Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Gynecologic Cancers

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

Faculty

Krishnansu S Tewari, MD
Courtney Arn, CNP

Moderator

Neil Love, MD

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Faculty

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

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

Courtney Arn, CNP
The James Cancer Hospital and Solove Research Institute
The Ohio State University
Columbus, Ohio

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Eisai Inc, GlaxoSmithKline and Merck.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, Genentech, a member of the Roche Group, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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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 Tewari — Disclosures

Advisory Committee	AbbVie Inc, Amgen Inc, AstraZeneca Pharmaceuticals LP, Clovis Oncology, Eisai Inc, Genentech, a member of the Roche Group, Merck, Tesaro, A GSK Company
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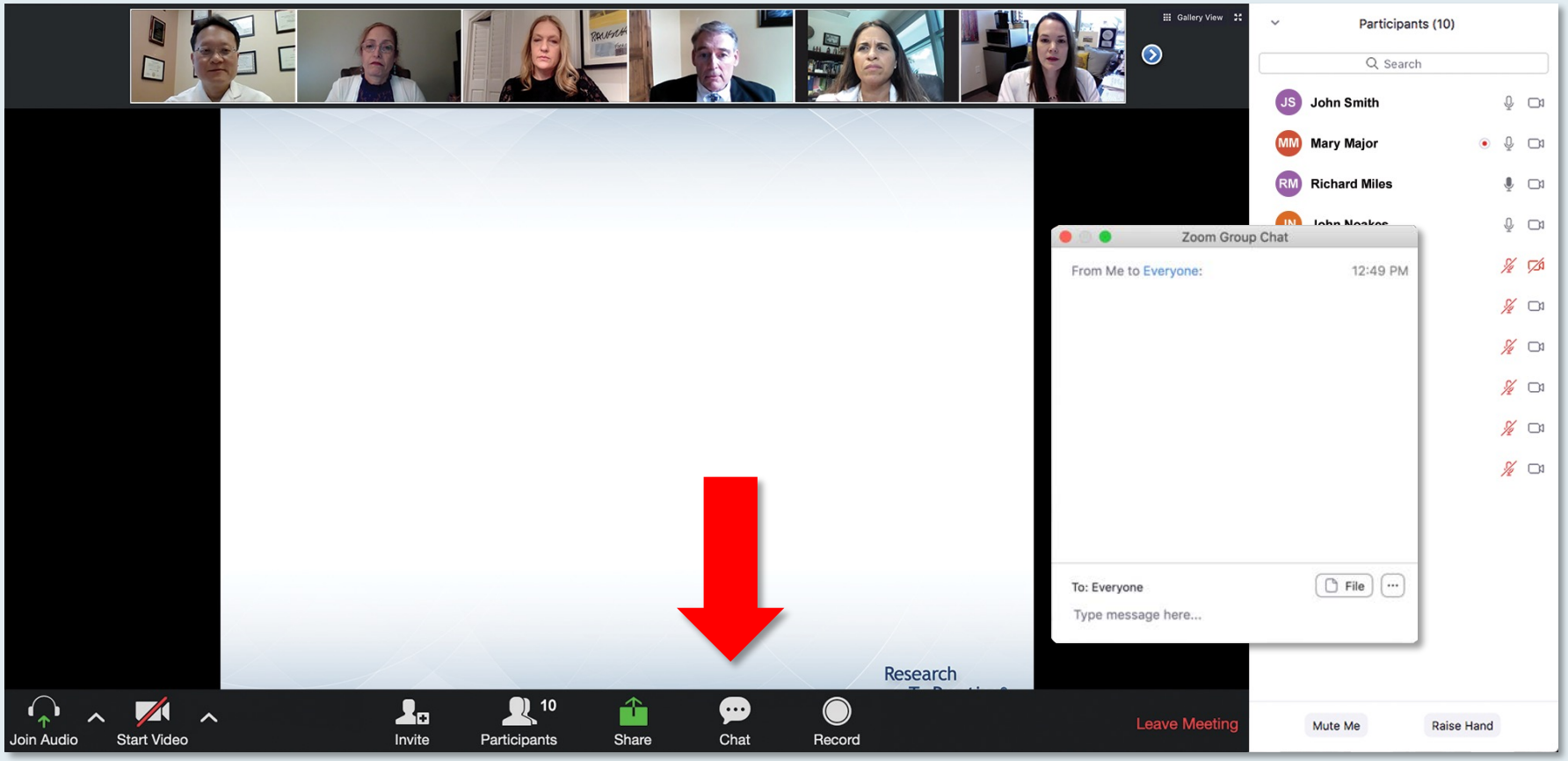
Speakers Bureau	AstraZeneca Pharmaceuticals LP, Clovis Oncology, Eisai Inc, Merck, Tesaro, A GSK Company

Ms Arn — Disclosures

No relevant conflicts of interest to disclose.

We Encourage Clinicians in Practice to Submit Questions



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

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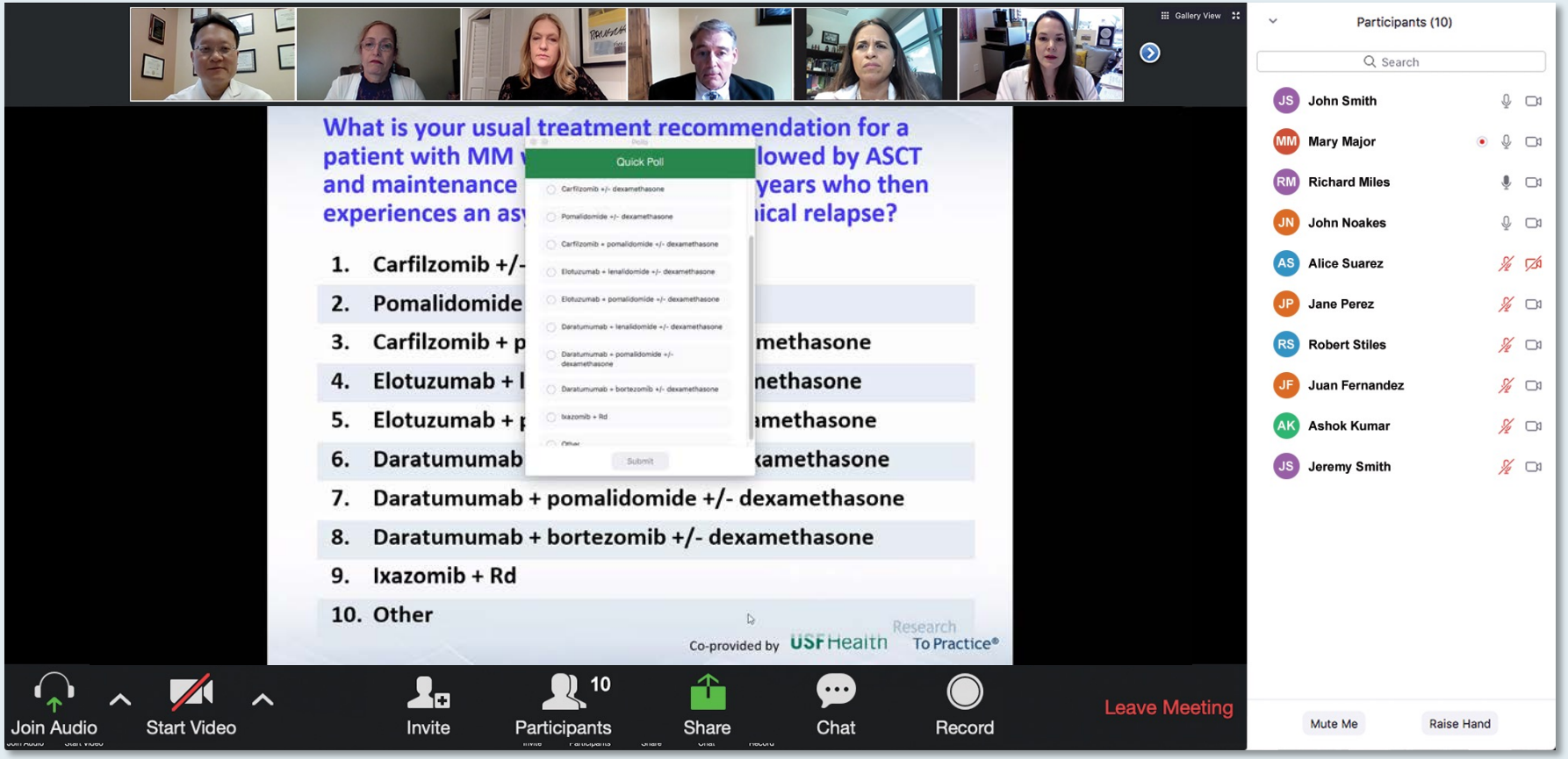
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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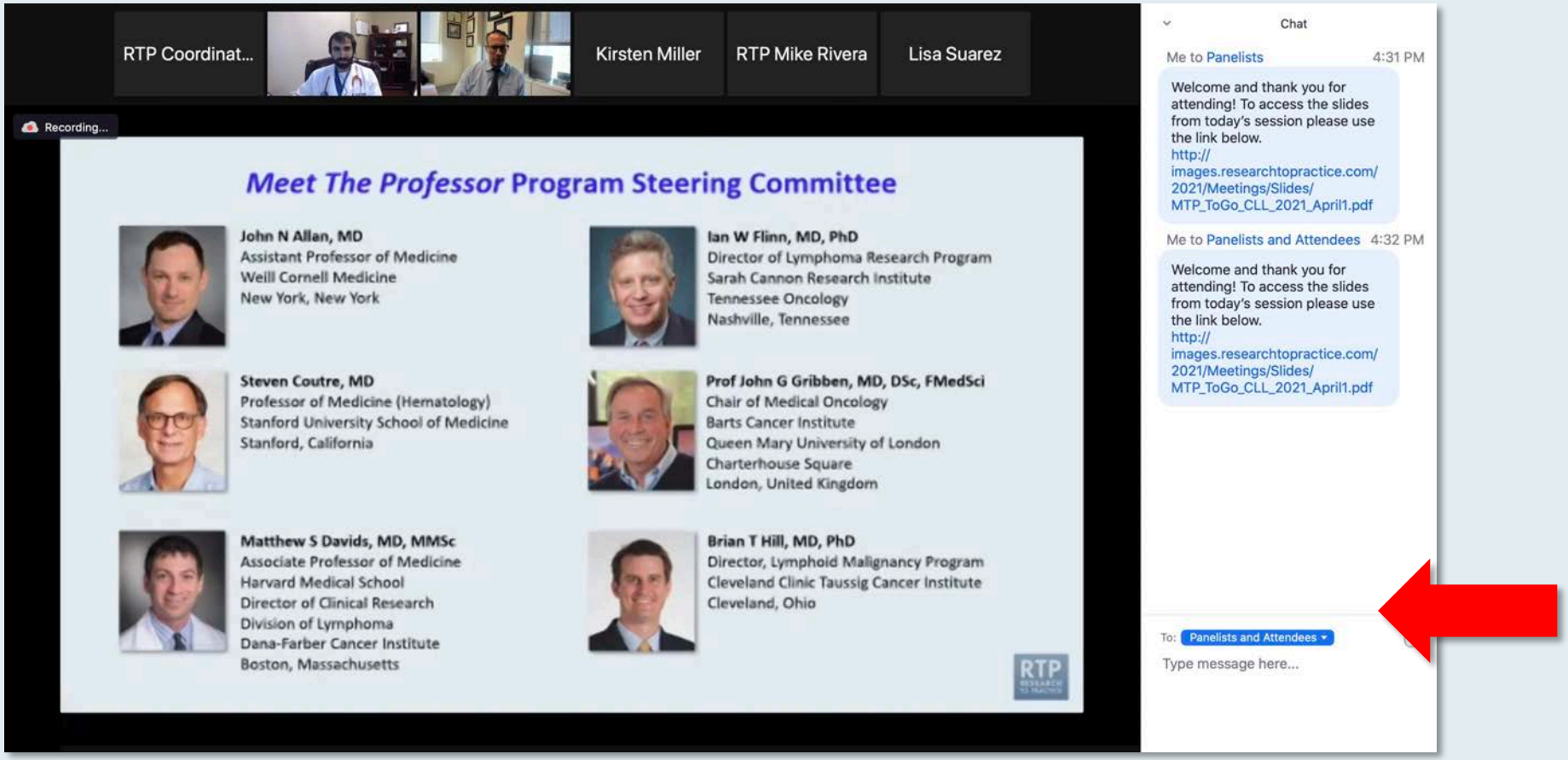
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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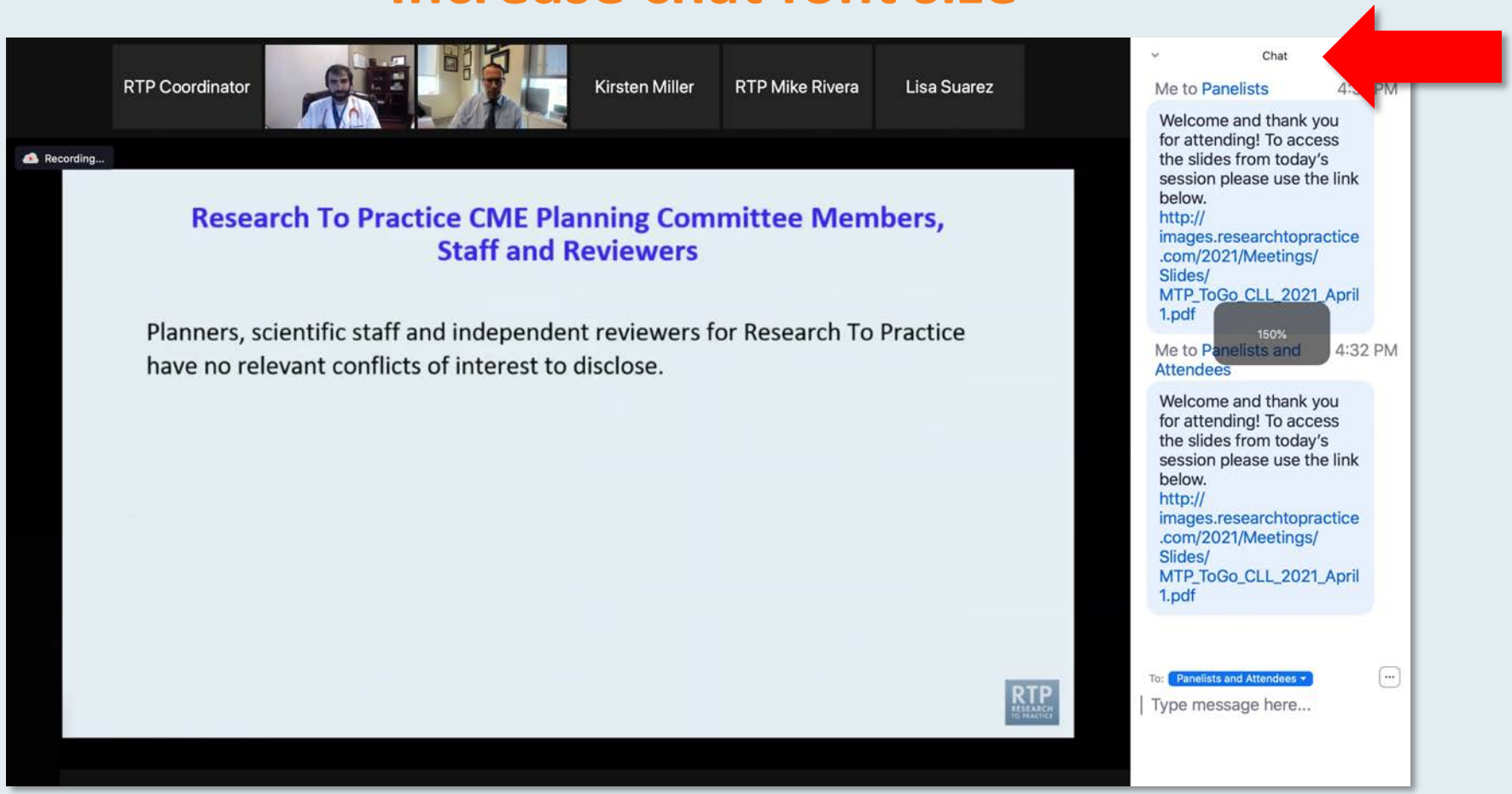
Familiarizing Yourself with the Zoom Interface

Increase chat font size



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

ONCOLOGY TODAY

WITH DR NEIL LOVE

PARP Inhibitors in Ovarian Cancer

DR ANTONIO GONZÁLEZ-MARTÍN
CLÍNICA UNIVERSIDAD DE NAVARRA

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

9 Exciting CME/MOC Events You Do Not Want to Miss

A Live Webinar Series Held in Conjunction with the 2021 ASCO Annual Meeting

Metastatic Castration-Resistant Prostate Cancer
Tuesday, July 20
5:00 PM – 6:00 PM ET

Bladder Cancer
Wednesday, July 21
5:00 PM – 6:00 PM ET

Endometrial and Cervical Cancers
Monday, July 26
5:00 PM – 6:00 PM ET

Targeted Therapy for Non-Small Cell Lung Cancer
Tuesday, July 27
5:00 PM – 6:00 PM ET

Immunotherapy and Other Nontargeted Approaches for Lung Cancer
Wednesday, July 28
5:00 PM – 6:00 PM ET

Mantle Cell, Diffuse Large B-Cell and Hodgkin Lymphoma
Monday, August 2
5:00 PM – 6:00 PM ET

Colorectal and Gastroesophageal Cancers
Tuesday, August 3
5:00 PM – 6:30 PM ET

Hepatocellular Carcinoma and Pancreatic Cancer
Wednesday, August 4
5:00 PM – 6:30 PM ET

Head and Neck Cancer
Wednesday, August 11
5:00 PM – 6:00 PM ET

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RESEARCH TO PRACTICE

Meet The Professor

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

Monday, July 19, 2021
5:00 PM – 6:00 PM ET

Faculty

Tanios Bekaii-Saab, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

A Conversation with the Investigators: Metastatic Castration-Resistant Prostate Cancer

Tuesday, July 20, 2021
5:00 PM – 6:00 PM ET

Faculty

Emmanuel S Antonarakis, MD
Johann de Bono, MBChB, MSc, PhD
Julie N Graff, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

A Conversation with the Investigators: Bladder Cancer

Wednesday, July 21, 2021
5:00 PM – 6:00 PM ET

Faculty

Petros Grivas, MD, PhD
Daniel P Petrylak, MD
Arlene Siefker-Radtke, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Thursday, July 22, 2021
5:00 PM – 6:00 PM ET

Faculty

David F McDermott, MD

Moderator

Neil Love, MD

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RESEARCH
TO PRACTICE

A Conversation with the Investigators: Endometrial and Cervical Cancers

Monday, July 26, 2021
5:00 PM – 6:00 PM ET

Faculty

Mansoor Raza Mirza, MD
David M O'Malley, MD
Angeles Alvarez Secord, MD, MHSc

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What General Medical Oncologists Want to Know About Targeted Therapy for Non-Small Cell Lung Cancer

Tuesday, July 27, 2021
5:00 PM – 6:00 PM ET

Faculty

Professor Solange Peters, MD, PhD
Zofia Piotrowska, MD, MHS
Gregory J Riely, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

What General Medical Oncologists Want to Know About Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Wednesday, July 28, 2021
5:00 PM – 6:00 PM ET

Faculty

Mark Awad, MD, PhD
David R Spigel, MD
Heather Wakelee, MD

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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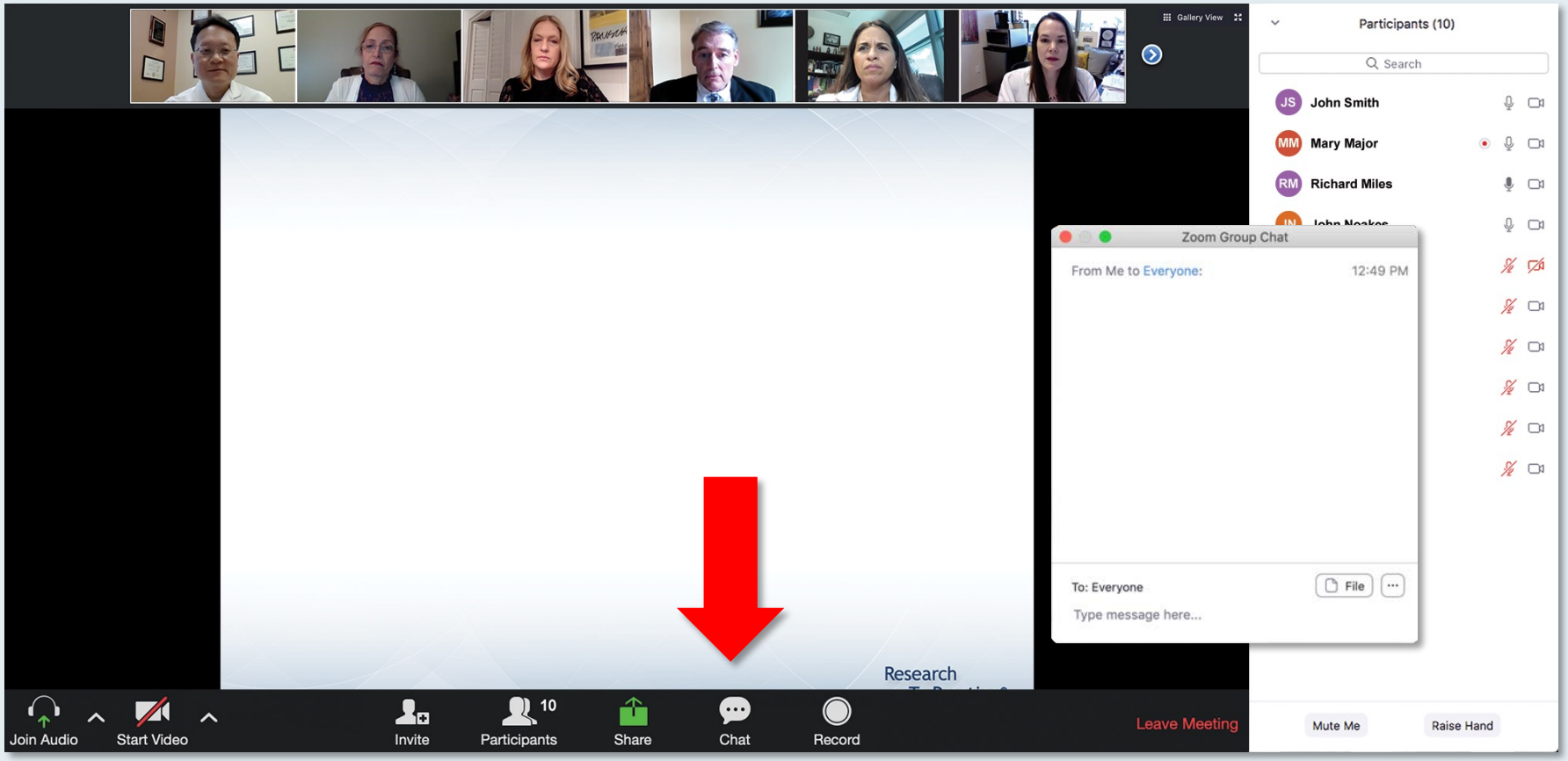

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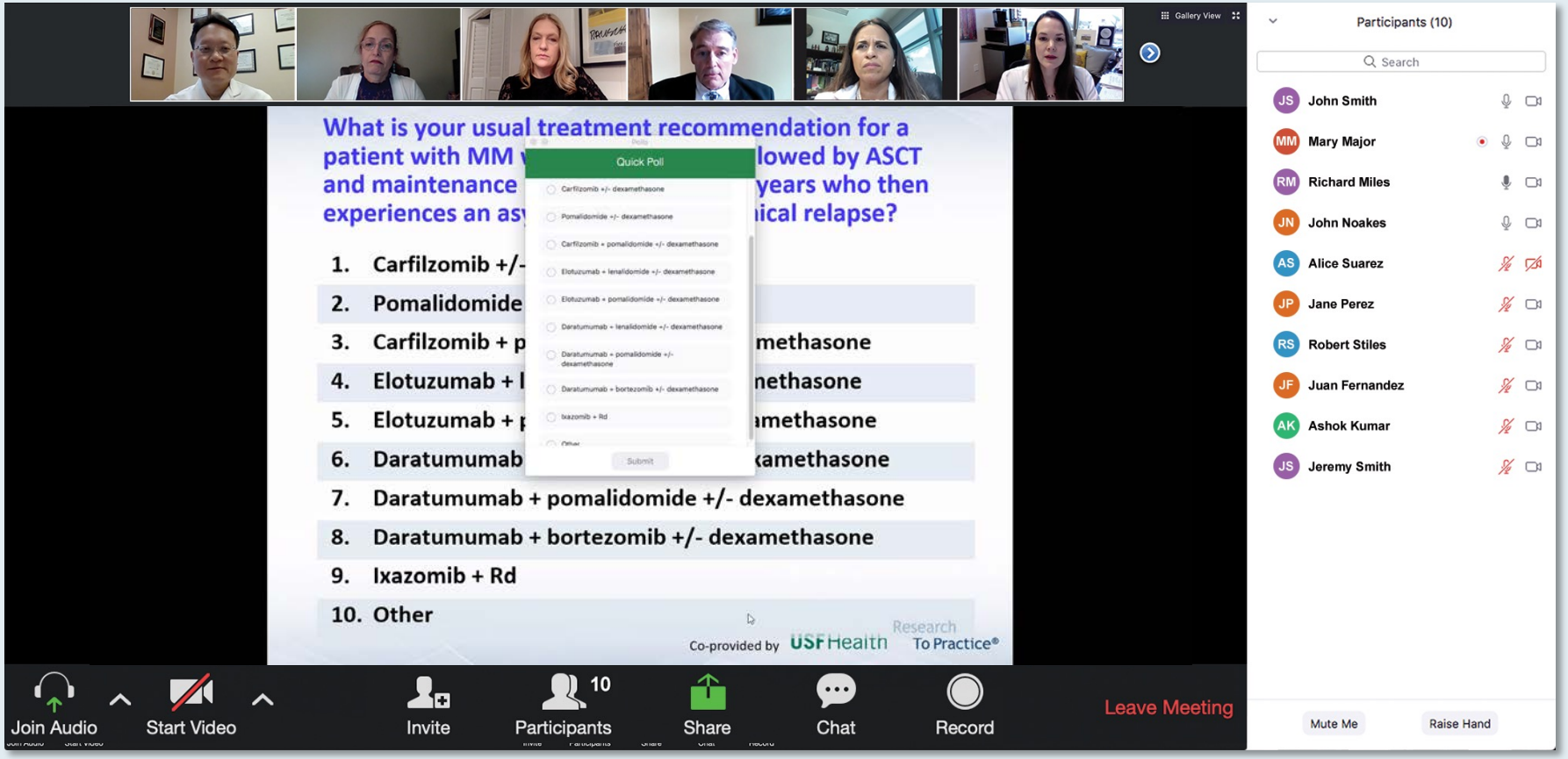

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Oncology Grand Rounds Nursing Webinar Series

Monday	Tuesday	Wednesday	Thursday	Friday
19	20 Breast Ca 8:30 AM Lung Ca 5:00 PM	21 AML 12:00 PM CRC and GE Ca 4:45 PM	22 Prostate Ca 8:30 AM Lymphomas 5:00 PM	23
26	27 Multiple Myeloma 8:30 AM Gynecologic Ca 5:00 PM	28 Bladder Ca 12:00 PM	29 CLL 8:30 AM CAR-T 5:00 PM	30

RTP RESEARCH TO PRACTICE

13th Annual Oncology Grand Rounds

A Complimentary NCPD Live Webinar Series
Held During the 46th Annual ONS Congress

Gynecologic Cancers

Tuesday, April 27, 2021
5:00 PM – 6:30 PM ET

Medical Oncologists

Robert L Coleman, MD
Thomas J Herzog, MD
Krishnansu S Tewari, MD

Oncology Nurse Practitioners

Paula J Anastasia, MN, RN, AOCN
Courtney Arn, CNP
Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC

Moderator

Neil Love, MD

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Paula J Anastasia, NP MN AOCN


Courtney R Arn, APRN-CNP


Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Agenda

Module 1: Ovarian Cancer

- Case 1: A 51-year-old woman with Stage IIIC ovarian cancer and a germline BRCA1 mutation
- Case 2: A 72-year-old woman with Stage IIIC HRD-positive ovarian cancer

Module 2: Endometrial Cancer

- Case 3: An 81-year-old woman with recurrent endometrial cancer, MMR proficient
- Case 4: A 55-year-old woman with recurrent endometrial cancer, MSI-High

Module 3: Cervical Cancer – Relapsed Disease

- Case 5: A 58-year-old woman with recurrent cervical cancer, PD-L1-positive
- Case 6: A 37-year-old woman with recurrent cervical cancer, PD-L1-negative

Agenda

Module 1: Ovarian Cancer

- Case 1: A 51-year-old woman with Stage IIIC ovarian cancer and a germline BRCA1 mutation
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- Case 4: A 55-year-old woman with recurrent endometrial cancer, MSI-High

Module 3: Cervical Cancer – Relapsed Disease

- Case 5: A 58-year-old woman with recurrent cervical cancer, PD-L1-positive
- Case 6: A 37-year-old woman with recurrent cervical cancer, PD-L1-negative

At a minimum, all patients with ovarian cancer should have the following assay(s) conducted at diagnosis regardless of family history of cancer.

1. BRCA germline testing
2. BRCA somatic testing
3. Multiplex germline testing
4. Multiplex somatic testing
5. Both 1 and 2
6. Both 3 and 4
7. I don’t know

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Bevacizumab can be particularly effective in patients with ovarian cancer who have ascites and/or pleural effusion…

1. Agree
2. Disagree
3. I don’t know

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In general, postoperative, postchemotherapy primary maintenance therapy with a PARP inhibitor is considered standard for patients with a germline or somatic BRCA mutation.

1. Agree
2. Disagree
3. I don’t know

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What was the duration of treatment with olaparib and niraparib in the Phase III trials evaluating maintenance therapy with PARP inhibitors after debulking surgery and first-line platinum-based chemotherapy?

1. 2 years for both
2. 3 years for both
3. 2 years for olaparib, 3 years for niraparib
4. 2 years for niraparib, 3 years for olaparib
5. I don’t know

Which of the following PARP inhibitors is approved to treat recurrent ovarian cancer?

1. Olaparib
2. Niraparib
3. Rucaparib
4. All of the above
5. I don’t know

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Case Presentation – Ms Arn: A 51-year-old woman with Stage IIIC ovarian cancer and a germline BRCA1 mutation

- Married social worker and mother of a 9-year-old son is diagnosed with high-grade adenocarcinoma of the ovary
- Neoadjuvant carboplatin/paclitaxel x 4 cycles → interval tumor reduction surgery → carboplatin/paclitaxel x 3 cycles
- Maintenance olaparib
- Risk of MDS and/or AML associated with PARP inhibitors

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Case Presentation – Ms Arn: A 72-year-old woman with Stage IIIC HRD-positive ovarian cancer

- 11/2019: Stage IIIC ovarian cancer s/p TAH/BSO with complete miscroscopic resection
- HRD-positive
- Carboplatin/paclitaxel/bevacizumab x 6
- Maintenance olaparib/bevacizumab x 1 year
- Disease progression → entering a clinical trial

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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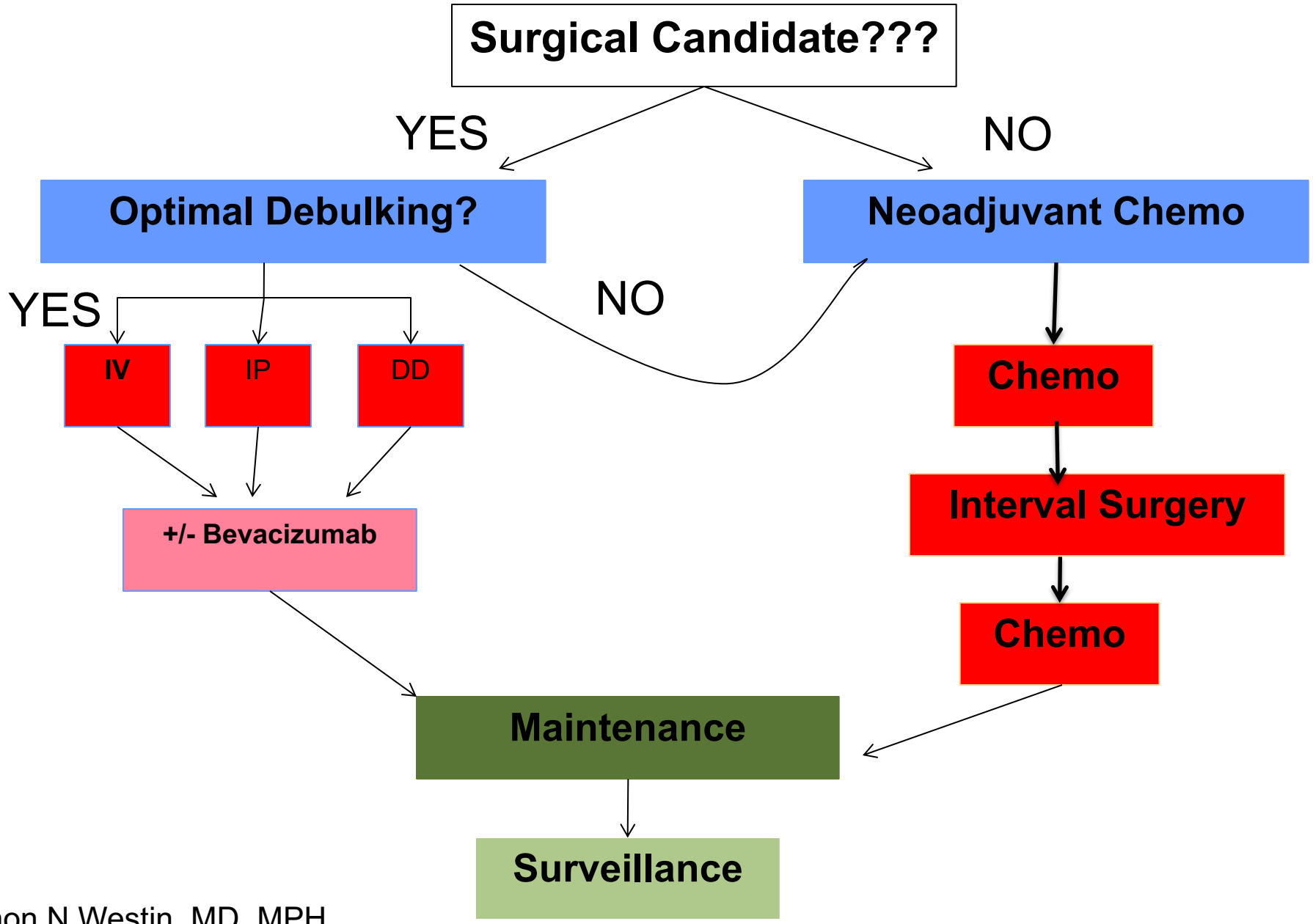
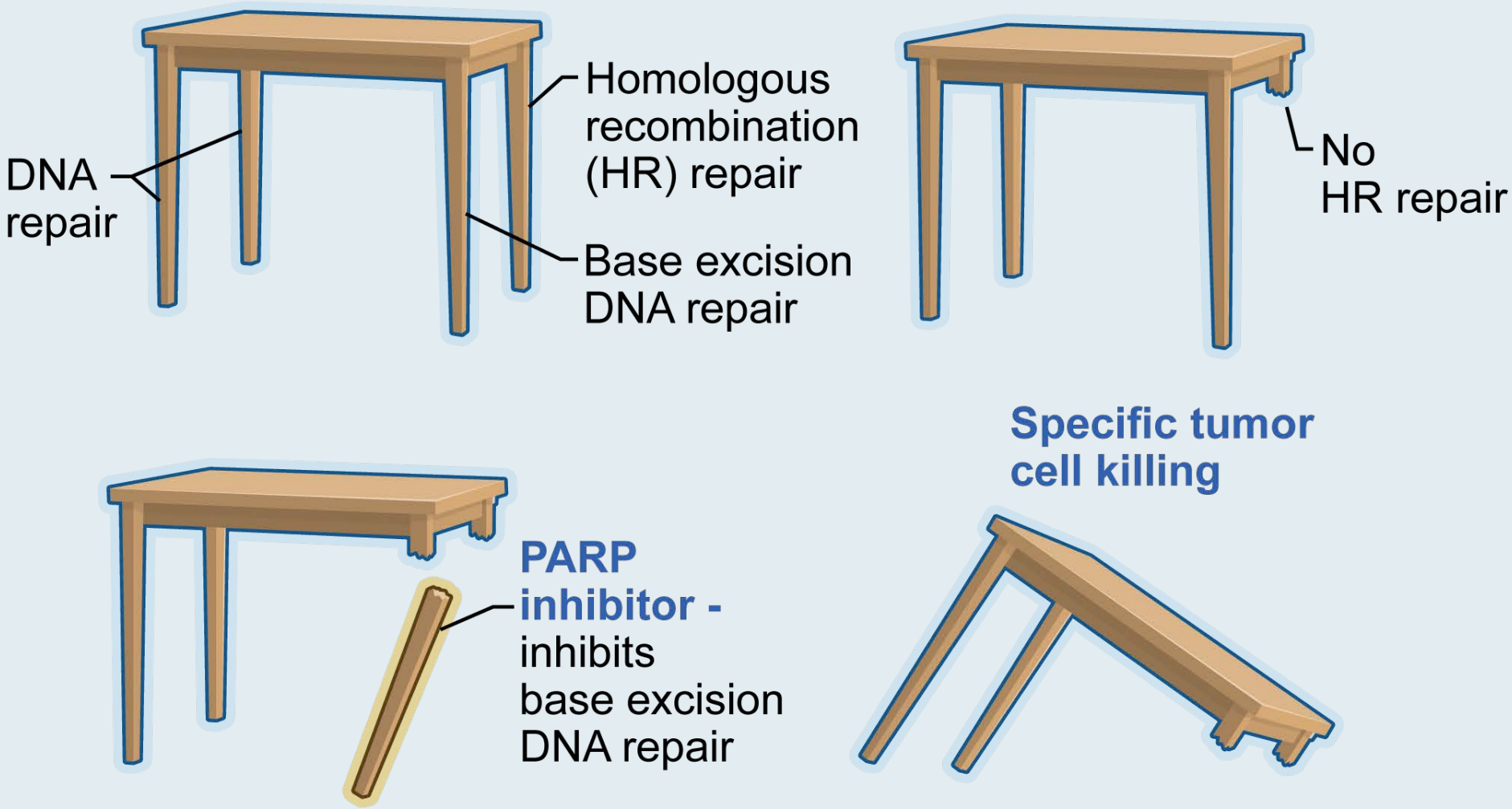
New Advanced Ovarian Cancer



Courtesy, Shannon N Westin, MD, MPH

Mechanism of Cell Death from Synthetic Lethality Induced by PARP Inhibition



Courtesy of Jenny C Chang, MD

Current FDA-Approved and Investigational PARP Inhibitors: Differences

PARP inhibitor	FDA approvals	PARP trapping potency	PARPi target selectivity (strength of binding)	Dose
Olaparib	Ovarian, breast, pancreatic, prostate	1	Potent PARP1 inhibitor, less selective	300 mg BID
Rucaparib	Ovarian, prostate	1	Potent PARP1 inhibitor, less selective	600 mg BID
Niraparib	Ovarian	~2	Selective inhibitor of PARP1 and 2	300 mg qd
Veliparib	None	<0.2	Potent PARP1 inhibitor, less selective	400 mg BID
Talazoparib	Breast	~100	Potent PARP1 inhibitor, less selective	1 mg qd

Lim JSJ, Tan DSP. *Cancers* 2017;9(8):pii:E109.

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Phase III First-Line PARPi Maintenance Trials

Study Design	SOLO-1 (N=451)	PAOLA-1 (N=612)	PRIMA (N=620)	VELIA (N=1140)
Treatment arms vs placebo	**Olaparib (n=260)**	**Bevacizumab ± Olaparib**	**Niraparib**	**Veliparib**
Patient Population	*BRCA* mutation	All comers	All comers	*All comers*
Treatment Duration	24 months	15 months for Bev 24 months for Olaparib	36 months or until PD	24 months

Burger RA, *N Engl J Med* 2011; Norquist B *Clin Cancer Res* 2018*; Bevacizumab* prescribing information; Moore K, NEJM 2018; Gonzalez-Martin NEJM 2019; Ray-Coquard NEJM 2019; Coleman NEJM 2019

Courtesy of Shannon N Westin, MD, MPH

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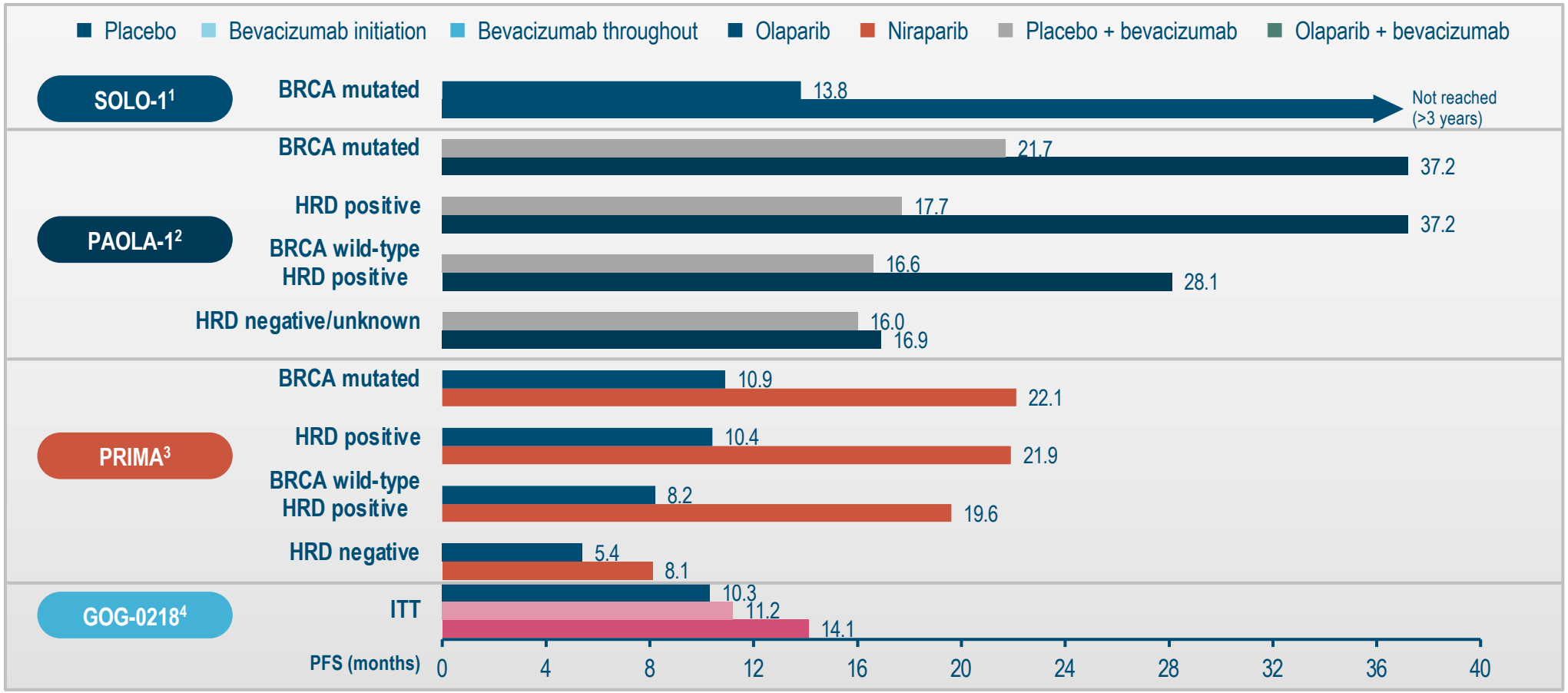
SUMMARY OF APPROVED MAINTENANCE STUDIES IN THE FIRST-LINE



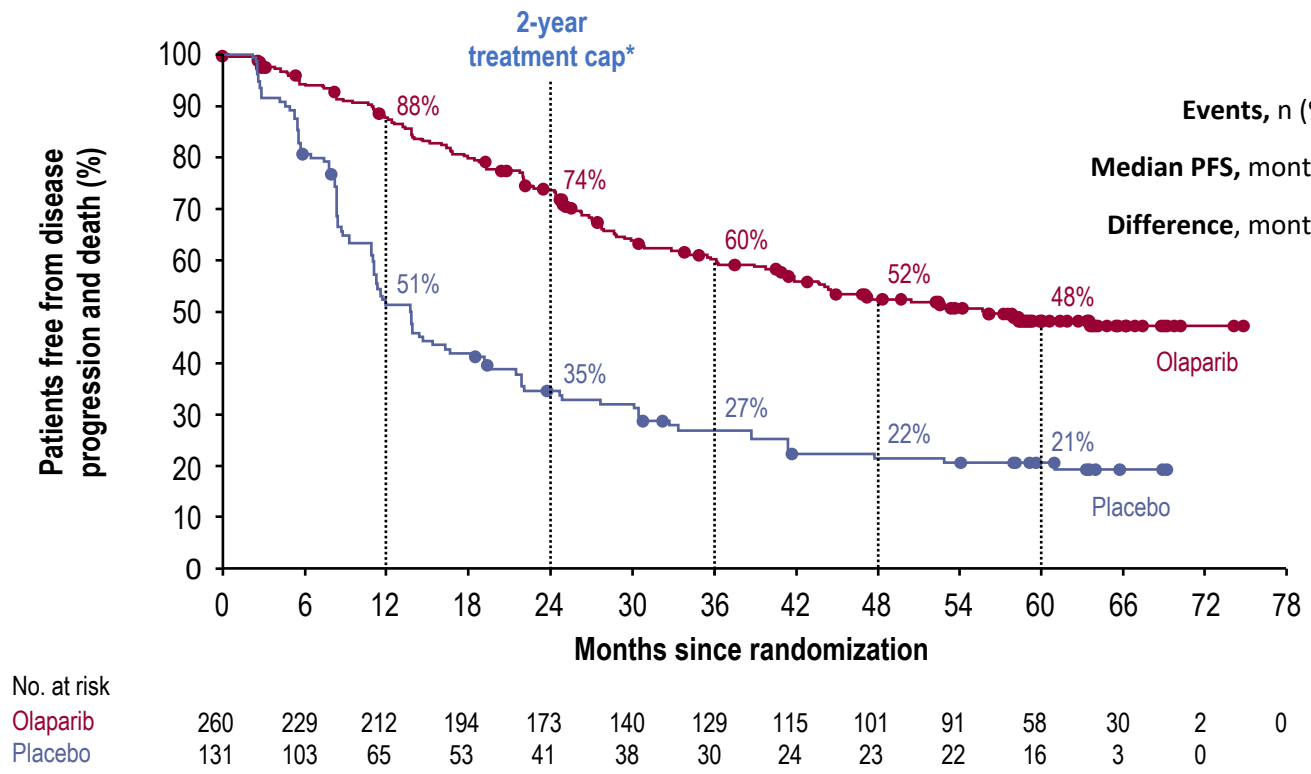
Comparisons across trials should not be made as trials were not head-to-head.

BRCA, breast cancer gene; HRD, homologous recombination deficiency; ITT, intent-to-treat; PFS, progression-free survival

1. Moore K, et al. N Engl J Med 2018;379:2495–2505; 2. Ray-Coquard IL, et al. N Engl J Med 2019; 381:2416–2428; 3. Gonzalez-Martin A, et al. N Engl J Med 2019;381:2391–2402; 4. Burger RA, et al. N Engl J Med 2011;365:2473–2483

Courtesy of Robert L Coleman, MD

Phase 3 SOLO1: PFS at 5 Years of Follow-Up



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	118 (45)	100 (76)
Median PFS, months	**56.0**	**13.8**
Difference, months	42.2	
HR 0.33 (95% CI 0.25–0.43)		

Median treatment duration:
Olaparib, 24.6 months
Placebo†, 13.9 months

*13 patients, all in the olaparib arm, continued study treatment past 2 years; †n=130 (safety analysis set)
Investigator-assessed by modified RECIST v1.1. DCO: 5 March 2020

Median follow-up for PFS: olaparib, 4.8 y; placebo, 5.0 years.

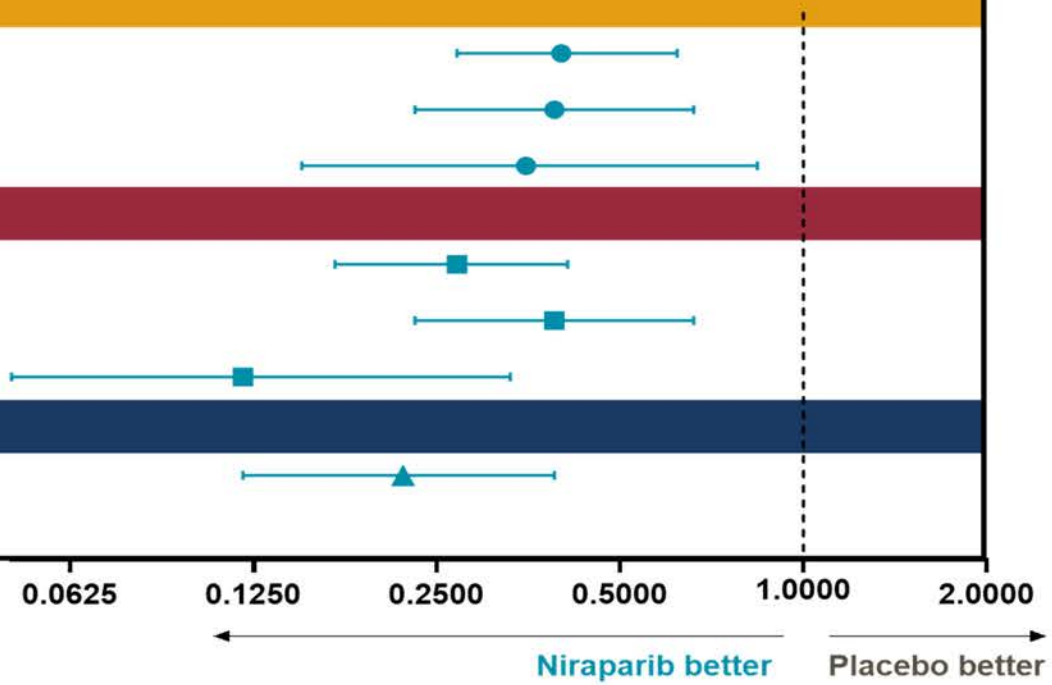
Banerjee S, et al. ESMO 2020.

Courtesy of Michael J Birrer, MD, PhD

ASCO 2021 UPDATE - PRIMA

Progression-Free Survival in Patients with *BRCA*m Ovarian Cancer

	Niraparib		Placebo		Hazard ratio for PFS (95% CI)
	n/N	mPFS, mo	n/N	mPFS, mo	
PRIMA (1L maintenance)					
*BRCA*m	49/152	22.1	40/71	10.9	0.40 (0.27–0.62)
BRCA1	40/105	19.6	26/43	8.4	0.39 (0.23–0.66)
BRCA2	9/47	NE	14/28	13.6	0.35 (0.15–0.84)
NOVA (2L maintenance)					
g*BRCA*m	59/138	21.0	44/65	5.5	0.27 (0.17–0.41)
BRCA1	41/84	12.9	27/43	5.8	0.39 (0.23–0.66)
BRCA2	16/50	NE	13/18	5.4	0.12 (0.05–0.33)
NORA[1] (2L maintenance)					
g*BRCA*m[a]	24/65	NE	28/35	5.5	0.22 (0.12–0.39)



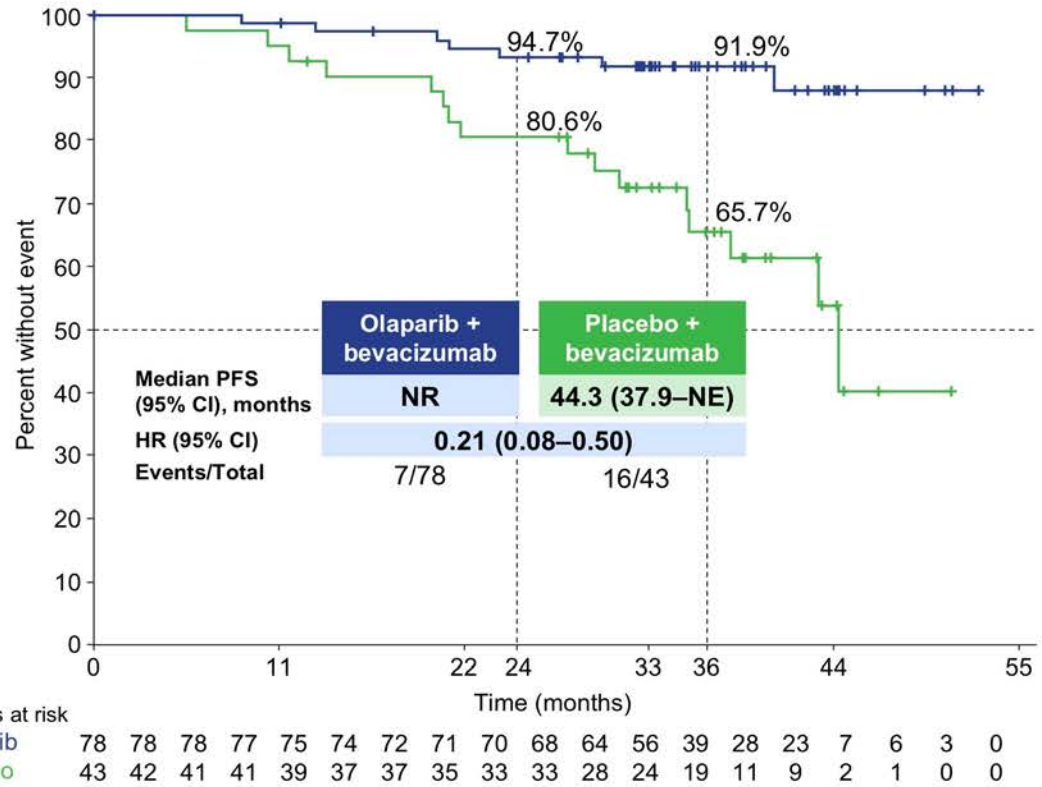
PFS was measured by blinded independent central review. Horizontal lines represent 95% CIs.
[a]*BRCA1* and *BRCA2* data are not currently available.
1L, first-line; 2L, second-line; g, germline; m, mutated; mPFS, median progression-free survival; NE, not estimable; PFS, progression-free survival.
[1]Wu XH, et al. *Ann Oncol* 2021;32(4):512–521.

Courtesy of Michael J Birrer, MD, PhD

ASCO 2021 UPDATE – PAOLA-1

PFS2 by FIGO stage and surgical outcome in patients with HRD-positive tumors

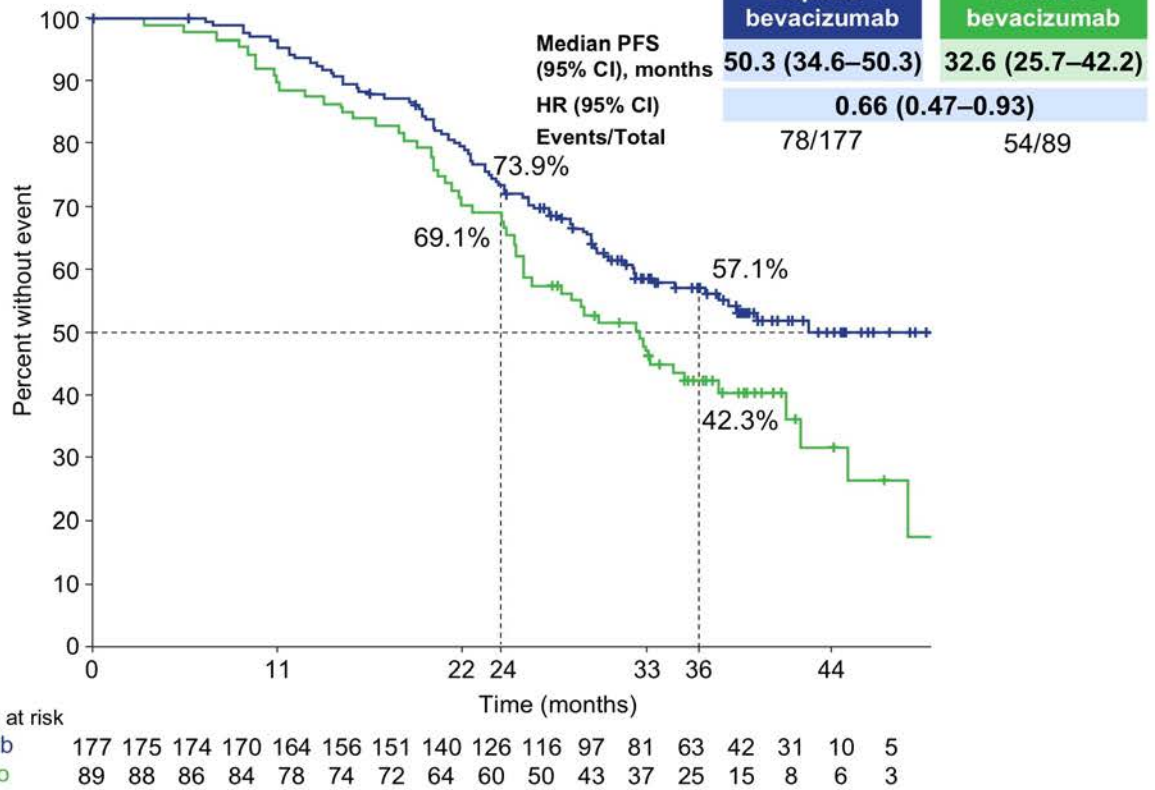
Lower risk*



Patients at risk

Olaparib	78	78	78	77	75	74	72	71	70	68	64	56	39	28	23	7	6	3	0
Placebo	43	42	41	41	39	37	37	35	33	33	28	24	19	11	9	2	1	0	0

Higher risk†



Patients at risk

Olaparib	177	175	174	170	164	156	151	140	126	116	97	81	63	42	31	10	5		
Placebo	89	88	86	84	78	74	72	64	60	50	43	37	25	15	8	6	3		

The median time from the first cycle of chemotherapy to randomization was 7 months. *Patients with HRD-positive tumors who had stage III disease and complete resection following upfront surgery (median follow-up overall: 37.0 months); †Stage III patients with residual disease after upfront surgery or who received neoadjuvant chemotherapy, or HRD-positive stage IV patients (median follow-up overall: 37.5 months).
NR, not reached; PFS2, second progression-free survival.

Courtesy of Michael J Birrer, MD, PhD

Tolerability of PARP Inhibitors

- Fatigue: usually plateaus after two weeks
- Nausea: may require daily anti-emetics – have used transdermal patch in a few patients
- Hematologic: monitor monthly, may consider weekly for 1st month. Hold dose for grade 2 hematologic events, Reduce dose in half if dose delay
- AML/MDS: refer patient to hematologist if blood counts do not return within 4 weeks. 2% study subjects were diagnosed

Courtesy of Paula J Anastasia, MN, RN, AOCN

SOLO-1 Trial 5-Year Update: Safety Profile

n (%)	Olaparib (n=260)	Placebo (n=130)
Any AE	256 (98)	120 (92)
Grade ≥3 AE	103 (40)	25 (19)
Serious AE	55 (21)	17 (13)
AE leading to dose interruption	136 (52)	22 (17)
AE leading to dose reduction	75 (29)	4 (3)
AE leading to treatment discontinuation	30 (12)	4 (3)
MDS/AML	3 (1)	0 (0)
New primary malignancy	7 (3)	5 (4)

No additional cases of MDS/AML reported; incidence remained <1.5%

Follow-up for MDS/AML continued until death due to any cause

Banerjee S et al. ESMO 2020;Abstract 811MO.

Dose Adjustments for Adverse Events

Olaparib dose reductions	Dose (tablet)
Starting dose	300 mg BID
First dose reduction	250 mg BID
Second dose reduction	200 mg BID

Niraparib dose reductions	Dose
Starting dose	300 mg daily
First dose reduction	200 mg daily
Second dose reduction	100 mg daily

Rucaparib dose reductions	Dose
Starting dose	600 mg twice daily
First dose reduction	500 mg twice daily
Second dose reduction	400 mg twice daily
Third dose reduction	300 mg twice daily

Courtesy, Shannon N Westin, MD, MPH

FDA Prescribing Information.

Agenda

Module 1: Ovarian Cancer

- Case 1: A 51-year-old woman with Stage IIIC ovarian cancer and a germline BRCA1 mutation
- Case 2: A 72-year-old woman with Stage IIIC HRD-positive ovarian cancer

Module 2: Endometrial Cancer

- Case 3: An 81-year-old woman with recurrent endometrial cancer, MMR proficient
- Case 4: A 55-year-old woman with recurrent endometrial cancer, MSI-High

Module 3: Cervical Cancer – Relapsed Disease

- Case 5: A 58-year-old woman with recurrent cervical cancer, PD-L1-positive
- Case 6: A 37-year-old woman with recurrent cervical cancer, PD-L1-negative

Checkpoint inhibitors are approved for and commonly used in cervical and endometrial cancer but not ovarian cancer.

1. Agree
2. Disagree
3. I don’t know

RTP
RESEARCH
TO PRACTICE

Case Presentation – Ms Arn: An 81-year-old woman with recurrent endometrial cancer, MMR proficient

- Divorced older woman s/p hysterectomy and adjuvant chemotherapy for Stage IA endometrial cancer experiences metastatic recurrence
- Lenvatinib/pembrolizumab
- Supportive care for patients and their ability to maintain independence

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

RTP
RESEARCH
TO PRACTICE

Case Presentation – Ms Arn: A 55-year-old woman with recurrent endometrial cancer, MSI-High

- A wife and nurse, without any children, who enjoys traveling
- 2014: Stage IVB, grade 1 adenocarcinoma of the endometrium s/p robotic hysterectomy/BOS with PPALN and extensive lymph node debulking
- Carboplatin/paclitaxel x 6, EBRT, VcBT, with complete response
- 4/2020 CT: Lesion in the spleen → Splenectomy and splenic colon flexure mobilization
  - Pathology c/w metastatic well-differentiated adenocarcinoma, MSI-High
- Pembrolizumab 200 mg q3 weeks

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

RTP
RESEARCH
TO PRACTICE

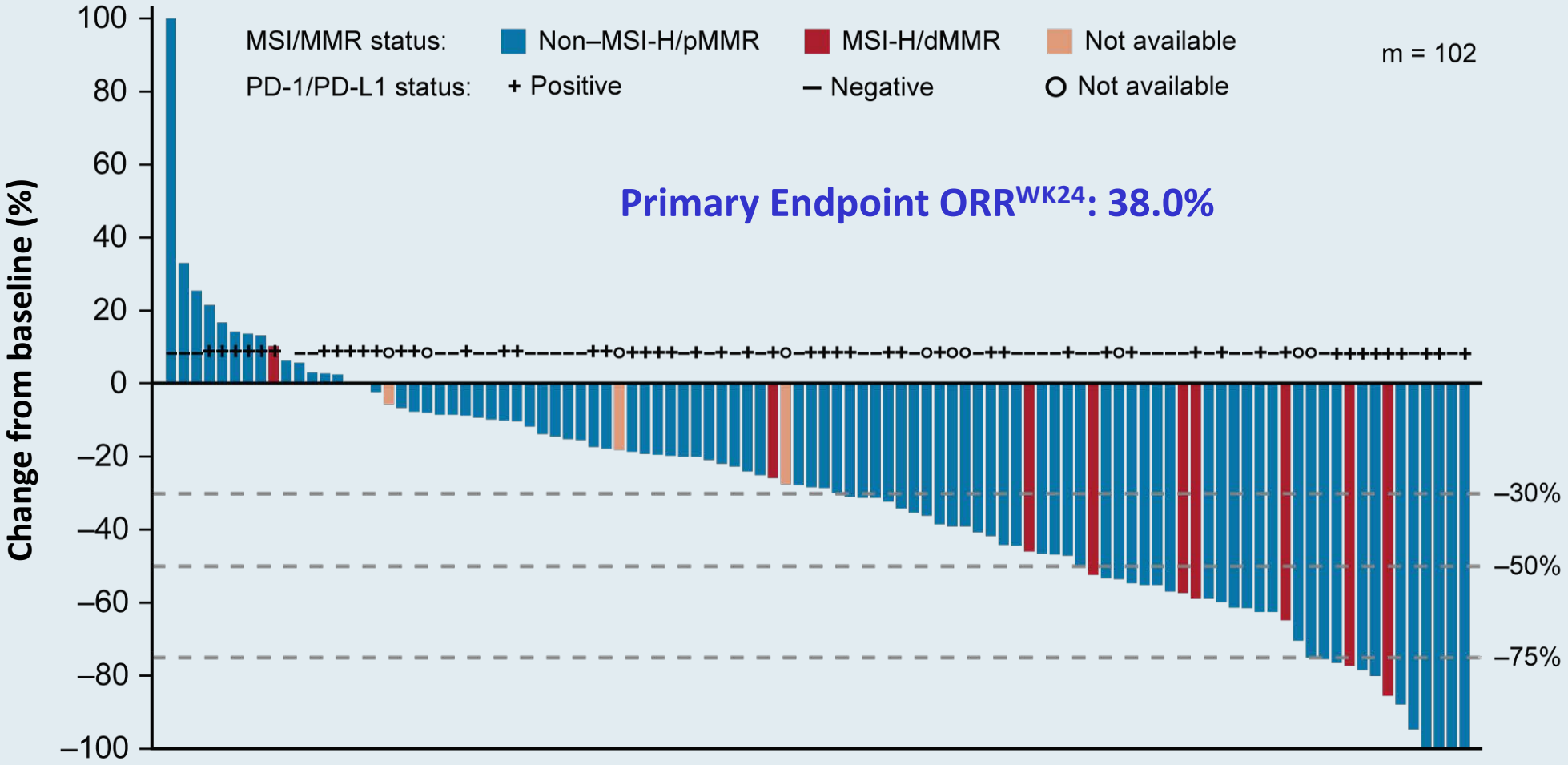
original reports

Lenvatinib Plus Pembrolizumab in Patients With Advanced Endometrial Cancer

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

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

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



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

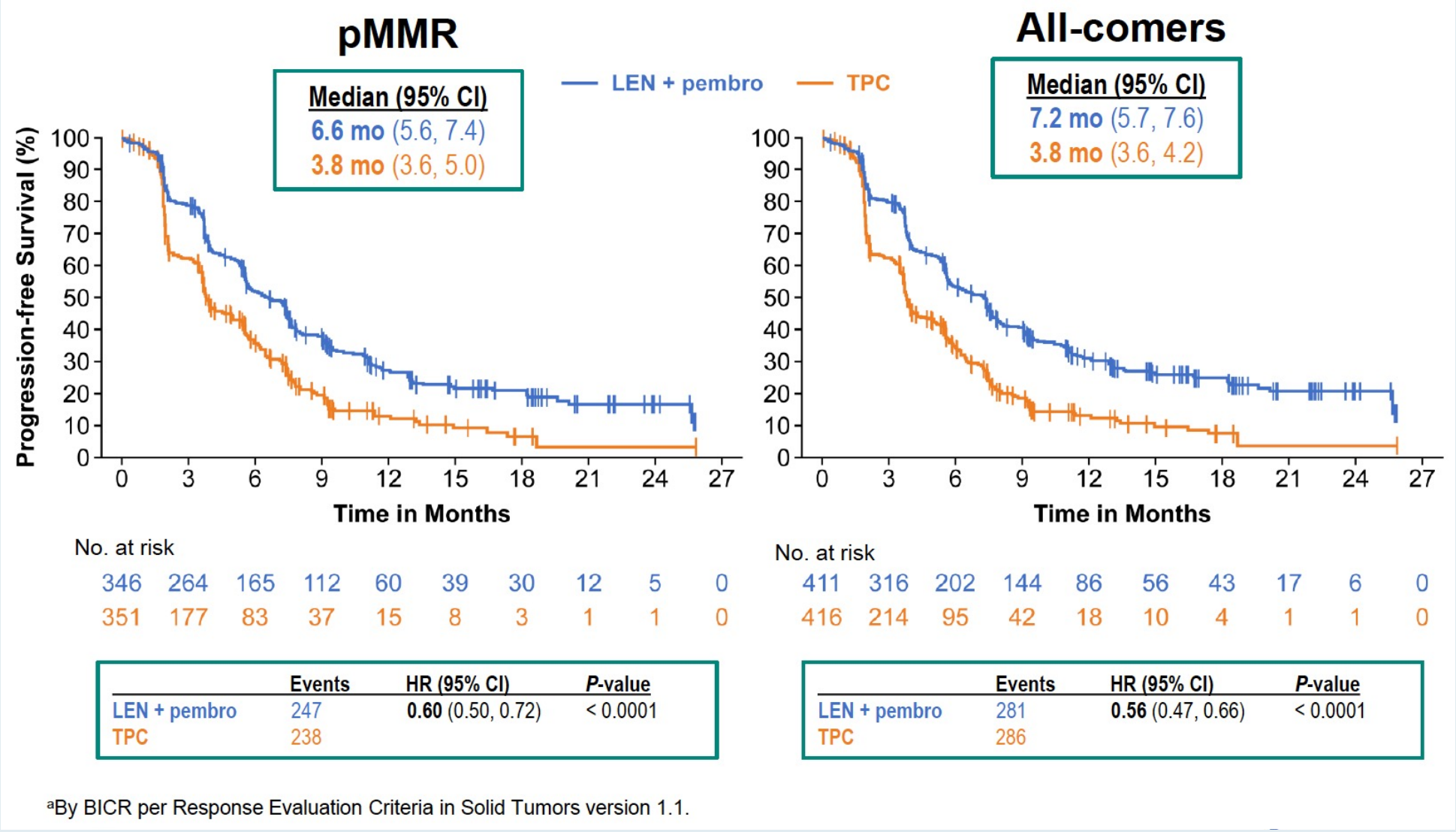
RTP RESEARCH TO PRACTICE

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

Makker V et al.

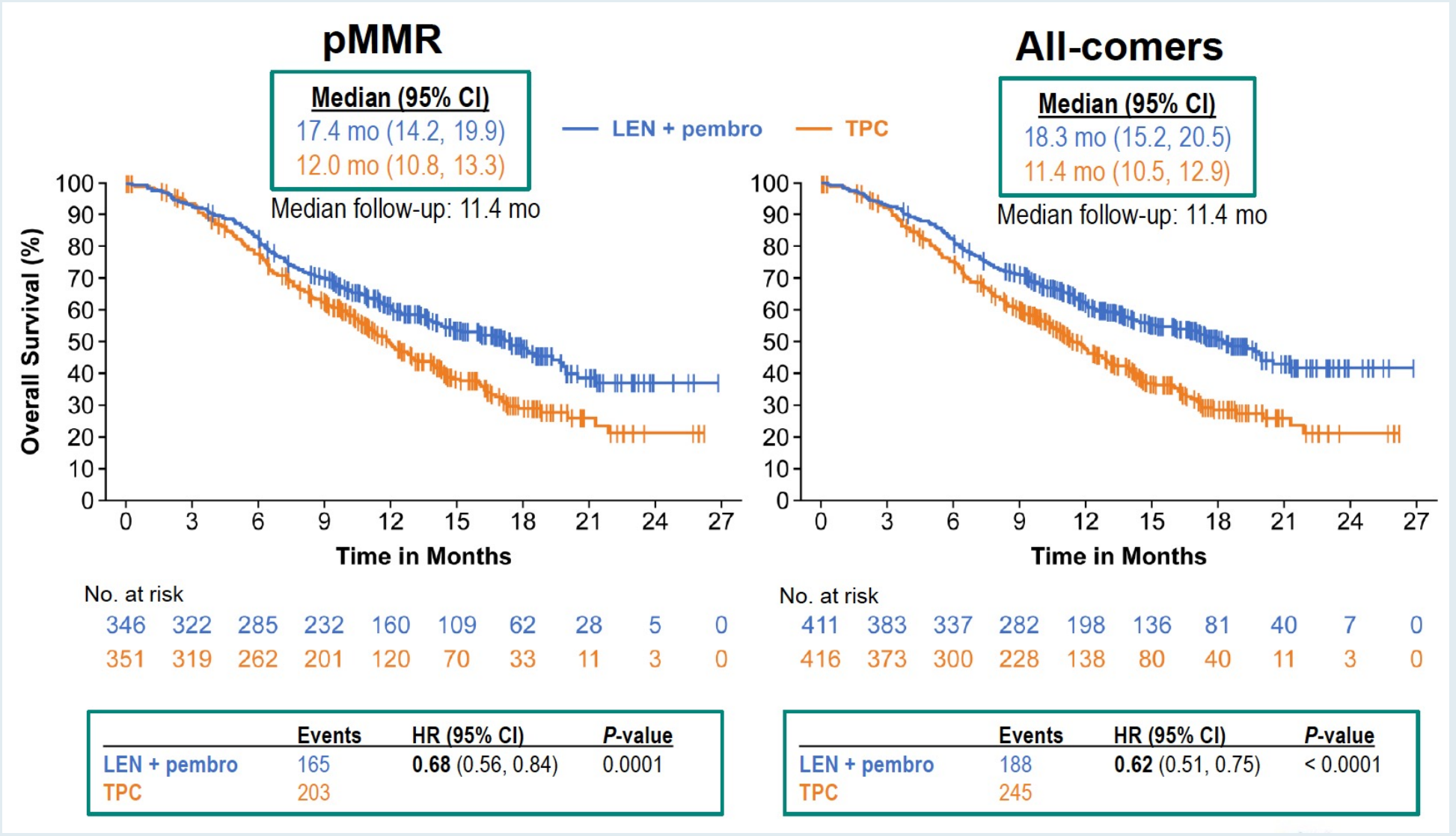
SGO 2021;Abstract 11512.

Study 309/KEYNOTE-775: Progression-Free Survival



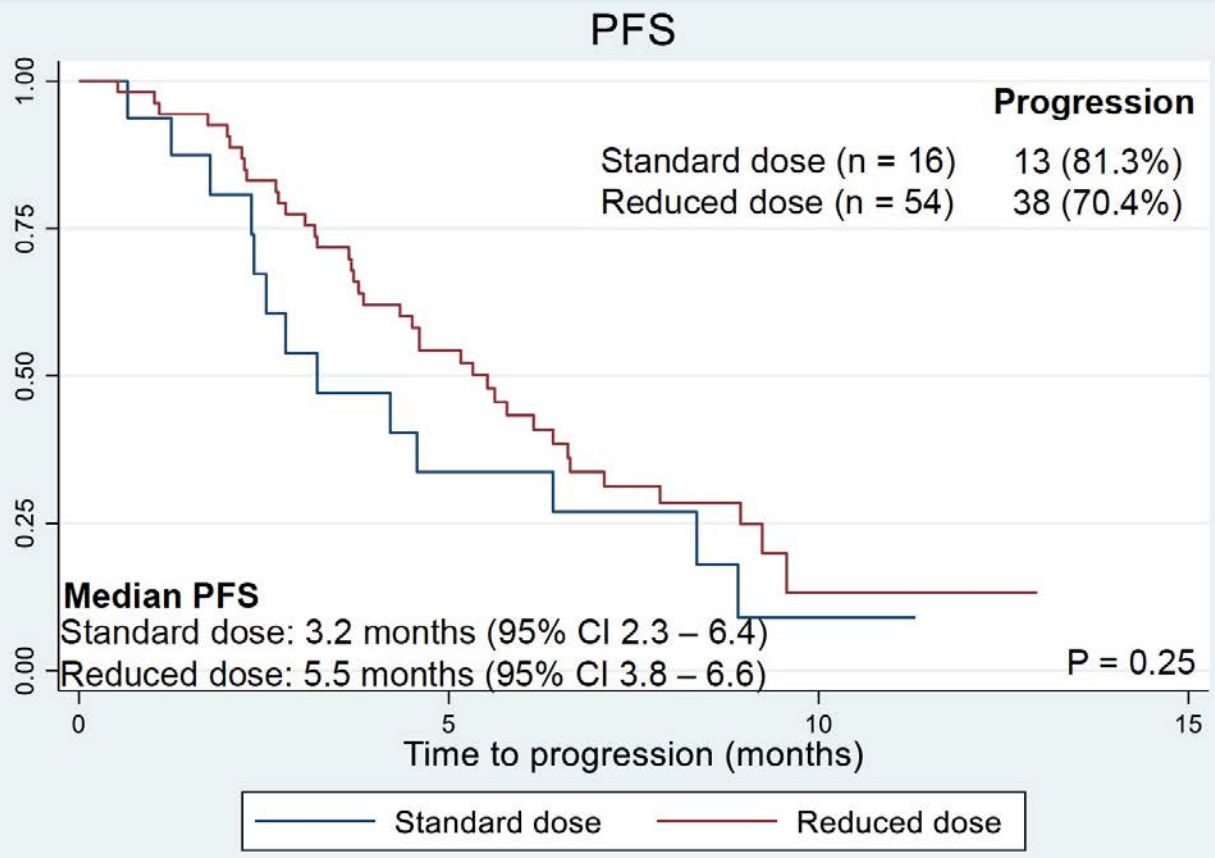
Makker V et al. SGO 2021;Abstract 11512.

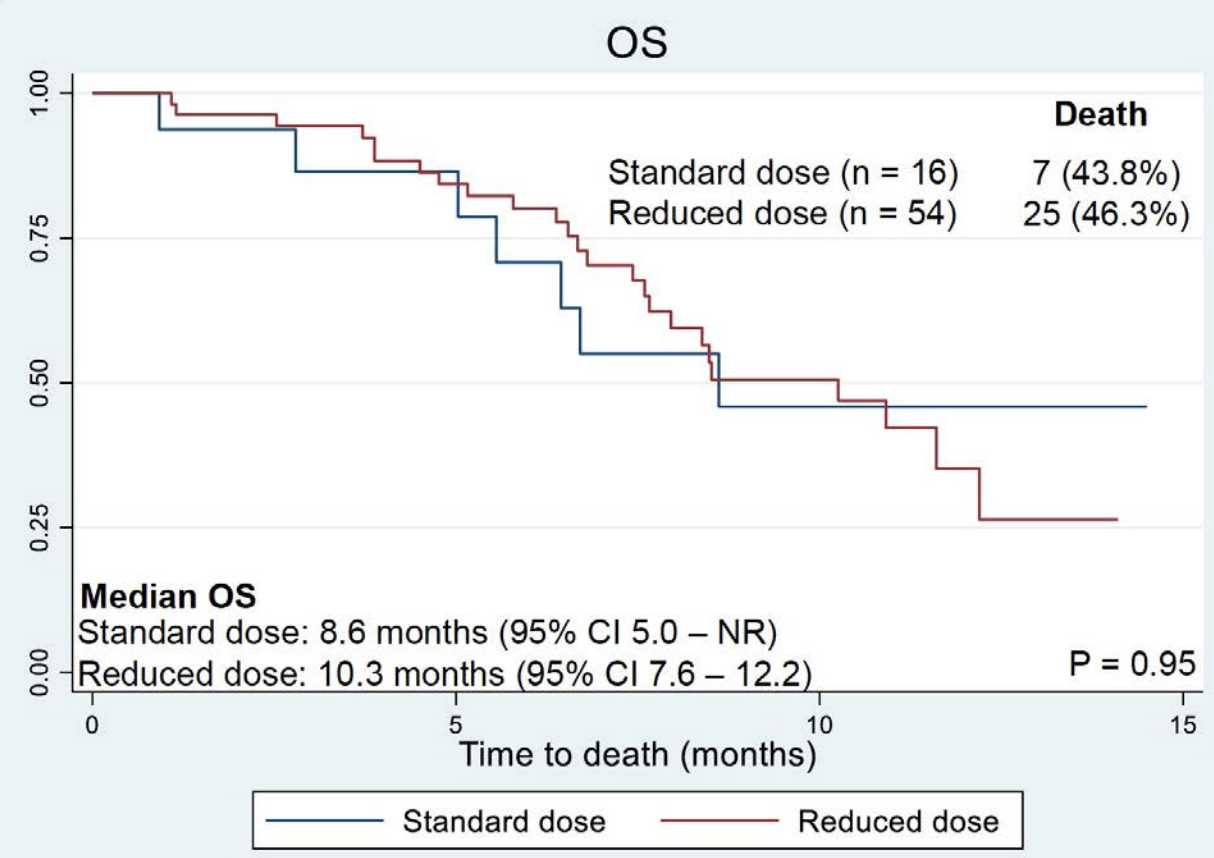
Study 309/KEYNOTE-775: Overall Survival



Makker V et al. SGO 2021;Abstract 11512.

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



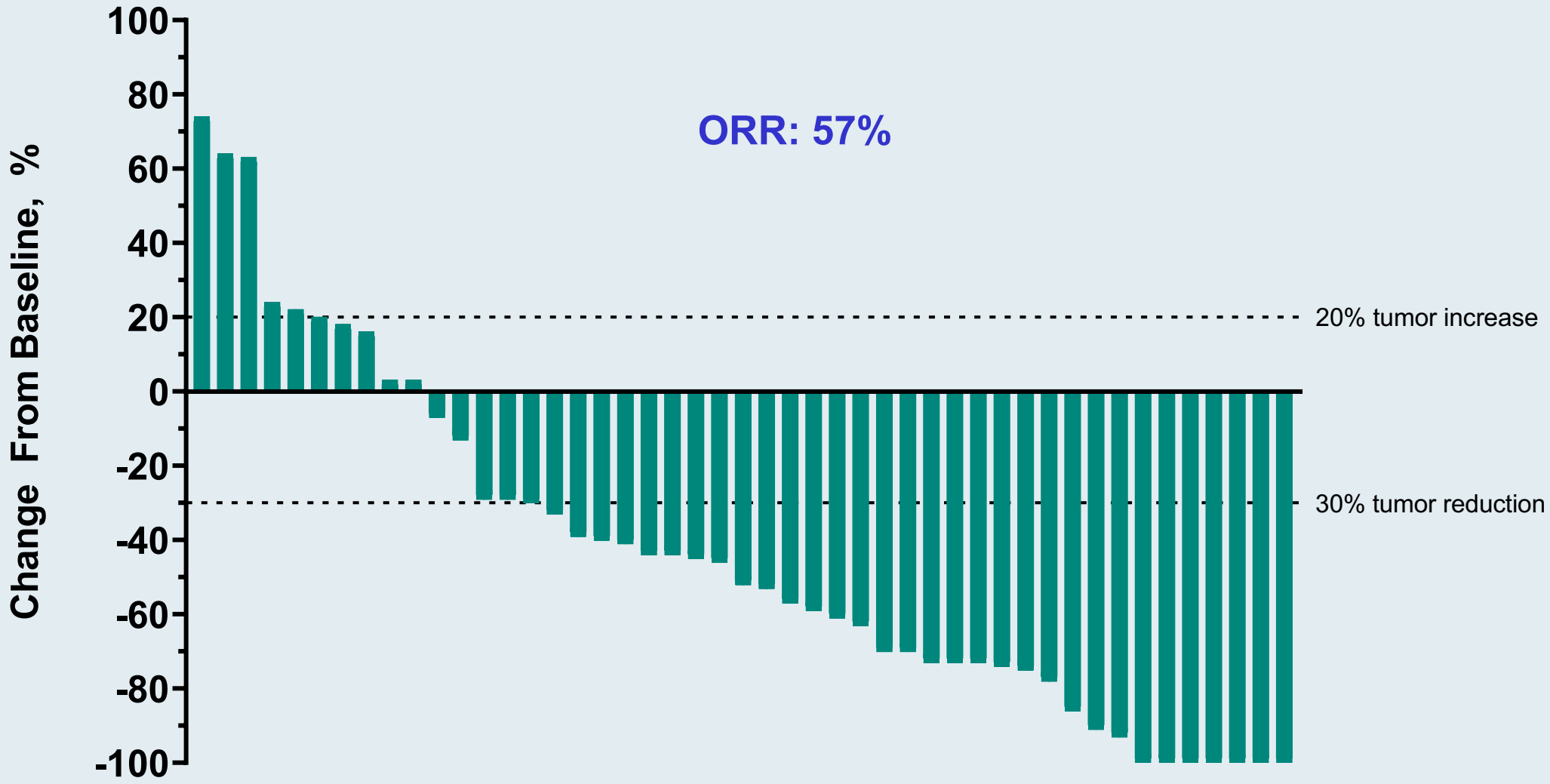


- Reduced starting dose of lenvatinib was associated with longer time to treatment toxicity and fewer dose de-escalations.
- "Published studies and these results may support using lenvatinib at a starting dose of 14 mg daily in clinical practice."

How JA et al. SGO 2021;Abstract 10775.

RTP RESEARCH TO PRACTICE

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



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

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Dostarlimab-gxly for dMMR Endometrial Cancer

Press Release – April 22, 2021

"The Food and Drug Administration granted accelerated approval to dostarlimab-gxly for adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer, as determined by an FDA-approved test, that has progressed on or following a prior platinum-containing regimen.

Efficacy was evaluated based on cohort (A1) in GARNET Trial (NCT02715284), a multicenter, multicohort, open-label trial in patients with advanced solid tumors. The efficacy population consisted of 71 patients with dMMR recurrent or advanced endometrial cancer who progressed on or after a platinum-containing regimen. Patients received dostarlimab-gxly, 500 mg intravenously, every 3 weeks for 4 doses followed by 1,000 mg intravenously every 6 weeks.

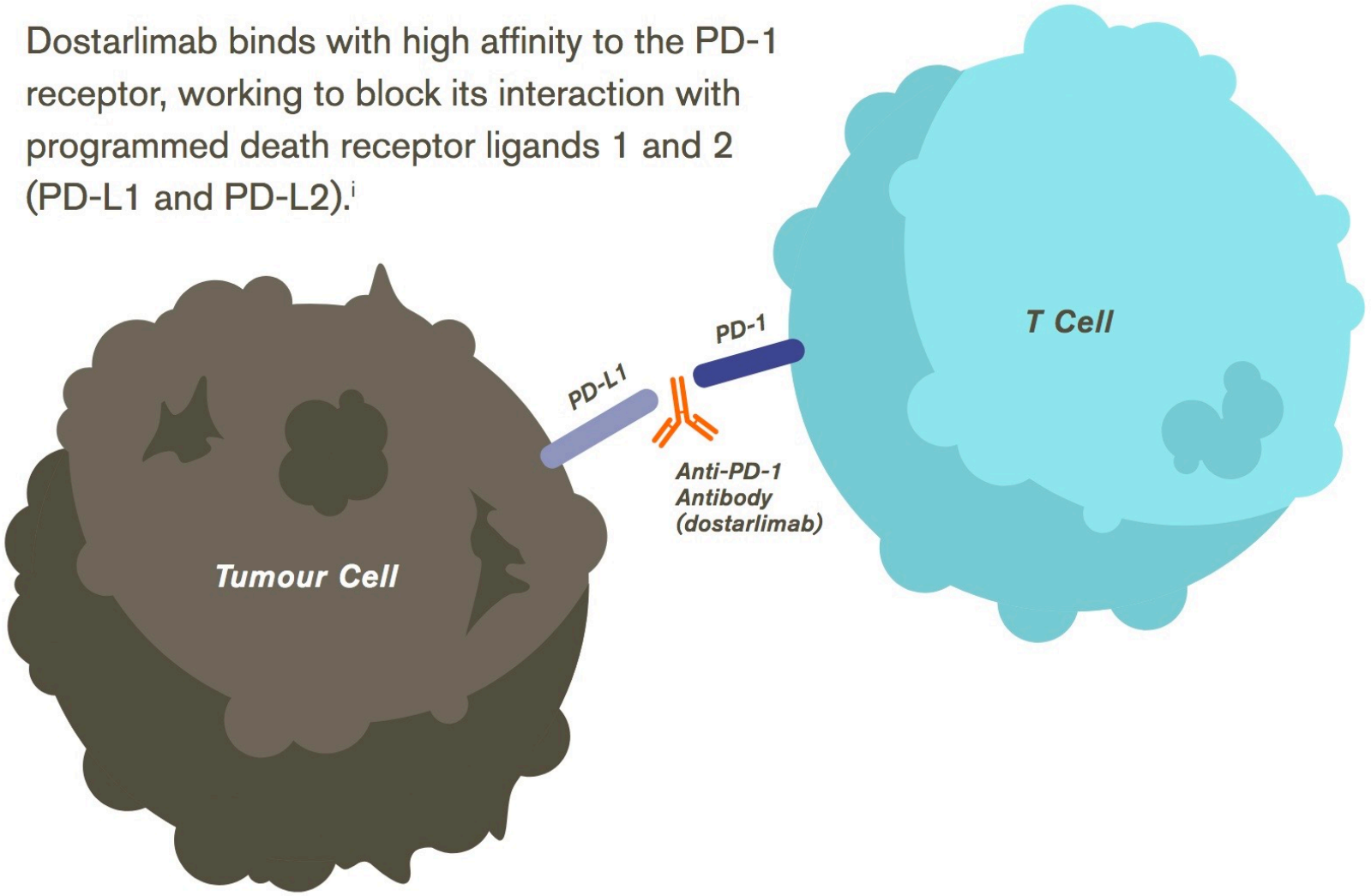
The main efficacy endpoints were overall response rate (ORR) and duration of response (DOR), as assessed by blinded independent central review (BICR) according to RECIST 1.1. Confirmed ORR was 42.3%. The complete response rate was 12.7% and partial response rate was 29.6%. Median DOR was not reached, with 93.3% of patients having durations ≥6 months (range: 2.6 to 22.4 months, ongoing at last assessment)."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-dostarlimab-gxly-dmmr-endometrial-cancer?utm_medium=email&utm_source=govdelivery

RTP RESEARCH TO PRACTICE

Dostarlimab Mechanism of Action

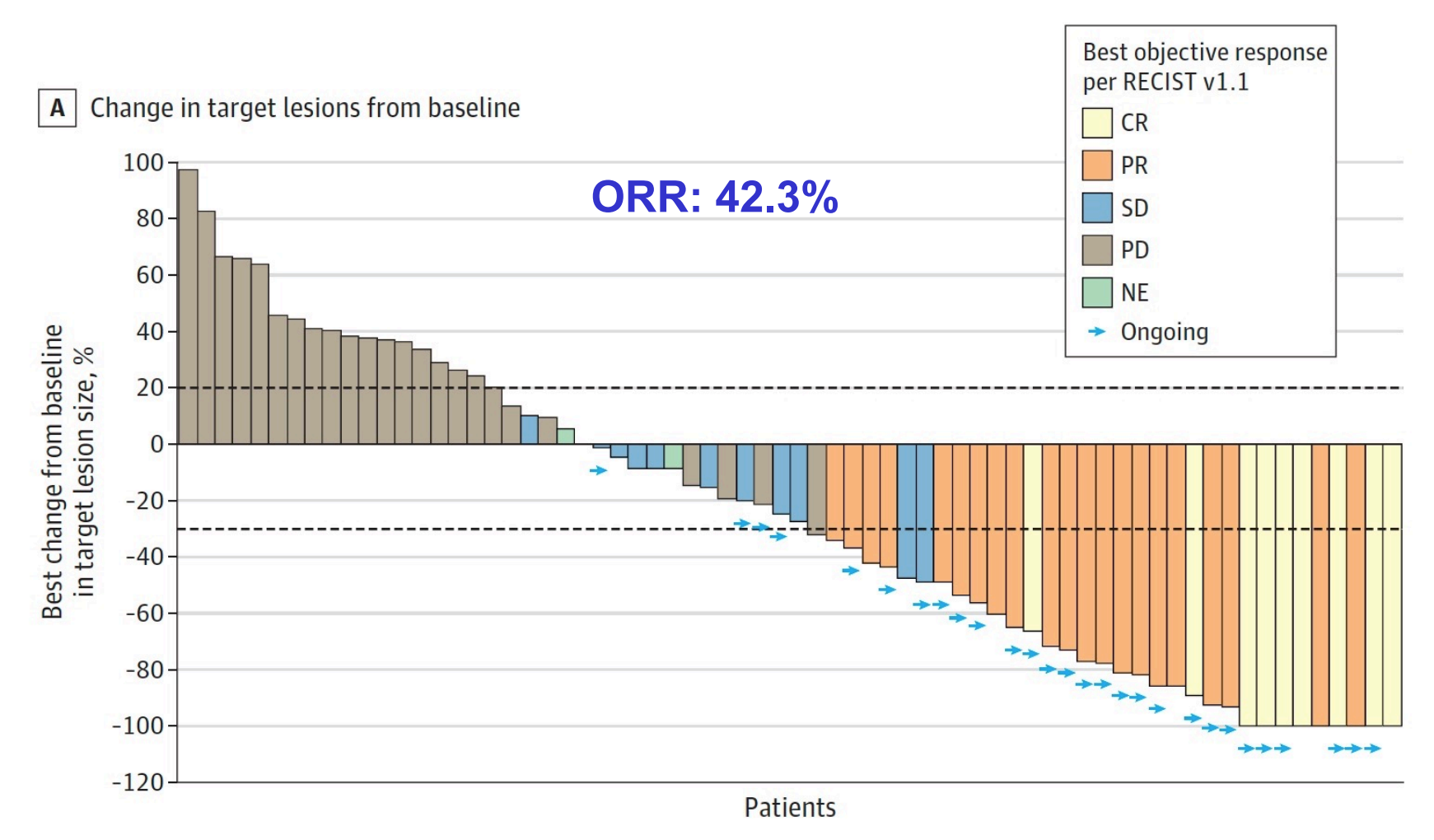
Dostarlimab binds with high affinity to the PD-1 receptor, working to block its interaction with programmed death receptor ligands 1 and 2 (PD-L1 and PD-L2).[i]



https://us.gsk.com/media/5875/dostarlimab-infographic_approved-0422.pdf

RTP RESEARCH TO PRACTICE

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



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

RTP RESEARCH TO PRACTICE

GARNET Study of Dostarlimab: Immune-Related Secondary Endpoints

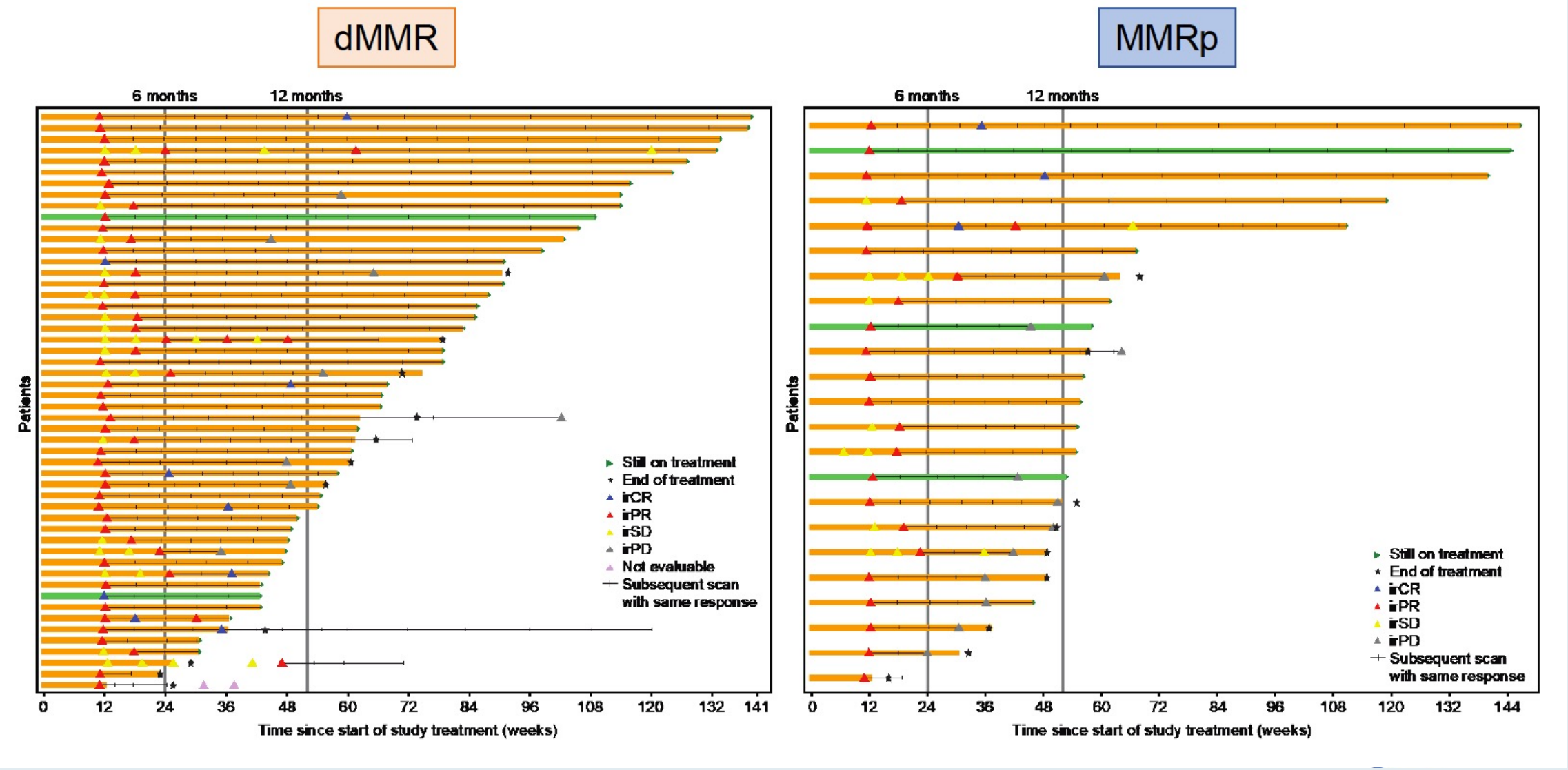
(irRECIST by investigator assessment)		
Variable	dMMR N=110	MMRp N=144
Follow-up, median (range), months	16.5 (0.03–30.6)	13.7 (0.03–33.1)
irORR, n (%)	50 (45.5)	20 (13.9)
irCR	7 (6.4)	3 (2.1)
irPR	43 (39.1)	17 (11.8)
irSD	20 (18.2)	41 (28.5)
irPD	36 (32.7)	63 (43.8)
NE	4 (3.6)	20 (13.9)
irDCR,[a] n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

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

Pothuri B et al. SGO 2021;Abstract 10417.

RTP RESEARCH TO PRACTICE

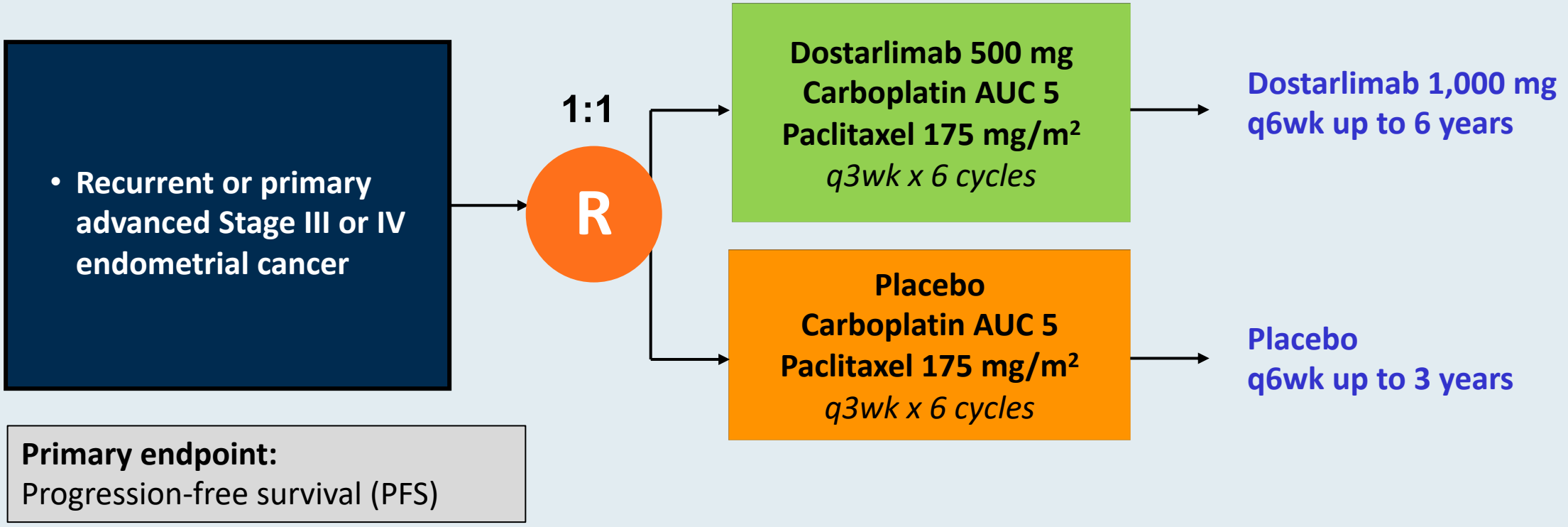
GARNET: Duration of Response with Dostarlimab



Pothuri B et al. SGO 2021;Abstract 10417.

RTP RESEARCH TO PRACTICE

ENGOT-EN6/NSGO-RUBY Phase III Schema of Dostarlimab



Mirza MR et al. ASCO 2020;Abstract TPS6107.

Agenda

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- Case 1: A 51-year-old woman with Stage IIIC ovarian cancer and a germline BRCA1 mutation
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- Case 5: A 58-year-old woman with recurrent cervical cancer, PD-L1-positive
- Case 6: A 37-year-old woman with recurrent cervical cancer, PD-L1-negative

Pembrolizumab is approved as second-line treatment for metastatic cervical cancer…

1. In all patients
2. In patients with elevated PD-L1 levels
3. In combination with chemotherapy
4. All of the above
5. I don’t know

One of the most common autoimmune toxicities associated with checkpoint inhibitors is thyroid dysfunction.

1. Agree
2. Disagree
3. I don’t know

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Recently presented results from a Phase III trial demonstrated clinical benefit with cemiplimab monotherapy in patients with recurrent or metastatic cervical cancer and which of the following tumor histologies?

1. Adenocarcinoma
2. Squamous cell carcinoma
3. Both 1 and 2
4. I don’t know

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TO PRACTICE

Case Presentation – Ms Arn: A 58-year-old woman with recurrent cervical cancer, PD-L1-positive

- Initially diagnosed with Stage IB2 cervical cancer and completed chemoradiation followed by 4 cycles of carboplatin/paclitaxel
- Disease recurrence 2 years later → gemcitabine/cisplatin → PD
- PD-L1-positive → pembrolizumab x 2 years with complete response

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

RTP
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TO PRACTICE

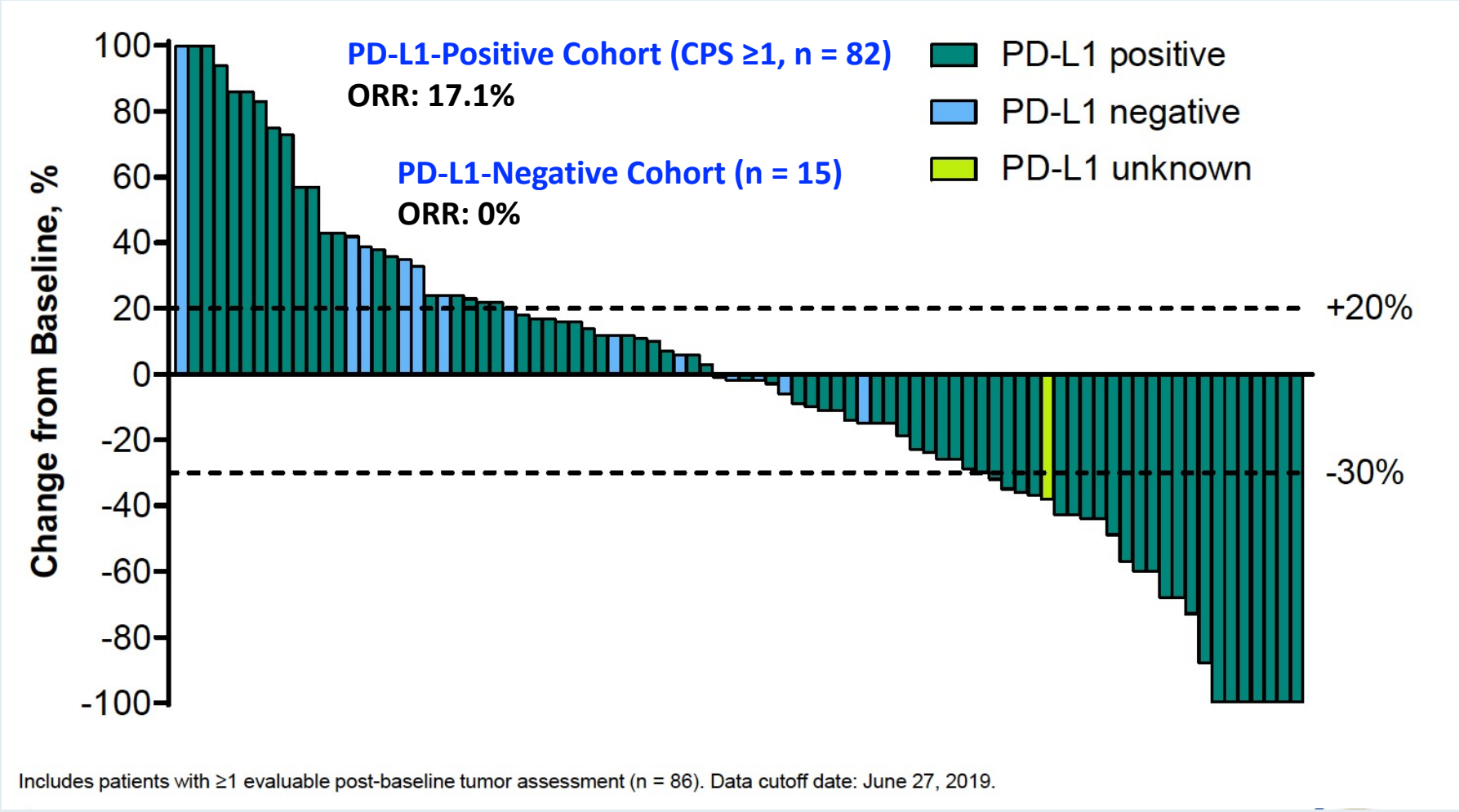
Case Presentation – Ms Arn: A 37-year-old woman with recurrent cervical cancer, PD-L1-negative

- Young mother of 2 children initially diagnosed with PD-L1-negative, Stage IIIB cervical cancer who completed chemoradiation
- Multiple metastatic disease recurrences in the lung and spine treated with chemotherapy and radiation; poor performance status
- Enrolled in clinical trial of tisotumab vedotin with good response and symptom improvement

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

RTP
RESEARCH
TO PRACTICE

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



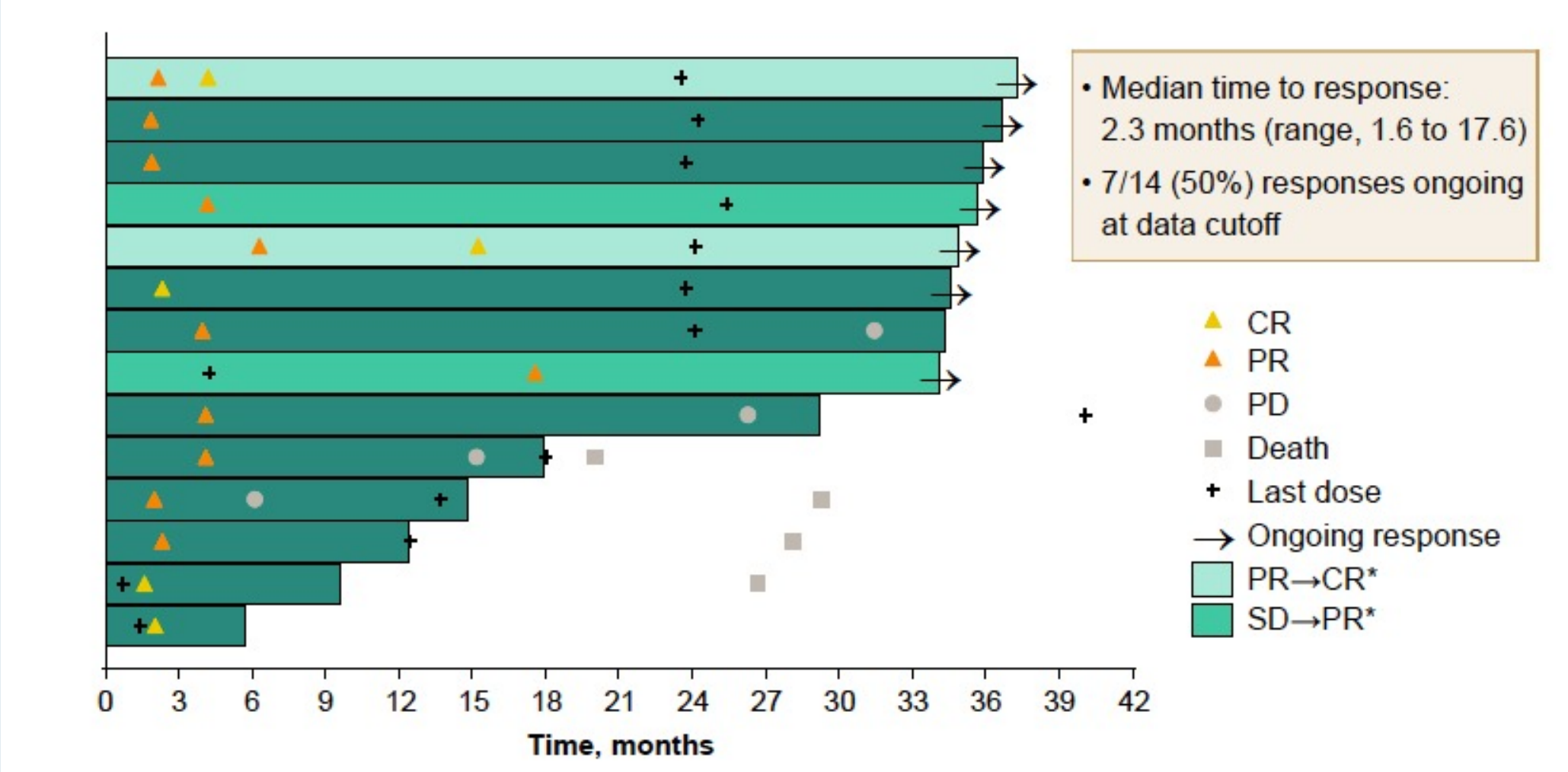
Includes patients with ≥1 evaluable post-baseline tumor assessment (n = 86). Data cutoff date: June 27, 2019.

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

Chung HC et al. SGO 2021;Abstract 10440.

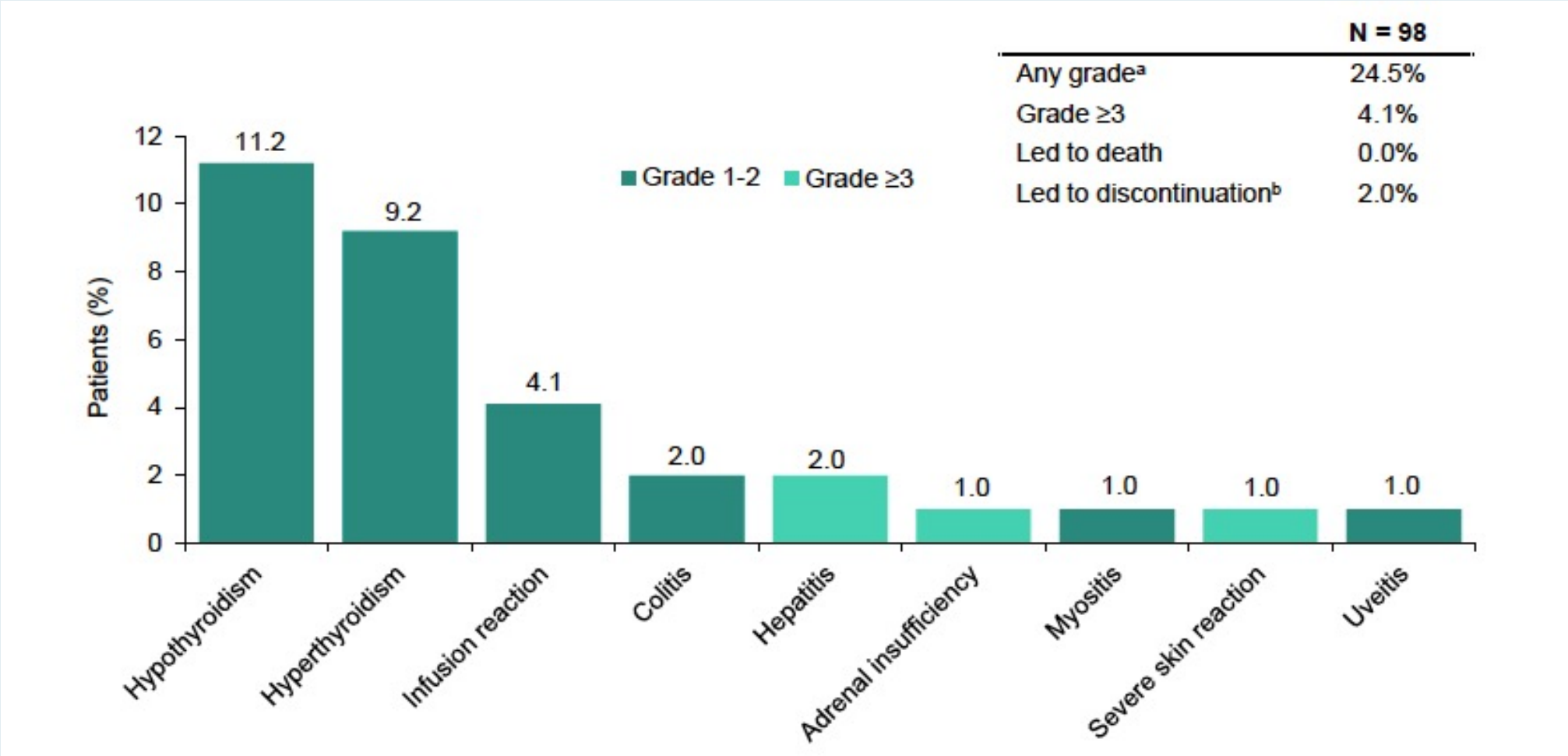
RTP RESEARCH TO PRACTICE

Phase II KEYNOTE-158: Time to Response and Duration of Response with Pembrolizumab



Chung HC et al. SGO 2021;Abstract 10440.

Phase II KEYNOTE-158: Immune-Mediated Adverse Events and Infusion Reactions



Includes events of any grade that occurred in ≥1 patient

Chung HC et al. SGO 2021;Abstract 10440.

Phase III KEYNOTE-826 Trial Met Dual Primary Endpoints of Overall Survival (OS) and Progression-Free Survival (PFS) in Patients With Persistent, Recurrent or Metastatic Cervical Cancer

Press Release – June 22, 2021

The Phase 3 KEYNOTE-826 trial investigating pembrolizumab in combination with platinum-based chemotherapy (paclitaxel plus cisplatin or paclitaxel plus carboplatin) with or without bevacizumab, met its primary endpoints of overall survival (OS) and progression-free survival (PFS) for the first-line treatment of patients with persistent, recurrent or metastatic cervical cancer.

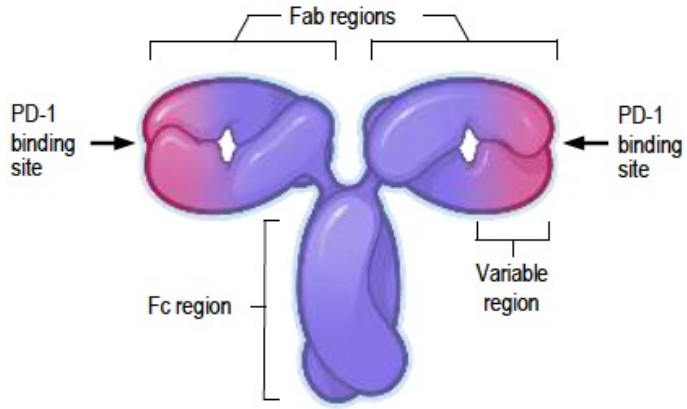
Based on an interim analysis conducted by an independent Data Monitoring Committee, pembrolizumab plus platinum-based chemotherapy with or without bevacizumab demonstrated statistically significant and clinically meaningful improvements in OS and PFS compared to the same platinum-based chemotherapy regimens with or without bevacizumab alone, regardless of PD-L1 status; pembrolizumab is the first anti-PD-1/PD-L1 therapy to demonstrate this. The safety profile of pembrolizumab in this trial was consistent with that observed in previously reported studies. Results will be presented at an upcoming medical meeting and will be submitted to regulatory authorities.

https://www.businesswire.com/news/home/20210622005214/en/Merck-Announces-Phase-3-KEYNOTE-826-Trial-Met-Dual-Primary-Endpoints-of-Overall-Survival-OS-and-Progression-Free-Survival-PFS-in-Patients-With-Persistent-Recurrent-or-Metastatic-Cervical-Cancer

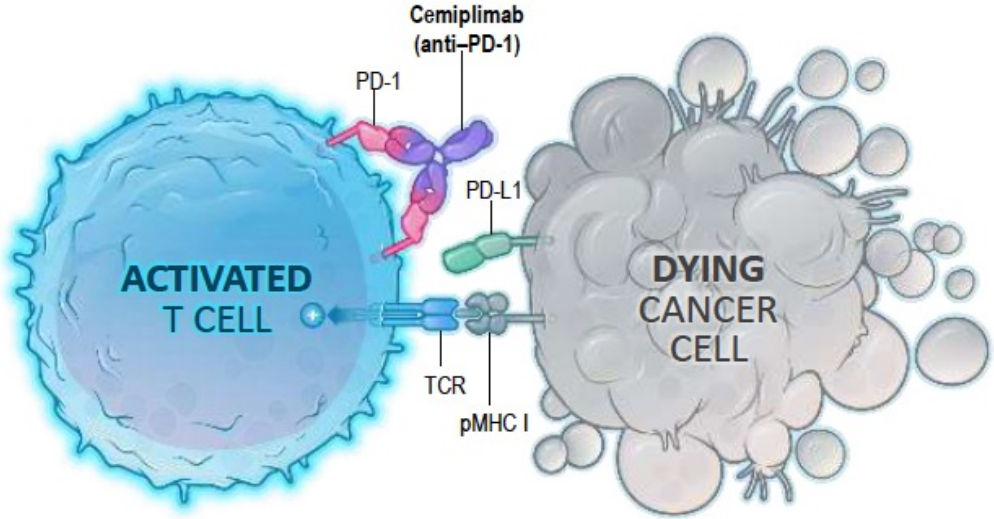
RTP RESEARCH TO PRACTICE

CEMIPLIMAB: MECHANISM OF ACTION

Cemiplimab Molecular Structure



Cemiplimab Mechanism of Action



- High-affinity, human, hinge-stabilised IgG4 monoclonal antibody to the PD-1 receptor[1]
- Phase 1 R/M cervical cancer (n=23; includes Dose Escalation + Expansion Cohorts)[2]
  - Safety profile similar to that of other PD-1 inhibitors[2]
  - 17% ORR[2]

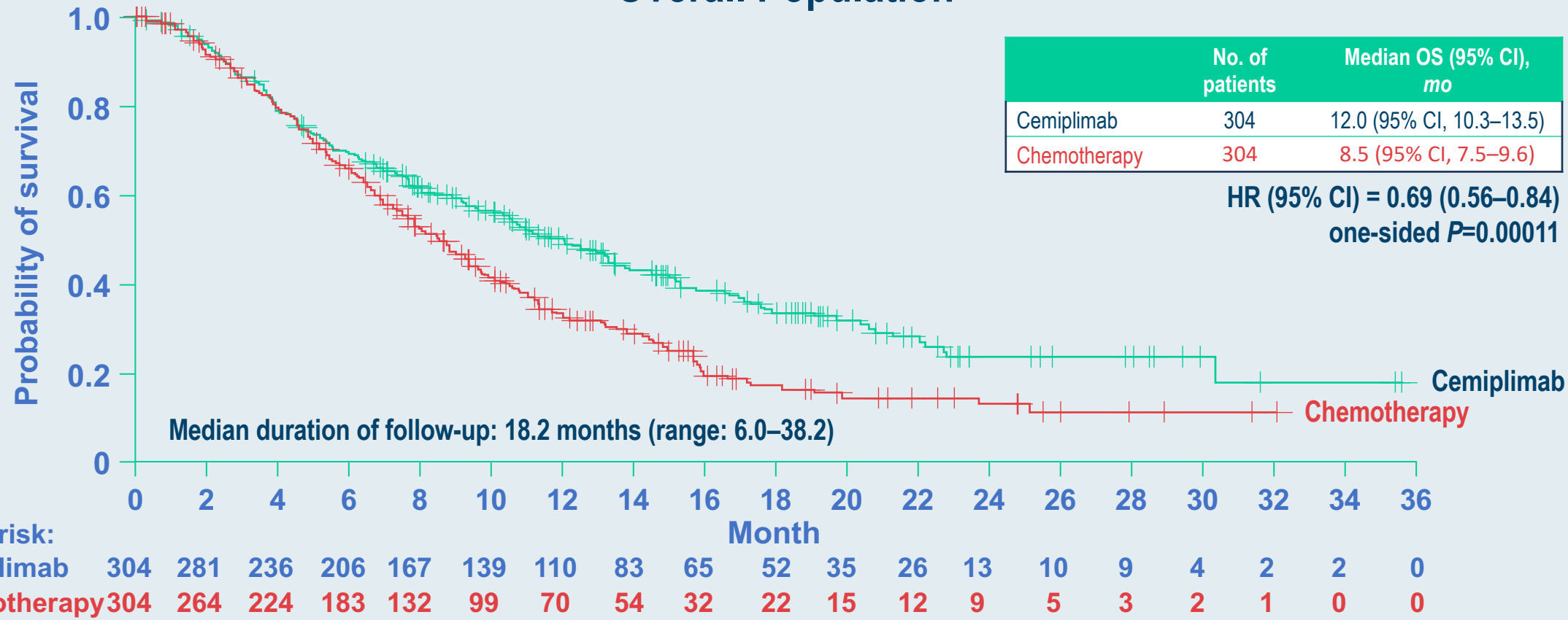
Ig, immunoglobin; Fc, fragment crystallizable; ORR, objective response rate; PD-1, programmed cell death-1; PD-L1, PD-ligand 1; pMHC I, peptide-bound major histocompatibility complex I; R/M, recurrent or metastatic; TCR, T-cell receptor.

1. Burova E et al. *Mol Cancer Ther.* 2017;16:861–870. 2. Rischin D et al. *Gynecol Oncol.* 2020;159:322–328.

EMPOWER: OVERALL SURVIVAL

- At second interim analysis (85% of total OS events), IDMC recommended trial be stopped early for efficacy

Overall Population



	No. of patients	Median OS (95% CI), *mo*
Cemiplimab	304	12.0 (95% CI, 10.3–13.5)
Chemotherapy	304	8.5 (95% CI, 7.5–9.6)

HR (95% CI) = 0.69 (0.56–0.84)
one-sided *P*=0.00011

No. at risk:

Cemiplimab	304	281	236	206	167	139	110	83	65	52	35	26	13	10	9	4	2	2	0
Chemotherapy	304	264	224	183	132	99	70	54	32	22	15	12	9	5	3	2	1	0	0

EMPOWER: OBJECTIVE RESPONSE RATE

By investigator assessment	Overall population	
	Cemiplimab (n=304)	Chemotherapy (n=304)
Response		
Objective response rate (ORR:CR+PR)	50 (16.4)	19 (6.3)
95% CI for ORR[a]	(12.5, 21.1)	(3.8, 9.6)
Best overall tumour response, n (%)		
Complete response (CR)[b]	10 (3.3)	3 (1.0)
Partial response (PR)[b]	40 (13.2)	16 (5.3)
Stable disease (SD)[c]	125 (41.1)	148 (48.7)
Progressive disease (PD)	105 (34.5)	88 (28.9)
Not evaluable (NE)	24 (7.9)	49 (16.1)
Stratified CMH test one-sided *P*-value[d]	0.00004	
Odds ratio (95% CI)[d]	2.984 (1.707, 5.215)	
KM estimated median DOR, months (95% CI)[e]	16.4 (12.4, NE)	6.9 (5.1, 7.7)
Median observed time to response, months (range)	2.7 (1.2–11.4)	1.6 (1.2–9.0)

- ORR of SCC population
  - Cemiplimab: 17.6% (95% CI: 13.0–23.0)
  - Chemotherapy: 6.7% (95% CI: 3.9–10.7)
- ORR of AC population
  - Cemiplimab: 12.3% (95% CI: 5.5–22.8)
  - Chemotherapy: 4.5% (95% CI: 0.9–12.7)

EMPOWER: ADVERSE EVENTS

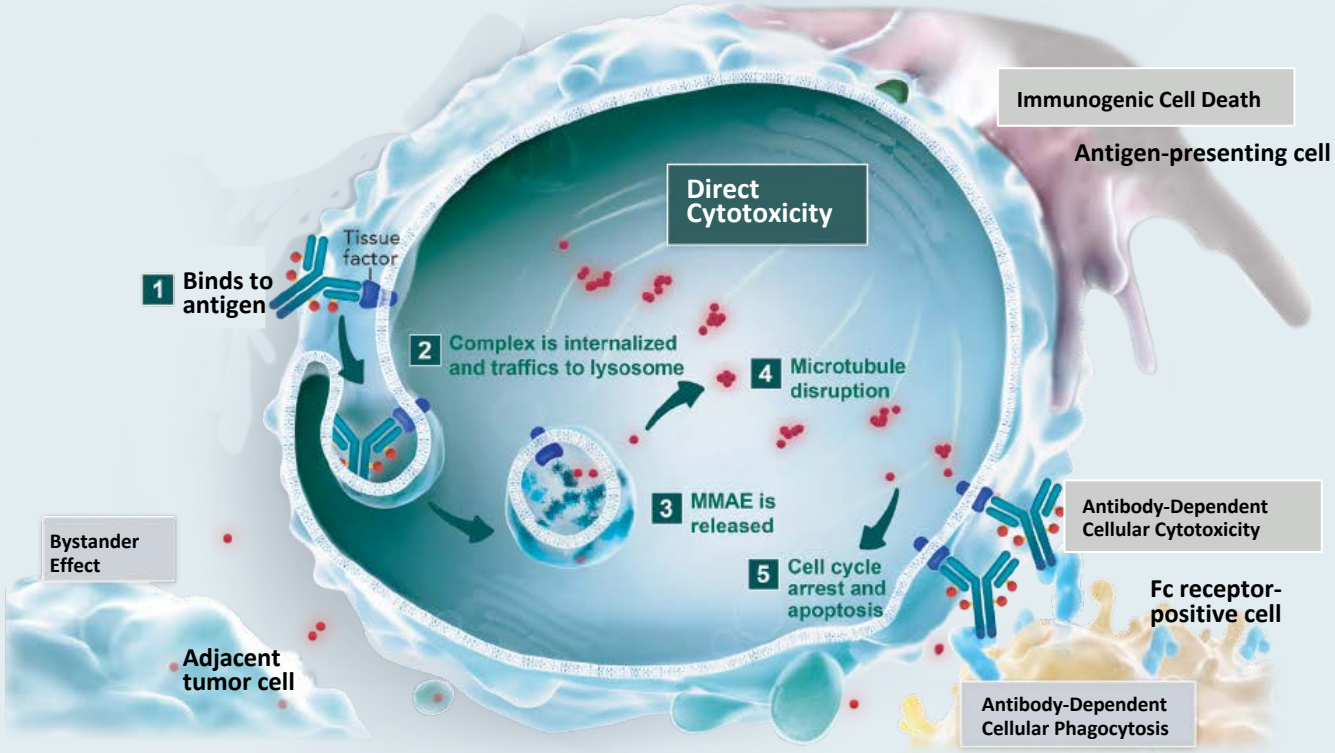
n (%), unless stated	Cemiplimab (n=300)		Chemotherapy (n=290)	
Median duration of exposure (range), weeks	15.2 (1.4–100.7)		10.1 (1.0–81.9)	
Treatment-emergent AEs, regardless of attribution	**Any grade**	**Grade 3–5**	**Any grade**	**Grade 3–5**
Overall	265 (88.3)	135 (45.0)	265 (91.4)	155 (53.4)
Led to discontinuation	26 (8.7)	20 (6.7)	15 (5.2)	11 (3.8)
Led to death	5 (1.7)	5 (1.7)	2 (0.7)	2 (0.7)
Treatment-related AEs				
Overall	170 (56.7)	44 (14.7)	236 (81.4)	117 (40.3)
Led to discontinuation	17 (5.7)	12 (4.0)	10 (3.4)	8 (2.8)
Led to death	0	0	2 (0.7)	2 (0.7)
Sponsor-identified immune-related AEs				
Overall	48 (16.0)	18 (6.0)	2 (0.7)	2 (0.7)
Led to discontinuation	15 (5.0)	11 (3.7)	2 (0.7)	2 (0.7)
Led to death	0	0	0	0

Treatment-emergent AEs in ≥15% of patients in either arm, n (%)	Cemiplimab (n=300)		Chemotherapy (n=290)	
	Any grade	**Grade 3–5**	**Any grade**	**Grade 3–5**
Overall	265 (88.3)	135 (45.0)	265 (91.4)	155 (53.4)
Anaemia	75 (25.0)	36 (12.0)	129 (44.5)	78 (26.9)
Nausea	55 (18.3)	1 (0.3)	97 (33.4)	6 (2.1)
Fatigue	50 (16.7)	4 (1.3)	45 (15.5)	4 (1.4)
Vomiting	48 (16.0)	2 (0.7)	68 (23.4)	7 (2.4)
Decreased appetite	45 (15.0)	1 (0.3)	46 (15.9)	2 (0.7)
Constipation	45 (15.0)	0	59 (20.3)	1 (0.3)
Pyrexia	35 (11.7)	1 (0.3)	61 (21.0)	0
Asthenia	33 (11.0)	7 (2.3)	44 (15.2)	3 (1.0)
Neutropenia	6 (2.0)	3 (1.0)	44 (15.2)	26 (9.0)

- There were no new immune-related AEs that are not well described for the PD-1/PD-L1 inhibitor class

Mechanism of Action of Tisotumab Vedotin

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

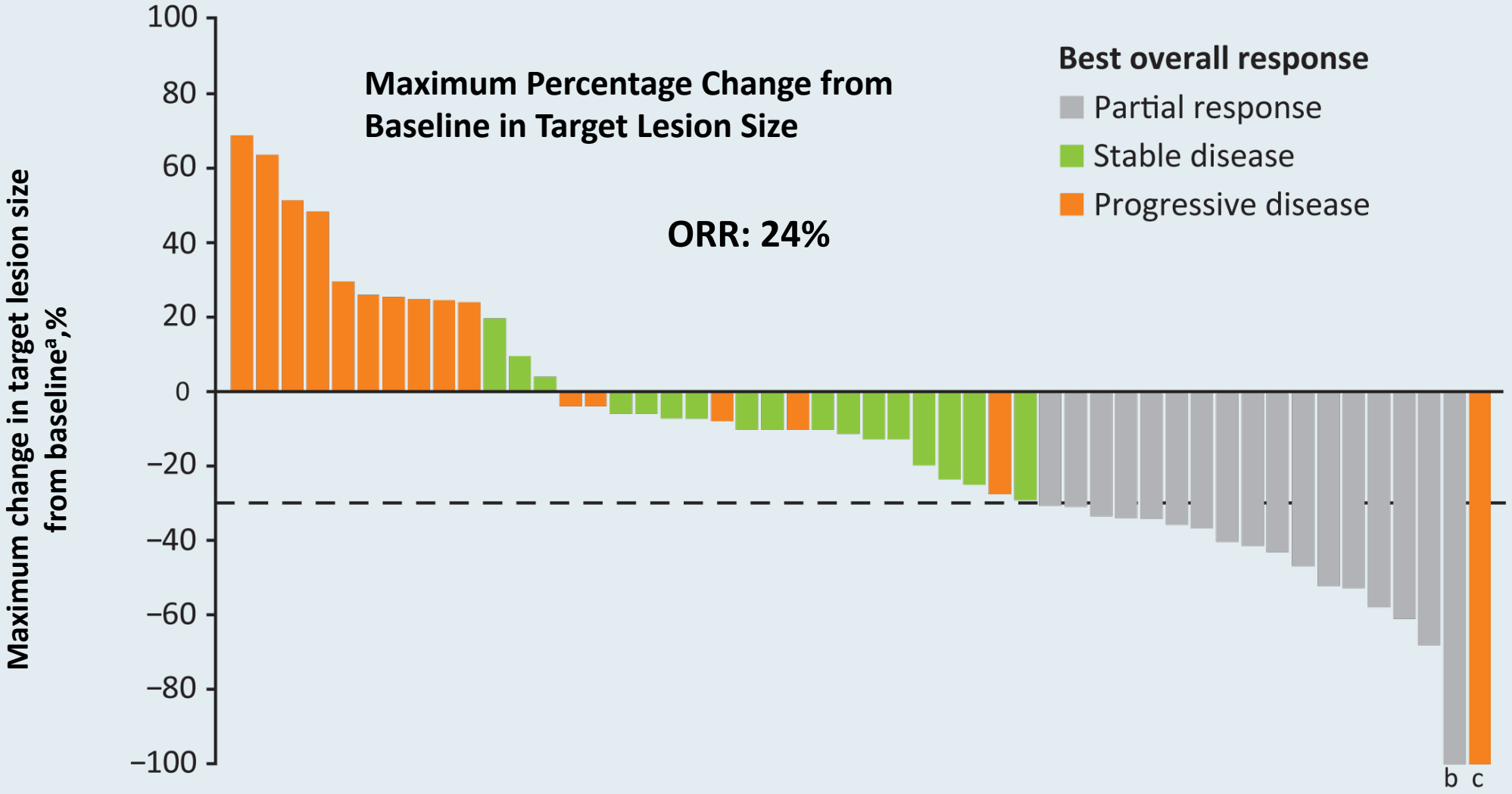


1. Förster Y, et al. *Clin Chim Acta,* 2006. 2. Cocco E, et al. *BMC Cancer,* 2011.
3. Breij EC, et al. *Cancer Res,* 2014. 4. De Goeij BE, et al. *Mol Cancer Ther,* 2015.

Courtesy of David M O'Malley, MD

RTP RESEARCH TO PRACTICE

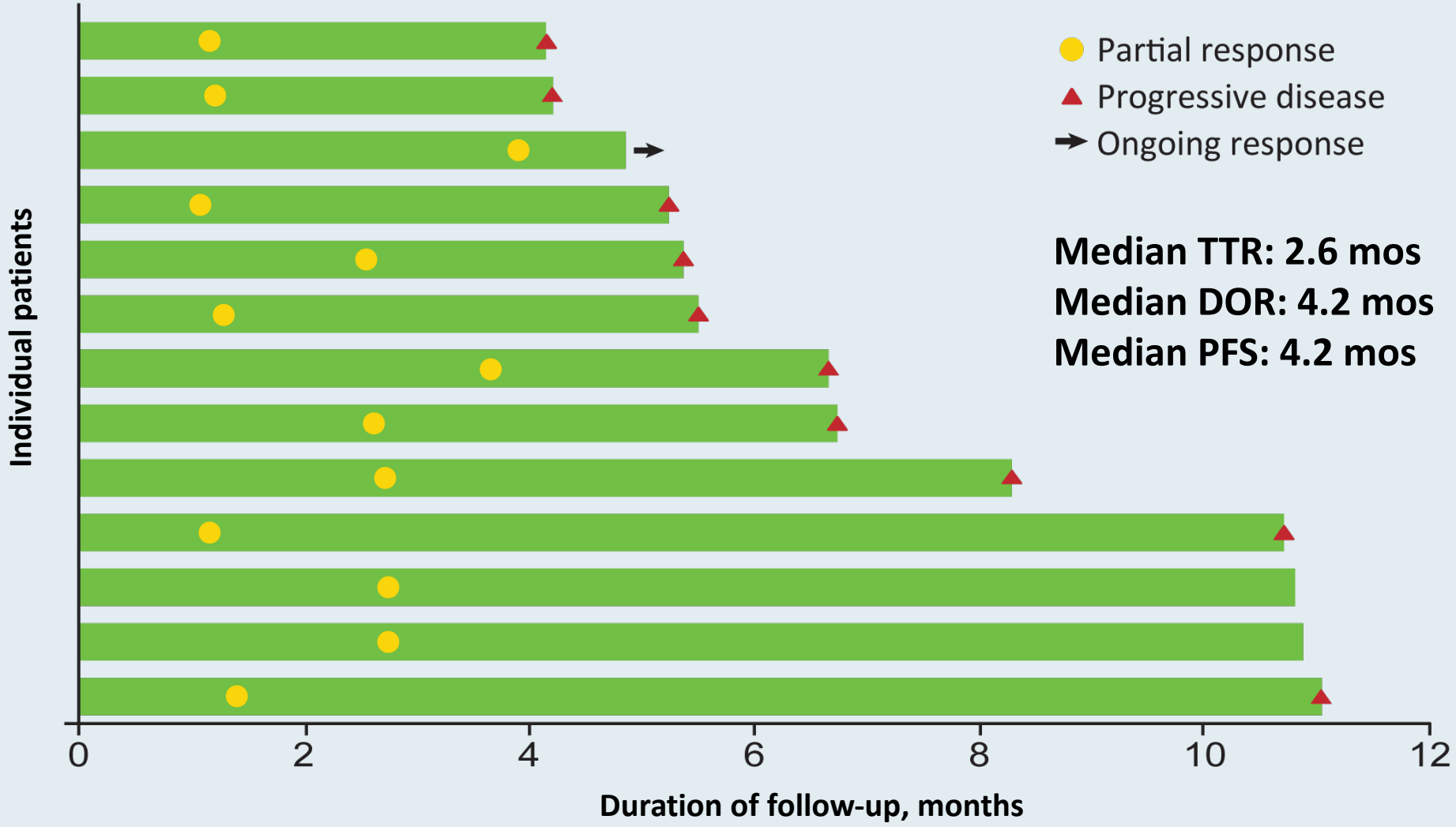
innovaTV 201: Best Overall Response to TV



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

RTP RESEARCH TO PRACTICE

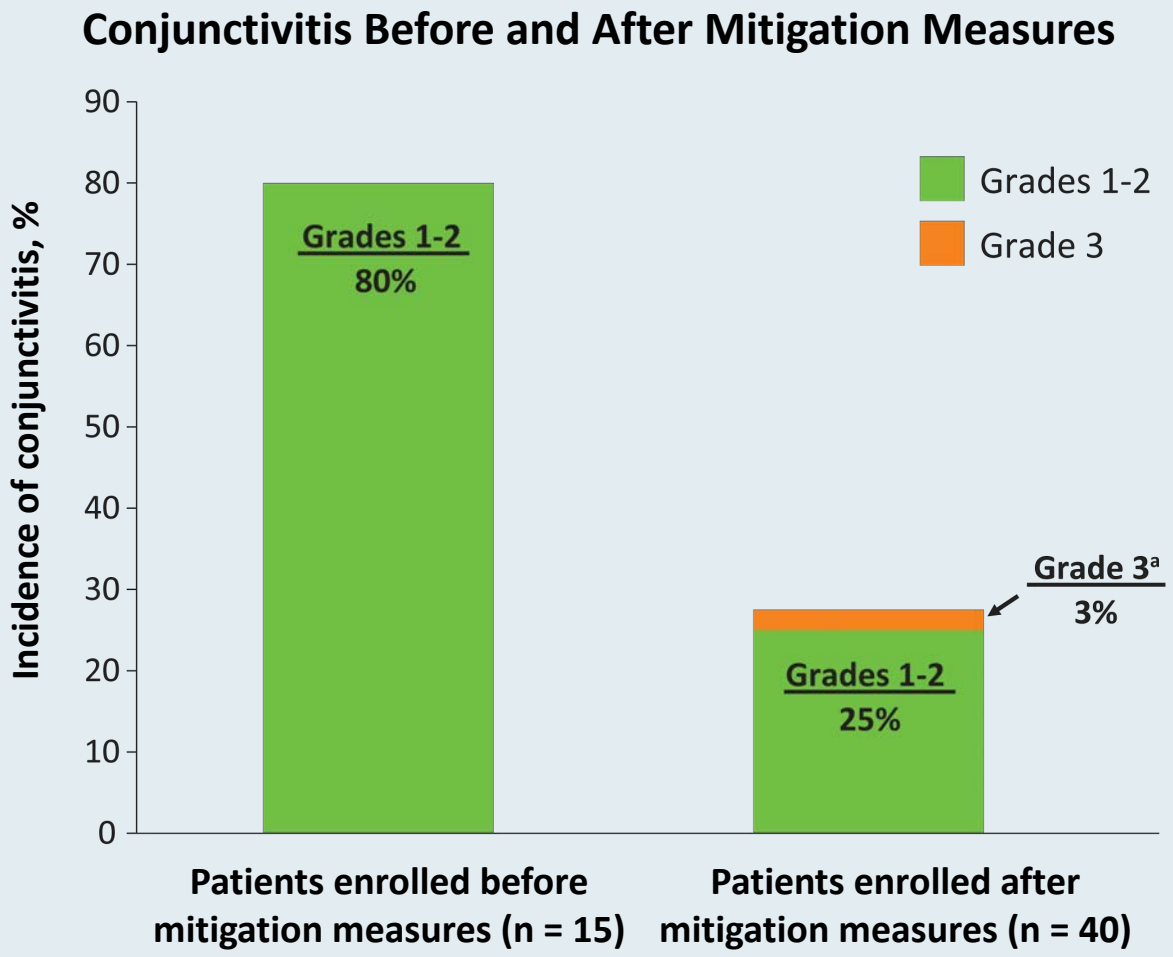
innovaTV 201: Time to Response and Duration of Response in Patients with a Confirmed PR to TV



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

innovaTV 201: Treatment-Emergent Adverse Events

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



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

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

RTP RESEARCH TO PRACTICE

Meet The Professor

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

Monday, July 19, 2021
5:00 PM – 6:00 PM ET

Faculty

Tanios Bekaii-Saab, MD

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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