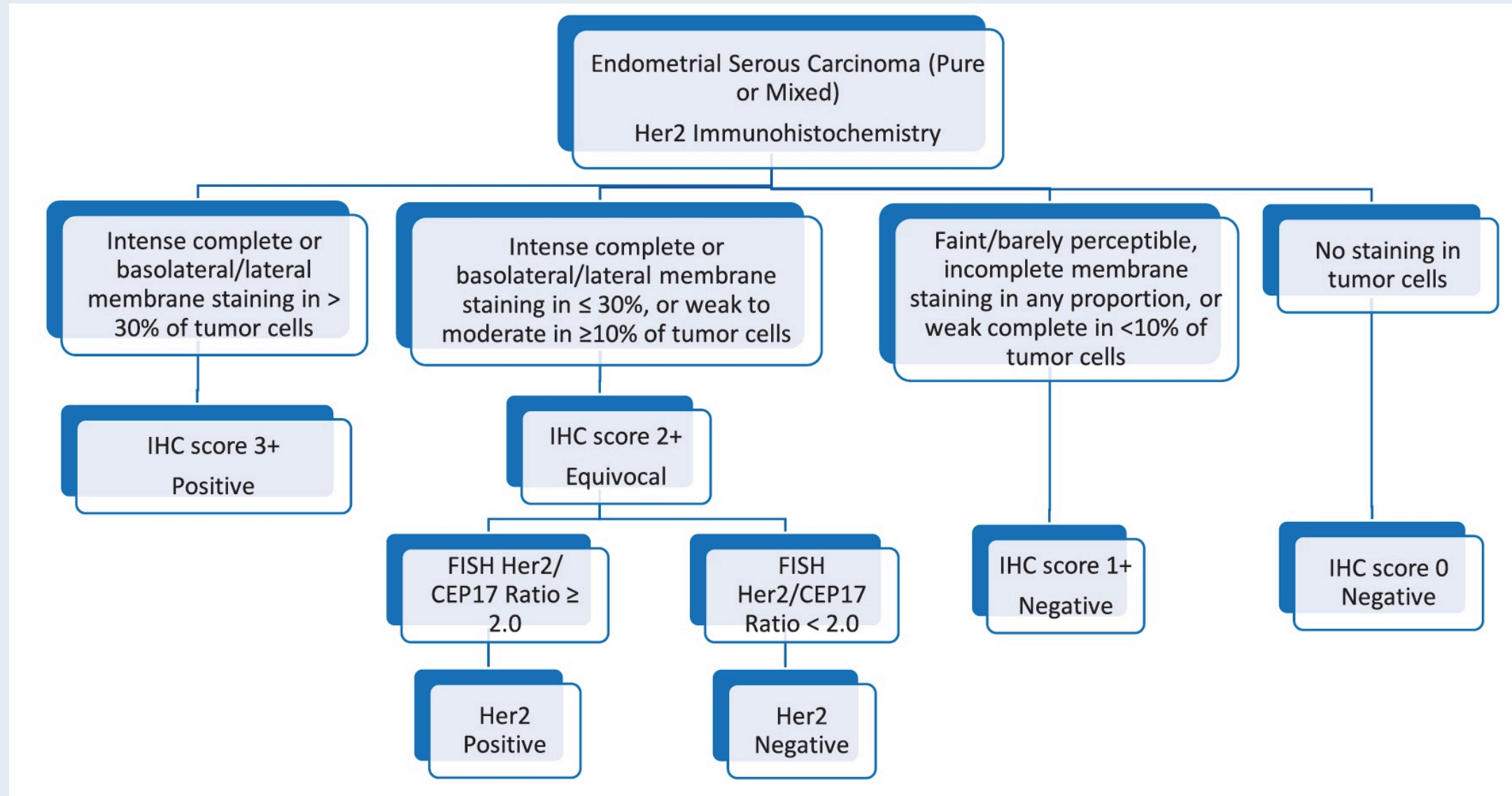
HER2 Testing in Endometrial Serous Carcinoma

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.

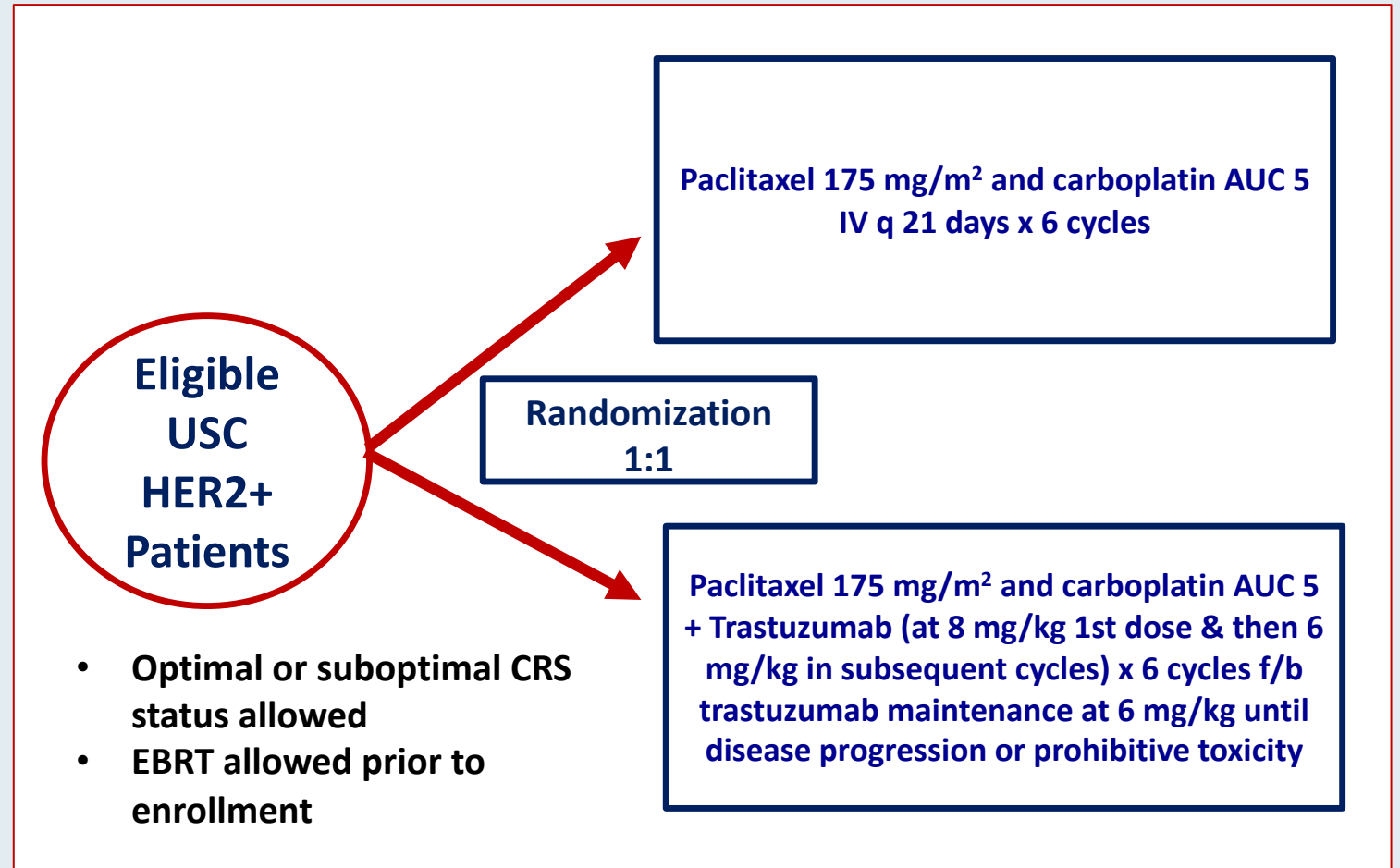
Proposed HER2 Testing Algorithm for Endometrial Serous Carcinoma



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

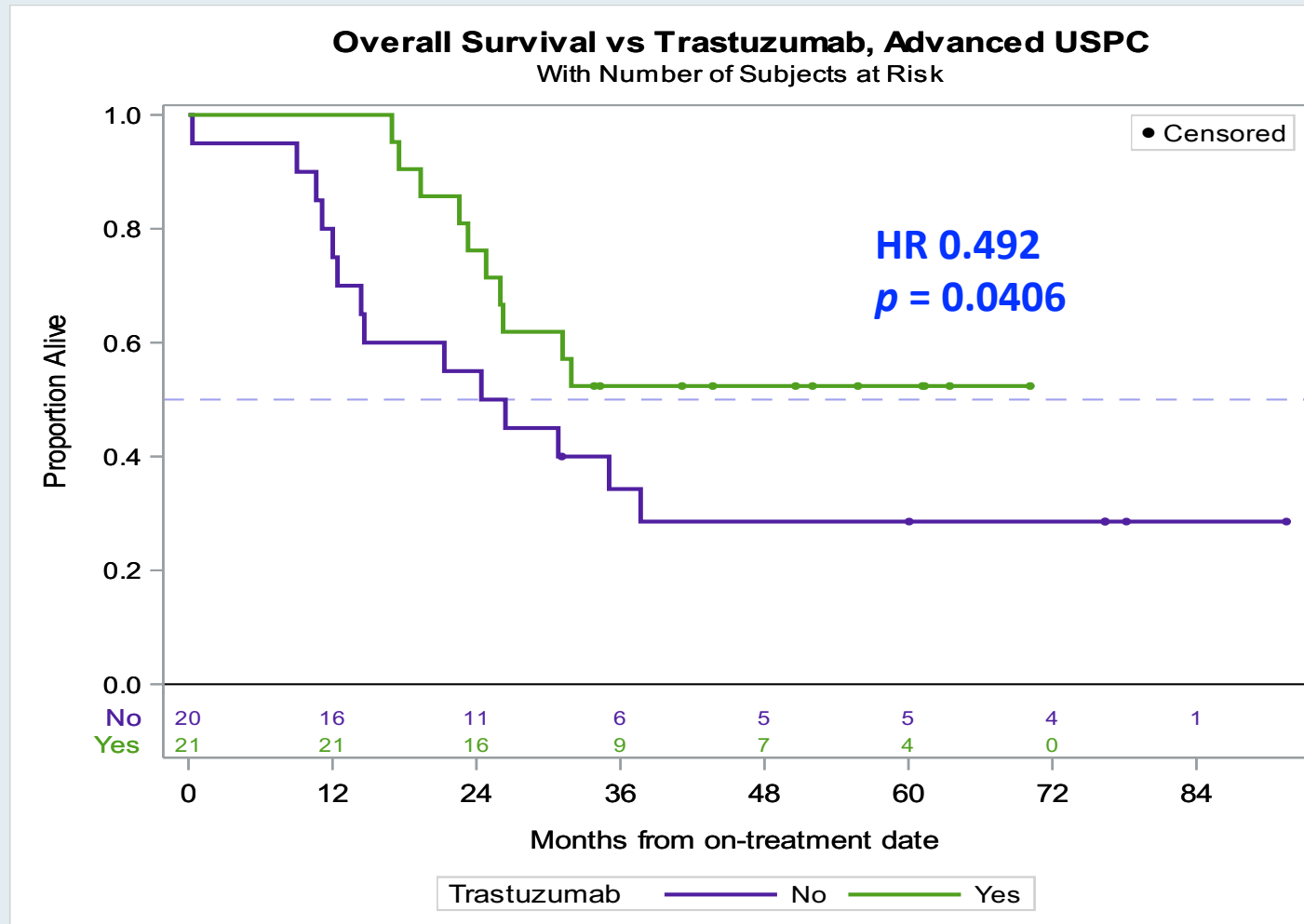
Eligibility

- 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



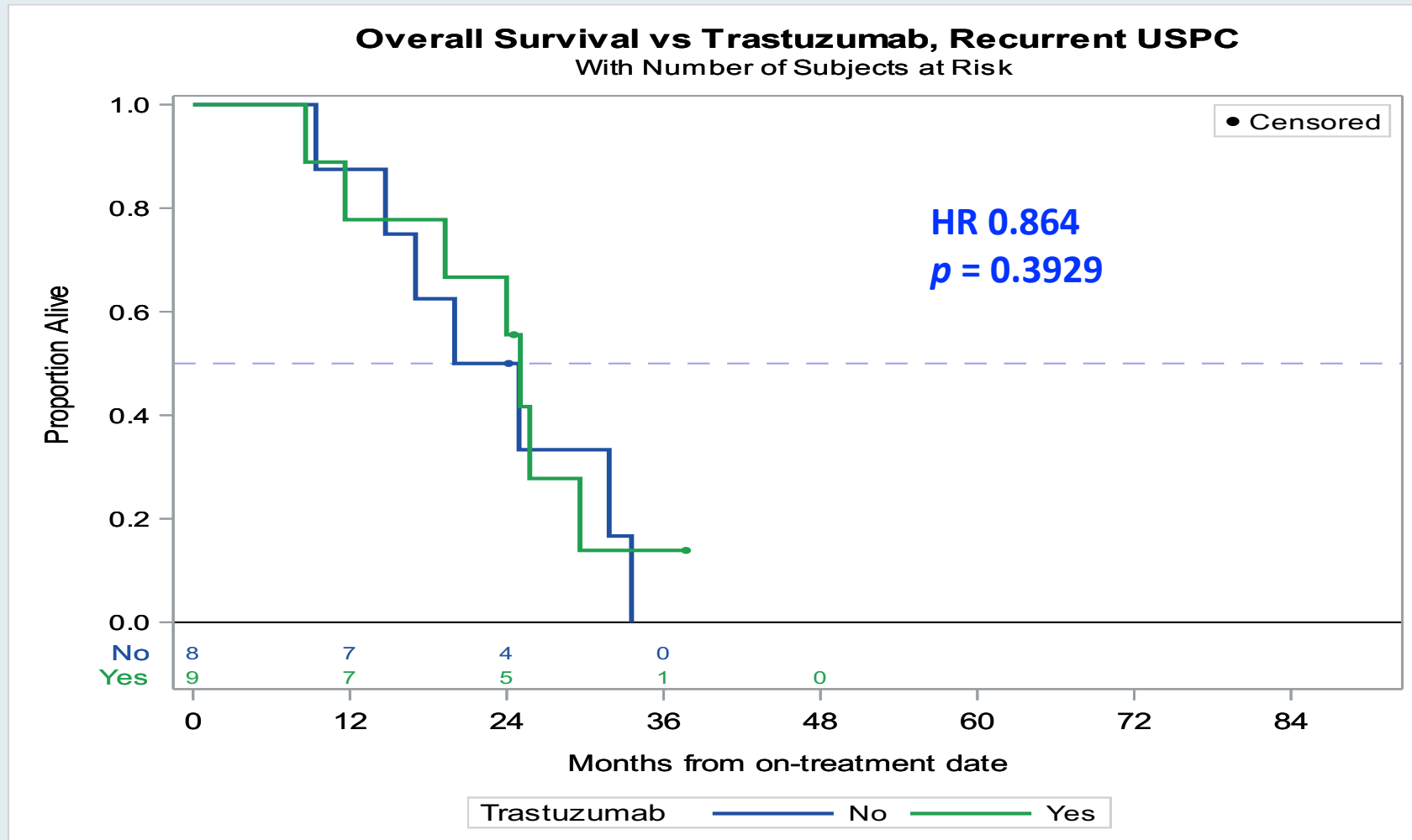
Overall Survival with the Addition of Trastuzumab to Carboplatin/Paclitaxel for Advanced Uterine Serous Papillary Carcinoma (USPC)

- 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)



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

- No significant OS benefit was observed in the recurrence cohort



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)

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

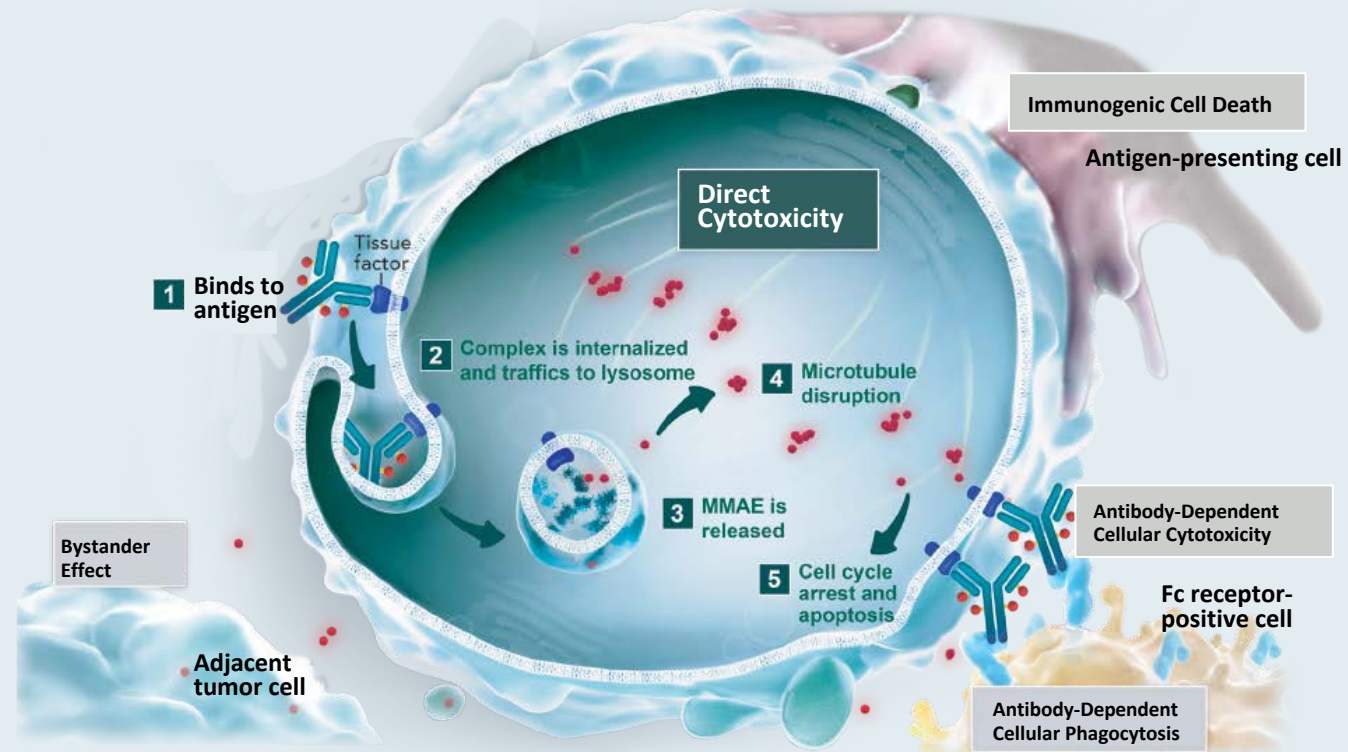
Primary endpoint: ORR

Secondary endpoints include DOR, PFS, OS, DCR

Tisotumab Vedotin and Other Novel Agents in Gynecologic Cancers

Mechanism of Action of Tisotumab Vedotin

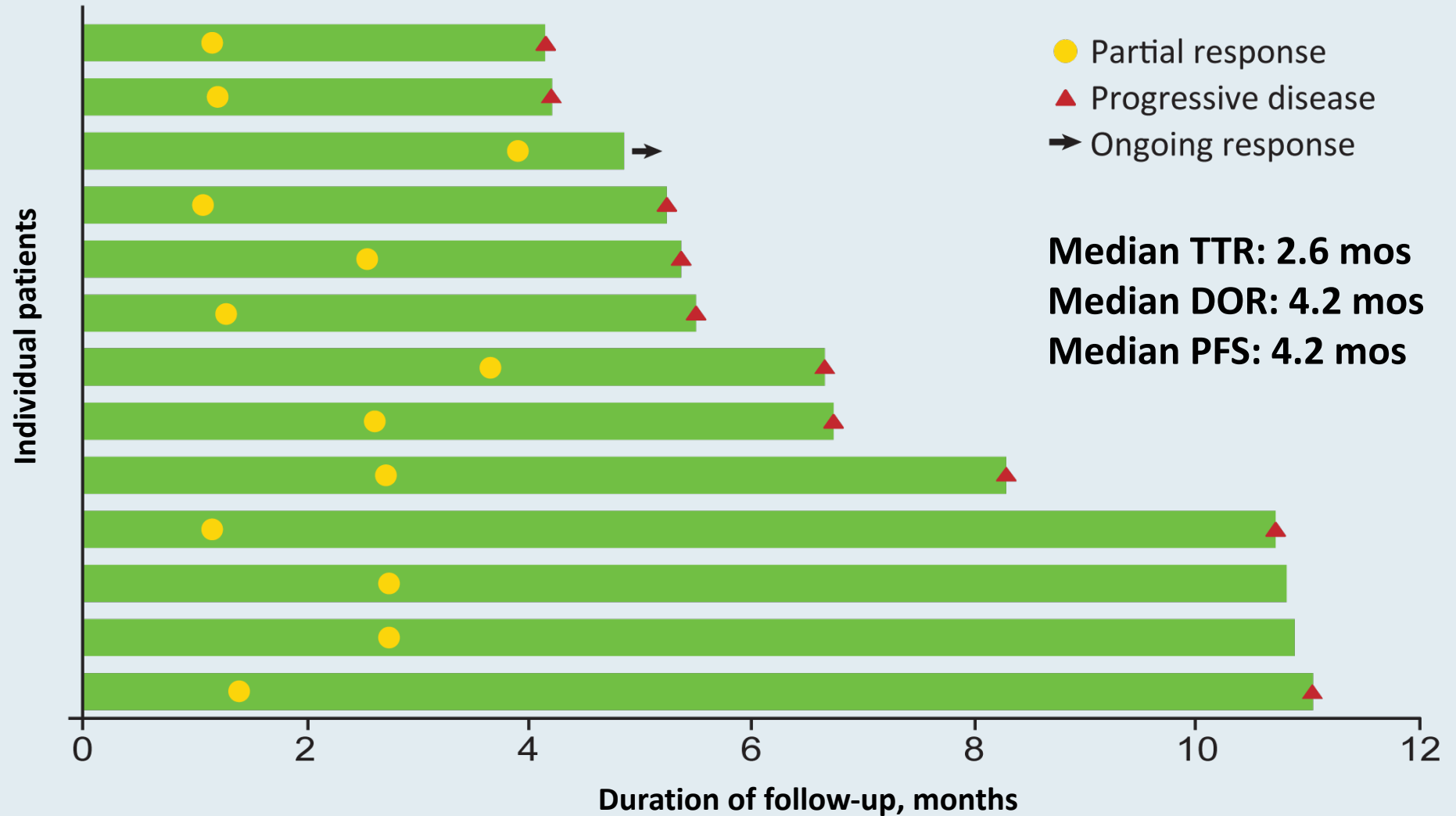
- Tissue factor (TF) is aberrantly expressed in a broad range of solid tumours, including cervical cancer,^{1,2} and TF expression has been associated with higher tumour stage and grade, higher metastatic burden and poor prognosis²
- TF expression in cervical cancer makes TF a novel target for patients 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}



innovaTV 201: Best Overall Response to TV

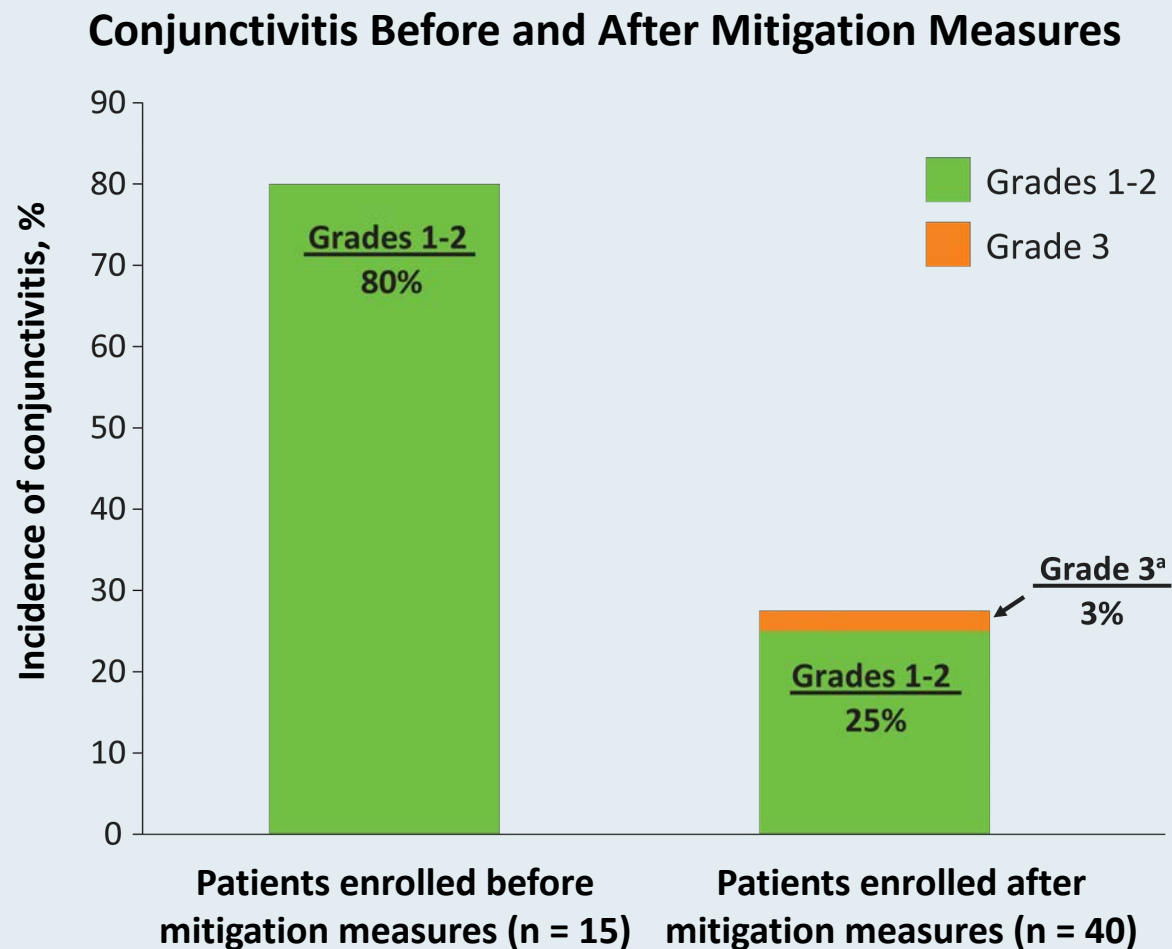


innovaTV 201: Time to Response and Duration of Response in Patients with a Confirmed PR to TV



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



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

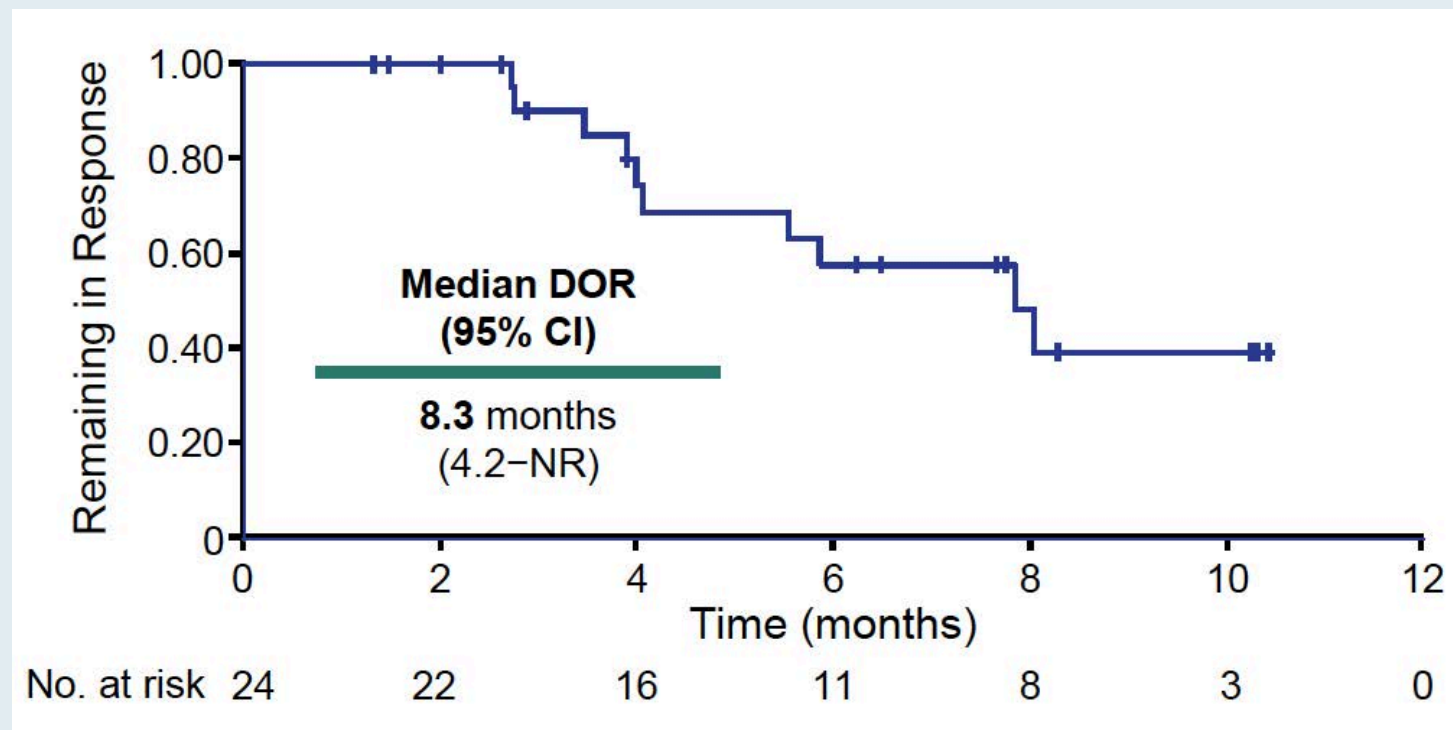
Coleman RL et al.

ESMO 2020;Abstract LBA32.

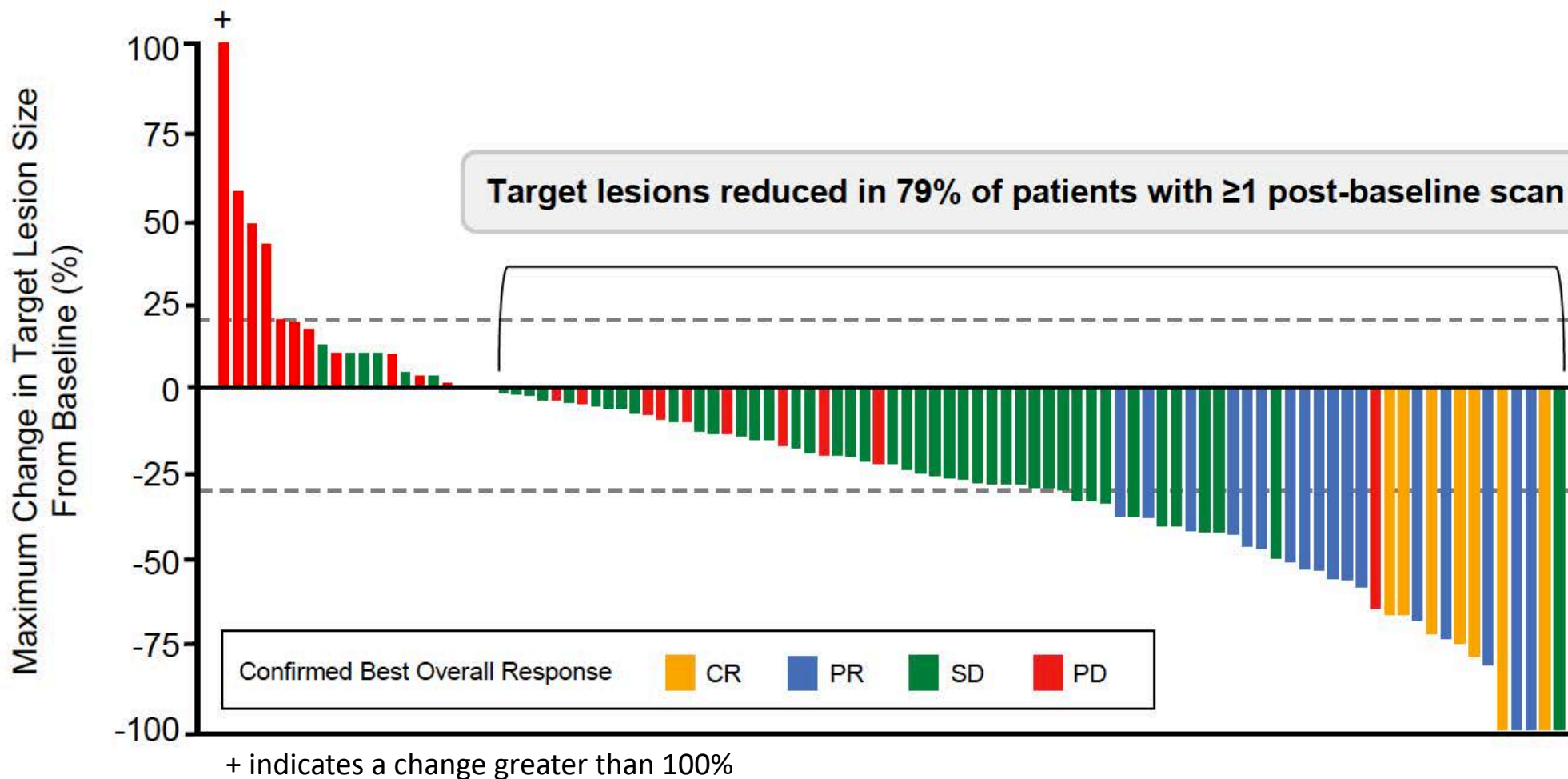
innovaTV 204: Antitumor Activity by IRC Assessment

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

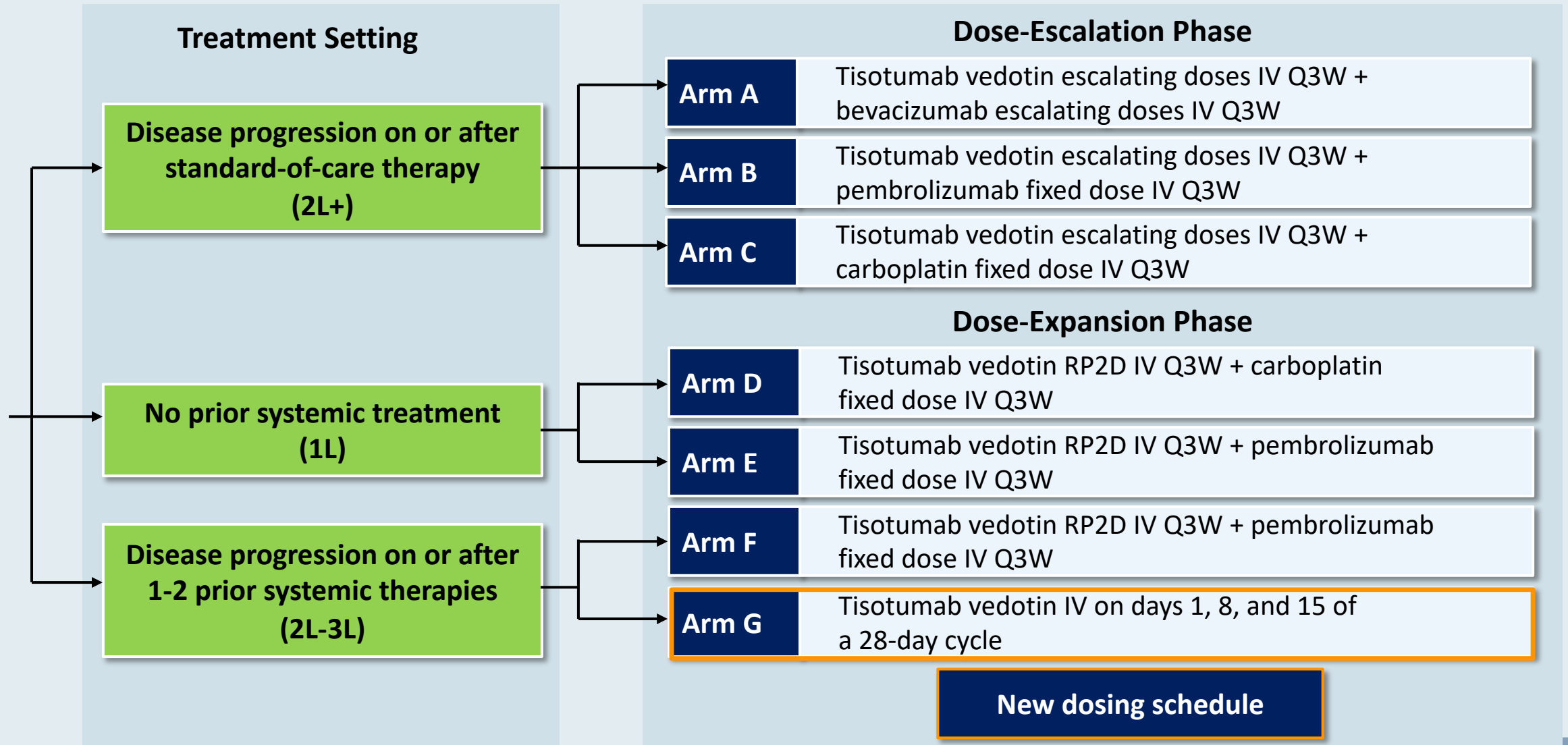
Duration of Response



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



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



Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

**Thursday, December 10, 2020
8:30 PM – 10:00 PM ET**

Faculty

Carey K Anders, MD

Erika Hamilton, MD

Sara Hurvitz, MD

Mark D Pegram, MD

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

Thank you for joining us!

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