Thank you for joining us.
The program will commence momentarily.

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

A Meet The Professor Series

Michael J Birrer, MD, PhD
Vice Chancellor, UAMS
Director, Winthrop P Rockefeller Cancer Institute
Director, Cancer Service Line
University of Arkansas for Medical Sciences
Little Rock, Arkansas

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Commercial Support

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Dr Love — Disclosures

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Upcoming Live Webinars

Monday, August 31, 2020
12:00 PM – 1:00 PM ET

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

Faculty
Joseph Mikhael, MD

Moderator
Neil Love, MD

Thursday, September 3, 2020
12:00 PM – 1:00 PM ET

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

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

Faculty
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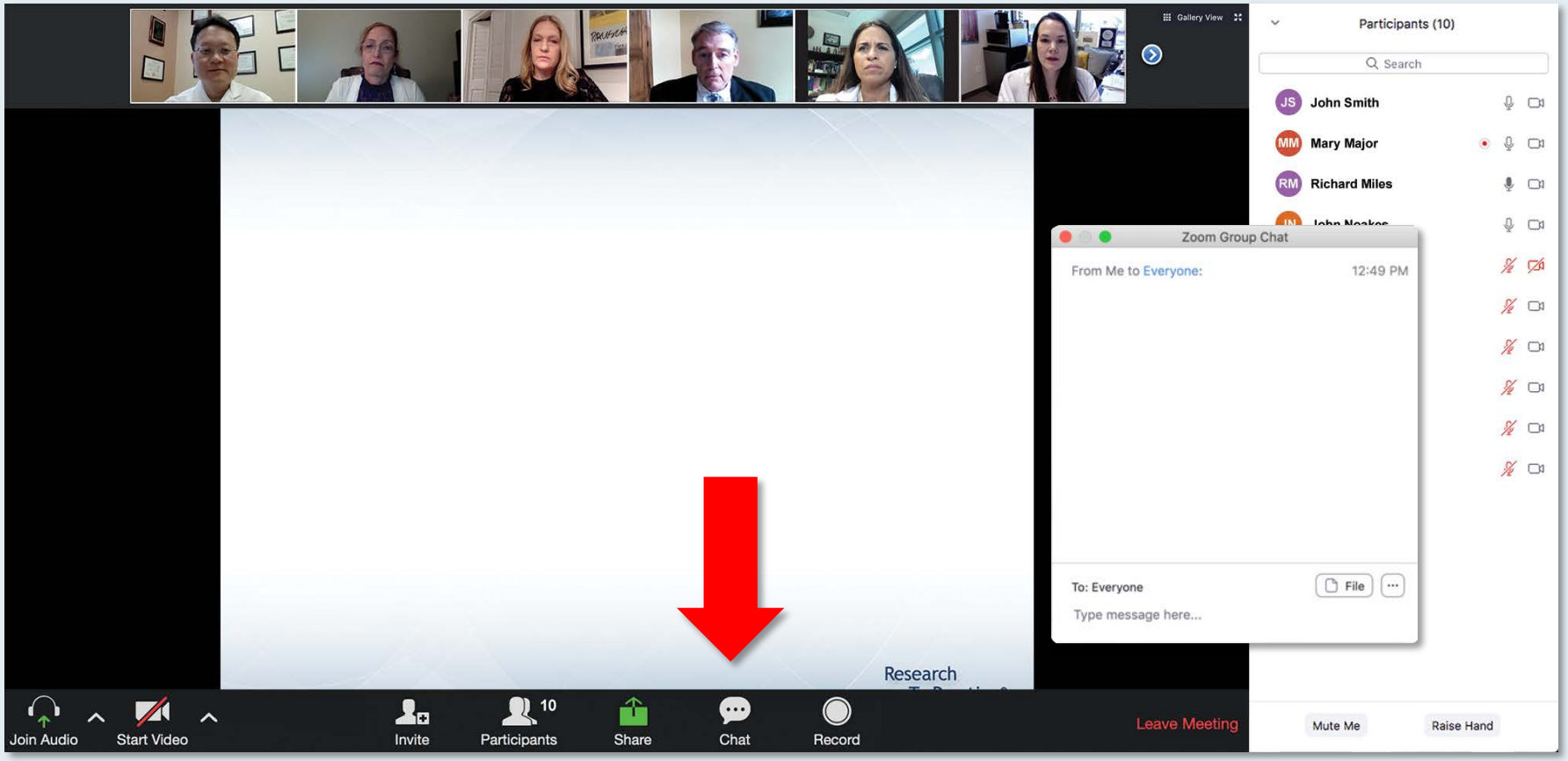
We Encourage Clinicians in Practice to Submit Questions



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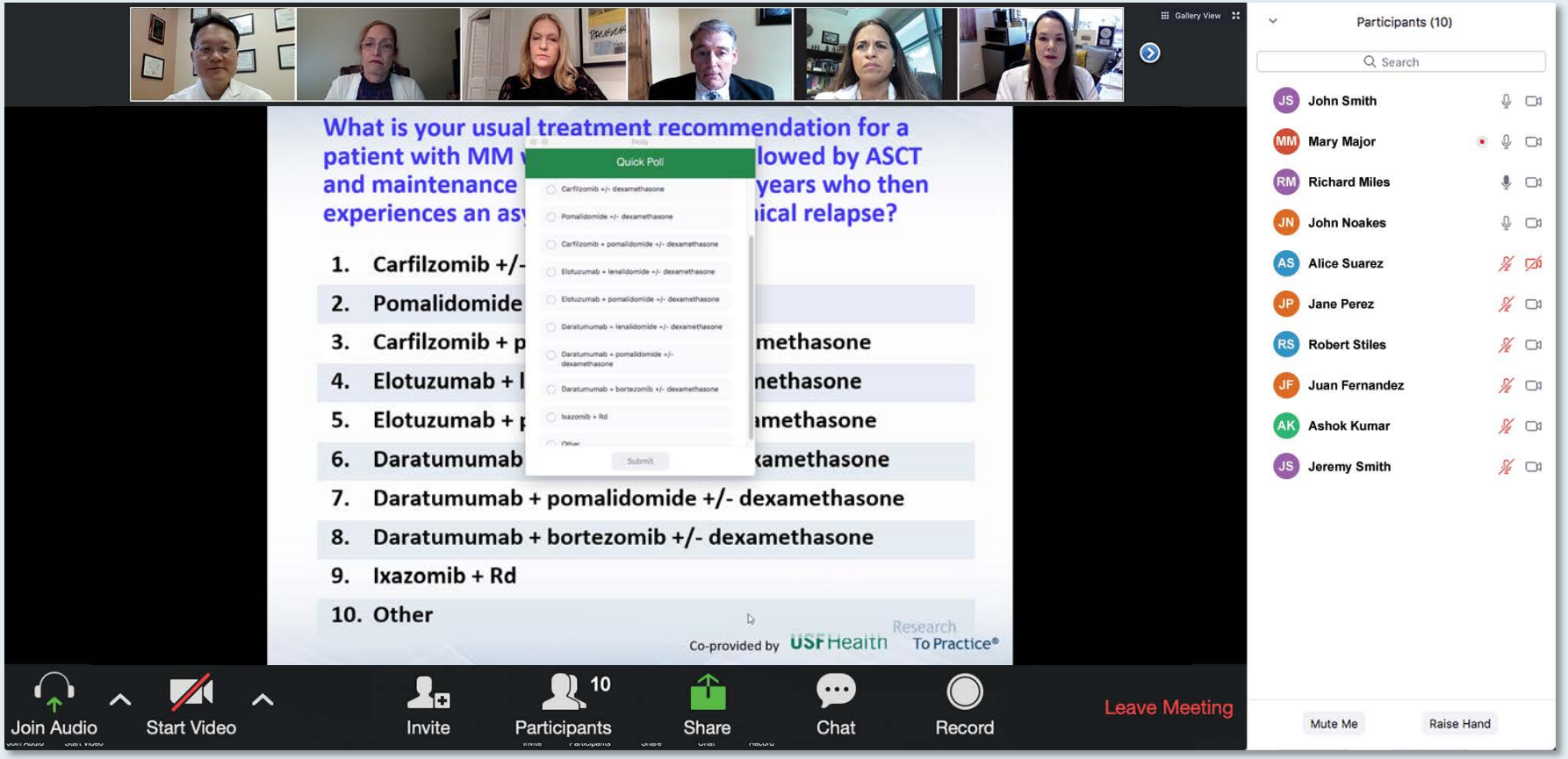
Familiarizing yourself with the Zoom interface

How to answer poll questions



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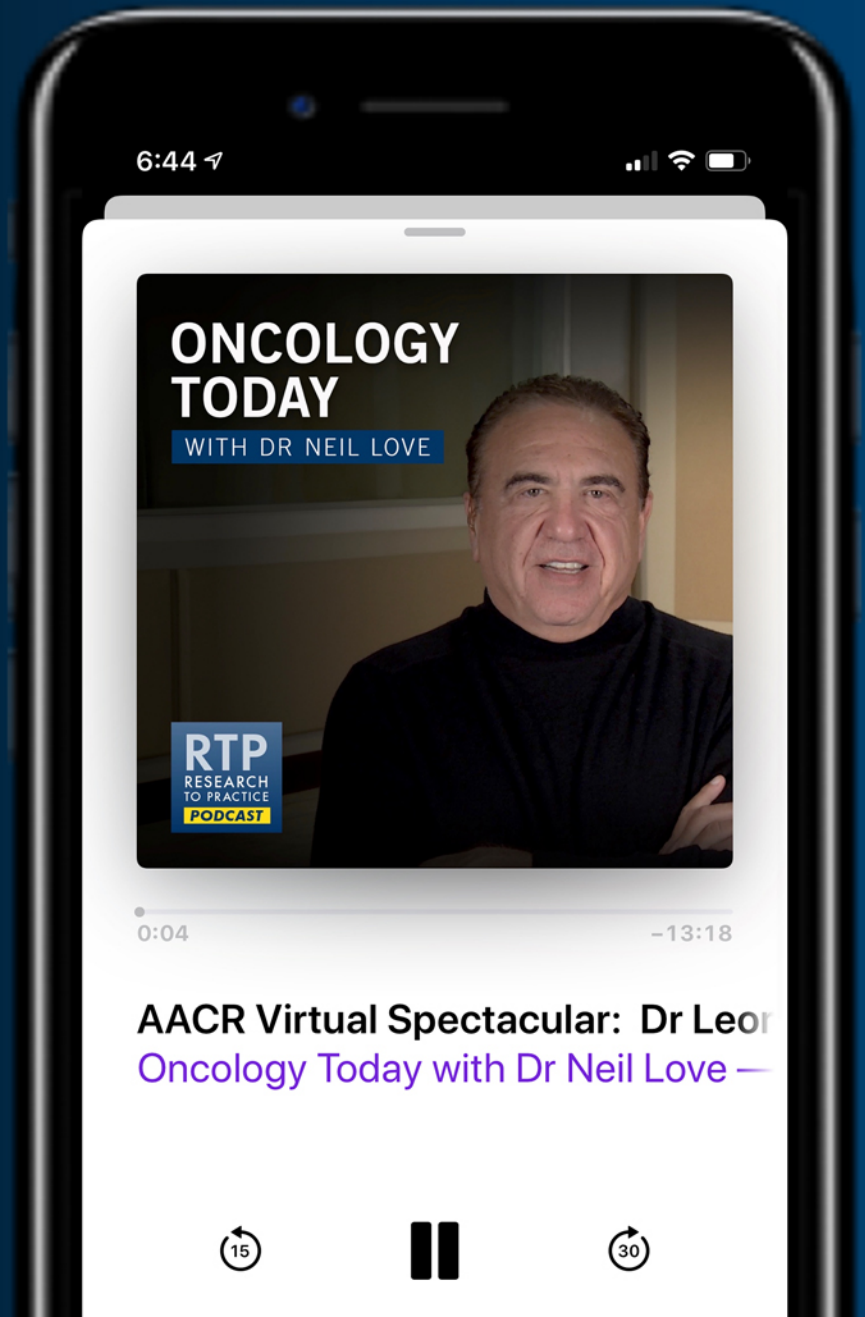

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Professor Ignace Vergote
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Gynaecological Oncologist
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Leuven, Belgium

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

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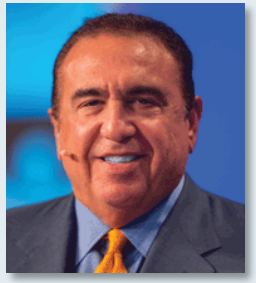
Meet The Professor Program Moderator



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

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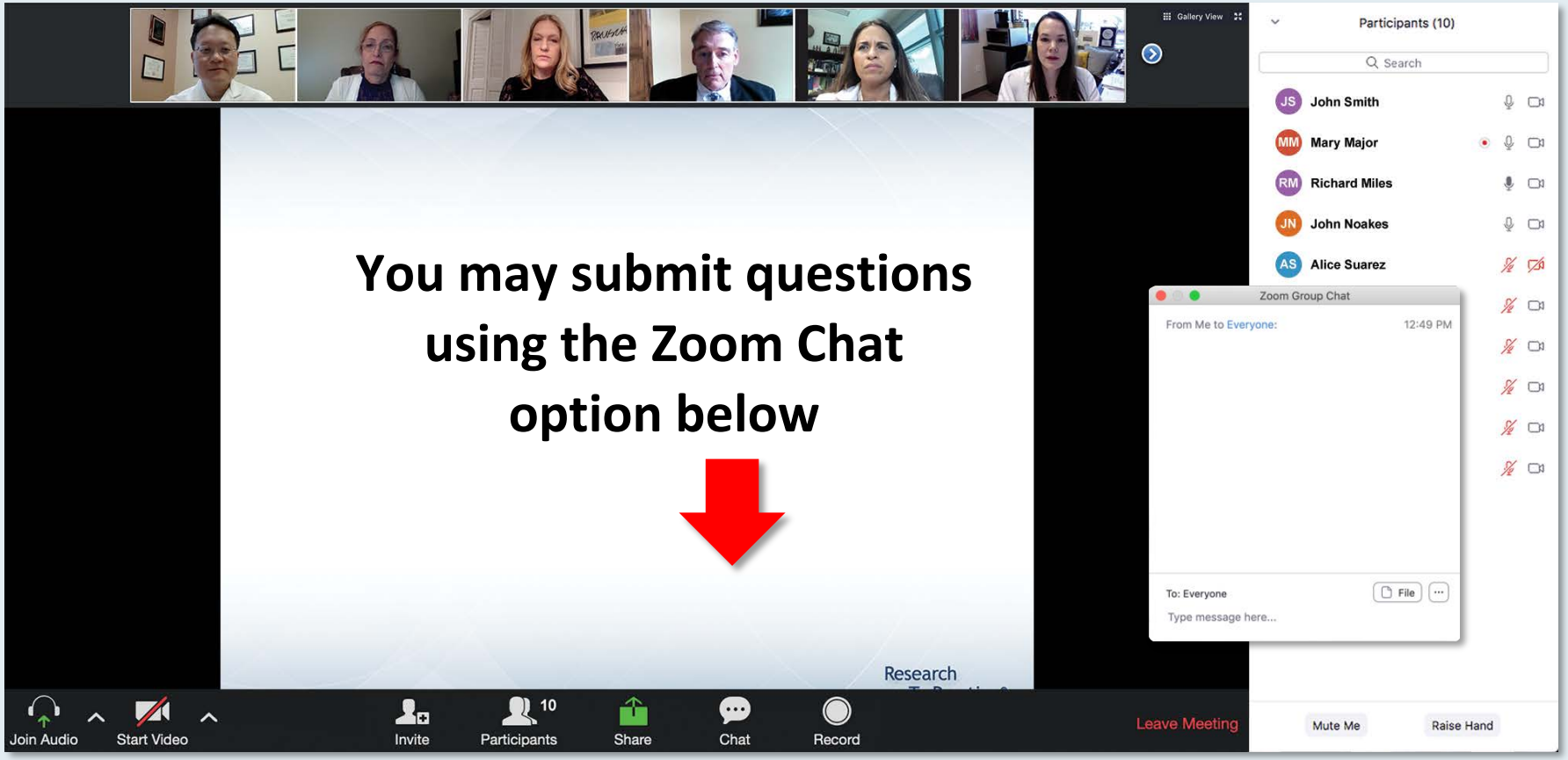

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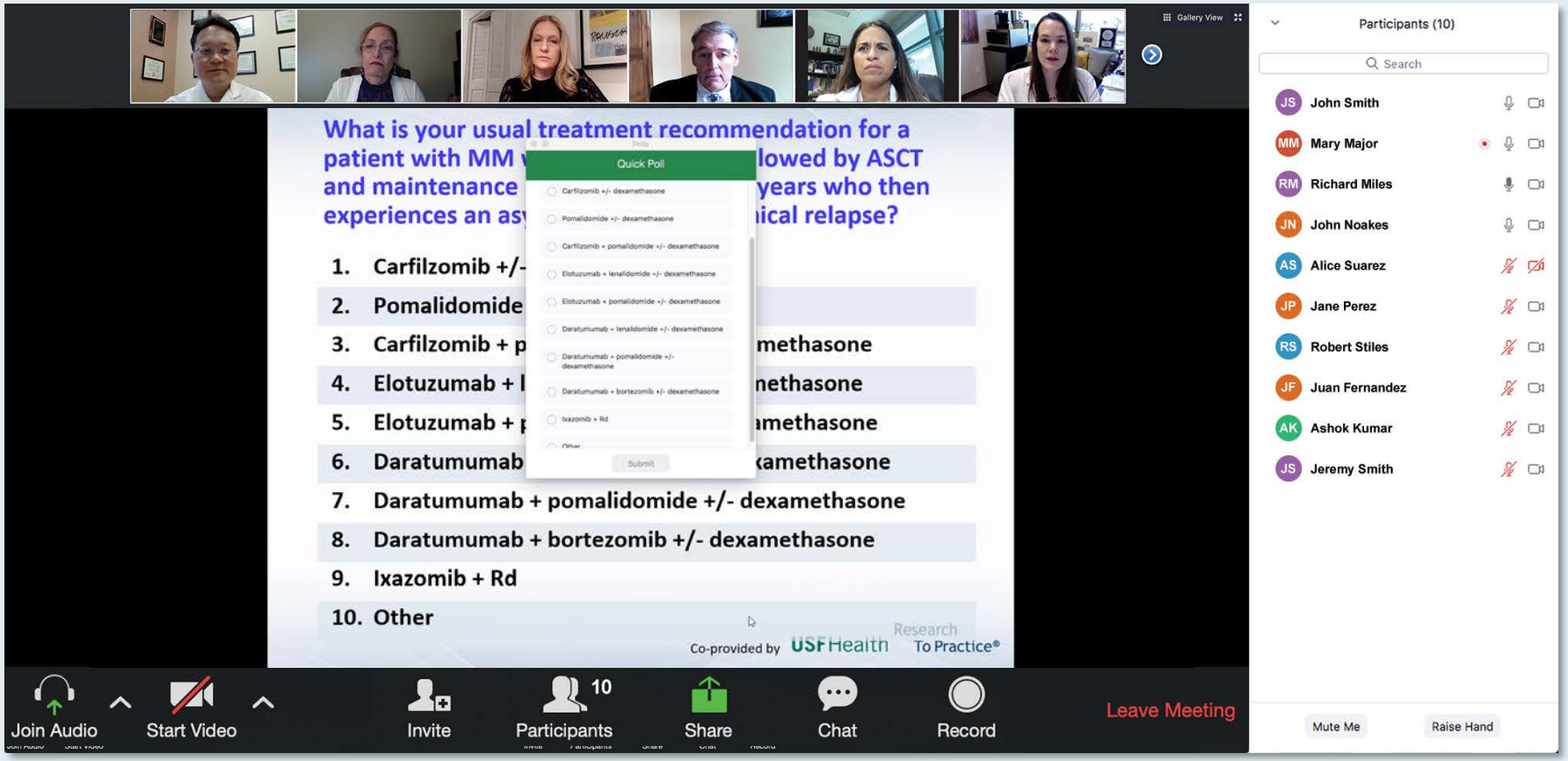

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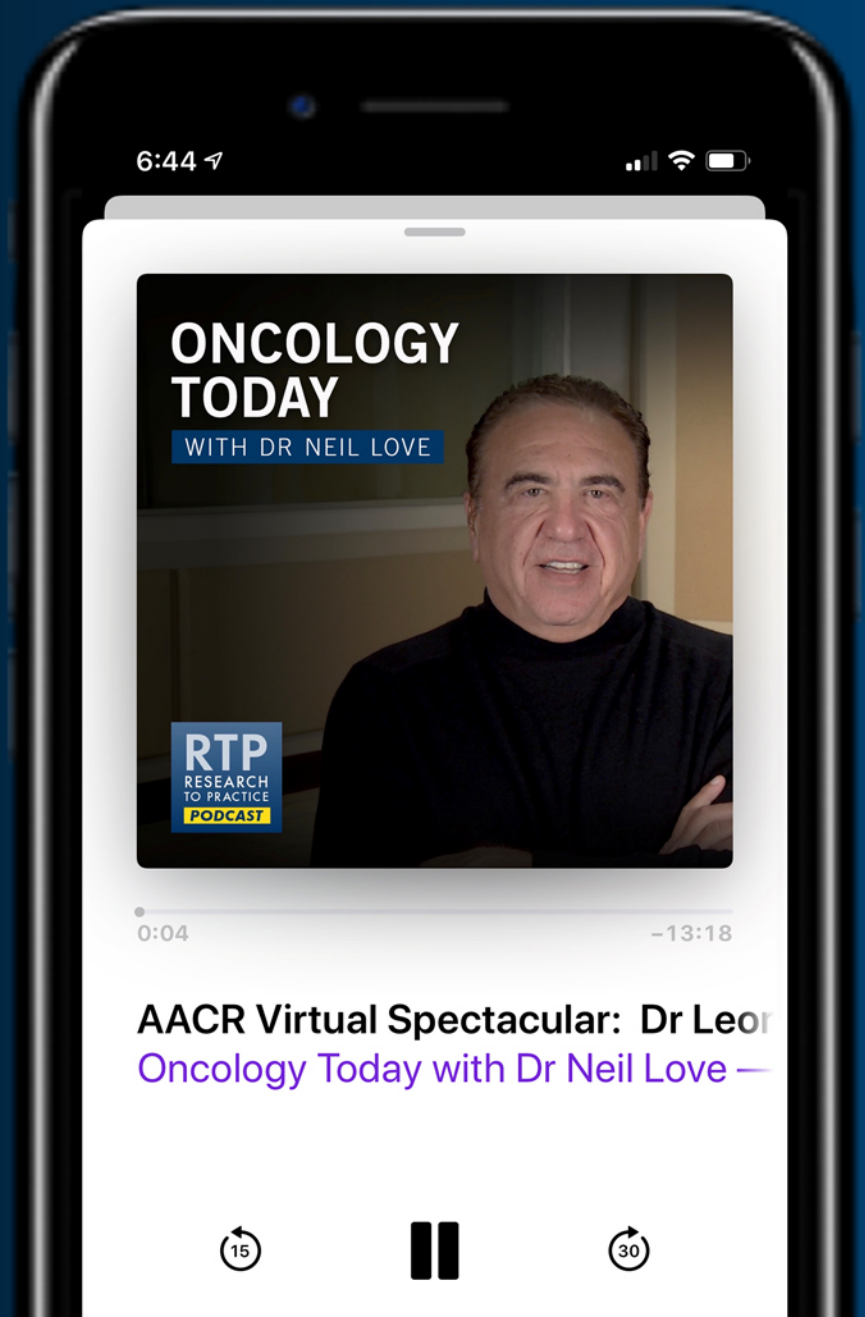

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Contributing Oncologist

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

Meet The Professor with Dr Birrer

MODULE 1: Anti-PD-1/PD-L1 Checkpoint Inhibitors for Gynecologic Cancers

- Recent relevant data sets
- Pembrolizumab (KEYNOTE-158) or dostarlimab (GARNET) for MSI-H or dMMR endometrial cancer (EC)
- KEYNOTE-146: Pembrolizumab/lenvatinib for EC without MSI-H/dMMR; ongoing studies (KEYNOTE-775, LEAP-001)
- FDA approval of pembrolizumab for cervical cancer; ongoing studies (BEATcc, KEYNOTE-826, CALLA)
- KEYNOTE-100 trial: Pembrolizumab for advanced recurrent ovarian cancer
- Emerging data from JAVELIN Ovarian 200, TOPACIO, MEDIOLA trials in ovarian cancer
- Key ongoing studies (FIRST, MOONSTONE, ATHENA, DUO-O) in ovarian cancer

MODULE 2: HER2-Positive Endometrial Cancer

- Recent relevant data sets
- Randomized Phase II trial of carboplatin/paclitaxel +/- trastuzumab in HER2-positive uterine serous carcinoma

MODULE 3: Tisotumab Vedotin and Other Novel Agents in Gynecologic Cancers

- Recent relevant data sets
- Emerging clinical data with tisotumab vedotin; ongoing innovaTV 205 study

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Case Presentation – Dr Slomovitz: A woman with chemoresistant metastatic choriocarcinoma

Brian M Slomovitz, MD

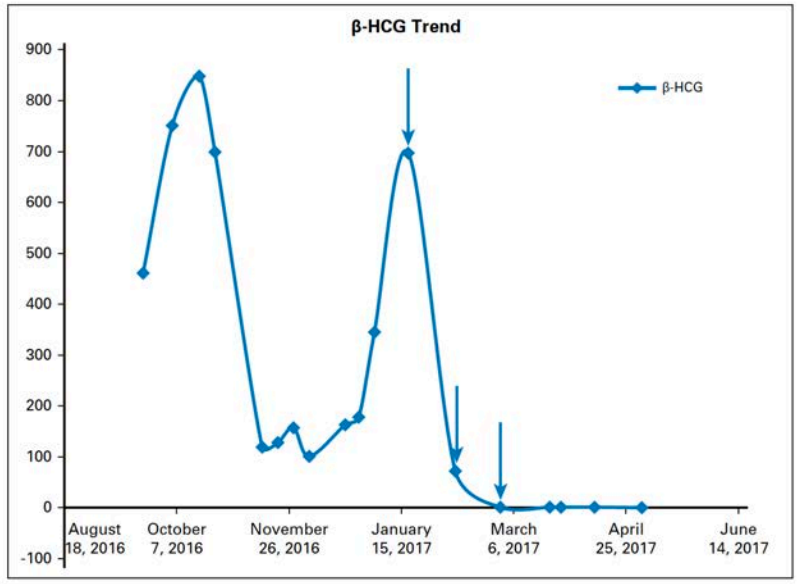
A new mom thought her cancer was a death sentence. This new therapy saved her

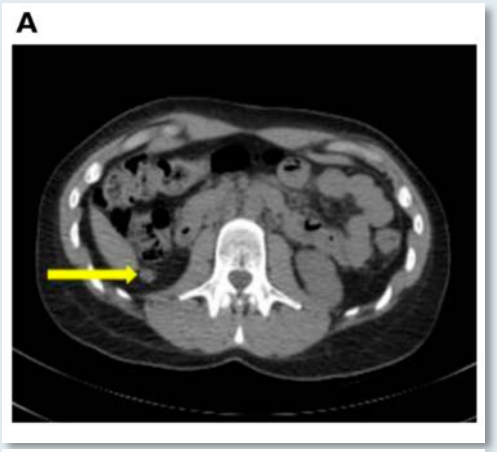
BY ANA VECIANA-SUAREZ

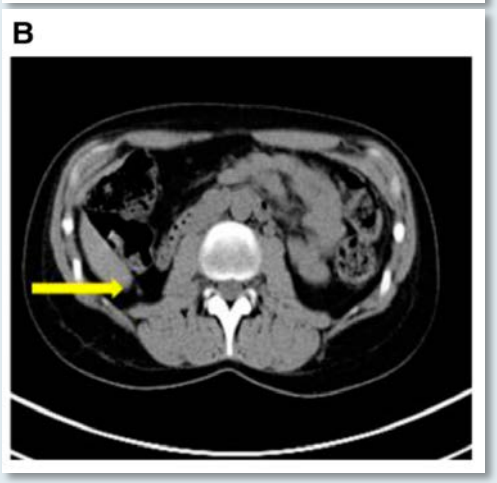
MAY 20, 2019 06:30 AM, UPDATED MAY 21, 2019 07:35 PM

Alessandra Valerio, cancer survivor, son, Louis, and husband Jorge Perez. Alessandra was diagnosed with choriocarcinoma, a rare pregnancy–related cancer that forms when cells, formerly part of the placenta, turn malignant.

Complete Serologic Response to Pembrolizumab in a Woman With Chemoresistant Metastatic Choriocarcinoma







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Case Presentation – Dr Slomovitz: A 63-year-old woman with recurrent endometrial cancer

Brian M Slomovitz, MD

- Presents to her GYN with postmenopausal bleeding
- EMB: grade 3 endometrial cancer
- Pre-op CT: No evidence of metastatic disease
- Robotic hysterectomy and staging, no visible cancer
- Pathology: Stage IB grade 3 endometrioid endometrial cancer, nodes negative
- Received vaginal cuff radiation post operatively
- 6 month later complained of vague abdominal pain
- CT: omental mass, carcinomatosis, CT guided biopsy: Confirmed recurrent G3 EEC
- Somatic NGS: +dMMR
- Carboplatin/paclitaxel, with complete response, but 4 months later liver metastases
- Doxorubicin x 3 cycles, with progressive disease
- Pembrolizumab, with stable disease after 4 cycles

Question

- Is there a role for first-line pembrolizumab in these patients?

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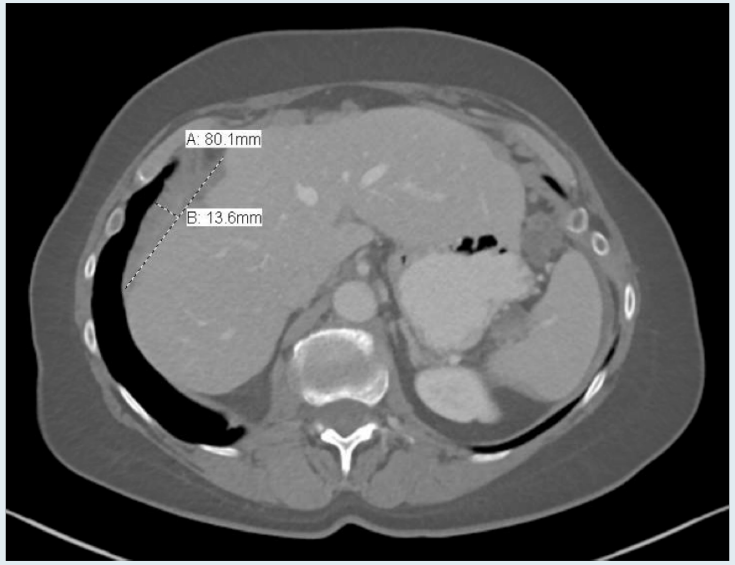
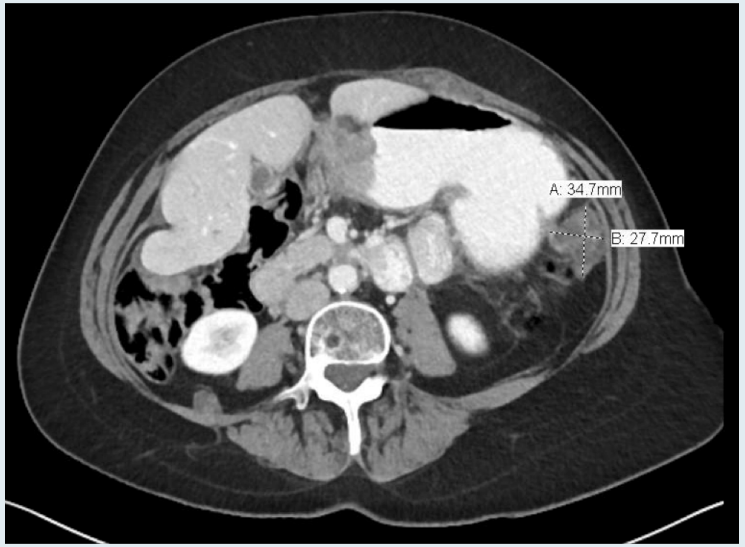
Case Presentation – Dr Birrer: A 51-year-old woman with MSI-high endometrial cancer

- G2 EMCA → CT scan negative for metastatic disease
- RTLH/BSO/LND → Stage IIIC2 (positive pelvic/paraaortic lymph nodes)
- Adjuvant treatment: carbo/paclitaxel x 6 cycles followed by whole pelvic xRT
- Post treatment scan: NED
- 12 month f/u visit – CT scan shows intra-abdominal recurrence
- She was treated with anti-PD-1 single agent

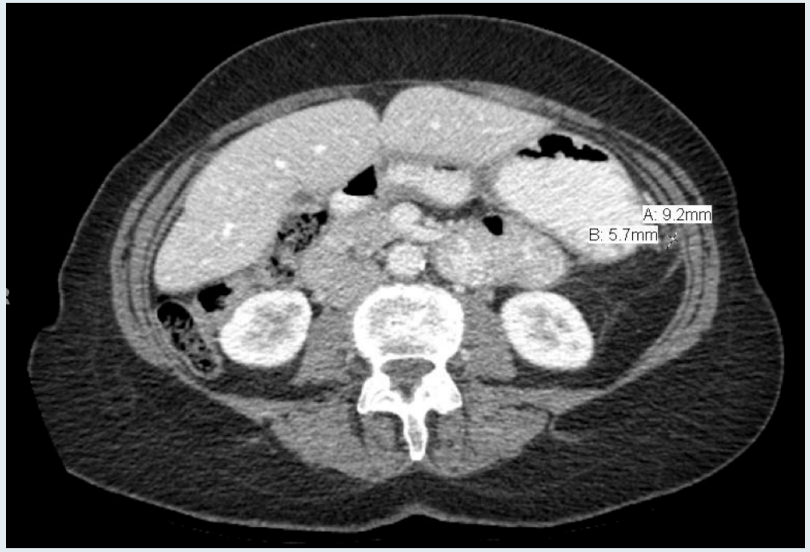
Case Presentation – Dr Birrer: A 51-year-old woman with MSI-high endometrial cancer

Before starting anti PD-1





After 12 months of anti-PD-1



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Case Presentation – Dr Slomovitz: A 68-year-old woman with recurrent endometrial cancer

Brian M Slomovitz, MD

- Grade 2 endometrial adenocarcinoma → Robotic hysterectomy, SLNB
- Pathology: Deeply invasive G 2 endometrial adenocarcinoma with 80% depth of invasion through the uterine wall. +LVSI, -cervix, Pelvic node +
- Stage IIIC1 disease; MMR proficient; ER+, PR+
- Chemotherapy and WPRT → 12 months later presents with cough
  - CT chest: Diffuse pulmonary metastases
- Pembrolizumab/Lenvatinib

Questions

- Which would you use first in a patient who is hormone receptor-positive – immunotherapy or hormonal therapy?
- In a hypertensive patient who is being managed with 2 antihypertensives, is lenvatinib contraindicated?
- How liberal are you with the use of steroids for the diarrhea that is inevitably seen with these 2 drugs? How quickly should we use steroids to manage autoimmune colitis? How do you determine if the diarrhea is from pembro or lenvatinib, and how does that affect your management approach?

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Case Presentation – Dr Birrer: A 41-year-old woman with MSS endometrial cancer

- Biopsy proven G3 EMCA → CT scan negative for metastatic disease → proceed with surgery
- Surgery: RTLH/BSO/blSLND → Stage IIIC1 (positive pelvic lymph node)
- Adjuvant treatment: carbo/paclitaxel x 6 cycles
- Post treatment scan: NED
- 3 f/u month visit – she is in pain, frequent nausea → CT scan

Case Presentation – Dr Birrer: A 41-year-old woman with MSS endometrial cancer

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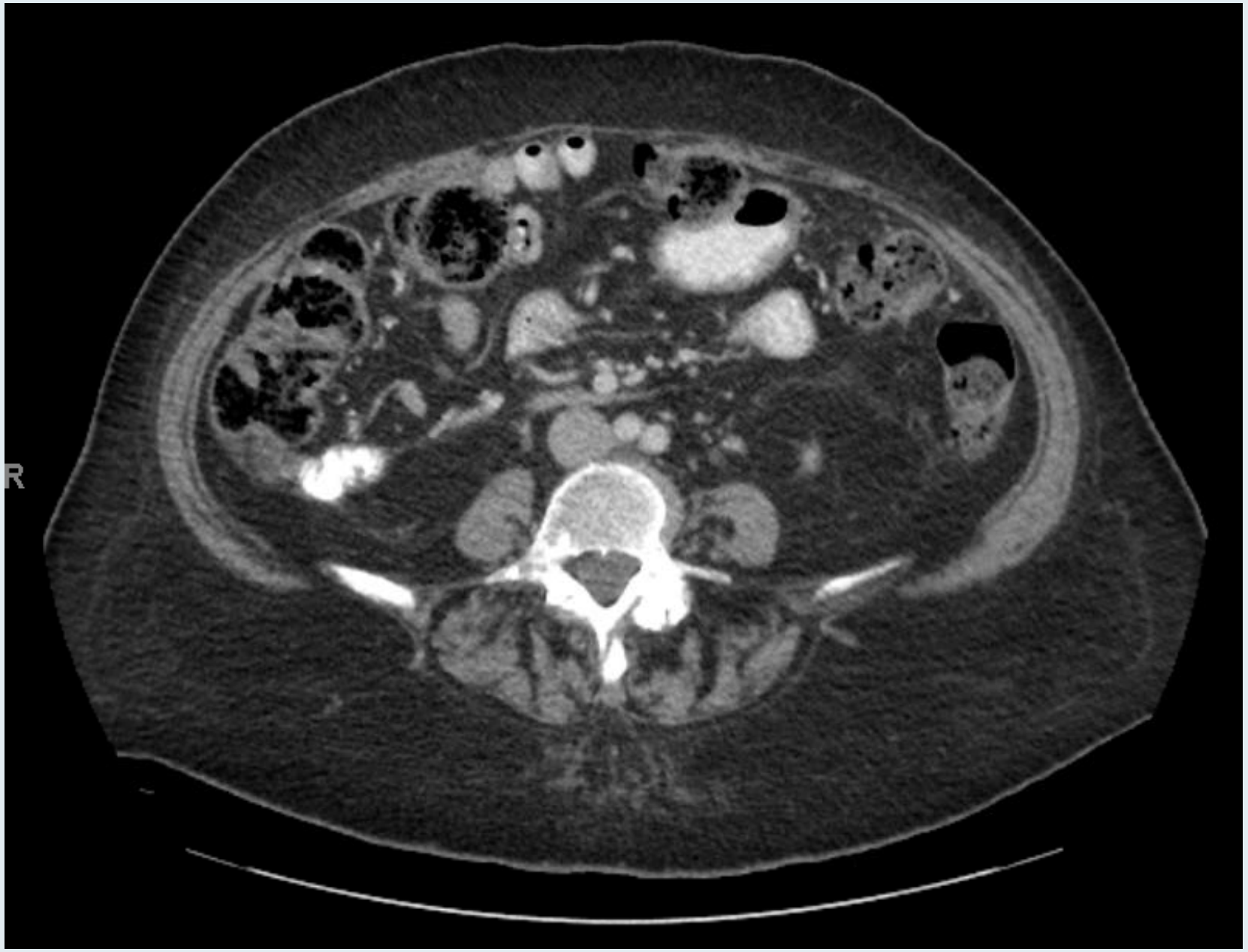
Case Presentation – Dr Birrer: A 41-year-old woman with MSS endometrial cancer (continued)

- Biopsy done → metastatic high-grade carcinoma consistent with known uterine primary
- IHC: ER neg
- NGS: amplification of AKT2, FGFR1, CCNE, MSI-S, TMB low
- Started her on Lenvatinib/pembro
- Developed HTN controlled by two anti-HTNs; grade 2 diarrhea—dose reduced to 14 mg lenvatinib
- Re-scan after 4 months

Case Presentation – Dr Birrer: A 41-year-old woman with MSS endometrial cancer



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?

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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…

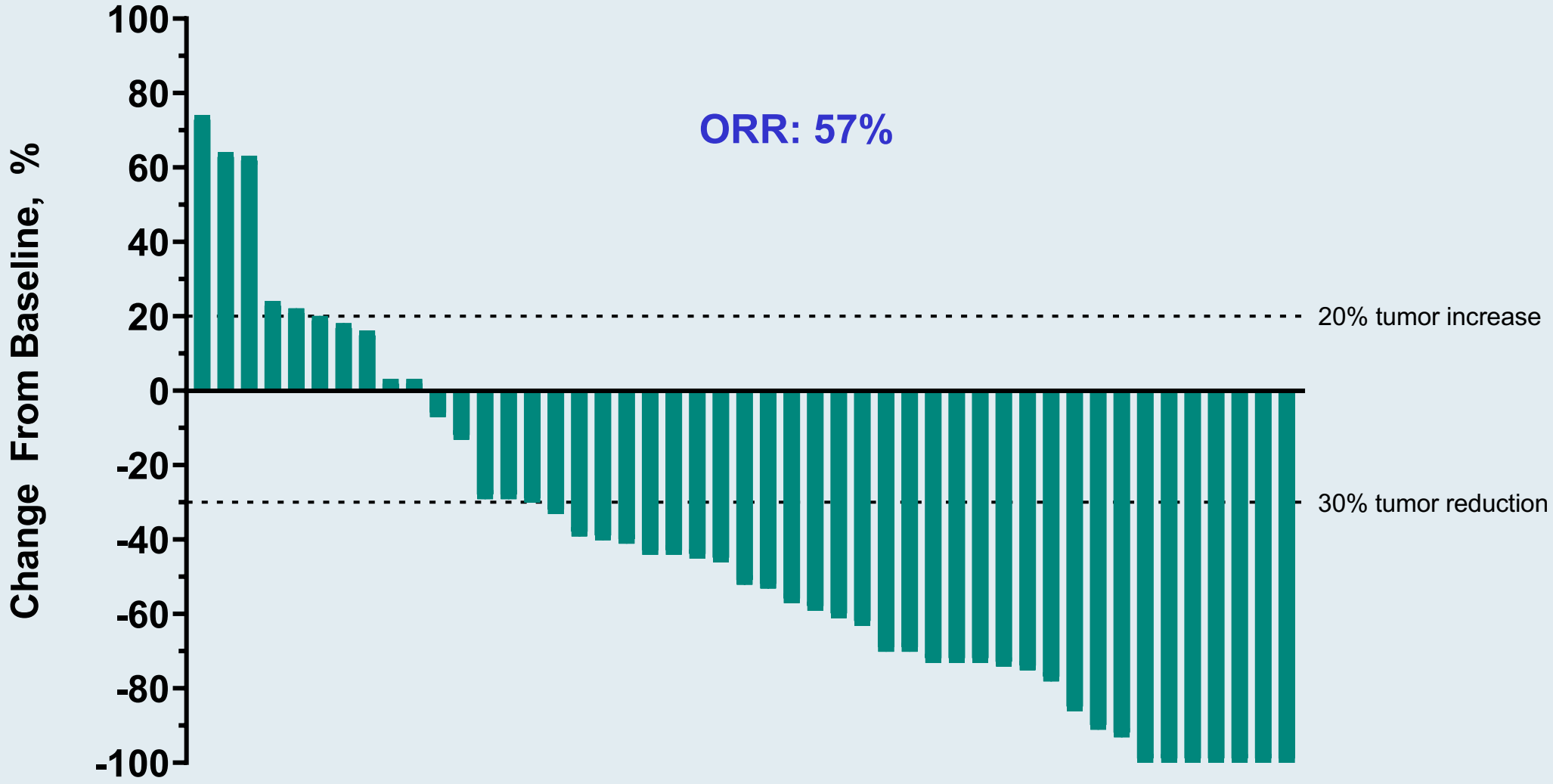
	Microsatellite stable (MSS)	MSI high (MSI-H)
 MICHAEL J BIRRER, MD, PHD	Lenvatinib/pembrolizumab	Pembrolizumab
 ROBERT L COLEMAN, MD	Lenvatinib/pembrolizumab	Pembrolizumab
 ANA OAKNIN, MD, PHD	Lenvatinib/pembrolizumab	Dostarlimab
 DAVID M O'MALLEY, MD	Lenvatinib/pembrolizumab	Pembrolizumab
 MATTHEW A 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
 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

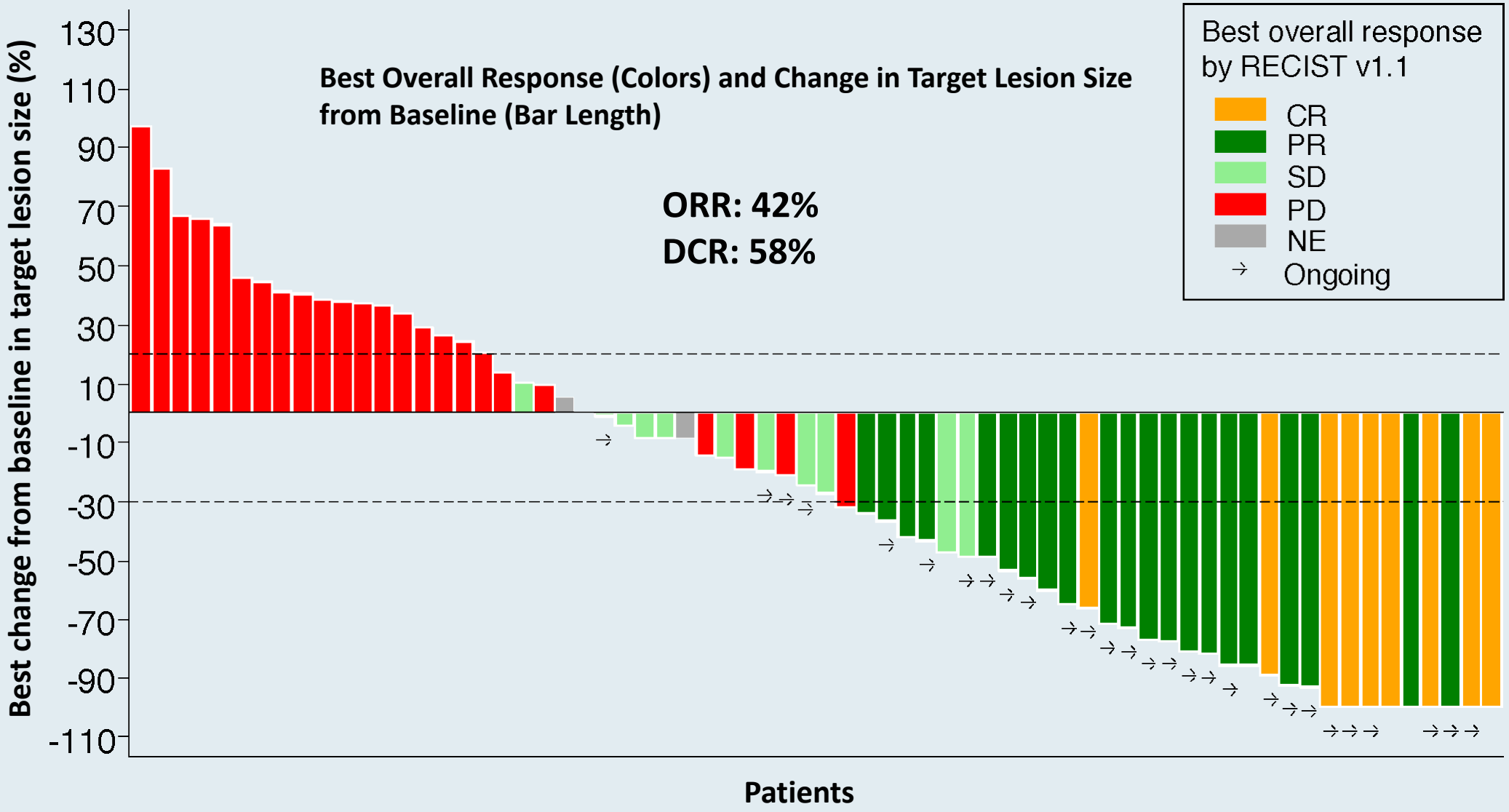
Recent Relevant Data Sets

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.

GARNET: Dostarlimab in Recurrent or Advanced dMMR Endometrial Cancer



Oaknin A et al. SGO 2020;Abstract LBA9.

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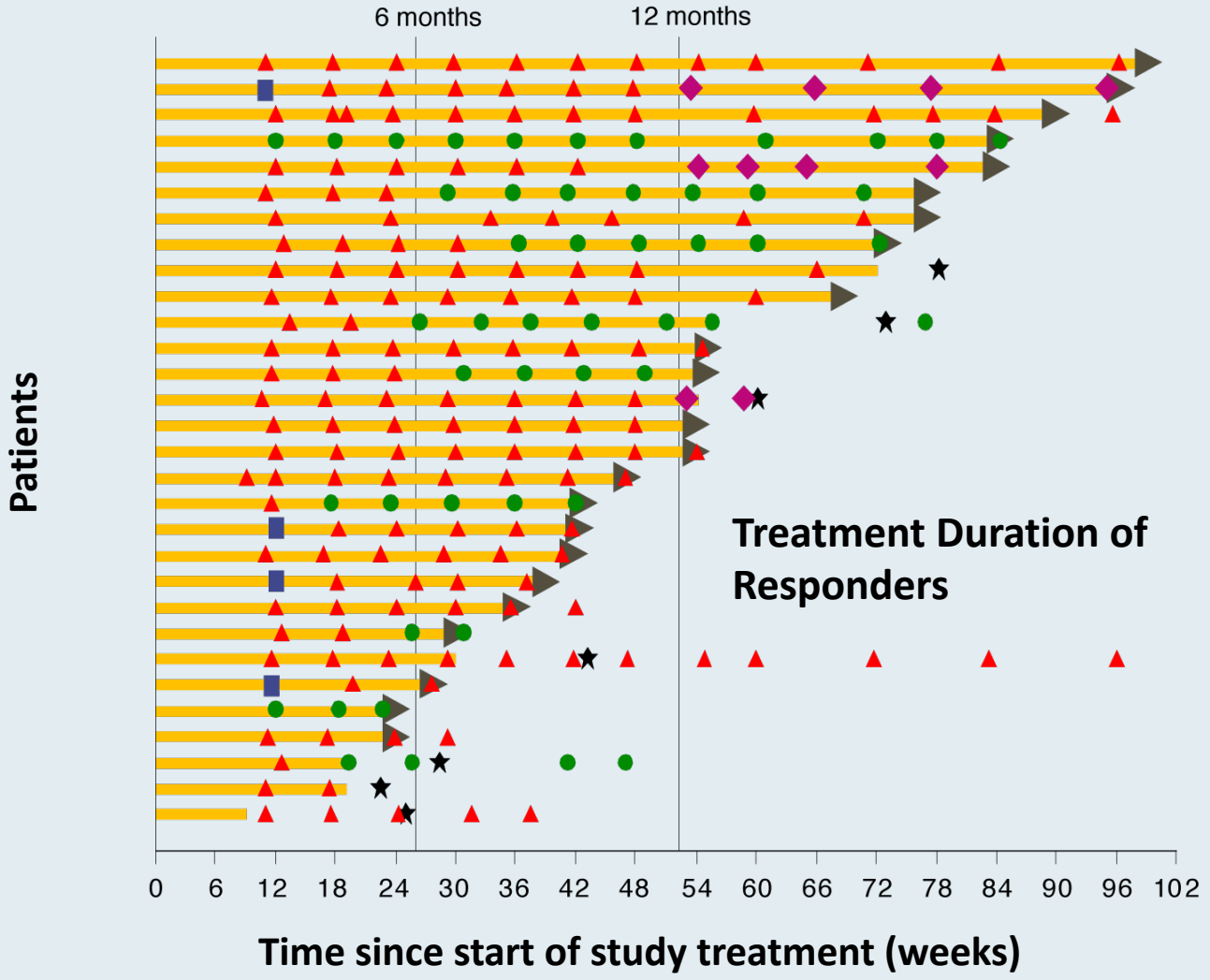
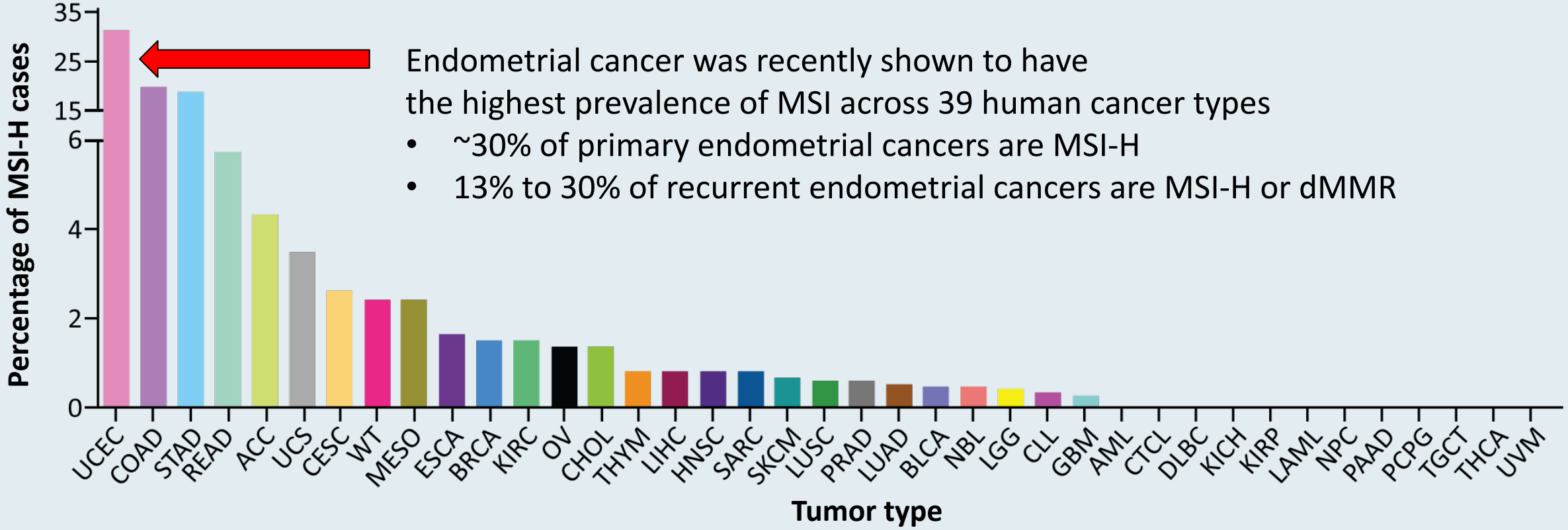


- Median follow-up is 11.2 mos
- Median DOR not reached (1.87+ to 19.61+ mos)
- 25 of 30 (83%) responders remain in response as of the data cutoff
- Deepening of responses:
  - **SD → PR**: 4 patients
  - **PR → CR:** 7 patients

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



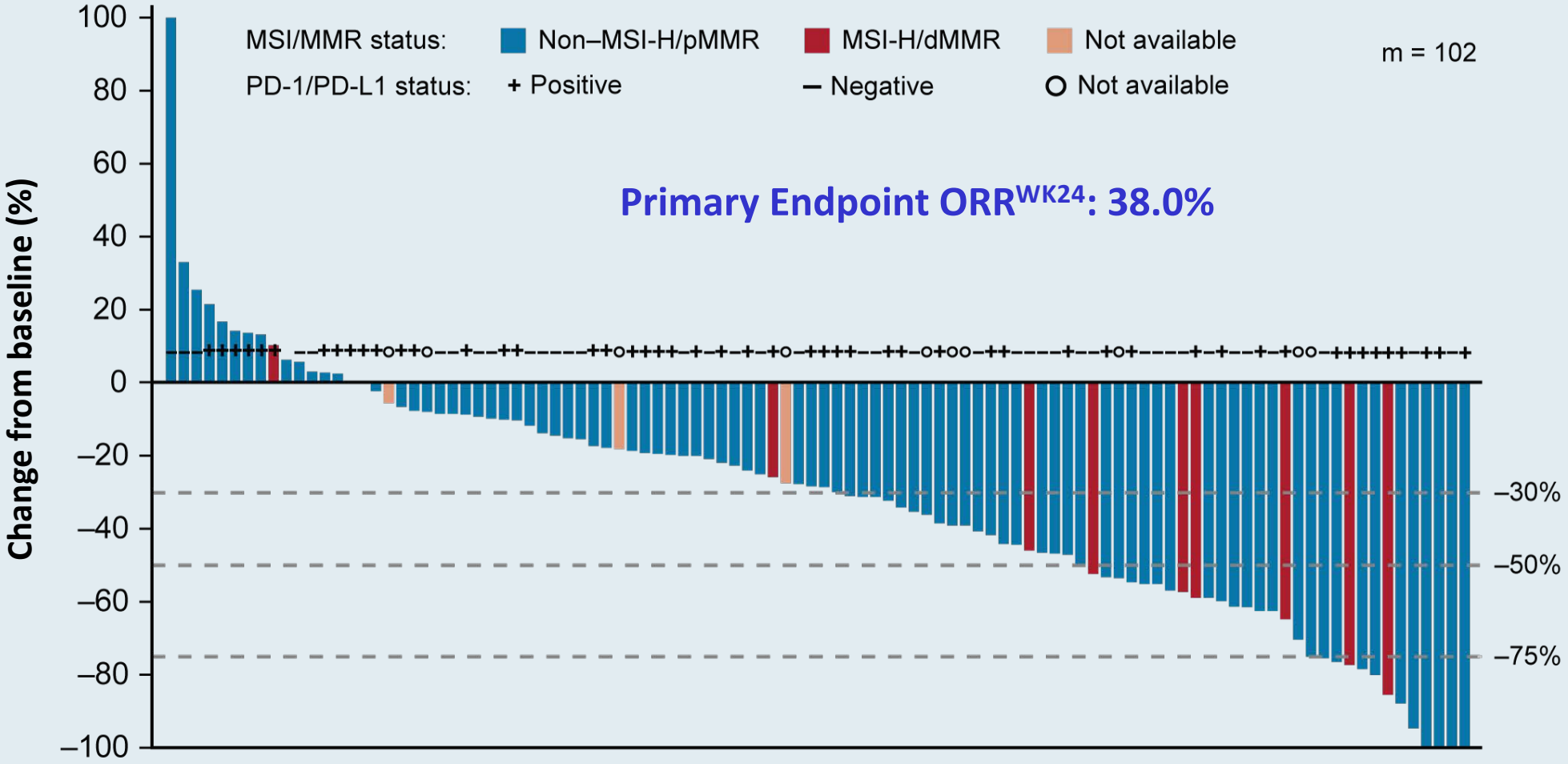
Endometrial cancer was recently shown to have the highest prevalence of MSI across 39 human cancer types

- ~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.

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].

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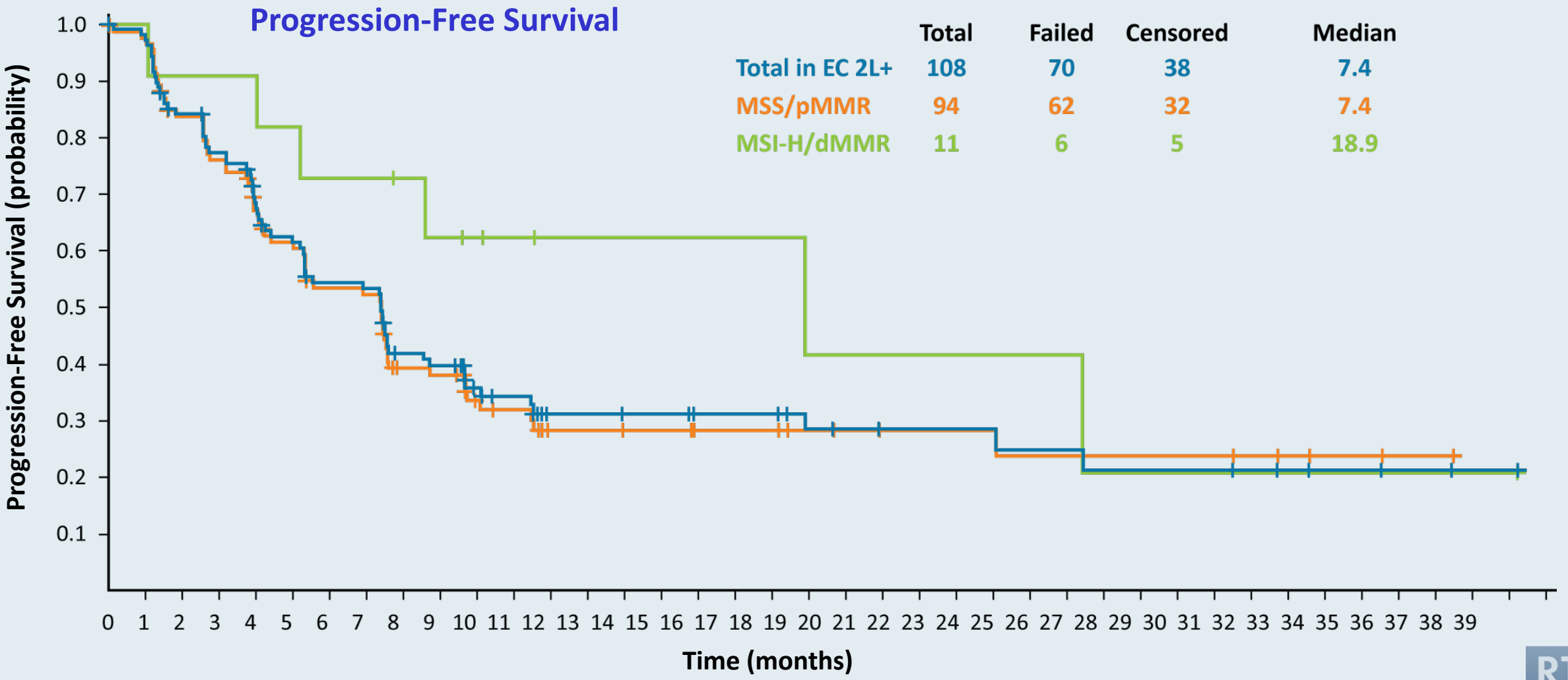

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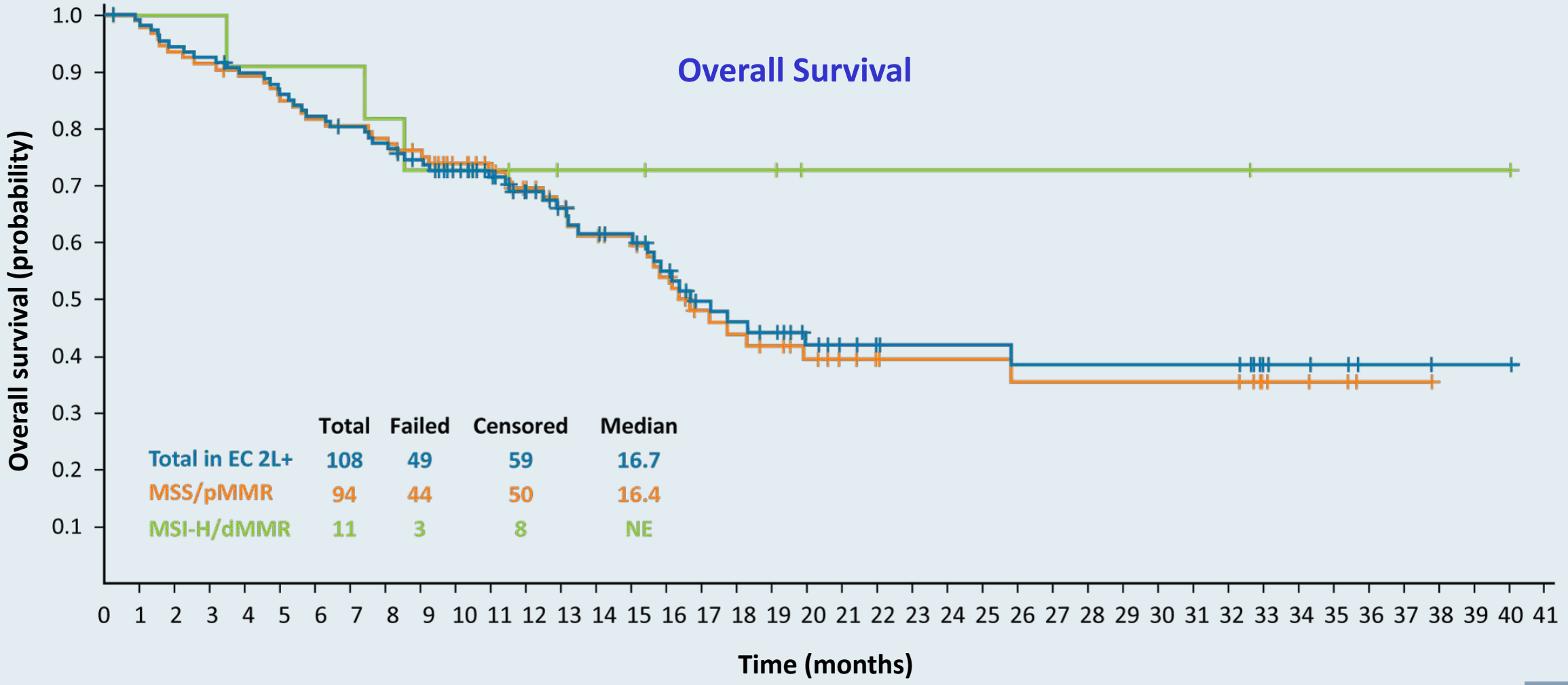

Makker V et al. *J Clin Oncol* 2020;[Online ahead of print].

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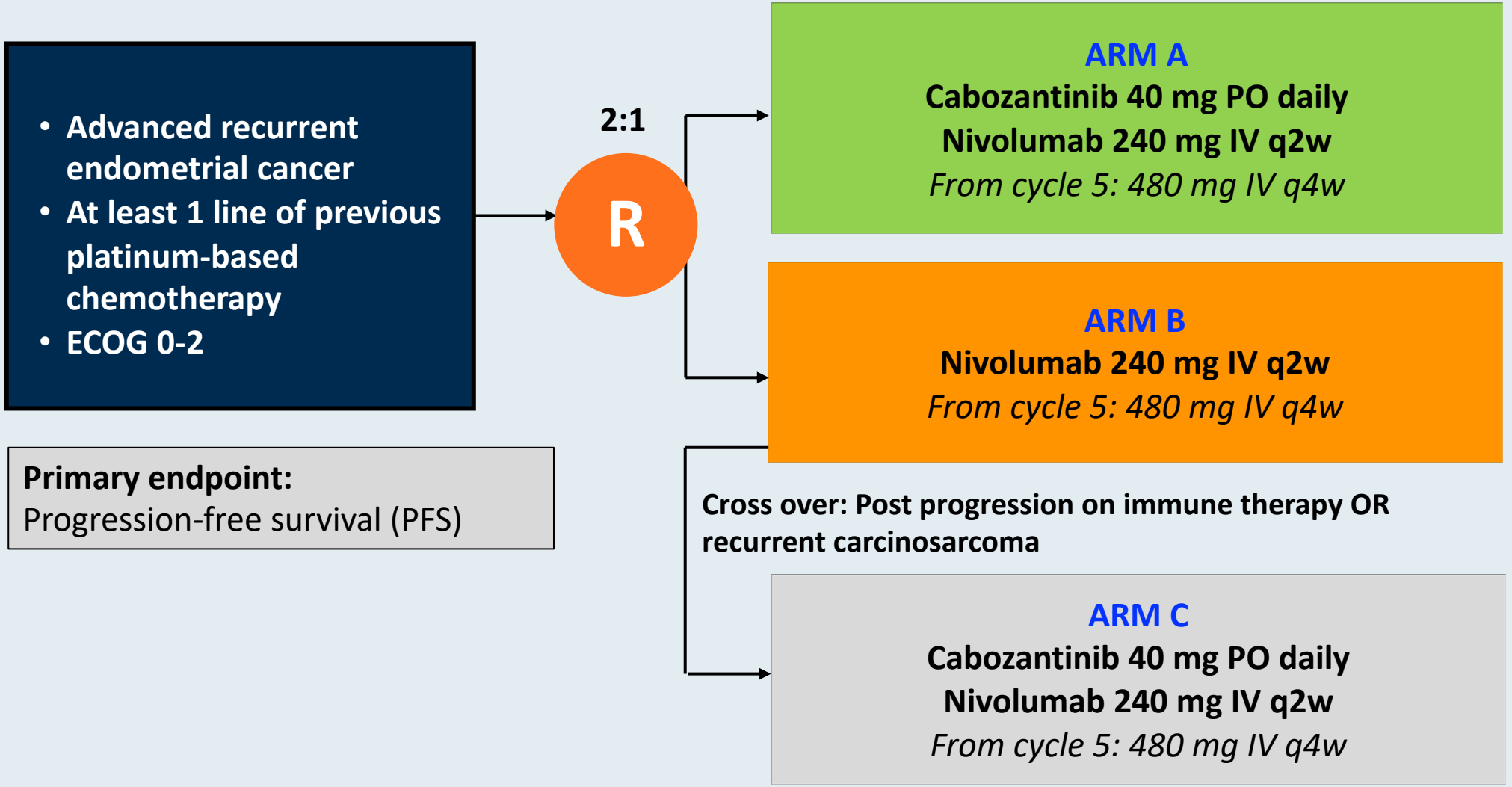
NCI 10104: A Randomized Phase 2 Study of Cabozantinib in Combination with Nivolumab in Advanced, Recurrent Metastatic Endometrial Cancer

Lheureux S et al.

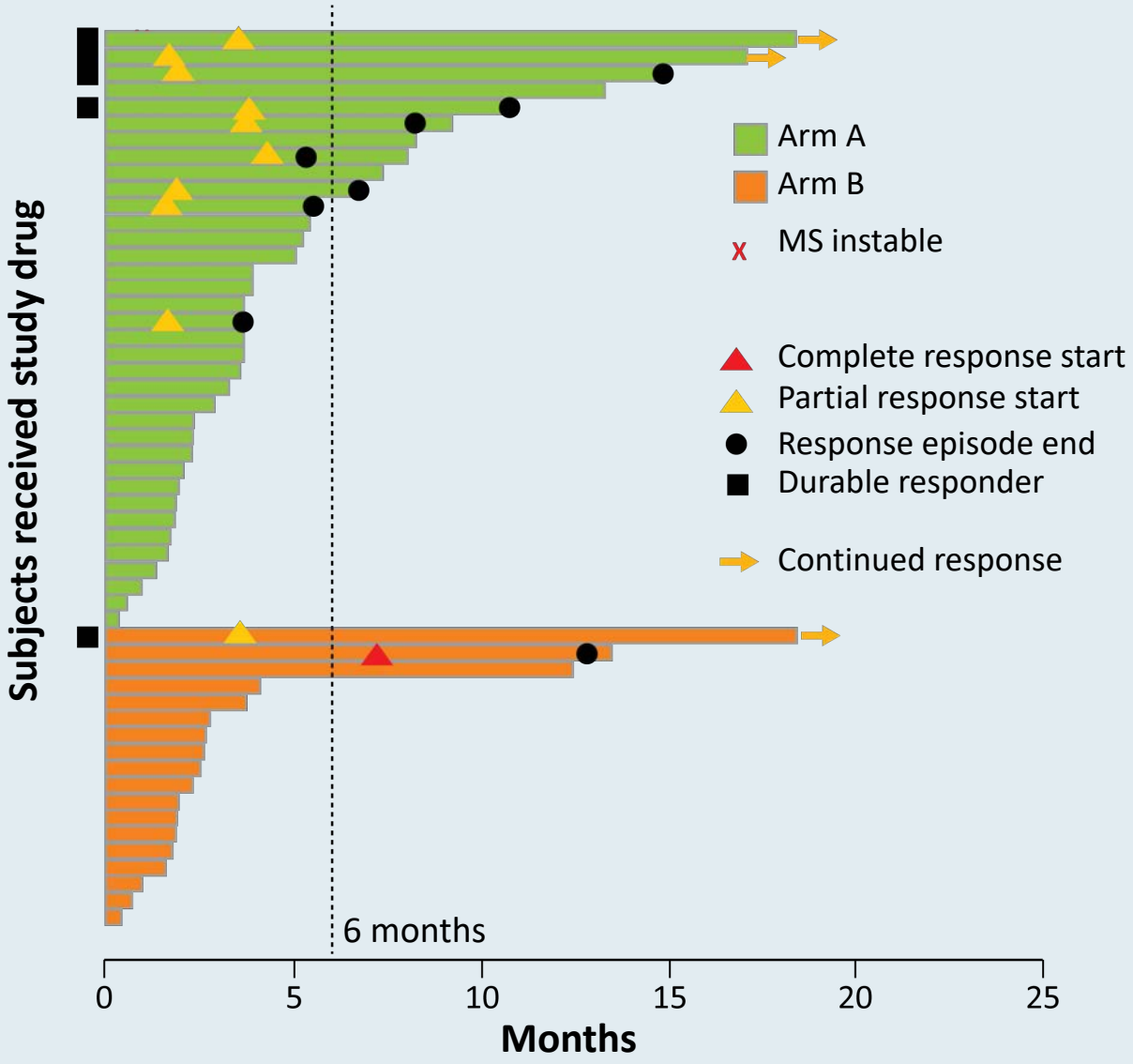
ASCO 2020;Abstract 6010.

NCI 10104 Phase II Study Schema



Lheureux S et al. ASCO 2020;Abstract 6010.

NCI 10104: Response Rate and Duration and Survival Analyses



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

* HR: 0.59, significant

† Immature, 55% events

Lheureux S et al. ASCO 2020;Abstract 6010.

Select Ongoing Phase III Immune Checkpoint Inhibitor Combination Studies

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

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

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

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
 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
 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?

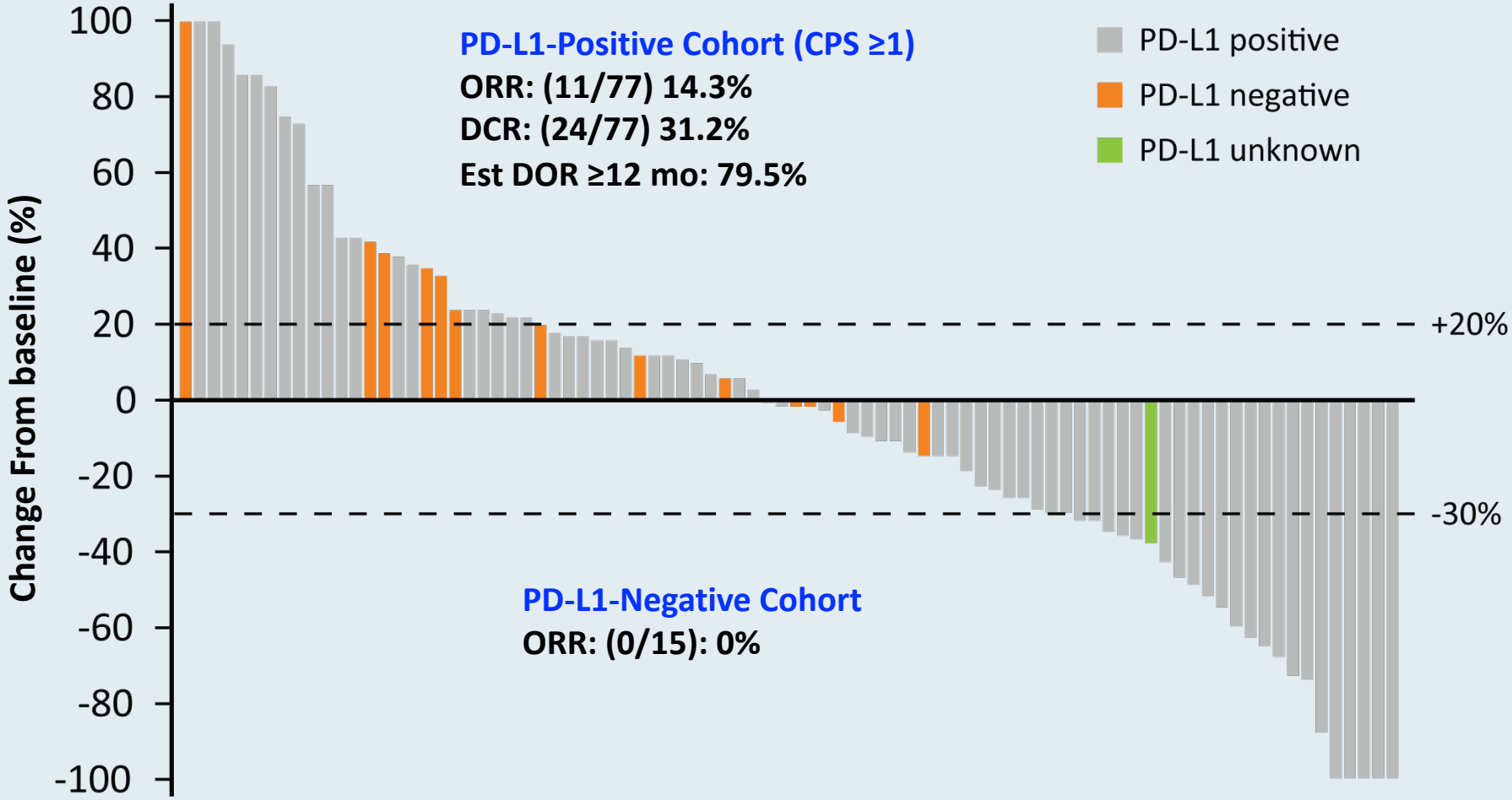
1. Other chemotherapy
2. Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
3. Pembrolizumab
4. Other

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
 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 (if possible, in combination with pembrolizumab)

Recent Relevant Data Sets

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

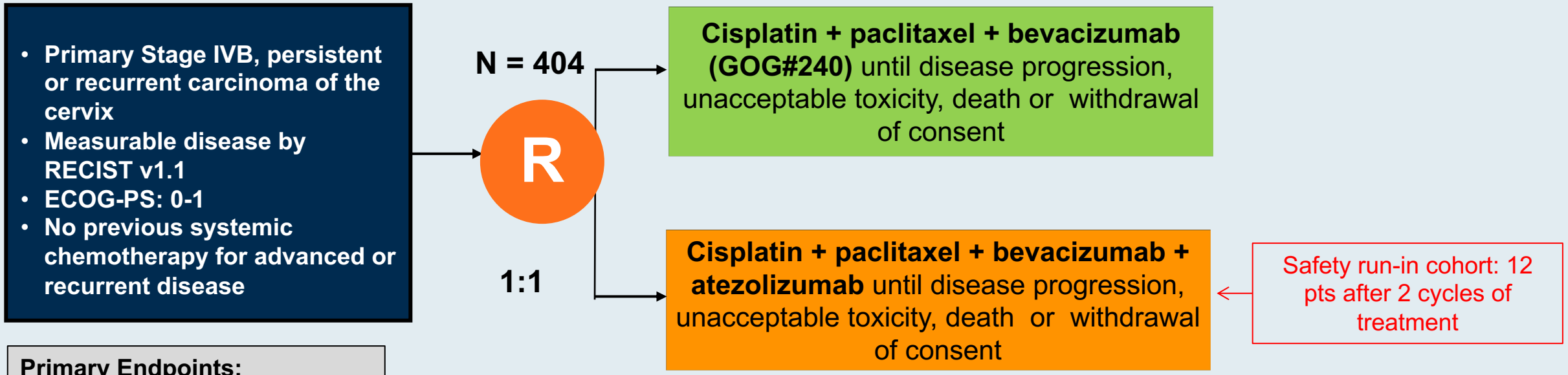


Combined Positive Score (CPS) = PD-L1+ cells (tumor cells, lymphocytes, macrophages) / Total number of tumor cells x 100

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

RTP RESEARCH TO PRACTICE

BEATcc Phase III Randomized Front-Line Trial of Atezolizumab



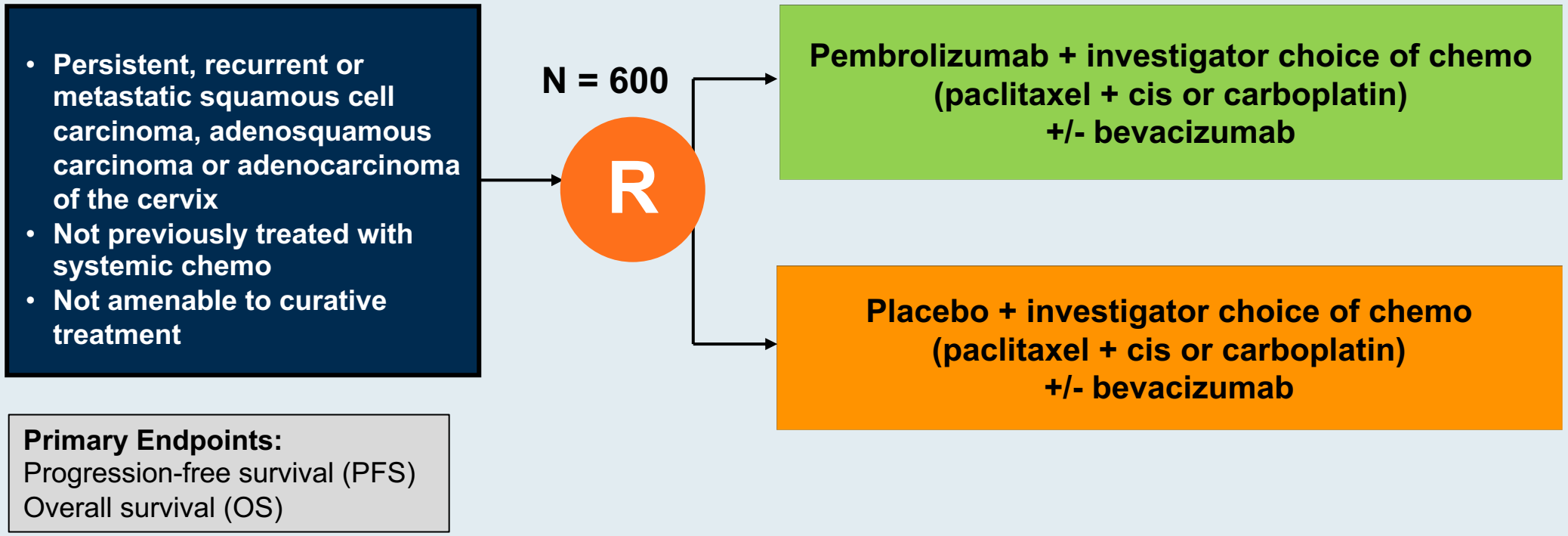
Primary Endpoints:
Overall survival (OS)
Secondary Endpoints:
- PFS
- ORR
- DOR
- Safety
- HR-QOL

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

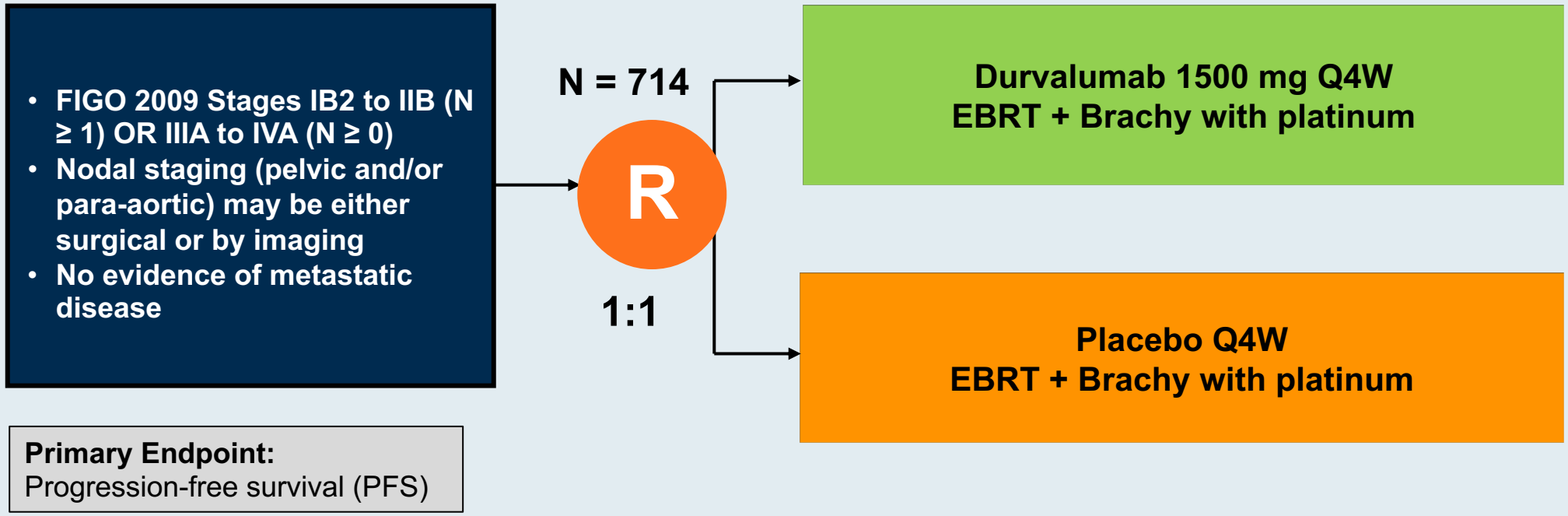
KEYNOTE-826 Phase III Schema



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

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
 MATTHEW A POWELL, MD	Yes
 BRIAN M SLOMOVITZ, MD	No
 KRISHNANSU S TEWARI, MD	No
 PROFESSOR IGNACE VERGOTE	No

Recent Relevant Data Sets

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.

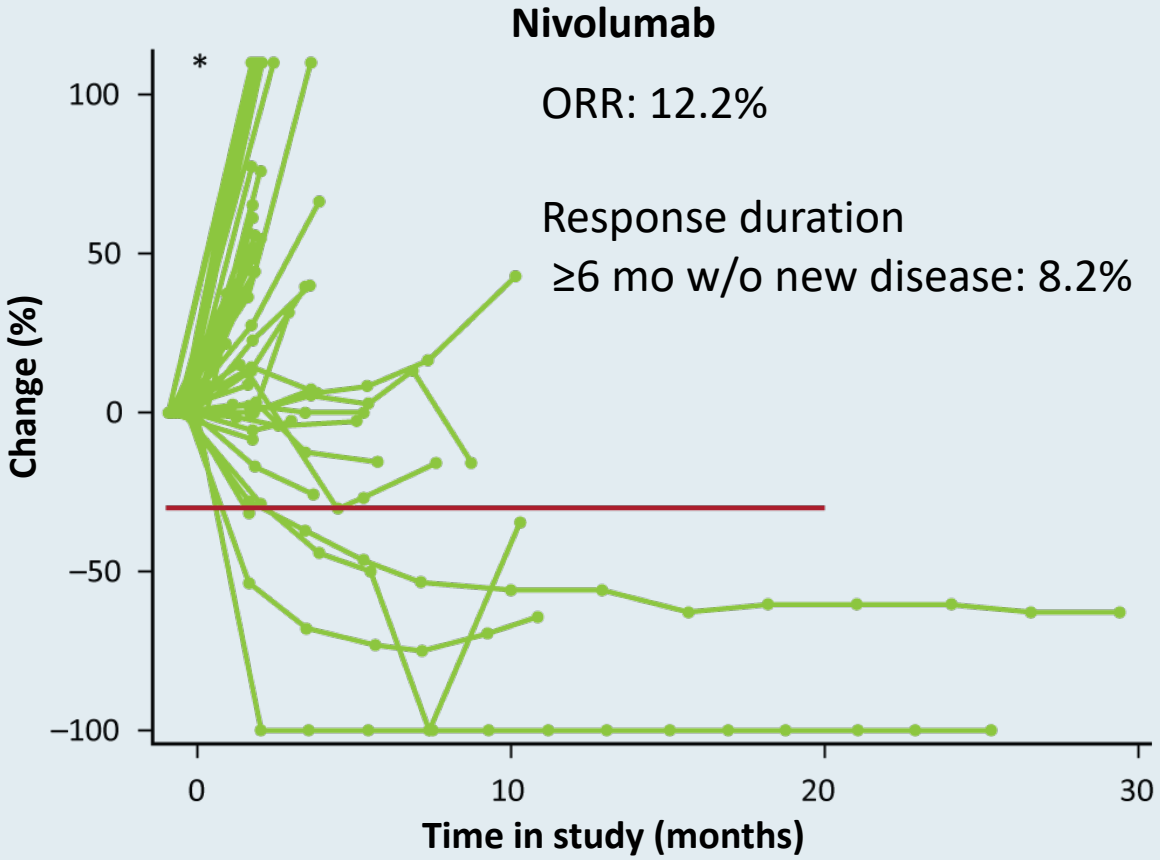
JAVELIN Ovarian 200: Avelumab Alone or in Combination with Pegylated Liposomal Doxorubicin (PLD) versus PLD Alone in Platinum-Resistant or Refractory OC

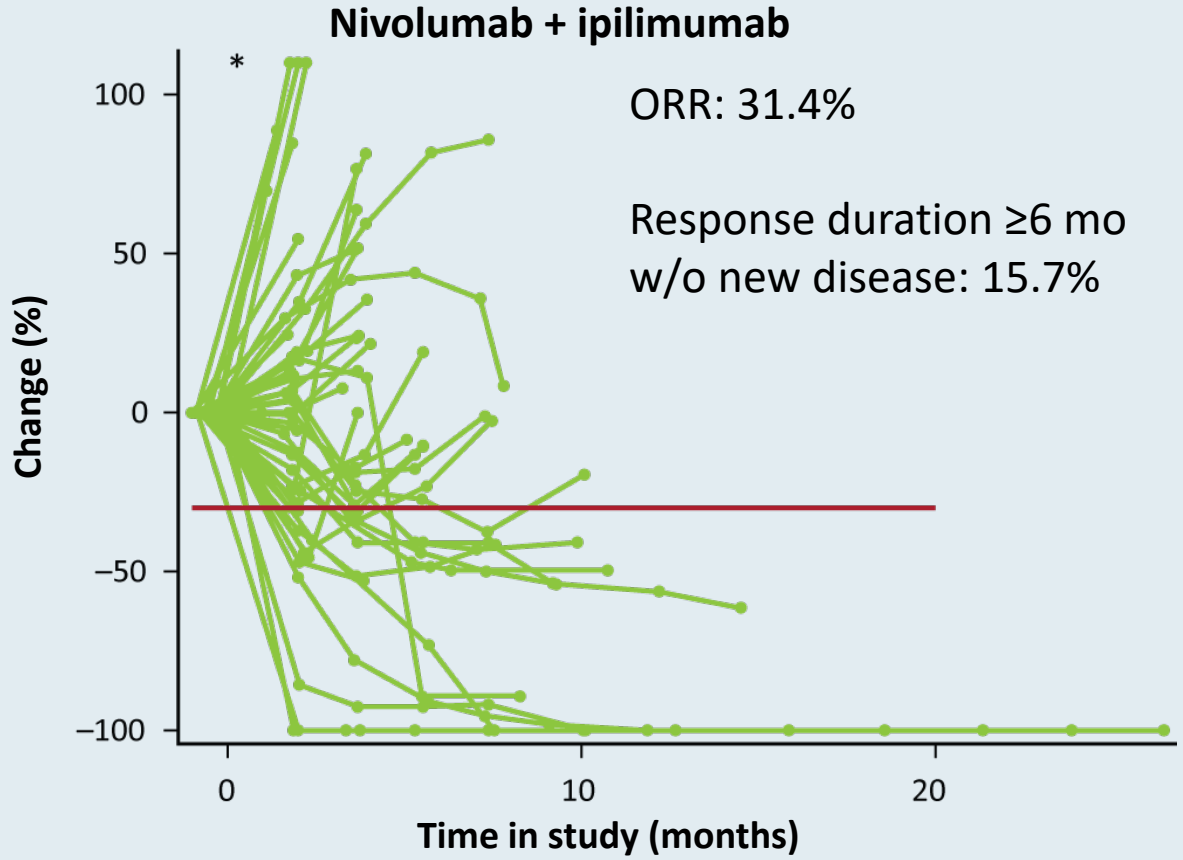
	Avelumab (n = 188)		Avelumab + PLD (n = 188)		PLD (n = 190)	
All patients						
Median OS	11.8 mo		15.7 mo		13.1 mo	
	HR: 1.14, *p* = 0.83		HR: 0.80, *p* = 0.21		Reference	
Median PFS	1.9 mo		3.7 mo		3.5 mo	
	HR: 1.68, *p* > 0.99		HR: 0.78, *p* = 0.03		Reference	
PD-L1 evaluable	**PD-L1+ (n = 91)**	**PD-L1-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



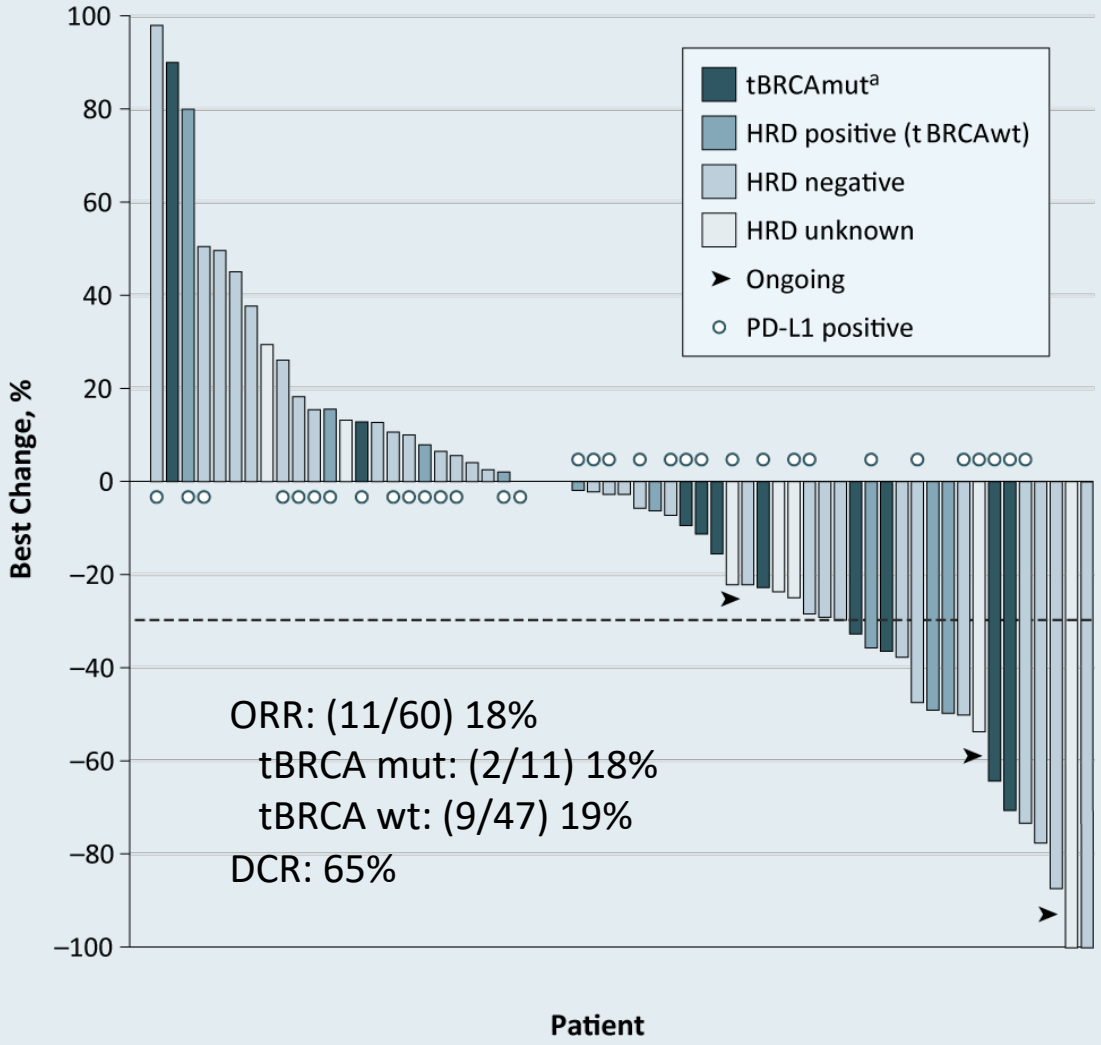


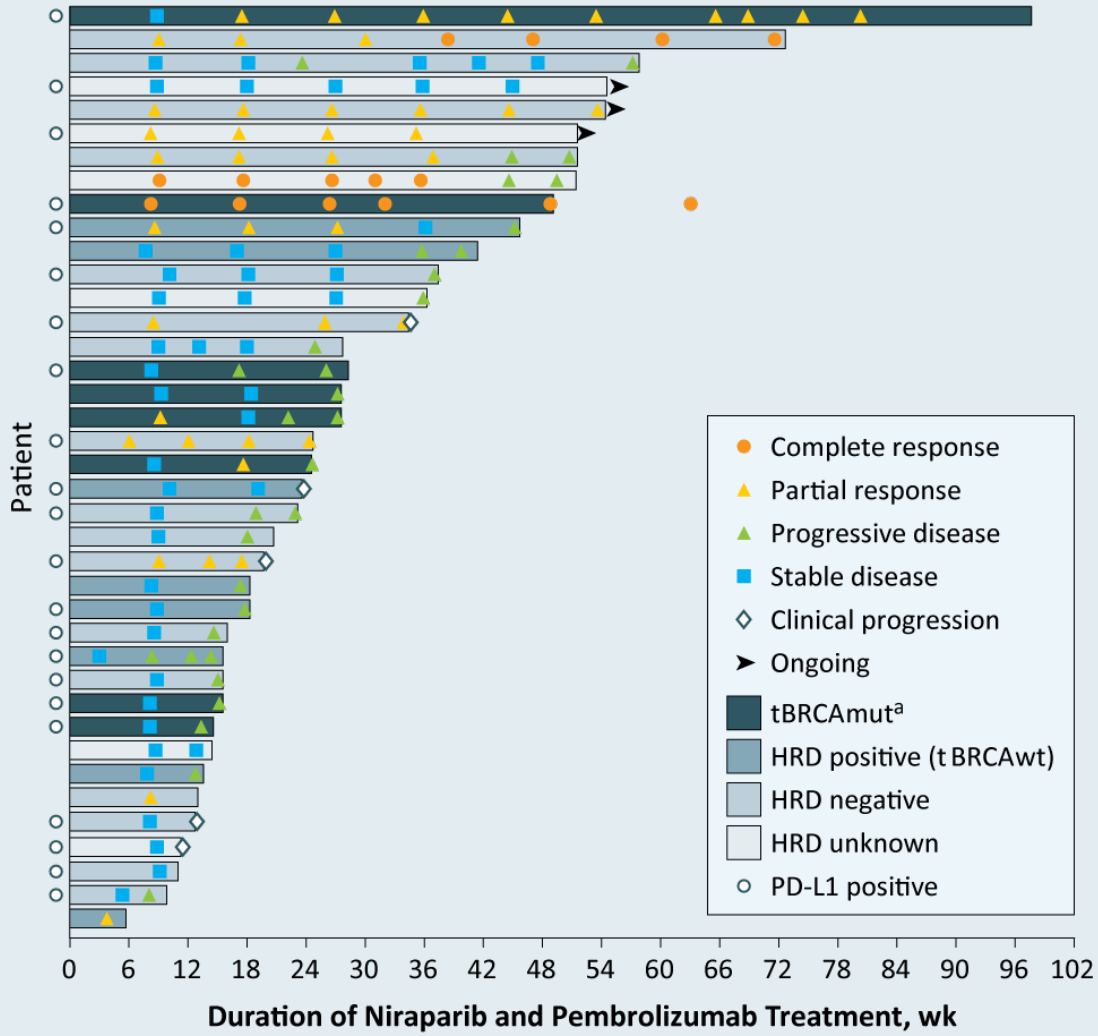
PD-L1 expression was not significantly associated with response in either treatment group

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

RTP RESEARCH TO PRACTICE

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

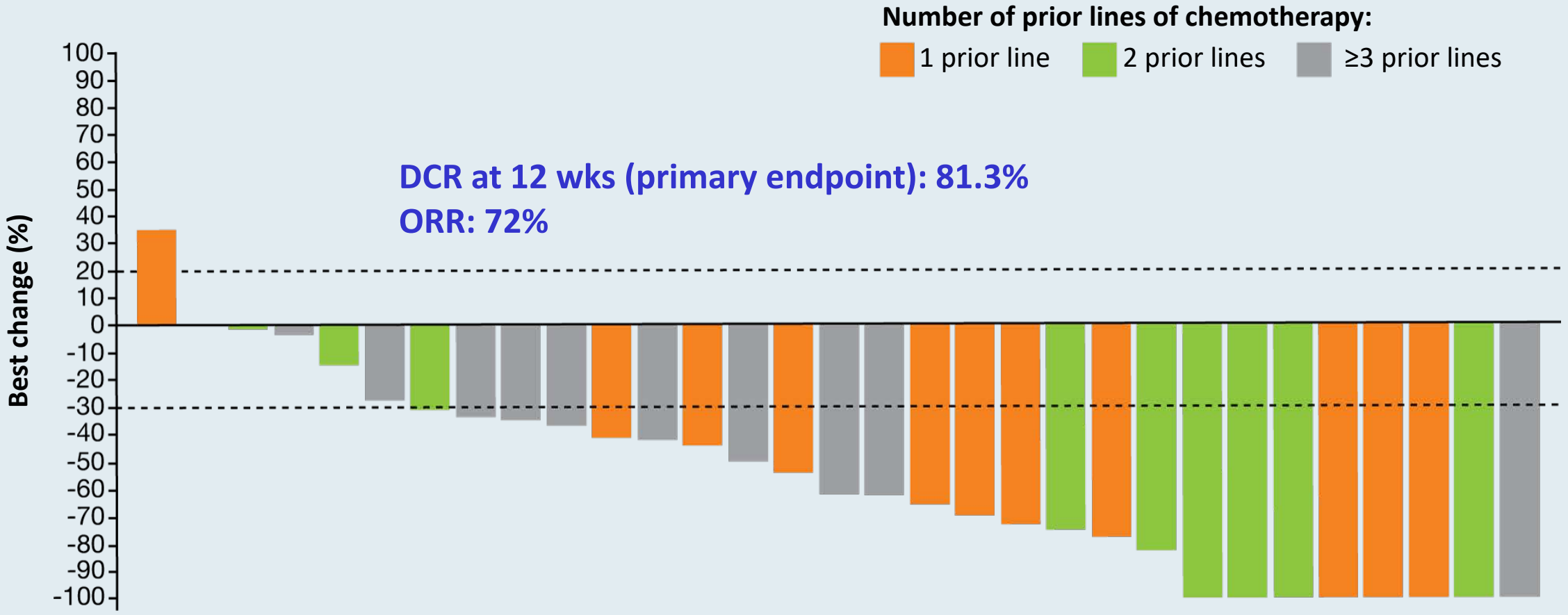




Konstantinopoulos PA, et al. *JAMA Oncol* 2019;5(8):1141-9.

RTP RESEARCH TO PRACTICE

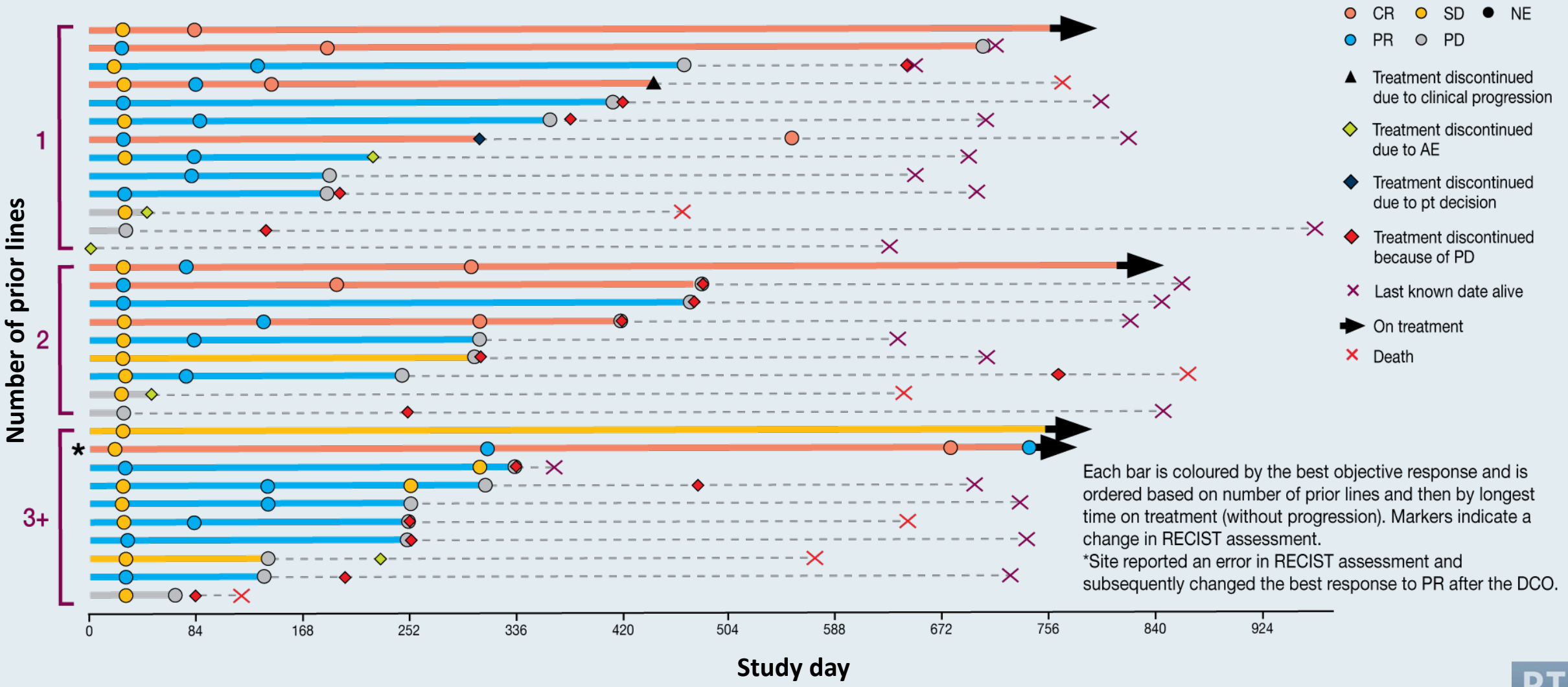
MEDIOLA: A Phase II Study of Olaparib and Durvalumab in gBRCA-Mutated Platinum-Sensitive Relapsed OC



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

RTP RESEARCH TO PRACTICE

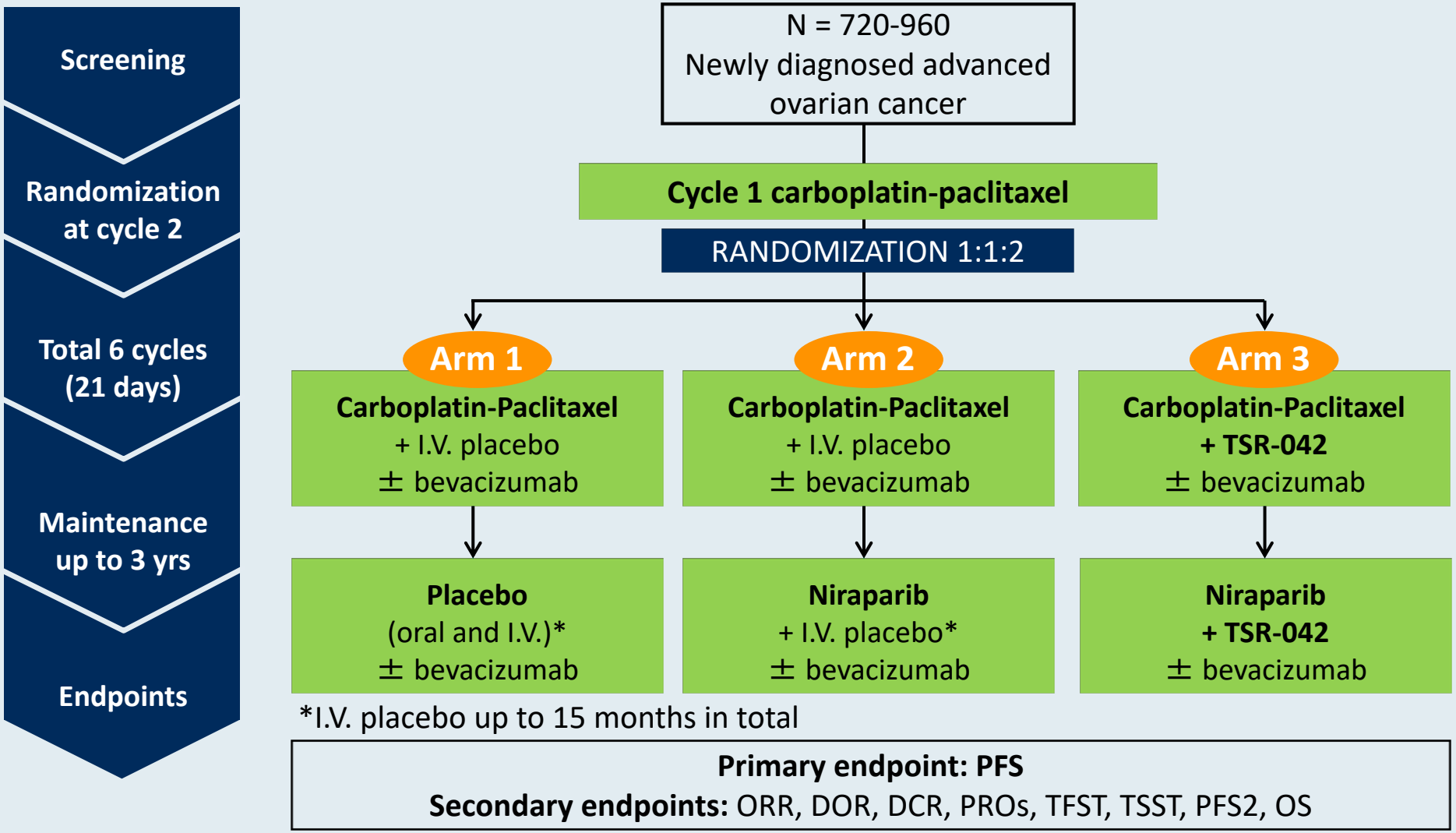
MEDIOLA: Time to Disease Progression or Treatment Discontinuation, Based on Number of Prior Lines of Therapy



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

RTP RESEARCH TO PRACTICE

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



www.clinicaltrials.gov/ct2/show/NCT03602859

Courtesy of Ursula Matulonis, MD

Phase II MOONSTONE Study Design

Eligibility

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

N=150

Niraparib + Dostarlimab

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

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

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

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

www.clinicaltrials.gov. Accessed August 2020.

Meet The Professor with Dr Birrer

MODULE 1: Anti-PD-1/PD-L1 Checkpoint Inhibitors for Gynecologic Cancers

- Recent relevant data sets
- Pembrolizumab (KEYNOTE-158) or dostarlimab (GARNET) for MSI-H or dMMR endometrial cancer (EC)
- KEYNOTE-146: Pembrolizumab/lenvatinib for EC without MSI-H/dMMR; ongoing studies (KEYNOTE-775, LEAP-001)
- FDA approval of pembrolizumab for cervical cancer; ongoing studies (BEATcc, KEYNOTE-826, CALLA)
- KEYNOTE-100 trial: Pembrolizumab for advanced recurrent ovarian cancer
- Emerging data from JAVELIN Ovarian 200, TOPACIO, MEDIOLA trials in ovarian cancer
- Key ongoing studies (FIRST, MOONSTONE, ATHENA, DUO-O) in ovarian cancer

MODULE 2: HER2-Positive Endometrial Cancer

- Recent relevant data sets
- Randomized Phase II trial of carboplatin/paclitaxel +/- trastuzumab in HER2-positive uterine serous carcinoma

MODULE 3: Tisotumab Vedotin and Other Novel Agents in Gynecologic Cancers

- Recent relevant data sets
- Emerging clinical data with tisotumab vedotin; ongoing innovaTV 205 study

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Case Presentation – Dr Slomovitz: A thin 64-year-old woman with uterine serous carcinoma

Brian M Slomovitz, MD

- Presents to her GYN with postmenopausal bleeding
- EMB: serous carcinoma
- Pre-op CT: No evidence of metastatic disease
- Robotic hysterectomy and staging, no visible cancer
- Pathology: 7/12 mm invasion of carcinoma, negative cervix, right sentinel lymph node positive for carcinoma
- HER-2/neu IHC: 3+ staining
- Adjuvant therapy: Carboplatin/paclitaxel/trastuzumab
- Currently: NED

Questions

- Do you do HER2/neu testing on all of your patients with uterine serous carcinoma? And if so, how are you using that information in the earlier- versus advanced-stage settings?
- For a thin patient with endometrial cancer, are you concerned that the cancer may not be an estrogen-driven tumor? Would it effect your management?

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Recent Relevant Data Sets

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

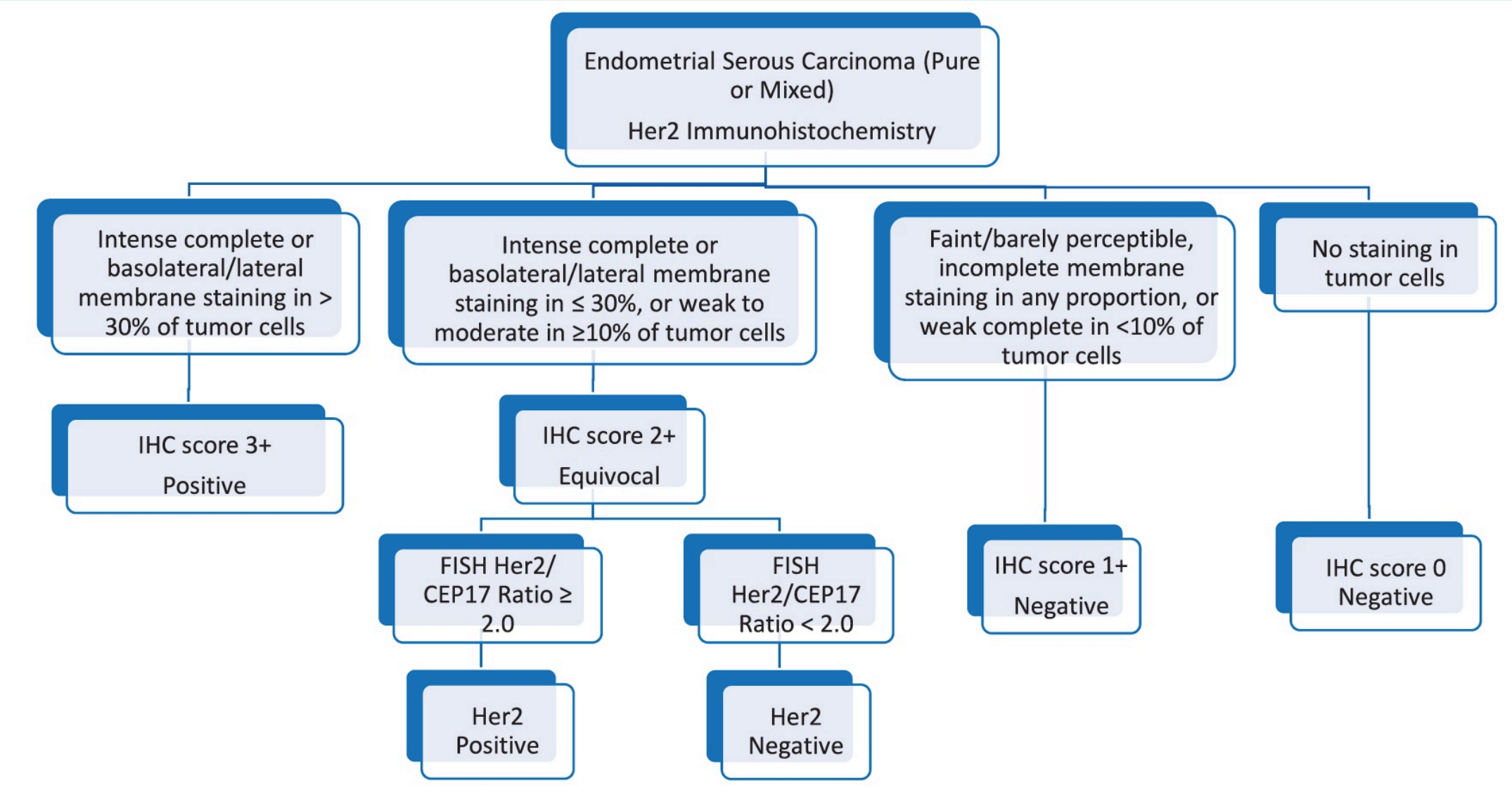
	Breast (ASCO/CAP 2018)[23]	Gastric (ASCO/CAP 2016)[36]	Colorectal (HERACLES Trial)[39]	Endometrial Serous (Fader et al Clinical Trial)[21]
HER2 IHC 3+	>10% circumferential, strong, complete	≥10%, strong complete, or basolateral/lateral	≥50% strong complete, or basolateral/lateral	>30% strong complete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



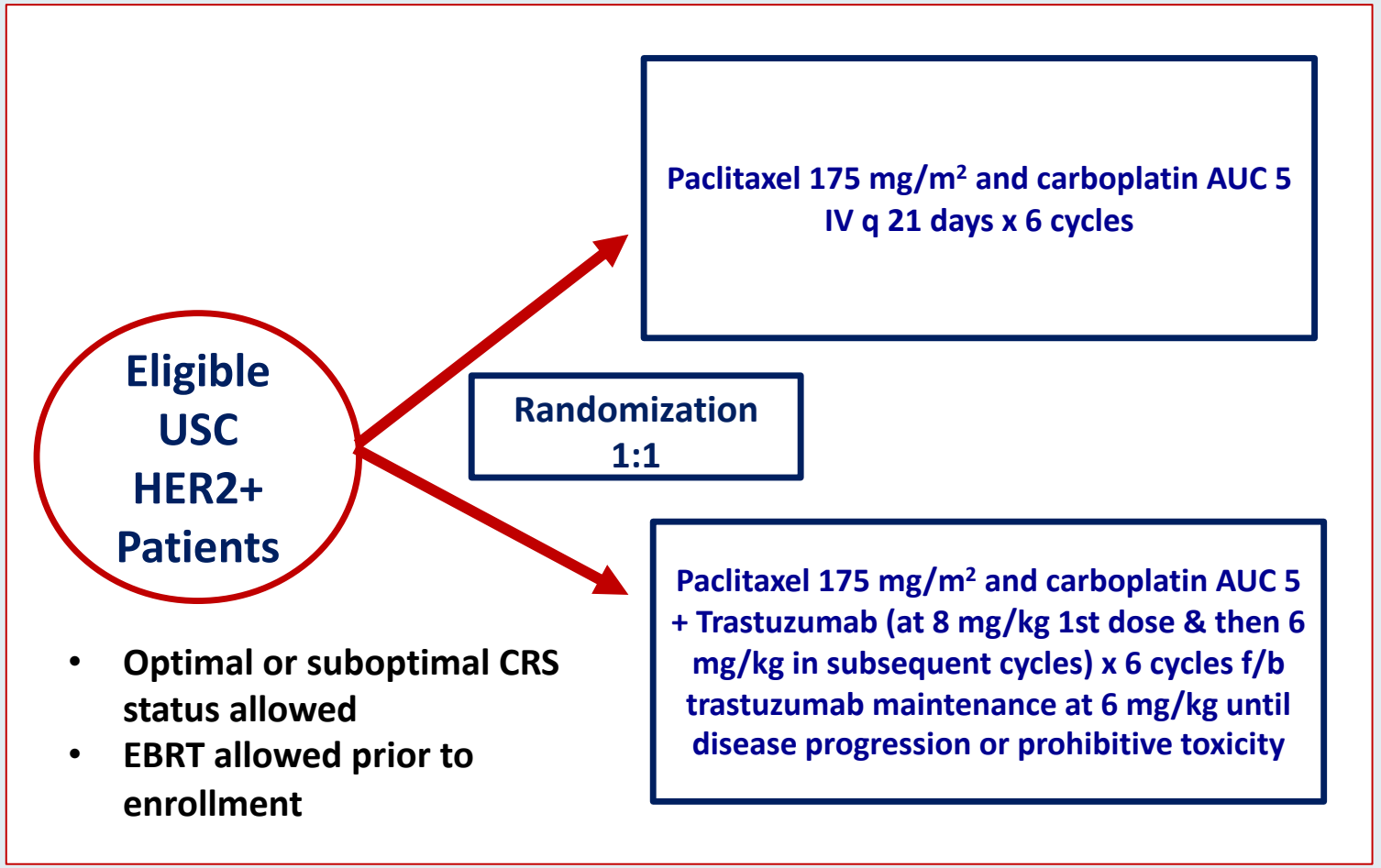
Buza N. *Arch Pathol Lab Med* 2020;[Online ahead of print].

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

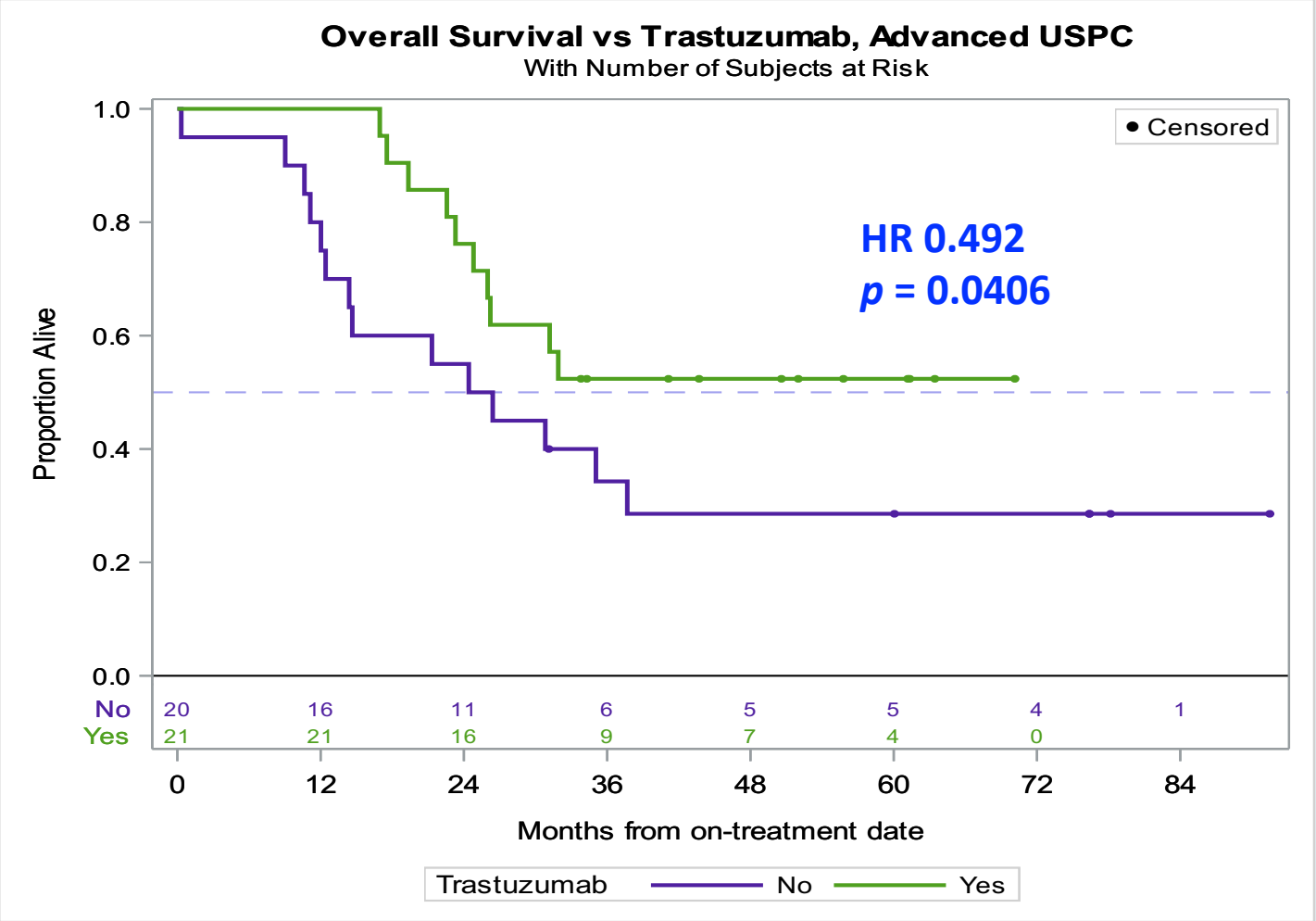


Fader AN et al. *Clin Cancer Res* 2020;26:3928-35.

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

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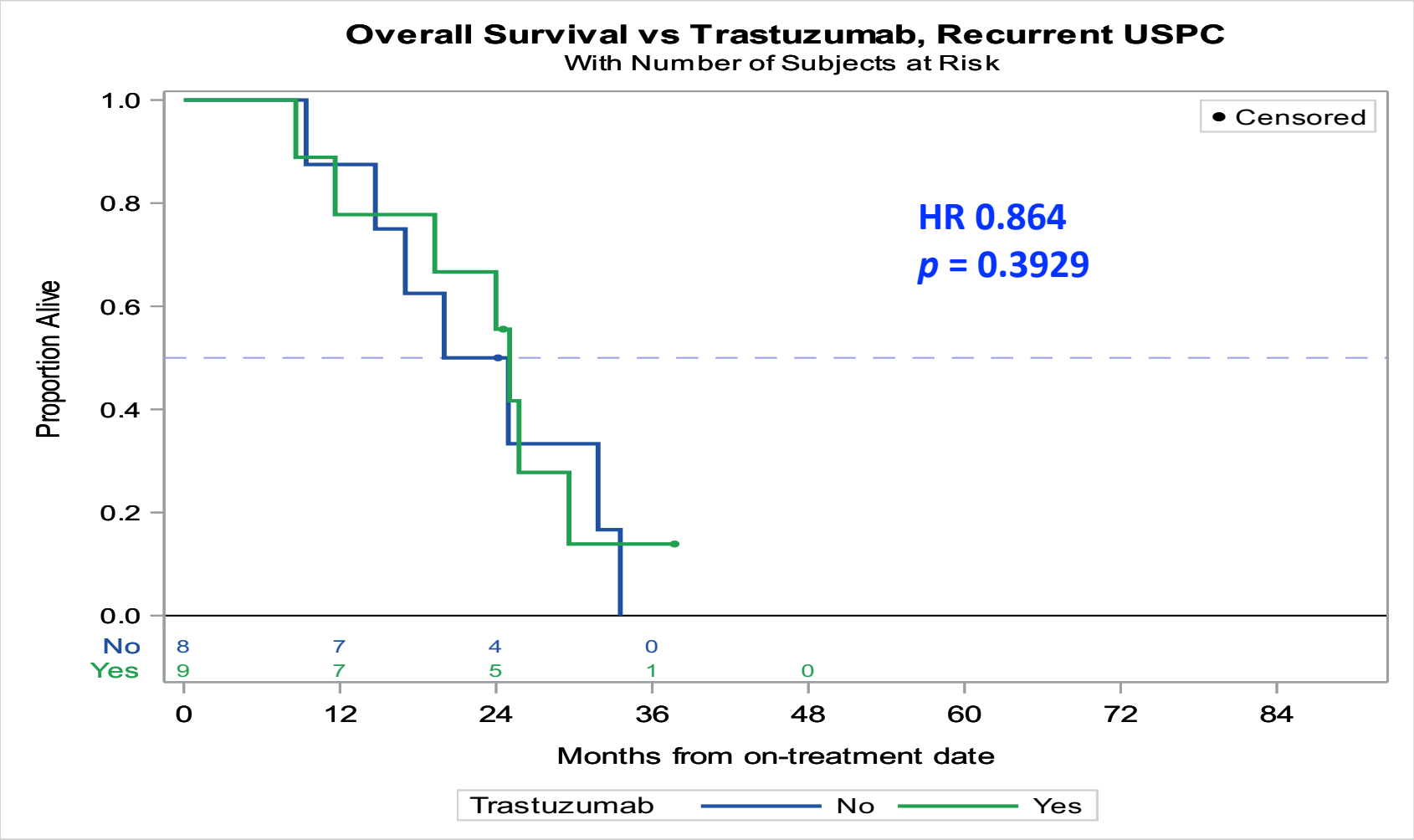
Overall Survival with the Addition of Trastuzumab to Carboplatin/Paclitaxel for Recurrent USPC

- No significant OS benefit was observed in the recurrence cohort



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

Courtesy of David M O'Malley, MD

Carboplatin/Paclitaxel/Trastuzumab: Summary

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

Fader AN et al. SGO 2020

Courtesy of David M O'Malley, MD

Phase II DESTINY-PanTumor02 Study Design

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

Eligibility

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

Trastuzumab deruxtecan

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

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

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

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Birrer

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Comments and Questions

Brian M Slomovitz, MD

RTP RESEARCH TO PRACTICE

Comments and Questions

Brian M Slomovitz, MD

RTP RESEARCH TO PRACTICE

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

 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
 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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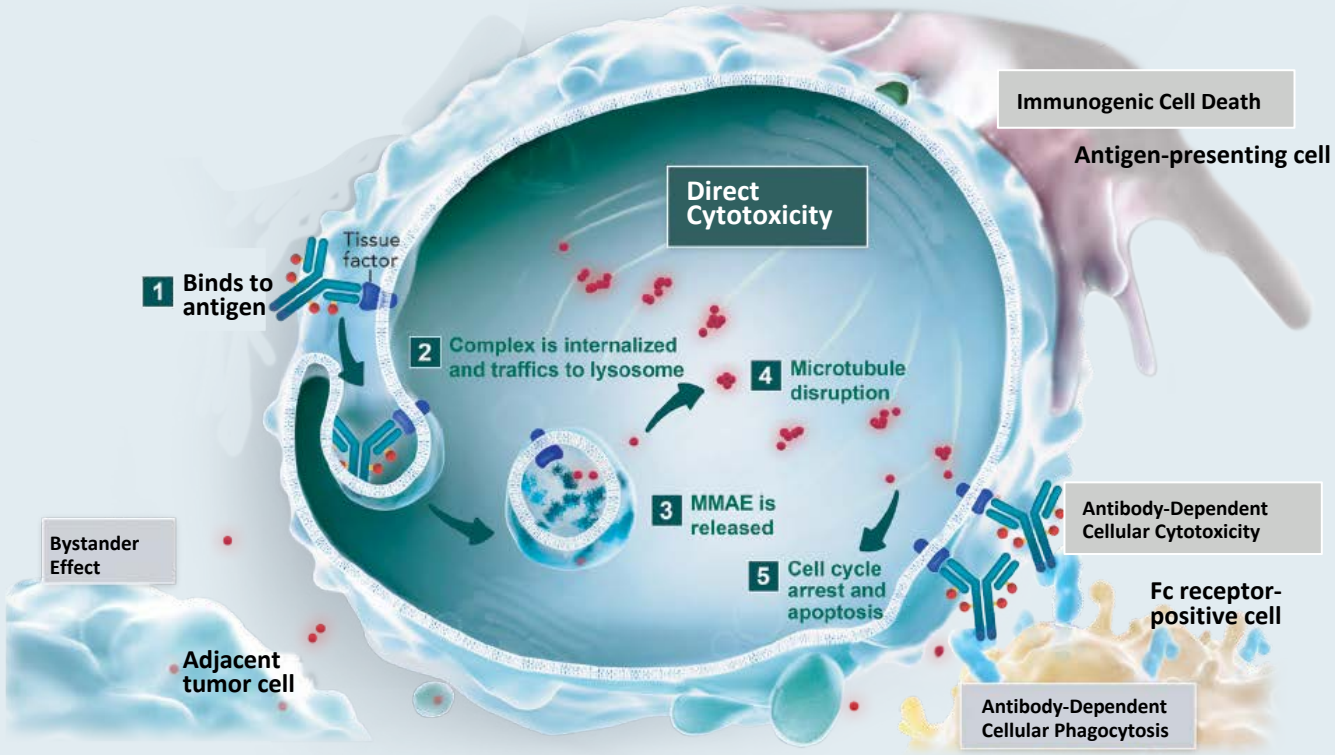
Recent Relevant Data Sets

Mechanism of Action of Tisotumab Vedotin

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

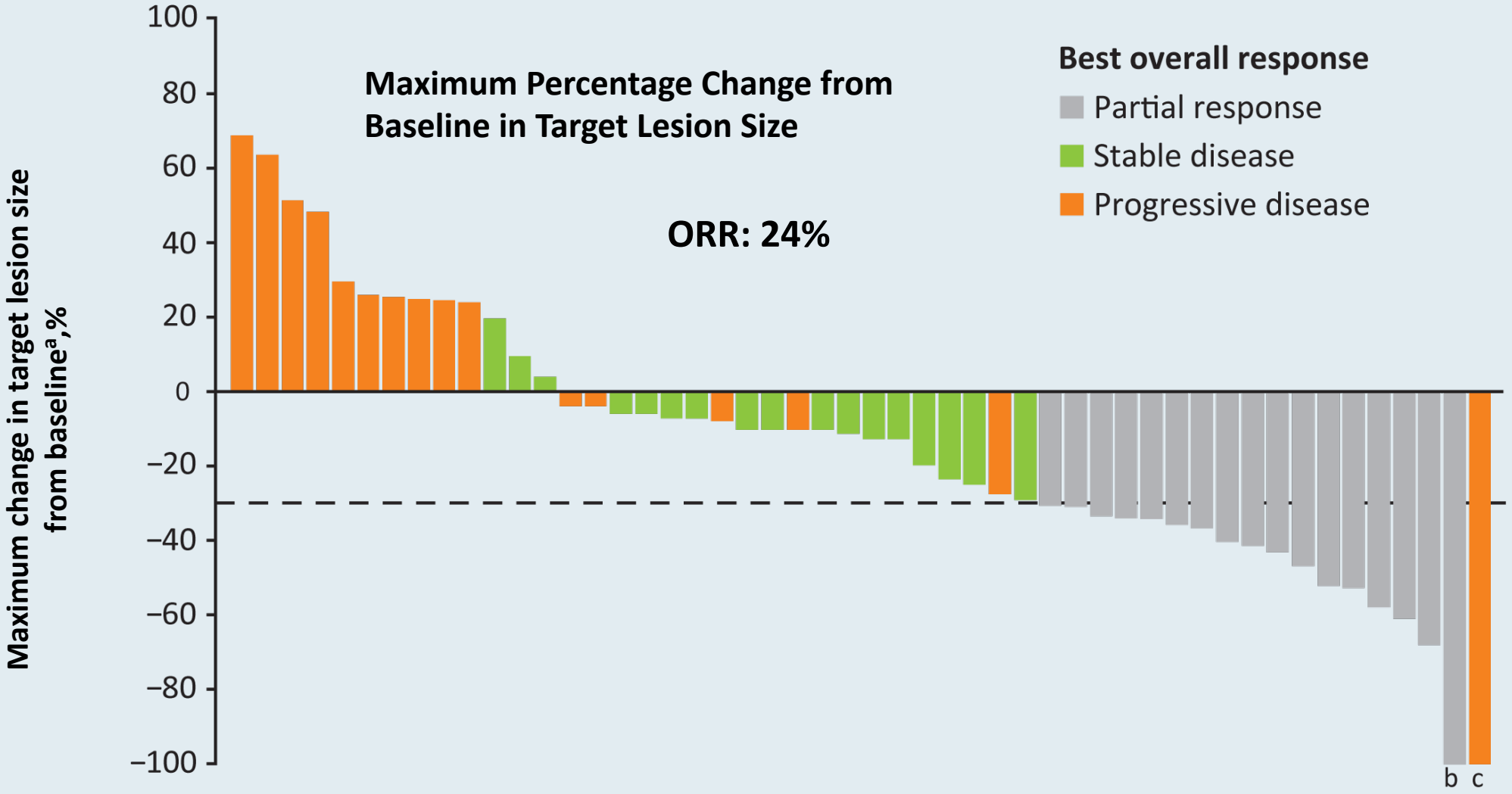


1. Förster Y, et al. *Clin Chim Acta,* 2006. 2. Cocco E, et al. *BMC Cancer,* 2011.
3. Breij EC, et al. *Cancer Res,* 2014. 4. De Goeij BE, et al. *Mol Cancer Ther,* 2015.

Courtesy of David M O'Malley, MD

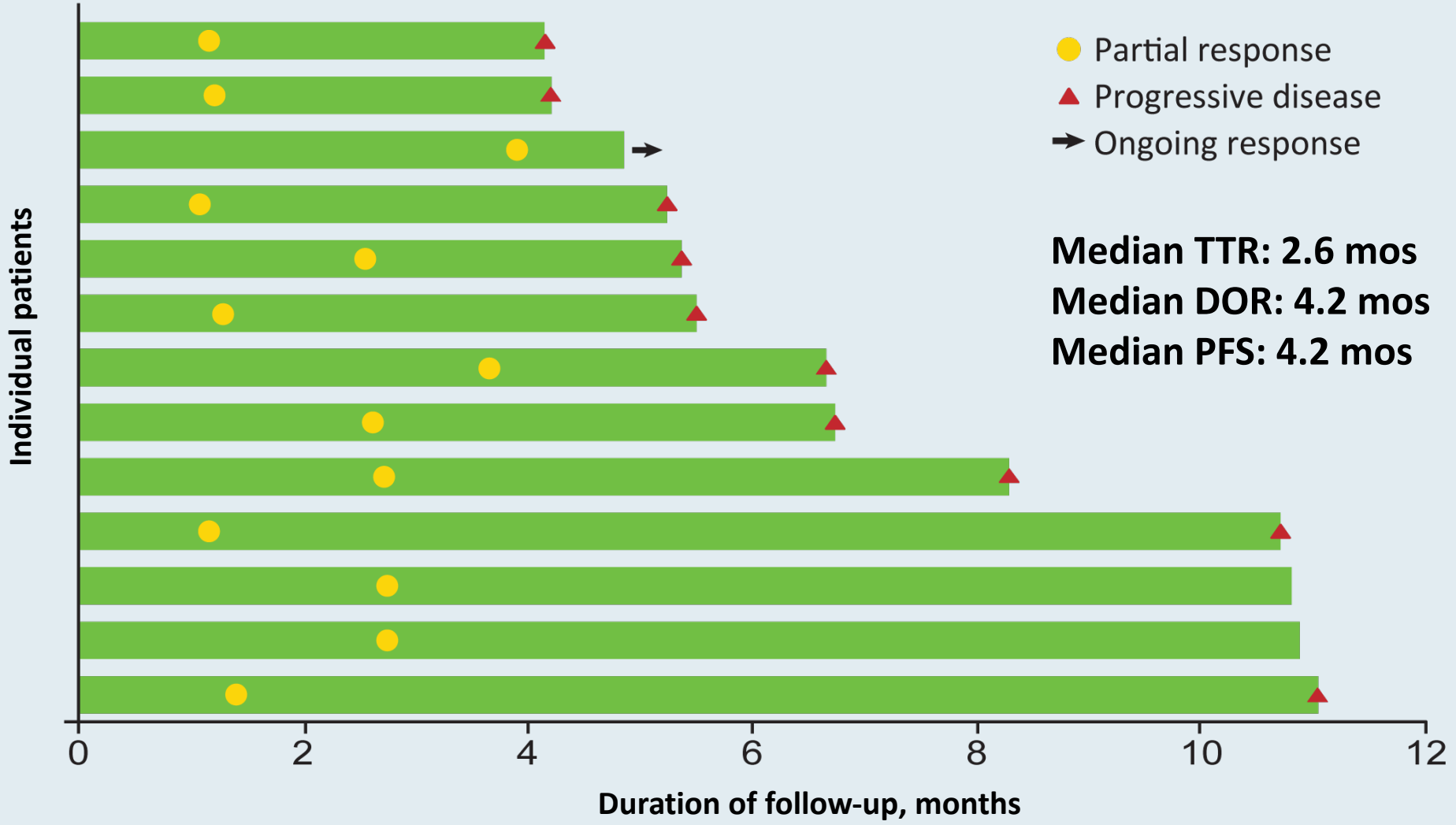
RTP RESEARCH TO PRACTICE

innovaTV 201: Best Overall Response to TV



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

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.

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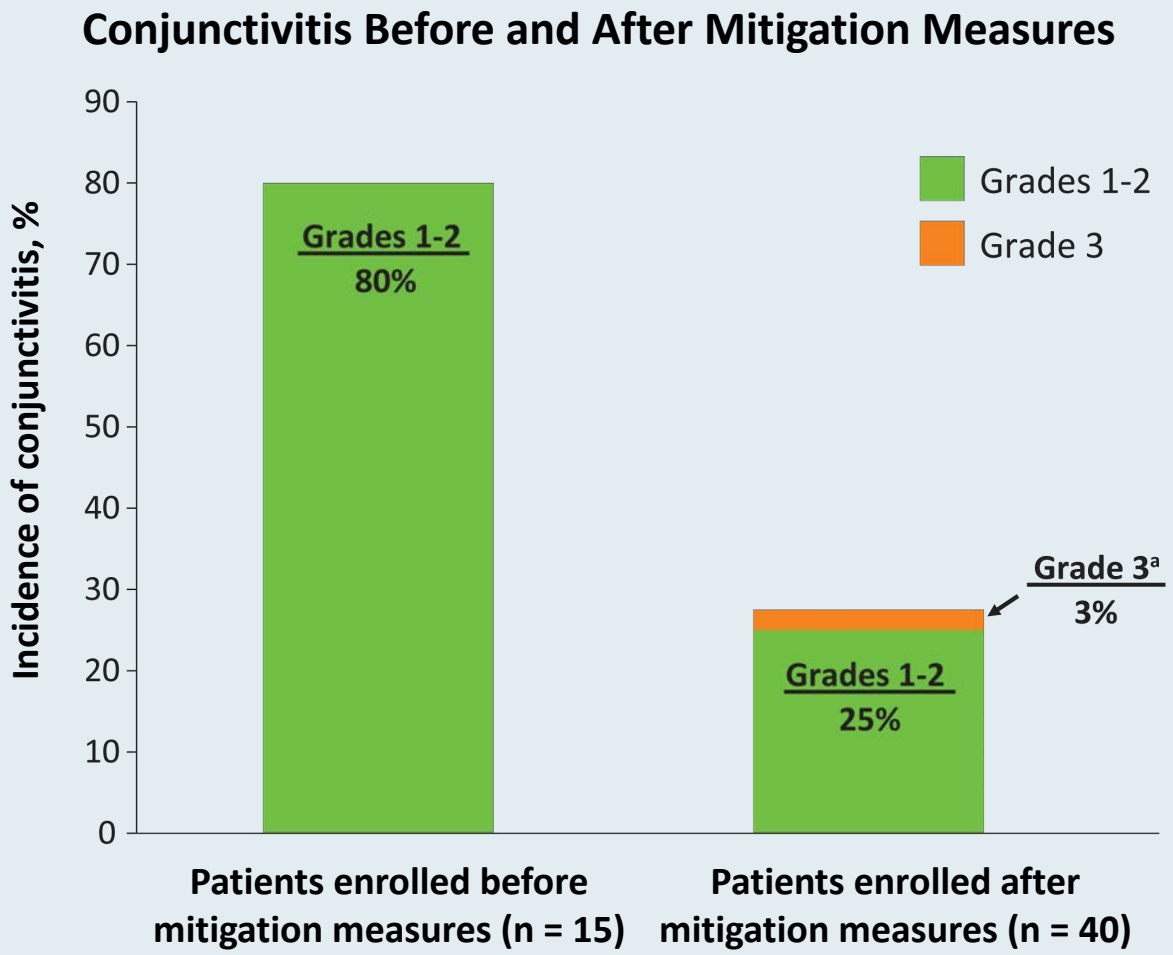
innovaTV 201: Treatment-Emergent Adverse Events

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



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

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

RTP RESEARCH TO PRACTICE

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

Press Release – June 30, 2020

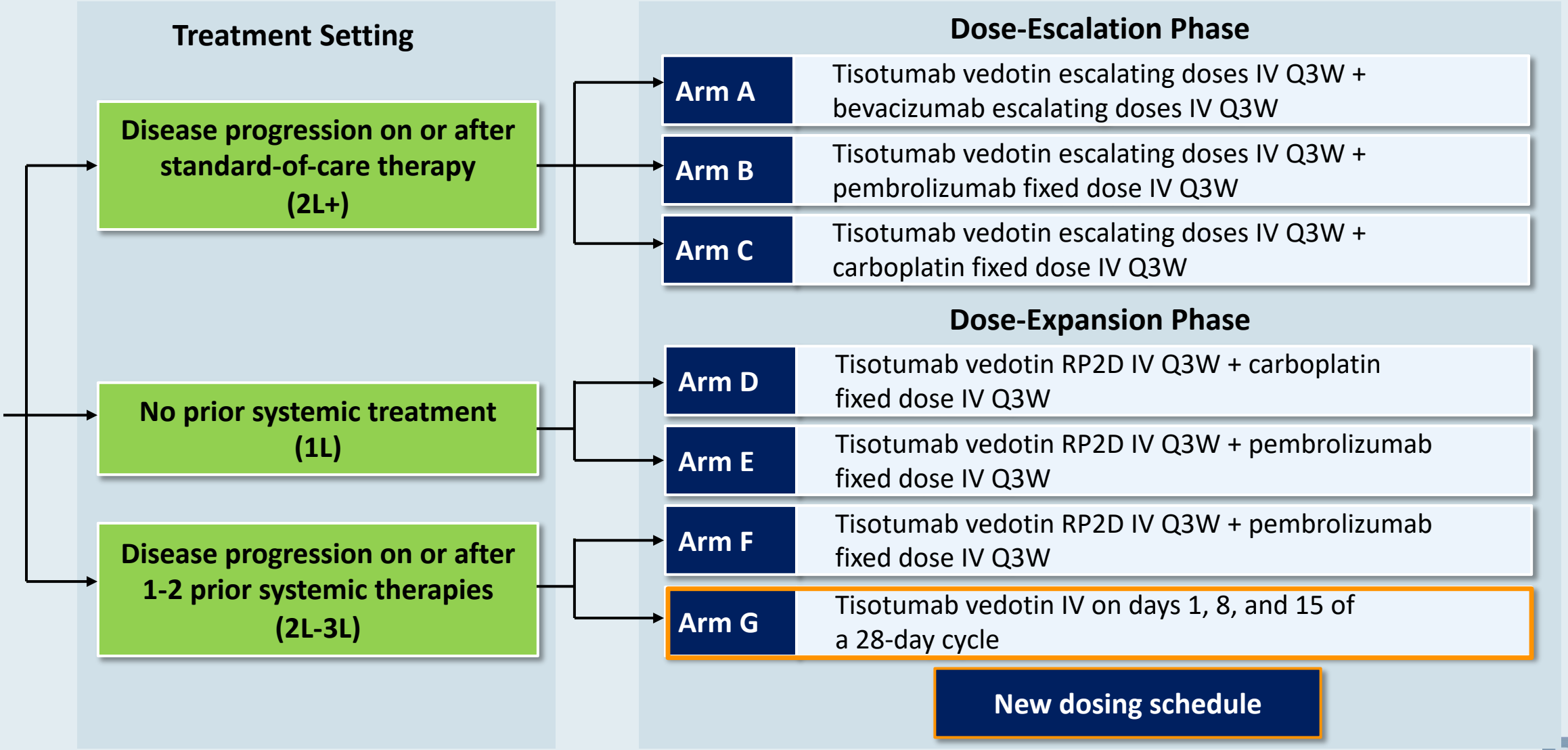
"Positive topline results [were announced] from the single-arm, phase 2 innovaTV 204 trial evaluating tisotumab vedotin administered every 3 weeks for the treatment of patients who have relapsed or progressed on or after prior treatment for recurrent or metastatic cervical cancer.

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

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

RTP RESEARCH TO PRACTICE

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



Courtesy of David M O'Malley, MD

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

A Meet The Professor Series

Monday, August 31, 2020
12:00 PM – 1:00 PM ET

Faculty
Joseph Mikhael, MD

Moderator
Neil Love, MD

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Thank you for joining us!

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

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