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

Gynecologic Cancers

Tuesday, January 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Robert L Coleman, MD
Richard T Penson, MD, MRCP

Moderator

Neil Love, MD

RTP Year in Review 2020

Commercial Support

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

Dr Love — Disclosures

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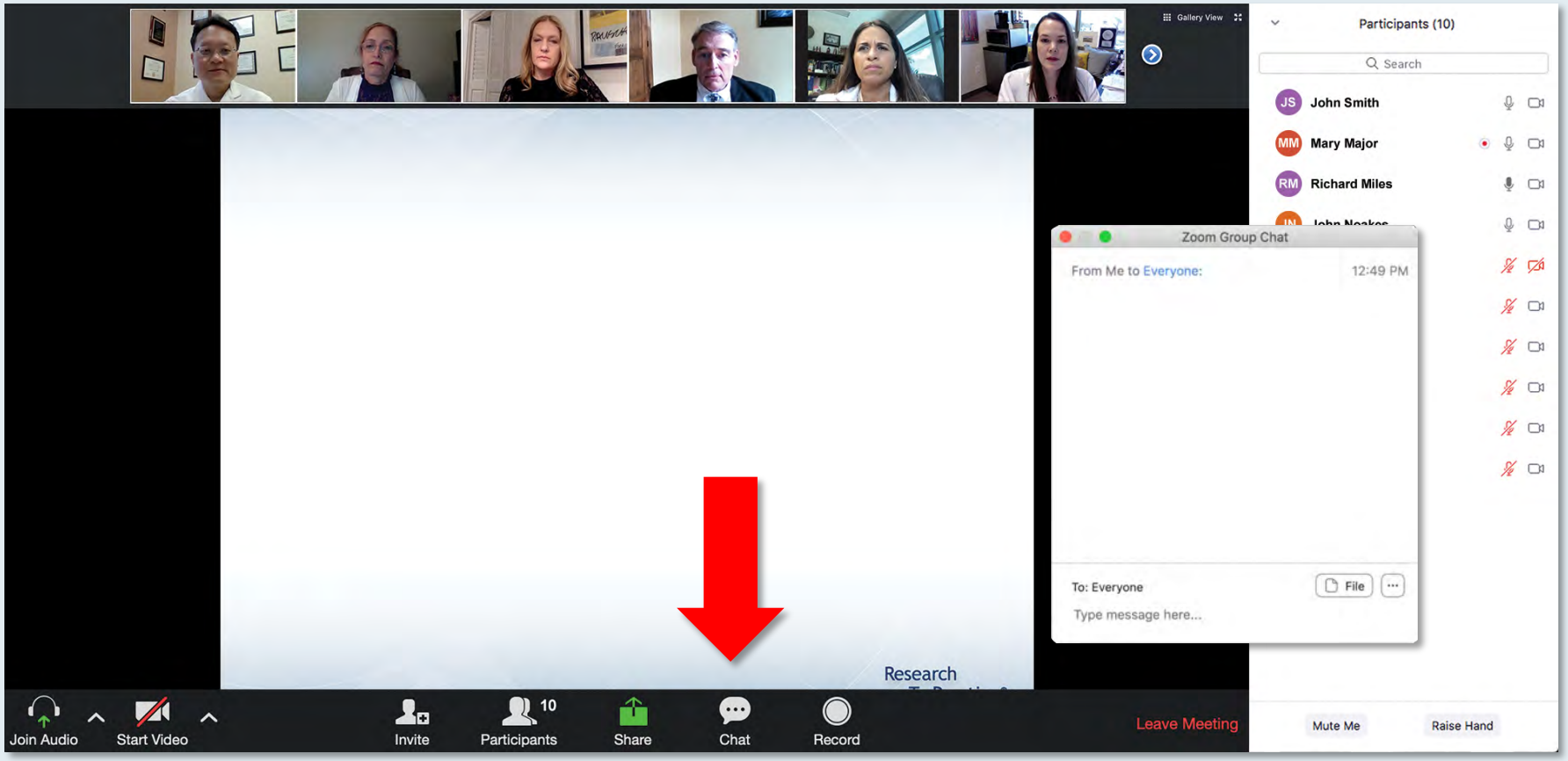

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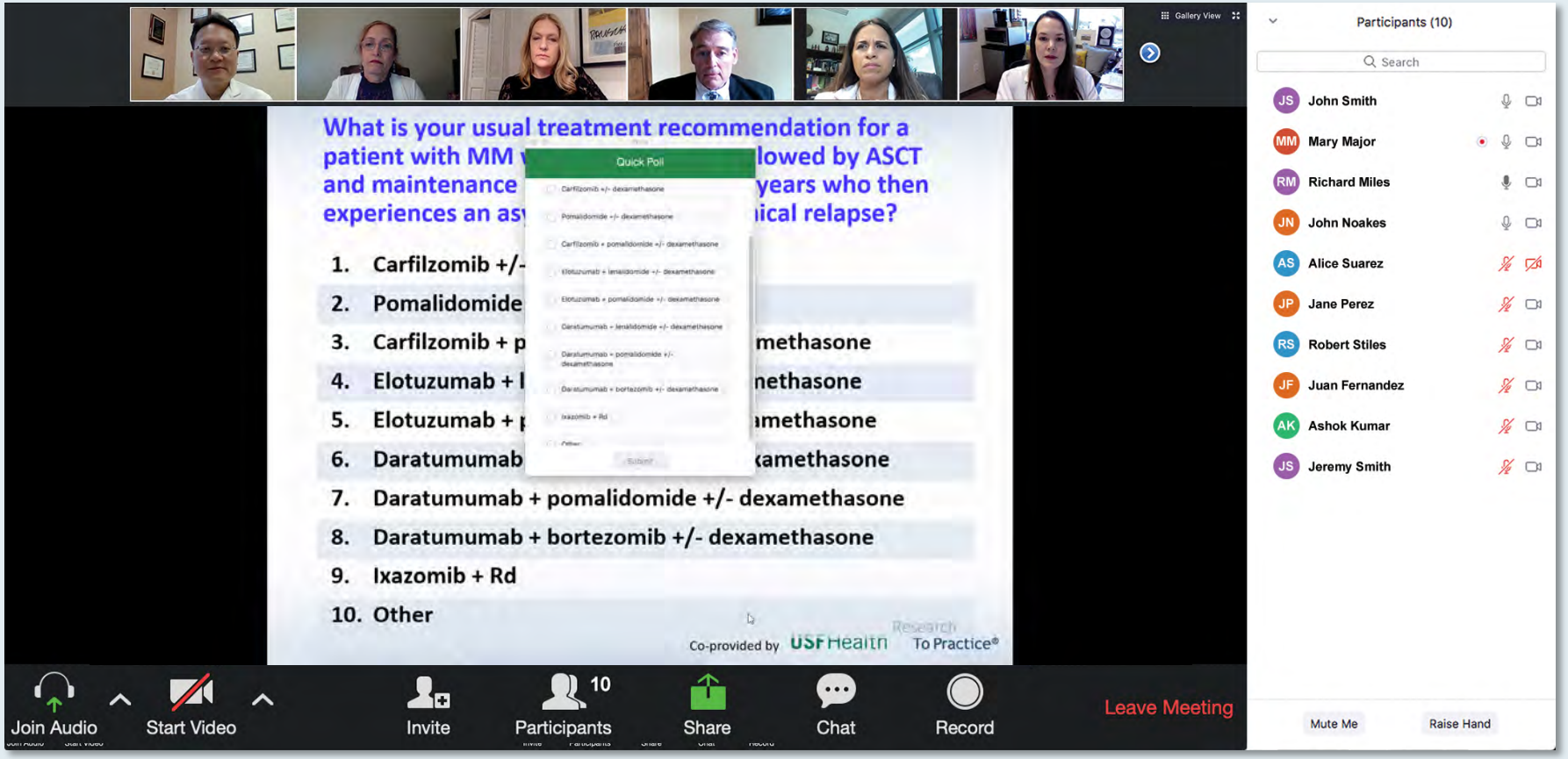
How to answer poll questions



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ONCOLOGY TODAY

WITH DR NEIL LOVE

THE ROLE OF PARP INHIBITION IN THE MANAGEMENT OF OVARIAN CANCER

DR URSULA MATULONIS

DANA-FARBER CANCER INSTITUTE

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

Lymphomas

Thursday, January 14, 2021
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Sonali M Smith, MD

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Neil Love, MD

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

Nontargeted Therapy for Lung Cancer

Tuesday, January 19, 2021
5:00 PM – 6:00 PM ET

Faculty

Matthew Gubens, MD, MS
Suresh S Ramalingam, MD

Moderator

Neil Love, MD

RTP Year in Review 2020

Recent Advances in Hematologic Oncology: A 4-Part Live Webinar Series Reviewing Key Data and Presentations from the 62nd ASH Annual Meeting

Part 1 — Acute Myeloid Leukemia

Wednesday, January 20, 2021
5:00 PM – 6:00 PM ET

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Eytan M Stein, MD
Andrew H Wei, MBBS, PhD

Moderator

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RTP RESEARCH TO PRACTICE

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Chronic Lymphocytic Leukemia

Thursday, January 21, 2021
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Jennifer Woyach, MD

Moderator

Neil Love, MD

RTP Year in Review 2020

Meet The Professor
Management of Ovarian Cancer

Friday, January 22, 2021
1:15 PM – 2:15 PM ET

Faculty

Professor Jonathan A Ledermann, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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YiR Gynecologic Cancers Faculty

Robert L Coleman, MD
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US Oncology Research
Gynecologic Oncology
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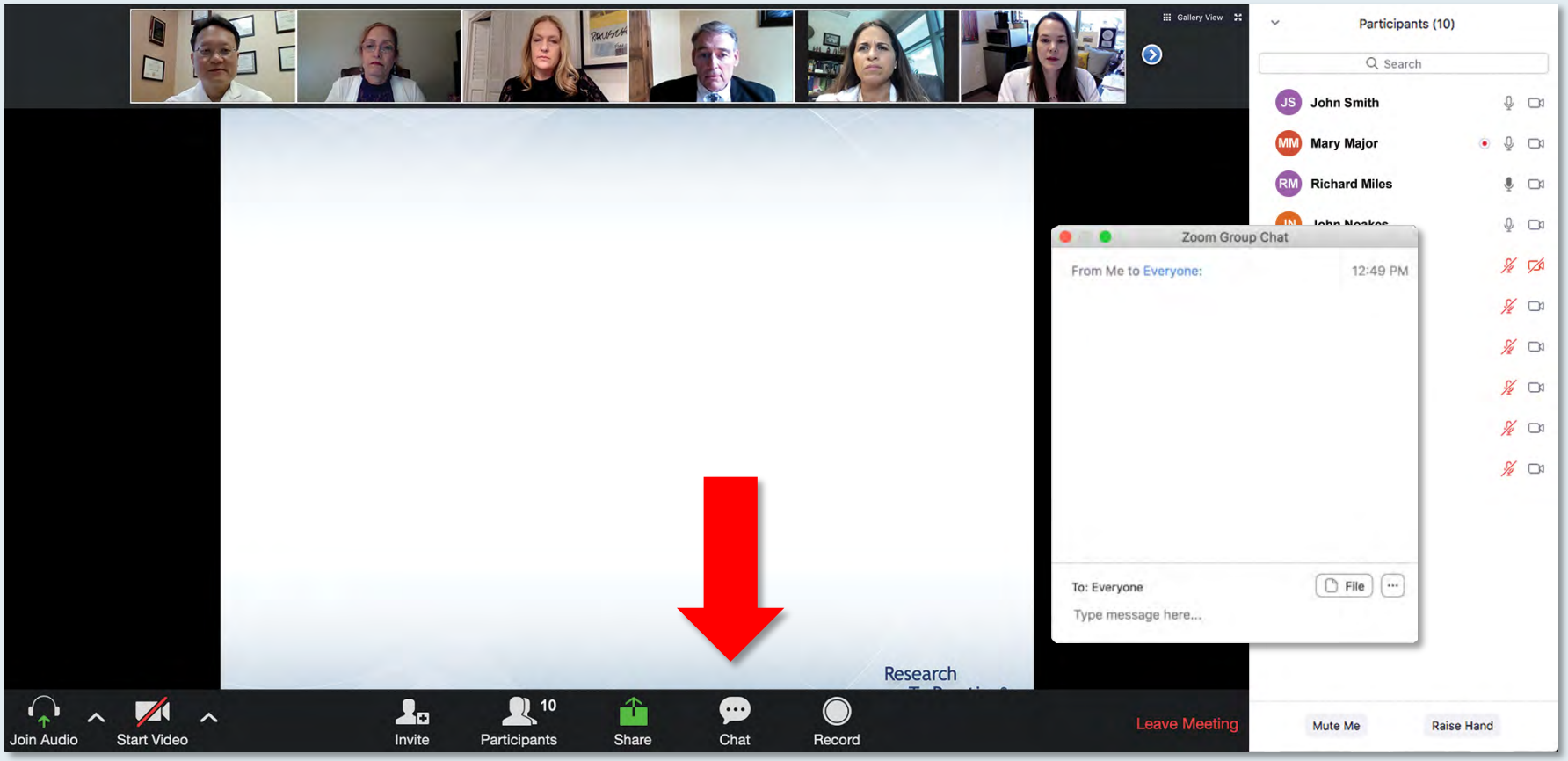
Richard T Penson, MD, MRCP
Associate Professor of Medicine
Harvard Medical School
Clinical Director, Medical Gynecologic Oncology
Massachusetts General Hospital
Boston, Massachusetts

We Encourage Clinicians in Practice to Submit Questions



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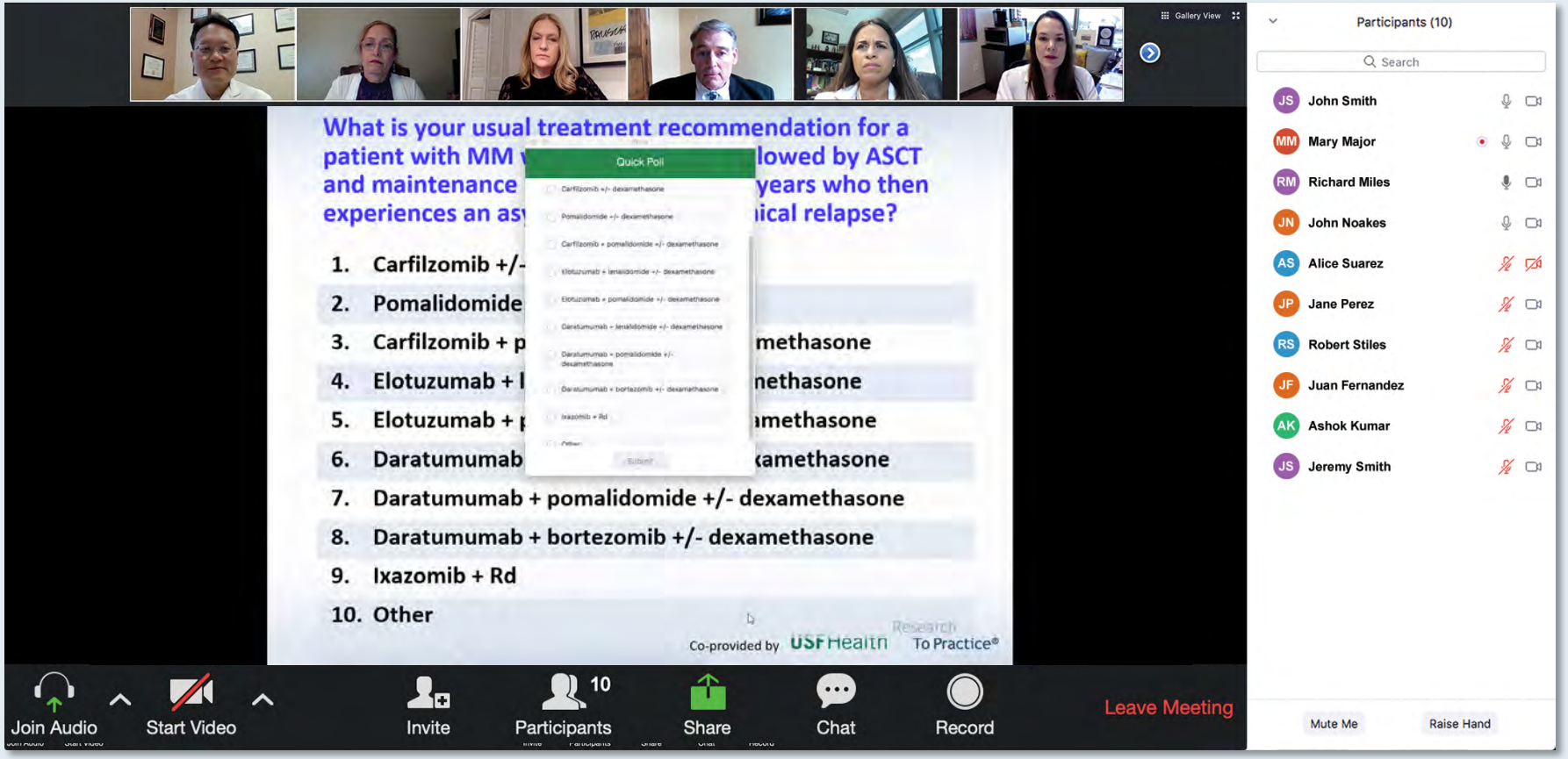

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- Module 1: PARP inhibitors — Maintenance therapy
- Module 2: PARP inhibitors — Combination with anti-PD-1/PD-L1 antibodies
- Module 3: Checkpoint inhibitors
- Module 4: Mirvetuximab soravtansine

Treatment of Endometrial and Cervical Cancers

- Module 5: Endometrial cancer — Immune checkpoint inhibitors +/- lenvatinib
- Module 6: Cervical cancer — Antibody-drug conjugates, immune checkpoint inhibitors

Agenda

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Module 6: Cervical cancer — Antibody-drug conjugates, immune checkpoint inhibitors

Module 1: PARP inhibitors – Maintenance therapy

- **Key Relevant Data Sets**
  - SOLO-1: Five-year follow-up
  - PRIMA: Niraparib – efficacy by BRCA and HR status
  - OVARIO: Niraparib + bevacizumab

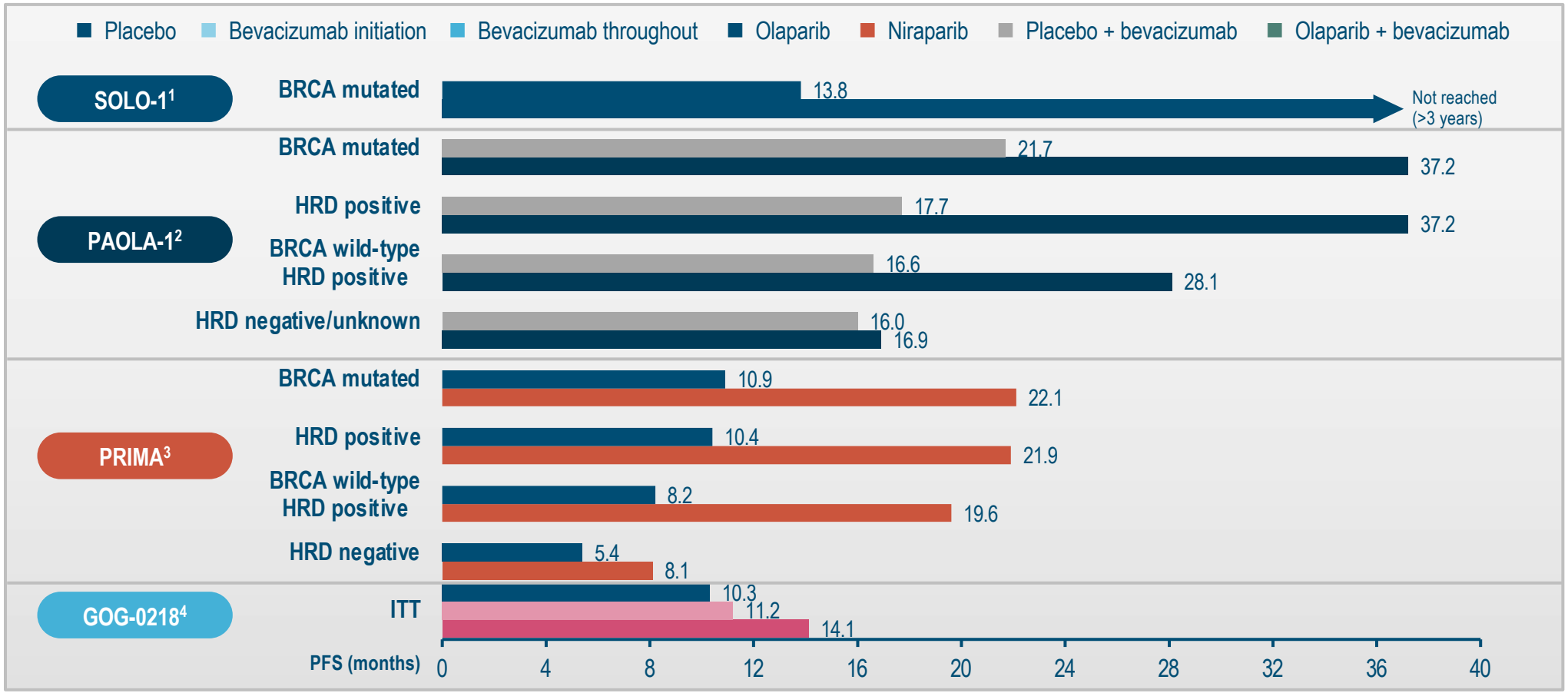
Phase III First-Line Maintenance Trials

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

Courtesy of Shannon N Westin, MD, MPH

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

SUMMARY OF APPROVED MAINTENANCE STUDIES IN THE FIRST-LINE



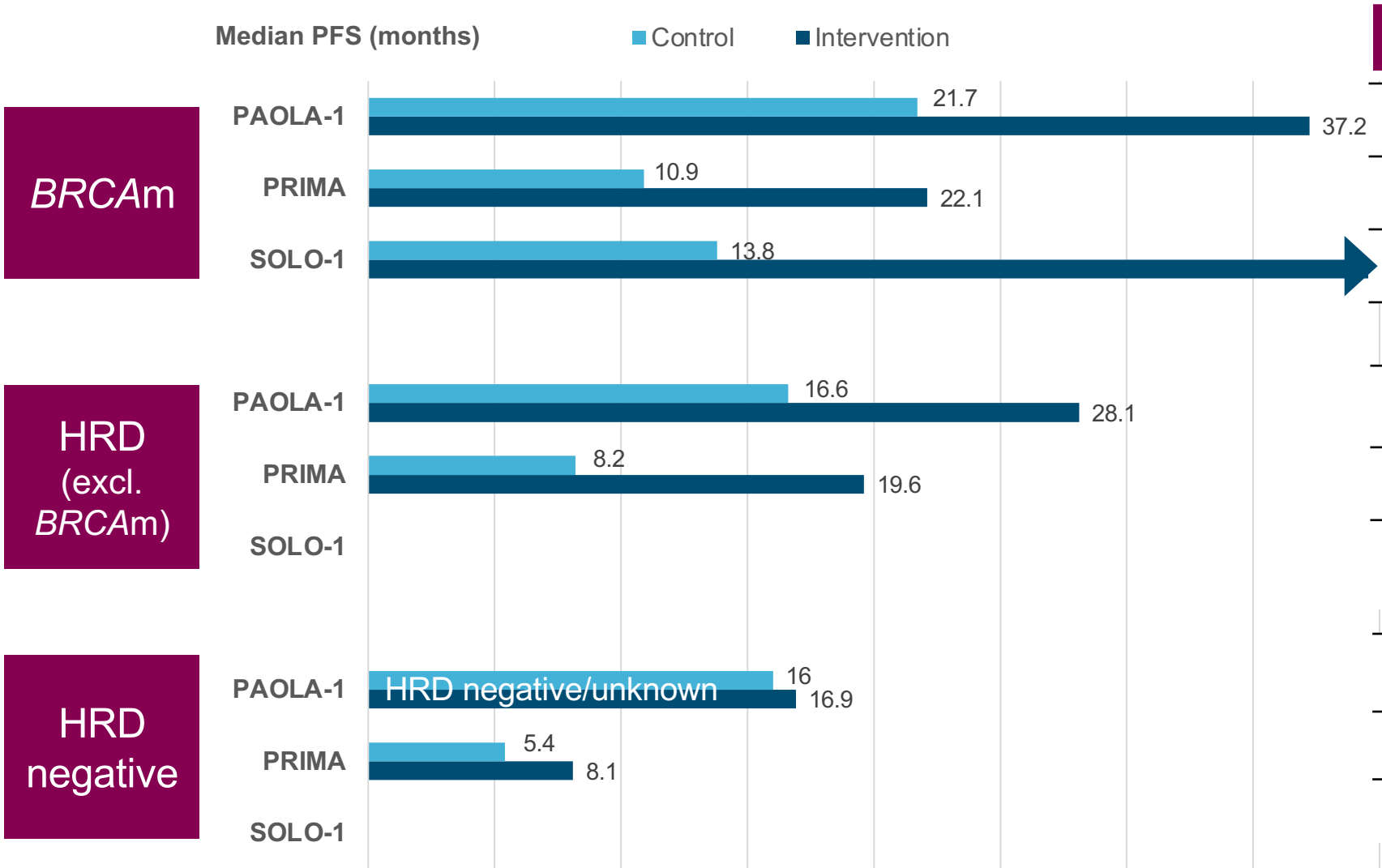
Comparisons across trials should not be made as trials were not head-to-head.

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

PREDICTIVE BIOMARKER: BRCA-MUTATION



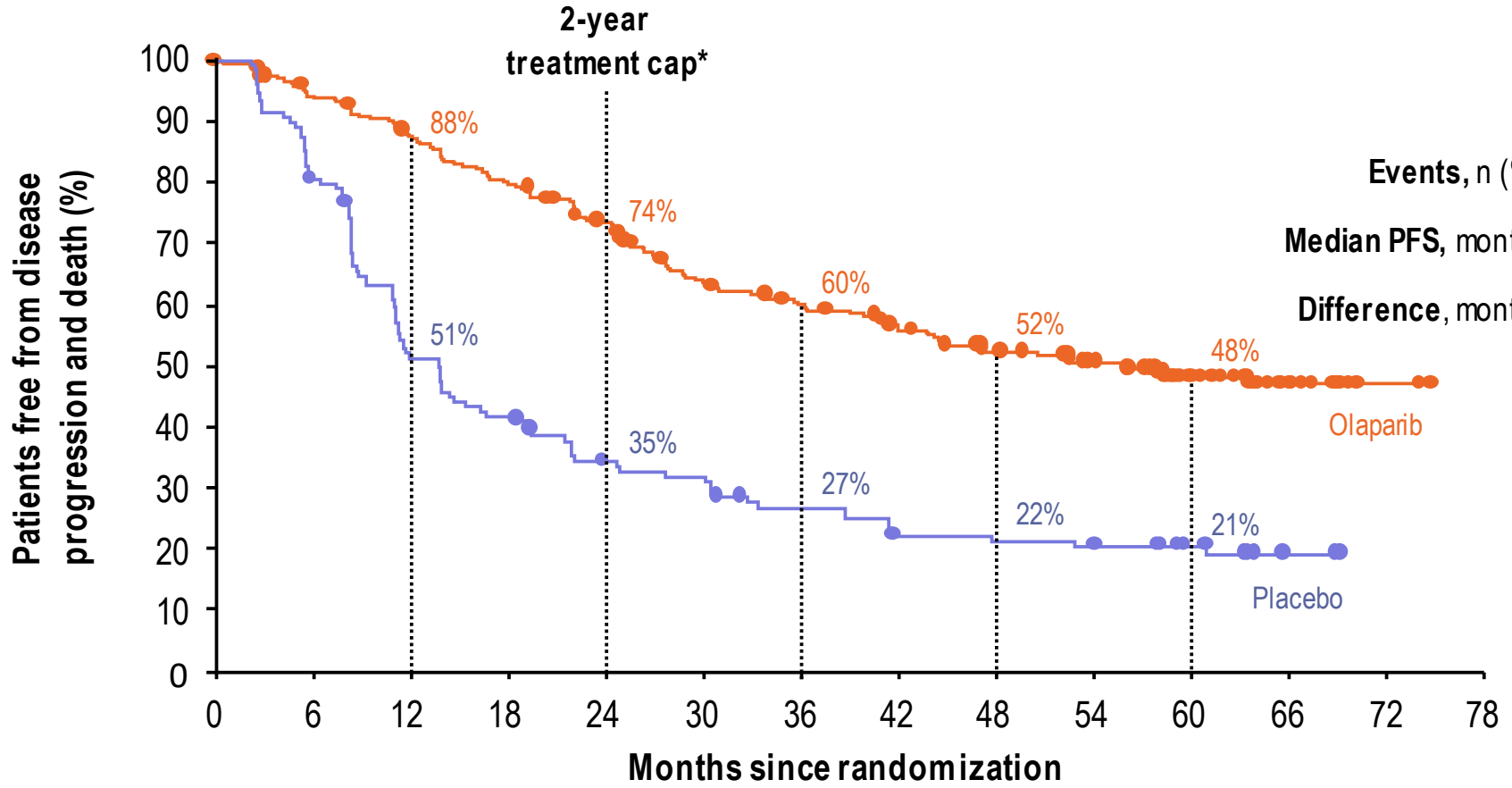
Δ mPFS (mo)	HR
15.5	0.31
11.2	0.40
NE	0.30
11.5	0.43
11.4	0.50
0.9	0.92
2.7	0.68

BRCA = breast cancer susceptibility gene; BRCAm = BRCA mutation; HRD = homologous recombination deficiency; mPFS = median progression-free survival; PARP = poly ADP-ribose polymerase.

1. Moore K et al. N. Engl. J. Med. 2018;379:2495-2505; 2. Gonzalez-Martin A, et al. N Engl J Med. 2019;381(25):2391-2402; 3. Gonzalez-Martin A, et al. Presented at: ESMO; 27 September–1 October 2019; Barcelona, Spain. Abstract LBA1;
4. Ray-Coquard I, et al. N Engl J Med. 2019;381:2416-28; 5. Ray-Coquard I, et al. Presented at: ESMO; 27 September–1 October 2019; Barcelona, Spain. Abstract LBA2

Courtesy of Robert L Coleman, MD

SOLO-1: PFS benefit of maintenance Olaparib was sustained beyond the end of treatment



	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

No. at risk

Olaparib	260	229	212	194	173	140	129	115	101	91	58	30	2	0
Placebo	131	103	65	53	41	38	30	24	23	22	16	3	0	

*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

Courtesy of Robert L Coleman, MD

VIRTUAL 2020 ESMO congress

SOLO-1

Secondary efficacy outcomes* support the observed PFS benefit

	Overall		Patients in CR at baseline	
PFS2	Olaparib (n=260)	Placebo (n=131)	Olaparib (n=189)	Placebo (n=101)
Events, n (%)	80 (31)	61 (47)	49 (26)	45 (45)
Event free at 5 years, %	64	41	68	44
Median, months	NR	42.1	NR	52.9
	HR 0.46 (95% CI 0.33–0.65)		**HR 0.48** (95% CI 0.32–0.71)	
TSST				
Events, n (%)	95 (37)	77 (59)	64 (34)	56 (55)
Event free at 5 years, %	62	36	65	39
Median, months	NR	40.7	NR	47.7
	HR 0.46 (95% CI 0.34–0.63)		**HR 0.50** (95% CI 0.35–0.72)	

Safety profile remained consistent with the primary DCO

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

*Measured from randomization. AE, adverse event; AML, acute myeloid leukaemia; CR, complete response; MDS, myelodysplastic syndrome. DCO: 5 March 2020

Banerjee, ESMO 2020

Courtesy of Robert L Coleman, MD

Myelodysplastic syndrome and acute myeloid leukaemia in patients treated with PARP inhibitors: a safety meta-analysis of randomised controlled trials and a retrospective study of the WHO pharmacovigilance database

Pierre-Marie Morice, Alexandra Leary, Charles Dolladille, Basile Chrétien, Laurent Poulain, Antonio González-Martín, Kathleen Moore, Eileen Mary O'Reilly, Isabelle Ray-Coquard, Joachim Alexandre

PARP inhibitors—understanding the risk of myelodysplastic syndrome and acute myeloid leukaemia

Lancet Haematol **2020;[Epub ahead of print].**

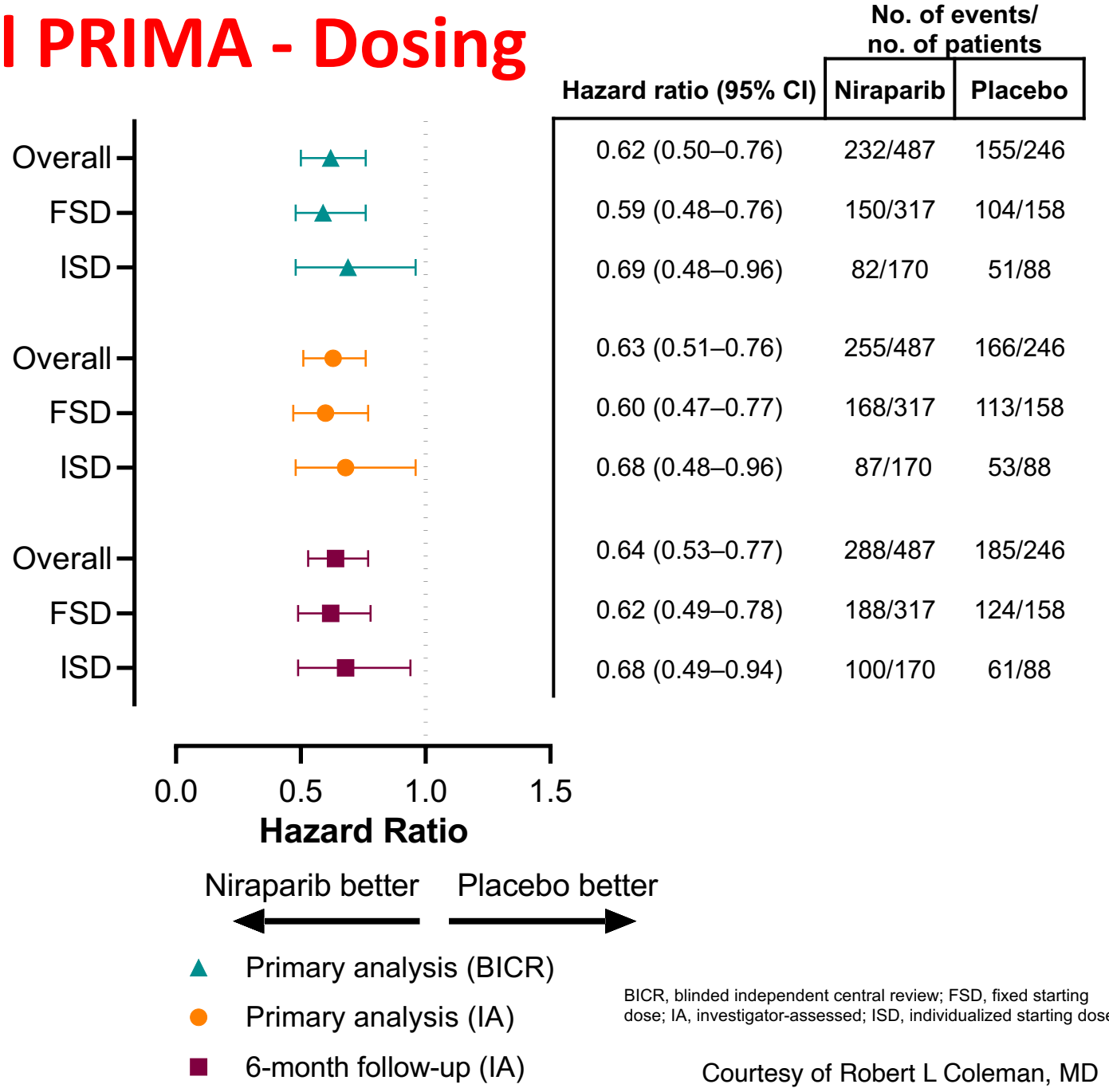
Incidence of MDS and AML Across PARP Inhibitor Groups

- PARP inhibitor groups: 0.73% (95% CI 0.50-1.07; I^2 = 0%, χ^2 p = 0.87; 21 events out of 4,533 patients)
- Placebo groups: 0.47% (0.26-0.85; I^2 = 0%, χ^2 p = 1.00; 3 events out of 2,774 patients)

Morice PM et al. *Lancet Haematol* 2020;[Epub ahead of print].

Progression-Free Survival PRIMA - Dosing

- No evidence of treatment difference was seen between starting dose regimens
  - A test of treatment interactions between FSD and ISD subgroups did not demonstrate statistical significance at the pre-specified 0.10 level (*P*=0.30)
- BICR and IA PFS were highly concordant
- Primary and updated IA PFS demonstrated sustained efficacy of ISD



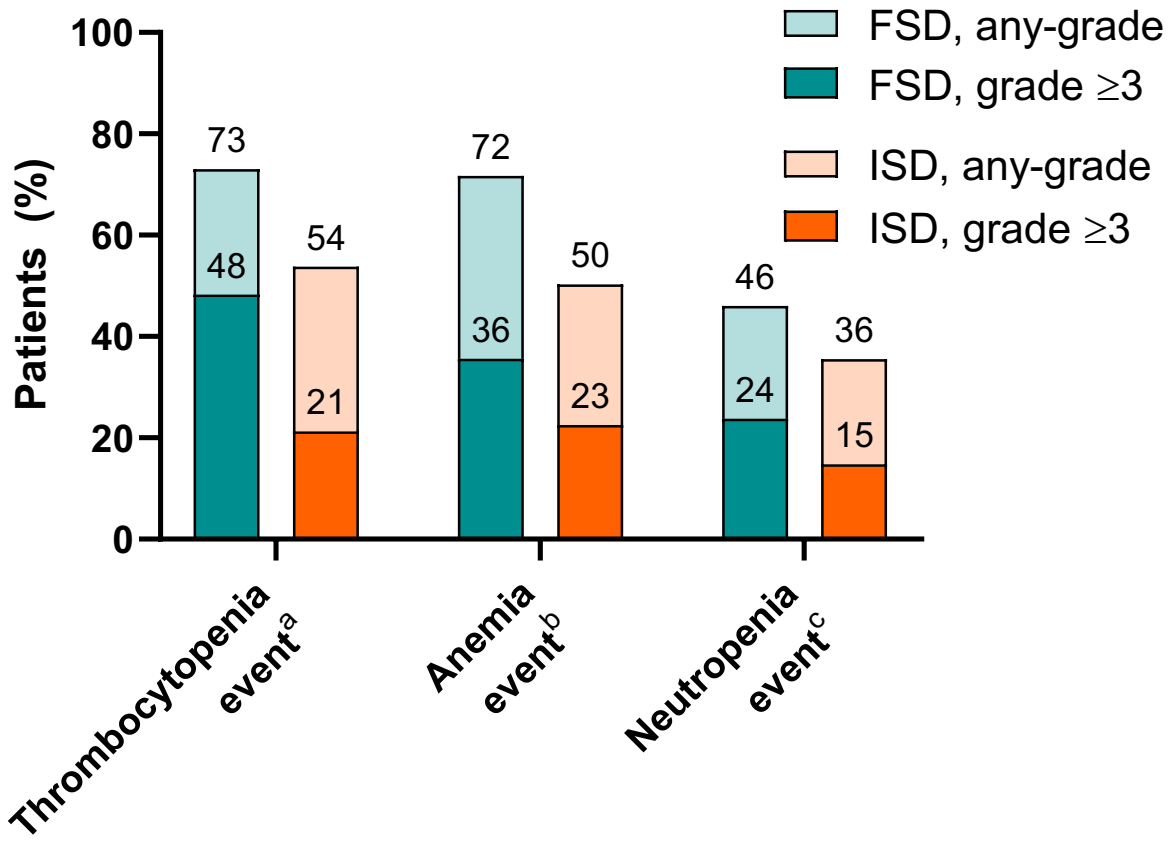
BICR, blinded independent central review; FSD, fixed starting dose; IA, investigator-assessed; ISD, individualized starting dose.

Graybill, IGCS 2020

Courtesy of Robert L Coleman, MD

PRIMA: Safety

- Incidence of any-grade and grade ≥3 hematological TEAEs were reduced with ISD
  - Grade ≥3 thrombocytopenia events reduced from 48.3% to 21.3%
  - Grade ≥3 anemia events reduced from 35.6% to 22.5%
  - Grade ≥3 neutropenia events reduced from 23.8 to 14.8%

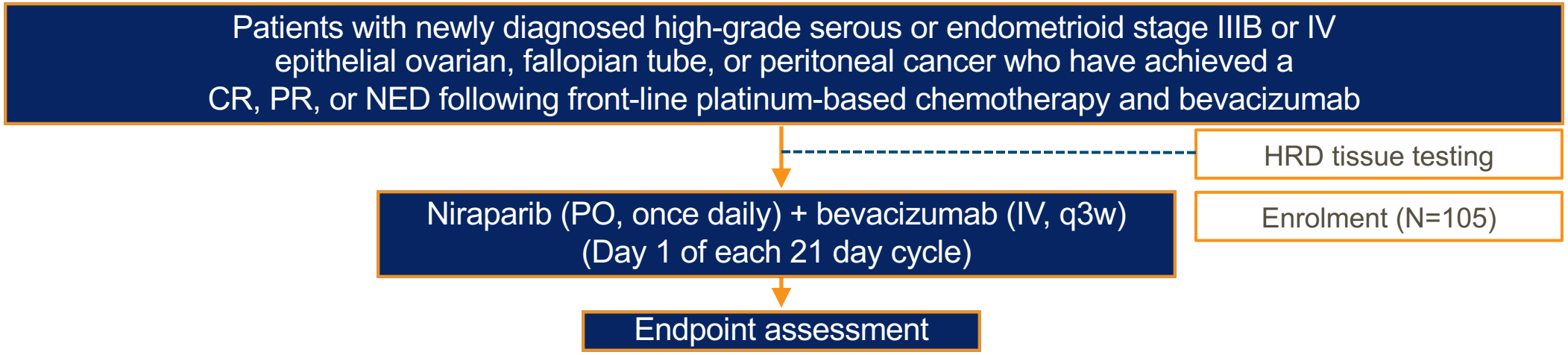


Graybill, IGCS 2020

[a]Includes thrombocytopenia and platelet count decreased; [b]Includes anemia and hemoglobin decreased; [c]Includes neutropenia and neutrophil count decreased.
FSD, fixed starting dose; ISD, individualized starting dose.

Courtesy of Robert L Coleman, MD

OVARIO – Trial design and endpoints



Primary endpoint	• Progression-free survival (PFS) rate at 18 months
Key secondary endpoints	• PFS • Overall survival (OS) • Time to first subsequent therapy (TFST) • Time to second subsequent therapy (TSST) • Safety, Incidence of treatment-emergent adverse events (TEAEs) • Functional assessment of cancer therapy – ovarian cancer symptom index (FOSI) • RECIST or CA-125 PFS by RECIST v1.1 per investigator or CA-125 measurement using GCIG criteria
Exploratory endpoints	• PFS rate at 6 and 12 months

Hardesty MM et al. SGO 2020;Abstract 4.

Courtesy of Robert L Coleman, MD

A 60-year-old woman with Stage IIIC ovarian cancer and a germline BRCA mutation is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

1. Carboplatin/paclitaxel
2. Carboplatin/paclitaxel → olaparib
3. Carboplatin/paclitaxel → niraparib
4. Carboplatin/paclitaxel + bevacizumab → olaparib
5. Carboplatin/paclitaxel + bevacizumab → niraparib
6. Carboplatin/paclitaxel + bevacizumab → bevacizumab/olaparib
7. Carboplatin/paclitaxel + bevacizumab → bevacizumab/niraparib
8. Other

A 60-year-old woman with Stage IIIC ovarian cancer (BRCA wild type, HRD-negative) is s/p optimal debulking surgery with a normal CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

1. Carboplatin/paclitaxel
2. Carboplatin/paclitaxel → olaparib
3. Carboplatin/paclitaxel → niraparib
4. Carboplatin/paclitaxel + bevacizumab → olaparib
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6. Carboplatin/paclitaxel + bevacizumab → bevacizumab/olaparib
7. Carboplatin/paclitaxel + bevacizumab → bevacizumab/niraparib
8. Other

A 60-year-old woman with Stage IIIC ovarian cancer and a somatic BRCA mutation is s/p suboptimal debulking surgery with an elevated CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy?

1. Carboplatin/paclitaxel
2. Carboplatin/paclitaxel → olaparib
3. Carboplatin/paclitaxel → niraparib
4. Carboplatin/paclitaxel + bevacizumab → olaparib
5. Carboplatin/paclitaxel + bevacizumab → niraparib
6. Carboplatin/paclitaxel + bevacizumab → bevacizumab /olaparib
7. Carboplatin/paclitaxel + bevacizumab → bevacizumab /niraparib
8. Other

Agenda

Management of Ovarian Cancer

Module 1: PARP inhibitors — Maintenance therapy

Module 2: PARP inhibitors — Combination with anti-PD-1/PD-L1 antibodies

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Module 4: Mirvetuximab soravtansine

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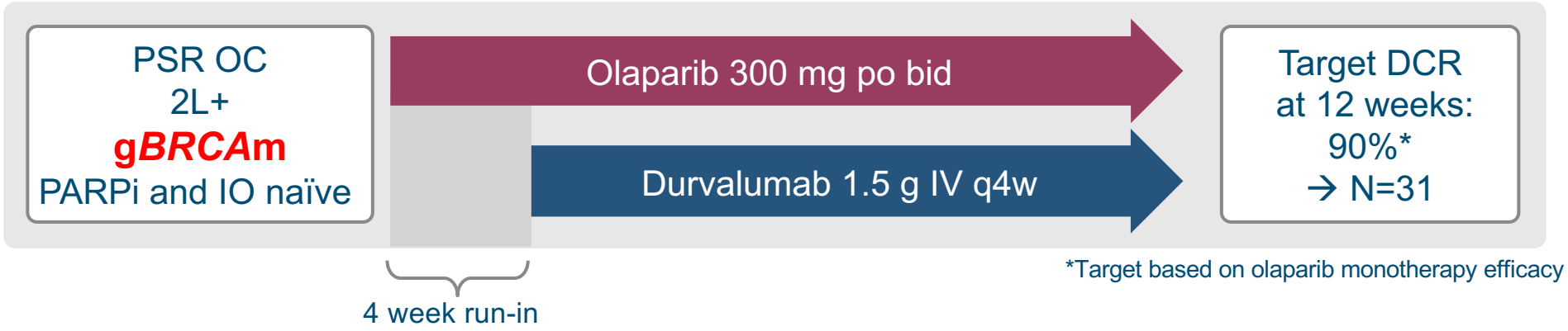
Module 6: Cervical cancer — Antibody-drug conjugates, immune checkpoint inhibitors

Module 2: PARP inhibitors – Combination with anti-PD-1/PD-L1 antibodies

- **Key Relevant Data Set**
  - MEDIOLA: Olaparib + durvalumab +/- bevacizumab for relapsed ovarian cancer
  - TOPACIO: Niraparib + pembrolizumab for platinum-resistant ovarian cancer

MEDIOLA

Initiation of therapy at the time of relapse



- Primary endpoints: DCR at 12 weeks, safety
- Secondary endpoints: DCR at 28 weeks, ORR, DoR, PFS, OS, PD-L1 expression
- Exploratory endpoints: TILs

DCR, disease control rate; DoR, duration of response; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; po, oral; TILs, tumor-infiltrating lymphocytes

Lancet Onc 2020

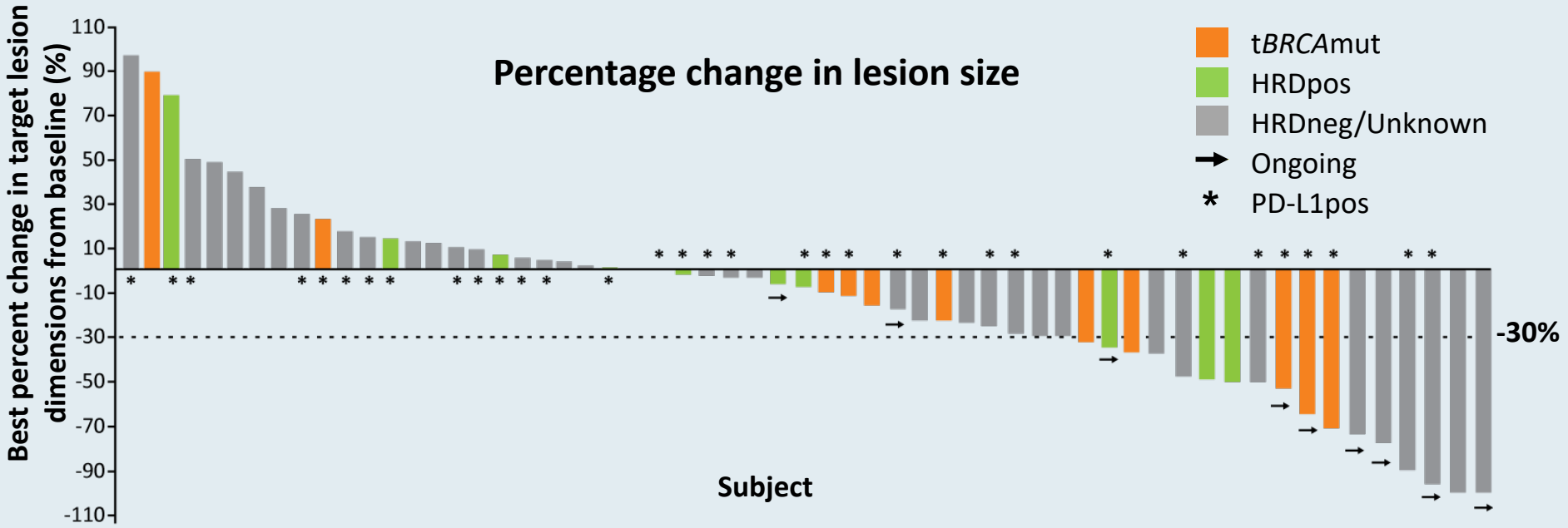
Courtesy of Robert L Coleman, MD

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

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

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

TOPACIO (KEYNOTE-162): A Phase I/II Study of Niraparib with Pembrolizumab for Recurrent, Platinum-Resistant OC



Response	All patients	tBRCAmut	HRD-pos	tBRCAwt	HRD-neg
ORR	18%	18%	14%	19%	19%

Konstantinopoulos P et al. *JAMA Oncol* 2019;5(8):1141-49; ASCO 2018;Abstract 106.

Agenda

Management of Ovarian Cancer

Module 1: PARP inhibitors — Maintenance therapy

Module 2: PARP inhibitors — Combination with anti-PD-1/PD-L1 antibodies

Module 3: Checkpoint inhibitors

Module 4: Mirvetuximab soravtansine

Treatment of Endometrial and Cervical Cancers

Module 5: Endometrial cancer — Immune checkpoint inhibitors +/- lenvatinib

Module 6: Cervical cancer — Antibody-drug conjugates, immune checkpoint inhibitors

Module 3: Checkpoint inhibitors

- **Key Relevant Data Sets**
  - KEYNOTE-100: Pembrolizumab for advanced recurrent ovarian cancer
  - NRG Oncology study: Nivolumab +/- ipilimumab for recurrent ovarian cancer

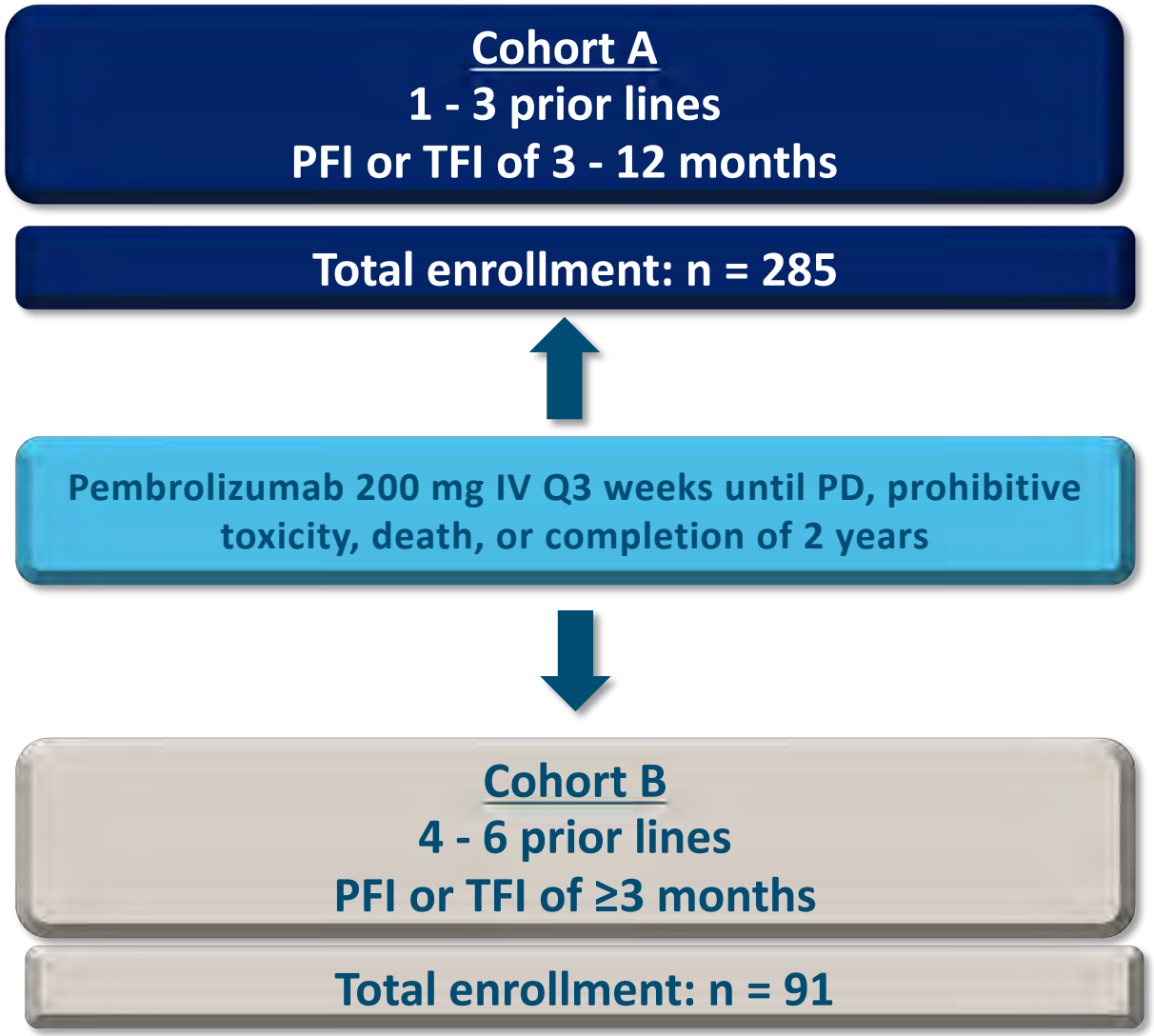
KEYNOTE-100 (NCT02674061): Phase 2, Two-Cohort Study of Pembrolizumab for Recurrent Advanced Ovarian Cancer

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:

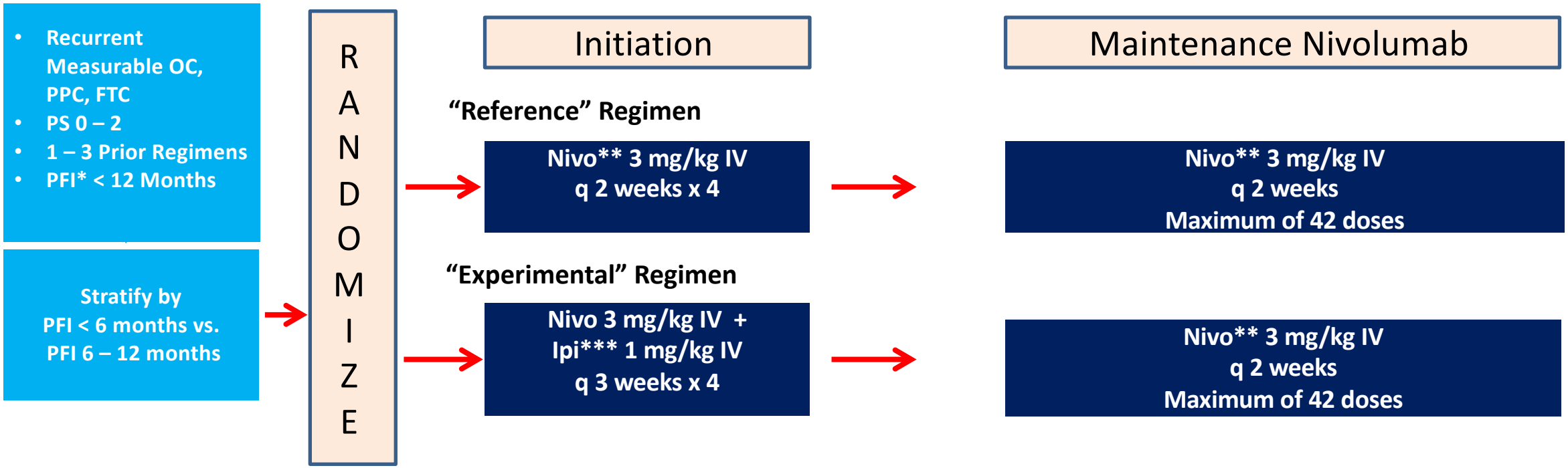
- Mucinous histology
- No bowel obstruction within 3 months
- No active autoimmune disease
- No active CNS metastases and/or carcinomatous meningitis



Courtesy of Robert L Coleman, MD

Matulonis UA, et al. J Clin Oncol. 2018;36(15)5511.; Lederman JA, et al. Ann Oncol. 2018;29(8):vii728.; Matulonis UA, et al. SGO 2019; Abstract 26.; Matulonis UA, et al. Ann Oncol. 2019;30(7)L1080-1087.

Final Preview of NRG GY003: Phase II Randomized Trial of Nivolumab with or without Ipilimumab in Patients with Persistent or Recurrent Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancer



Courtesy of Robert L Coleman, MD

Burger, IGCS, Kyoto, Japan 2018

GY003: Phase II (Ipi/nivo vs nivo)

- N = 100 patients
  - 49 pts Nivo “control”
  - 51 pts Ipi/Nivo
- Demographics
  - Median age: 62
  - HGSOC: 82%
- Response window 6 months
- Gr 3+ toxicity
  - 27 (55%) Nivolumab
  - 34 (67%) in combination
  - No Grade 5 events

Outcome	Nivo	Ipi + Nivo
Response	6/49 **(12%)**	16/51 **(31%)**
HR_{PFS}	0.53 (0.34-0.82)	
HR_{Death}	0.79 (0.44-1.42)	

Courtesy of Robert L Coleman, MD

Zamairin J Clin Oncol 2020

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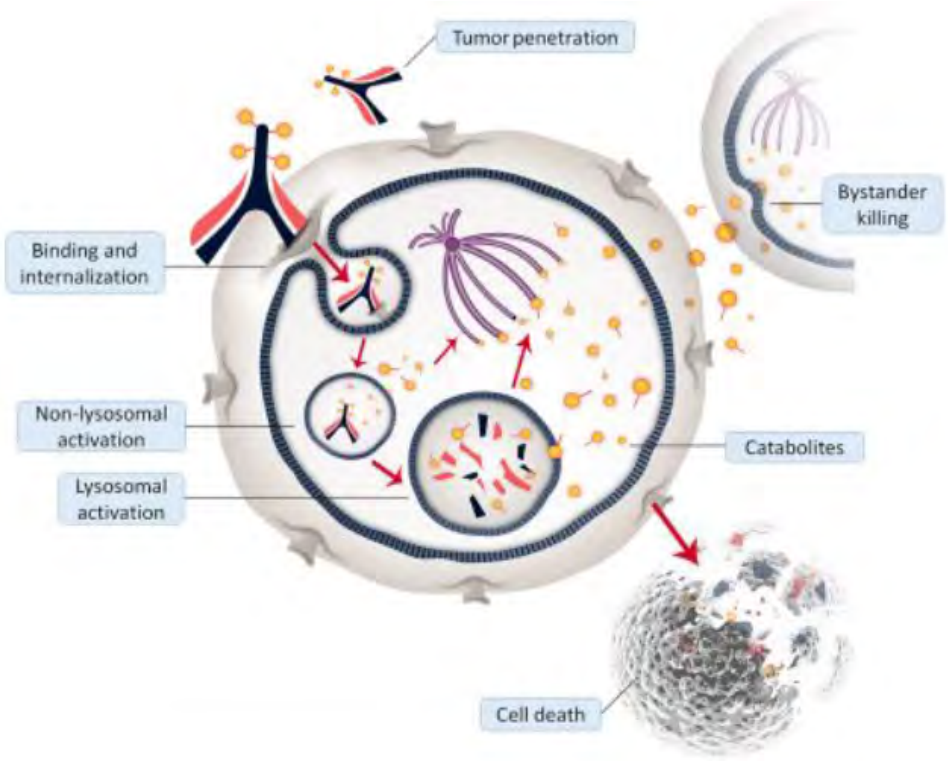
Module 4: Mirvetuximab soravtansine

- **Key Relevant Data Set**
  - Mirvetuximab soravtansine + bevacizumab for platinum-resistant ovarian cancer

Mirvetuximab Soravtansine (MIRV) In Combination With Bevacizumab In Patients With Platinum Agnostic Ovarian Cancer



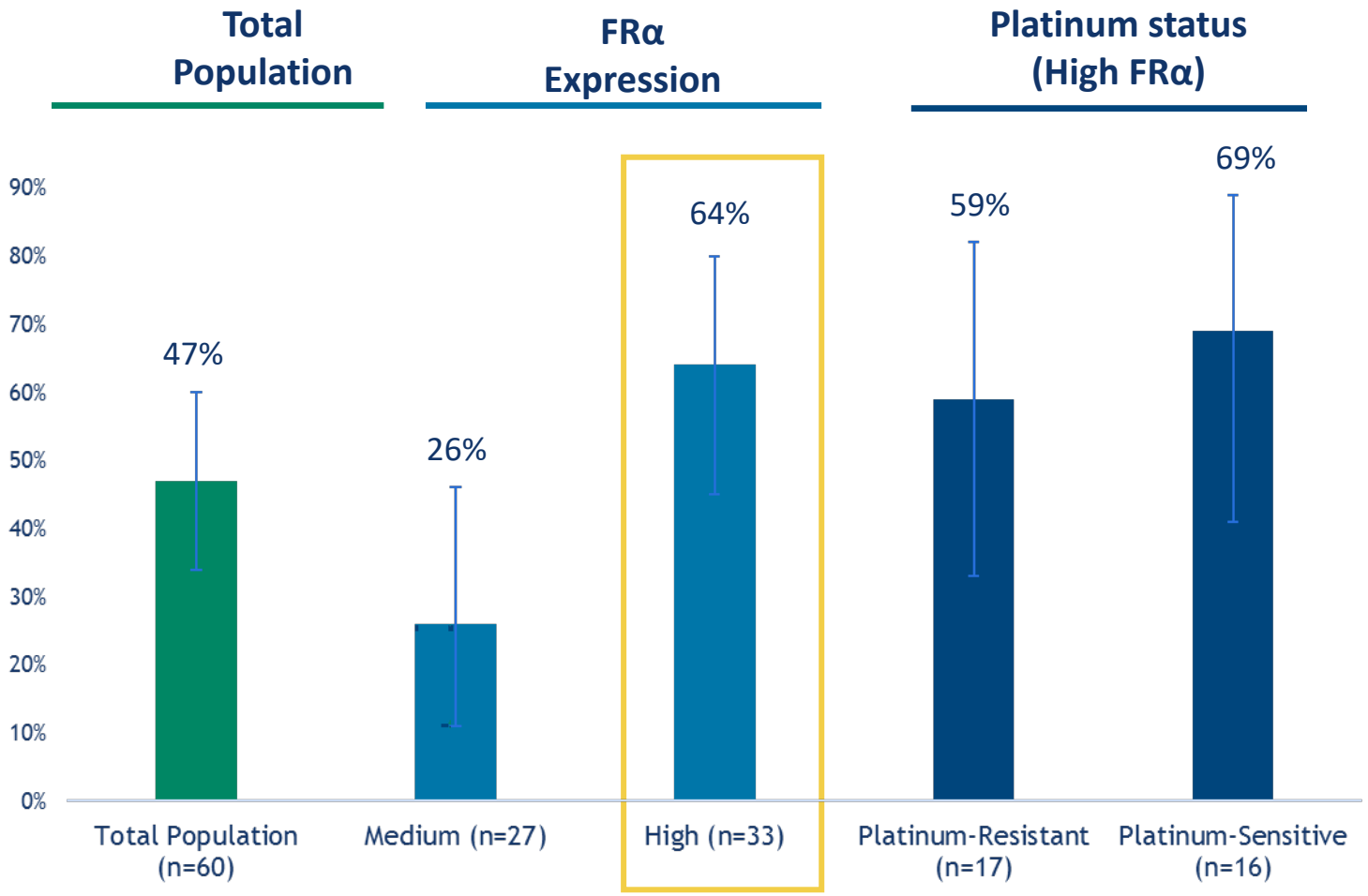
Enrolled patients with folate receptor medium to high expressing tumors
Allowed both plat sens and plat resistant tumors

Characteristic	N=60
Age (median)	60 (44-83)
ECOG PS	
0	75%
1	25%
# prior therapies	
1	33%
2	37%
≥3	30%
FR alpha	
med	45%
high	55%
Prior regimens	
Platinums	100%
Taxanes	98%
Bevacizumab	40%
PARPi	32%
Platinum Free Interval	
< 6 months	53%
6-12 months	33%
> 12 months	13%

Courtesy of Robert L Coleman, MD

Gilbert et al. ASCO 2020 (virtual) Chicago Abstract 6004

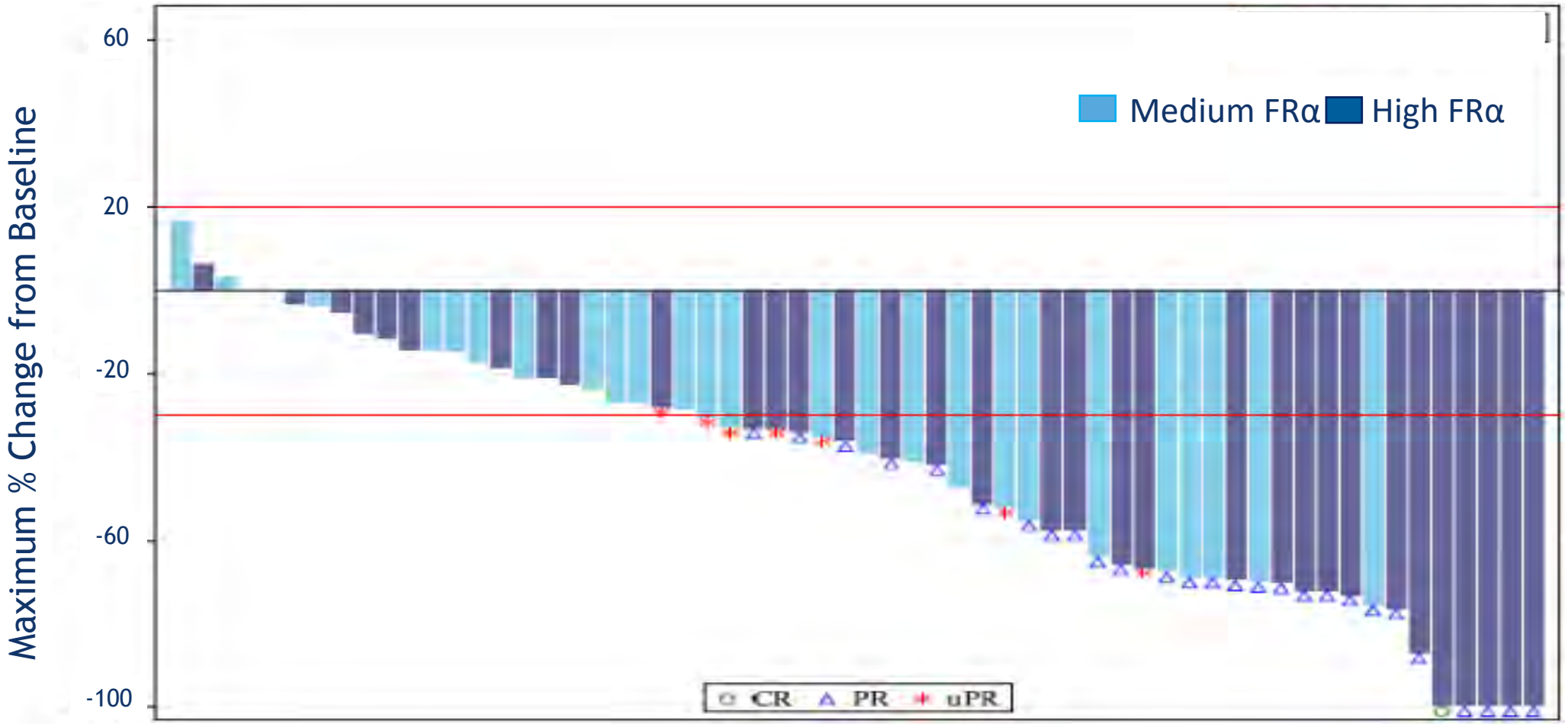
ORR by FRα Expression and Platinum Status with MIRV/Bev



- 47% ORR (28/60) for overall cohort
- 64% ORR (21/33) in high FRα pts
  - 59% ORR (10/17) in-platinum-resistant subset
  - 69% ORR (11/16) in platinum-sensitive subset
- With a median follow-up of 8.5 months, the duration of response and progression free survival data are immature

Courtesy of Robert L Coleman, MD

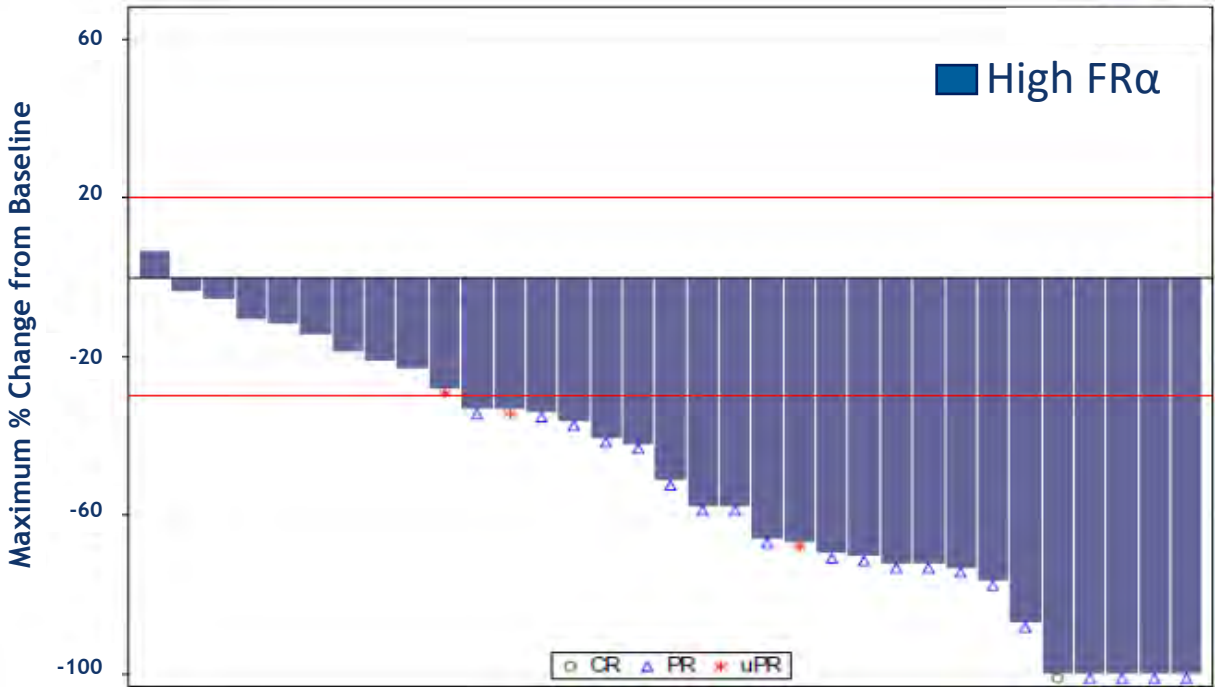
Maximum Tumor Change (%) in Target Lesions from Baseline with MIRV/Bev

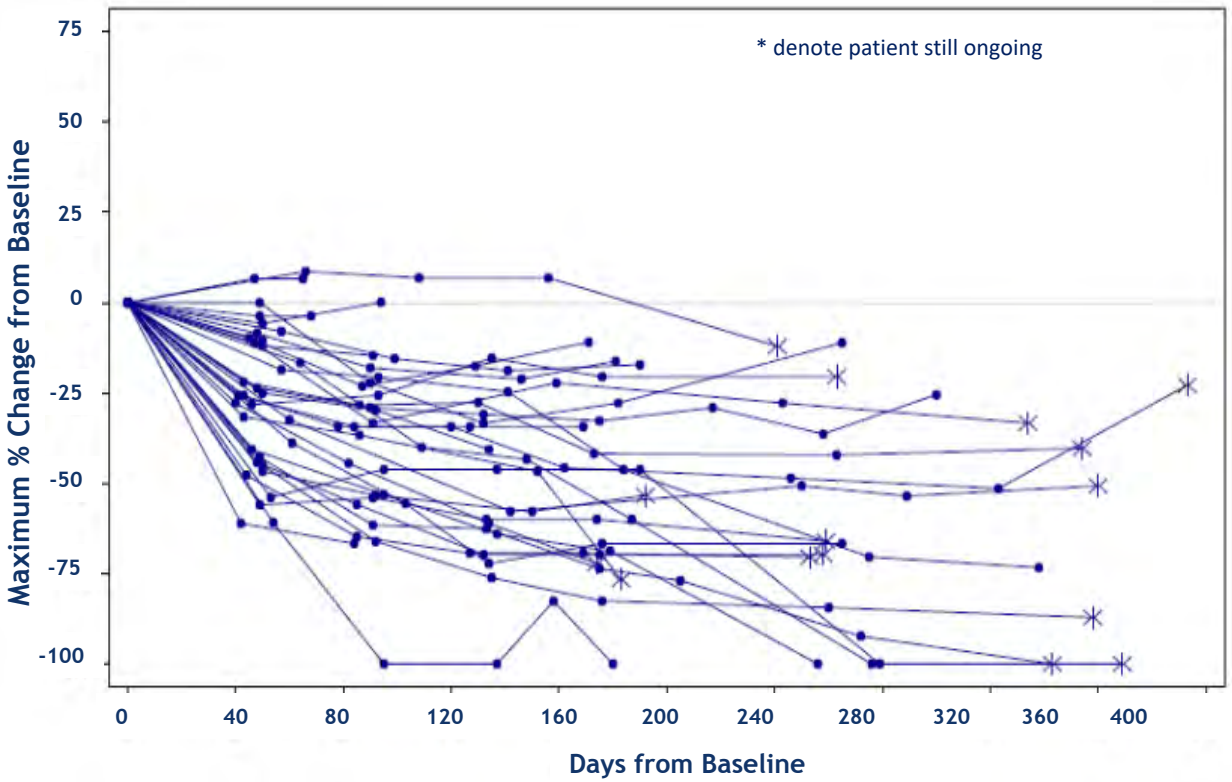


- 92% (55/60) of patients demonstrated tumor reduction
- Deeper tumor responses in high FRα pts

Courtesy of Robert L Coleman, MD

Depth and Duration of Tumor Reduction with MIRV/Bev in High FRα Patients





- More durable tumor reductions in high FRα, with 46% of high FRα (vs 26% of medium FRα) remaining on treatment
- With a median duration of follow-up of 8.5 months, duration of response (DOR) and progression free survival (PFS) are immature

Courtesy of Robert L Coleman, MD

MIRV/Bev: Treatment-Related Emergent Adverse Events

	All Grades		Grade 3/4	
Adverse Event	N	%	No.	%
Diarrhea	41	68	1	2
Blurred vision	38	63	1	2
Fatigue	35	58	3	5
Nausea	33	55	0	0
Peripheral neuropathy*	26	43	1	2
Keratopathy†	26	43	0	0
Dry eye	21	35	3	5
Headache	21	35	0	0
Decreased appetite	19	32	0	0
Hypertension	17	28	7	12
AST increased	17	28	2	3
Vomiting	16	27	0	0
Abdominal pain	16	27	0	0
Neutropenia	14	23	6	10
ALT increased	13	22	3	5
Dysphonia	13	22	0	0
Visual acuity reduced	13	22	0	0
Thrombocytopenia	13	22	2	3

AST, aspartate aminotransferase; ALT, alanine aminotransferase;
*Includes neuropathy peripheral, peripheral sensory neuropathy, paresthesia, and hypoesthesia

- Most AEs were low grade
  - GI and Ocular
  - Ocular AE class effect of ADC but manageable with local drops
- Grade 3+ events were infrequent
  - 12% hypertension
  - 10% myelosuppression
  - Pneumonitis
    - Grade 3: None
    - Grade 1: 3pts
    - Grade 2: 1pt
- Thirteen patients (22%) discontinued bevacizumab and/or MIRV due to treatment-related AEs

Gilbert L et al. ASCO 2020;Abstract 6004.

MIRV/Bev: Treatment-Related Emergent Adverse Events

- Most AEs were low grade:
  - GI and ocular
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Gilbert L et al. ASCO 2020;Abstract 6004.

Agenda

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Module 6: Cervical cancer — Antibody-drug conjugates, immune checkpoint inhibitors

Module 5: Endometrial cancer — Immune checkpoint inhibitors with and without lenvatinib

- **Key Relevant Data Sets**
  - KEYNOTE-158: Pembrolizumab for non-CRC MSI-high/dMMR cancers
  - KEYNOTE-146: Lenvatinib + pembrolizumab for advanced endometrial cancer (EC)
  - LEAP-005: Lenvatinib + pembrolizumab for previously treated advanced solid tumors
  - Avelumab for recurrent EC
  - Dostarlimab for dMMR recurrent EC
  - ENGOT-EN6: Dostarlimab + chemotherapy for recurrent or primary advanced EC

rapid communications

Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/ Mismatch Repair–Deficient Cancer: Results From the Phase II KEYNOTE-158 Study

Aurelien Marabelle, MD, PhD[1]; Dung T. Le, MD[2]; Paolo A. Ascierto, MD[3]; Anna Maria Di Giacomo, MD[4]; Ana De Jesus-Acosta, MD[2]; Jean-Pierre Delord, MD, PhD[5]; Ravit Geva, MD, MSc[6]; Maya Gottfried, MD[7]; Nicolas Penel, MD, PhD[8]; Aaron R. Hansen, MBBS[9]; Sarina A. Piha-Paul, MD[10]; Toshihiko Doi, MD, PhD[11]; Bo Gao, MBBS, PhD[12]; Hyun Cheol Chung, MD, PhD[13]; Jose Lopez-Martin, MD, PhD[14]; Yung-Jue Bang, MD, PhD[15]; Ronnie Shapira Frommer, MD[16]; Manisha Shah, MD[17]; Razi Ghori, PhD[18]; Andrew K. Joe, MD[18]; Scott K. Pruitt, MD, PhD[18]; and Luis A. Diaz Jr, MD[19]

J Clin Oncol 2020;38(1):1-10

Courtesy of Richard T Penson, MD, MRCP

KEYNOTE-158: Tumor Type Specific Antitumor Activity

TABLE 3. Antitumor Activity for Tumor Types With Greatest Enrollment

Tumor Type	No.	CR, No.	PR, No.	ORR, % (95% CI)	Median PFS, Months (95% CI)	Median OS, Months (95% CI)	Median DOR, Months (range)
Endometrial	49	8	20	57.1 (42.2 to 71.2)	25.7 (4.9 to NR)	NR (27.2 to NR)	NR (2.9 to 27.0+)
Gastric	24	4	7	45.8 (25.6 to 67.2)	11.0 (2.1 to NR)	NR (7.2 to NR)	NR (6.3 to 28.4+)
Cholangiocarcinoma	22	2	7	40.9 (20.7 to 63.6)	4.2 (2.1 to NR)	24.3 (6.5 to NR)	NR (4.1+ to 24.9+)
Pancreatic	22	1	3	18.2 (5.2 to 40.3)	2.1 (1.9 to 3.4)	4.0 (2.1 to 9.8)	13.4 (8.1 to 16.0+)
Small intestine	19	3	5	42.1 (20.3 to 66.5)	9.2 (2.3 to NR)	NR (10.6 to NR)	NR (4.3+ to 31.3+)
Ovarian	15	3	2	33.3 (11.8 to 61.6)	2.3 (1.9 to 6.2)	NR (3.8 to NR)	NR (4.2 to 20.7+)
Brain	13	0	0	0.0 (0.0 to 24.7)	1.1 (0.7 to 2.1)	5.6 (1.5 to 16.2)	–

9%

KEYNOTE-100
Matulonis UA, et al. Ann Oncol. 2019;30(7):1080-1087

Marabelle A, et al. J Clin Oncol 2020;38(1):1-10

Courtesy of Richard T Penson, MD, MRCP

KEYNOTE-158: Toxicities

TABLE 4. Incidence of Adverse Events

Adverse Event	Patients (N = 233) Any Grade, No. (%)	Patients (N = 233) Grade 3-4*, No. (%)
Treatment-related adverse events		
Any	151 (64.8)	34 (14.6)
Occurring in ≥ 5% of patients		
Fatigue	34 (14.6)	2 (0.9)
Pruritus	30 (12.9)	0
Diarrhea	28 (12.0)	0
Asthenia	25 (10.7)	1 (0.4)
Hypothyroidism	19 (8.2)	0
Arthralgia	18 (7.7)	0
Nausea	15 (6.4)	0
Rash	12 (5.2)	0

Marabelle A, et al. J Clin Oncol 2020;38(1):1-10

Courtesy of Richard T Penson, MD, MRCP

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):2981-2992

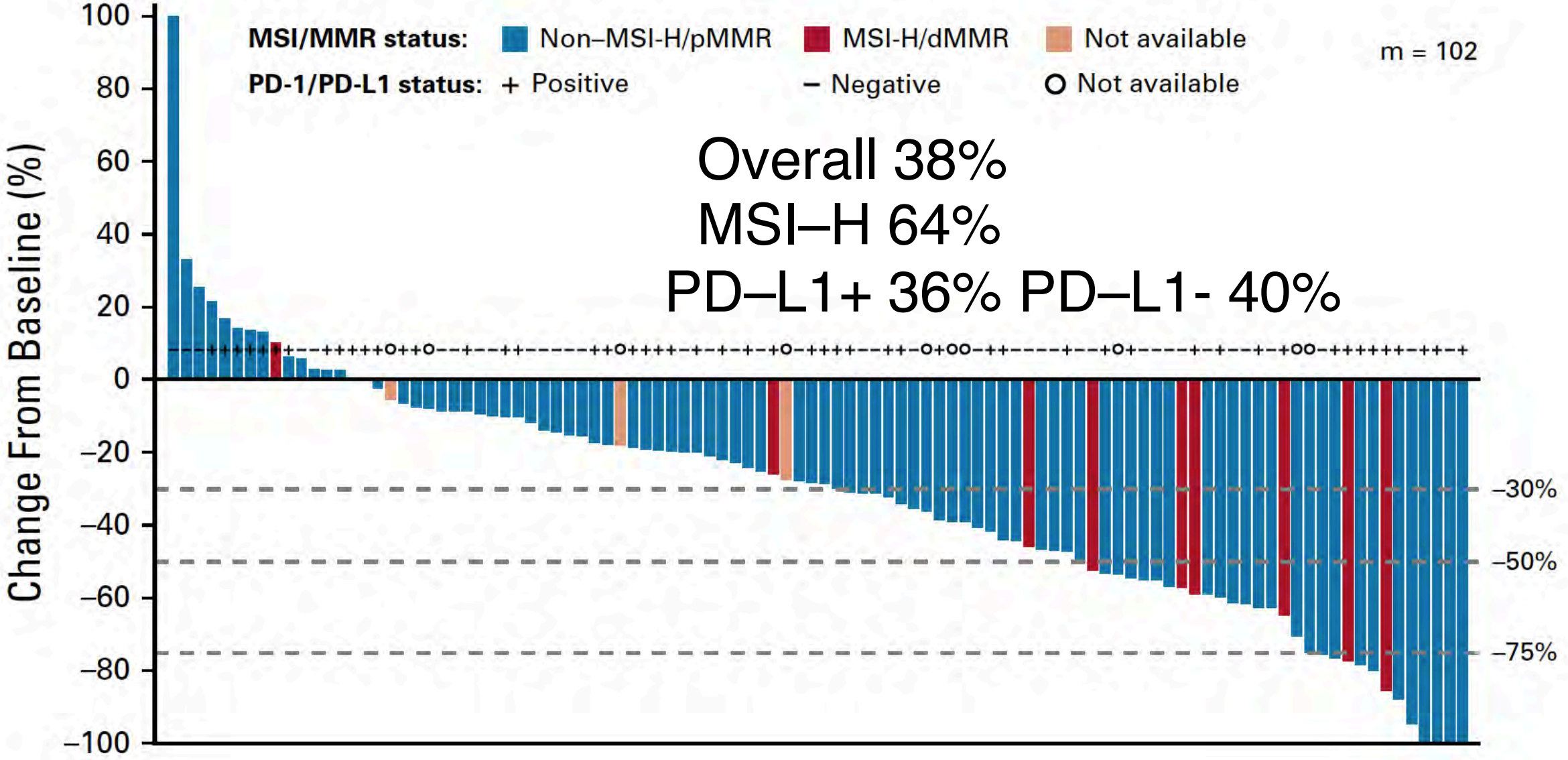
Lenvatinib 20 mg PO QD pembrolizumab 200 mg IV Q21

Primary end point: ORRWk24

n=108

Courtesy of Richard T Penson, MD, MRCP

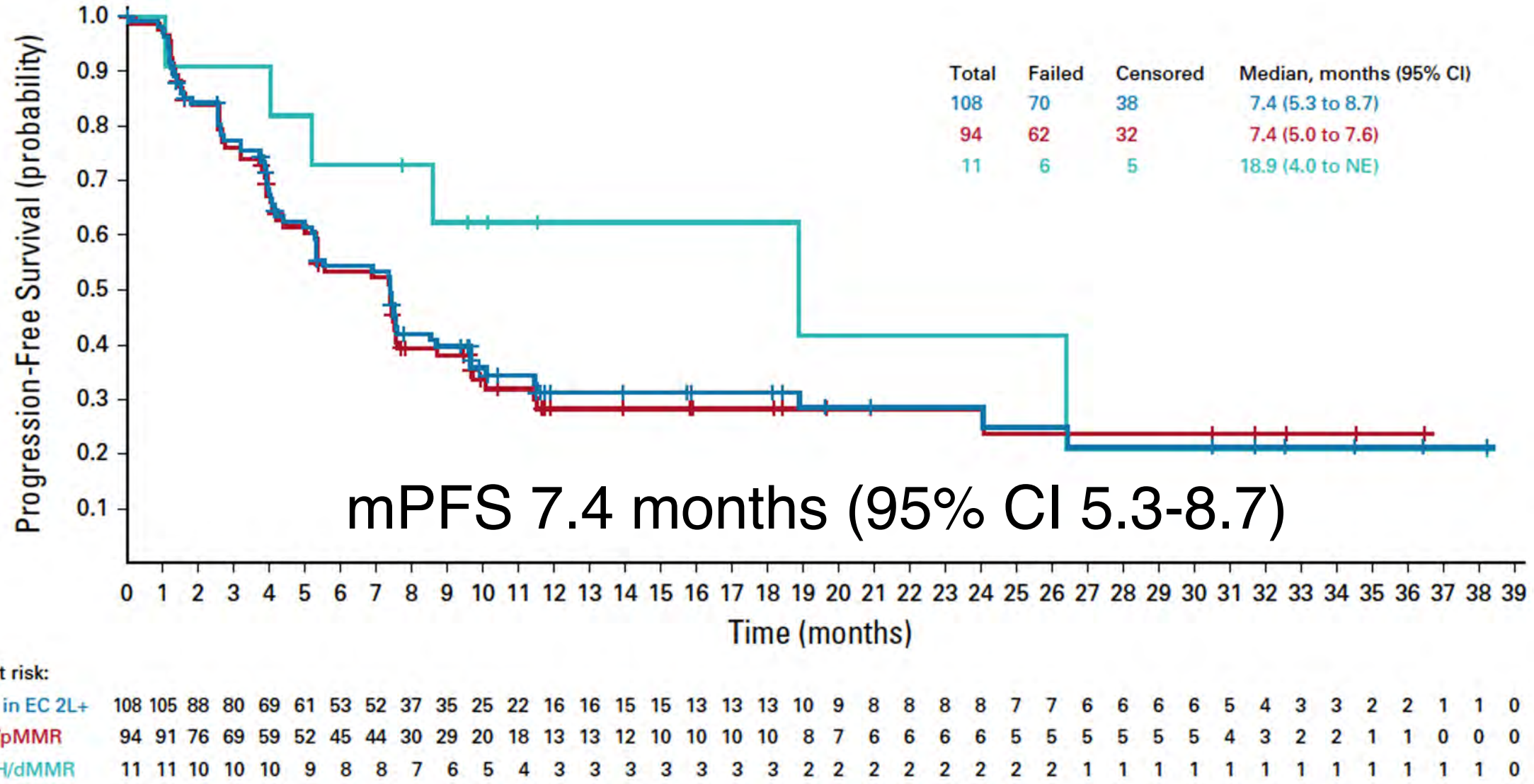
KEYNOTE-146: Objective Response Rate (ORRWk24)



Makker, et al. J Clin Oncol 2020;38(26):2981-2992

Courtesy of Richard T Penson, MD, MRCP

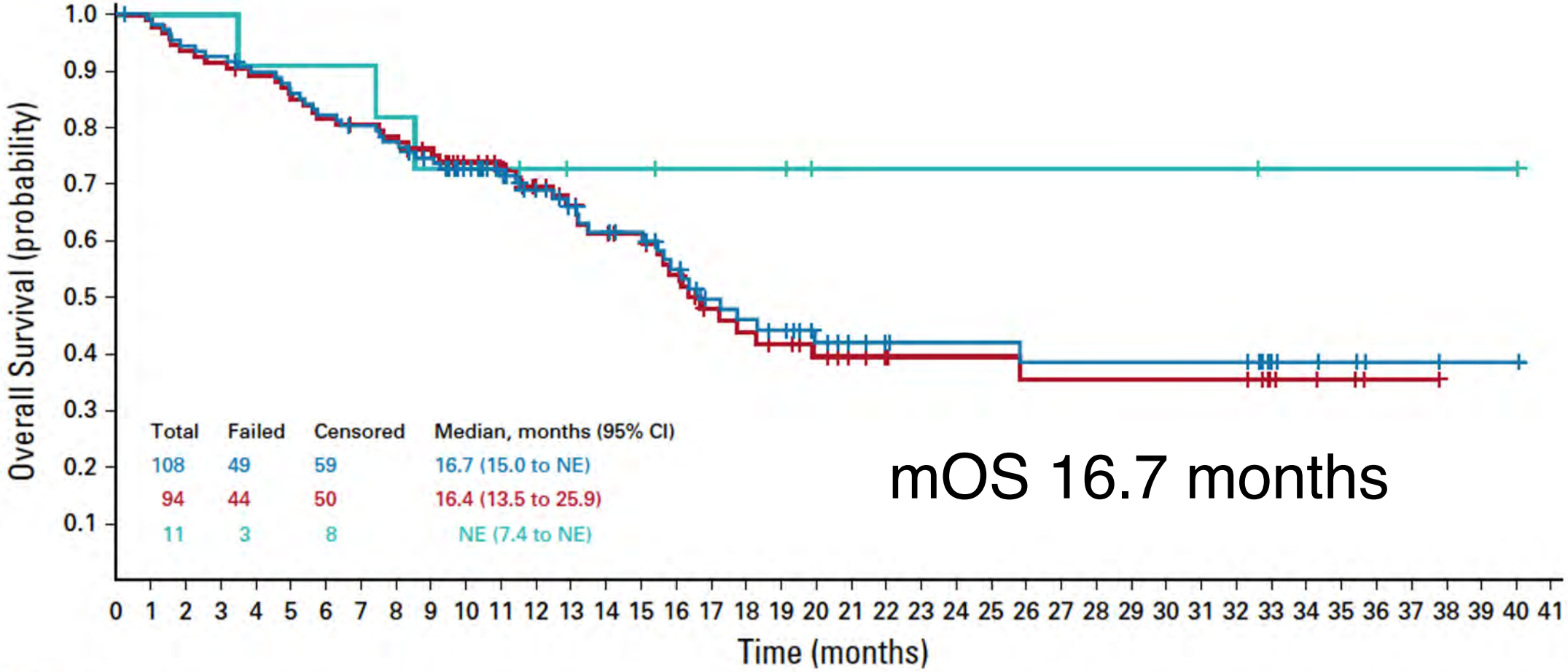
KEYNOTE-146: Progression Free Survival



Makker, et al. J Clin Oncol 2020;38(26):2981-2992

Courtesy of Richard T Penson, MD, MRCP

KEYNOTE-146: Overall Survival



mOS 16.7 months

No. at risk:

Total in EC 2L+	108	106	101	99	95	91	87	84	81	76	66	59	51	45	41	39	33	27	25	23	18	15	13	12	12	12	11	11	11	11	11	11	11	6	5	4	2	2	1	1	1	0
MSS/pMMR	94	92	87	85	82	78	75	73	71	67	57	52	45	40	36	34	29	23	21	19	16	13	11	10	10	10	9	9	9	9	9	9	9	5	4	3	1	1	0	0	0	0
MSI-H/dMMR	11	11	11	11	10	10	10	10	9	8	8	7	6	5	5	5	4	4	4	4	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	0

Makker, et al. J Clin Oncol 2020;38(26):2981-2992

Courtesy of Richard T Penson, MD, MRCP

KEYNOTE-146: Select Treatment-Related Adverse Events

	Previously Treated EC[a] (n = 108)		All EC (N = 124)	
Preferred Term or Basket	**Any Grade**	**Grade 3/4**	**Any Grade**	**Grade 3/4**
Patients with any treatment-related TEAEs	105 (97.2)	75 (69.4)	120 (96.8)	83 (66.9)
Hypertension[b]	66 (61.1)	35 (32.4)	74 (59.7)	39 (31.5)
Diarrhea	57 (52.8)	7 (6.5)	65 (52.4)	8 (6.5)
Fatigue	56 (51.9)	9 (8.3)	59 (47.6)	9 (7.3)
Decreased appetite	51 (47.2)	0	59 (47.6)	0
Hypothyroidism[c]	48 (44.4)	1 (0.9)	54 (43.5)	1 (0.8)
Nausea	43 (39.8)	3 (2.8)	48 (38.7)	3 (2.4)
Stomatitis	36 (33.3)	0	39 (31.5)	0
Pain and arthralgia[d]	34 (31.5)	2 (1.9)	37 (29.8)	2 (1.6)
Dysphonia	30 (27.8)	0	34 (27.4)	0
PPE and severe skin reactions[e]	29 (26.9)	5 (4.6)	32 (25.8)	6 (4.8)
Vomiting	29 (26.9)	0	31 (25.0)	0

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

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

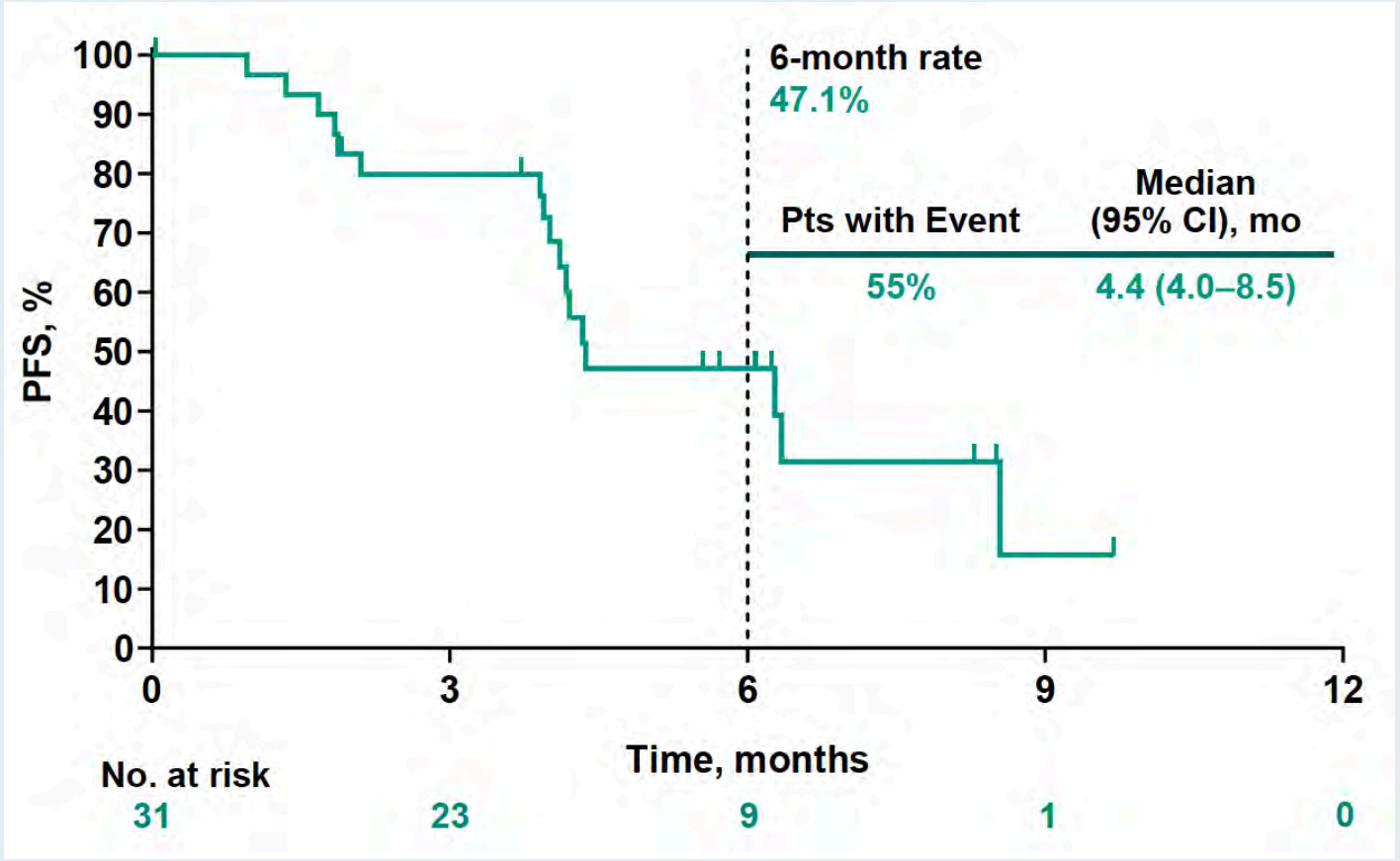
Lwin Z et al.

ESMO 2020;Abstract LBA41.

LEAP-005: Antitumor Activity in Ovarian Cancer Cohort

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

PFS: 4L Ovarian Cohort (n = 31)



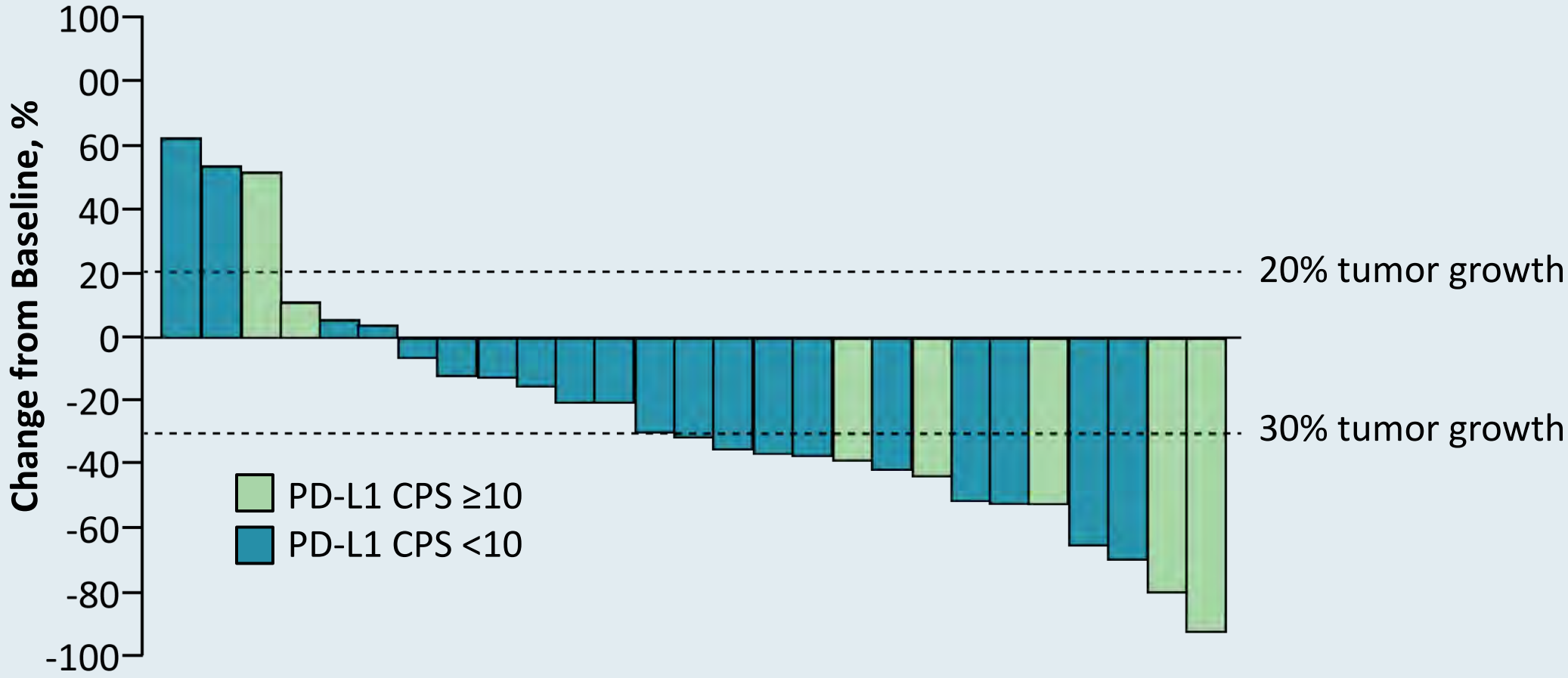
Lwin Z et al. *ESMO* 2020;Abstract LBA41.

Lenvatinib plus Pembrolizumab for Previously Treated, Advanced Triple-Negative Breast Cancer: Early Results from the Multicohort Phase 2 LEAP-005 Study

Chung HC et al.

SABCS 2020;Abstract PS12-07.

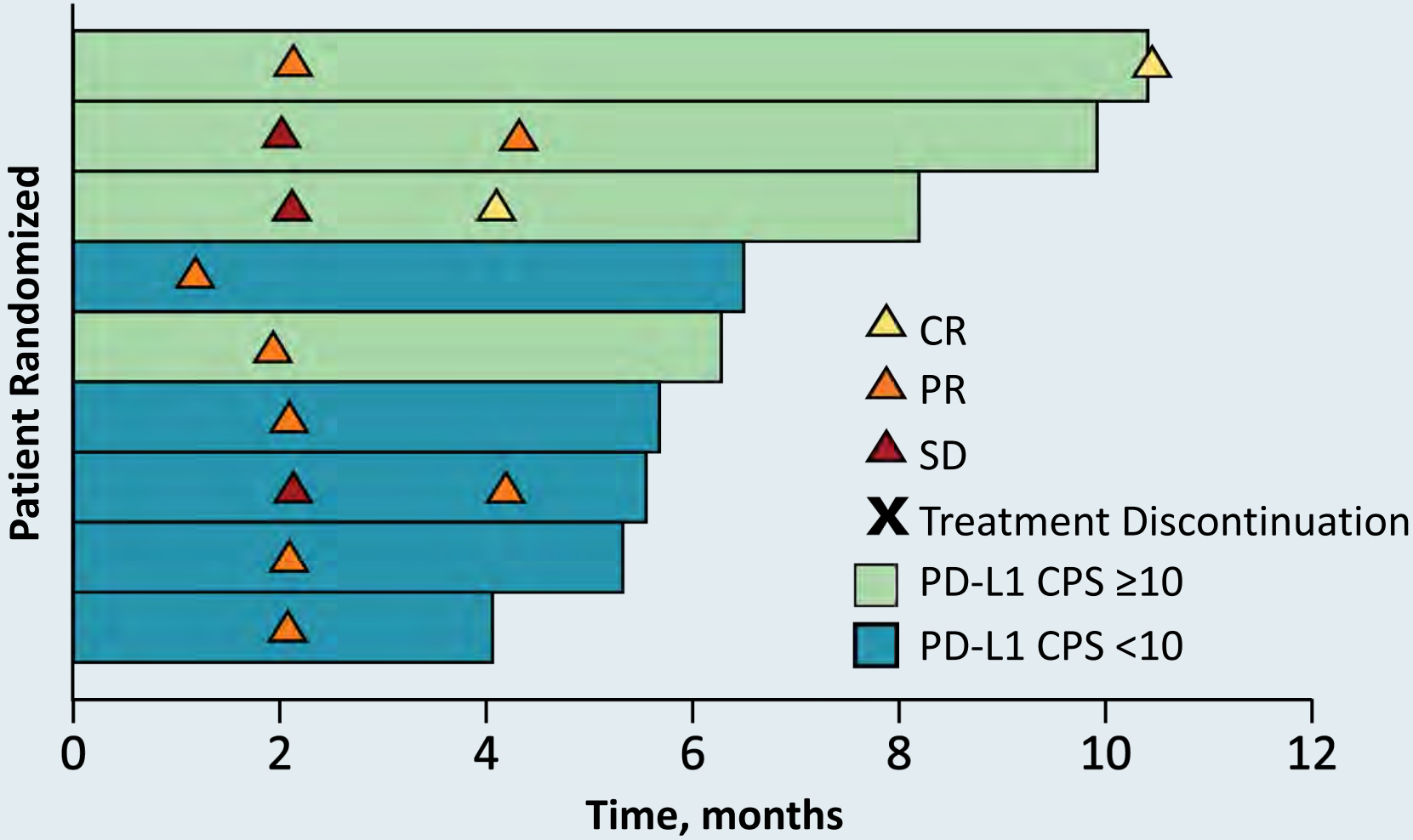
LEAP-005: Best Percentage Change from Baseline in Target Lesion Size



Includes patients with one or more evaluable post-baseline imaging assessment (n = 27).

Chung HC et al. SABCS 2020;Abstract PS12-07.

LEAP-005: Treatment Duration and Response Evaluation



Chung HC et al. SABCS 2020;Abstract PS12-07.

original report

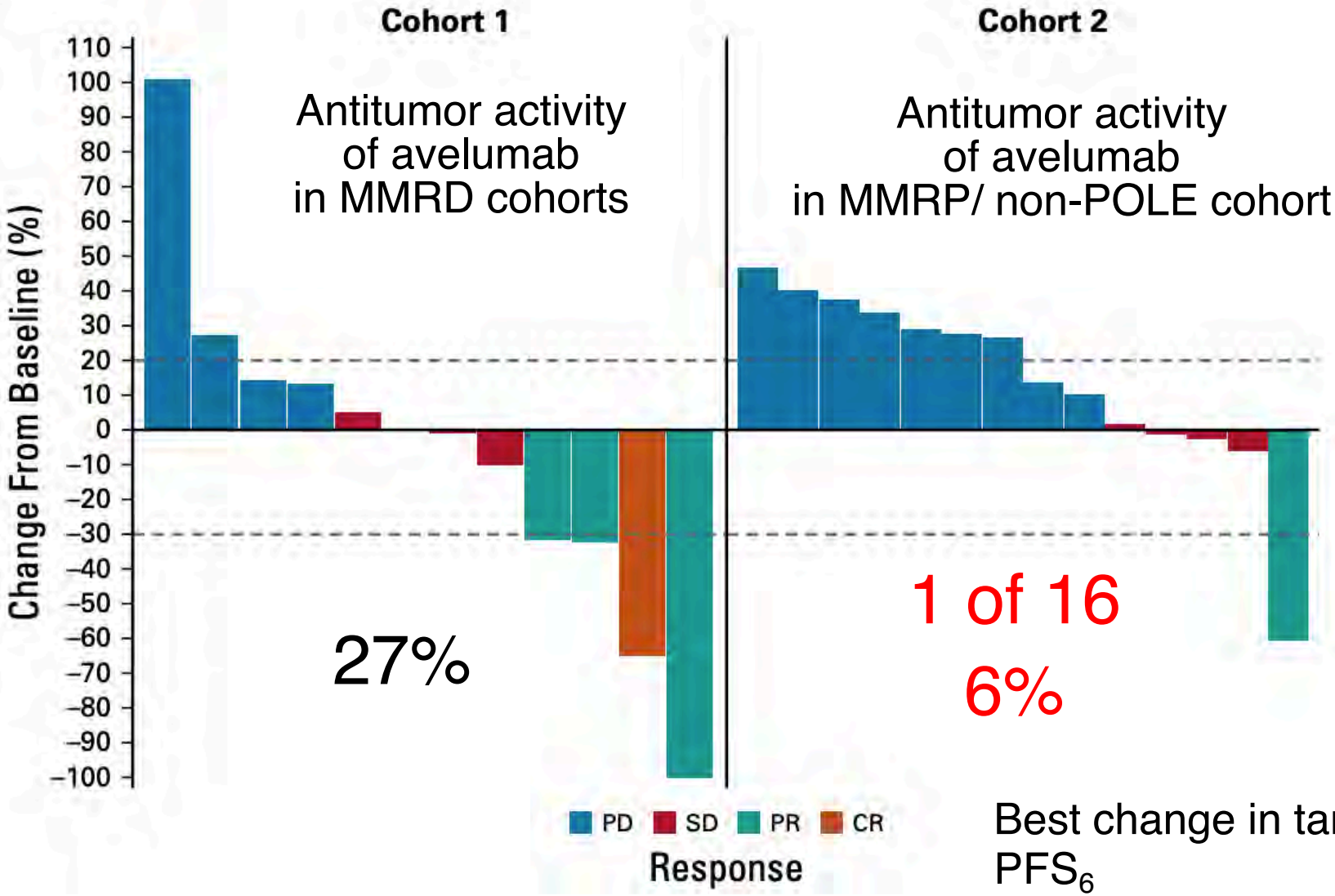
Phase II Study of Avelumab in Patients With Mismatch Repair Deficient and Mismatch Repair Proficient Recurrent/Persistent Endometrial Cancer

Panagiotis A. Konstantinopoulos, MD, PhD[1]; Weixiu Luo, MS[1]; Joyce F. Liu, MD[1]; Doga C. Gulhan, PhD[2]; Carolyn Krasner, MD[1]; Jeffrey J. Ishizuka, MD, DPhil[1]; Allison A. Gockley, MD[3]; Mary Buss, MD, MPH[4]; Whitfield B. Growdon, MD[5]; Heather Crowe[5]; Susana Campos, MD, MPH[1]; Neal I. Lindeman, MD[3]; Sarah Hill, MD, PhD[3]; Elizabeth Stover, MD, PhD[1]; Susan Schumer, MD[1]; Alexi A. Wright, MD, MPH[1]; Jennifer Curtis, MS[1]; Roxanne Quinn[1]; Christin Whalen, RN[1]; Kathryn P. Gray, PhD[1]; Richard T. Penson, MD[5]; Stephen A. Cannistra, MD[4]; Gini F. Fleming, MD[6]; and Ursula A. Matulonis, MD[1]

J Clin Oncol 2019;37(30):2786-94

Courtesy of Richard T Penson, MD, MRCP

Objective Response Rate: Avelumab



Best change in target lesions
PFS_6

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

Courtesy of Richard T Penson, MD, MRCP

JAMA Oncology | Original Investigation

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

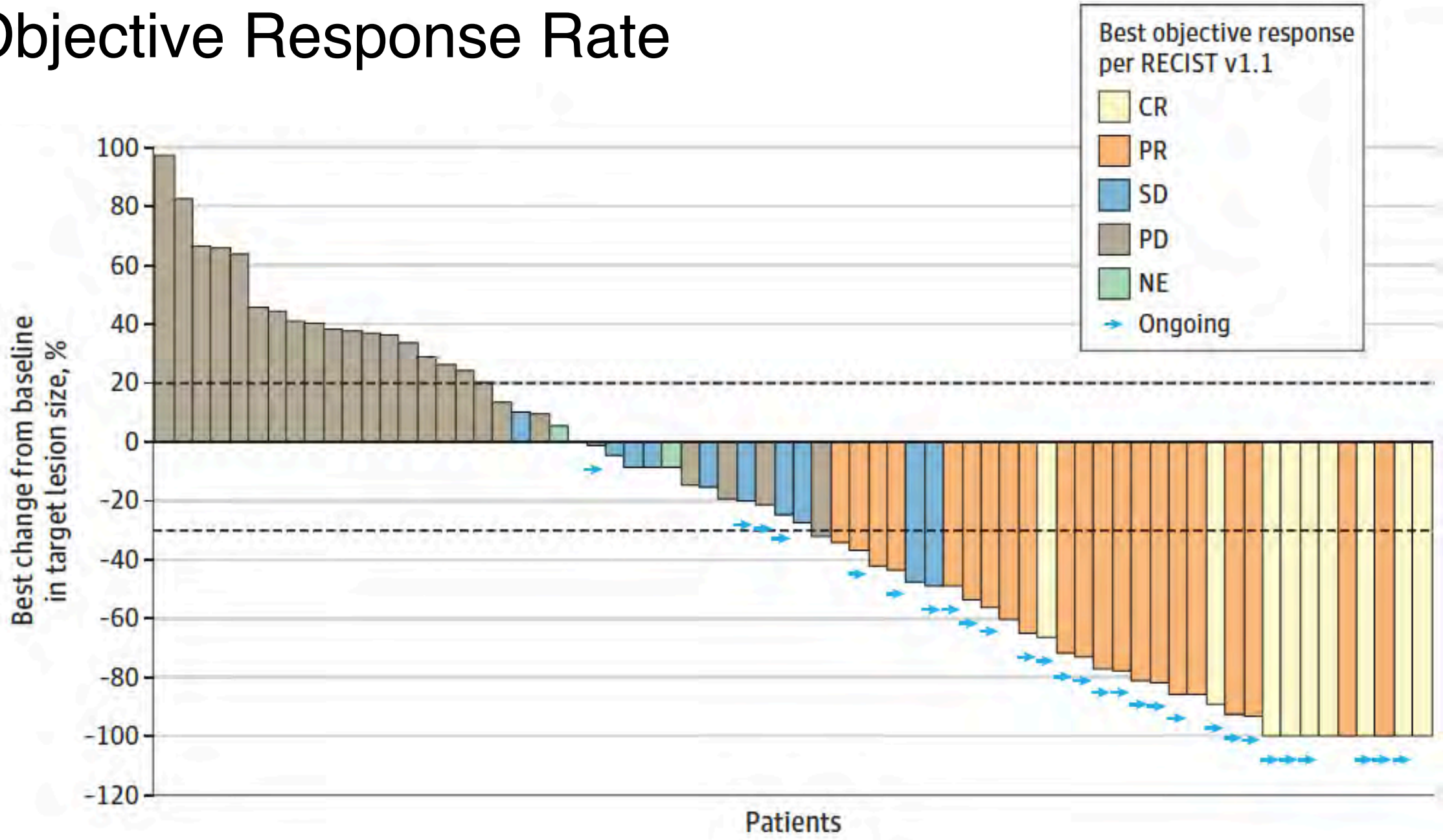
A Nonrandomized Phase 1 Clinical Trial

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

JAMA Oncol 2020;6(11):1-7

Courtesy of Richard T Penson, MD, MRCP

Objective Response Rate



Oaknin A, et al. JAMA Oncol 2020;6(11):1-7

Courtesy of Richard T Penson, MD, MRCP

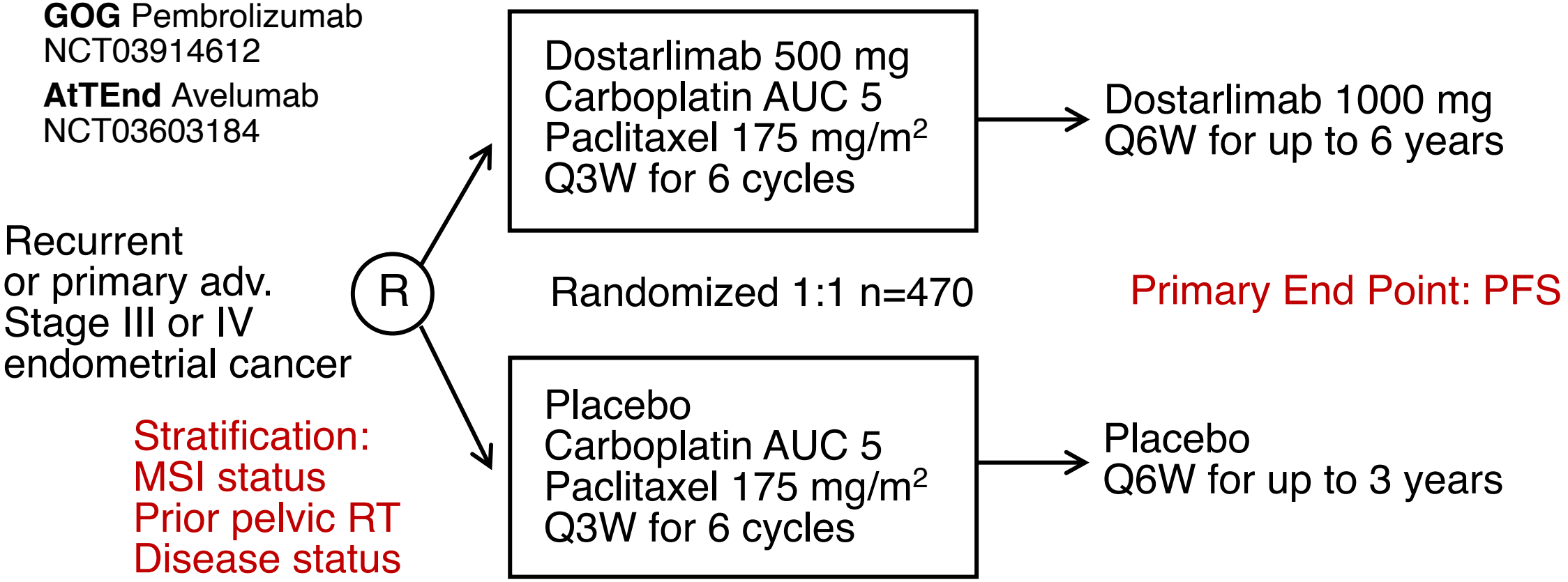
RUBY
CARESTONE CLINICAL TRIAL

NCT03981796

GOG Pembrolizumab
NCT03914612

AtTEnd Avelumab
NCT03603184

Mirza MR, et al. ENGOT-EN6/NSGO-RUBY
A Phase III, randomized, double-blind, multicenter study of dostarlimab + carbo-paclitaxel versus placebo + carbo-paclitaxel in recurrent or primary advanced EC. ASCO 2020;Abs TPS6107.



NSGO-CTU Nordic Society of Gynaecological Oncology - Clinical Trial Unit
ENGOT European Network of Gynaecological Oncological Trial groups
GOG FOUNDATION Transforming the standard of care

Courtesy of Richard T Penson, MD, MRCP

In general, what treatment would you recommend for a patient with microsatellite-stable (MSS) 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 microsatellite instability (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

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

Agenda

Management of Ovarian Cancer

- Module 1: PARP inhibitors — Maintenance therapy
- Module 2: PARP inhibitors — Combination with anti-PD-1/PD-L1 antibodies
- Module 3: Checkpoint inhibitors
- Module 4: Mirvetuximab soravtansine

Treatment of Endometrial and Cervical Cancers

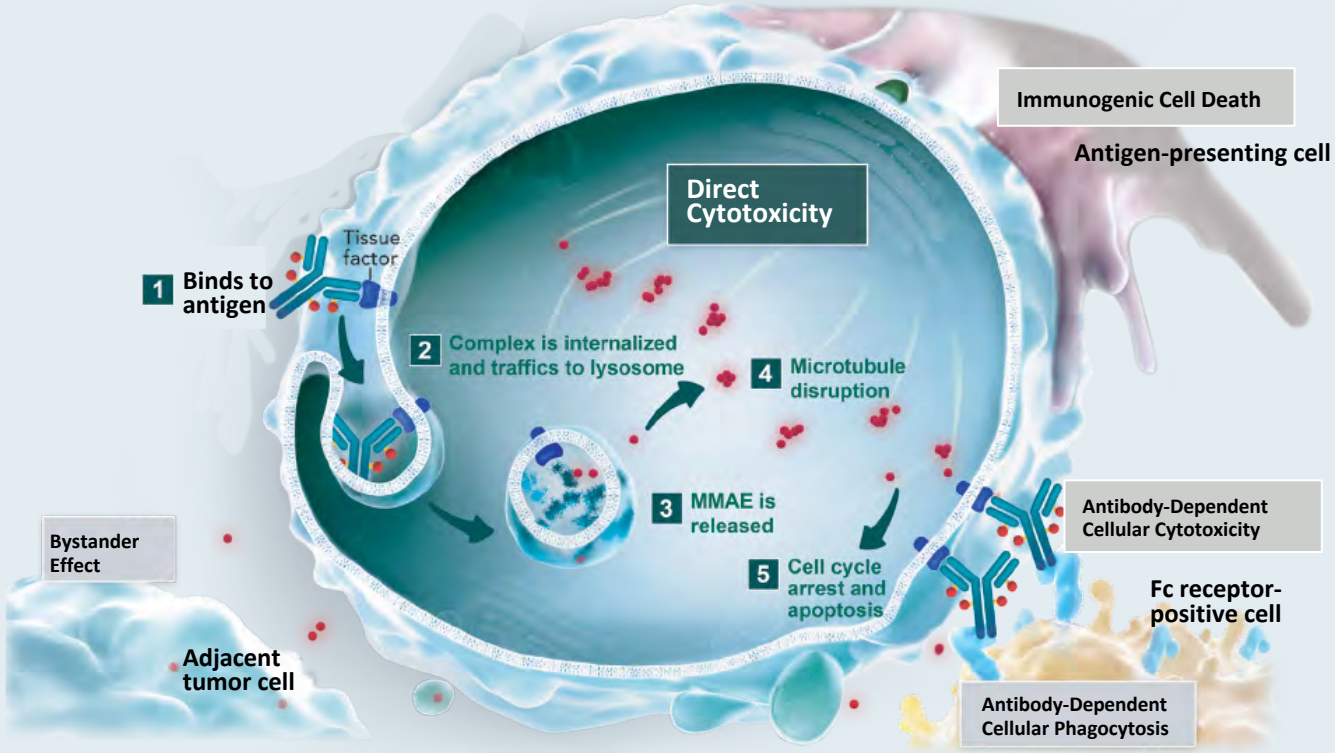
- Module 5: Endometrial cancer — Immune checkpoint inhibitors +/- lenvatinib
- **Module 6: Cervical cancer — Antibody-drug conjugates, immune checkpoint inhibitors**

Module 6: Cervical cancer — Antibody-drug conjugates, immune checkpoint inhibitors

- **Key Relevant Data Sets**
  - Tisotumab vedotin for previously treated recurrent or metastatic cervical cancer
  - innovaTV 204: Tisotumab vedotin
  - innovaTV 205: Tisotumab vedotin +/- bevacizumab, pembrolizumab or carboplatin
  - KEYNOTE-158: Pembrolizumab for previously treated advanced cervical cancer

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.

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

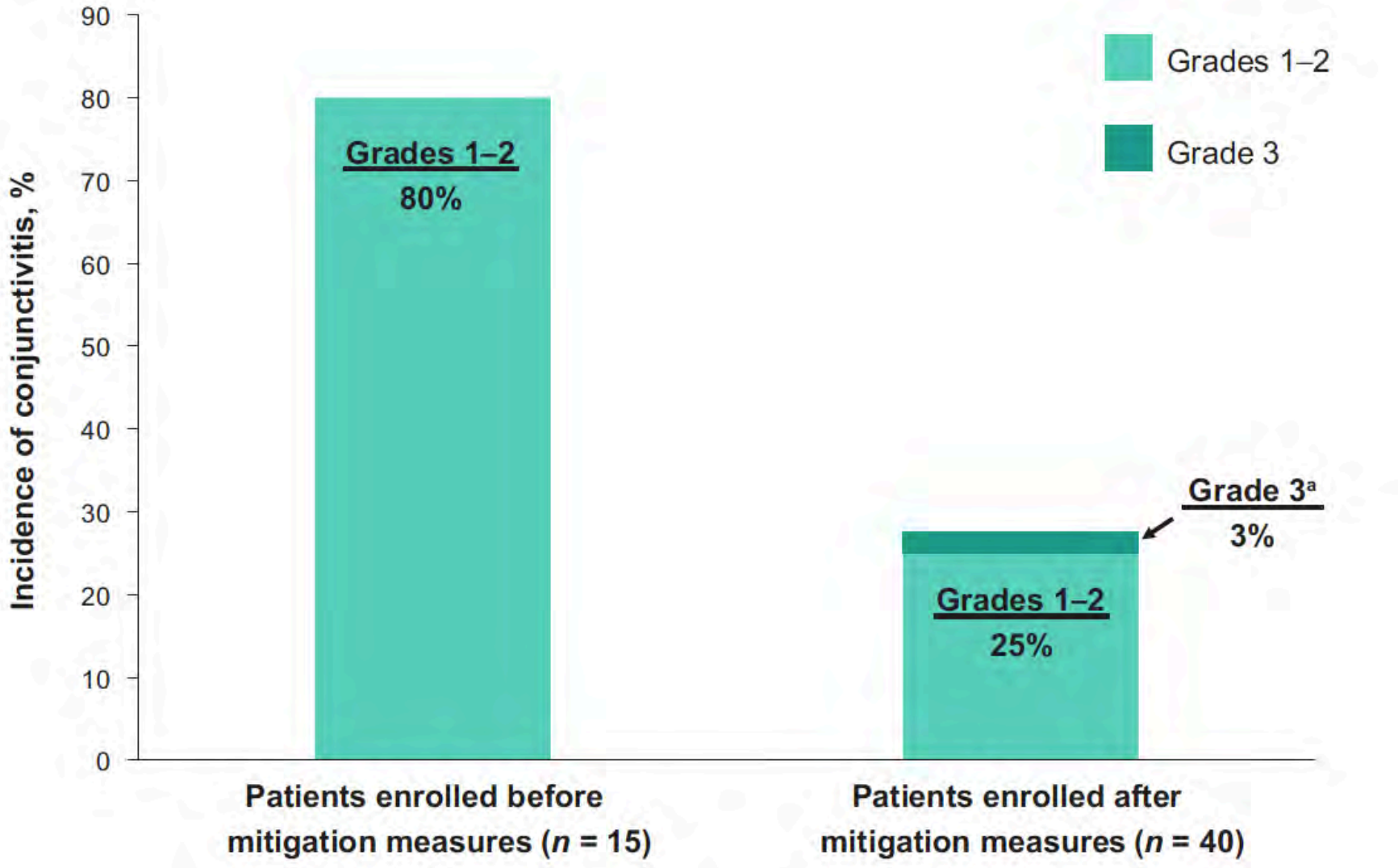
Tisotumab Vedotin in Previously Treated Recurrent or Metastatic Cervical Cancer

David S. Hong[1], Nicole Concin[2], Ignace Vergote[2], Johann S. de Bono[3], Brian M. Slomovitz[4], Yvette Drew[5], Hendrik-Tobias Arkenau[6], Jean-Pascal Machiels[7], James F. Spicer[8], Robert Jones[9], Martin D. Forster[10], Nathalie Cornez[11], Christine Gennigens[12], Melissa L. Johnson[13], Fiona C. Thistlethwaite[14], Reshma A. Rangwala[15], Srinivas Ghatta[16], Kristian Windfeld[17], Jeffrey R. Harris[18], Ulrik Niels Lassen[19], and Robert L. Coleman[20]

Clin Cancer Res 2020;26:1220–8

Courtesy of Richard T Penson, MD, MRCP

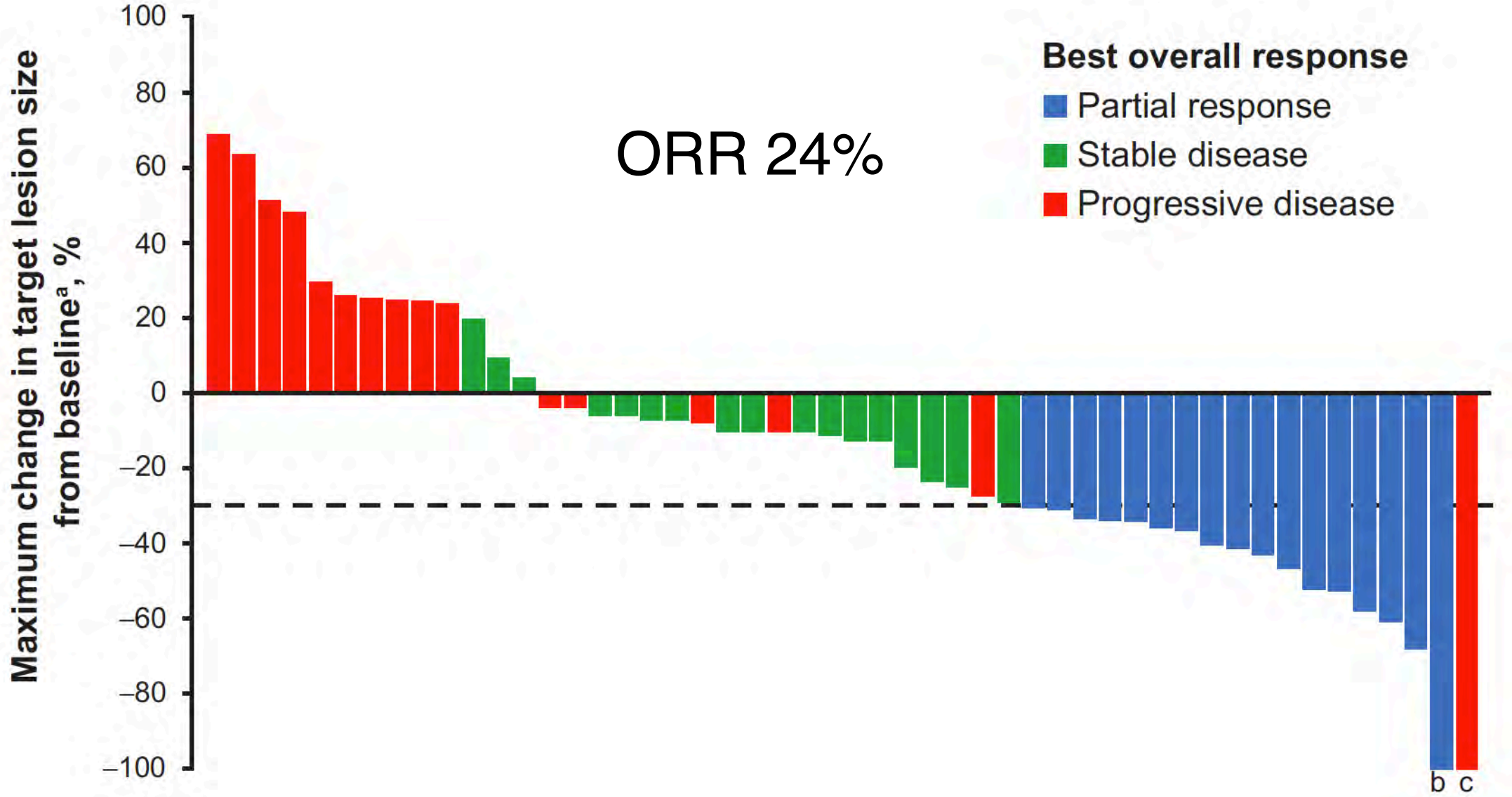
Toxicity



Hong DS, et al. Clin Cancer Res 2020;26:1220–8

Courtesy of Richard T Penson, MD, MRCP

Objective Response Rate



Hong DS, et al. Clin Cancer Res 2020;26:1220–8

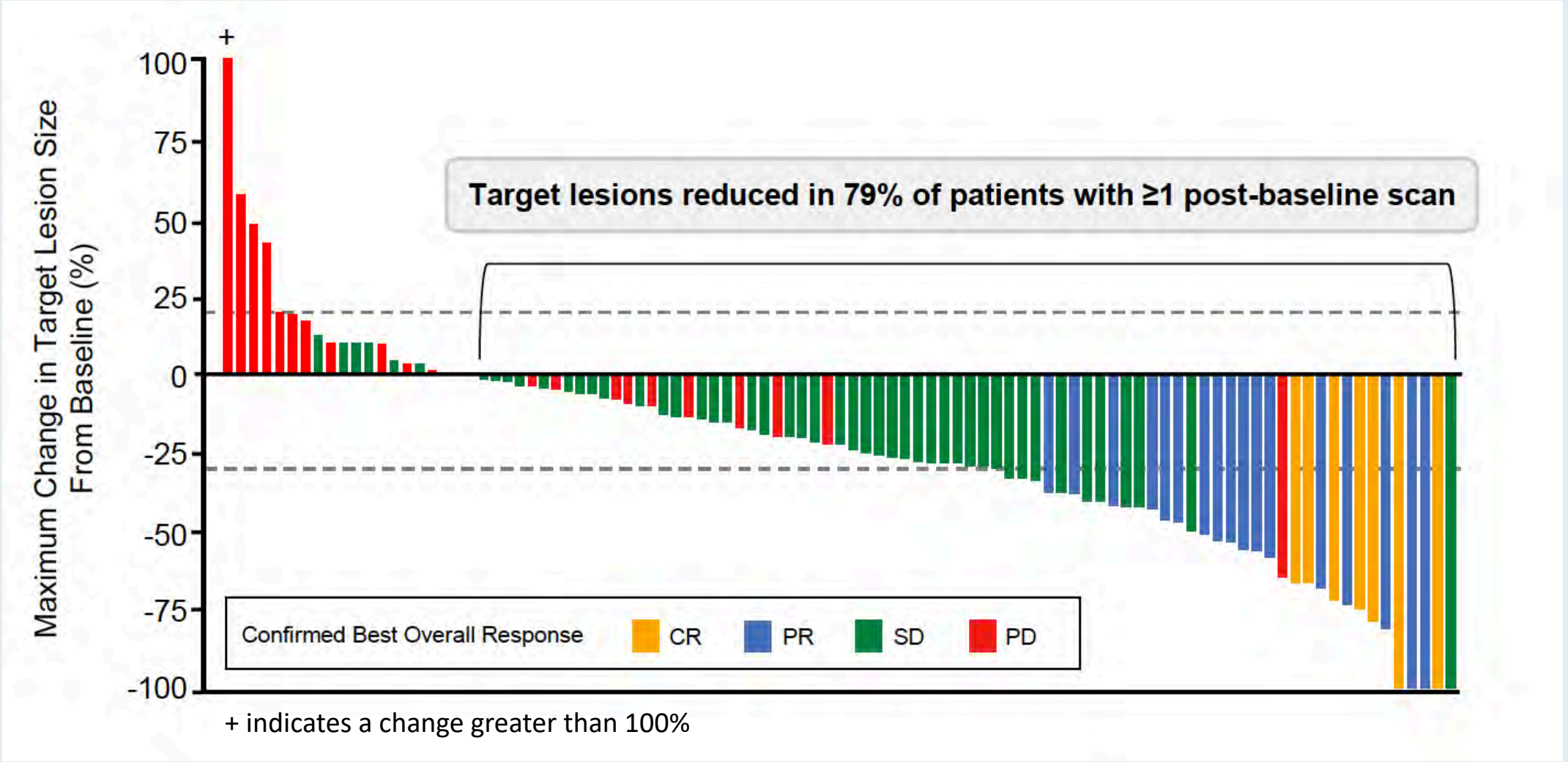
Courtesy of Richard T Penson, MD, MRCP

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: Maximum Change in Target Lesion Size by IRC Assessment



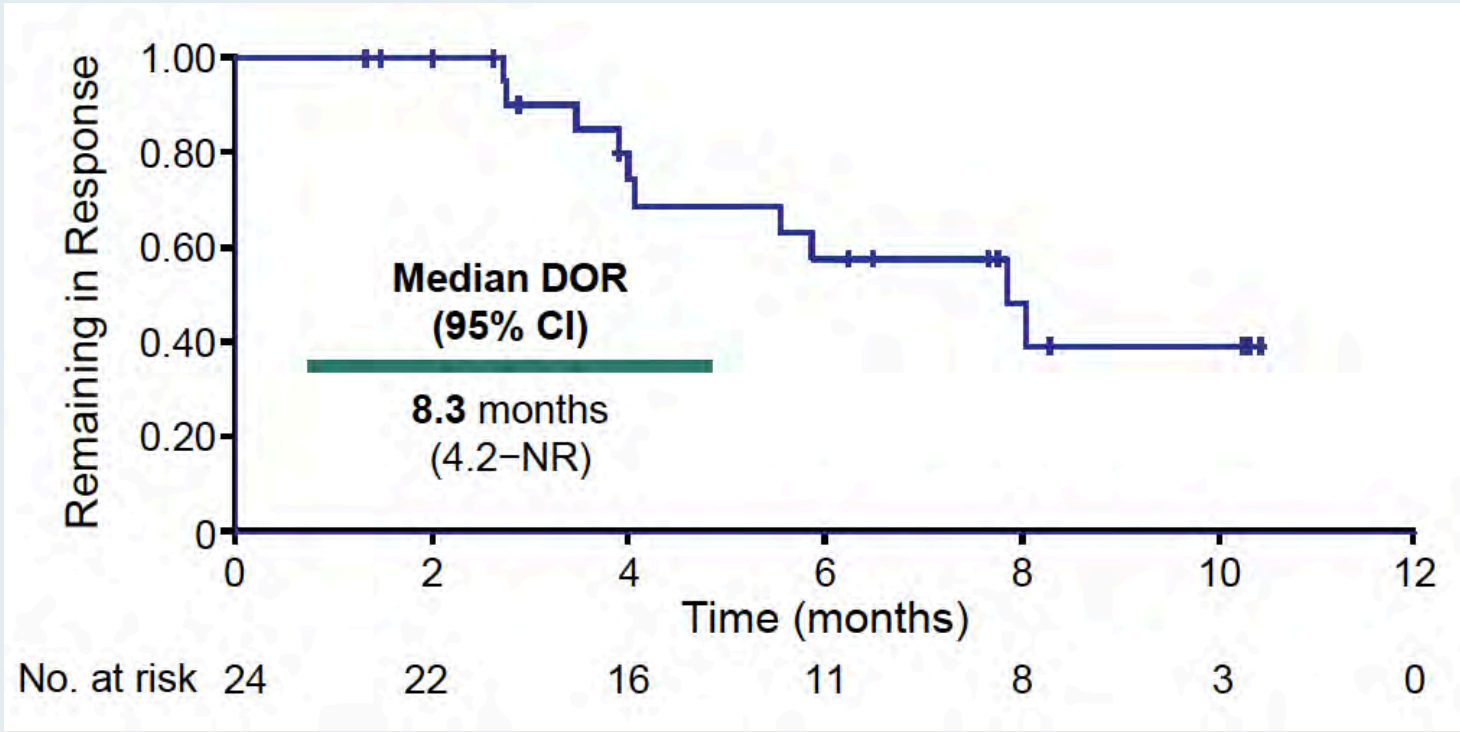
+ indicates a change greater than 100%

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

innovaTV 204: Antitumor Activity by IRC Assessment

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

Duration of Response



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

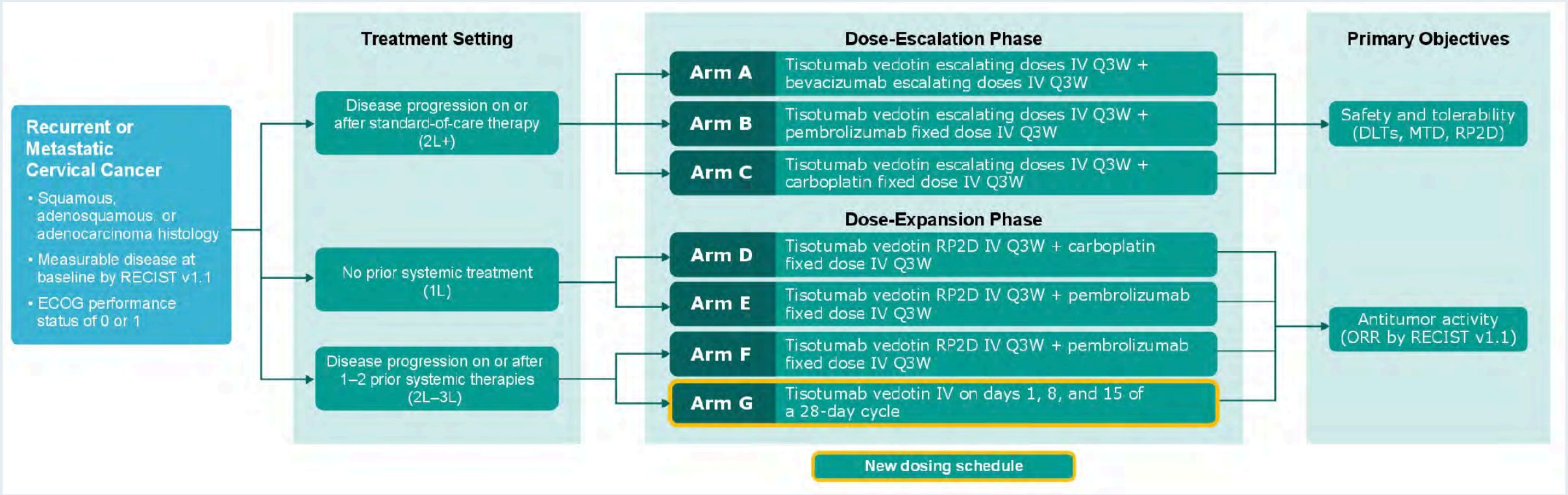
Phase Ib/II Trial of Tisotumab Vedotin ± Bevacizumab, Pembrolizumab, or Carboplatin in Recurrent or Metastatic Cervical Cancer (innova TV 205/ENGOT-cx8/ GOG-3024)

Vergote I et al.

ASCO 2020;Abstract TPS6095.

innovaTV 205: Phase Ib/II Trial Schema

Trial Identifier: NCT03786081



Vergote I et al. *ASCO* 2020;Abstract TPS6095.

original report

Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study

Hyun Cheol Chung, MD, PhD[1]; Willeke Ros, MSc[2]; Jean-Pierre Delord, MD, PhD[3]; Ruth Perets, MD, PhD[4]; Antoine Italiano, MD, PhD[5]; Ronnie Shapira-Frommer, MD[6]; Lyudmila Manzuk, MD[7]; Sarina A. Piha-Paul, MD[8]; Lei Xu, PhD[9]; Susan Zeigenfuss, RN[9]; Scott K. Pruitt, MD, PhD[9]; and Alexandra Leary, MD, PhD[10]

J Clin Oncol 2019;37(17):1470-8

Courtesy of Richard T Penson, MD, MRCP

KEYNOTE-158: Objective Response Rate

12%

Antitumor Activity	Total Population (N = 98)*	Total (n = 82)	Previously Treated (n = 77)†	PD-L1–Negative Population (n = 15)
ORR	12 (12.2)	12 (14.6)	11 (14.3)	0 (0.0)
95% CI	6.5 to 20.4	7.8 to 24.2	7.4 to 24.1	0.0 to 21.8
DCR	30 (30.6)	27 (32.9)	24 (31.2)	3 (20.0)
95% CI	21.7 to 40.7	22.9 to 44.2	21.2 to 42.7	4.3 to 48.1
Best overall response				
CR	3 (3.1)	3 (3.7)	2 (2.6)	0 (0.0)
PR	9 (9.2)	9 (11.0)	9 (11.7)	0 (0.0)
SD	18 (18.4)	15 (18.3)	13 (16.9)	3 (20.0)
Progressive disease	55 (56.1)	44 (53.7)	42 (54.5)	10 (66.7)
Not able to be evaluated‡	5 (5.1)	4 (4.9)	4 (5.2)	1 (6.7)
Not able to be assessed§	8 (8.2)	7 (8.5)	7 (9.1)	1 (6.7)
Time to response, months‖				—
Median	2.1	2.1	2.2	
Range	1.6-4.1	1.6-4.1	1.6-4.1	
Duration of response, months‖¶				—
Median	NR	NR	NR	
Range	≥ 3.7 to ≥ 18.6	≥ 3.7 to ≥ 18.6	4.1 to ≥ 18.6	
Estimated rate of response duration, months‖¶				—
≥ 6	10 (90.9)	10 (90.9)	10 (90.9)	
≥ 9	9 (90.9)	9 (90.9)	9 (90.9)	
≥ 12	7 (79.5)	7 (79.5)	7 (79.5)	

Chung HC, et al. J Clin Oncol 2019;37(17):1470-8

Courtesy of Richard T Penson, MD, MRCP

KEYNOTE-158: Objective Response Rate

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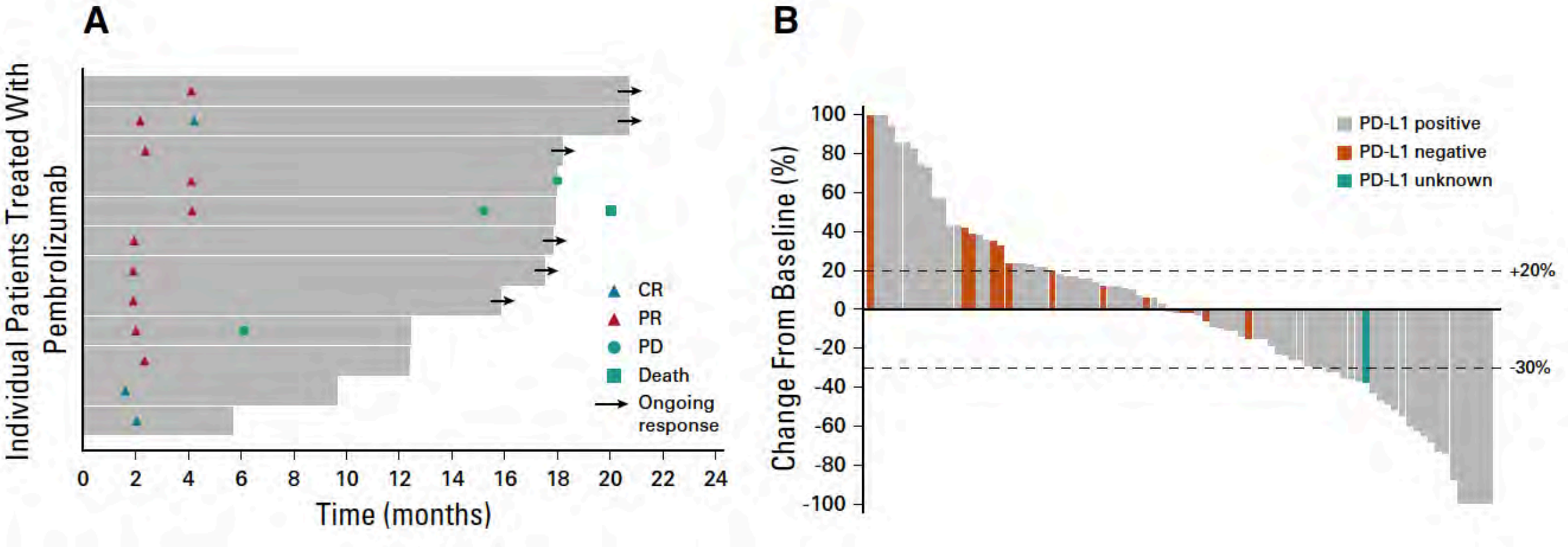
Chung HC, et al. J Clin Oncol 2019;37(17):1470-8

Courtesy of Richard T Penson, MD, MRCP

KEYNOTE-158: Duration of Response



Chung HC, et al. J Clin Oncol 2019;37(17):1470-8

Courtesy of Richard T Penson, MD, MRCP

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?

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

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

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

Lymphomas

Thursday, January 14, 2021
5:00 PM – 6:00 PM ET

Faculty

Christopher R Flowers, MD, MS
Sonali M Smith, MD

Moderator

Neil Love, MD

RTP Year in Review 2020

Thank you for joining us!

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

RTP Year in Review 2020