

Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Joyce F Liu, MD, MPH

Associate Chief and Director of Clinical Research
Division of Gynecologic Oncology
Dana-Farber Cancer Institute
Boston, Massachusetts

Commercial Support

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

Dr Love — Disclosures

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

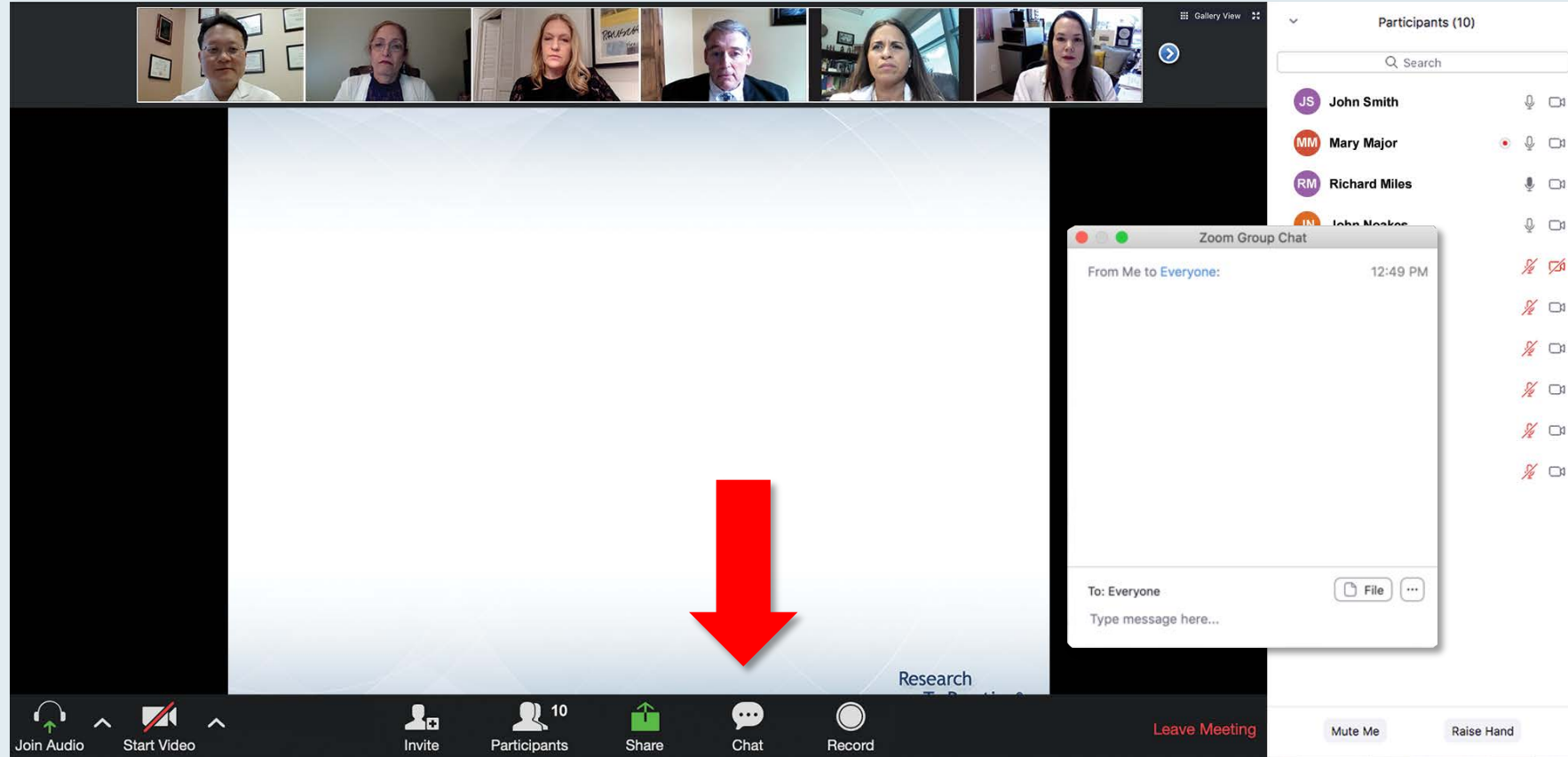
Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Liu — Disclosures

Advisory Committee	AstraZeneca Pharmaceuticals LP, Eisai Inc, Epsila Bio, Genentech, a member of the Roche Group, GlaxoSmithKline, Regeneron Pharmaceuticals Inc
Consulting Agreement	Genentech, a member of the Roche Group

We Encourage Clinicians in Practice to Submit Questions



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

Familiarizing Yourself with the Zoom Interface

How to answer survey or poll questions

Meet The Professionals
Optimizing the Selection and Sequencing of Therapy for Patients with Gastrointestinal Cancer

Wednesday, August 25,
5:00 PM – 6:00 PM EST

Faculty
Wells A Messersmith, MD

Moderator
Neil Love, MD

Quick Survey

- Carboplatin +/- docetaxel
- Pomalidomide +/- dexamethasone
- Carboplatin + pomalidomide +/- dexamethasone
- Eltuzumab + lenalidomide +/- dexamethasone
- Eltuzumab + pomalidomide +/- dexamethasone
- Daratumumab + lenalidomide +/- dexamethasone
- Daratumumab + pomalidomide +/- dexamethasone
- Daratumumab + bortezomib +/- dexamethasone
- Isatuximab + Rd

Submit

Participants (10)

- John Smith
- Mary Major
- Richard Miles
- John Noakes
- Alice Suarez
- Jane Perez
- Robert Stiles
- Juan Fernandez
- Ashok Kumar
- Jeremy Smith

Regulatory and reimbursement issues aside, what would you recommend for a 65-year-old patient with clear cell renal cell carcinoma (ccRCC) if follow-up 3 years later is found to have asymptomatic disease (PS 0)?

Quick Poll

- Nivolumab/ipilimumab
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Clinicians in the audience, please click your answer choice for the premeeting survey as well as the live polling questions.

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

The screenshot shows a Zoom meeting interface. At the top, there are video thumbnails for participants: RTP Coordinat..., Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. A 'Recording...' indicator is visible on the left. The main content is a slide titled 'Meet The Professor Program Steering Committee' with six members listed:

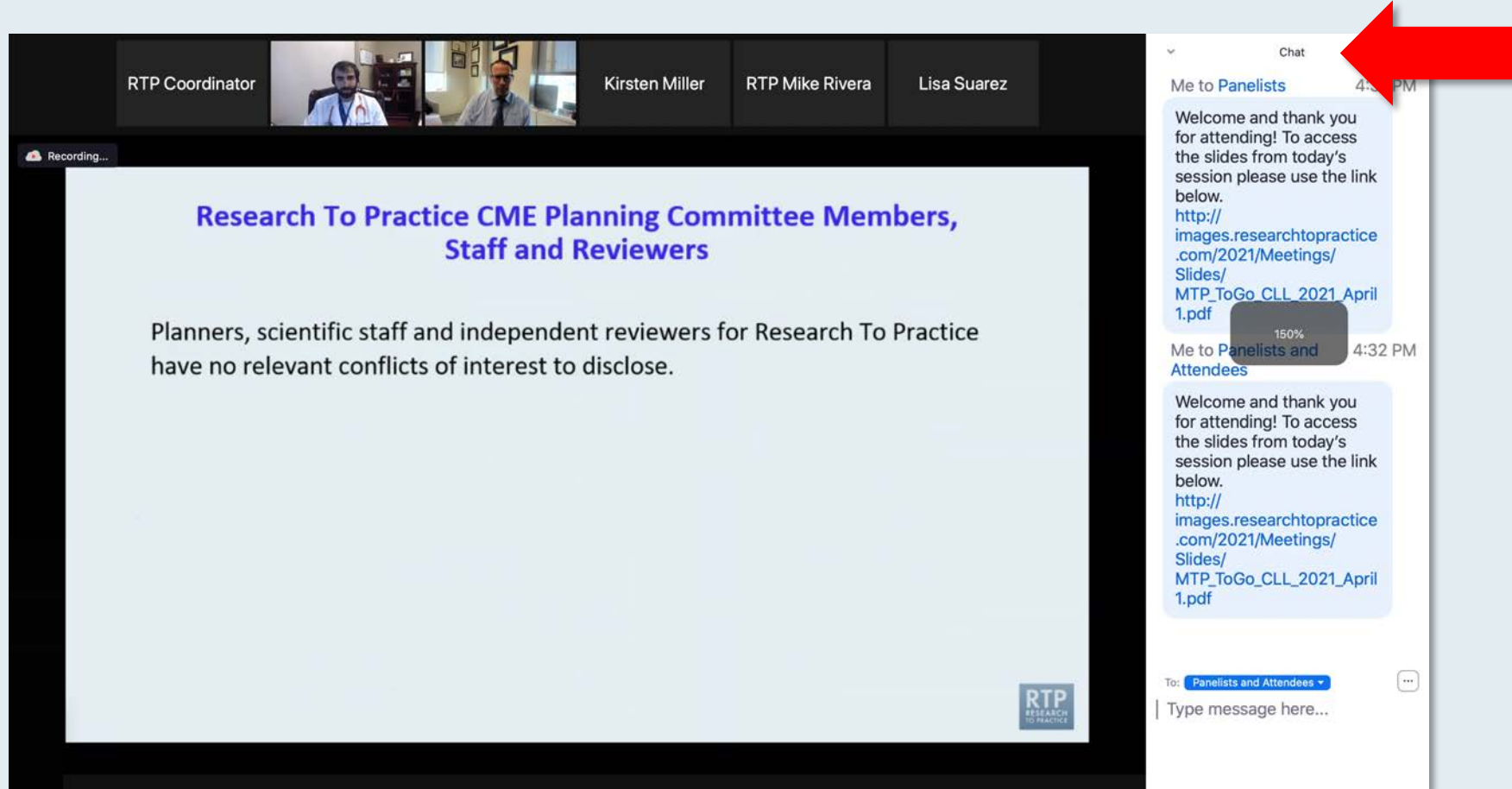
- John N Allan, MD**
Assistant Professor of Medicine
Weill Cornell Medicine
New York, New York
- Ian W Flinn, MD, PhD**
Director of Lymphoma Research Program
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee
- Steven Coutre, MD**
Professor of Medicine (Hematology)
Stanford University School of Medicine
Stanford, California
- Prof John G Gribben, MD, DSc, FMedSci**
Chair of Medical Oncology
Barts Cancer Institute
Queen Mary University of London
Charterhouse Square
London, United Kingdom
- Matthew S Davids, MD, MMSc**
Associate Professor of Medicine
Harvard Medical School
Director of Clinical Research
Division of Lymphoma
Dana-Farber Cancer Institute
Boston, Massachusetts
- Brian T Hill, MD, PhD**
Director, Lymphoid Malignancy Program
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio

The chat window on the right is expanded, showing messages from 'Me to Panelists' and 'Me to Panelists and Attendees'. A red arrow points to the white line above the 'Type message here...' input box, indicating how to expand the chat area.

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

Familiarizing Yourself with the Zoom Interface

Increase chat font size



The screenshot displays a Zoom meeting interface. At the top, there are video thumbnails for participants: RTP Coordinator, Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. Below the thumbnails is a slide titled "Research To Practice CME Planning Committee Members, Staff and Reviewers". The slide content reads: "Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose." A "Recording..." indicator is visible in the top left of the slide area. On the right side, the Zoom chat window is open, showing a message from "Me to Panelists" with a timestamp of 4:32 PM. The message content is: "Welcome and thank you for attending! To access the slides from today's session please use the link below. http://images.researchtopractice.com/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April 1.pdf". A red arrow points to the chat window, specifically to the font size adjustment icon (a small square with a plus sign) located above the message. The chat window also shows a "150%" font size indicator and a "Type message here..." input field at the bottom.

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

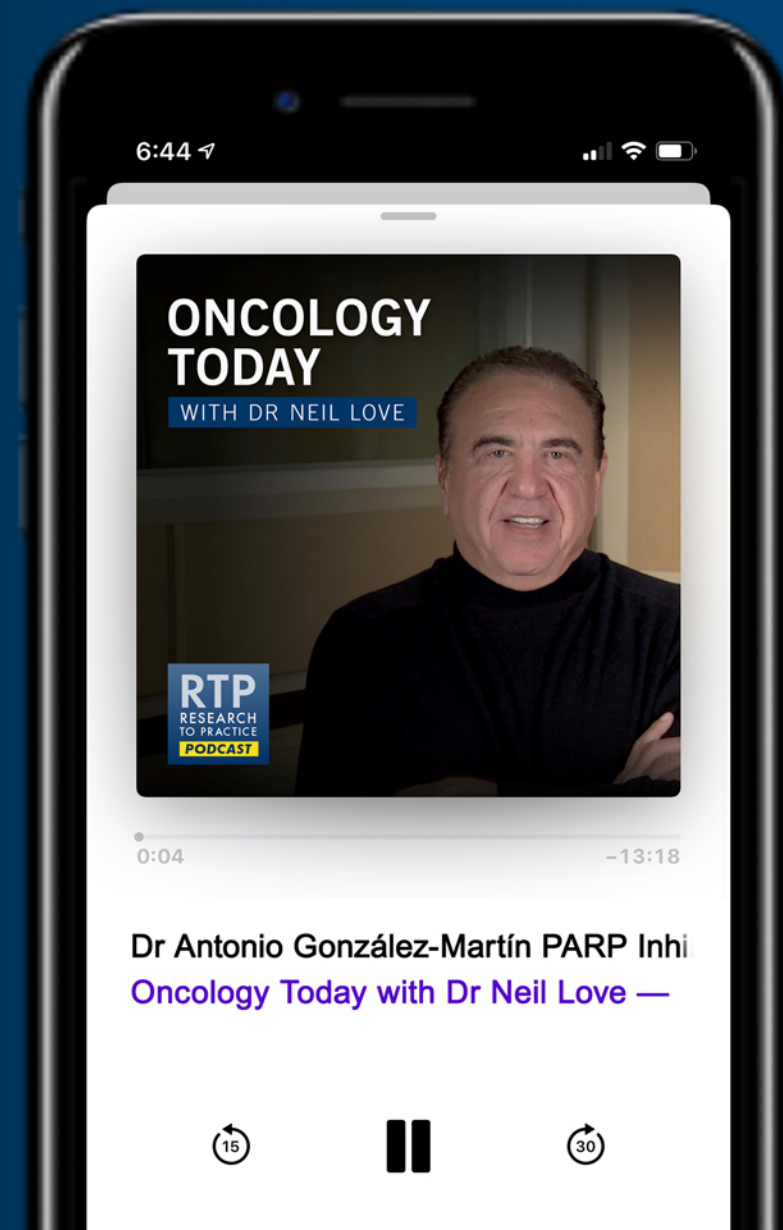
ONCOLOGY TODAY

WITH DR NEIL LOVE

PARP Inhibitors in Ovarian Cancer



DR ANTONIO GONZÁLEZ-MARTÍN
CLÍNICA UNIVERSIDAD DE NAVARRA



Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes

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**Wednesday, September 8, 2021
7:30 PM – 9:00 PM Central Time**

Faculty

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Daniel A Pollyea, MD, MS

David Sallman, MD

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Moderator

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Exploring Key Issues Affecting the Care of Patients with Metastatic Colorectal Cancer with BRAF Mutations

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Expert Second Opinion: Investigators Discuss Available Clinical Research in the Care of Patients with Early-Stage Non-Small Cell Lung Cancer

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Additional faculty to be announced

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Neal D Shore, MD

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Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

**Thursday, September 16, 2021
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Moderator

Neil Love, MD

Thank you for joining us!

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

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Meet The Professor Program Participating Faculty



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Professor of Oncology
Professor of Gynecology and Obstetrics
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Johns Hopkins Sidney Kimmel Comprehensive
Cancer Center
Baltimore, Maryland



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



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



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



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

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, Gyn 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

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

We Encourage Clinicians in Practice to Submit Questions

The image shows a Zoom meeting interface. At the top, there is a gallery view of six participants. The main area of the screen is a white slide with the text: "You may submit questions using the Zoom Chat option below". A large red arrow points downwards from this text. On the right side, there is a "Participants (10)" list with names and initials: John Smith (JS), Mary Major (MM), Richard Miles (RM), John Noakes (JN), and Alice Suarez (AS). Below the participants list, a "Zoom Group Chat" window is open, showing a message from "Me to Everyone" at 12:49 PM. The chat window has a text input field and a "File" button. At the bottom of the screen, the Zoom control bar is visible, including buttons for "Join Audio", "Start Video", "Invite", "Participants", "Share", "Chat", "Record", "Leave Meeting", "Mute Me", and "Raise Hand".

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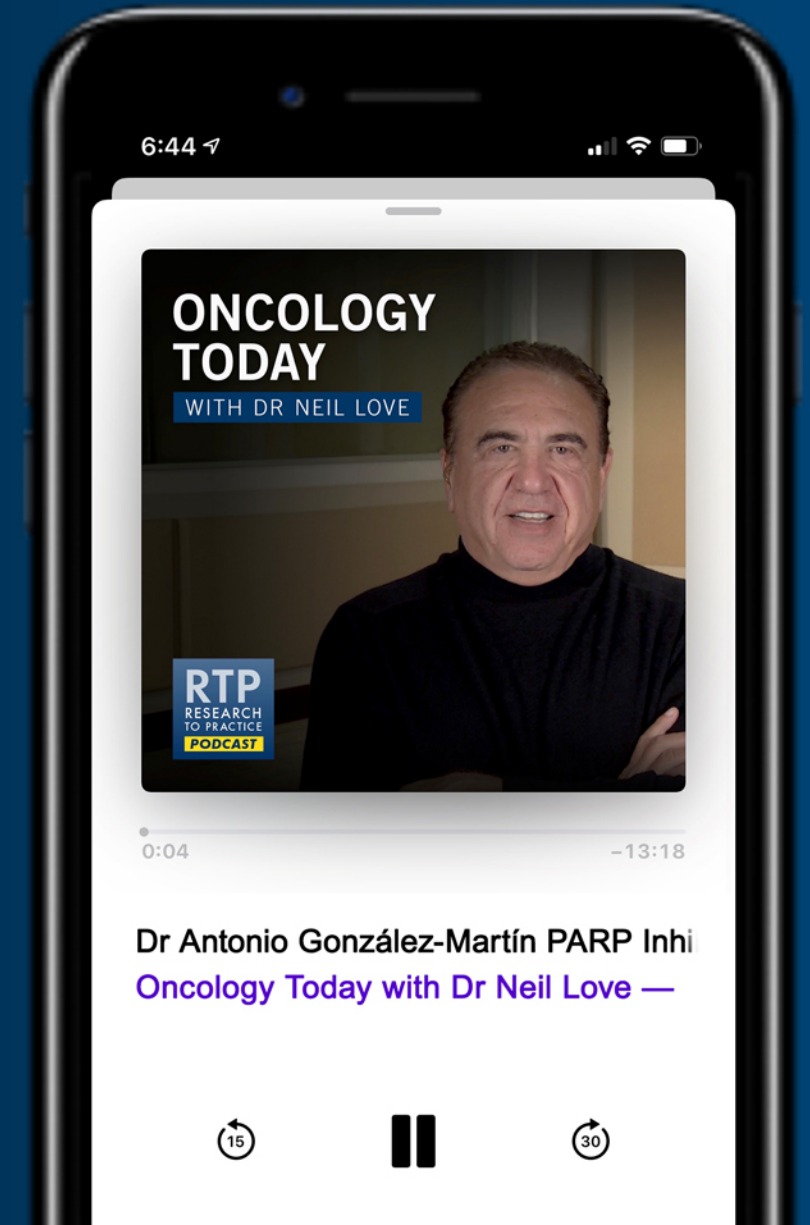
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Linda R Duska, MD, MPH
Professor of Obstetrics and Gynecology
Division of Gynecologic Oncology
University of Virginia School of Medicine
Charlottesville, Virginia



Heidi E Godoy, DO
Women's Cancer Care Associates
Albany, New York



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



Bhavana Pothuri, MD

Professor, Department of Obstetrics and Gynecology
Division of Gynecologic Oncology
New York University Grossman School of Medicine
New York, New York



Nasfat Shehadeh, MD

Medical Oncologist
Oncology Specialists of Charlotte
Charlotte, North Carolina



Shannon N Westin, MD, MPH

Associate Professor
Director, Early Drug Development
Department of Gynecologic Oncology and Reproductive Medicine
The University of Texas MD Anderson Cancer Center
Houston, Texas

Meet The Professor with Dr Liu

MODULE 1: Cases from the Practices of Gynecologic and Medical Oncologists

Cervical Cancer

- Dr Westin: A 52-year-old woman with metastatic squamous cell carcinoma of the cervix
- Dr Penson: A 39-year-old woman with metastatic squamous cell carcinoma of the cervix – PD-L1-negative
- Dr Godoy: A 72-year-old woman with metastatic squamous cell carcinoma of the vulva – PD-L1 50%

Endometrial Cancer

- Dr Shehadeh: An 84-year-old woman with metastatic adenocarcinoma of the uterus – MSI-H, TMB-H, PD-L1-negative
- Dr Pothuri: A 78-year-old woman with HER2-positive metastatic endometrial cancer – MSI-H/dMMR, TMB high, BRCA WT
- Dr Penson: A 74-year-old woman with MSS endometrioid adenocarcinoma – PD-L1 0%
- Dr Duska: A 60-year-old woman with metastatic, MSS carcinosarcoma
- Dr Duska: A 69-year-old woman with ER/PR-positive metastatic endometrioid adenocarcinoma – MMR proficient

MODULE 2: Journal Club with Dr Liu

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

MODULE 4: Key Recent Data Sets

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Phase III KEYNOTE-826 Trial of First-Line Pembrolizumab with Chemotherapy with and without Bevacizumab Improves Survival in Cervical Cancer

Press Release – June 22, 2021

“The pivotal Phase 3 KEYNOTE-826 trial investigating pembrolizumab, an anti-PD-1 therapy, in combination with platinum-based chemotherapy (paclitaxel plus cisplatin or paclitaxel plus carboplatin) with or without bevacizumab, met its primary endpoints of overall survival (OS) and progression-free survival (PFS) for the first-line treatment of patients with persistent, recurrent or metastatic cervical cancer. Based on an interim analysis conducted by an independent Data Monitoring Committee, pembrolizumab plus platinum-based chemotherapy with or without bevacizumab demonstrated statistically significant and clinically meaningful improvements in OS and PFS compared to the same platinum-based chemotherapy regimens with or without bevacizumab alone, regardless of PD-L1 status... The safety profile of pembrolizumab in this trial was consistent with that observed in previously reported studies. Results will be presented at an upcoming medical meeting and will be submitted to regulatory authorities.”

Case Presentation – Dr Westin: A 52-year-old woman with metastatic squamous cell carcinoma of the cervix



Dr Shannon Westin

- Diagnosed with metastatic Grade 3 squamous cell carcinoma of the cervix
- Cisplatin/paclitaxel/bevacizumab x 6, with near CR → Bevacizumab maintenance x 12 months
 - Proteinuria

Questions

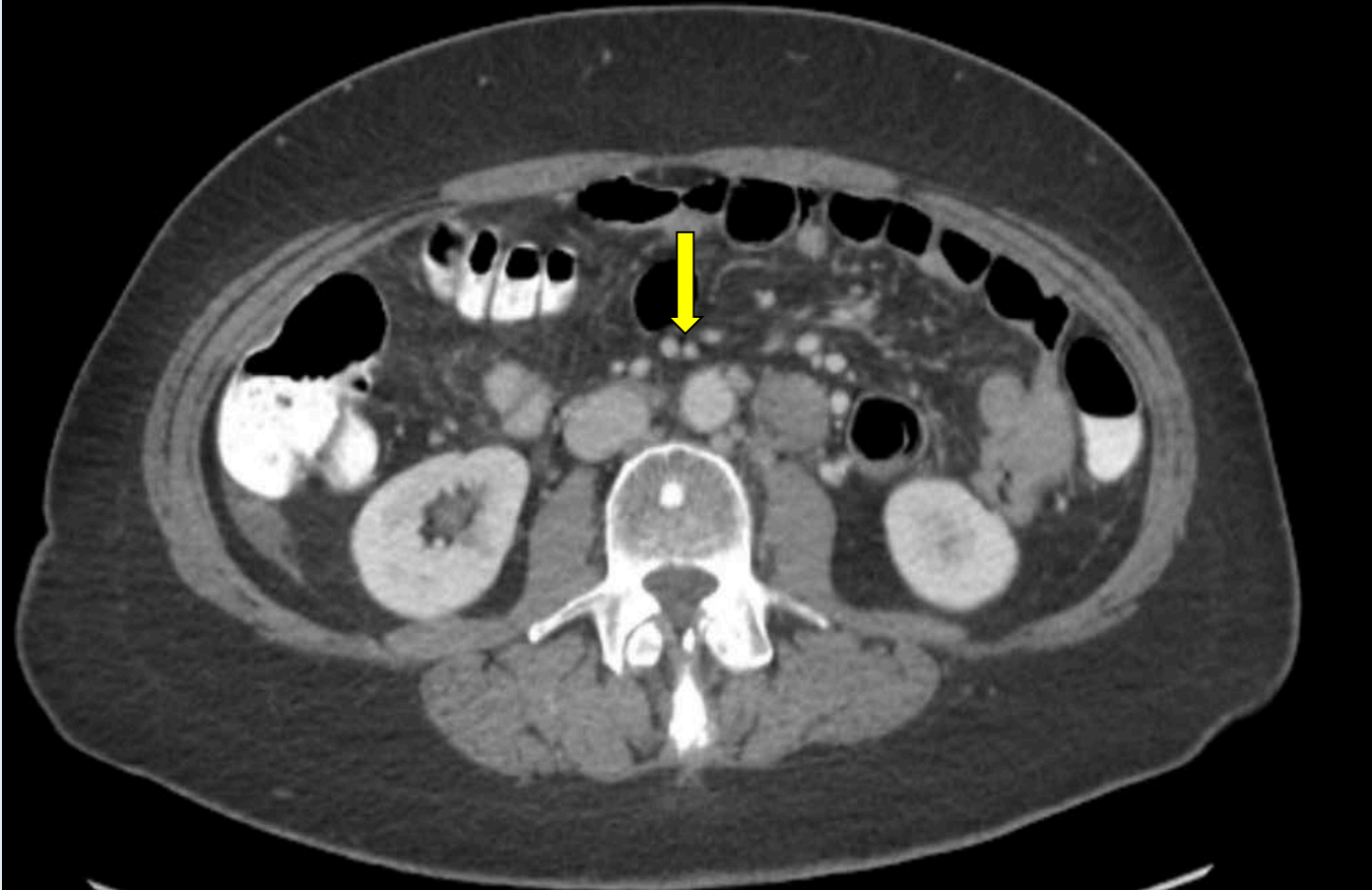
- How long would you continue the maintenance bevacizumab – indefinitely or for a certain amount of time?

Case Presentation – Dr Westin: A 52-year-old woman with metastatic squamous cell carcinoma of the cervix



Dr Shannon Westin

Omental disease along the colon, peritoneal nodularity



Case Presentation – Dr Penson: A 39-year-old woman with metastatic squamous cell carcinoma of the cervix, PD-L1-negative



Dr Richard Penson

- 2016: Diagnosed with Stage IB1, Grade 2-3 squamous cell carcinoma of the cervix
- RT/cisplatin
- 2018: Carboplatin/paclitaxel/bevacizumab
- 2019: Pembrolizumab, with poor response
- 2020: Gemcitabine/cisplatin
- 2020: Clinical trial of HPV vaccine (PDS0101), IL-2 and bifunctional fusion protein targeting PD-L1 and TGFb (M7824)
- 2020: Capecitabine

Questions

- How do you think about pembrolizumab, particularly in a patient without PD-L1 staining for positivity, where the chance of at least tumor shrinkage, if not clinical benefit, is very low?
- In a young, fit person with good organ function, what's your “go-to” choice? Do you use tisetumab or something else?

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

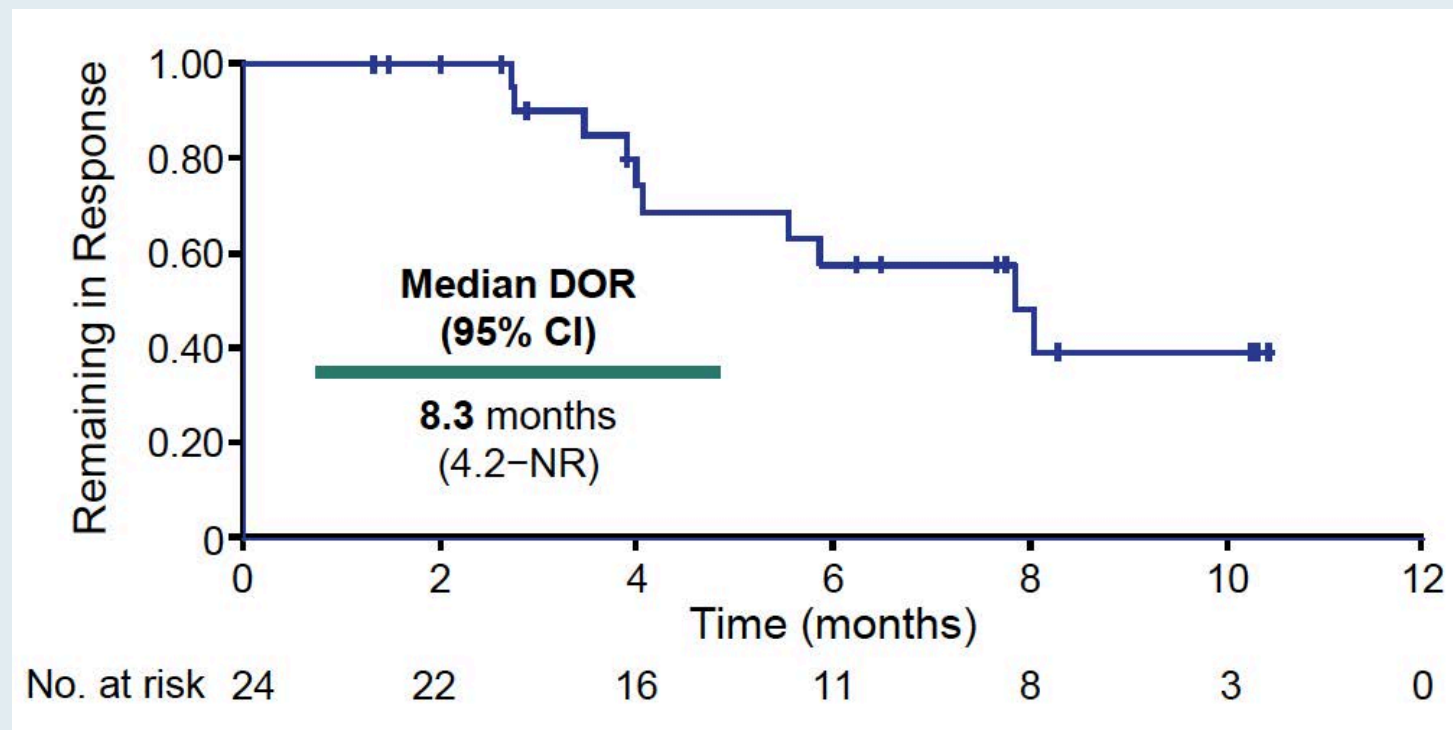
Coleman RL et al.

ESMO 2020;Abstract LBA32.

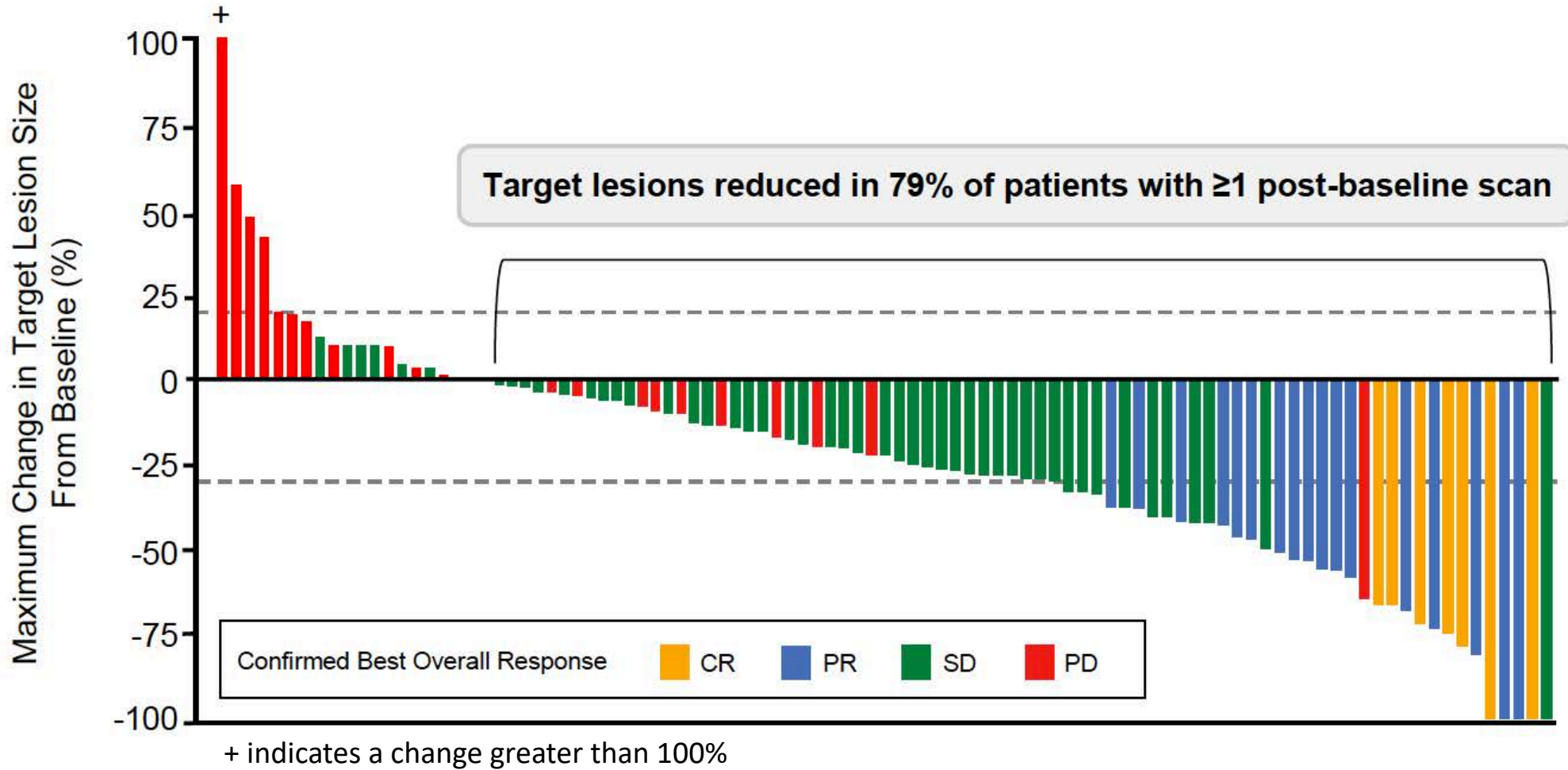
innovaTV 204: Antitumor Activity by IRC Assessment

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

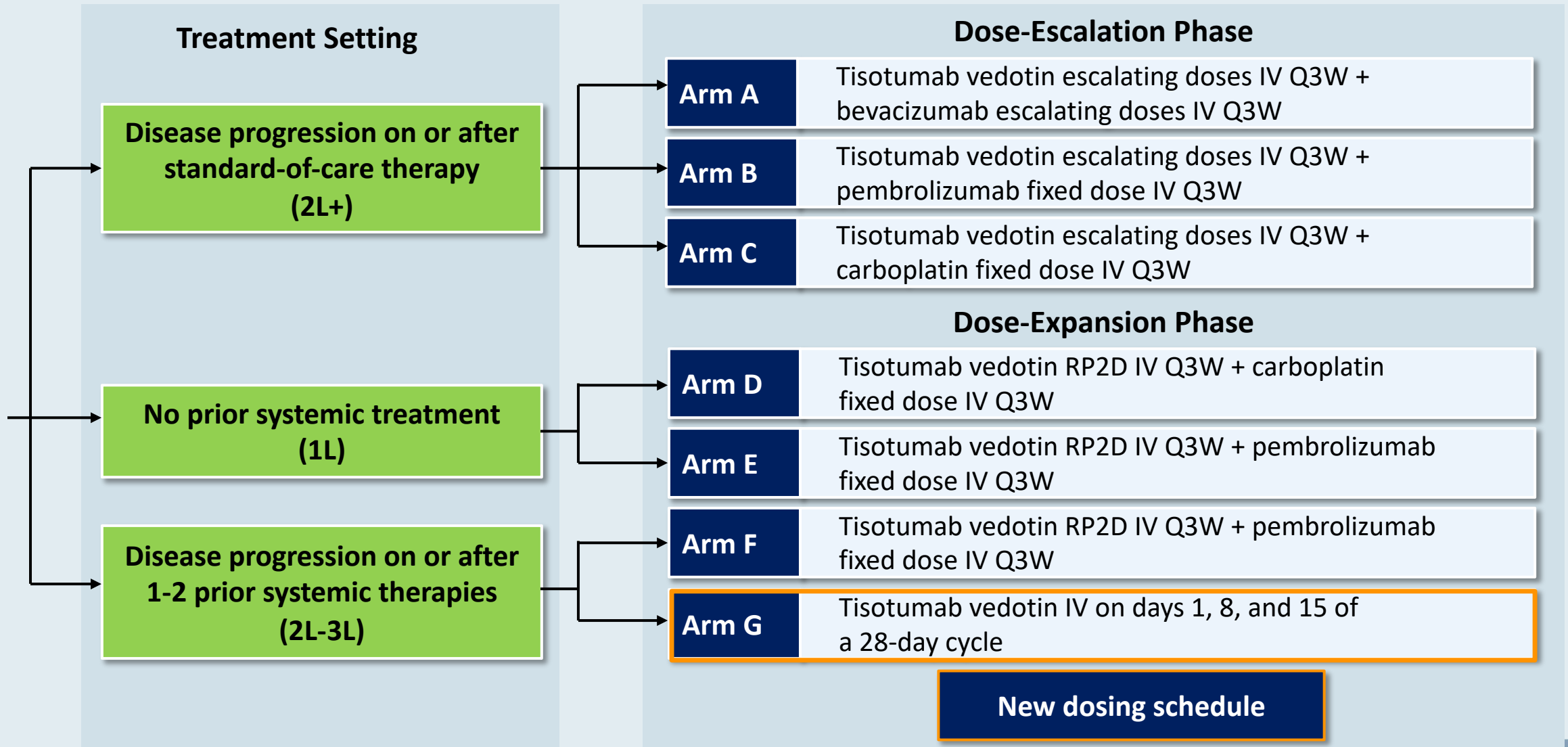
Duration of Response



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



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

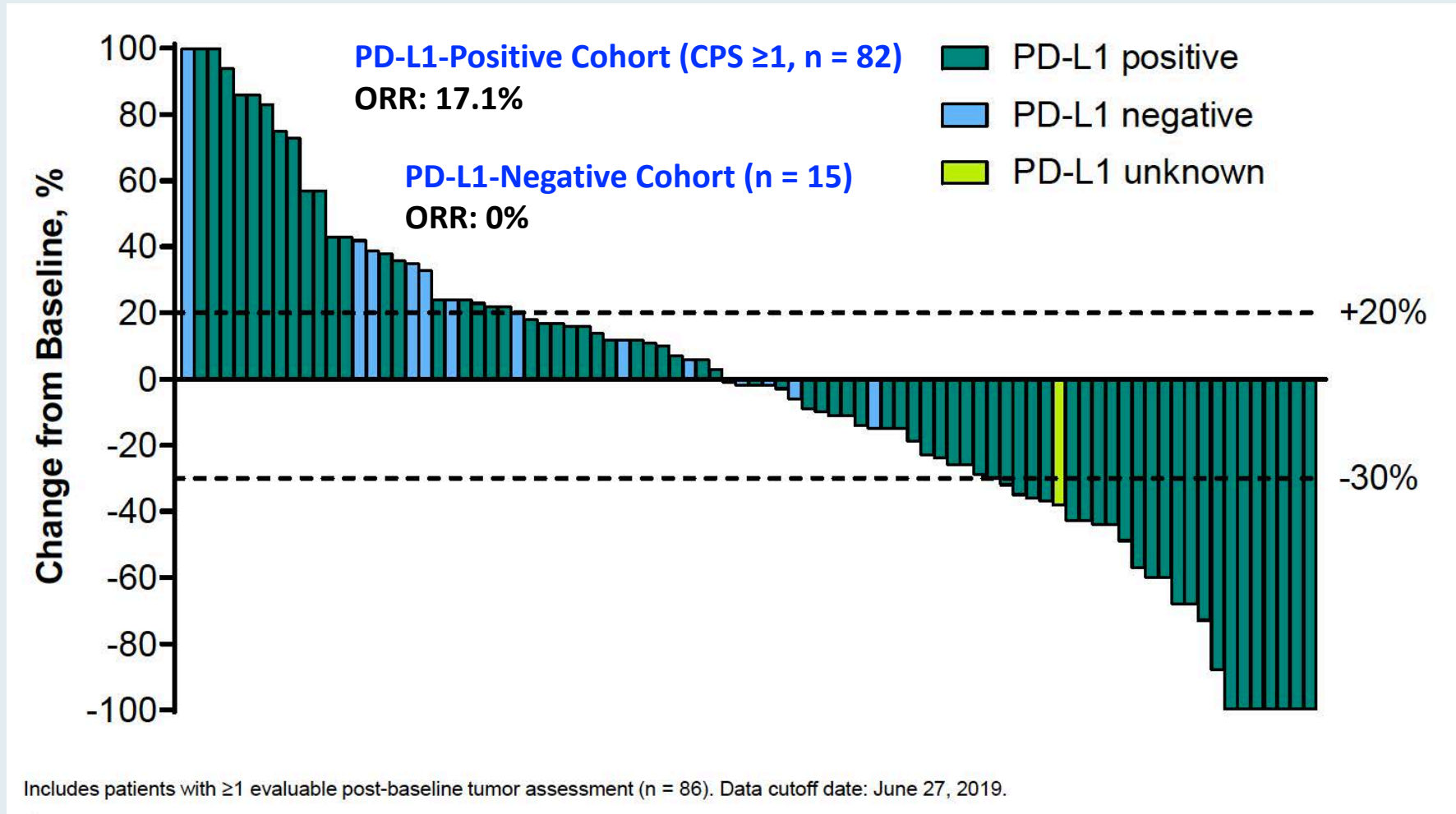


Pembrolizumab Treatment of Advanced Cervical Cancer: Updated Results from the Phase II KEYNOTE-158 Study

Chung HC et al.

SGO 2021;Abstract 10440.

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



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

ESMO VIRTUAL PLENARY

12 & 13 May 2021



Krishnansu Tewari

ESMO VIRTUAL PLENARY



EMPOWER-CERVICAL 1/GOG-3016/ENGOT-CX9: RESULTS OF PHASE 3 TRIAL OF CEMIPIMAB 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

12 May 2021



*Contributed equally to this presentation.

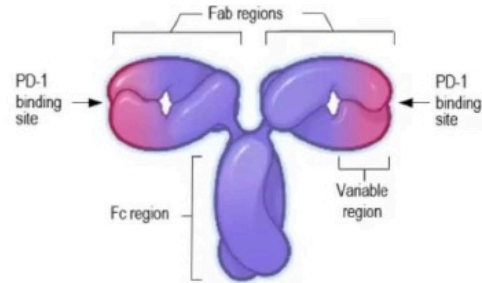
This study (NCT03257267) was sponsored by Regeneron Pharmaceuticals, Inc. and Sanofi.



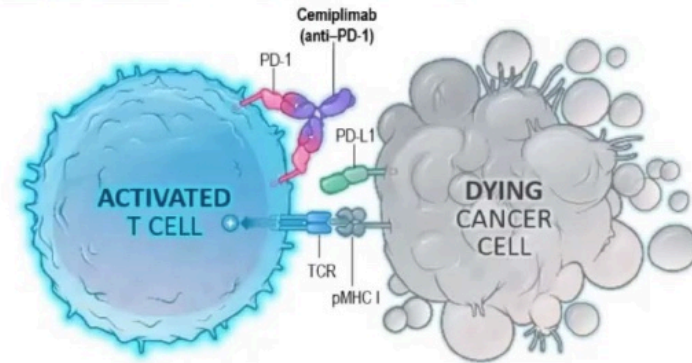
Krishnansu Tewari

CEMIPLIMAB

Cemiplimab Molecular Structure



Cemiplimab Mechanism of Action



- ♦ High-affinity, human, hinge-stabilised IgG4 monoclonal antibody to the PD-1 receptor¹
- ♦ Phase 1 R/M cervical cancer (n=23; includes Dose Escalation + Expansion Cohorts)²
 - ♦ Safety profile similar to that of other PD-1 inhibitors²
 - ♦ 17% ORR²

Ig, immunoglobulin; 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.



Krishnansu Tewari

OVERALL SURVIVAL

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

SCC Population



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



Krishnansu Tewari

OVERALL SURVIVAL



*Stratified by geographic region (North America vs Asia vs ROW) and Histology (SCC vs AC) according to interactive web response system. ¹From randomisation to data cutoff date. AC, adenocarcinoma or adenosquamous carcinoma; CI, confidence interval; HR, hazard ratio; mo, month; OS, overall survival; ROW, rest of world; SCC, squamous cell carcinoma.

Case Presentation – Dr Godoy: A 72-year-old woman with metastatic squamous cell carcinoma of the vulva – PD-L1 50%



Dr Heidi Godoy

- PMH: Lichen sclerosis, s/p clobetasol and estradiol cream with no improvement after 4 months, lesion on the right side of the vulva
- 5/2014 Biopsy: Stage IB squamous cell carcinoma of the vulva, with no residual disease s/p vulvectomy
- 9/2017 Vulvar biopsy: Squamous cell carcinoma
- 10/2017: Radical vulvectomy/distal urethrectomy, with positive margins
- 1/2018: Cisplatin/RT
- 10/2018: Hyperbaric O2 planned x 30
- 1/2019: Recurrence, with extensive disease spread to vagina and perineum
- 4/2019: Carboplatin/paclitaxel/bevacizumab
- NGS: PD-L1 TPS 50%
- 7/2019: Pembrolizumab, with response x 6 months followed by disease progression and referral to hospice

Endometrial Cancer

Case Presentation – Dr Shehadeh: An 84-year-old woman with metastatic adenocarcinoma of the uterus – MSI-H, TMB high, PD-L1-negative



Dr Nasfat Shehadeh

- 2/2018: Presents with large pelvic mass, fistula between mass and colon, abscess requiring diverting colostomy
 - Biopsy: Poorly differentiated adenocarcinoma of the uterus, MMR-proficient
- Carboplatin/paclitaxel x 4, with minor response, continued to be symptomatic
- 4/2018 NGS: MSI-high, TMB 18 mut/Mb, PD-L1-negative, non-germline BRCA2-positive (sporadic?), PI3K and PTEN mutations
- 6/2018: Pembrolizumab, with great response, no pain, improved QoL
- 9/2019: Colostomy reversed
- 3/2020: Pembrolizumab discontinued, in CR, due to COVID-19 pandemic

Questions

- Would you discontinue the immunotherapy in a patient who achieved a CR and is doing well?
- If she progresses down the road, could I use a PARP inhibitor in this patient? Are the PI3 kinase and PTEN mutations actionable?

Case Presentation – Dr Shehadeh: An 84-year-old woman with metastatic adenocarcinoma of the uterus – MSI-H, TMB high, PD-L1-negative



Dr Nasfat Shehadeh

BIOMARKER HIGHLIGHTS		
Lineage Relevant Biomarkers		
MSI	NGS	High
Total Mutational Load		High 18 Mutations/MB
Other Notable Biomarker Results		
PD-L1	IHC	Negative 0, 100%
ARID1A	NGS	Mutated, Pathogenic Exon 16 p.R1335X
BRCA2	NGS	Mutated, Pathogenic Exon 10 p.V323fs
CIC	NGS	Mutated, Pathogenic Exon 4 p.N193fs
	NGS	Mutated, Pathogenic Exon 5 p.R215W
CTNNB1	NGS	Mutated, Pathogenic Exon 3 p.G34E
KMT2D	NGS	Mutated, Pathogenic Exon 31 p.A2119fs

Other Notable Biomarker Results (cont)		
PIK3CA	NGS	Mutated, Pathogenic Exon 2 p.R108H
PTEN	NGS	Mutated, Pathogenic Exon 5 p.R130G
RNF43	NGS	Mutated, Pathogenic Exon 9 p.G659fs
ATM	NGS	Mutation Not Detected
BRAF	NGS	Mutation Not Detected
BRCA1	NGS	Mutation Not Detected
EGFR	NGS	Mutation Not Detected
KRAS	NGS	Mutation Not Detected
NRAS	NGS	Mutation Not Detected
ERBB2 (Her2/Neu)	NGS	Amplification Not Detected
ERCC1	IHC	Negative 0, 100%
RHM1	IHC	Positive 2+, 75%
TOPO1	IHC	Positive 2+, 75%
TS	IHC	Positive 2+, 25%

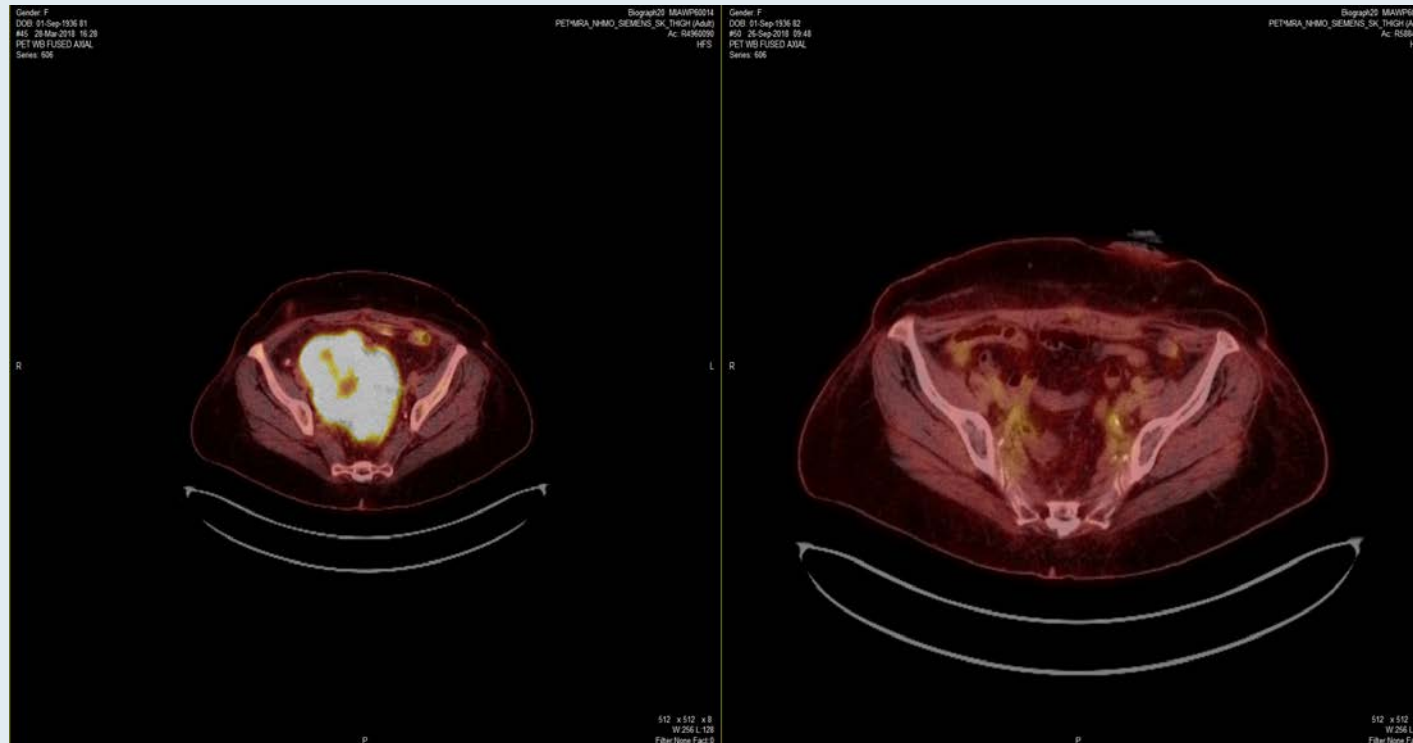
Case Presentation – Dr Shehadeh: An 84-year-old woman with metastatic adenocarcinoma of the uterus – MSI-H, TMB high, PD-L1-negative



Dr Nasfat Shehadeh

PET scan before surgery:
Large active mass
3/28/2018

PET scan after therapy



Case Presentation – Dr Pothuri: A 78-year-old woman with HER2-positive metastatic endometrial cancer – MSI-H/dMMR, TMB high, BRCA wild type



Dr Bhavana Pothuri

- 9/2016: Diagnosed with Stage IIA, grade 2 endometrial cancer, s/p hysterectomy BSO, LND
- 2/2017: Sandwich RT
- 5/2017: Carboplatin/paclitaxel x 6
- Germline genetic testing: Negative
- NGS: HER2-positive, MSI-High, TMB-High,
- 6/2018: Recurrence
- 9/2018: Pembrolizumab x 6, with CR on 1/2019
- 2/2109: Hospitalized with influenza A encephalitis, with significant neurologic deficit
 - Pembrolizumab discontinued and still NED 2 years after her last treatment

ASCO 2021;Abstract 2565

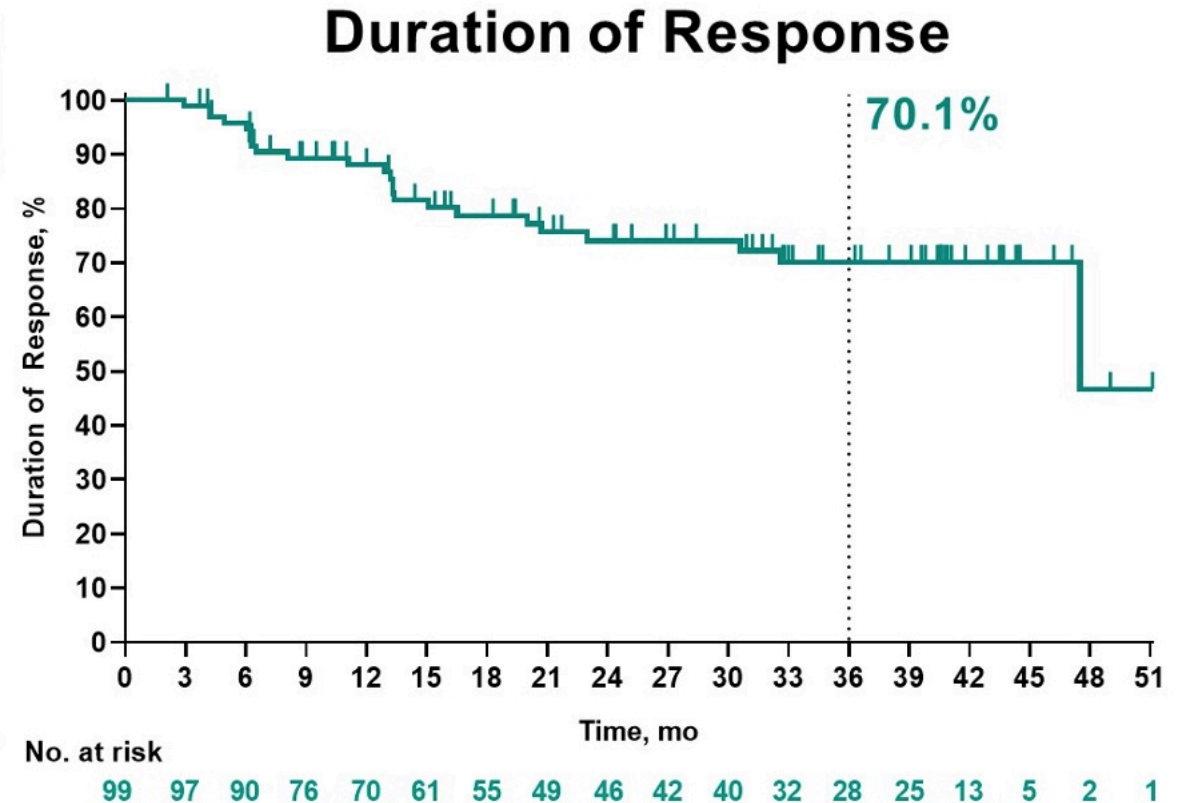
Pembrolizumab in Microsatellite Instability High/Mismatch Repair–Deficient Cancers: Updated Analysis From Phase 2 KEYNOTE-158 Study

M. Maio¹; P.A. Ascierto²; L. Manzyuk³; D. Motola-Kuba⁴; N. Penel⁵; P.A. Cassier⁶; G. Mendonca Bariani⁷; A. De Jesus Acosta⁸; T. Doi⁹; F. Longo Muñoz¹⁰; W.H. Miller, Jr¹¹; D.-Y. Oh¹²; M. Gottfried¹³; R. Wang¹⁴; F. Jin¹⁴; K. Norwood¹⁴; A. Marabelle¹⁵

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



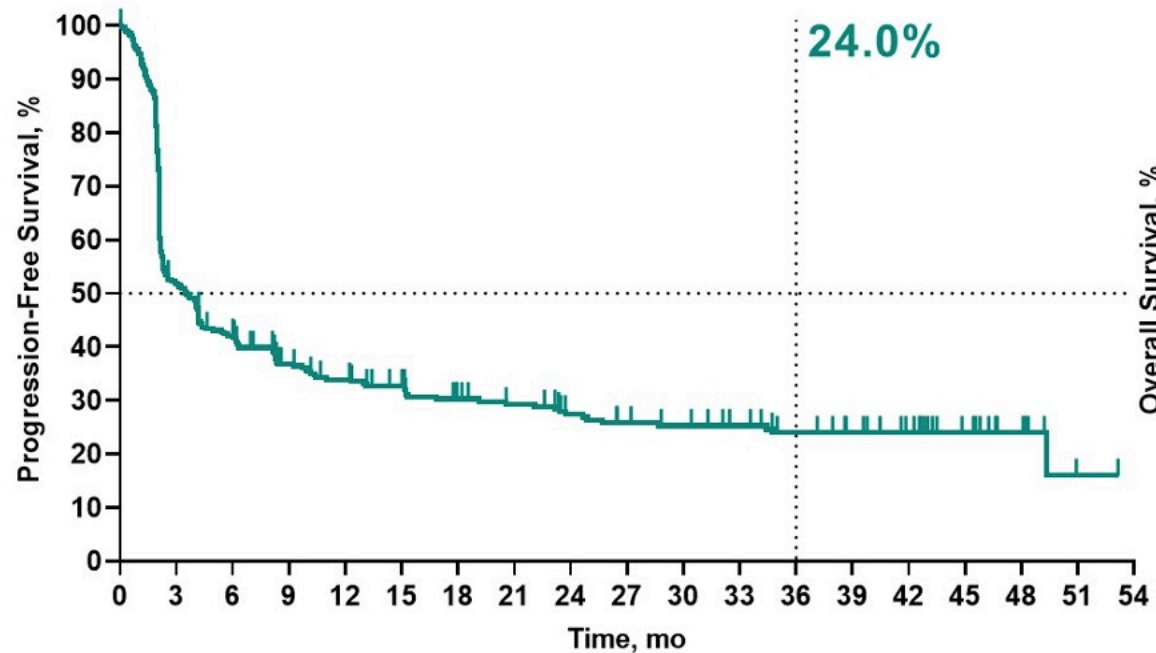
CI, confidence interval. “+” indicates no PD by the time of last disease assessment.

^aPatients who had no postbaseline imaging assessment.

Data cutoff: October 5, 2020

KEYNOTE-158: Updated Survival Analyses

Progression-Free Survival

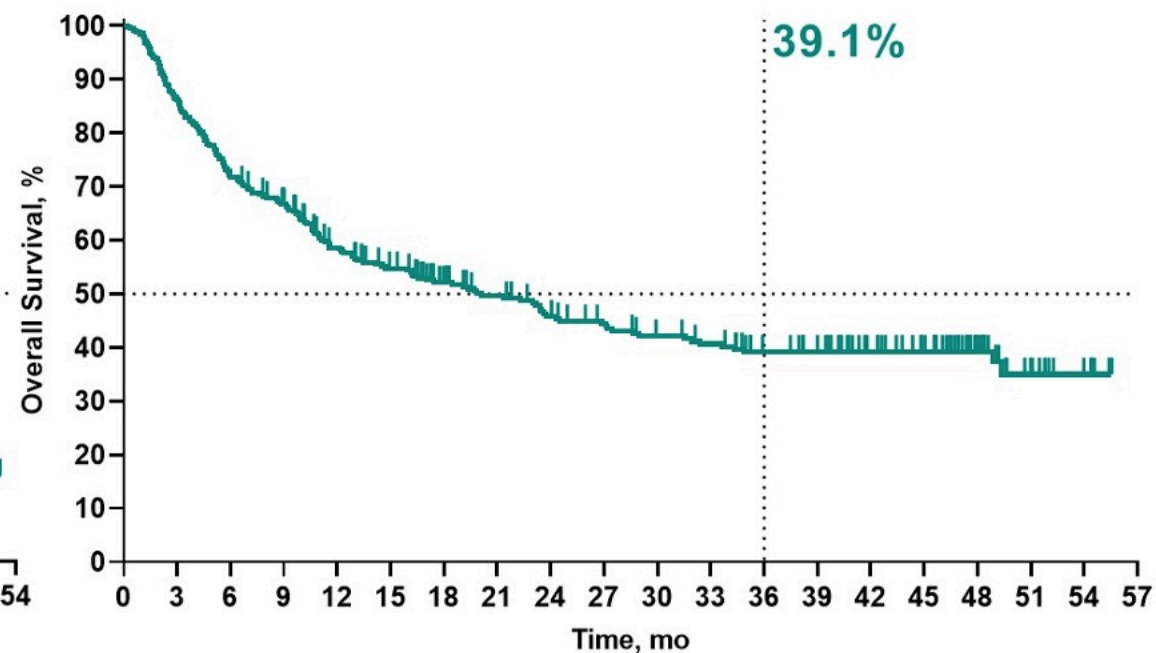


No. at risk

321 165 132 104 92 83 67 62 53 48 45 41 35 31 26 14 7 1 0

Median (95% CI): 3.5 (2.3–4.2) mo

Overall Survival



321 277 230 208 170 151 131 117 105 97 89 84 73 68 56 47 28 11 5 0

Median (95% CI): 20.1 (14.1–27.1) mo

Data cutoff: October 5, 2020

Case Presentation – Dr Penson: A 74-year-old woman with MSS endometrioid endometrial adenocarcinoma – PD-L1 0%



Dr Richard Penson

- 2013: Diagnosed with Stage IA, grade 2 MSS endometrioid adenocarcinoma
- Robotic-assisted laparoscopic hysterectomy, BSO, brachytherapy
- 2017: Carboplatin/paclitaxel
- 2017: Phase I study of lenvatinib/pembrolizumab x 12, with “spectacular” response
 - Hypothyroidism, hypertension, Grade 3 myalgias, gastric perforation
- 2017-Present: Continues pembrolizumab q6wks
- NGS assay: PIK3CA, PTEN, BRCA2, ARID1A, APC mutations

Questions

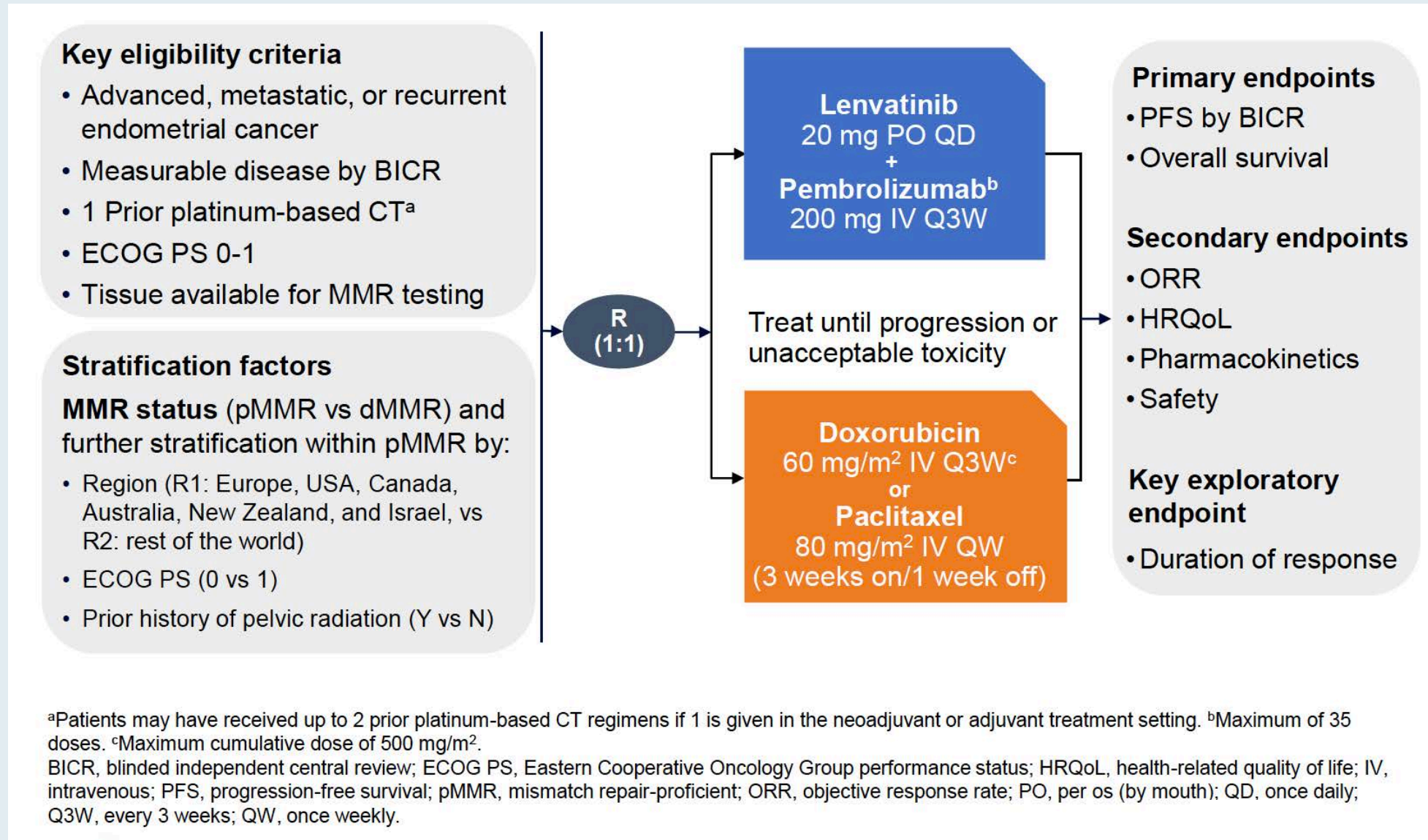
- As you approach the 2-year milestone with immunotherapy, do you stop treatment?

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

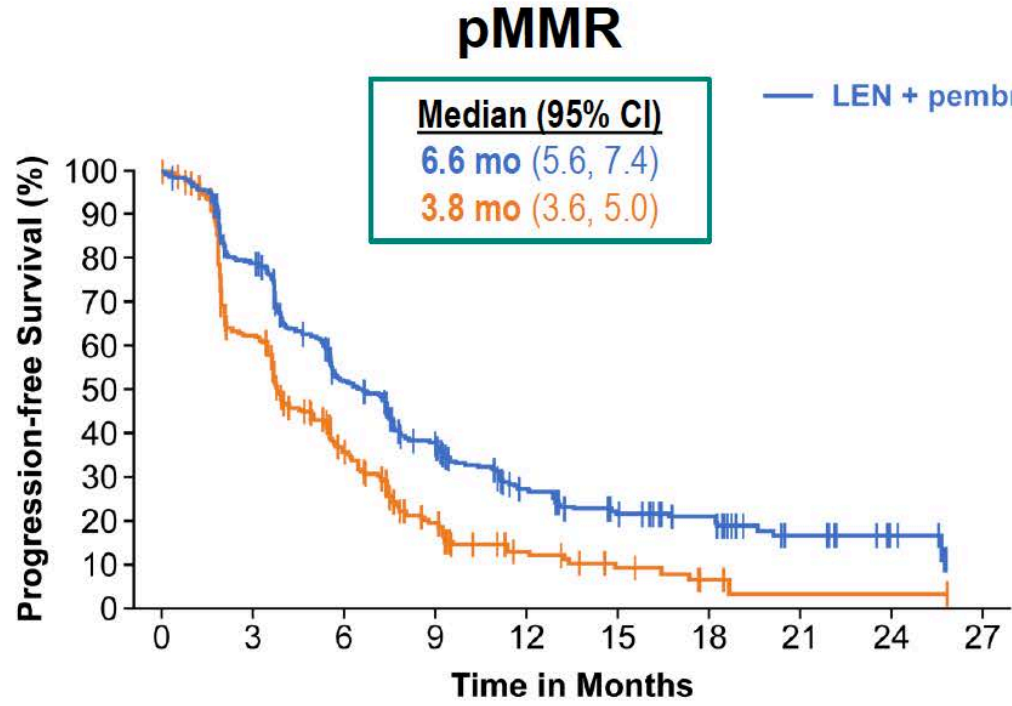
Makker V et al.

SGO 2021;Abstract 11512.

Study 309/KEYNOTE-775: Phase III Trial Schema



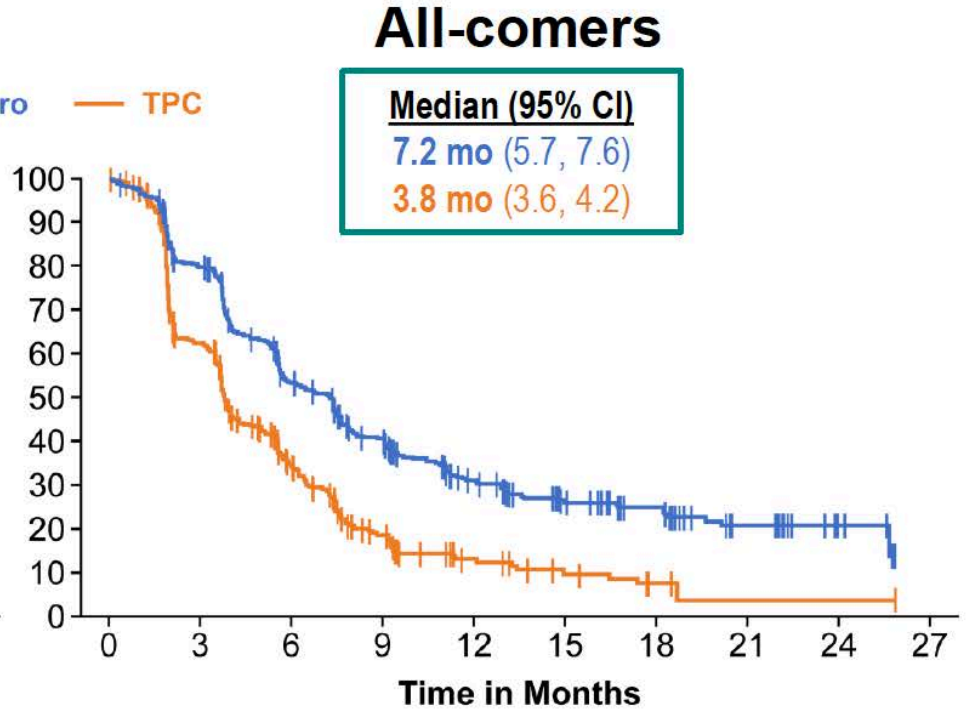
Study 309/KEYNOTE-775: Progression-Free Survival



No. at risk

346	264	165	112	60	39	30	12	5	0
351	177	83	37	15	8	3	1	1	0

	Events	HR (95% CI)	P-value
LEN + pembro	247	0.60 (0.50, 0.72)	< 0.0001
TPC	238		



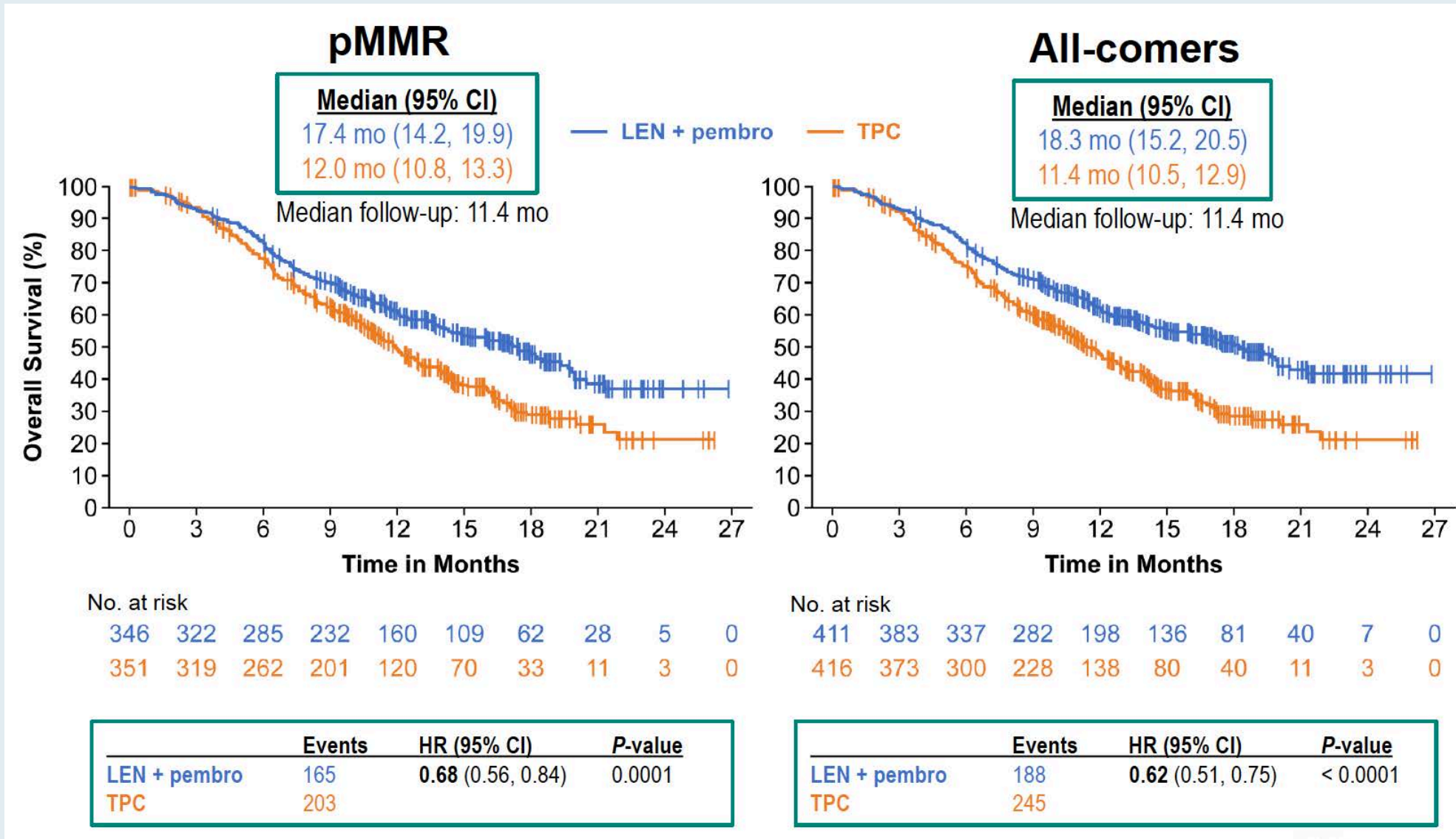
No. at risk

411	316	202	144	86	56	43	17	6	0
416	214	95	42	18	10	4	1	1	0

	Events	HR (95% CI)	P-value
LEN + pembro	281	0.56 (0.47, 0.66)	< 0.0001
TPC	286		

^aBy BICR per Response Evaluation Criteria in Solid Tumors version 1.1.

Study 309/KEYNOTE-775: Overall Survival



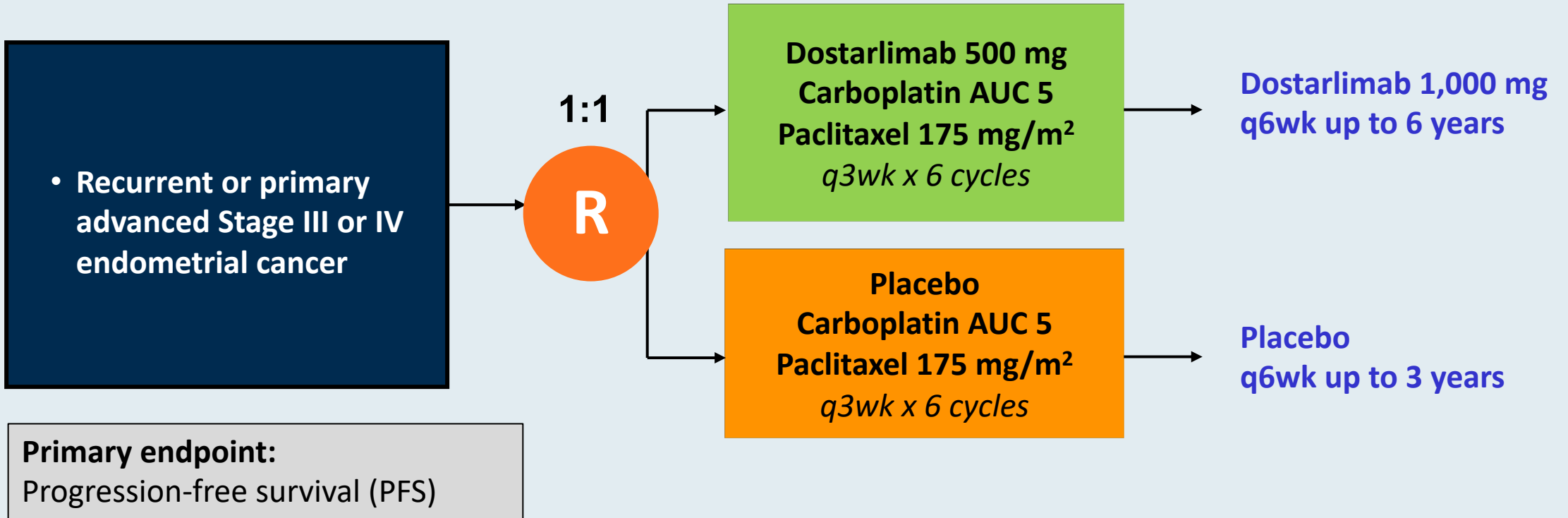
Case Presentation – Dr Duska: A 60-year-old woman with metastatic, MSS carcinosarcoma



Dr Linda Duska

- PMH: Dyslipidemia, hypertension, seizure disorder, stroke, smoker
- Presents with progressive fatigue, nausea, abdominal pain
- Endometrial biopsy: Carcinosarcoma (malignant mixed Mullerian tumor), microsatellite stable
- CT: Bulky mass in the uterus extending to pelvis and lower abdomen c/w metastatic disease
- Enrolled on RUBY trial: carboplatin/paclitaxel +/- dostarlimab

ENGOT-EN6/NSGO-RUBY Phase III Schema



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

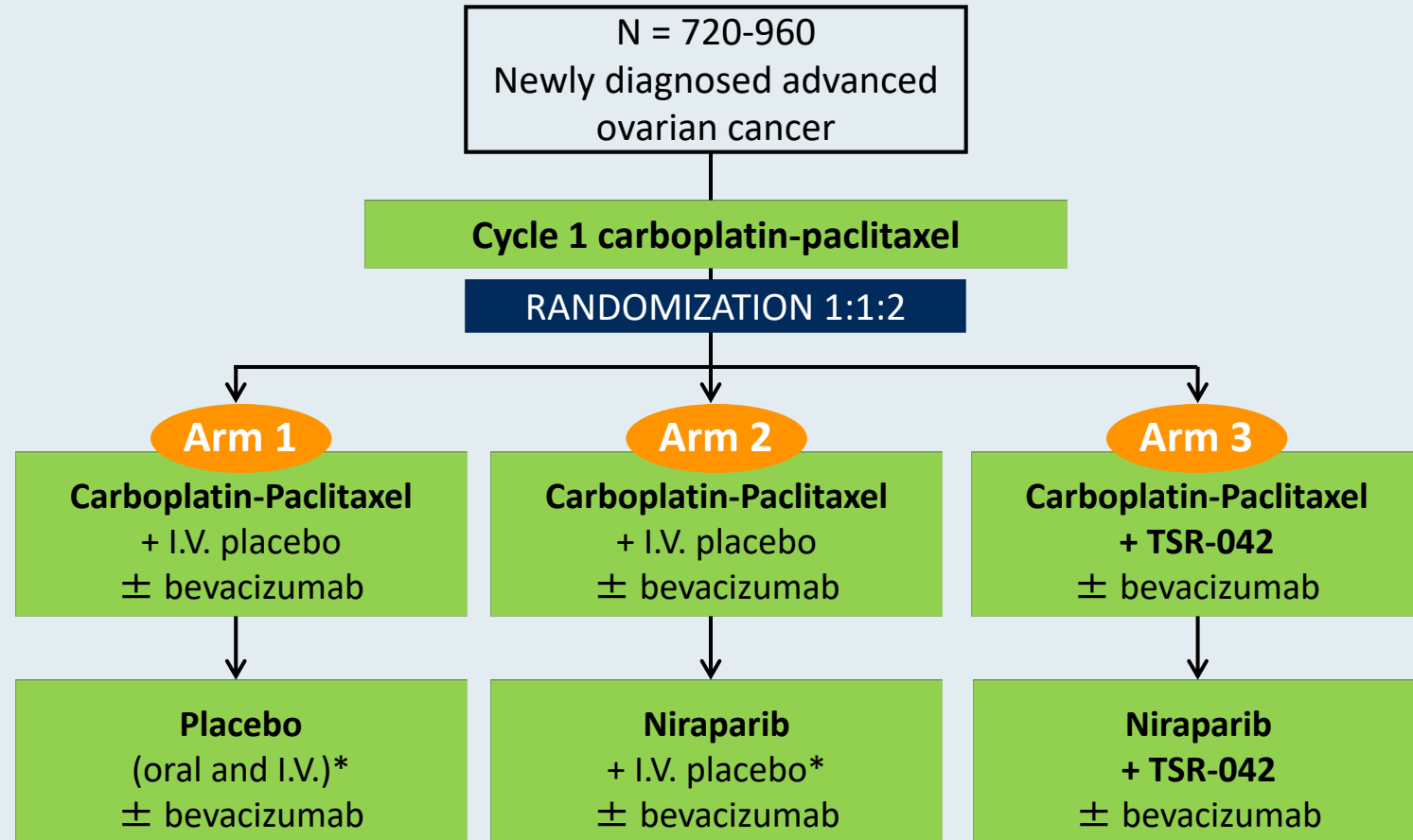
Press Release – April 22, 2021

“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).”

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



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

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

Case Presentation – Dr Duska: A 69-year-old woman with ER/PR-positive metastatic endometrioid adenocarcinoma – MMR proficient



Dr Linda Duska

- PMH: Hyperlipidemia, nephrolithiasis, recurrent UTI, prior lumpectomy
- Postmenopausal bleeding → Endometrial biopsy: Grade 1 endometrioid adenocarcinoma
- Laparoscopic TLH/BSO BPLND: Grade 1, Stage IB, ER/PR-positive, MMR-proficient
- Nine years later: Presents with cough
- Chest x-ray: Multiple lung nodules, biopsy-confirmed metastatic adenocarcinoma c/w endometrial primary
- Tamoxifen/megesterol acetate, with decreasing disease one year later

Meet The Professor with Dr Liu

MODULE 1: Cases from the Practices of Gynecologic and Medical Oncologists

Cervical Cancer

- Dr Westin: A 52-year-old woman with metastatic squamous cell carcinoma of the cervix
- Dr Penson: A 39-year-old woman with metastatic squamous cell carcinoma of the cervix – PD-L1-negative
- Dr Godoy: A 72-year-old woman with metastatic squamous cell carcinoma of the vulva – PD-L1 50%

Endometrial Cancer

- Dr Shehadeh: An 84-year-old woman with metastatic adenocarcinoma of the uterus – MSI-H, TMB-H, PD-L1-negative
- Dr Pothuri: A 78-year-old woman with HER2-positive metastatic endometrial cancer – MSI-H/dMMR, TMB high, BRCA WT
- Dr Penson: A 74-year-old woman with MSS endometrioid adenocarcinoma – PD-L1 0%
- Dr Duska: A 60-year-old woman with metastatic, MSS carcinosarcoma
- Dr Duska: A 69-year-old woman with ER/PR-positive metastatic endometrioid adenocarcinoma – MMR proficient

MODULE 2: Journal Club with Dr Liu

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

MODULE 4: Key Recent Data Sets

Journal Club with Dr Liu – Part 1

ASCO 2021 Annual Meeting: A review and summary of selected abstracts

Trials in Progress

- innovaTV 301: Ongoing trial of tisotumab vedotin vs investigator's choice of chemotherapy for second- or third-line recurrent or metastatic cervical cancer (CC). Abstract TPS5596.
- ROCSAN: Dostarlimab/niraparib vs niraparib vs chemotherapy for endometrial/ovarian carcinosarcoma after ≥ 1 line of platinum-based chemotherapy. Abstract TPS5604.
- KEYNOTE-B21: Pembrolizumab with adjuvant chemotherapy \pm RT for newly diagnosed high-risk endometrial cancer (EC). Abstract TPS5608.
- ENGOT-OV54/Swiss-GO-2/MATAO Including LOGOS (Low-Grade Ovarian Cancer Substudy): Maintenance therapy with aromatase inhibitor for epithelial ovarian cancer (OC). Abstract TPS5598.
- Paclitaxel/carboplatin and maintenance letrozole vs letrozole monotherapy for Stage II-IV primary low-grade serous carcinoma of the ovary or peritoneum. Abstract TPS5601.
- AdvanTIG-202: Anti-TIGIT monoclonal antibody ociperlimab with anti-PD-1 monoclonal antibody tislelizumab for previously treated recurrent or metastatic CC. Abstract TPS5595.

Journal Club with Dr Liu – Part 1

ASCO 2021 Annual Meeting: A review and summary of selected abstracts

Other Abstracts

- NEOPEMBROV: Neoadjuvant chemotherapy \pm pembrolizumab (P) \rightarrow Interval debulking surgery and standard systemic therapy \pm P for advanced high-grade serous carcinoma. Abstract 5500.
- Anlotinib with sintilimab for recurrent advanced CC. Abstract 5524.
- OUTBACK: Adjuvant chemotherapy after chemoradiation as primary treatment for locally advanced CC. Abstract LBA3.
- TAPUR: Pertuzumab with trastuzumab for uterine cancer with ERBB2 or ERBB3 amplification, overexpression or mutation. Abstract 5508.
- Mirvetuximab soravtansine/bevacizumab for platinum-agnostic OC: Final analysis. Abstract 5504.
- Optimal treatment duration of bevacizumab combined with carboplatin/paclitaxel for epithelial OC. Abstract 5501.
- TOTEM: Intensive vs minimalist follow-up for patients who receive treatment for EC. Abstract 5506.

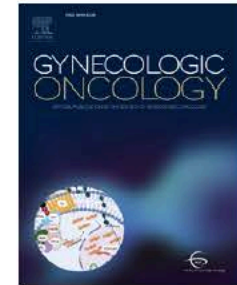


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Meeting Report

The American Society of Clinical Oncology 2021 annual (virtual) meeting: A review and summary of selected abstracts

Ritu Salani ^{a,*}, Joyce F. Liu ^b

Tisotumab Vedotin versus Investigator's Choice Chemotherapy in Second- or Third-Line Recurrent or Metastatic Cervical Cancer (innovaTV 301/ENGOT-cx12/GOG 3057, Trial in Progress)

Vergote I et al.

ASCO 2021;Abstract TPS5596.

ROCSAN Trial (GINECO-EN203b/ENGOT-EN8): A Multicentric Randomized Phase II/III Evaluating Dostarlimab in Combination with Niraparib versus Niraparib Alone Compared to Chemotherapy in the Treatment of Endometrial/Ovarian Carcinosarcoma After at Least One Line of Platinum Based Chemotherapy

Ray-Coquard IL et al.

ASCO 2021;Abstract TPS5604.

ENGOT-en11/GOG-3053/KEYNOTE-B21: Phase 3 Study of Pembrolizumab or Placebo in Combination with Adjuvant Chemotherapy with/without Radiotherapy in Patients with Newly Diagnosed High-Risk Endometrial Cancer

Gorp TV et al.

ASCO 2021;Abstract TPS5608.

ENGOT-ov54/Swiss-GO-2/MATAO Including LOGOS (Low-Grade Ovarian Cancer Sub-study): Maintenance Therapy with Aromatase Inhibitor in Epithelial Ovarian Cancer — A Randomized, Double-Blinded, Placebo-Controlled, Multicenter Phase III Trial

Heinzelmann-Schwarz VA et al.
ASCO 2021;Abstract TPS5598.

A Randomized Phase III, Two-Arm Trial of Paclitaxel, Carboplatin, and Maintenance Letrozole versus Letrozole Monotherapy in Patients with Stage II-IV, Primary Low-Grade Serous Carcinoma of the Ovary or Peritoneum

Fader AM et al.

ASCO 2021;Abstract TPS5601.

AdvanTIG-202: A Phase 2 Study Investigating Anti-TIGIT Monoclonal Antibody Ociperlimab plus Anti-PD-1 Monoclonal Antibody Tislelizumab in Patients with Previously Treated Recurrent or Metastatic Cervical Cancer

Wu L et al.

ASCO 2021;Abstract TPS5595.

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 \pm P for Advanced High-Grade Serous Carcinoma (HGSC): A GINECO Study

Ray-Coquard IL et al.

ASCO 2021;Abstract 5500.

Anlotinib plus Sintilimab in Patients with Recurrent Advanced Cervical Cancer: A Prospective, Multicenter, Single-Arm, Phase II Clinical Trial

Xu Q et al.

ASCO 2021;Abstract 5524.

Adjuvant Chemotherapy Following Chemoradiation as Primary Treatment for Locally Advanced Cervical Cancer Compared to Chemoradiation Alone: The Randomized Phase III OUTBACK Trial (ANZGOG 0902, RTOG 1174, NRG 0274)

Mileshkin LR et al.

ASCO 2021;Abstract LBA3.

Pertuzumab plus Trastuzumab (P + T) in Patients (Pts) with Uterine Cancer (UC) with *ERBB2* or *ERBB3* Amplification, Overexpression or Mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Ali-Ahmad HM et al.

ASCO 2021;Abstract 5508.

Mirvetuximab Soravtansine, a Folate Receptor Alpha (FR α)-Targeting Antibody-Drug Conjugate (ADC), in Combination with Bevacizumab in Patients (pts) with Platinum-Agnostic Ovarian Cancer: Final Analysis

O'Malley DM et al.

ASCO 2021;Abstract 5504.

Optimal Treatment Duration of Bevacizumab (BEV) Combined with Carboplatin and Paclitaxel in Patients (pts) with Primary Epithelial Ovarian (EOC), Fallopian Tube (FTC) or Peritoneal Cancer (PPC): A Multicenter Open-Label Randomized 2-Arm Phase 3 ENGOT/GCIG Trial of the AGO Study Group, GINECO, and NSGO (AGO-OVAR 17/BOOST, GINECO OV118, ENGOT Ov-15, NCT01462890)

Pfisterer J et al.

ASCO 2021;Abstract 5501.

Intensive versus Minimalist Follow-Up in Patients Treated for Endometrial Cancer: A Multicentric Randomized Controlled Trial (The TOTEM Study—NCT00916708)

Zola P et al.

ASCO 2021;Abstract 5506.

Journal Club with Dr Liu – Part 2

- OPAL Cohort A: Dostarlimab, bevacizumab and niraparib for platinum-resistant OC
- Mirvetuximab soravtansine/pembrolizumab for MSS EC
- Phase II study of talazoparib and avelumab for MSS recurrent/persistent EC
- Avelumab/axitinib in mismatch repair-proficient recurrent or persistent EC
- Adapting protein sequences for optimized therapeutic efficacy

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. Konecny¹¹

Poster #23

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

SGO
2021 VIRTUAL ANNUAL MEETING
ON WOMEN'S CANCER®

Abstract 10415

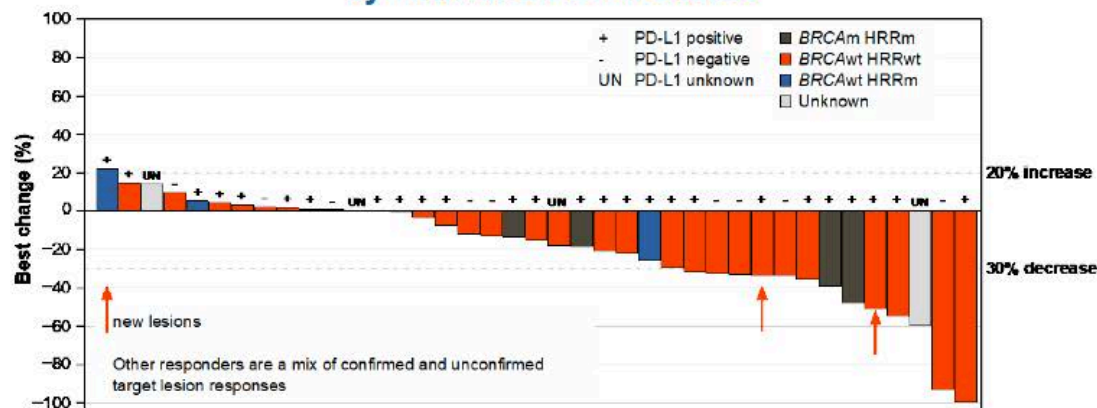


Antitumor Activity

- 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



BRCAm, BRCA mutation; BRCAwt, BRCA wild type; HRRm, homologous recombination repair mutation; HRRwt, homologous recombination repair wild type; PD-L1, programmed death ligand 1.



A Phase 2, Two-Stage Study of Mirvetuximab Soravtansine (IMGN853) in Combination with Pembrolizumab in Patients with Microsatellite Stable (MSS) Endometrial Cancer (EC)

Porter RL et al.

ASCO 2021;Abstract TPS5611.

VIRTUAL
2020

ESMO congress

Abstract LBA35

**Phase 2 study of PARP inhibitor Talazoparib
and PD-L1 inhibitor Avelumab in patients
(pts) with Recurrent Microsatellite Stable
(MSS) Endometrial Cancer**

Panagiotis Konstantinopoulos MD, PhD

Director of Translational Research
Gynecologic Oncology Program
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School



A Phase 2, Two-Stage Study of Avelumab and Axitinib in Patients with Mismatch Repair Proficient (MMR-P) Recurrent or Persistent Endometrial Cancer (EC)

Lee EK et al.

ASCO 2021;Abstract TPS5609.

Meet The Professor with Dr Liu

MODULE 1: Cases from the Practices of Gynecologic and Medical Oncologists

Cervical Cancer

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- Dr Penson: A 74-year-old woman with MSS endometrioid adenocarcinoma – PD-L1 0%
- Dr Duska: A 60-year-old woman with metastatic, MSS carcinosarcoma
- Dr Duska: A 69-year-old woman with ER/PR-positive metastatic endometrioid adenocarcinoma – MMR proficient

MODULE 2: Journal Club with Dr Liu

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

MODULE 4: Key Recent Data Sets

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

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

In general, what treatment would you recommend for a patient with 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**

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

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

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

A patient with PD-L1-positive metastatic cervical cancer experiences disease progression on platinum-based therapy and has significant symptoms from her disease. If tisetumab vedotin and cemiplimab were accessible, what would likely be your next line of treatment?

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

Do you generally evaluate microsatellite instability status in your patients with advanced ovarian cancer?

1. Yes

2. No

Do you generally evaluate microsatellite instability status in your patients with advanced ovarian cancer?

 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

Meet The Professor with Dr Liu

MODULE 1: Cases from the Practices of Gynecologic and Medical Oncologists

Cervical Cancer

- Dr Westin: A 52-year-old woman with metastatic squamous cell carcinoma of the cervix
- Dr Penson: A 39-year-old woman with metastatic squamous cell carcinoma of the cervix – PD-L1-negative
- Dr Godoy: A 72-year-old woman with metastatic squamous cell carcinoma of the vulva – PD-L1 50%

Endometrial Cancer

- Dr Shehadeh: An 84-year-old woman with metastatic adenocarcinoma of the uterus – MSI-H, TMB-H, PD-L1-negative
- Dr Pothuri: A 78-year-old woman with HER2-positive metastatic endometrial cancer – MSI-H/dMMR, TMB high, BRCA WT
- Dr Penson: A 74-year-old woman with MSS endometrioid adenocarcinoma – PD-L1 0%
- Dr Duska: A 60-year-old woman with metastatic, MSS carcinosarcoma
- Dr Duska: A 69-year-old woman with ER/PR-positive metastatic endometrioid adenocarcinoma – MMR proficient

MODULE 2: Journal Club with Dr Liu

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Anti-PD-1/PD-L1 Checkpoint Inhibitors in 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.

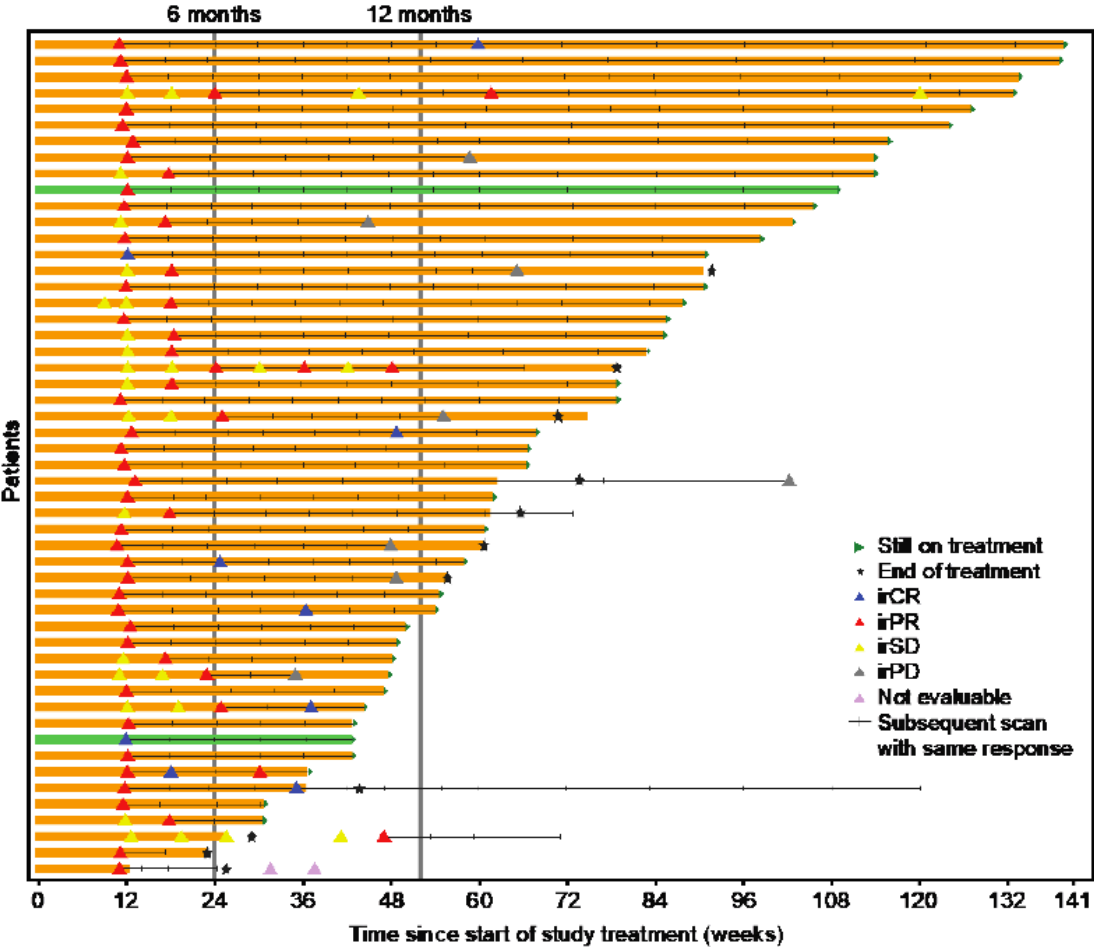
GARNET: Immune-Related Secondary Endpoints

(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

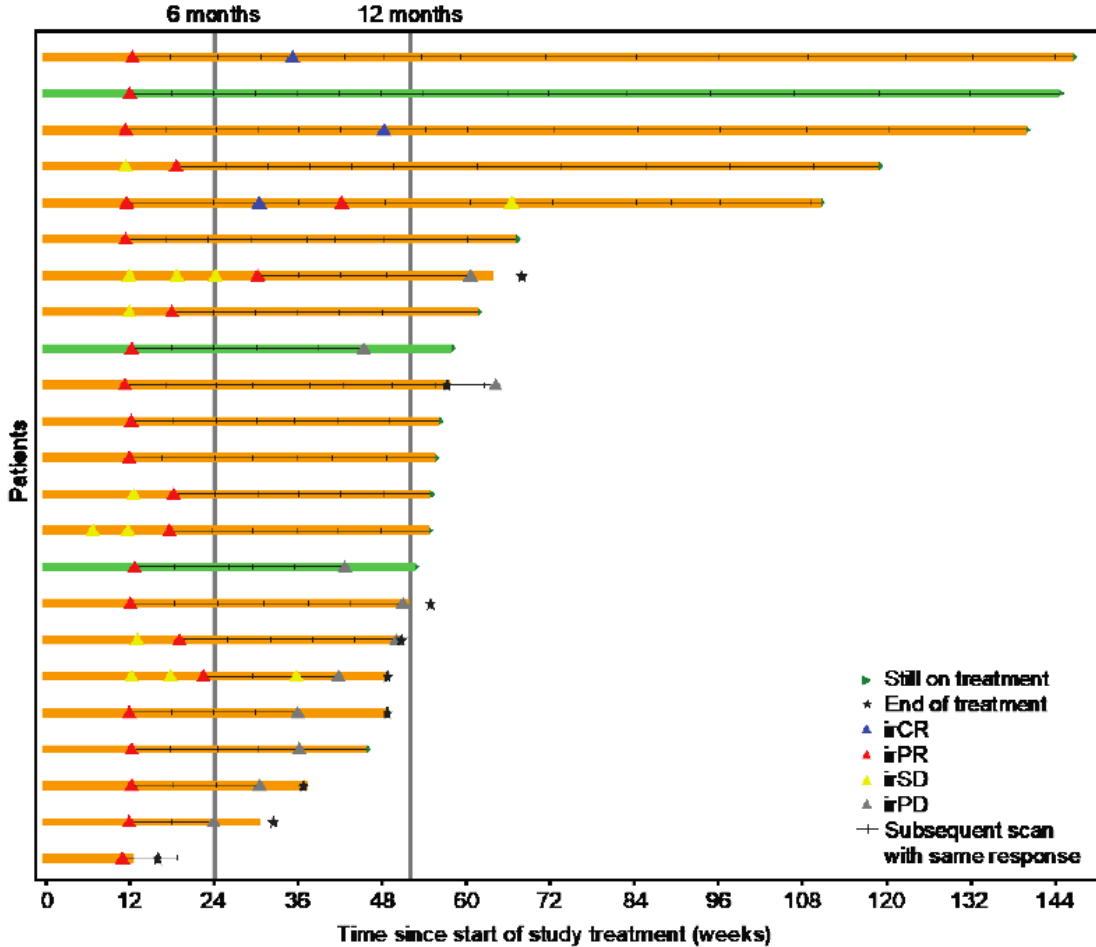
^aIncludes CR, PR, and SD \geq 12 weeks; ^bOnly includes responders.

GARNET: Duration of Response

dMMR

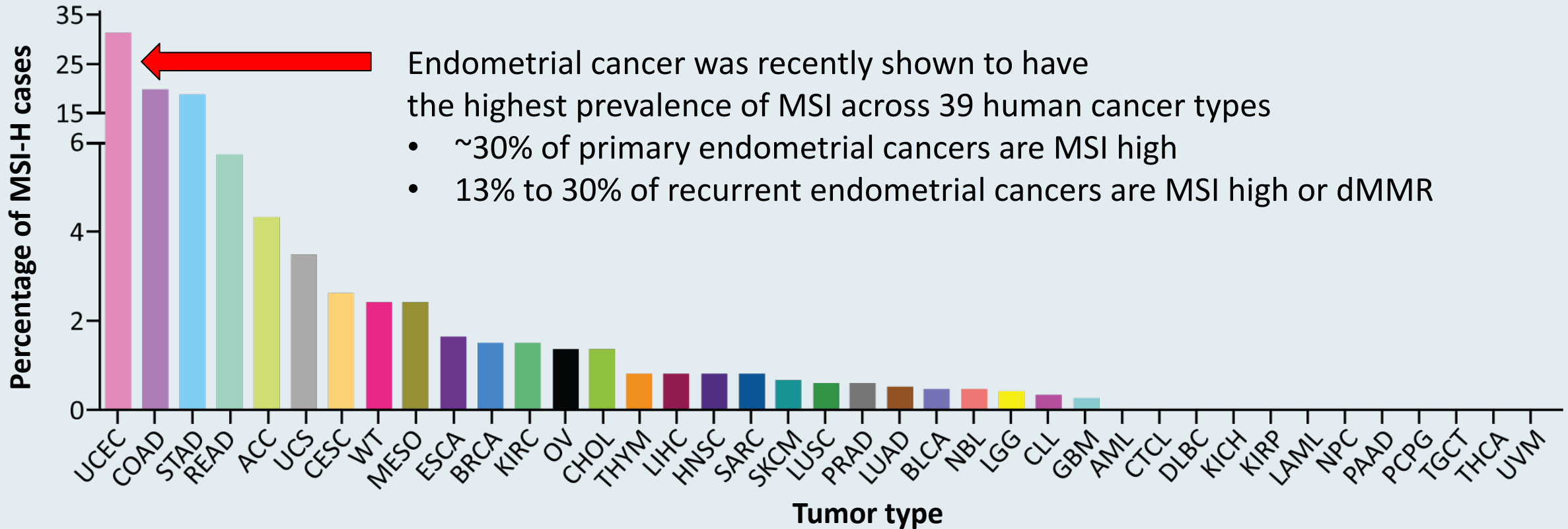


MMRp



High MSI Across 39 Cancer Types

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



UCEC = uterine corpus endometrial carcinoma

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

Phase III Trial of Cemiplimab Monotherapy in Advanced Cervical Cancer Stopped Early for Positive Result on Overall Survival

Press Release – March 15, 2021

“Positive results demonstrating an overall survival (OS) benefit from the Phase 3 trial investigating the PD-1 inhibitor cemiplimab monotherapy compared to chemotherapy, in patients previously treated with chemotherapy whose cervical cancer is recurrent or metastatic were announced today. The trial will be stopped early based on a unanimous recommendation by the Independent Data Monitoring Committee (IDMC), and the data will form the basis of regulatory submissions in 2021 ...

“This is the largest Phase 3 randomized clinical trial in advanced cervical cancer and included women (median age: 51 years) with either squamous cell carcinoma or adenocarcinoma. Patients were randomized to receive cemiplimab monotherapy (350 mg every 3 weeks) or an investigator's choice of commonly used chemotherapy (pemetrexed, vinorelbine, topotecan, irinotecan or gemcitabine). Compared to chemotherapy, patients receiving cemiplimab experienced: Total population: 31% reduced risk of death; Squamous cell carcinoma: 27% reduced risk of death; Adenocarcinoma: 44% reduced risk of death. The primary endpoint for the trial was OS, analyzed first among patients with squamous cell carcinoma, then in the total population...

“Detailed results will be presented at an upcoming medical meeting.”

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

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

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

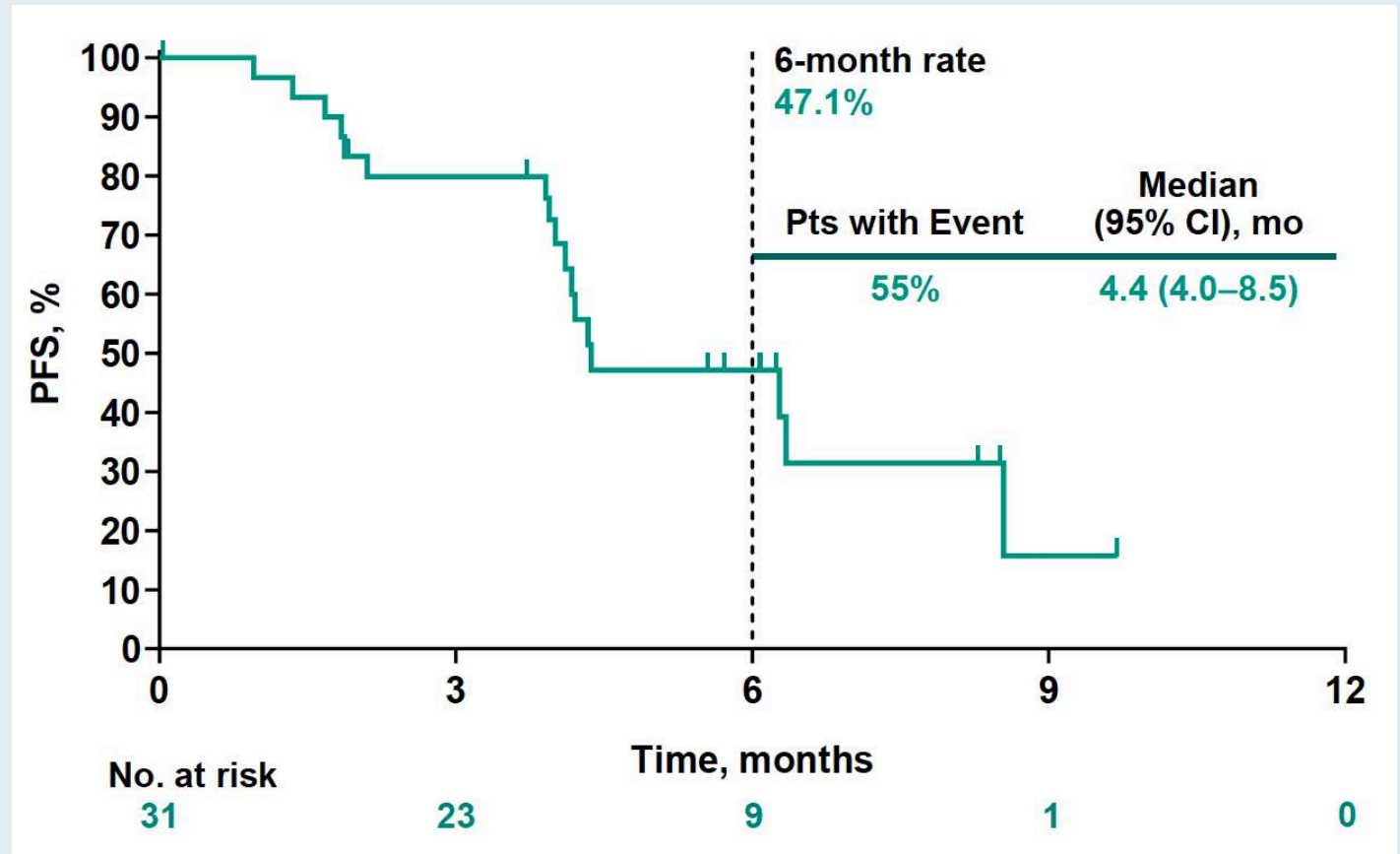
Lwin Z et al.

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)



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-COQUARD¹, Aude-Marie SAVOYE², Marie-Ange MOURET-REYNIER³, Sylvie CHABAUD⁴, Olfia DERBEL⁵, Elsa KALBACHER⁶, Marianne LEHEURTEUR⁷, Alejandra MARTINEZ⁸, Corina CORNILA⁹, Mathilde MARTINEZ¹⁰, Leila BENGRINE LEFEVRE¹¹, Frank PRIOU¹², Nicolas CLOAREC¹³, Laurence VENAT-BOUVET¹⁴, Frederic SELLE¹⁵, Dominique BERTON¹⁶, Olivier COLLARD¹⁷, Florence JOLY¹⁸, Olivier TREDAN¹⁹

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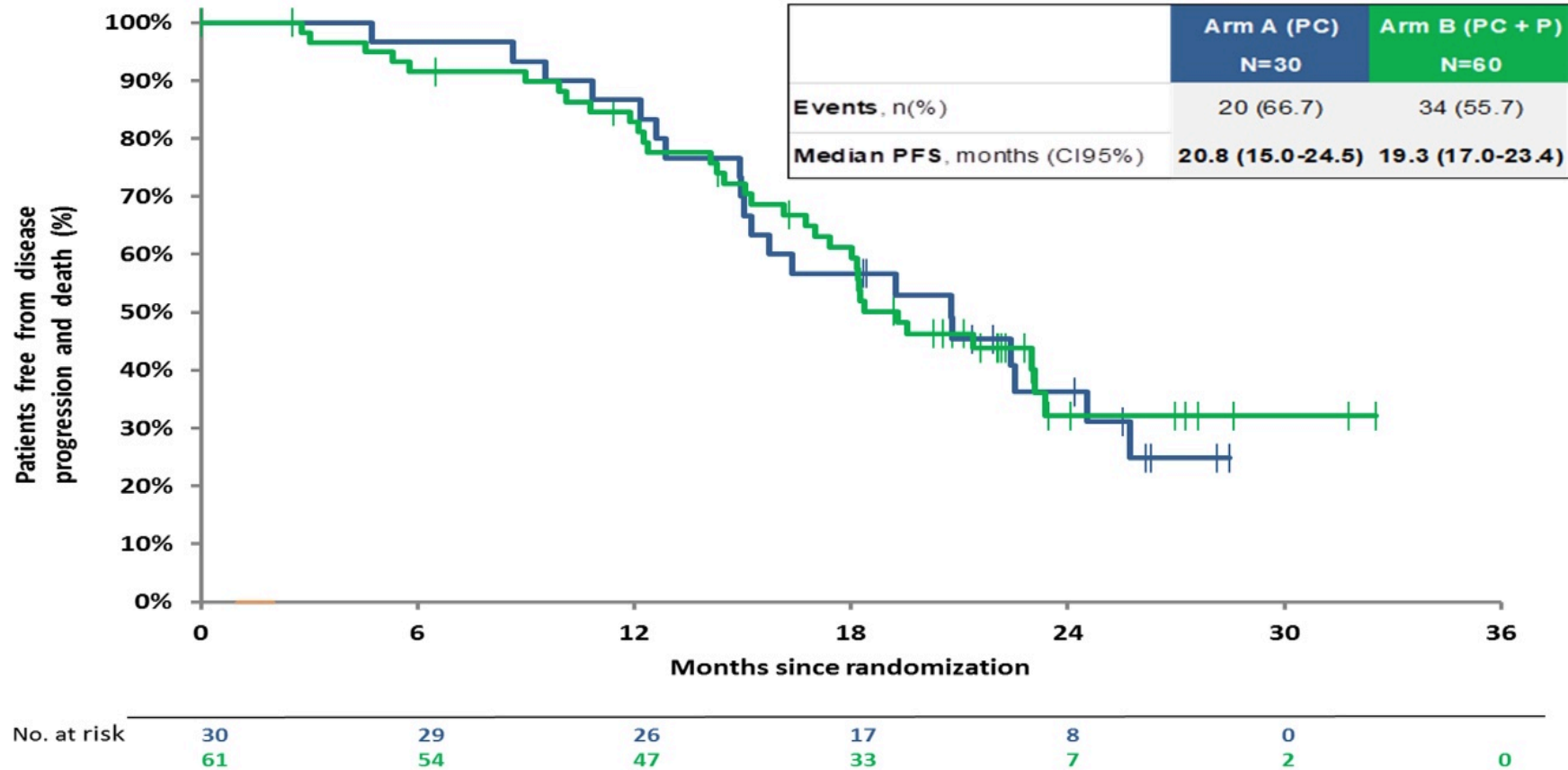
Isabelle Ray-Coquard, Centre Leon Bérard

May, 2021

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)

NEOPEMBROV: Progression-Free Survival



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

Presented By: Isabelle Ray-Coquard

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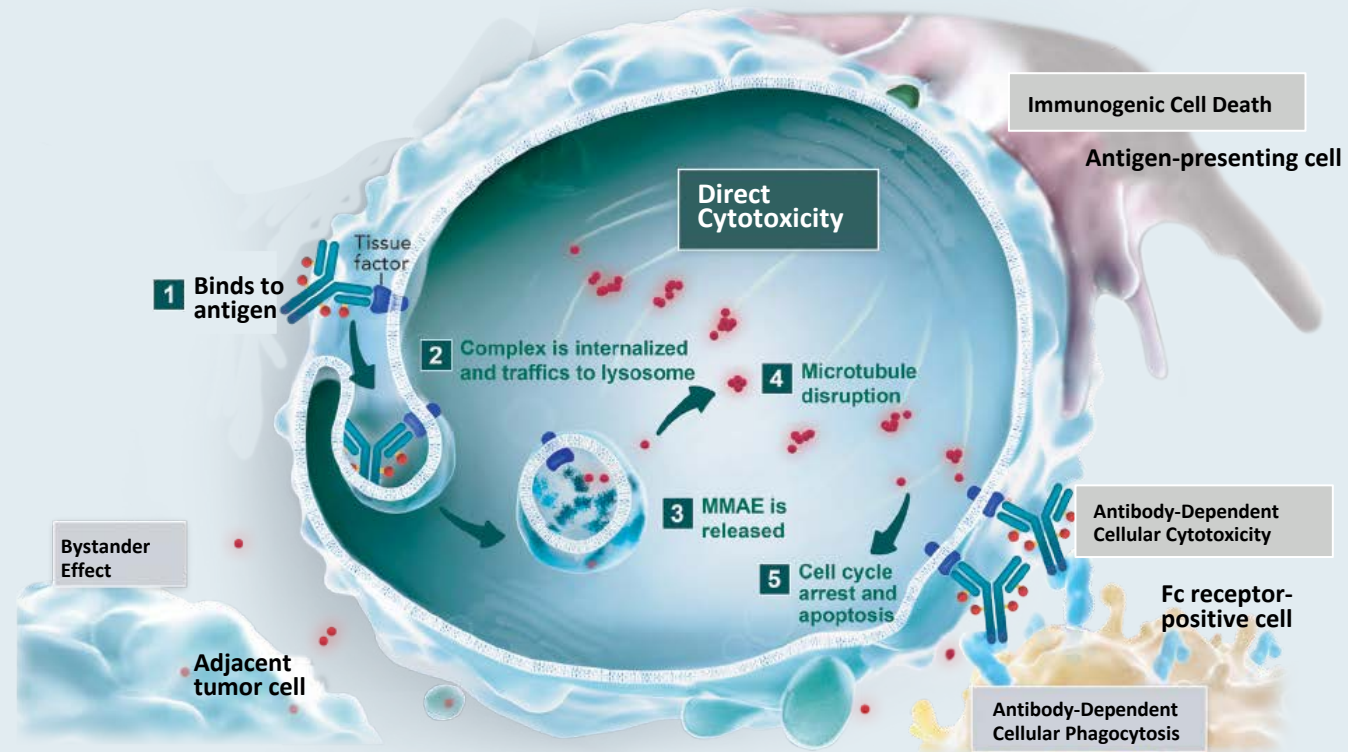
2021 ASCO[®]
ANNUAL MEETING

RTP
RESEARCH
TO PRACTICE

Tisotumab Vedotin and Other Novel Agents in Gynecologic Cancers

Mechanism of Action of Tisotumab Vedotin

- Tissue factor (TF) is aberrantly expressed in a broad range of solid tumours, including cervical cancer,^{1,2} and TF expression has been associated with higher tumour stage and grade, higher metastatic burden and poor prognosis²
- TF expression in cervical cancer makes TF a novel target for patients with cervical cancer
- ADC targets TF
 - Monoclonal Antibody targets TF
 - Payload: Microtubule disrupting MMAE
- Allowing for direct cytotoxicity and bystander killing, as well as antibody-dependent cellular cytotoxicity^{3,4}



Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes

*A Virtual CME Satellite Symposium During the Society of
Hematologic Oncology 2021 Annual Meeting*

**Wednesday, September 8, 2021
7:30 PM – 9:00 PM Central Time**

Faculty

Courtney D DiNardo, MD, MSCE

Daniel A Pollyea, MD, MS

David Sallman, MD

Eunice S Wang, MD

Moderator

Neil Love, MD

Thank you for joining us!

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