Meet The Professor
Immunotherapy and Novel Agents in Gynecologic Cancers

Martee L Hensley, MD, MSc
Attending Physician, Gynecologic Medical Oncology
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Cornell Medical College
New York, New York

Commercial Support

This activity is supported by educational grants from Eisai Inc, Merck, Seagen Inc and Tesaro, A GSK Company.

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Dr Love — Disclosures

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Dr Hensley — Disclosures

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Strategic Advisory Board	GlaxoSmithKline

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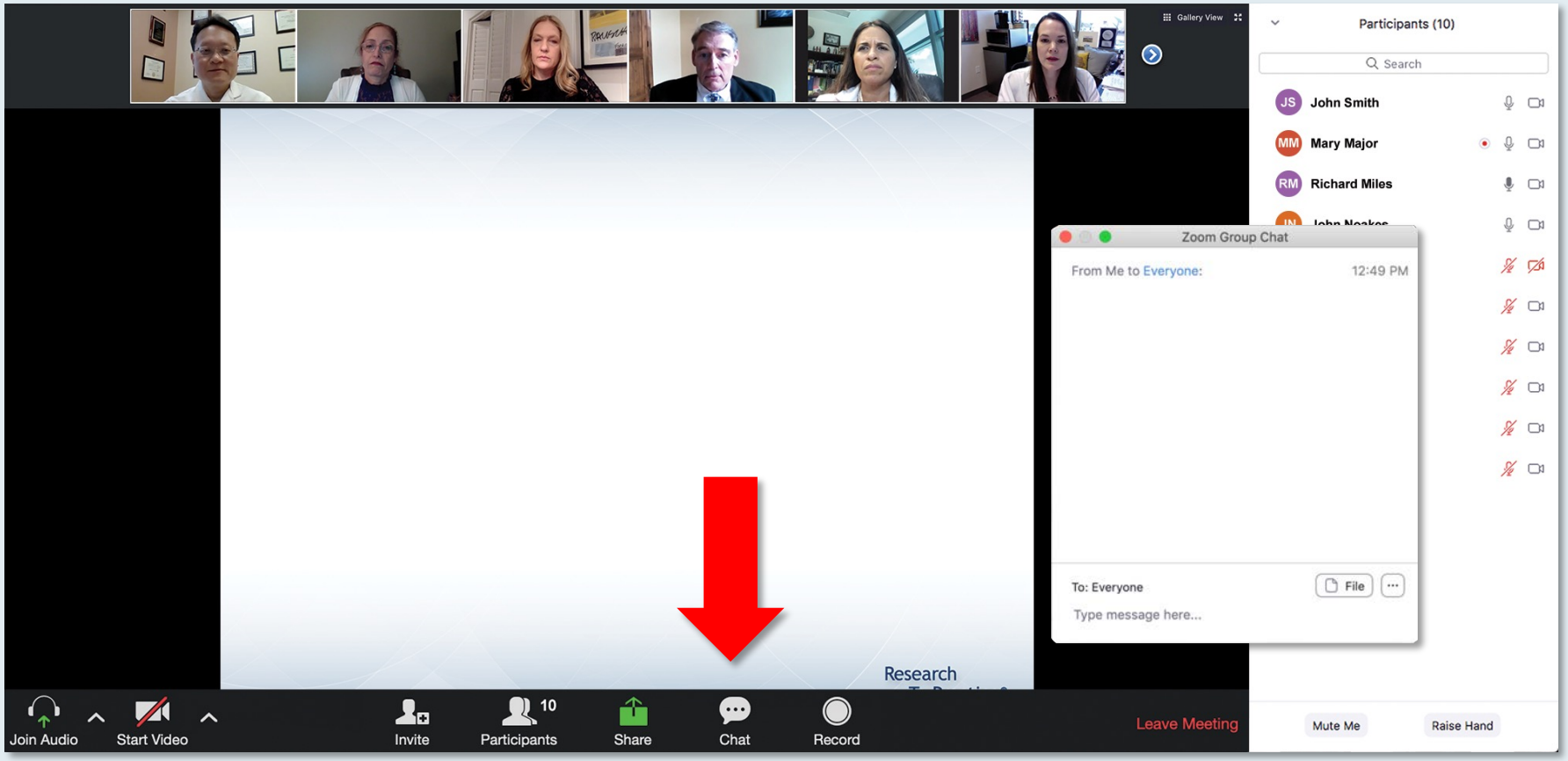

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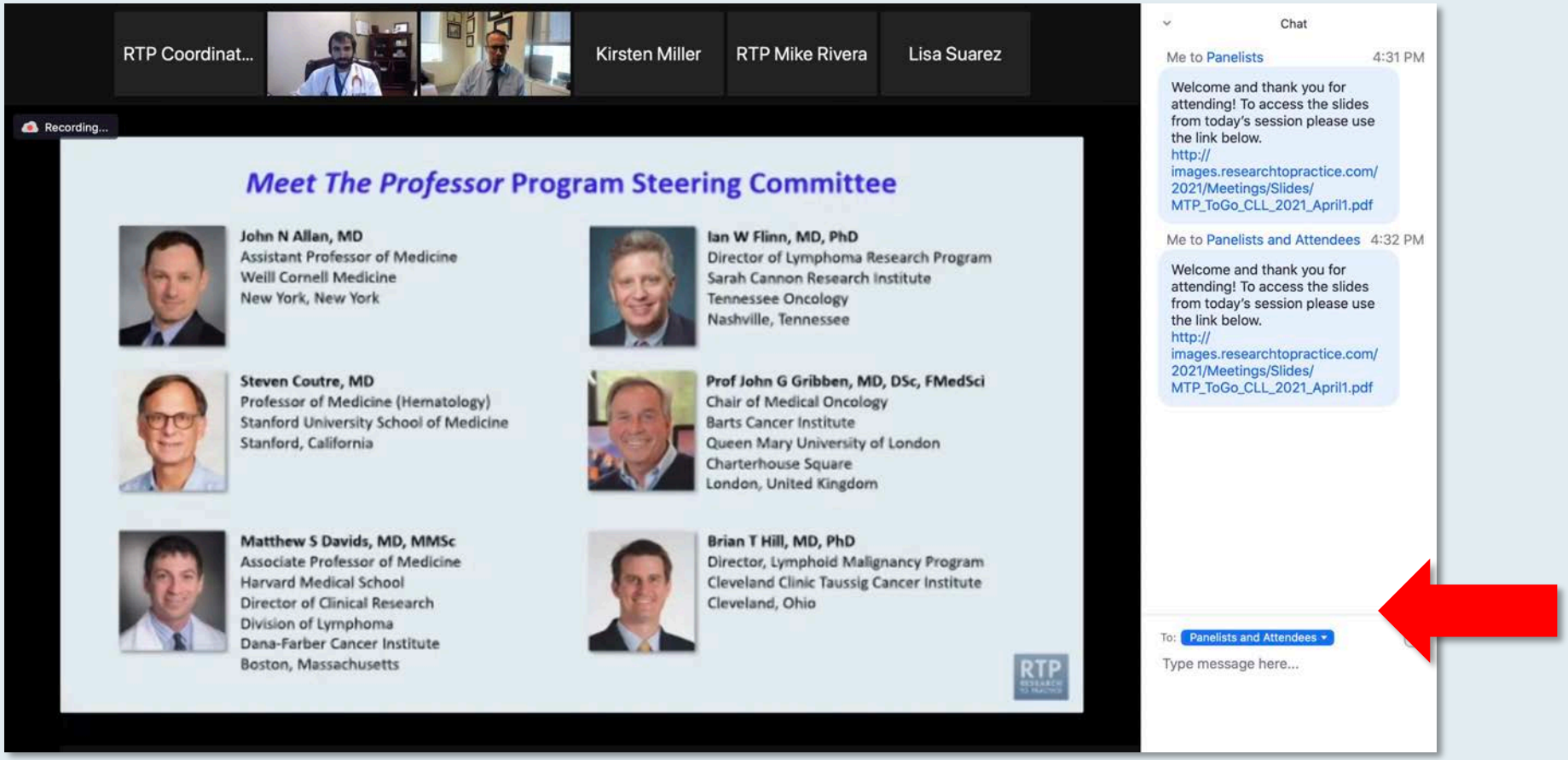

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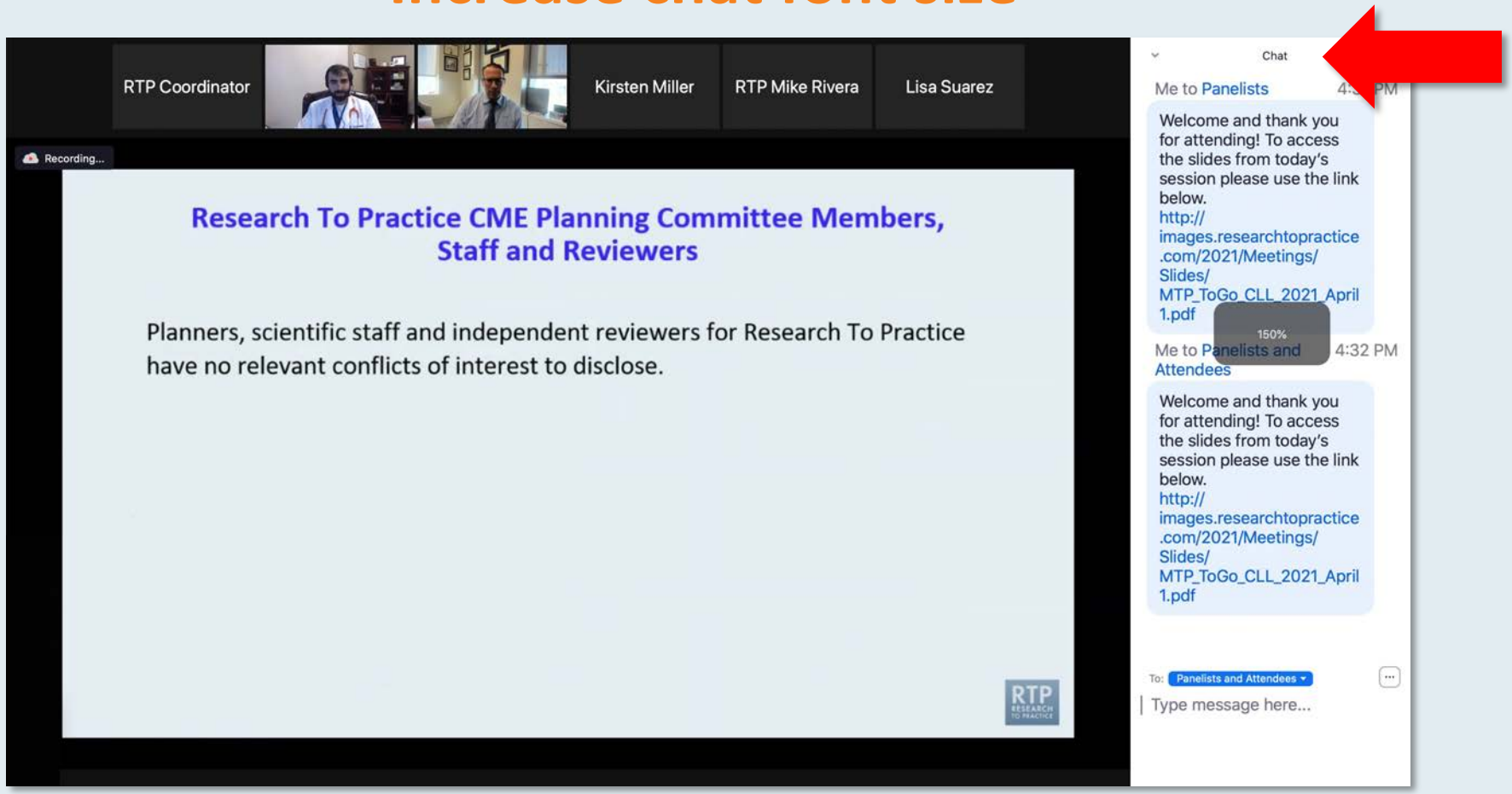

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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Key Presentations on Gynecologic Cancers from the 2021 ASCO Annual Meeting

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UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

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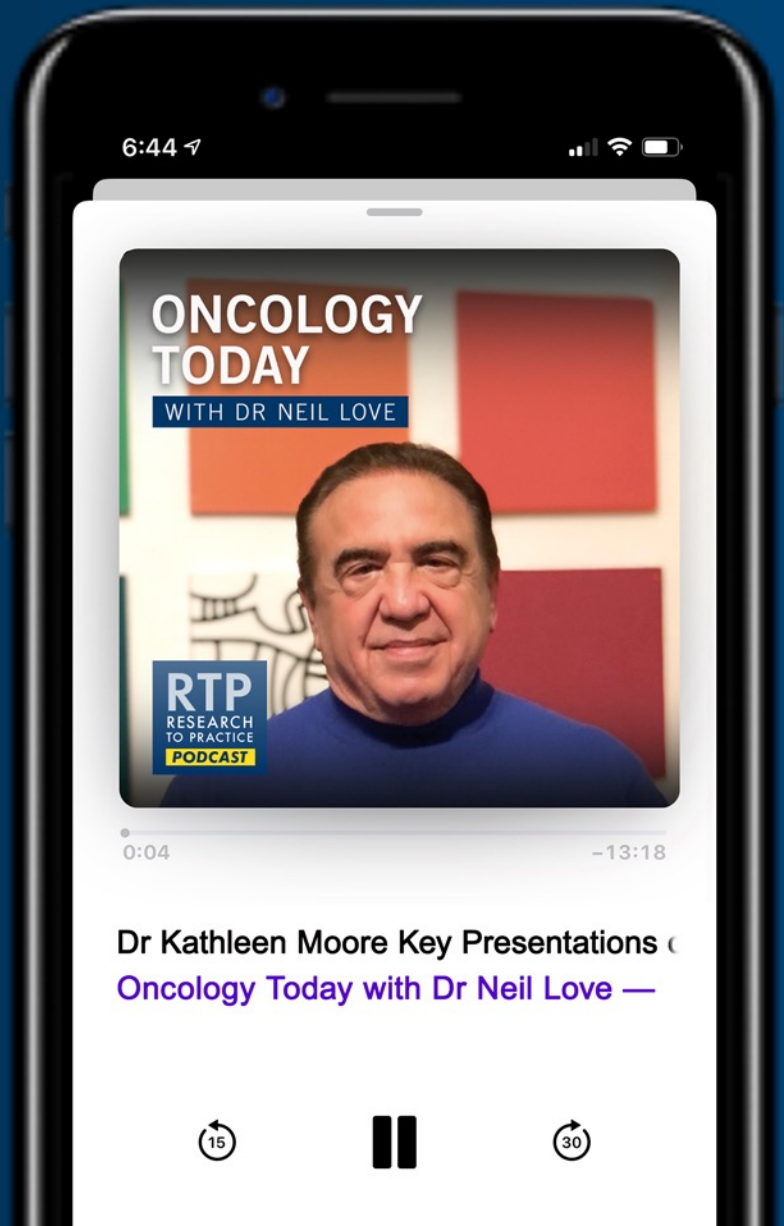

Meet The Professor

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

Monday, September 27, 2021
5:00 PM – 6:00 PM ET

Faculty

Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Optimizing the Selection and Sequencing of Therapy for Patients with Triple-Negative Breast Cancer

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Moderator

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Virginia Kaklamani, MD, DSc

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Additional faculty to be announced.

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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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Professor of Medicine
Weill Cornell Medical College
New York, New York

Meet The Professor Program Participating Faculty

Deborah K Armstrong, MD
Professor of Oncology
Professor of Gynecology and Obstetrics
Skip Viragh Outpatient Cancer Building
Johns Hopkins Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

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

Robert L Coleman, MD
Chief Scientific Officer
US Oncology Research
Gynecologic Oncology
The Woodlands, Texas

Martee L Hensley, MD, MSc
Attending Physician, Gynecologic Medical Oncology
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Cornell Medical College
New York, New York

Gottfried E Konecny, MD
Professor-in-Residence
Division of Hematology-Oncology
Department of Medicine, David Geffen School of Medicine
UCLA Medical Center
Los Angeles, California

Joyce F Liu, MD, MPH
Associate Chief and Director of Clinical Research
Division of Gynecologic Oncology
Dana-Farber Cancer Institute
Boston, Massachusetts

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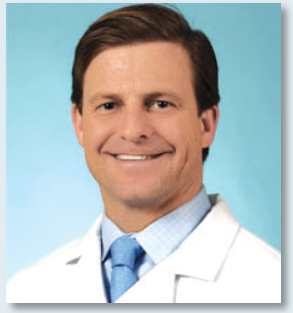
Meet The Professor Program Participating Faculty

Bradley J Monk, MD
Professor, Division of Gynecologic Oncology
Arizona Oncology (US Oncology Network)
University of Arizona College of Medicine
Creighton University School of Medicine at St Joseph's Hospital
Medical Director, US Oncology Network (McKesson) Gynecologic Program
Co-Director, GOG Partners
Member, Board of Directors, GOG Foundation
Phoenix, Arizona

David M O'Malley, MD
Professor
Division Director, Gynecologic Oncology
Co-Director, Gynecologic Oncology Phase I Program
The Ohio State University and The James Cancer Center
Columbus, Ohio

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

Ana Oaknin, MD, PhD
Head of Gynaecologic Cancer Programme
Vall d'Hebron Institute of Oncology
Hospital Universitari Vall d'Hebron
Vall d'Hebron Barcelona Hospital Campus
Barcelona, Spain



Matthew A Powell, MD
Professor and Chief
Division of Gynecologic Oncology
Washington University School of Medicine
St Louis, Missouri

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Meet The Professor Program Participating Faculty

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

Professor Ignace Vergote
Chairman, Department of Obstetrics and Gynaecology
Gynaecological Oncologist
Leuven Cancer Institute
University Hospital Leuven
Leuven, Belgium

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

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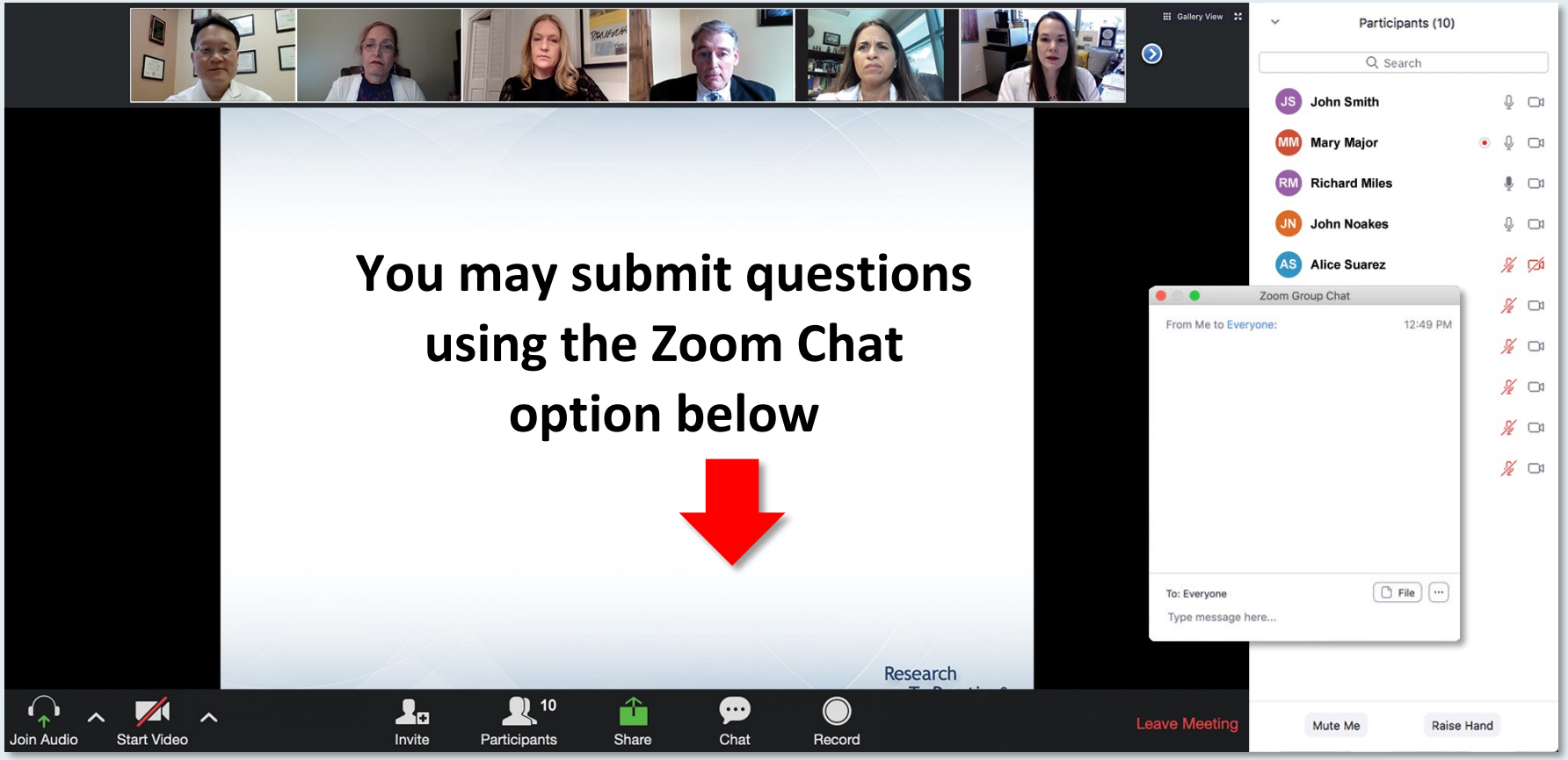

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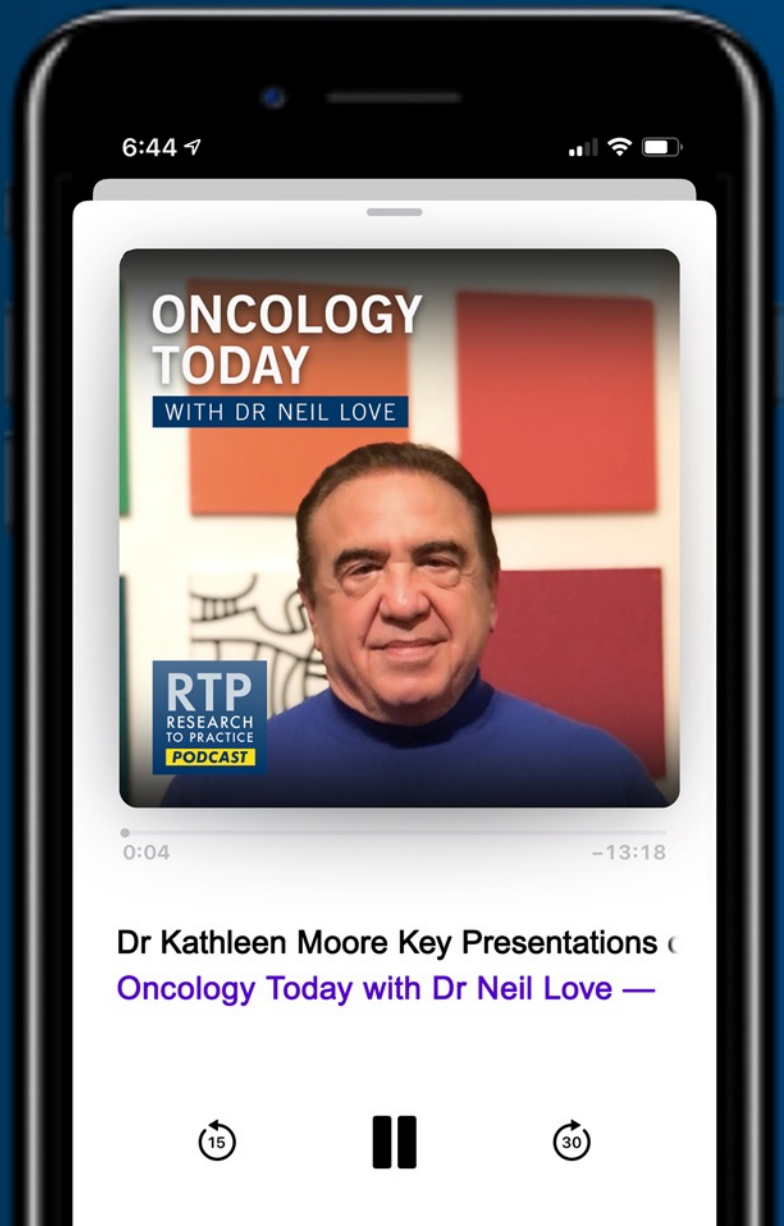

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Module 1: Breast Cancer – 9:30 AM – 10:20 AM

Module 2: Lung Cancer – 10:30 AM – 11:20 AM

Module 3: Gastrointestinal Cancers – 11:30 AM – 12:20 PM

Module 4: Genitourinary Cancers – 12:30 PM – 1:20 PM

Module 5: CLL and Lymphomas – 1:30 PM – 2:20 PM

Module 6: Multiple Myeloma – 2:30 PM – 3:20 PM

Module 7: AML and MDS – 3:30 PM – 4:20 PM

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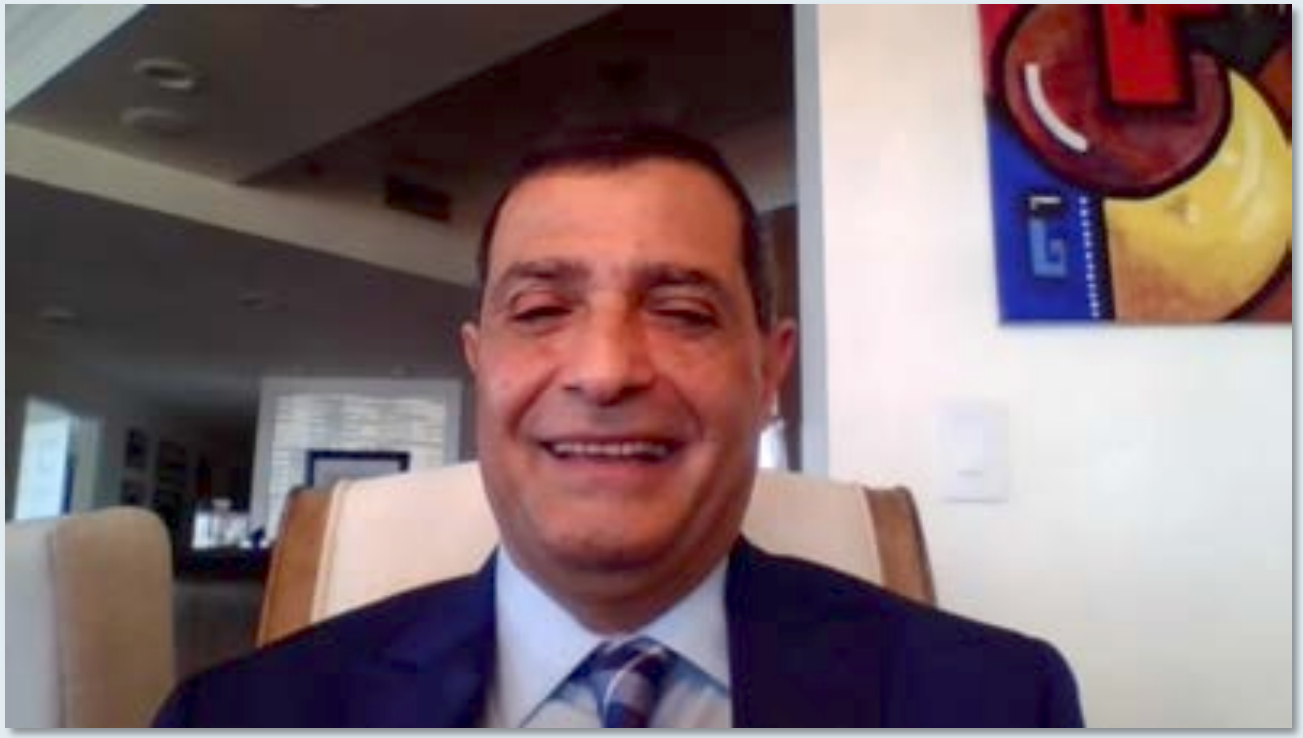

Atif Hussein, MD, MMM
Program Director, Hematology/Oncology Fellowship
Medical Director, Oncology Clinical Research
Chairman, Cancer Committee
Memorial Healthcare System
Clinical Associate Professor
Florida International University Herbert Wertheim College of Medicine
Hollywood, Florida

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Meet The Professor with Dr Hensley

MODULE 1: Cervical Cancer

- A 54-year-old woman with recurrent cervical squamous cell carcinoma – PD-L1 CPS: 100
- ESMO 2021 Highlights and Key Data Sets

MODULE 2: Endometrial Cancer

- A 65-year-old woman with MSS metastatic uterine adenocarcinoma who receives pembrolizumab/lenvatinib
- A 55-year-old woman with MSI-high, MMR-deficient uterine adenocarcinoma who receives pembrolizumab
- ESMO 2021 Highlights and Key Data Sets

MODULE 3: Uterine Sarcoma

- A 54-year-old woman with recurrent uterine high-grade stromal sarcoma

MODULE 4: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 5: Other Key Recent Data Sets

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Case Presentation – Dr Hussein: A 54-year-old woman with recurrent cervical squamous cell carcinoma – PD-L1 CPS 100

Dr Atif Hussein

- 2/2019: Moderately to poorly differentiated cervical squamous cell carcinoma
- 4/2019 – 8/2019: Concurrent radiation therapy and weekly cisplatin → carboplatin/paclitaxel x 3
- 12/2019: PD → carboplatin/paclitaxel/bevacizumab x 6 cycles → maintenance bevacizumab
- 6/2020: PD with worsening retroperitoneal lymph nodes and new hilar adenopathy
- 6/2020: PD-L1 CPS 100 → pembrolizumab, with complete response

Questions

- How long do you continue checkpoint inhibitors in patients with recurrent cervical cancer who are in complete response and tolerating therapy well?
- Is there any differential response to checkpoint inhibitor based on the pathologic subtype of cervical cancer — squamous versus adenocarcinoma versus adenosquamous?
- What therapy would you recommend to this patient upon recurrence? What's the role of tisotumab vedotin in this patient if she recurs?
- What are the most common side effects of tisotumab vedotin? How severe are the ocular toxicities? Are these dose limiting or result in discontinuation? How do you manage them? Has tisotumab vedotin been combined with other agents?

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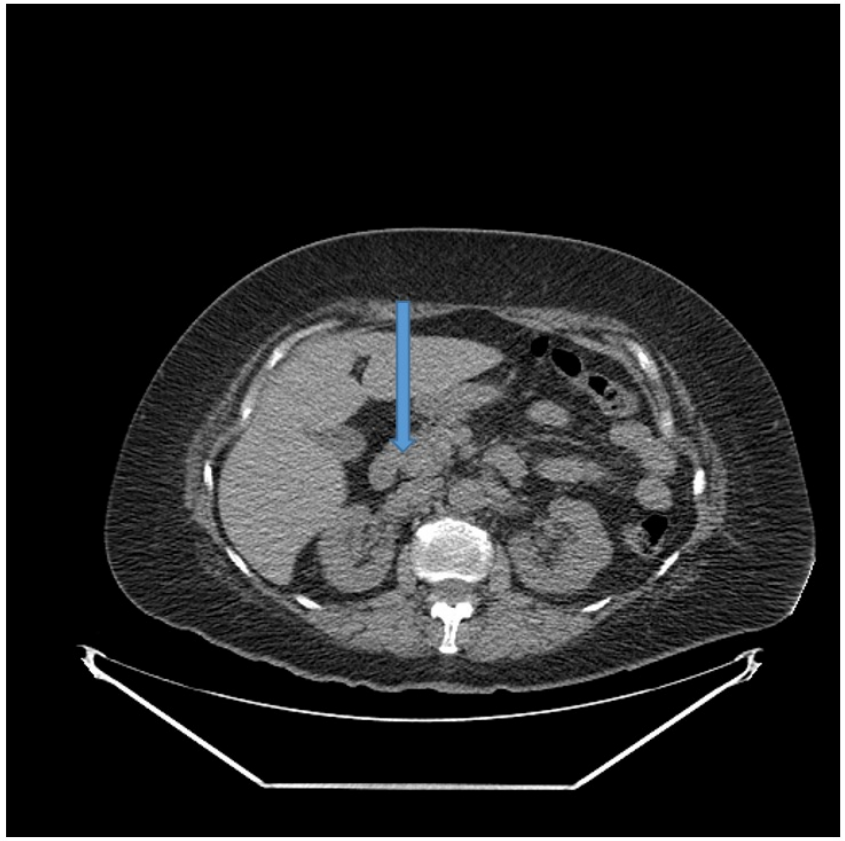
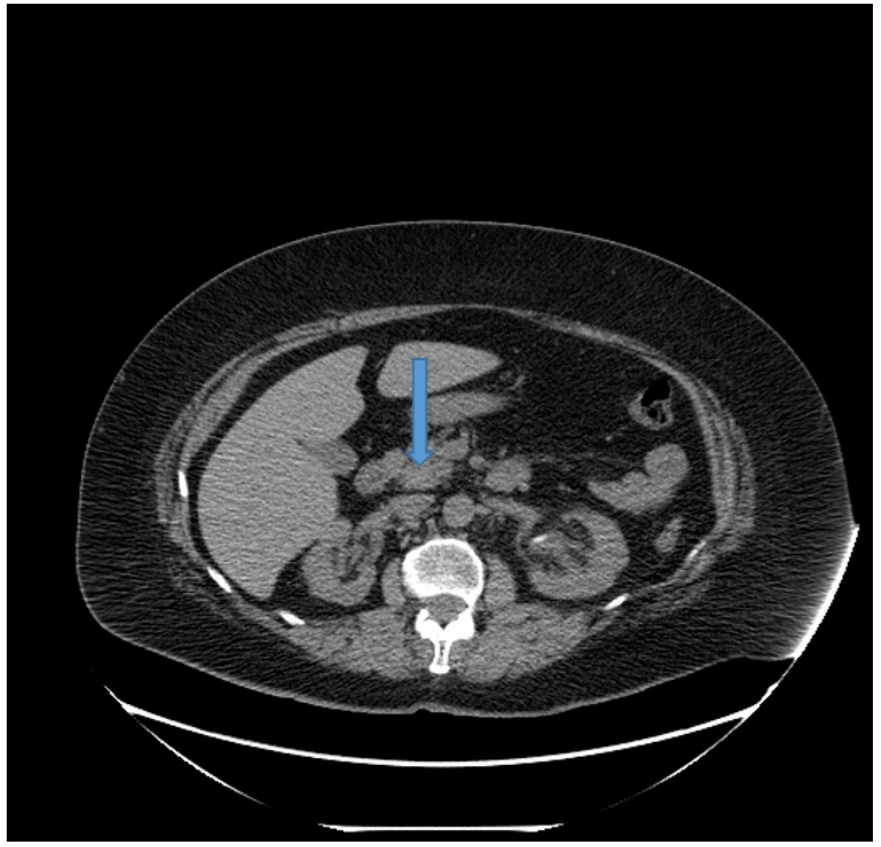
Case Presentation – Dr Hussein: A 54-year-old woman

Dr Atif Hussein

CT scans 12/2019 and 08/2021 showing complete response to pembrolizumab





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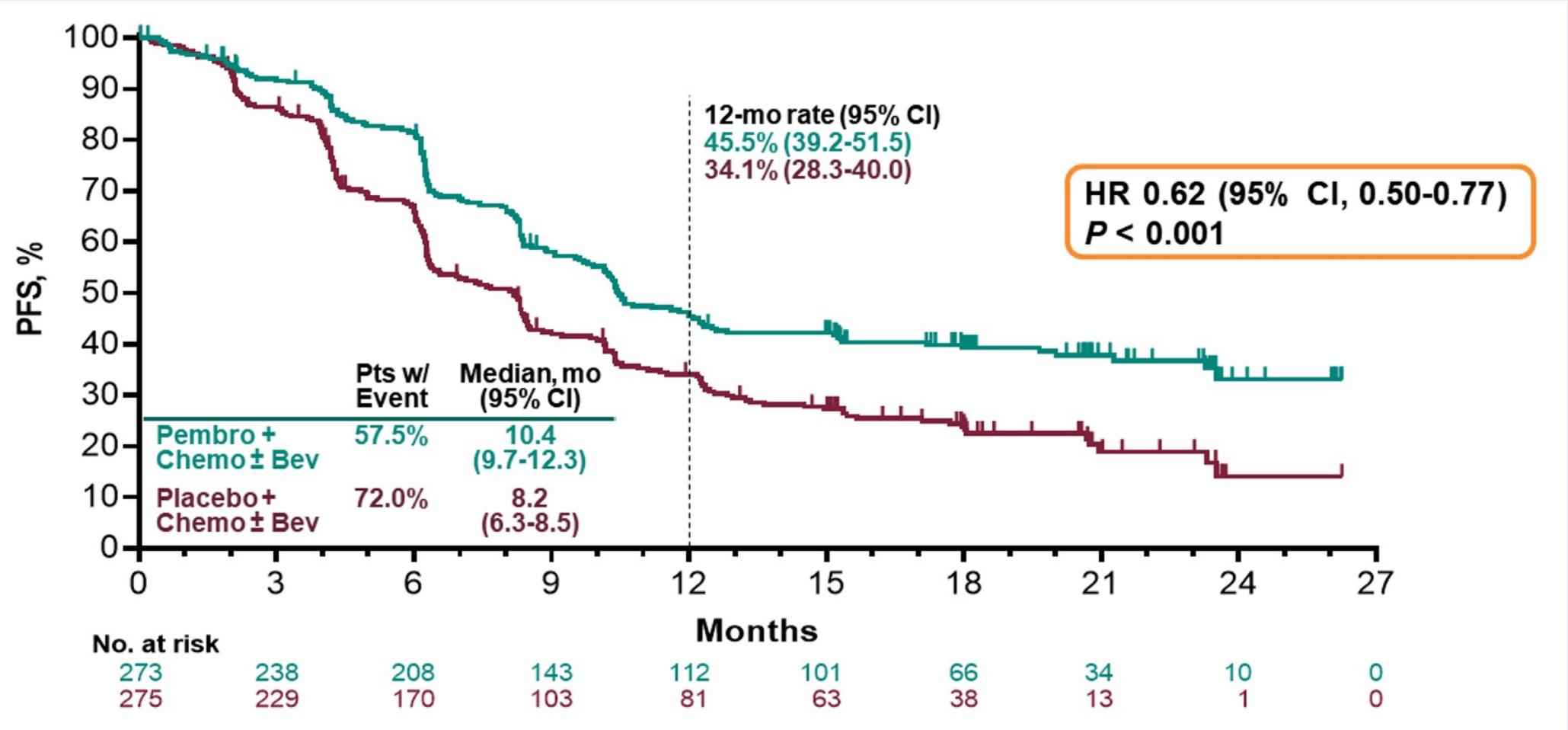
ESMO 2021;Abstract LBA2

Pembrolizumab plus Chemotherapy versus Placebo plus Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Randomized, Double-Blind, Phase 3 KEYNOTE-826 Study

Nicoletta Colombo,[1] Coraline Dubot,[2] Domenica Lorusso,[3] Valeria Caceres,[4] Kosei Hasegawa,[5] Ronnie Shapira-Frommer,[6] Krishnansu S. Tewari,[7] Pamela Salman,[8] Edwin Hoyos Usta,[9] Eduardo Yañez,[10] Mahmut Gümüş,[11] Mivael Olivera Hurtado de Mendoza,[12] Vanessa Samouëlian,[13] Vincent Castonguay,[14] Alexander Arkhipov,[15] Sarper Toker,[16] Kan Li,[16] Stephen M. Keefe,[16] Bradley J. Monk,[17] on behalf of the KEYNOTE-826 Investigators

[1]University of Milan-Bicocca and European Institute of Oncology (IEO) IRCCS, Milan, Italy; [2]Institut Curie Saint-Cloud, Saint-Cloud, France, Group d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO); [3]Fondazione Policlinico Universitario A Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; [4]Instituto de Oncología Angel H. Roffo, Buenos Aires, Argentina; [5]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [6]Ella Lemelbaum Institute for Immuno-Oncology, Sheba Medical Center, Ramat Gan, Israel; [7]University of California, Irvine, Orange, CA, USA; [8]Oncovida Cancer Center, Providencia, Chile; [9]IMAT Oncomedica S.A., Monteria, Colombia; [10]Universidad de la Frontera, Temuco, Chile; [11]Istanbul Medeniyet University Hospital, Istanbul, Turkey; [12]Instituto Nacional de Enfermedades Neoplásicas, INEN, Lima, Perú; [13]Centre Hospitalier de l'Université de Montréal (CHUM), Centre de Recherche de l'Université de Montréal (CRCHUM), Université de Montréal, Montréal, QC, Canada; [14]Centre Hospitalier Universitaire de Québec, Université Laval, Québec City, QC, Canada; [15]Medical Rehabilitation Center under the Ministry of Health of Russian Federation, Moscow, Russia; [16]Merck & Co., Inc., Kenilworth, NJ, USA; [17]Arizona Oncology (US Oncology Network), University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA

KEYNOTE-826: PFS in PD-L1 CPS ≥1 Population



Colombo N et al. ESMO 2021;Abstract LBA2.

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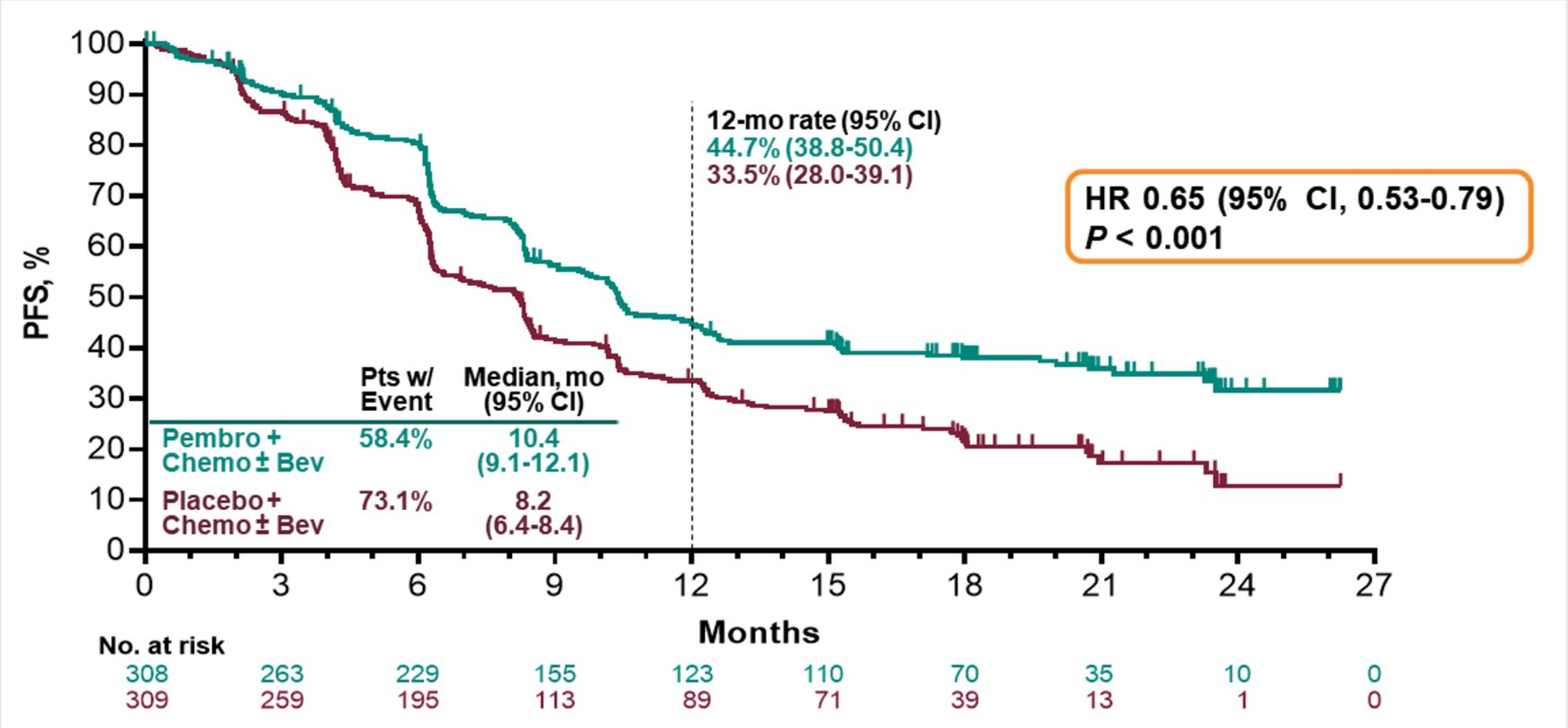
KEYNOTE-826: PFS in All-Comer Population



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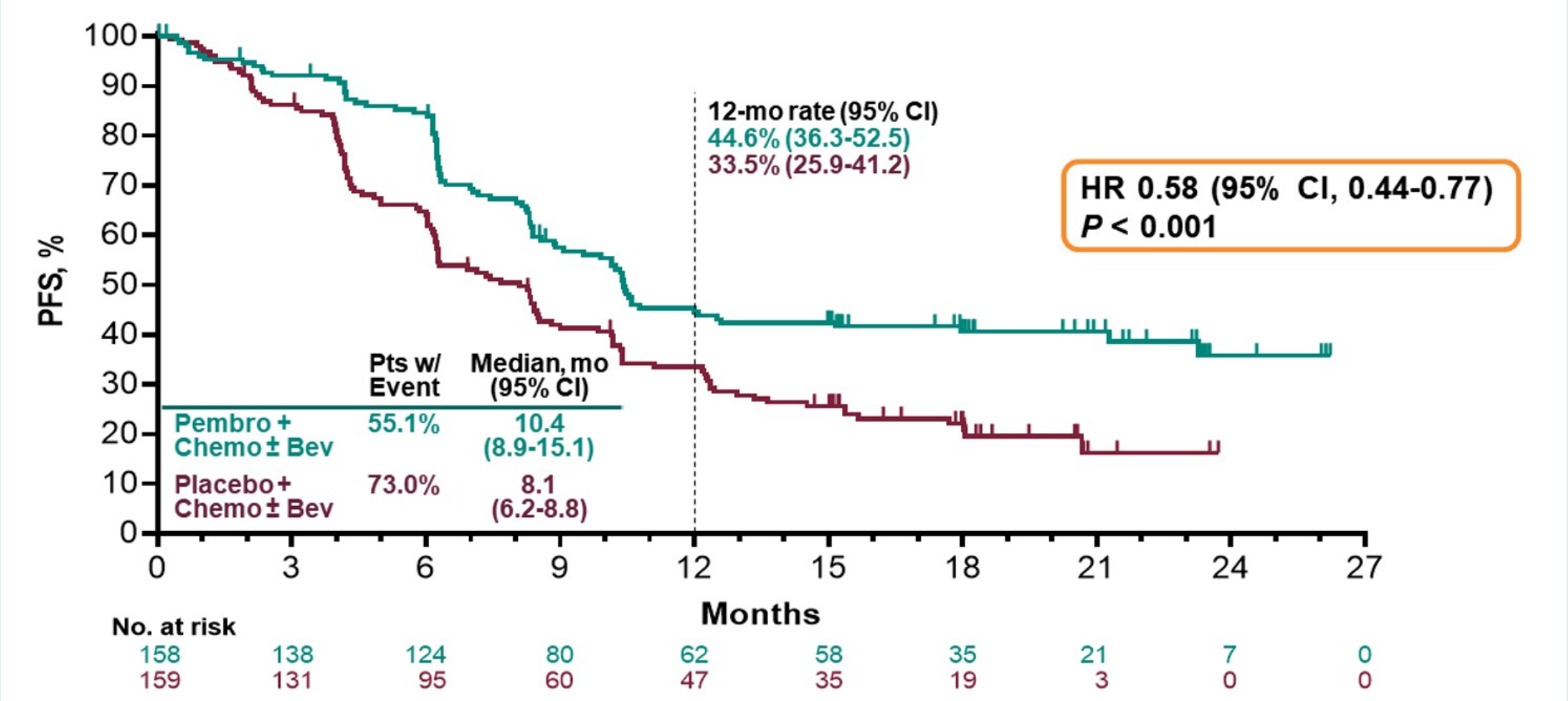
KEYNOTE-826: PFS in PD-L1 CPS ≥10 Population



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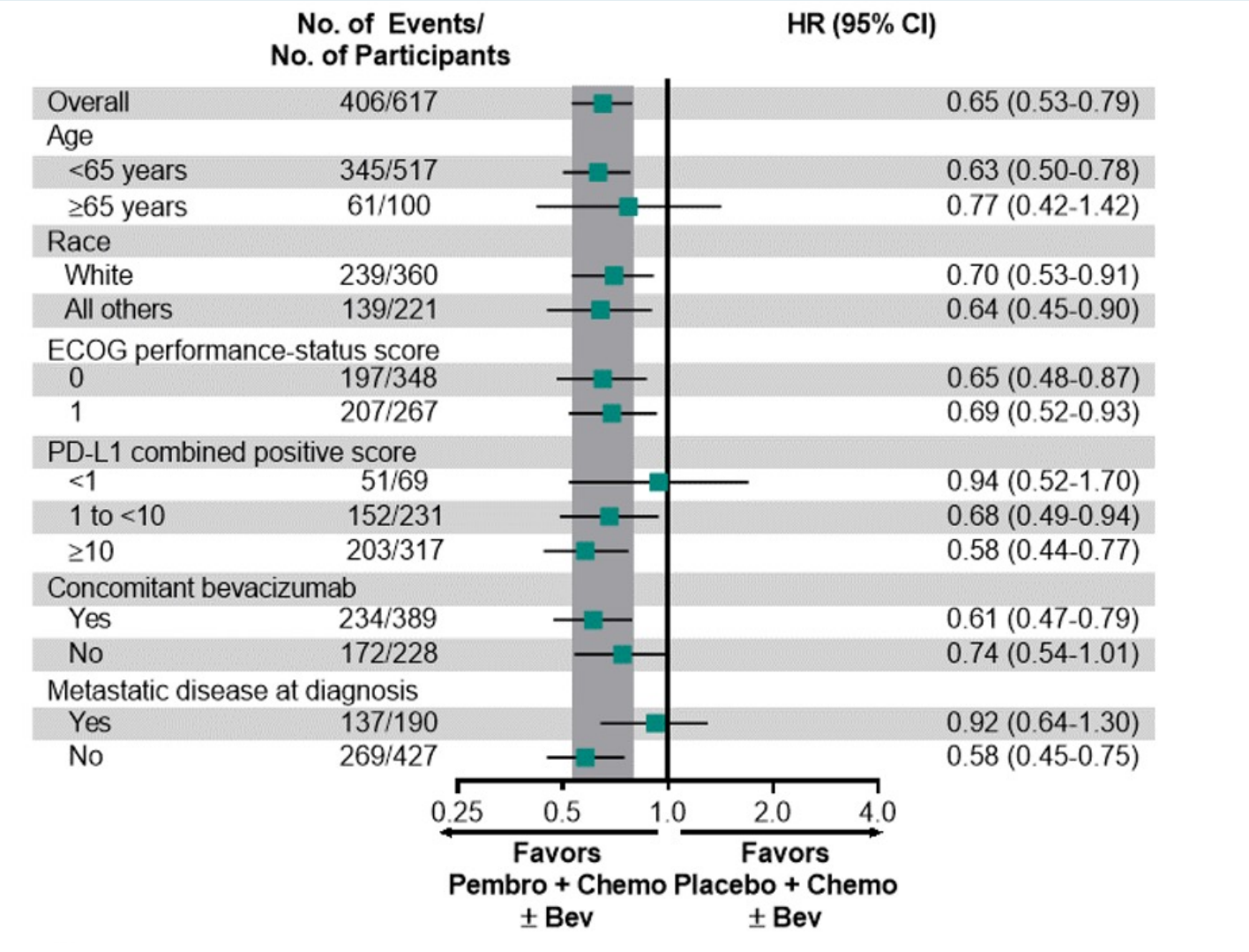
KEYNOTE-826: PFS Protocol-Specified Subroups
All-Comer Population



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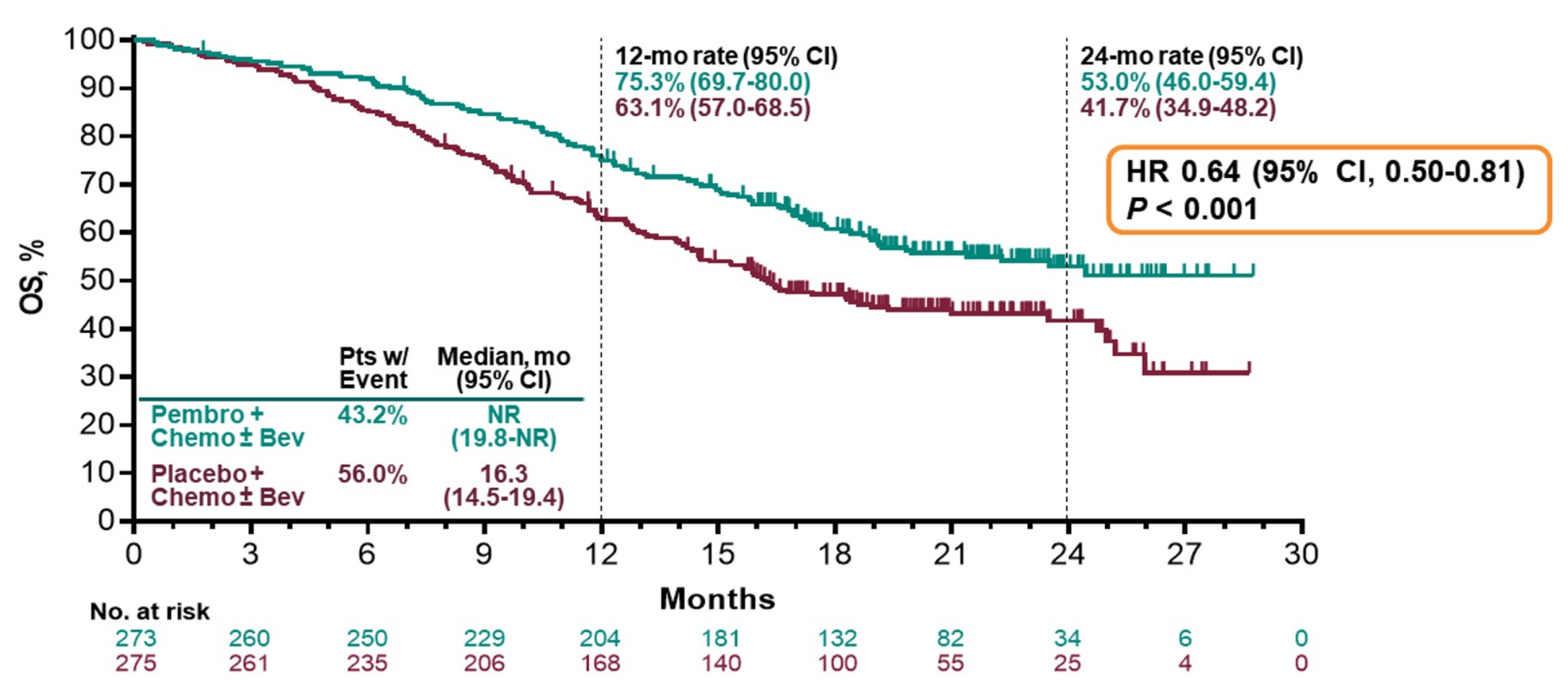
KEYNOTE-826: OS in PD-L1 CPS ≥1 Population



Significant benefit was also observed in the protocol-specified primary analysis populations of all comers and PD-L1 CPS ≥10.

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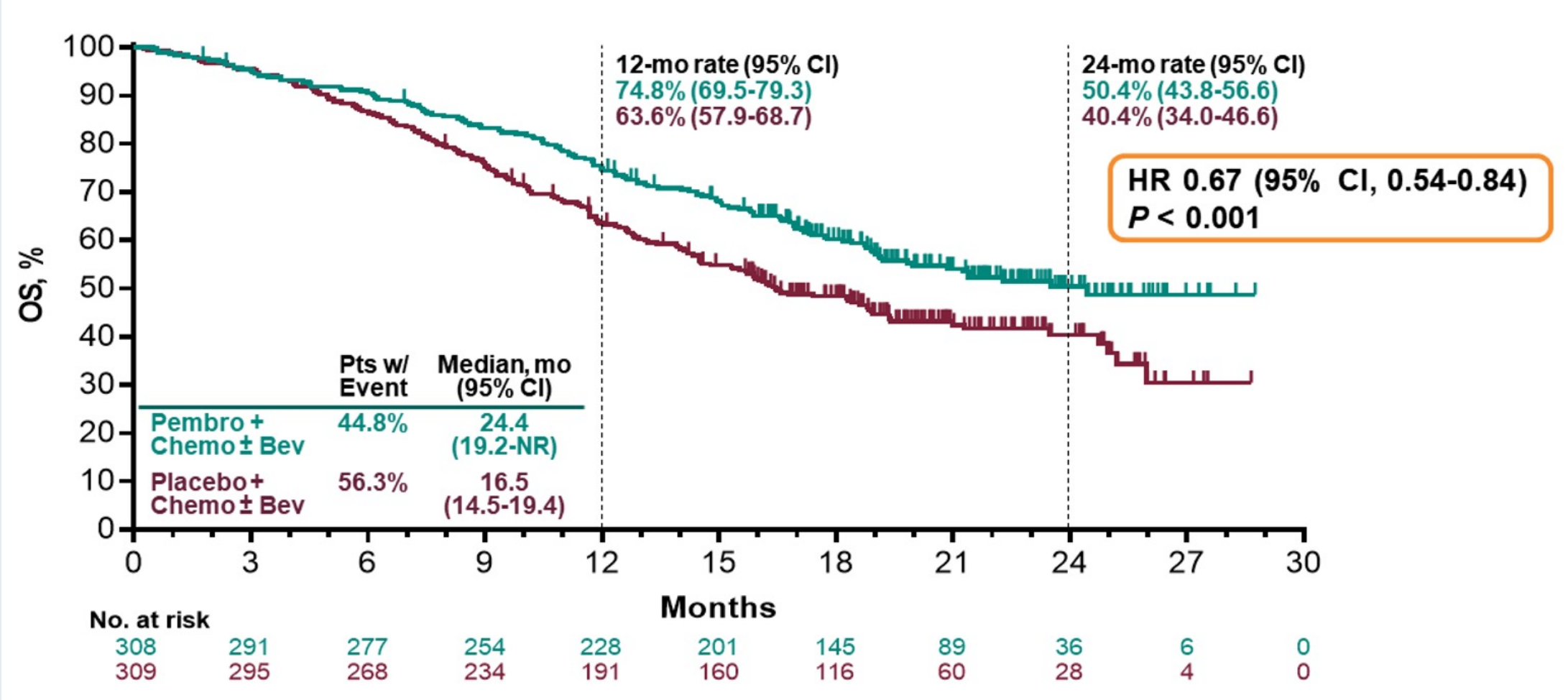
KEYNOTE-826: OS in All-Comer Population



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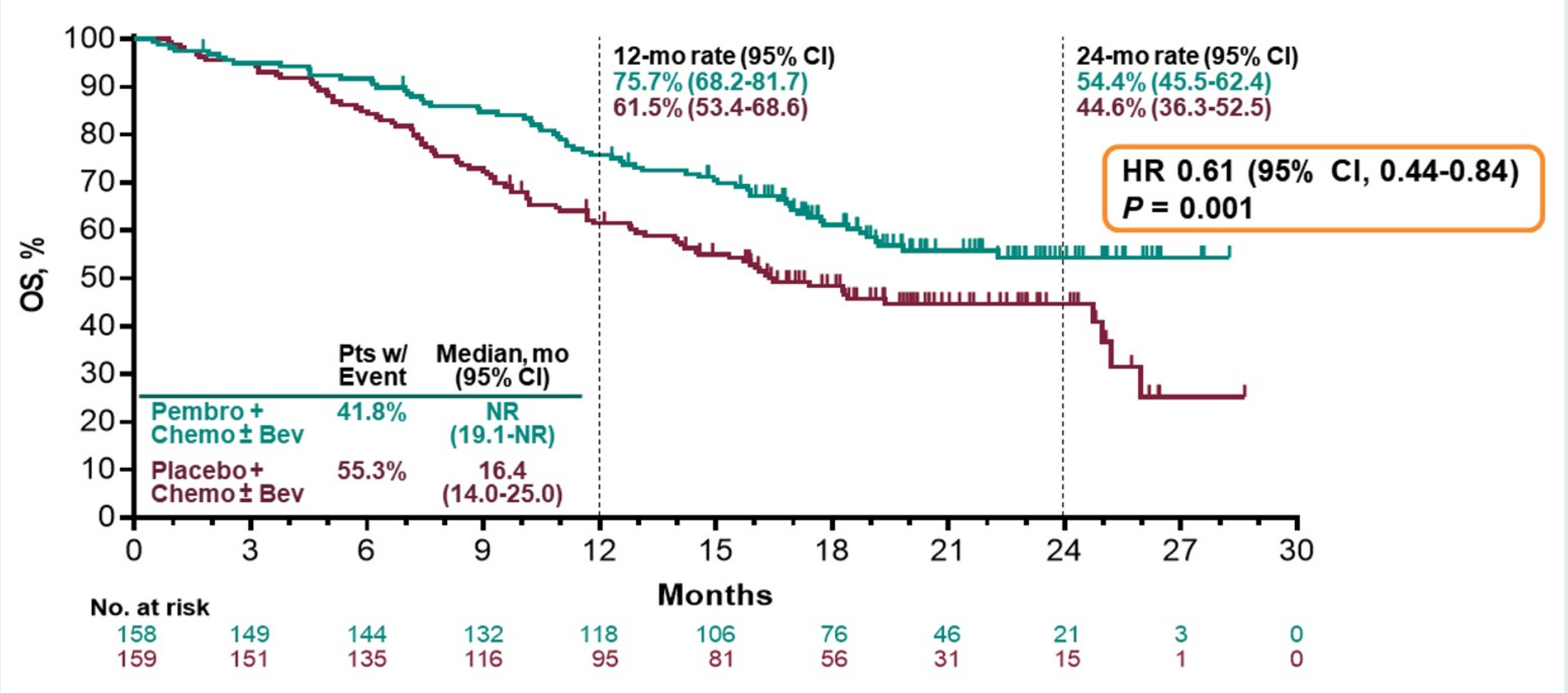

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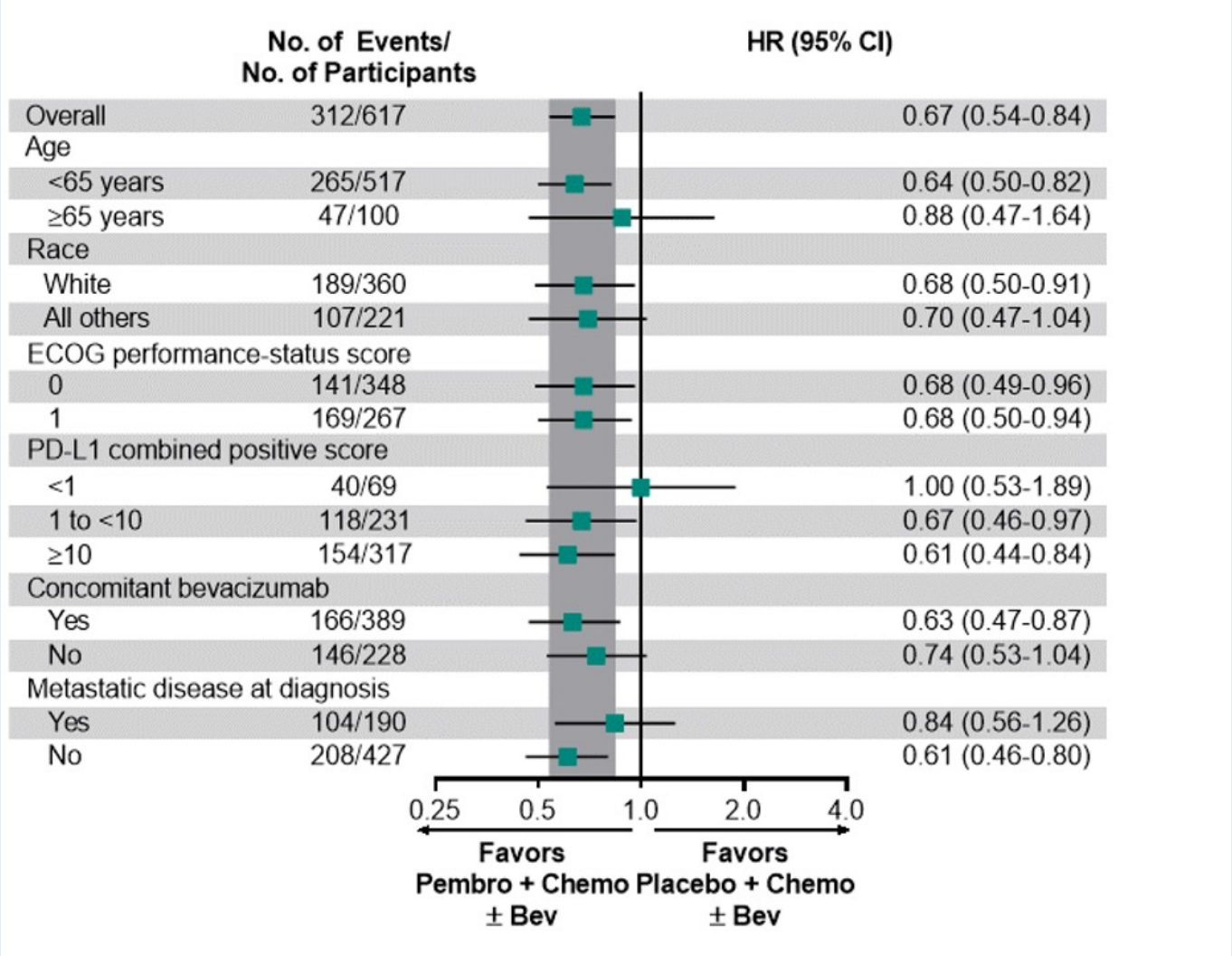

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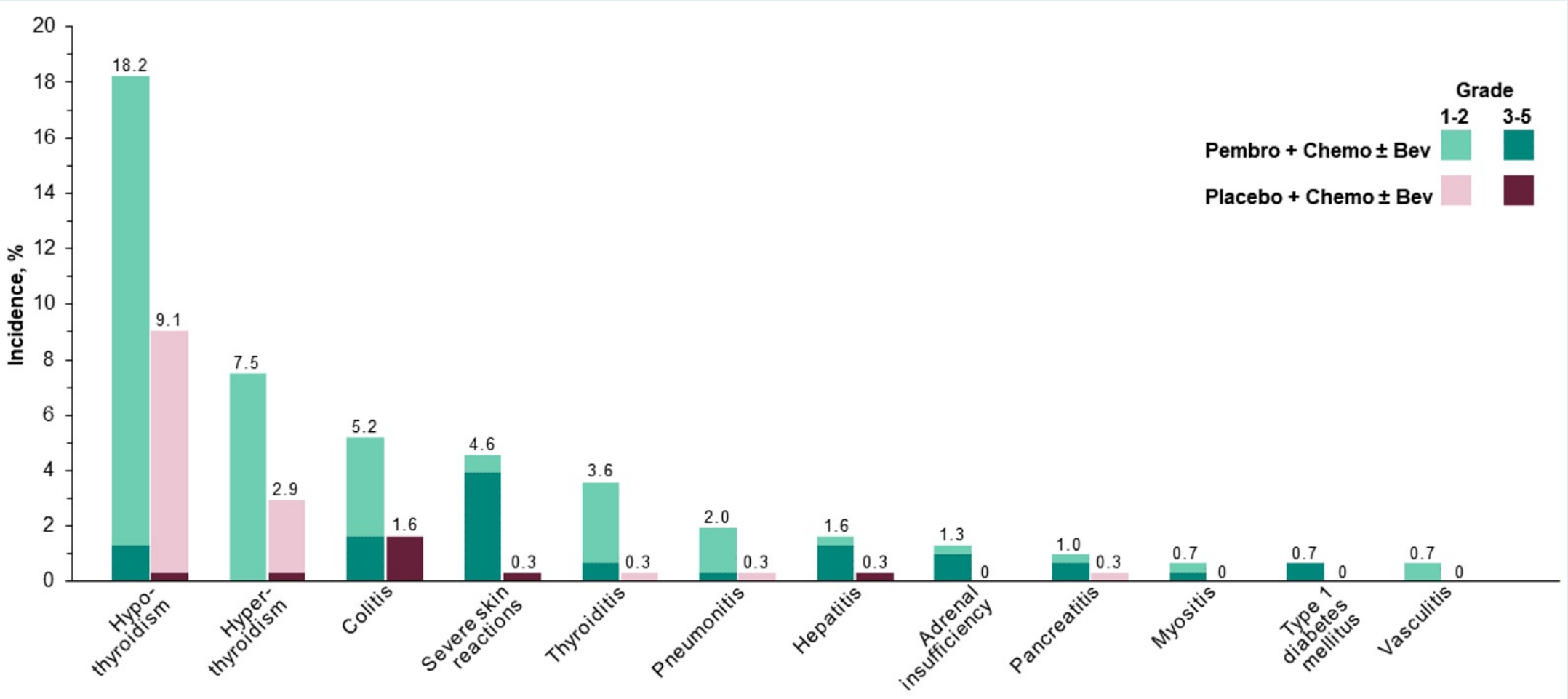
KEYNOTE-826: Immune-Mediated AEs
Incidence ≥2 Patients in Either Arm



Colombo N et al. ESMO 2021;Abstract LBA2.

ESMO 2021;Abstract VP4

2021 ESMO congress

EMPOWER GOG FOUNDATION ENGOT European Network of Gynaecological Oncological Trial groups

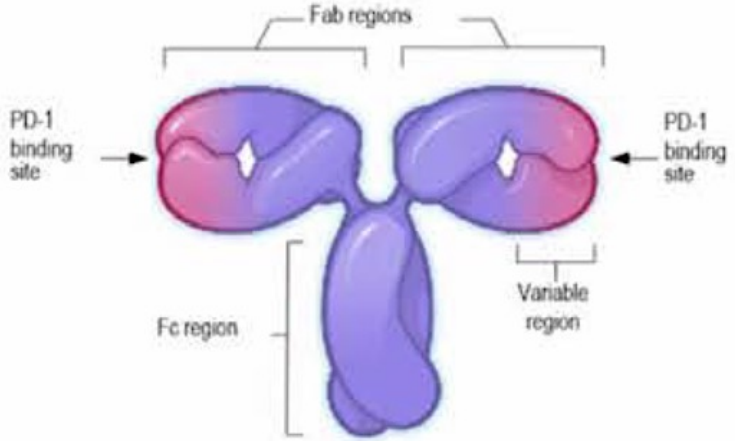
EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9: Results of Phase 3 trial of cemiplimab vs investigator's choice (IC) chemotherapy (chemo) in recurrent/metastatic (R/M) cervical carcinoma

Krishnansu S Tewari,*† Bradley J Monk,* Ignace Vergote, Austin Miller, Andreia Cristina de Melo, Hee Seung Kim, Yong Man Kim, Alla Lisyanskaya, Vanessa Samouëlian, Domenica Lorusso, Fernanda Damian, Chih-Long Chang, Evgeniy A Gotovkin, Shunji Takahashi, Daniella Ramone, Joanna Pikiel, Beata Maćkowiak-Matejczyk, Eva Maria Guerra, Nicoletta Colombo, Yulia Makarova, Jingjin Li, Shaheda Jamil, Vladimir Jankovic, Chieh-I Chen, Frank Seebach, David M Weinreich, George D Yancopoulos, Israel Lowy, Melissa Mathias, Matthew G Fury, and Ana Oaknin

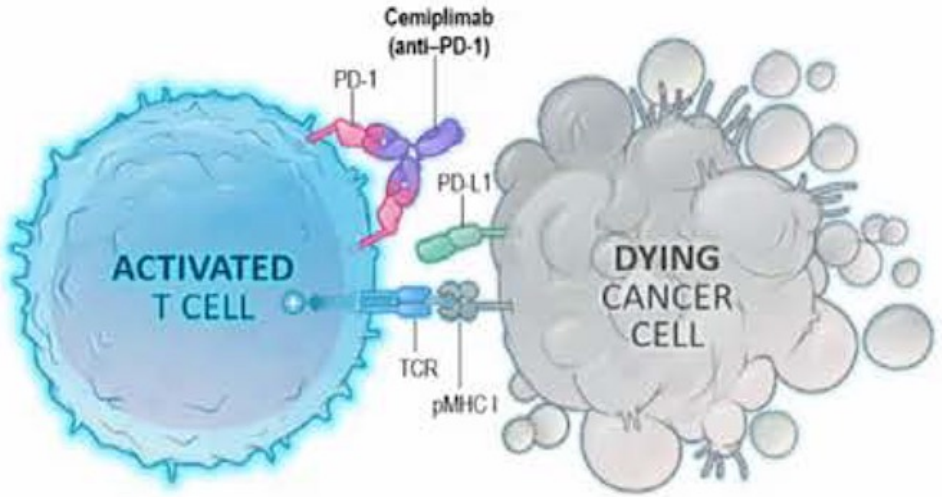
*Contributed equally to this presentation.
†Department of Obstetrics & Gynecology, University of California, Irvine.
Portions of the following were previously presented at the May 2021 ESMO Virtual Plenary.

Cemiplimab

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]

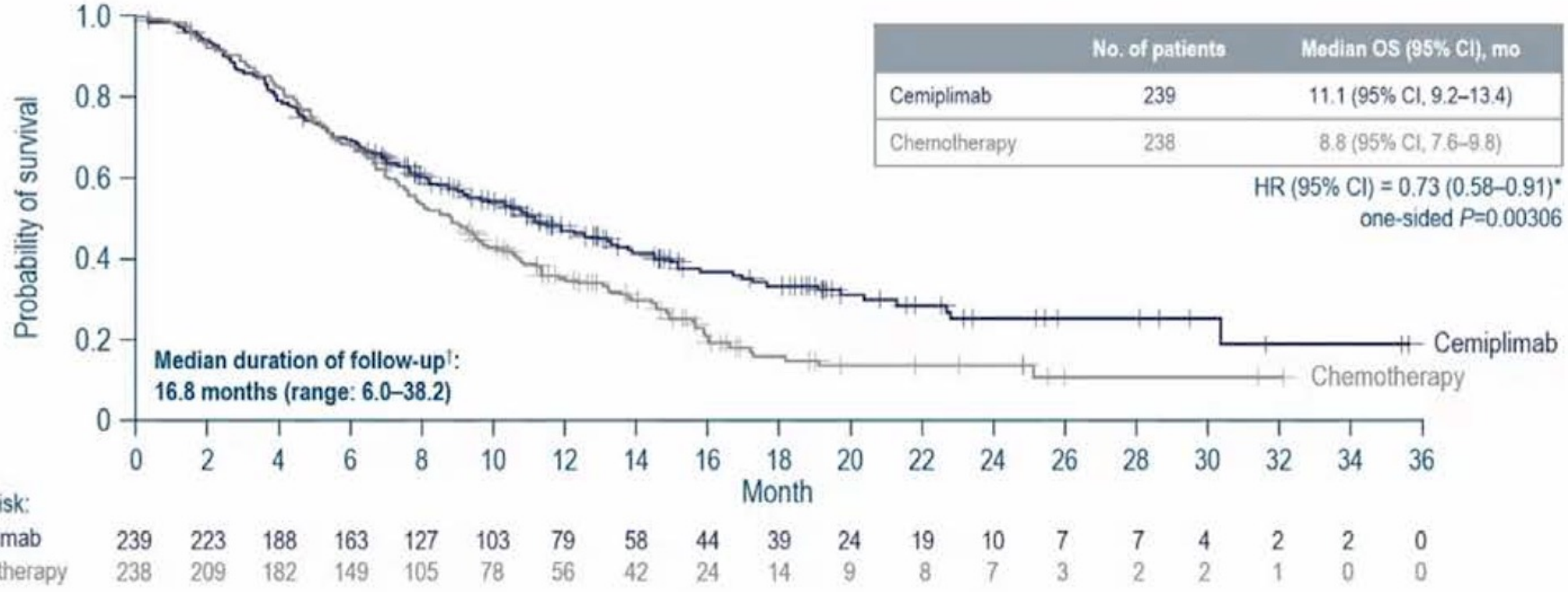
Ig, immunoglobin; Fc, fragment crystallizable; ORR, objective response rate; PD-1, programmed cell death-1; PD-L1, PD-ligand 1; pMHC I, peptide-bound major histocompatibility complex I; R/M, recurrent or metastatic; TCR, T-cell receptor.

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

Tewari KS et al. ESMO 2021;Abstract VP4.

Survival Analysis for SCC Population

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



	No. of patients	Median OS (95% CI), mo
Cemiplimab	239	11.1 (95% CI, 9.2–13.4)
Chemotherapy	238	8.8 (95% CI, 7.6–9.8)

HR (95% CI) = 0.73 (0.58–0.91)*
one-sided *P*=0.00306

*Stratified by geographic region (North America vs Asia vs ROW) according to interactive web response system. †From randomisation to data cutoff date.
Data cutoff date: 4 Jan 2021.
CI, confidence interval; HR, hazard ratio; IDMC, Independent Data Monitoring Committee; mo, month; OS, overall survival; ROW, rest of world; SCC, squamous cell carcinoma.

Tewari KS et al. ESMO 2021;Abstract VP4.

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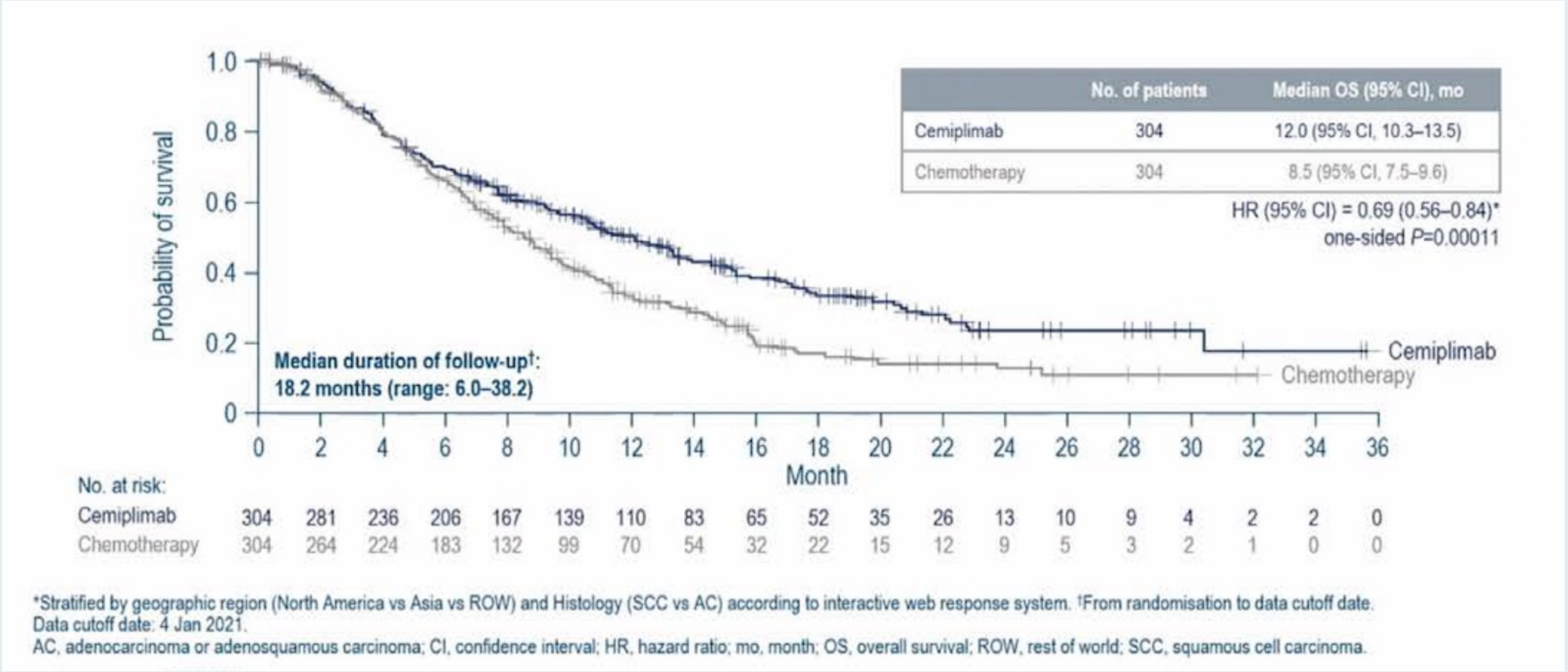
Survival Analysis for the Total Population



	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)

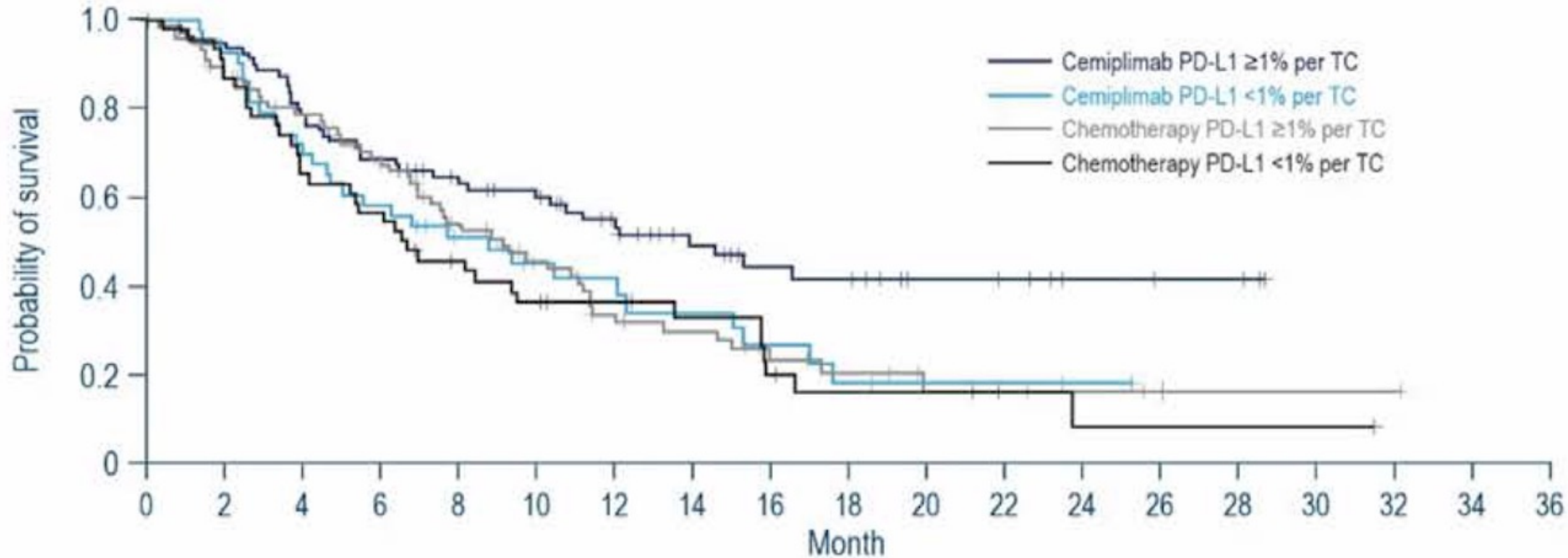
HR (95% CI) = 0.69 (0.56–0.84)*
one-sided *P*=0.00011

*Stratified by geographic region (North America vs Asia vs ROW) and Histology (SCC vs AC) according to interactive web response system. †From randomisation to data cutoff date.
Data cutoff date: 4 Jan 2021.
AC, adenocarcinoma or adenosquamous carcinoma; CI, confidence interval; HR, hazard ratio; mo, month; OS, overall survival; ROW, rest of world; SCC, squamous cell carcinoma.

Tewari KS et al. ESMO 2021;Abstract VP4.

RTP RESEARCH TO PRACTICE

Survival Analysis by PD-L1 Status



No. at risk:																			
Cemiplimab PD-L1 ≥1% per TC	82	78	65	55	45	39	30	22	16	15	10	9	4	3	3	0	0	0	0
Cemiplimab PD-L1 <1% per TC	44	41	30	25	18	13	11	9	6	4	3	3	1	0	0	0	0	0	0
Chemotherapy PD-L1 ≥1% per TC	80	69	58	50	36	28	20	16	10	8	5	5	4	2	1	1	1	0	0
Chemotherapy PD-L1 <1% per TC	48	40	30	26	19	15	12	10	6	4	4	2	1	1	1	1	0	0	0

*Associations between efficacy outcomes and PD-L1 expression (detected using the SP263 monoclonal antibody) in tumor cells was evaluated using exploratory analyses.
Of 608 randomized patients, 254 had valid baseline PD-L1 samples: cemiplimab (n=126) and chemotherapy (n=128).
Data cutoff date: 4 Jan 2021.
PD-L1, programmed cell death-ligand 1; TC, tumor cells.

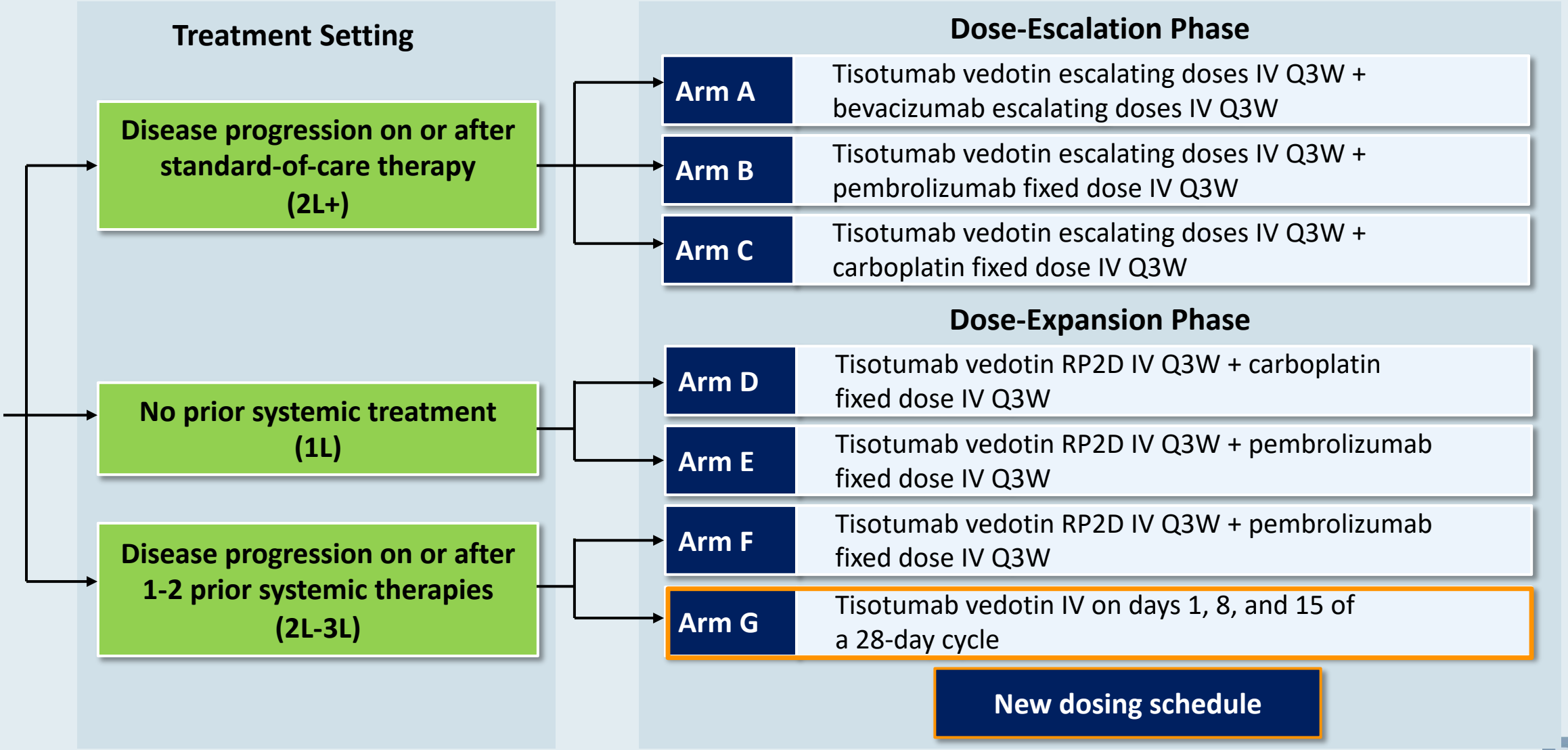
Tewari KS et al. ESMO 2021;Abstract VP4.

Other ESMO 2021 Highlights

- O'Malley D et al. **Balstilimab (anti-PD-1) in combination with zalifrelimab (anti-CTLA-4): Final results from a phase II study in patients (pts) with recurrent/metastatic (R/M) cervical cancer (CC).** ESMO 2021;Abstract 724MO.

- Vergote IB et al. **Tisotumab vedotin (TV) + carboplatin (Carbo) in first-line (1L) or + pembrolizumab (Pembro) in previously treated (2L/3L) recurrent or metastatic cervical cancer (r/mCC): Interim results of ENGOT-Cx8/GOG-3024/innovaTV 205 study.** ESMO 2021;Abstract 723MO.

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



Courtesy of David M O'Malley, MD

FDA Accelerated Approval Granted to Tisotumab Vedotin-tftv for Previously Treated Recurrent or Metastatic Cervical Cancer

Press Release – September 20, 2021

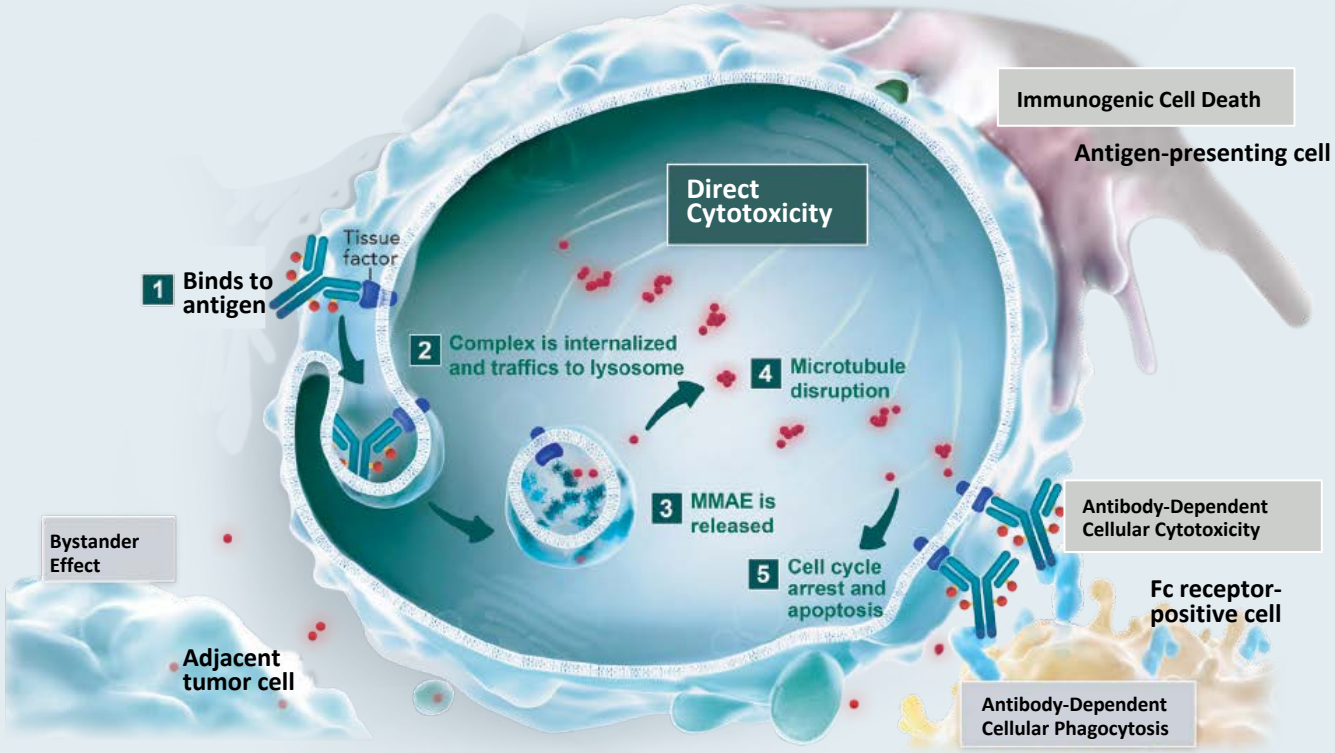
"[It was announced today that the FDA] has granted accelerated approval to tisotumab vedotin-tftv, the first and only approved antibody-drug conjugate (ADC) for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. Tisotumab vedotin-tftv is approved under the FDA's Accelerated Approval Program based on tumor response and the durability of the response. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials."

The accelerated approval is based on results from the innovaTV 204 trial. InnovaTV 301, a global, randomized Phase III clinical trial intended to support global registrations, is under way. The prescribing information for tisotumab vedotin-tftv includes a BOXED WARNING for ocular toxicity and warnings for peripheral neuropathy, hemorrhage, pneumonitis and embryo-fetal toxicity.

https://investor.seagen.com/press-releases/news-details/2021/Seagen-and-Genmab-Announce-FDA-Accelerated-Approval-for-TIVDAK-tisotumab-vedotin-tftv-in-Previously-Treated-Recurrent-or-Metastatic-Cervical-Cancer/default.aspx

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

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

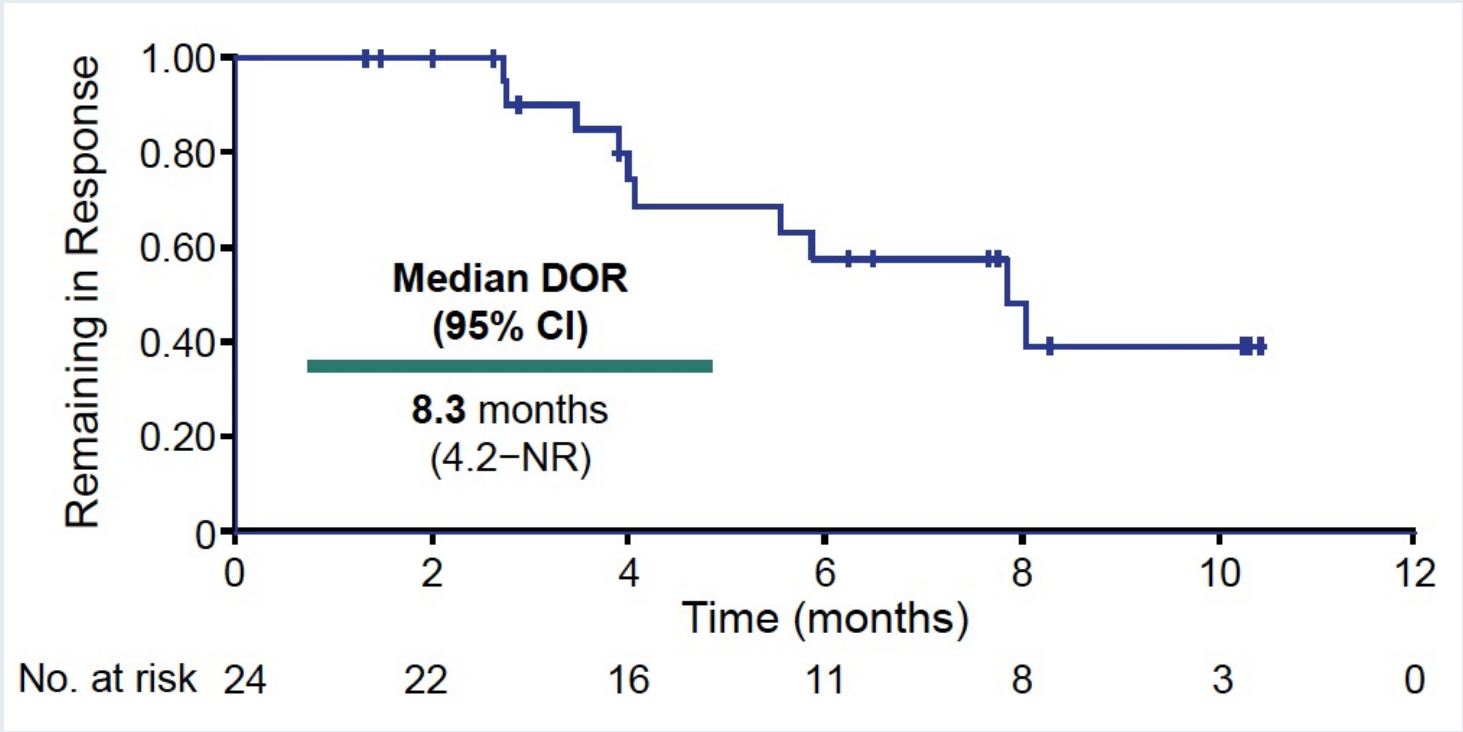
Coleman RL et al.

ESMO 2020;Abstract LBA32.

innovaTV 204: Antitumor Activity by IRC Assessment

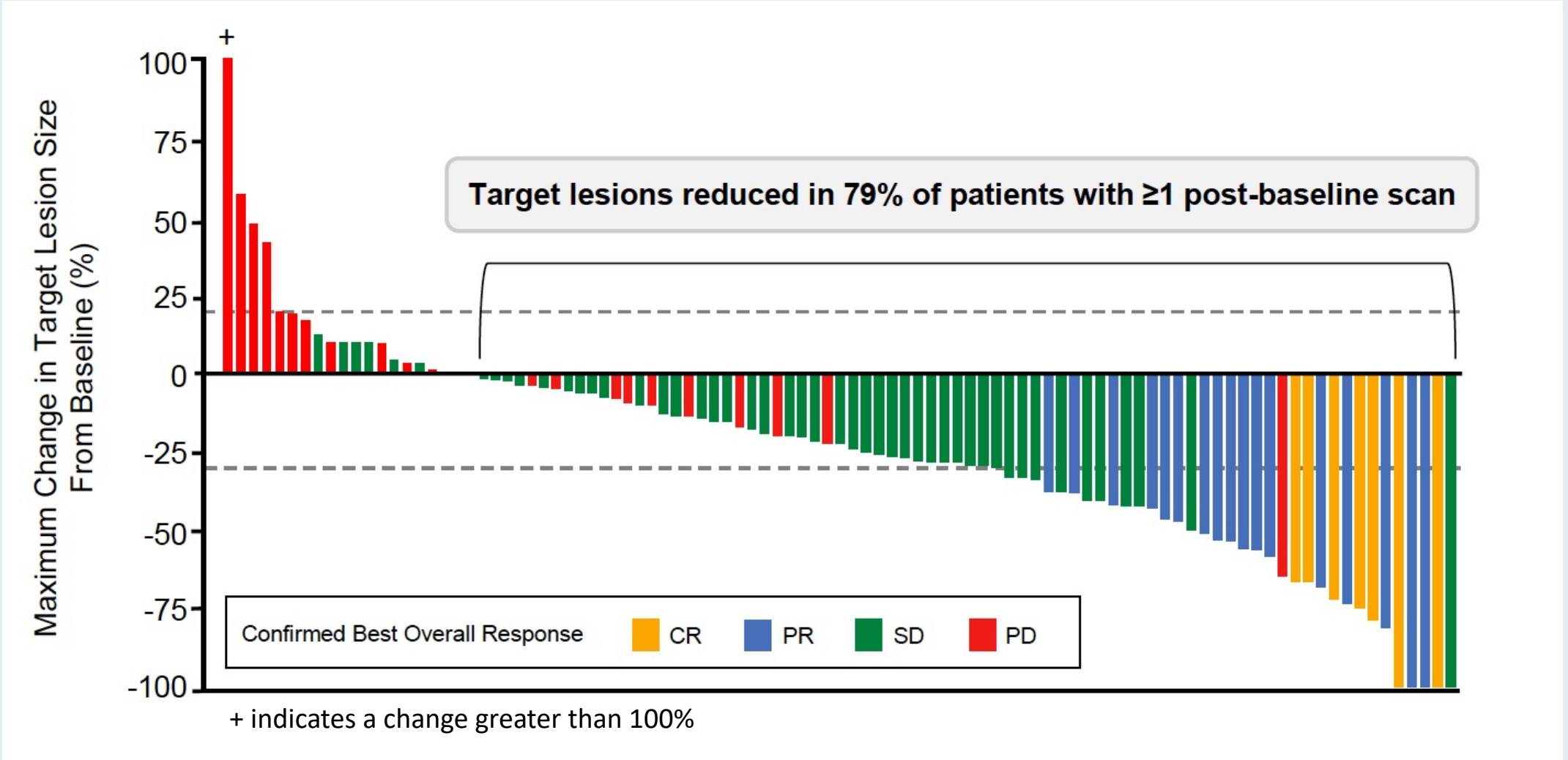
Clinical Variable	N = 101
Confirmed ORR	24%
CR	7%
PR	17%
SD	49%
PD	24%
Not evaluable	4%

Duration of Response



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

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



+ indicates a change greater than 100%

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

Meet The Professor with Dr Hensley

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- A 54-year-old woman with recurrent uterine high-grade stromal sarcoma

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MODULE 5: Other Key Recent Data Sets

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Case Presentation – Dr Hussein: A 65-year-old woman with MSS metastatic uterine adenocarcinoma who receives pembrolizumab/lenvatinib

Dr Atif Hussein

- Diagnosed with uterine adenocarcinoma, with biopsy-proven lung metastases, MSS, PD-L1: 12%
- Carboplatin/paclitaxel x 8, with excellent PR x 16 months
- Recurrence in retroperitoneum and lungs
- Lenvatinib (20 mg qd) and pembrolizumab (200 mg q3wks) x 11 months and ongoing
  - Dose reduction of lenvatinib, but recent increase in fatigue, hypertension
  - Patient inquiring about discontinuing lenvatinib, continuing pembrolizumab

Questions

- How long do you continue with lenvatinib and pembrolizumab? Would you be hesitant in reducing the dose of lenvatinib if the patient has side effects but is responding?
- Have you used this doublet to maximal response or tolerability and then dropped lenvatinib completely or reduced it to its lowest dose and continued with pembrolizumab?
- Do you use pembrolizumab 400 mg q6wks across the board, or only for select patients?

Case Presentation – Dr Hussein: A 55-year-old woman with MSI-high, MMR-deficient uterine adenocarcinoma who receives pembrolizumab

Dr Atif Hussein

- 5/2019: Diagnosed with endometroid adenocarcinoma
- TAH/BSO and lymphadenectomy, with 3/8 positive nodes
- 3/2020: Carboplatin/paclitaxel x 6 and pelvic RT, with no recurrent disease
- 5/2020 CT: PD in abdominal and cervical adenopathy
- Molecular testing: No clinically significant mutation identified; MSI-high, MONO-27 and NR-24 unstable
- NGS: No actionable mutations
- 5/2020: Pembrolizumab, x 15 months and ongoing, with CR after 3-4 months

Case Presentation – Dr Hussein: A 55-year-old woman with MSI-high, MMR-deficient uterine adenocarcinoma who receives pembrolizumab

Dr Atif Hussein

Questions

- How long do you continue pembrolizumab in patients who achieve a CR and are tolerating therapy well?
- How do you decide between pembrolizumab, nivolumab, and dostarlimab? Any difference in efficacy and/or safety?
- How do you use checkpoint inhibitors in patients with recurrent uterine adenocarcinoma who are microsatellite stable or mismatch repair proficient but with the mutations more than 10 per megabase based on one of the indications for pembrolizumab? Have you seen any clinically significant responses?
- Would you use dostarlimab in recurrent uterine adenocarcinoma that is MS stable or proficient MMR based on the GARNET study?
- How do you find the doses of dostarlimab using it initially every 3 weeks for 4 cycles and then you double the dose every 6 weeks?

RTP RESEARCH TO PRACTICE

ESMO 2021 Highlights

- Colombo N et al. **Outcomes by histology and prior therapy with lenvatinib plus pembrolizumab vs treatment of physician's choice in patients with advanced endometrial cancer (Study 309/KEYNOTE-775).** ESMO 2021;Abstract 726M0.
- Lorusso D et al. **Randomized phase III trial on niraparib-TSR-042 (dostarlimab) vs physician's choice chemotherapy in recurrent ovarian, fallopian tube or primary peritoneal cancer patients not candidate for platinum retreatment: NItCHE trial (MITO 33).** ESMO 2021;Abstract 816TiP.
- Mirza MR et al. **ENGOT-EN6/GOG-3031/NSGO-CTU-RUBY part 2: A phase III, randomized, double-blind study of dostarlimab + carboplatin-paclitaxel followed by dostarlimab + niraparib versus placebo (PBO) + carboplatin-paclitaxel followed by PBO in recurrent or advanced endometrial cancer (EC).** ESMO 2021;Abstract 820TiP.

FDA Grants Accelerated Approval to Dostarlimab-gxly for dMMR Advanced Solid Tumors

Press Release – August 17, 2021

"The Food and Drug Administration granted accelerated approval to dostarlimab-gxly for adult patients with mismatch repair deficient (dMMR) recurrent or advanced solid tumors, as determined by an FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options.

The FDA also approved the VENTANA MMR RxDx Panel as a companion diagnostic device to select patients with dMMR solid tumors for treatment with dostarlimab-gxly.

The efficacy of dostarlimab was evaluated in the GARNET Trial (NCT02715284), a non-randomized, multicenter, open-label, multi-cohort trial. The efficacy population consisted of 209 patients with dMMR recurrent or advanced solid tumors who progressed following systemic therapy and had no satisfactory alternative treatment.

The primary efficacy endpoints were overall response rate (ORR) and duration of response (DoR) as determined by blinded independent central review according to RECIST 1.1. The ORR was 41.6% (95% CI: 34.9, 48.6), with 9.1% complete response rate and 32.5% partial response rate. Median DOR was 34.7 months (range 2.6, 35.8+), with 95.4% of patients with duration ≥6 months."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-dostarlimab-gxly-dmmr-advanced-solid-tumors

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

Interim Analysis of the Immune-Related Endpoints of the Mismatch Repair Deficient (dMMR) and Proficient (MMRp) Endometrial Cancer Cohorts from the GARNET Study

Pothuri B et al.

SGO 2021;Abstract 10417.

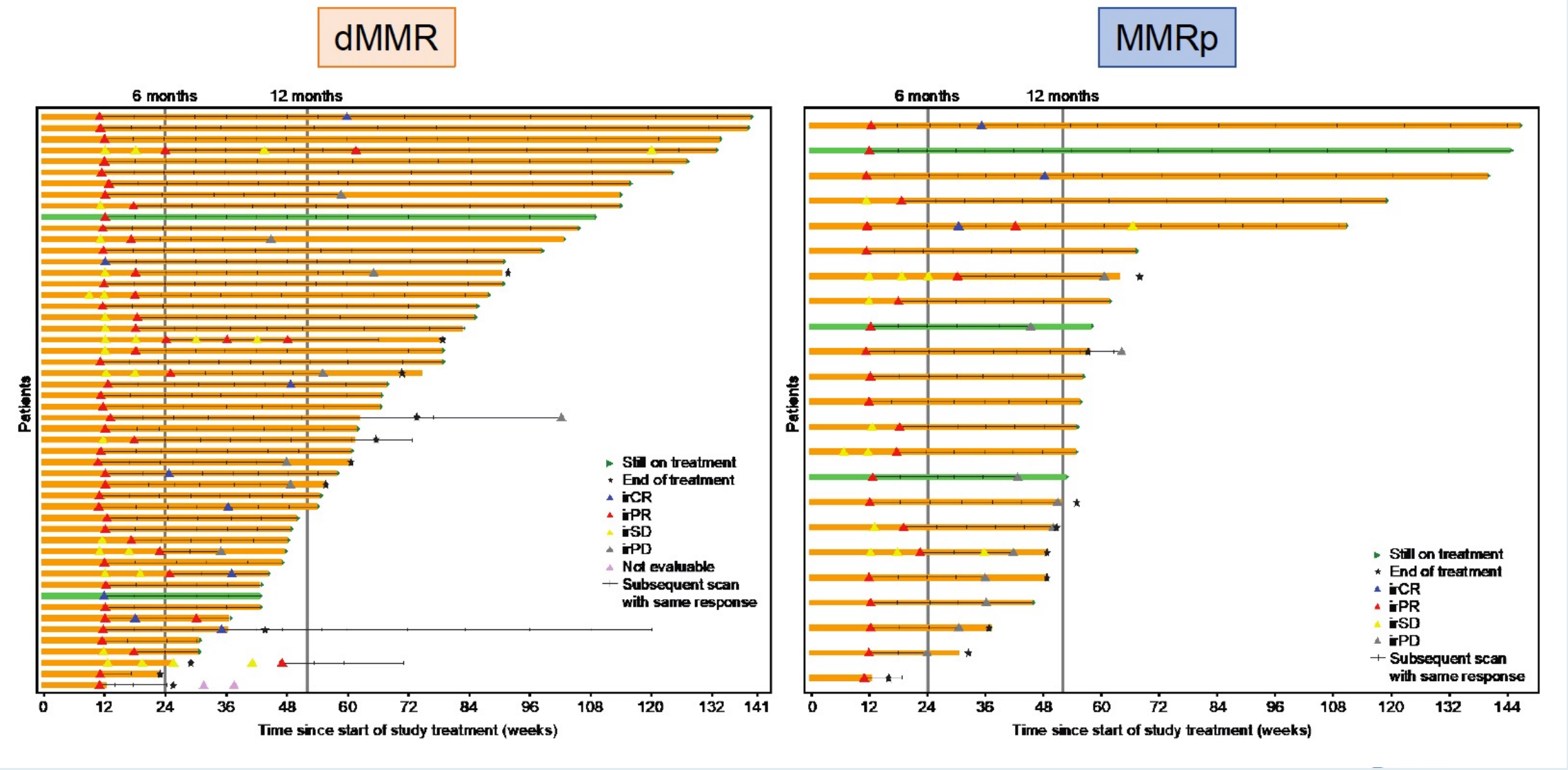
GARNET: Immune-Related Secondary Endpoints

(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.

GARNET: Duration of Response



Pothuri B et al. SGO 2021;Abstract 10417.

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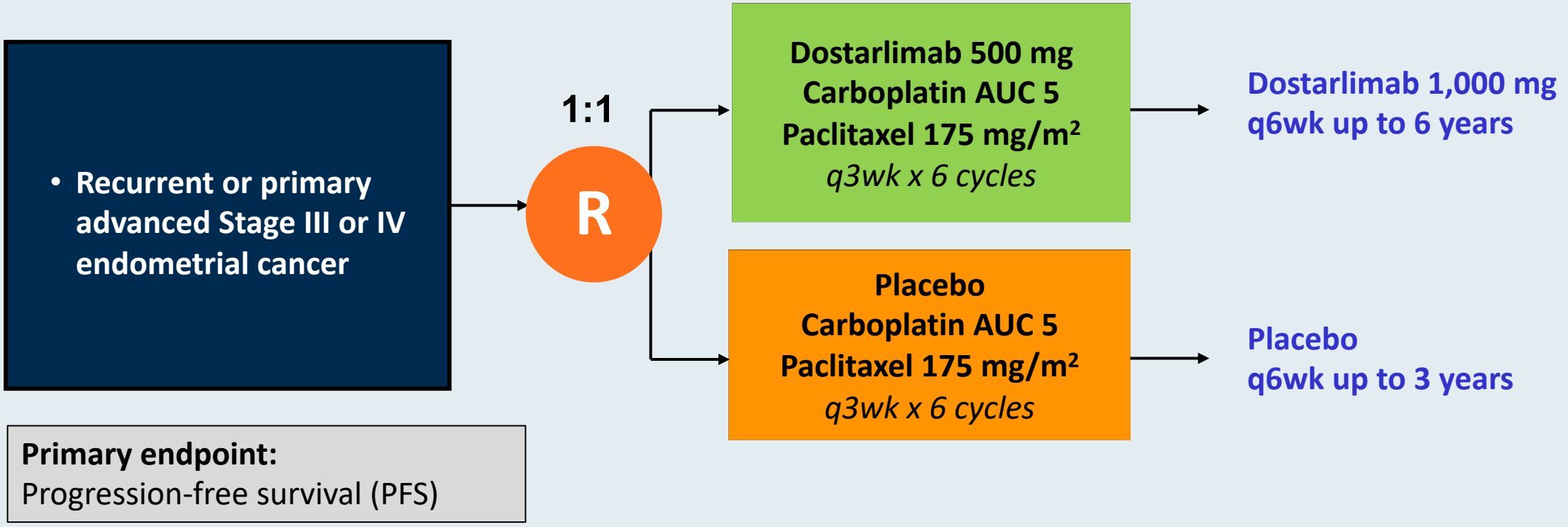
ENGOT-EN6/NSGO-RUBY Phase III Schema



Mirza MR et al. ASCO 2020;Abstract TPS6107.

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Case Presentation – Dr Hussein: A 54-year-old woman with recurrent uterine high-grade stromal sarcoma

Dr Atif Hussein

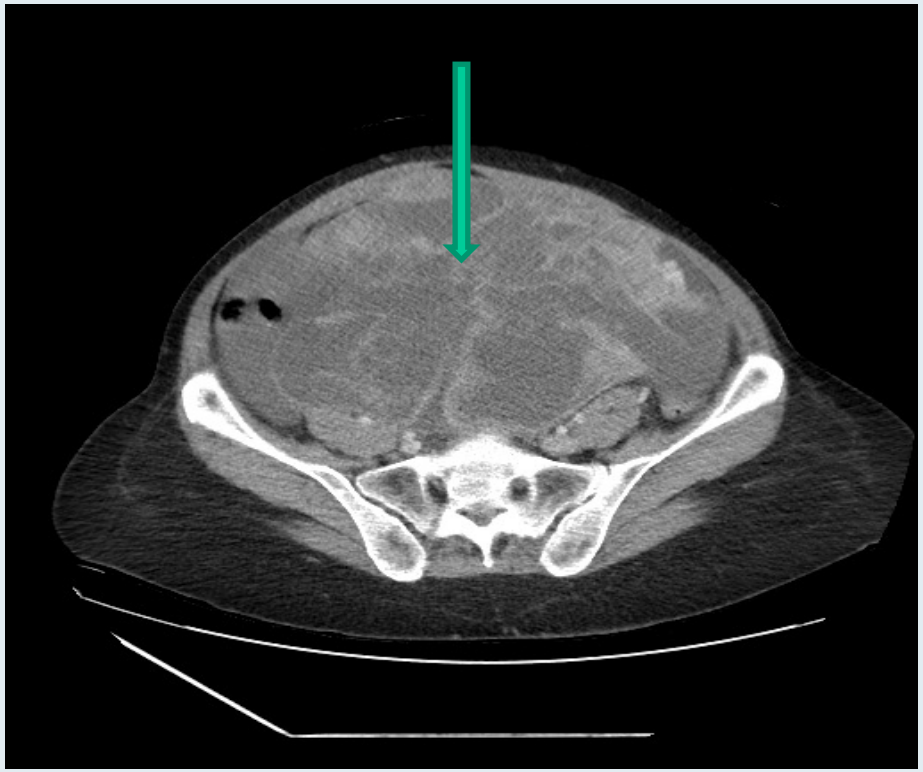
- 8/2018: Right leg pain x 1 month
- 9/2018: Diagnosed with undifferentiated high-grade stromal cell carcinoma
- NGS: No actionable targets, MSS, PD-L1 0%
- Doxorubicin/olaratumab x 6 → R0 surgery

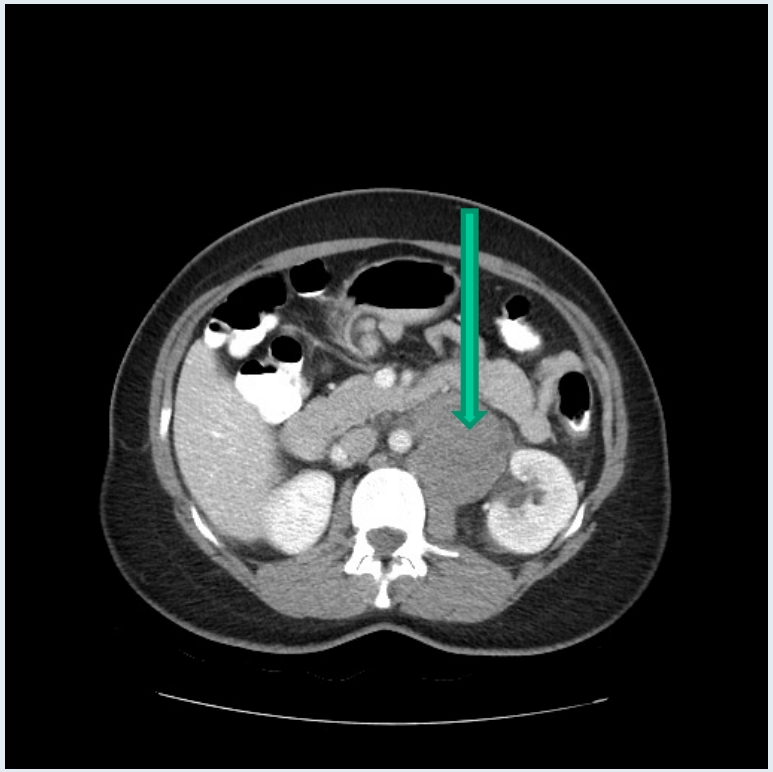
Case Presentation – Dr Hussein: A 54-year-old woman

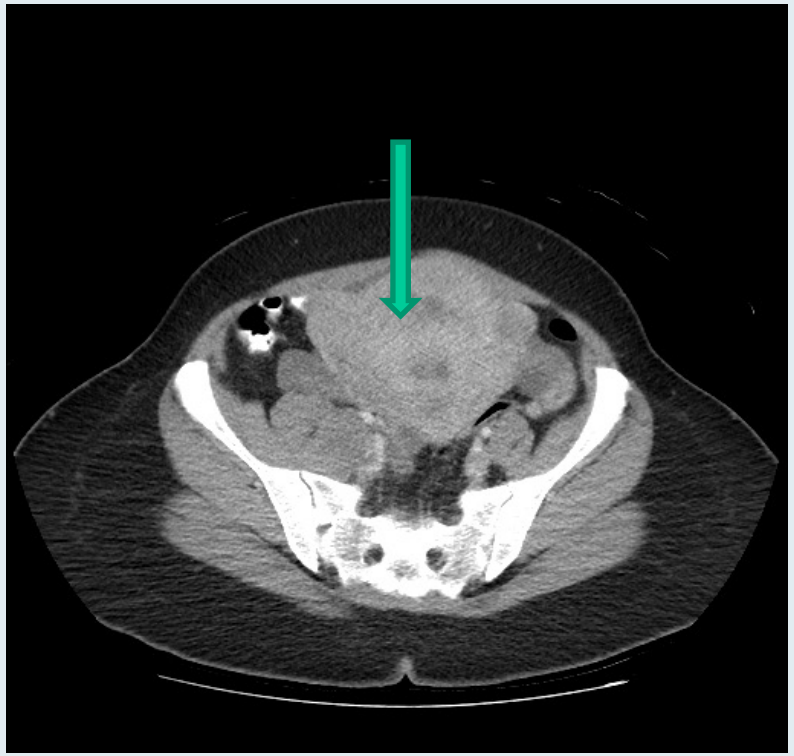
Dr Atif Hussein

Pelvic and abdominal masses at presentation

09/2018







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Case Presentation – Dr Hussein: A 54-year-old woman with recurrent uterine high-grade stromal sarcoma (continued)

Dr Atif Hussein

- 8/2018: Right leg pain x 1 month
- 9/2018: Diagnosed with undifferentiated high-grade stromal cell carcinoma
- NGS: No actionable targets, MSS, PD-L1 0%
- Doxorubicin/olaratumab x 6 → R0 surgery
- ***7/2019 PET/CT: New hypermetabolic right external iliac LAD → Gemcitabine/docetaxel***
- ***9/2019 CT chest/abdomen/pelvis: Increasing metastatic disease → RT to right pelvic mass***
- ***2/2020: Second resection***
- ***5/2020 CT: Large mass filling LUQ with infiltration into the spleen***
- ***6/2020: Third resection of splenic mass and splenectomy***
- ***9/2020 Imaging: Hepatic metastases → Pazopanib → 2/2021: PD, but pt refuses further therapy***
- ***Hospice, passes away***

Case Presentation – Dr Hussein: A 54-year-old woman with recurrent uterine high-grade stromal sarcoma (continued)

Dr Atif Hussein

Questions

- ***What would you have done if the patient had agreed to further chemotherapy after the doxorubicin and then the gemcitabine/docetaxel?***
- ***Do you treat those undifferentiated endometrial sarcomas like any other sarcomas? What's the role of eribulin, trabectedin, pazopanib in these patients? Have you seen significant responses?***
- ***Recently dislocation of (7;17) has been reported in a lot of these patients. What do you think the significance of this translocation is? Any data using immune checkpoint inhibitors in uterine stromal sarcoma, especially the undifferentiated type?***

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Case Presentation – Dr Hussein: A 54-year-old woman with recurrent uterine high-grade stromal sarcoma (continued)

Dr Atif Hussein

- 8/2018: Right leg pain x 1 month
- 9/2018 CT chest/abdomen/pelvis: Left bulky retroperitoneal para-aortic aortocaval lymphadenopathy, bulky adenopathy in right pelvis, enlarged uterine mass 7 x 8-cm
- Uterine biopsies: Undifferentiated high-grade stromal cell carcinoma
- NGS: No actionable targets, MSS, PD-L1 0%
- Doxorubicin/olaratumab x 6 → R0 surgery
- 7/2019 PET/CT: New hypermetabolic right external iliac LAD → Gemcitabine/docetaxel
- 9/2019 CT chest/abdomen/pelvis: Increasing metastatic disease → RT to right pelvic mass
- 2/2020: Second resection
- 5/2020 CT: Large mass filling LUQ with infiltration into the spleen
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- Hospice, passes away

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JOURNAL OF CLINICAL ONCOLOGY

ART OF ONCOLOGY

What Do You Say When She Is No Longer Living With Cancer?

Martee L. Hensley

Meet The Professor with Dr Hensley

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Cervical Cancer

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Regulatory and reimbursement issues aside, 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. Cemiplimab
5. 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?

 Dr Birrer	Pembrolizumab	 Dr Penson	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 Dr Coleman	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher	 Dr Powell	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 Dr Oaknin	Anti-PD-1/PD-L1 antibody in general	 Dr Slomovitz	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher
 Dr O'Malley	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher	 Dr Tewari	Test for PD-L1 CPS and administer pembrolizumab if 1% or higher

RTP RESEARCH TO PRACTICE

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 and cemiplimab were accessible, what would likely be your next line of treatment?

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

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Endometrial Cancer

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In general, what treatment would you recommend for a patient with microsatellite-stable metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel?

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

In general, what treatment would you recommend for a patient with metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel if their disease was microsatellite stable (MSS)?

 Dr Birrer	Lenvatinib/ pembrolizumab	 Dr Penson	Lenvatinib/ pembrolizumab
 Dr Coleman	Lenvatinib/ pembrolizumab	 Dr Powell	Lenvatinib/ pembrolizumab
 Dr Oaknin	Lenvatinib/ pembrolizumab	 Dr Slomovitz	Lenvatinib/ pembrolizumab
 Dr O'Malley	Lenvatinib/ pembrolizumab	 Dr Tewari	Lenvatinib/ pembrolizumab

RTP RESEARCH TO PRACTICE

In general, what treatment would you recommend for a patient with MSI-high metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel?

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

In general, what treatment would you recommend for a patient with metastatic endometrial cancer who experienced disease progression on carboplatin/paclitaxel if their disease was MSI high?

 Dr Birrer	Pembrolizumab	 Dr Penson	Pembrolizumab
 Dr Coleman	Pembrolizumab	 Dr Powell	Pembrolizumab
 Dr Oaknin	Dostarlimab	 Dr Slomovitz	Pembrolizumab
 Dr O'Malley	Pembrolizumab	 Dr Tewari	Pembrolizumab

RTP RESEARCH TO PRACTICE

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?

 Dr Birrer	Second line	 Dr Penson	First line
 Dr Coleman	Second line	 Dr Powell	Second line
 Dr Oaknin	Second line	 Dr Slomovitz	Second line
 Dr O'Malley	First line	 Dr Tewari	Second line

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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?

 Dr Birrer	Yes	 Dr Penson	Yes
 Dr Coleman	Yes	 Dr Powell	Yes
 Dr Oaknin	No	 Dr Slomovitz	No
 Dr O'Malley	Yes	 Dr Tewari	No

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Hensley

MODULE 1: Cervical Cancer

- A 54-year-old woman with recurrent cervical squamous cell carcinoma – PD-L1 CPS: 100
- ESMO 2021 Highlights and Key Data Sets

MODULE 2: Endometrial Cancer

- A 65-year-old woman with MSS metastatic uterine adenocarcinoma who receives pembrolizumab/lenvatinib
- A 55-year-old woman with MSI-high, MMR-deficient uterine adenocarcinoma who receives pembrolizumab
- ESMO 2021 Highlights and Key Data Sets

MODULE 3: Uterine Sarcoma

- A 54-year-old woman with recurrent uterine high-grade stromal sarcoma

MODULE 4: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 5: Other Key Recent Data Sets

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Anti-PD-1/PD-L1 Checkpoint Inhibitors in Endometrial Cancer

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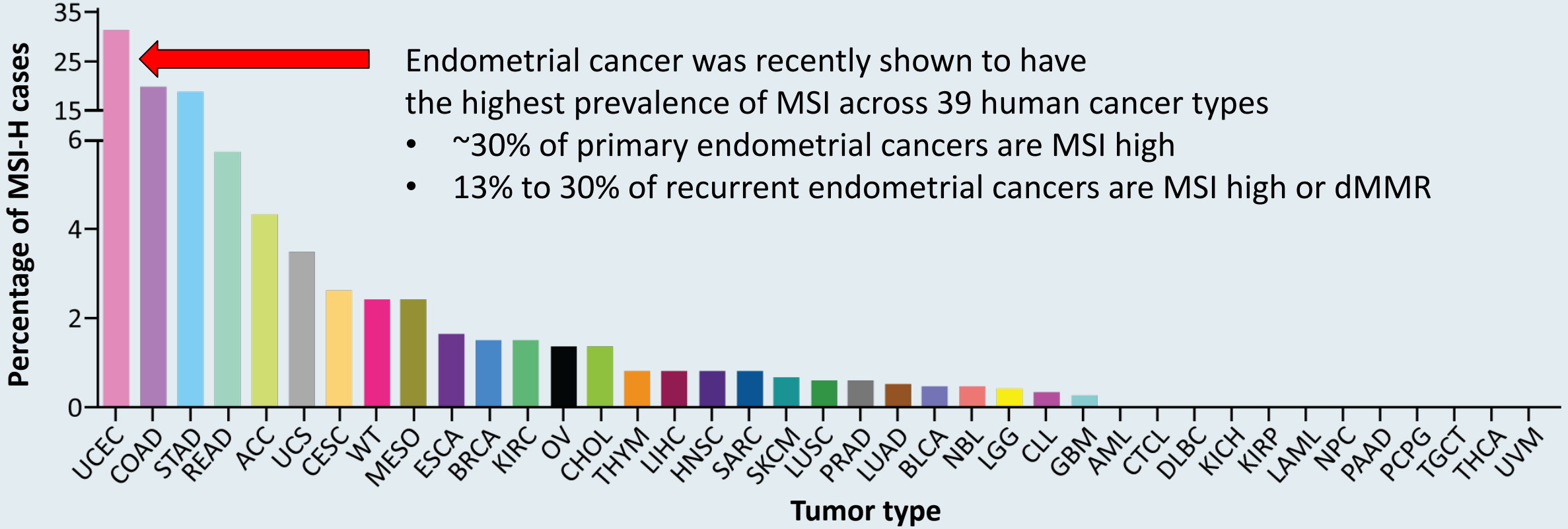
High MSI Across 39 Cancer Types

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



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

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

UCEC = uterine corpus endometrial carcinoma

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

RTP RESEARCH TO PRACTICE

ASCO 2021;Abstract 2565

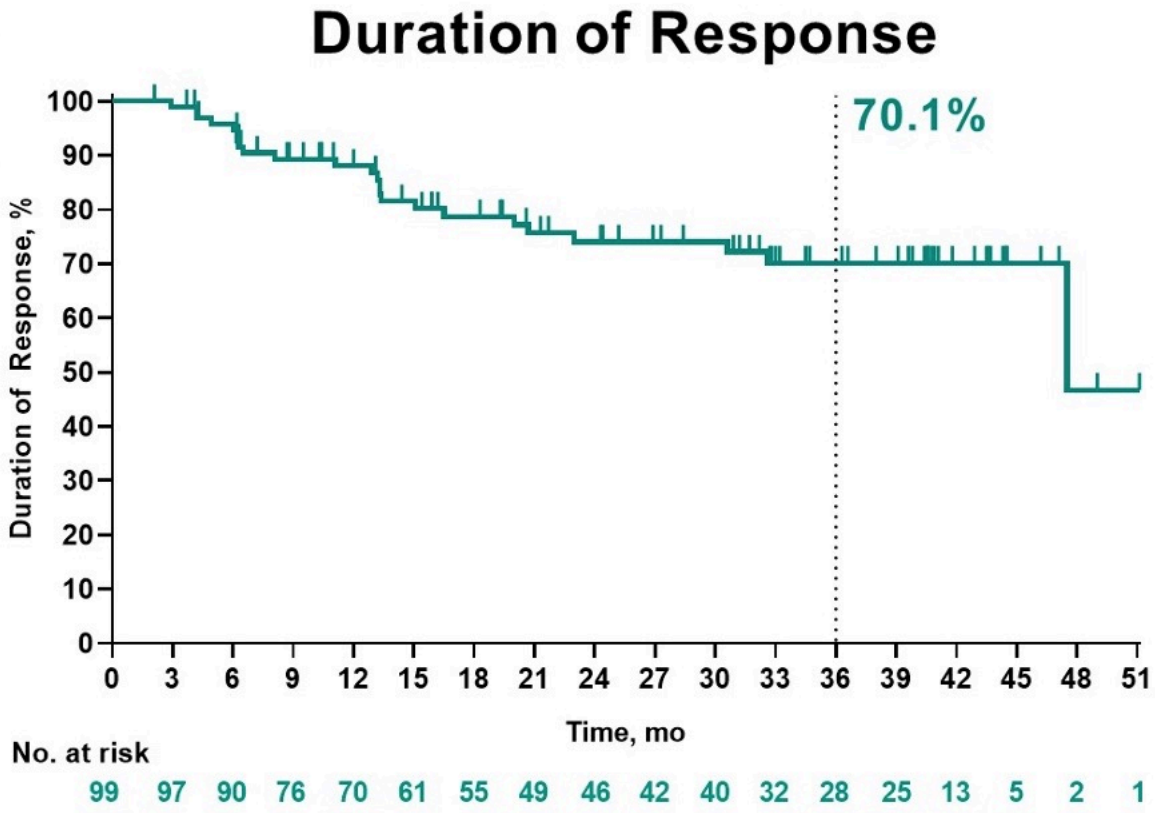
Pembrolizumab in Microsatellite Instability High/Mismatch Repair–Deficient Cancers: Updated Analysis From Phase 2 KEYNOTE-158 Study

M. Maio[1]; P.A. Ascierto[2]; L. Manzyuk[3]; D. Motola-Kuba[4]; N. Penel[5]; P.A. Cassier[6]; G. Mendonca Bariani[7]; A. De Jesus Acosta[8]; T. Doi[9]; F. Longo Muñoz[10]; W.H. Miller, Jr[11]; D.-Y. Oh[12]; M. Gottfried[13]; R. Wang[14]; F. Jin[14]; K. Norwood[14]; A. Marabelle[15]

[1]Center for Immuno-Oncology, University Hospital of Siena, Siena, Italy; [2]Istituto Nazionale Tumori Istituto di Ricovero e Cura a Carattere Scientifico Fondazione Pascale, Naples, Italy; [3]NN Blokhin National Medical Research Center of Oncology, Moscow, Russia; [4]COMOP A.C., Clinical Investigation, Mexico City, Mexico; [5]Centre Oscar Lambret and Lille University, Lille, France; [6]Department of Medical Oncology, Centre Léon Bérard, Lyon, France; [7]Instituto do Câncer do Estado de São Paulo, Universidade de São Paulo, São Paulo, Brazil; [8]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; [9]National Cancer Center Hospital East, Kashiwa, Japan; [10]Hospital Universitario Ramón y Cajal, IRYCIS, CIBERONC, Madrid, Spain; [11]Jewish General Hospital and McGill University, Montréal, QC, Canada; [12]Department of Internal Medicine, Seoul National University Hospital, and Cancer Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; [13]Meir Medical Center, Tel Aviv, Israel; [14]Merck & Co., Inc., Kenilworth, NJ, USA; [15]Gustave Roussy, Institut National de la Santé et de la Recherche Médicale U1015, Villejuif, France.

KEYNOTE-158: Updated Response Analyses

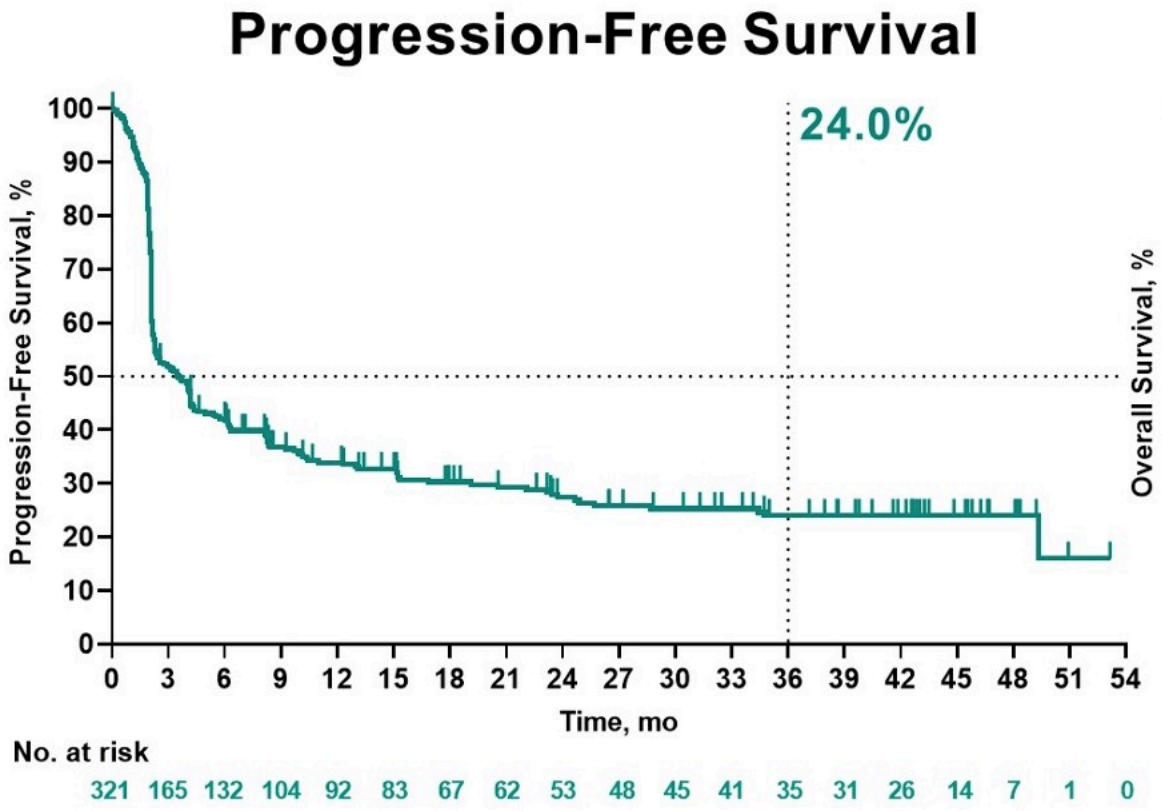
Efficacy Analysis Population	N = 321
ORR, % (95% CI)	**30.8 (25.8–36.2)**
CR	27 (8.4)
PR	72 (22.4)
SD	61 (19.0)
PD	131 (40.8)
Nonevaluable	3 (0.9)
No assessment[a]	27 (8.4)

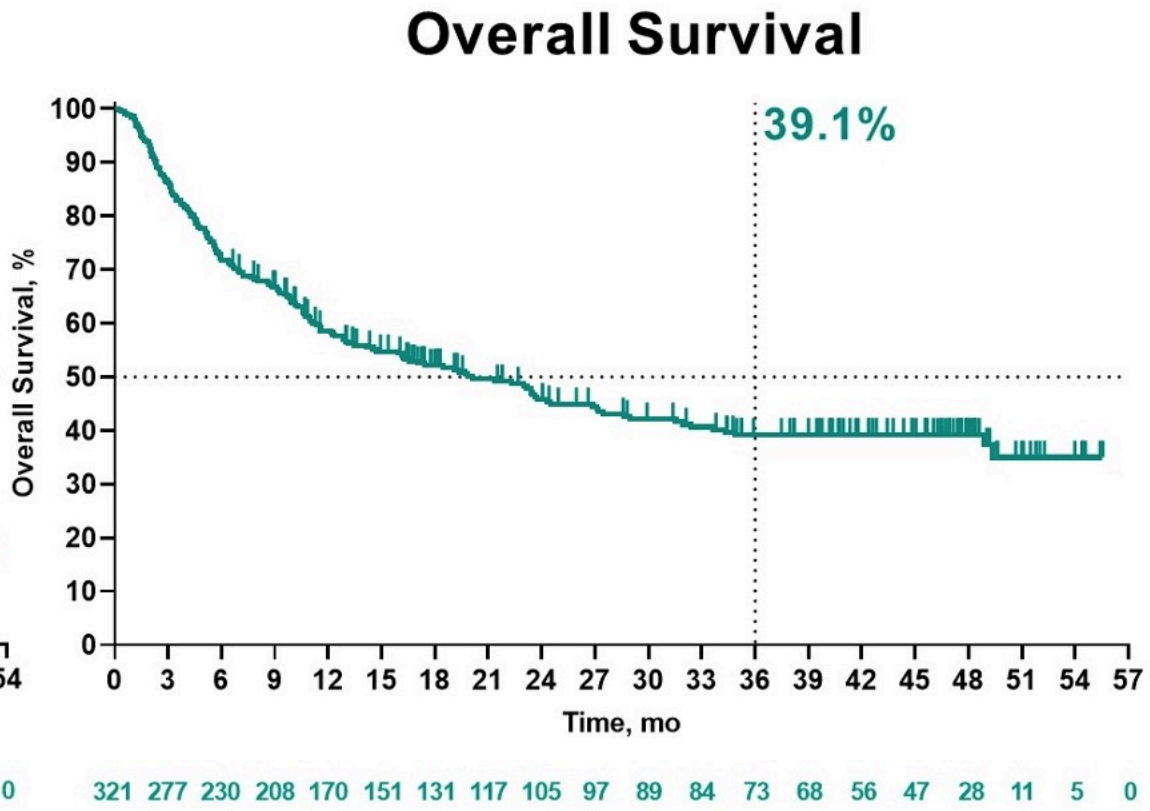


CI, confidence interval. "+" indicates no PD by the time of last disease assessment.
[a]Patients who had no postbaseline imaging assessment.
Data cutoff: October 5, 2020

Maio M et al. ASCO 2021;Abstract 2565.

KEYNOTE-158: Updated Survival Analyses





Data cutoff: October 5, 2020

Maio M et al. ASCO 2021;Abstract 2565.

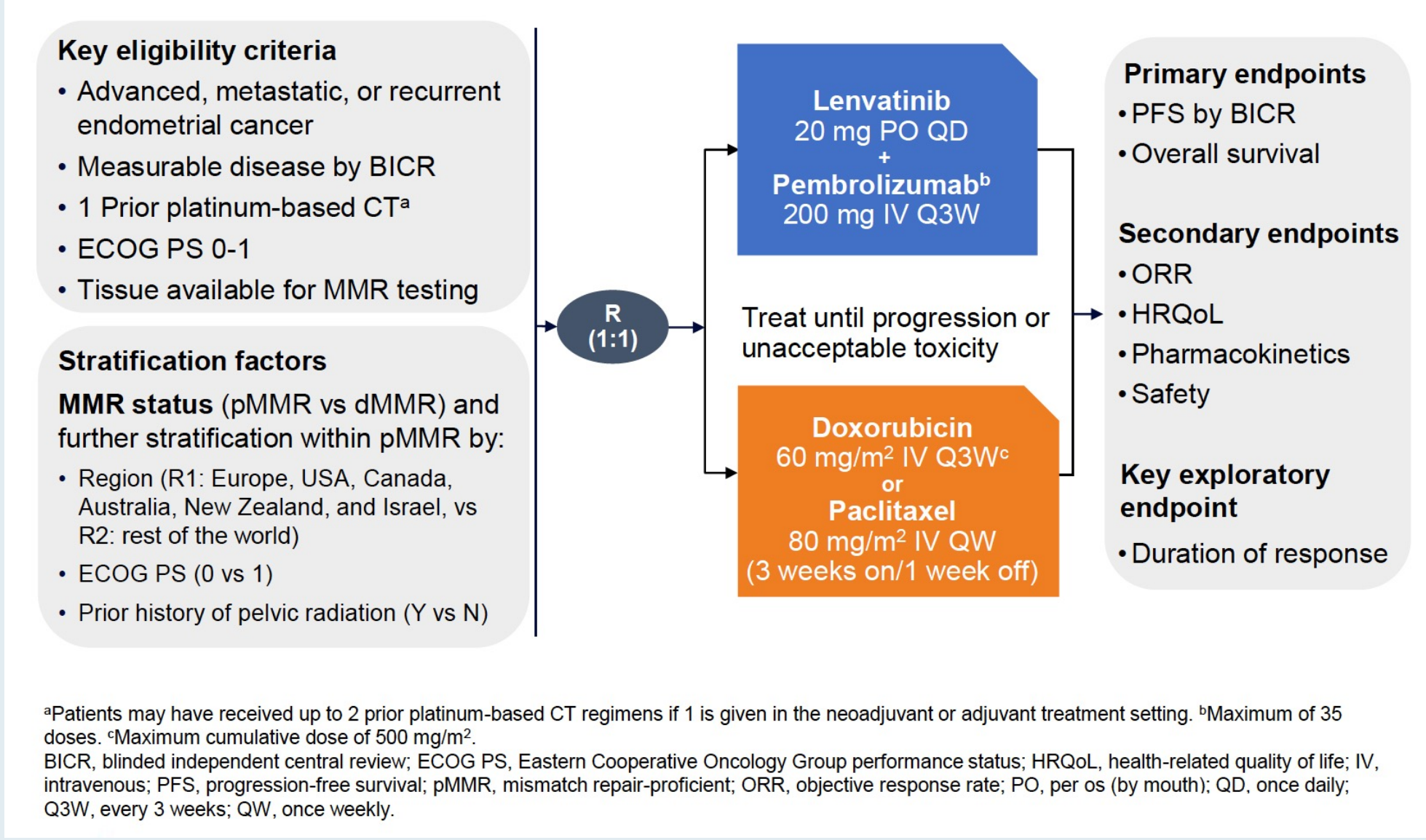
RTP RESEARCH TO PRACTICE

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.

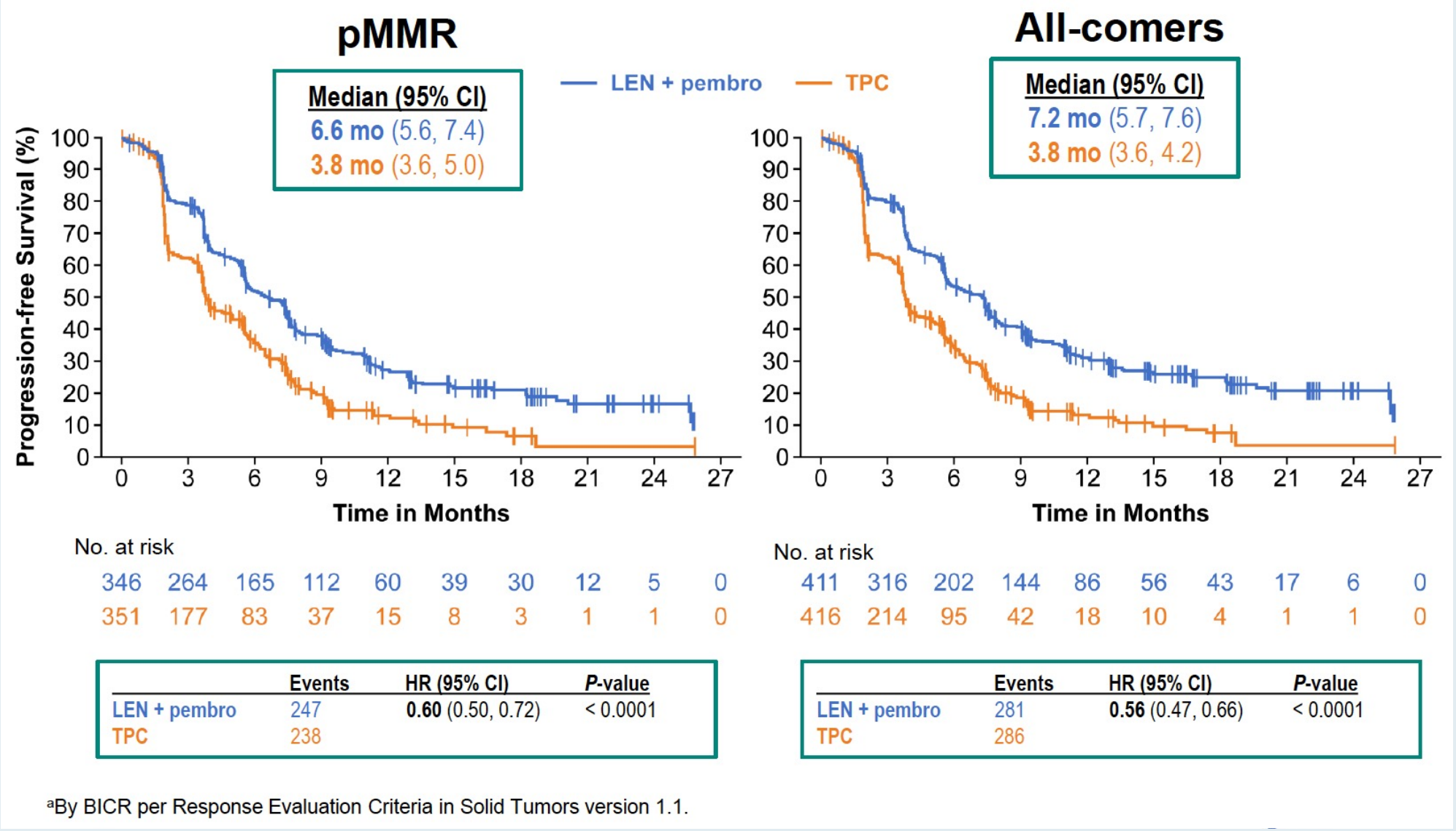
Study 309/KEYNOTE-775: Phase III Trial Schema



[a]Patients may have received up to 2 prior platinum-based CT regimens if 1 is given in the neoadjuvant or adjuvant treatment setting. [b]Maximum of 35 doses. [c]Maximum cumulative dose of 500 mg/m^2.
BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IV, intravenous; PFS, progression-free survival; pMMR, mismatch repair-proficient; ORR, objective response rate; PO, per os (by mouth); QD, once daily; Q3W, every 3 weeks; QW, once weekly.

Makker V et al. SGO 2021;Abstract 11512.

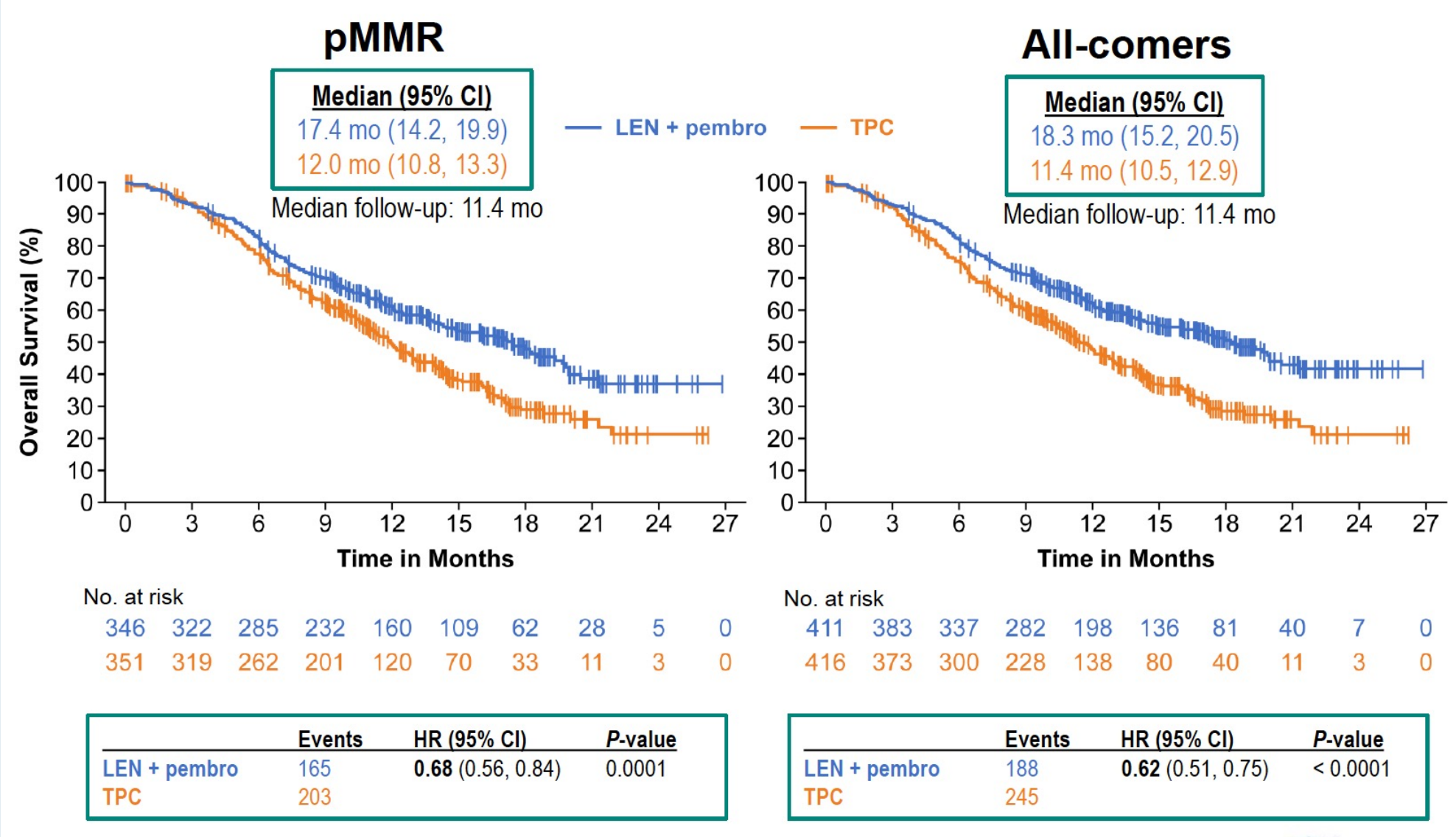
Study 309/KEYNOTE-775: Progression-Free Survival



[a]By BICR per Response Evaluation Criteria in Solid Tumors version 1.1.

Makker V et al. SGO 2021;Abstract 11512.

Study 309/KEYNOTE-775: Overall Survival



Makker V et al. SGO 2021;Abstract 11512.

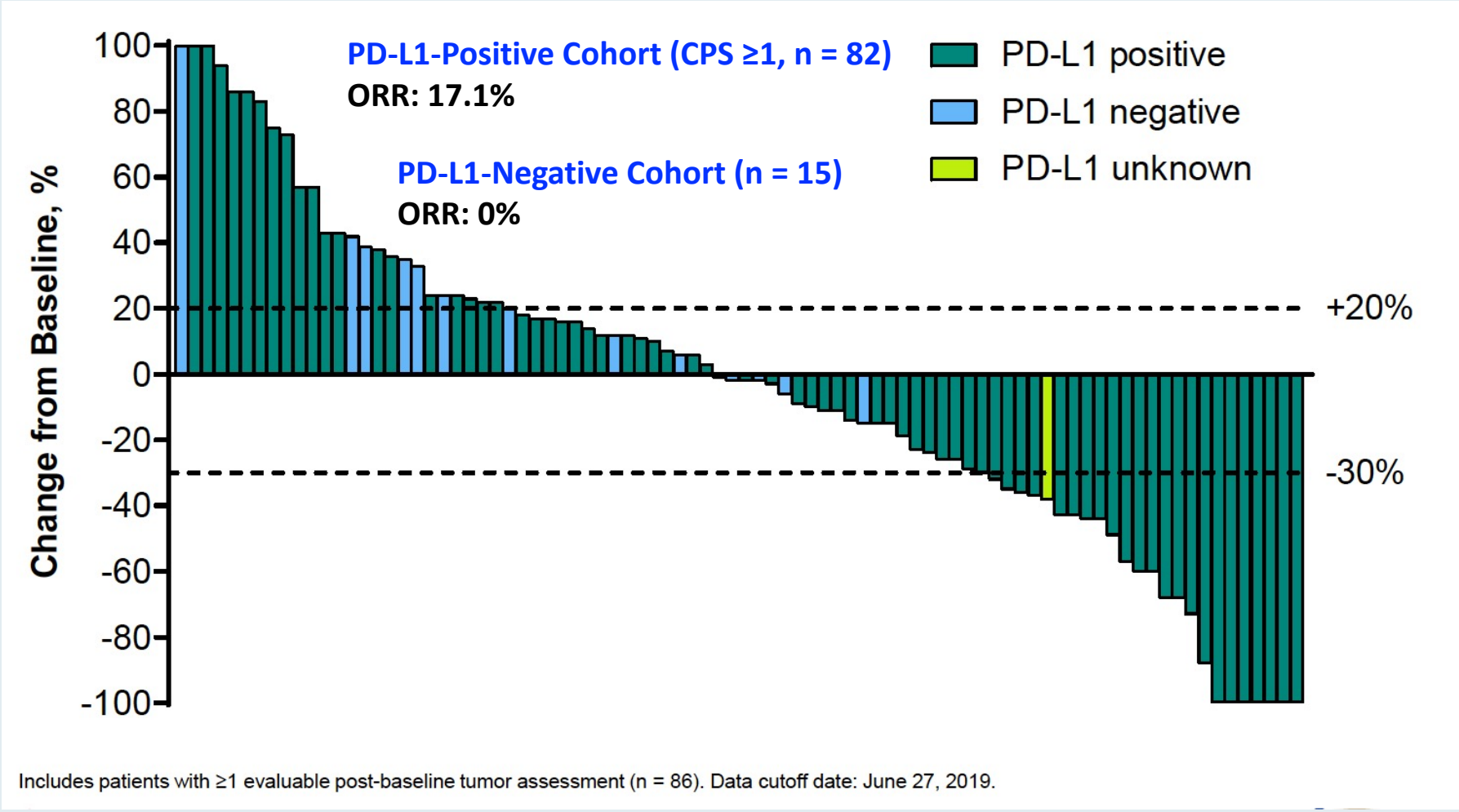
Immunotherapeutic Approaches in Cervical Cancer

Pembrolizumab Treatment of Advanced Cervical Cancer: Updated Results from the Phase II KEYNOTE-158 Study

Chung HC et al.

SGO 2021;Abstract 10440.

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

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

An Open-Label Phase 2 Study of Dostarlimab, Bevacizumab, and Niraparib Combination in Patients with Platinum-Resistant Ovarian Cancer: Cohort A of the OPAL Trial

Joyce F. Liu,[1] Stéphanie Gaillard,[2] Andrea E. Wahner Hendrickson,[3] John W. Moroney,[4] Oladapo Yeku,[5] Elisabeth Diver,[6] Camille Gunderson,[7] Rebecca Arend,[8] Elena Ratner,[9] Vivek Samnotra,[10] Divya Gupta,[10] Lena Evilevitch,[10] Zebin Wang,[10] Ping Wang,[10] Joseph Tang,[10] Emeline Bacqué,[10] Xiaohong Liu,[10] Gottfried E. Konecny[11]

Poster #23

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [3]Mayo Clinic Rochester, Rochester, NY, USA; [4]University of Chicago Medicine Comprehensive Cancer Center, Chicago, IL, USA; [5]Massachusetts General Cancer Center, Boston, MA, USA; [6]Stanford Women's Cancer Center, Palo Alto, CA, USA; [7]University of Oklahoma Stephenson Cancer Center, Oklahoma City, OK, USA; [8]The University of Alabama at Birmingham, UAB Comprehensive Cancer Center, Birmingham, AL, USA; [9]Yale University, New Haven, CT, USA; [10]GlaxoSmithKline, Waltham, MA, USA; [11]Ronald Reagan UCLA Medical Center, Los Angeles, CA, USA.

SGO 2021 VIRTUAL ANNUAL MEETING ON WOMEN'S CANCER®

Abstract 10415

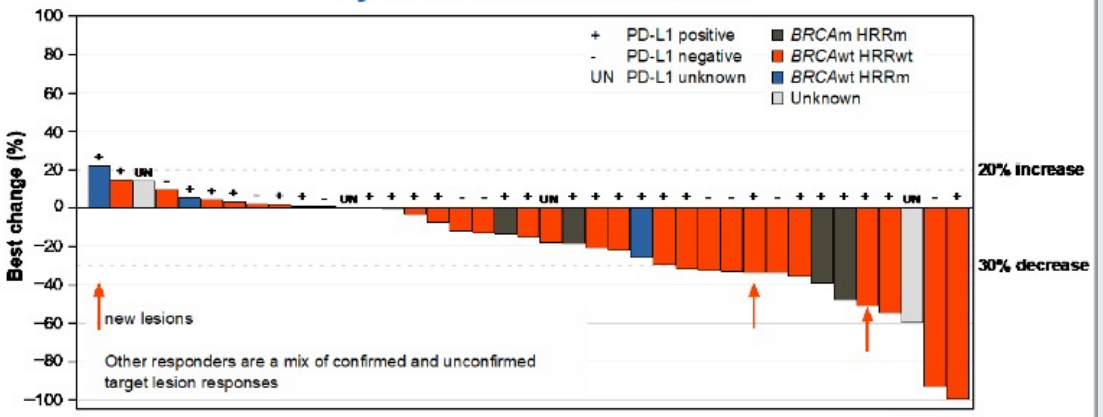
Society of Gynecologic Oncology

Antitumor Activity

- Antitumor activity was assessed in the response-evaluable population (n=39)
  - 2 patients in the safety population did not have a postbaseline scan and were excluded from the response-evaluable population
- Response data required that patients with a best response of complete response or partial response had a confirmation scan ≥4 weeks after the first scan in which a response was observed

Antitumor Activity per RECIST v1.1	
Variable, n (%)	**Response-evaluable population (n=39)**
Complete response	0
Partial response	7 (17.9)
Stable disease	23 (59.0)
Progressive disease	8 (20.5)
Inconclusive	1 (2.6)
ORR (90% CI), %	17.9 (8.7–31.1)
DCR (90% CI), %	76.9 (63.2–87.4)

Best Percent Change from Baseline Sum of Target Lesions by HRR and PD-L1 Status



*BRCA*m, *BRCA* mutation; *BRCA*wt, *BRCA* wild type; HRRm, homologous recombination repair mutation; HRRwt, homologous recombination repair wild type; PD-L1, programmed death ligand 1.

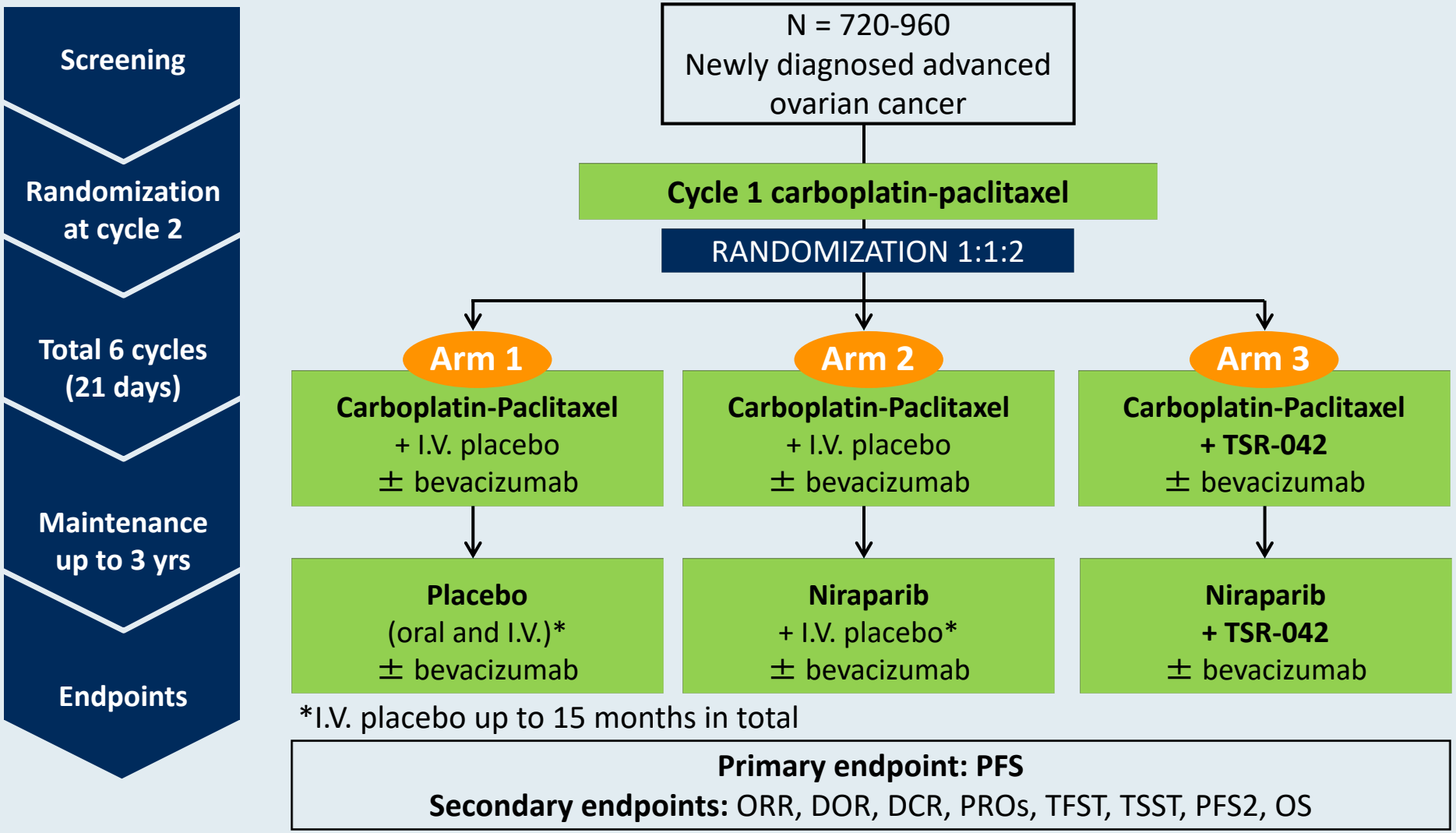
SGO 2021 VIRTUAL ANNUAL MEETING ON WOMEN'S CANCER®

Society of Gynecologic Oncology

Liu JF et al. SGO 2021;Abstract 10415.

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

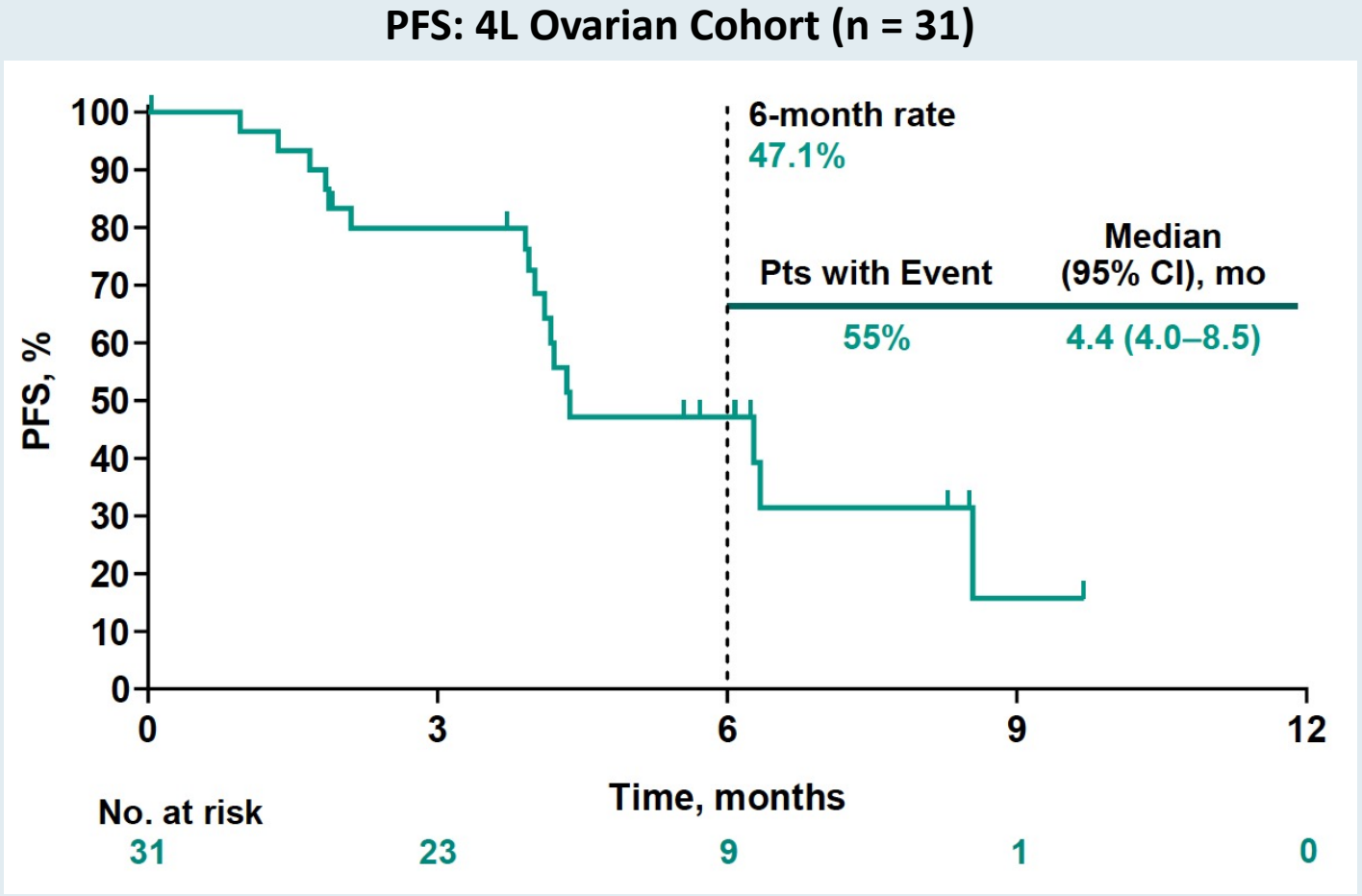
LEAP-005: Phase II Study of Lenvatinib (Len) plus Pembrolizumab (Pembro) in Patients (Pts) with Previously Treated Advanced Solid Tumours

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



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

2021 ASCO ANNUAL MEETING

Abstract 5500

GINECO

EFFICACY AND SAFETY RESULTS FROM NEOPEMBROV STUDY. A RANDOMIZED PHASE II TRIAL OF NEOADJUVANT CHEMOTHERAPY (CT) WITH OR WITHOUT PEMBROLIZUMAB (P) FOLLOWED BY INTERVAL DEBULKING SURGERY AND STANDARD SYSTEMIC THERAPY ± P FOR ADVANCED HIGH GRADE SEROUS CARCINOMA (HGSC). A GINECO STUDY.

Isabelle Laure RAY-COQUARD[1], Aude-Marie SAVOYE[2], Marie-Ange MOURET-REYNIER[3], Sylvie CHABAUD[4], Olfa DERBEL[5], Elsa KALBACHER[6], Marianne LEHEURTEUR[7], Alejandra MARTINEZ[8], Corina CORNILA[9], Mathilde MARTINEZ[10], Leila BENGRINE LEFEVRE[11], Frank PRIOU[12], Nicolas CLOAREC[13], Laurence VENAT-BOUVET[14], Frederic SELLE[15], Dominique BERTON[16], Olivier COLLARD[17], Florence JOLY[18], Olivier TREDAN[19]

Centre Léon Bérard. University Claude Bernard. Lyon. GINECO. France[1]; Institut Jean Godinot. Reims. GINECO. France[2]; Department of Medical Oncology. Centre Jean Perrin. Clermont-Ferrand. GINECO. France[3]; Departement of Clinical Research. Centre Léon-Bérard. Lyon. GINECO. France[4]; Institut de Cancérologie. Hôpital Privé Jean Mermoz. Lyon. GINECO. France[5]; CHU Jean Minjoz. Besançon. GINECO. France[6]; Centre Henri-Becquerel. Medical Oncology Department. Rouen. GINECO France[7]; Institut Claudius Régaud IUCT-O. Toulouse. GINECO France[8]; Centre Hospitalier Régional d'Orléans. Orleans. GINECO. France[9]; Clinique Pasteur. Toulouse. GINECO. France[10]; Centre Georges-François Leclerc. Dijon. GINECO.France[11]; CHD Vendée-Hôpital Les Oudairies. La Roche-Sur-Yon. GINECO. France[12]; Centre Hospitalier d'Avignon. Avignon. GINECO.France[13]; Centre Hospitalier Universitaire Dupuytren. Limoges. GINECO. France[14]; Groupe Hospitalier Diaconesses Croix Saint-Simon. Paris. GINECO. France[15]; Institut de Cancérologie de l'Ouest. Centre René Gauducheau. Saint-Herblain. GINECO. France[16]; Institut de Cancérologie de la Loire. St. Priest En Jarez. GINECO. France[17]; Department of Medical Oncology. Centre François Baclesse. Caen. GINECO. France[18]; Departement of Medical Oncology. Centre Léon Bérard. Lyon. GINECO. France[19]

Isabelle Ray-Coquard, Centre Leon Bérard

May, 2021

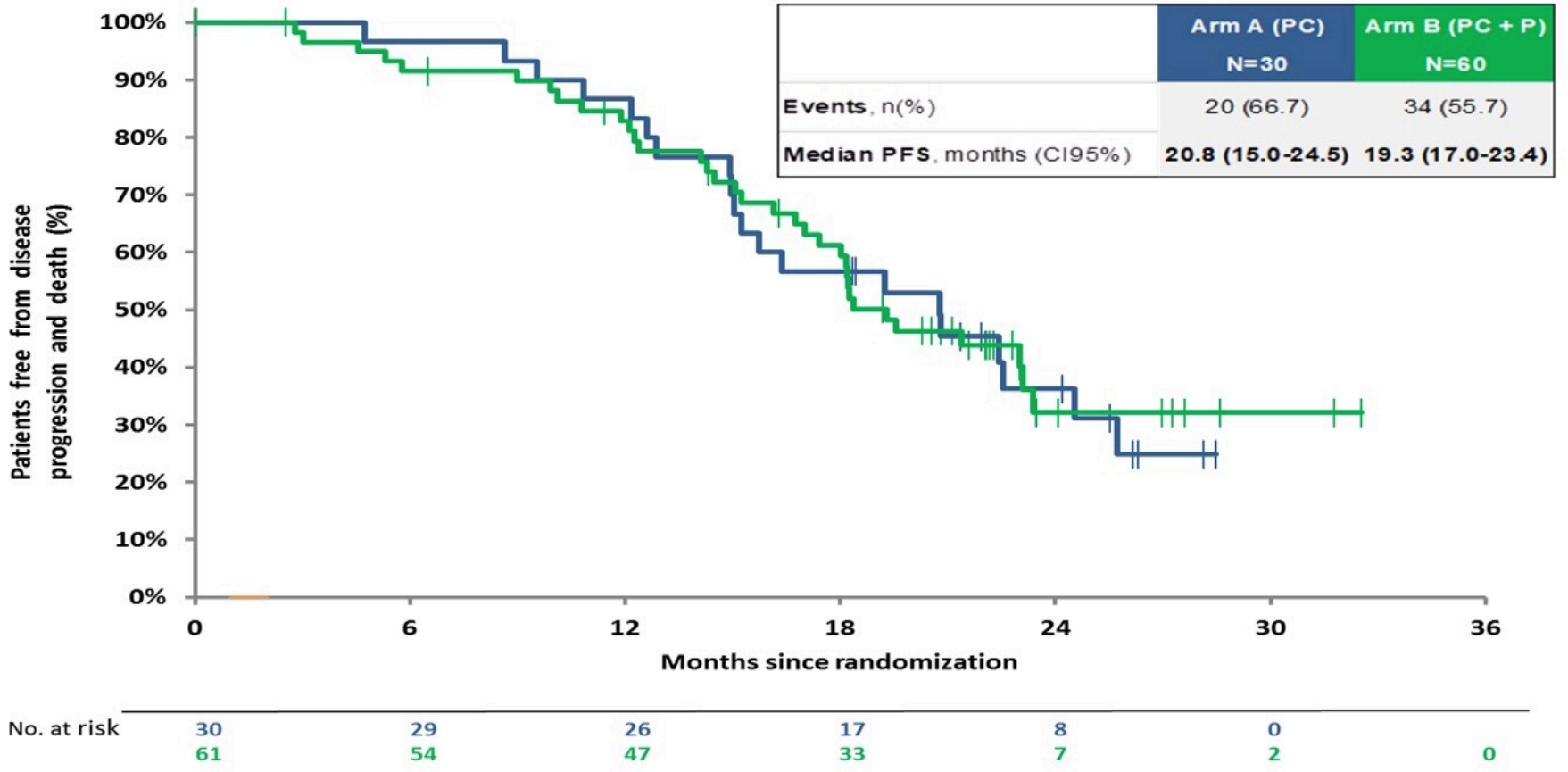
RTP RESEARCH TO PRACTICE

NEOPEMBROV: Response to CT with or without Bevacizumab with or without Pembrolizumab

	Arm A (CP ± Bev) N = 30	Arm B (CP+ P ± Bev) N = 61
Interval debulking surgery performed (%)		
Yes	29 (96.7)	58 (95.1)
No	1 (3.3)	3 (4.9)
Response at IDS (PCI Decrease)		
mean [std]	- 9.58 [8.58]	- 10.19 [9.27]
Not evaluable	3	6
Primary Endpoint (ITT) Rate of complete debulking % [95% CI]	***70% [53.5% -]***	***73.8% [62.9% -]***
Complete cytoreductive surgery (CC0)	21 (72.4)	45 (77.5)
CC1	0	2 (3.4)
CC ≥ 3 or biopsies only	8 (27.6)	11 (18.9)
	N = 29	N = 58
Response Rate after 4 cy NACT (RECIST) (%)		
Complete response	2 (6.9)	2 (3.3)
Partial response	16 (55.2)	42 (70.0)
Stable	11 (37.9)	14 (23.3)
Progression	0 (0.0)	2 (3.3)
Not evaluable	1	1
ORR (95% CI)	***62.1% [42.3-79.3]***	***73.3% [60.3-83.9]***
Best Overall Response (%)		
Complete response	22 (75.9)	45 (75.0)
Partial response	3 (10.3)	10 (16.7)
Stable	4 (13.8)	5 (8.3)
Not evaluable	1	1
CR+PR	*25 (83.3)*	*55 (90.1)*
Ca125 normalization	22 (73.3)	46 (75.4)

Ray-Coquard IL et al. ASCO 2021;Abstract 5500.

NEOPEMBROV: Progression-Free Survival



Median Follow-up of 22 months (min=6.8, max = 32.5)

Presented By: Isabelle Ray-Coquard

2021 ASCO ANNUAL MEETING

Ray-Coquard IL et al. ASCO 2021;Abstract 5500.

Meet The Professor

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

Monday, September 27, 2021
5:00 PM – 6:00 PM ET

Faculty

Zev Wainberg, MD, MSc

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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