# Year in Review: Gynecologic Oncology

A CME/MOC-Accredited Live Webinar

Tuesday, June 25, 2024 5:00 PM – 6:00 PM ET

Faculty Dana M Chase, MD



### Faculty



Dana M Chase, MD

Associate Professor Division of Gynecologic Oncology David Geffen School of Medicine at UCLA Los Angeles, California



MODERATOR Neil Love, MD Research To Practice Miami, Florida



### **Commercial Support**

This activity is supported by an educational grant from AstraZeneca Pharmaceuticals LP.



#### **Dr Love — Disclosures**

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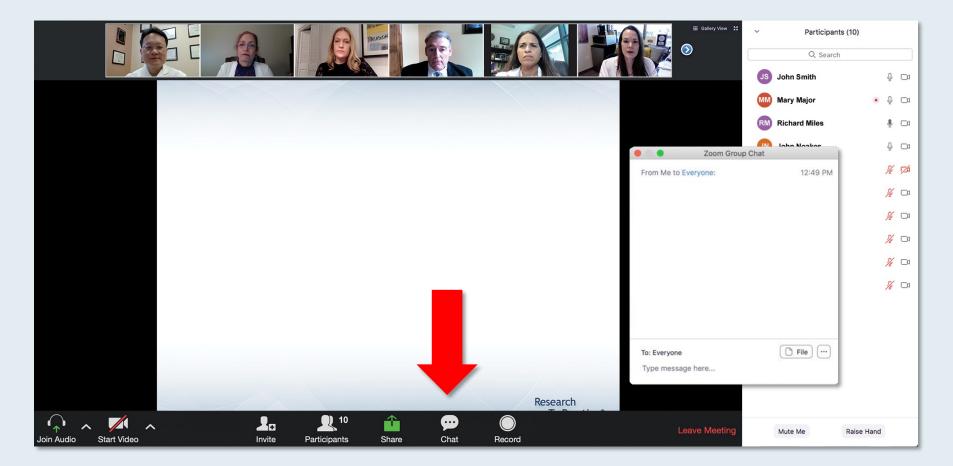


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Advisory Committees and Contracted Research	GSK, Merck
Consulting Agreements	AstraZeneca Pharmaceuticals LP, Eisai Inc, GSK
Speakers Bureaus	AstraZeneca Pharmaceuticals LP, Eisai Inc, GSK, ImmunoGen Inc, Merck, Myriad Genetic Laboratories Inc
Nonrelevant Financial Relationship	NRG Oncology



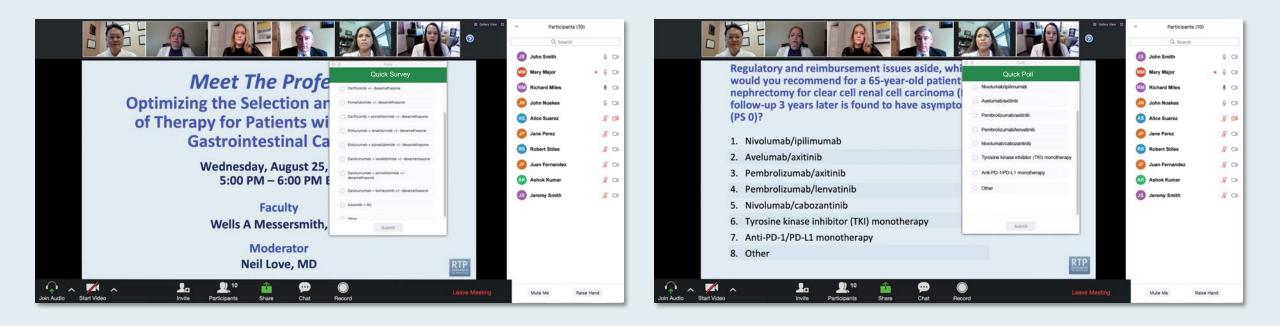
### We Encourage Clinicians in Practice to Submit Questions



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



## Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys





# **ONCOLOGY TODAY** WITH DR NEIL LOVE

Meet The Professor: Optimizing the Management of Ovarian Cancer — Part 4 of a 4-Part Series



DR BRADLEY J MONK FLORIDA CANCER SPECIALISTS & RESEARCH INSTITUTE









Dr Bradley J Monk – Meet The Profess Oncology Today with Dr Neil Love —

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# Year in Review: Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Tuesday, July 9, 2024 5:00 PM – 6:00 PM ET

Faculty Jesús G Berdeja, MD Thomas Martin, MD



Year in Review: Melanoma and Nonmelanoma Skin Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, July 10, 2024 5:00 PM – 6:00 PM ET

> Faculty Evan J Lipson, MD



Inside the Issue: Integrating Antibody-Drug Conjugates into the Management of HR-Positive and Triple-Negative Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 17, 2024 5:00 PM – 6:00 PM ET

### Faculty Professor Peter Schmid, FRCP, MD, PhD Sara M Tolaney, MD, MPH



## Inside the Issue: Integrating ALK-Targeted Therapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, July 18, 2024 5:00 PM – 6:00 PM ET

### Faculty

Professor Solange Peters, MD, PhD Professor Ben Solomon, MBBS, PhD



### Agenda

**INTRODUCTION: ASCO 2024 Review** 

**MODULE 1: Ovarian Cancer** 

**MODULE 2: HER2** as a Therapeutic Target

**MODULE 3: Endometrial Cancer** 

**MODULE 4: Cervical Cancer** 



## Thank you for joining us!

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



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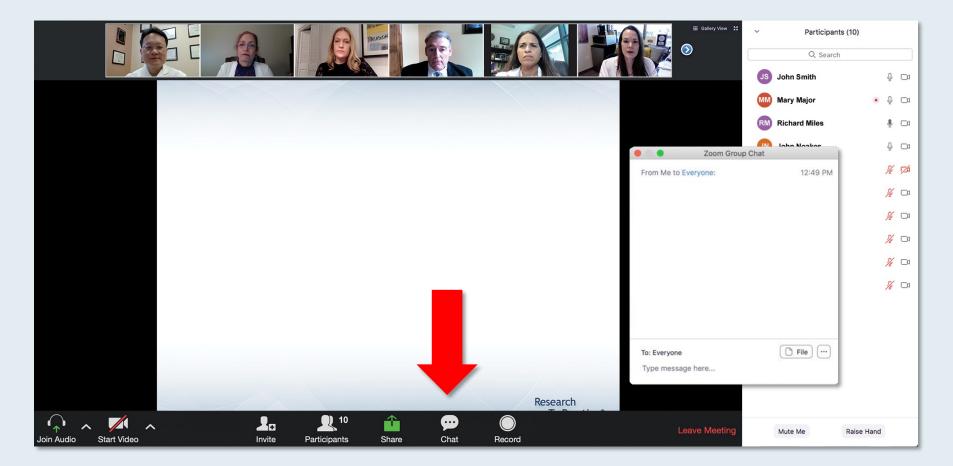
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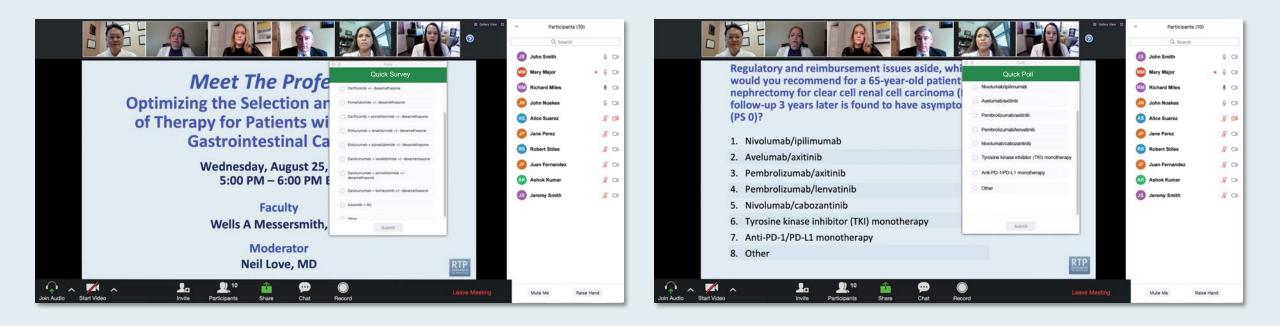
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# **ONCOLOGY TODAY** WITH DR NEIL LOVE

Meet The Professor: Optimizing the Management of Ovarian Cancer — Part 4 of a 4-Part Series



DR BRADLEY J MONK FLORIDA CANCER SPECIALISTS & RESEARCH INSTITUTE









Dr Bradley J Monk – Meet The Profess Oncology Today with Dr Neil Love —

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This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.



#### **Key Data Sets**

- Pfisterer J et al. Optimal treatment duration of bevacizumab as front-line therapy for advanced OC: AGO-OVAR 17 BOOST/GINECO OV118/ENGOT Ov-15 open-label randomized Phase III Trial. J Clin Oncol 2023;41(4):893-902.
- DiSilvestro P et al; SOLO1 Investigators. Overall survival with **maintenance olaparib** at a 7-year followup in patients with newly diagnosed advanced OC and a BRCA mutation: The **SOLO1**/GOG 3004 trial. *J Clin Oncol* 2023;41(3):609-17.
- González-Martín A et al. Progression-free survival and safety at 3.5 years of follow-up: Results from the randomised Phase III **PRIMA**/ENGOT-OV26/GOG-3012 trial of **niraparib maintenance** treatment in patients with newly diagnosed OC. *Eur J Cancer* 2023;189:112908.
- Ray-Coquard I et al. **Olaparib plus bevacizumab first-line maintenance** in ovarian cancer: Final overall survival results from the **PAOLA-1**/ENGOT-ov25 trial. *Ann Oncol* 2023;34(8):681-92.
- Harter P et al. Durvalumab with paclitaxel/carboplatin (PC) and bevacizumab (bev), followed by maintenance durvalumab, bev, and olaparib in patients (pts) with newly diagnosed advanced ovarian cancer (AOC) without a tumor BRCA1/2 mutation (non-tBRCAm): Results from the randomized, placebo (pbo)-controlled phase III DUO-O trial. ASCO 2023;Abstract LBA5506.



### Key Data Sets (Continued)

- Pujade-Lauraine E et al. **Maintenance olaparib rechallenge** in patients with platinum-sensitive relapsed ovarian cancer previously treated with a PARP inhibitor (**OReO**/ENGOT-ov38): A phase IIIb trial. *Ann Oncol* 2023;34(12):1152-64.
- Simpkins F et al. Combination ATR and PARP Inhibitor (CAPRI): A phase 2 study of ceralasertib plus olaparib

in patients with recurrent, platinum-sensitive epithelial ovarian cancer (cohort A). ASCO 2024;Abstract 5510.

- Moore KN et al. Mirvetuximab soravtansine in FRα-positive, platinum-resistant ovarian cancer. *N Engl J Med* 2023;389(23):2162-74.
- Meric-Bernstam F et al. Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: Primary results from the DESTINY-PanTumor02 phase II trial. J Clin Oncol 2024;42(1):47-58.
- Nishikawa T et al. Trastuzumab Deruxtecan for Human Epidermal Growth Factor Receptor 2-Expressing Advanced or Recurrent Uterine Carcinosarcoma (NCCH1615): The STATICE Trial. J Clin Oncol 2023; 41(15):2789-99.
- Van Nieuwenhuysen E et al. Durvalumab + carboplatin/paclitaxel (CP) followed by durvalumab ± olaparib as first-line treatment for newly diagnosed advanced or recurrent endometrial cancer (EC) in DUO-E: Results by BRCA1/BRCA2 mutation (BRCAm) status. ASCO 2024; Abstract 5595.

### **Key Data Sets (Continued)**

- Pepin JT et al. Safety and tolerability of durvalumab + carboplatin/paclitaxel followed by durvalumab
   + olaparib in patients with newly diagnosed advanced or recurrent endometrial cancer (EC) in the
   DUO-E/GOG-3041/ENGOT-EN10 trial. ASCO 2024;Abstract 5599.
- Westin SN et al. Durvalumab plus carboplatin/paclitaxel followed by maintenance durvalumab with or without olaparib as first-line treatment for advanced endometrial cancer: The phase III DUO-E trial. J Clin Oncol 2023;42;283-99.
- Eskander RN et al. **Overall survival** and **progression-free survival** by **PD-L1 status** among endometrial cancer patients treated with **pembrolizumab plus carboplatin/paclitaxel** as compared to carboplatin/paclitaxel plus placebo in the **NRG GY018** trial. SGO 2024; Late-breaking abstract.
- Makker V et al. Long-term follow-up of selinexor maintenance for patients with TP53wt advanced or recurrent endometrial cancer: A pre-specified subgroup analysis from the phase 3 ENGOT-EN5/GOG-3055/SIENDO study. ASCO 2024;Rapid Update.
- Makker V et al. Phase 3 **dose selection** for **selinexor** in **TP53wt endometrial cancer** based on exposure-response analysis. ASCO 2024;Abstract 5594.
- Lorusso D et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): A randomised, double-blind, phase 3 clinical trial. *Lancet* 2024;403:1341-50.

#### **Key Data Sets (Continued)**

- Oaknin A et al. Atezolizumab plus bevacizumab and chemotherapy for metastatic, persistent, or recurrent cervical cancer (BEATcc): A randomised, open-label, phase 3 trial. Lancet 2024;403:31-43.
- Sánchez LM et al. Tisotumab vedotin in 2L/3L recurrent or metastatic cervical cancer: Subsequent therapy data from ENGOT-cx12/GOG-3057/innovaTV 301. ASCO 2024;Abstract 5531.
- Vergote I et al. innovaTV 301/ENGOT-cx12/GOG-3057: A global, randomized, open-label, phase III study of tisotumab vedotin vs investigator's choice of chemotherapy in 2L or 3L recurrent or metastatic cervical cancer. ESMO 2023;Abstract LBA9.
- Vergote I et al. Tisotumab vedotin in combination with carboplatin, pembrolizumab, or bevacizumab in recurrent or metastatic cervical cancer: Results from the innovaTV 205/GOG-3024/ENGOT-cx8 study. *J Clin Oncol* 2023;41:5536-49.



### Agenda

**INTRODUCTION: ASCO 2024 Review** 

**MODULE 1: Ovarian Cancer** 

**MODULE 2: HER2** as a Therapeutic Target

**MODULE 3: Endometrial Cancer** 

**MODULE 4: Cervical Cancer** 



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### ASCO 2024 Review

- Lheureux S et al. Phase II randomized multi-centre study of neoadjuvant olaparib in patients with platinum sensitive relapsed high grade serous ovarian cancer: The NEO trial. ASCO 2024;Abstract 5506.
- Francoeur AA et al. Endometrial cancer and obesity trends in the United States in the 21st century. ASCO 2024; Abstract 5507.
- Rojas C et al. Vibostolimab coformulated with pembrolizumab (vibo/pembro) for previously treated advanced mismatch repair-deficient (dMMR) endometrial cancer: Results from cohort B1 of the phase 2 KEYVIBE-005 study. ASCO 2024;Abstract 5502.







Abstract 5506

## Phase II randomized multi-centre study of neoadjuvant olaparib in patients with platinum sensitive relapsed high grade serous ovarian cancer: The NEO Trial

Stephanie Lheureux, Taymaa May, Michelle K. Wilson, Diane M. Provencher, Susie Lau, Prafull Ghatage, Johanne I Weberpals, Susana N. Banerjee, lain A. McNeish, Neesha C. Dhani, Sarah Ferguson, Genevieve Bouchard-Fortier, Trevor John Pugh, Xiang Y Ye, Sarah Garisto, Judy Quintos, Janelle Ramsahai, Horace Wong, Valerie Bowering, Amit M. Oza



PRESENTED BY: Lheureux Stephanie, MD-PhD

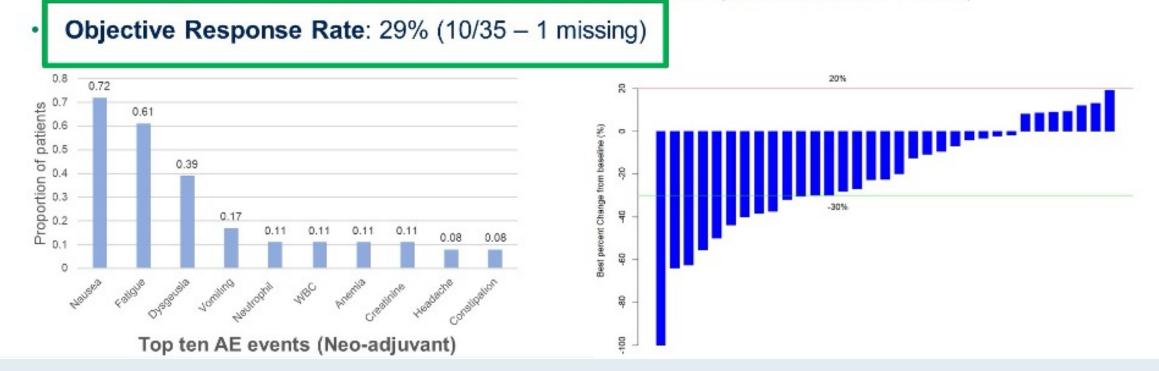




# **NEO Trial: Efficacy and Safety of Neoadjuvant Olaparib**

- Olaparib median duration : 40 (34-48) days
- Safety: No grade ≥3 AEs

2 patients (5%) had at least one dose modification (dose reduction & hold)





# **NEO Trial: Key Takeaways**

- Following secondary cytoreductive surgery, olaparib alone was as effective as chemotherapy followed by olaparib and associated with less toxicity.
- This study suggests the potential for a de-escalated approach with targeted therapy in this selected population.



Moroney JW. ASCO 2024 Highlights of the Day – Gynecologic Cancer, Discussant.



# Endometrial Cancer and Obesity Trends in the United States in the 21<sup>st</sup> Century

June 2, 2024

**ASCO Annual Meeting** 

Alex A. Francoeur MD

University of California Irvine

Cheng-I Liao, Jenny Chang, Caitlin R. Johnson, Kiran Clair, Krishnansu S. Tewari, Daniel S. Kapp, John K. Chan, Robert E. Bristow



# **Endometrial Cancer and Obesity Trends: Key Takeaways**

- Obesity rates are rising rapidly in the U.S. particularly among Black and Hispanic women
- Endometrioid endometrial adenocarcinoma incidence has risen rapidly over a similar time frame and is highly correlated with obesity in matched racial and age populations
- Though not scientifically causal, the relationship is so clear and the burden of disease is severe among young, vulnerable women that a call to action is warranted



Moroney JW. ASCO 2024 Highlights of the Day – Gynecologic Cancer, Discussant.

#### ASCO 2024 Abstract: 5502

Vibostolimab Coformulated With Pembrolizumab for Previously Treated Advanced Mismatch Repair– Deficient Endometrial Cancer: Results From Cohort B1 of the Phase 2 KEYVIBE-005 Study

Carlos Rojas<sup>1</sup>; Francois Ghiringhelli<sup>2</sup>; Mustafa Özgüroğlu<sup>3</sup>; Christian Caglevic<sup>4</sup>; Mahmut Gumus<sup>5</sup>; Diego Tosi<sup>6</sup>; Julien Grenier<sup>7</sup>; Alejandro Falcon Gonzalez<sup>8</sup>; Andres Fernando Arenas Arias<sup>9</sup>; Lucia Gonzalez Cortijo<sup>10</sup>; Andrew Robinson<sup>11</sup>; Javier Cuello Lopez<sup>12</sup>; Maria Bell<sup>13</sup>; Mariusz Kwiatkowski<sup>14</sup>; Mehmet Ali Nahit Sendur<sup>15</sup>; Qi Liu<sup>16</sup>; Tanya Keenan<sup>16</sup>; Robin Guo<sup>17</sup>



# **KEYVIBE-005: Key Takeaways**

- Co-formulated vibostolimab / pembrolizumab is active in checkpoint inhibitor (ICi) naïve patients following platinum-based chemotherapy
- This anti-TIGIT / anti PD-1 combination resulted in an impressive response rate (65%) in mostly 2<sup>nd</sup>/3<sup>rd</sup> line patients, with PFS durability *historically* similar to pembrolizumab monotherapy
- The combination is relatively tolerable, though clearly more toxic than pembrolizumab monotherapy



Moroney JW. ASCO 2024 Highlights of the Day – Gynecologic Cancer, Discussant.

# Agenda

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## **Bevacizumab as Front-Line Therapy for Advanced OC**

• Pfisterer J et al. **Optimal treatment duration of bevacizumab** as front-line therapy for advanced OC: AGO-OVAR 17 **BOOST**/GINECO OV118/ENGOT Ov-15 open-label randomized phase III trial. *J Clin Oncol* 2023;41(4):893-902.



# **DISCUSSION QUESTIONS**

- In what situations should bevacizumab be included as a component of front-line chemotherapy?
- How, if at all, do you factor in the KELIM score when deciding on a treatment approach?



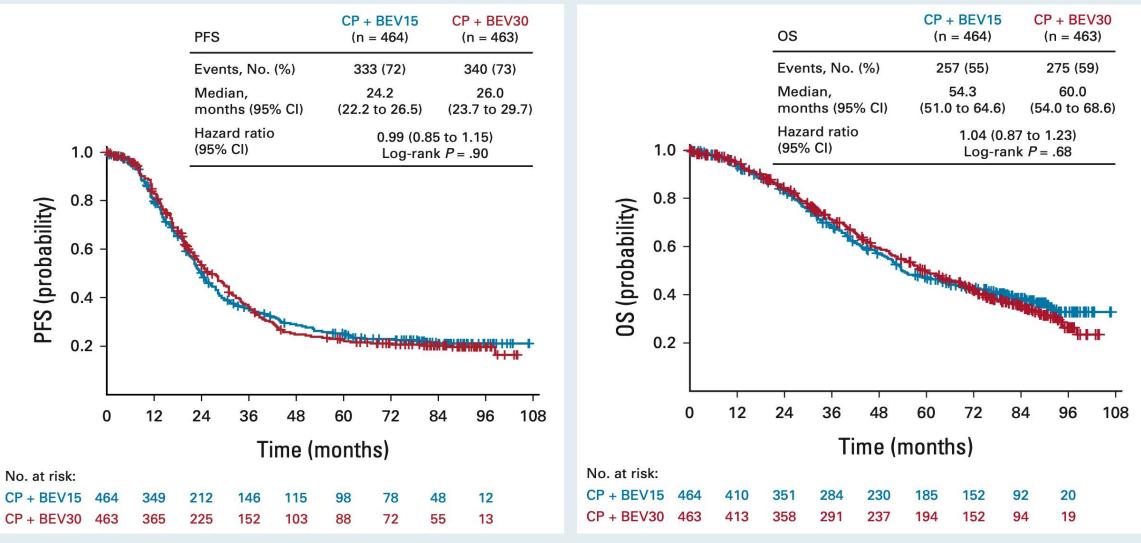
# Optimal Treatment Duration of Bevacizumab as Front-Line Therapy for Advanced Ovarian Cancer: AGO-OVAR 17 BOOST/GINECO OV118/ENGOT Ov-15 Open-Label Randomized Phase III Trial

Jacobus Pfisterer, MD<sup>1</sup>; Florence Joly, MD, PhD<sup>2</sup>; Gunnar Kristensen, MD<sup>3</sup>; Joern Rau, MSc<sup>4</sup>; Sven Mahner, MD<sup>5,6</sup>; Patricia Pautier, MD<sup>7</sup>; Ahmed El-Balat, MD<sup>8,9</sup>; Jean-Emmanuel Kurtz, MD<sup>10</sup>; Ulrich Canzler, MD<sup>11</sup>; Jalid Sehouli, MD<sup>12</sup>; Martin L. Heubner, MD<sup>13,14</sup>; Andreas D. Hartkopf, MD<sup>15,16</sup>; Klaus Baumann, MD<sup>17,18</sup>; Annette Hasenburg, MD<sup>19,20</sup>; Lars C. Hanker, MD<sup>21</sup>; Antje Belau, MD<sup>22,23</sup>; Barbara Schmalfeldt, MD<sup>24,25</sup>; Dominik Denschlag, MD<sup>26</sup>; Tjoung-Won Park-Simon, MD<sup>27</sup>; Frédéric Selle, MD<sup>28</sup>; Christian Jackisch, MD<sup>29</sup>; Alexander Burges, MD<sup>6</sup>; Hans-Joachim Lück, MD<sup>30</sup>; Günter Emons, MD<sup>31</sup>; Werner Meier, MD<sup>32,33</sup>; Martina Gropp-Meier, MD<sup>34</sup>; Willibald Schröder, MD<sup>35</sup>; Nikolaus de Gregorio, MD<sup>36,37</sup>; Felix Hilpert, MD<sup>38,39</sup>; and Philipp Harter, MD<sup>40</sup>

J Clin Oncol 2023;41(4):893-902.



# **ENGOT-OV15: Progression-Free Survival (PFS) and Overall Survival (OS) Outcomes in the ITT Population**



ITT = intention to treat; CP = carboplatin/paclitaxel; BEV = bevacizumab



Pfisterer J et al. J Clin Oncol 2023;41(4):893-902.

## **PARP Inhibitors as First-Line Maintenance for OC**

- DiSilvestro P et al; SOLO1 Investigators. Overall survival with **maintenance olaparib** at a 7-year followup in patients with newly diagnosed advanced OC and a BRCA mutation: The **SOLO1**/GOG 3004 trial. *J Clin Oncol* 2023;41(3):609-17.
- González-Martín A et al. Progression-free survival and safety at 3.5 years of follow-up: Results from the randomised Phase III **PRIMA**/ENGOT-OV26/GOG-3012 trial of **niraparib maintenance** treatment in patients with newly diagnosed OC. *Eur J Cancer* 2023;189:112908.
- Ray-Coquard I et al. **Olaparib plus bevacizumab first-line maintenance** in ovarian cancer: Final overall survival results from the **PAOLA-1**/ENGOT-ov25 trial. *Ann Oncol* 2023;34(8):681-92.
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# **DISCUSSION QUESTIONS**

- In general, what is your approach to primary PARP-inhibitor maintenance for patients with a germline or somatic BRCA mutation?
- What about patients without a BRCA mutation with HRD-positive disease?
- For patients who don't receive bevacizumab with chemotherapy, when should it be added to PARP-inhibitor maintenance?



# Overall Survival With Maintenance Olaparib at a 7-Year Follow-Up in Patients With Newly Diagnosed Advanced Ovarian Cancer and a BRCA Mutation: The SOLO1/GOG 3004 Trial Paul Disilvestro, MD<sup>1</sup>; Susana Banerjee, MD, PhD<sup>2</sup>; Nicoletta Colombo, MD, PhD<sup>3</sup>; Giovanni Scambia, MD<sup>4</sup>; Byoung-Gie Kim, MD, PhD<sup>5</sup>; Ana Oaknin, MD, PhD<sup>6</sup>; Michael Friedlander, MD<sup>7</sup>; Alla Lisyanskaya, MD<sup>8</sup>; Anne Floquet, MD<sup>9,10</sup>; Alexandra Leary, MD<sup>10,11</sup>;

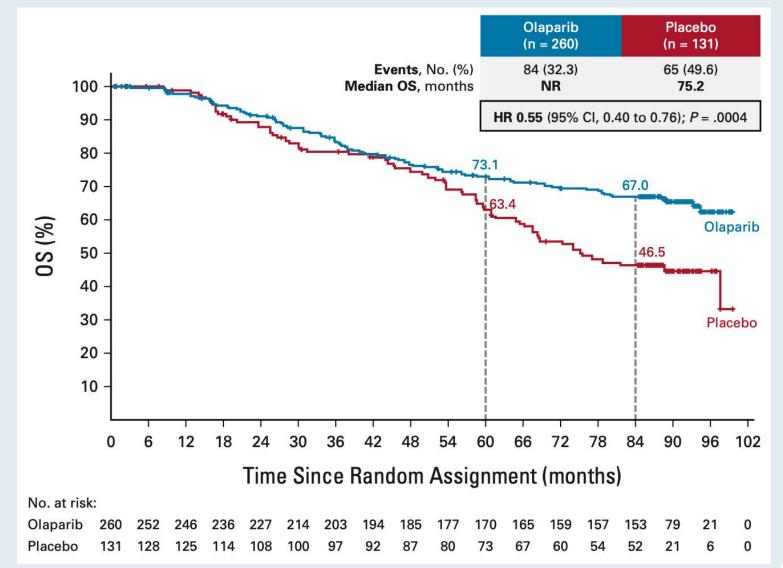
Paul DiSilvestro, MD<sup>1</sup>; Susana Banerjee, MD, PhD<sup>2</sup>; Nicoletta Colombo, MD, PhD<sup>3</sup>; Giovanni Scambia, MD<sup>4</sup>; Byoung-Gie Kim, MD, PhD<sup>5</sup>; Ana Oaknin, MD, PhD<sup>6</sup>; Michael Friedlander, MD<sup>7</sup>; Alla Lisyanskaya, MD<sup>8</sup>; Anne Floquet, MD<sup>9,10</sup>; Alexandra Leary, MD<sup>10,11</sup>; Gabe S. Sonke, MD, PhD<sup>12</sup>; Charlie Gourley, MD, PhD<sup>13</sup>; Amit Oza, MD<sup>14</sup>; Antonio González-Martín, MD, PhD<sup>15,16</sup>; Carol Aghajanian, MD<sup>17</sup>; William Bradley, MD<sup>18</sup>; Cara Mathews, MD<sup>1</sup>; Joyce Liu, MD<sup>19</sup>; John McNamara, MSc<sup>20</sup>; Elizabeth S. Lowe, MD<sup>21</sup>; Mei-Lin Ah-See, MB BChir, MD<sup>22</sup>; and Kathleen N. Moore, MD<sup>23</sup>; on behalf of the SOLO1 Investigators

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J Clin Oncol 2023;41(3):609-17.



## **SOLO-1: Long-Term OS Outcomes**





DiSilvestro P et al. J Clin Oncol 2023;41(3):609-17.

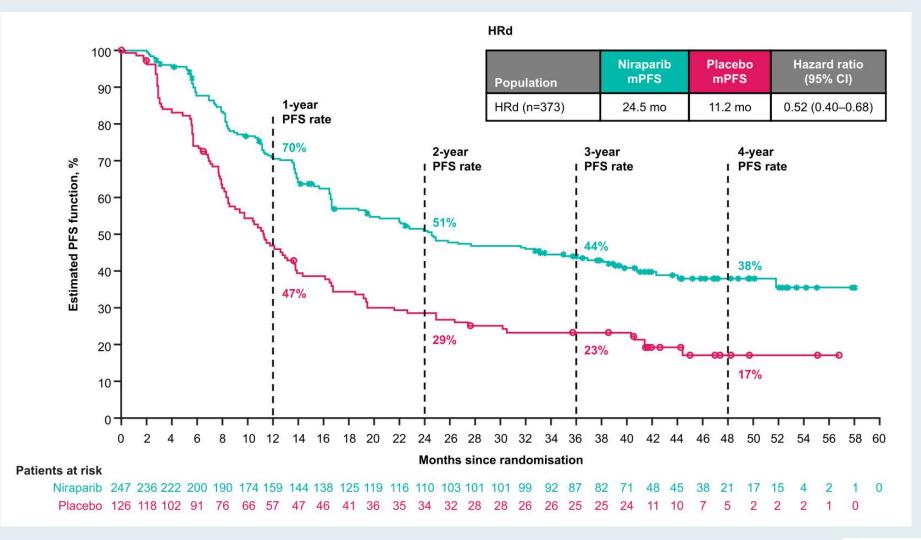
Progression-free survival and safety at 3.5 years of follow-up: results from the randomised phase 3 PRIMA/ENGOT-OV26/GOG-3012 trial of niraparib maintenance treatment in patients with newly diagnosed ovarian cancer

Antonio González-Martín<sup>a,\*</sup>, Bhavana Pothuri<sup>b</sup>, Ignace Vergote<sup>c</sup>, Whitney Graybill<sup>d</sup>, Domenica Lorusso<sup>e</sup>, Colleen C. McCormick<sup>f</sup>, Gilles Freyer<sup>g</sup>, Floor Backes<sup>h</sup>, Florian Heitz<sup>i,q</sup>, Andrés Redondo<sup>j</sup>, Richard G. Moore<sup>k</sup>, Christof Vulsteke<sup>1,r</sup>, Roisin E. O'Cearbhaill<sup>m</sup>, Izabela A. Malinowska<sup>n</sup>, Luda Shtessel<sup>n</sup>, Natalie Compton<sup>n</sup>, Mansoor R. Mirza<sup>o</sup>, Bradley J. Monk<sup>p</sup>

*Eur J Cancer* 2023;189:112908.



# **PRIMA/ENGOT-OV26: PFS in the Homologous Recombination-Deficient (HRd) Population**



mPFS = median progession-free survival



González-Martín A et al. Eur J Cancer 2023;189:112908.

# **DISCUSSION QUESTIONS**

- Do you believe there is therapeutic synergy between PARP inhibitors and anti-PD-1/PD-L1 antibodies?
- Based on available data from studies such as DUO-O, is there any current role for this strategy?





#### Durvalumab with paclitaxel/carboplatin and bevacizumab followed by maintenance durvalumab, bevacizumab and olaparib in patients with newly diagnosed advanced ovarian cancer without a tumor *BRCA1/BRCA2* mutation: results from the randomized, placebo-controlled Phase III DUO-O/ENGOT-ov46/AGO-OVAR 23/GOG-3025 trial

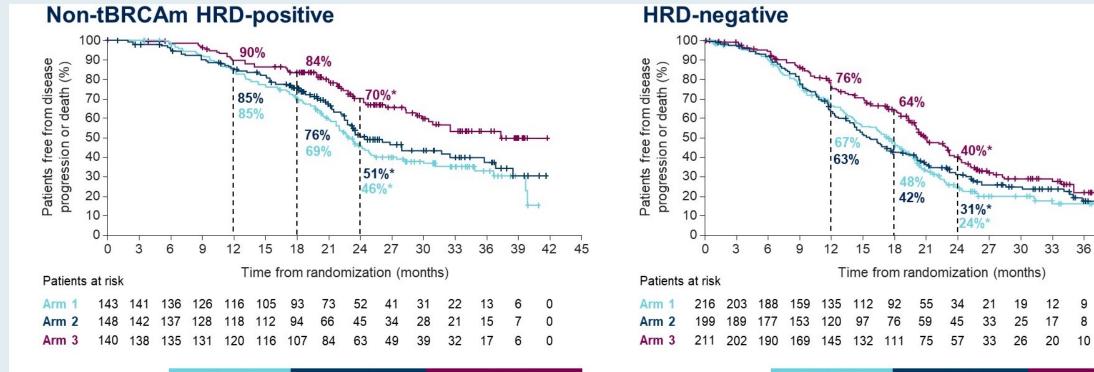
Philipp Harter,<sup>1</sup> Fabian Trillsch,<sup>2</sup> Aikou Okamoto,<sup>3</sup> Alexander Reuss,<sup>4</sup> Jae-Weon Kim,<sup>5</sup> Maria Jesús Rubio-Pérez,<sup>6</sup> Mehmet Ali Vardar,<sup>7</sup> Giovanni Scambia,<sup>8</sup> Olivier Trédan,<sup>9</sup> Gitte-Bettina Nyvang,<sup>10</sup> Nicoletta Colombo,<sup>11</sup> Anita Chudecka-Głaz,<sup>12</sup> Christoph Grimm,<sup>13</sup> Stephanie Lheureux,<sup>14</sup> Els Van Nieuwenhuysen,<sup>15</sup> Florian Heitz,<sup>16</sup> Robert M. Wenham,<sup>17</sup> Kimio Ushijima,<sup>18</sup> Emily Day,<sup>19</sup> Carol Aghajanian<sup>20</sup>

<sup>1</sup>Kliniken Essen-Mitte, Essen, and AGO, Germany; <sup>2</sup>University Hospital, LMU Munich, Munich, and AGO, Germany; <sup>3</sup>The Jikei University School of Medicine, Tokyo, and JGOG, Japan; <sup>4</sup>Coordinating Center for Clinical Trials of the Philipps-University of Marburg, Marburg, and ENGOT, Germany; <sup>5</sup> Seoul National University Hospital, Seoul, and KGOG, South Korea; <sup>6</sup>Reina Sofia University Hospital, Cordoba, and GEICO, Spain; <sup>7</sup>Medical Faculty, University of Cukurova, and Balcalı Hospital, Adana, and TRSGO, Turkey; <sup>8</sup>Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, and MITO, Italy; <sup>9</sup>Centre Léon Bérard, Centre de Recherche en Cancérologie de Lyon, Lyon, and GINECO, France; <sup>10</sup> Odense Universitetshospital, Odense, and NSGO, Denmark; <sup>11</sup>University of Milan-Bicocca and Istituto Europeo di Oncologia IRCCS, Milan, and MANGO, Italy; <sup>12</sup>SPSK Nr 2, Pomeranian Medical University, Szczecin, and PGOG, Poland; <sup>13</sup>Gynecologic Cancer Unit, Medical University Vienna, and AGO-Au, Austria; <sup>14</sup>Princess Margaret Hospital, Toronto, ON, and PMHC, Canada; <sup>15</sup>UZ Leuven, Leuven, and BGOG, Belgium, <sup>16</sup>Ev. Kliniken Essen-Mitte, Essen, and Charité Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin Institute of Health, Berlin, and AGO, Germany; <sup>17</sup>Moffitt Cancer Center, Tampa, FL, and GOG-F, USA; <sup>18</sup>Kurume University School of Medicine, Kurume, and JGOG, Japan; <sup>19</sup>Oncology Biometrics, AstraZeneca, Cambridge, UK; <sup>20</sup>Memorial Sloan Kettering Cancer Center, New York, NY, and GOG-F, USA

ClinicalTrials.gov identifier: NCT03737643



# **DUO-O: Subgroup Analysis of PFS by HRD status**



	Arm 1 PC + bev N=143	Arm 2 PC + bev + durva N=148	Arm 3 PC + bev + durva + ola N=140
Events, n (%)	86 (60)	69 (47)	49 (35)
Median PFS, months†	23.0	24.4 <sup>‡</sup>	37.3 <sup>‡</sup>
HR (95% CI) vs Arm 1		<b>0.82</b> (0.60–1.12)§	<b>0.51</b> (0.36–0.72)§

	N=216	N=199	N=211	
Events, n (%)	157 (73)	142 (71)	127 (60)	
Median PFS, months <sup>†</sup>	17.4	15.4	20.9	
HR (95% CI) vs Arm 1		<b>0.94</b> (0.75–1.18)§	<b>0.68</b> (0.54–0.86)§	

Arm 2

PC + bev + durva

Arm 1



39

3

Arm 3

PC + bev + durva + ola

42

0

45

0

0

# **DUO-O: Safety Summary**

	(chemothera	Overall py phase + main	tenance phase)	Ν	laintenance pha	ISE
AEs, n (%)	Arm 1 PC + bev N=376	<b>Arm 2</b> PC + bev + durva <b>N=373</b>	Arm 3 PC + bev + durva + ola <b>N=378</b>	Arm 1 PC + bev N=331	<b>Arm 2</b> PC + bev + durva <b>N=323</b>	<b>Arm 3</b> PC + bev + durva + ola <b>N=336</b>
Any-grade AE	373 (99)	371 (99)	375 (99)	308 (93)	303 (94)	328 (98)
Grade ≥3 AE	231 (61)	245 (66)	269 (71)	88 (27)	113 (35)	164 (49)
AE with outcome of death	4 (1)	9 (2)	6 (2)	2 (1)	3 (1)	4 (1)
Serious AE (including outcome of death)	128 (34)	161 (43)	148 (39)	50 (15)	91 (28)	83 (25)
AE of special interest to olaparib						
MDS/AML*	1 (<1)	0	2 (1)	1 (<1)	0	1 (<1)
New primary malignancies*	1 (<1)	1 (<1)	4 (1)	1 (<1)	1 (<1)	3 (1)
Pneumonitis	3 (1)	5 (1)	7 (2)	1 (<1)	3 (1)	6 (2)
Any immune-mediated AEs <sup>†</sup>	132 (35)	209 (56)	200 (53)	94 (28)	139 (43)	141 (42)
AEs leading to dose modification <sup>‡§</sup>	272 (72)	299 (80)	323 (85)	163 (49)	182 (56)	254 (76)
AEs leading to discontinuation <sup>‡</sup>	77 (20)	98 (26)	131 (35)	44 (13)	54 (17)	88 (26)
AEs leading to discontinuation of PC/bevacizumab	57 (15)	59 (16)	70 (19)	27 (8)	24 (7)	35 (10)
AEs leading to discontinuation of durvalumab/placebo	24 (6)	62 (17)	65 (17)	14 (4)	39 (12)	40 (12)
AEs leading to discontinuation of olaparib/placebo	15 (4)	19 (5)	62 (16)	14 (4)	19 (6)	61 (18)

Includes AEs with onset or worsening on or after the date of first dose of durvalumab/placebo or olaparib/placebo (overall) or first dose of olaparib/placebo (maintenance phase)

until initiation of the first subsequent anticancer therapy following last dose of study treatment or until the end of the safety follow-up period.

\*Includes events from first dose of durvalumab/olaparib/placebo until end of study; †Investigator-assessed; \*Based on action taken on AE CRF for at least one treatment. For durvalumab/placebo, dose modification includes

skipped or delayed doses, or interruption of the infusion; Seither dose reduction or dose interruption. AE, adverse event; AML, acute myeloid leukemia; CRF, case report form; MDS, myelodysplastic syndrome.



## **PARP Inhibitors for Recurrent Ovarian Cancer**

- Pujade-Lauraine E et al. Maintenance olaparib rechallenge in patients with platinum-sensitive relapsed ovarian cancer previously treated with a PARP inhibitor (OReO/ENGOT-ov38): A phase IIIb trial. Ann Oncol 2023;34(12):1152-64.
- Simpkins F et al. Combination ATR and PARP Inhibitor (CAPRI): A phase 2 study of ceralasertib plus olaparib in patients with recurrent, platinum-sensitive epithelial ovarian cancer (cohort A). ASCO 2024; Abstract 5510.



# **DISCUSSION QUESTION**

• Under what circumstances, if any, would you use a PARP inhibitor for a patient with recurrent ovarian cancer?





# 2023;34(12):1152-64



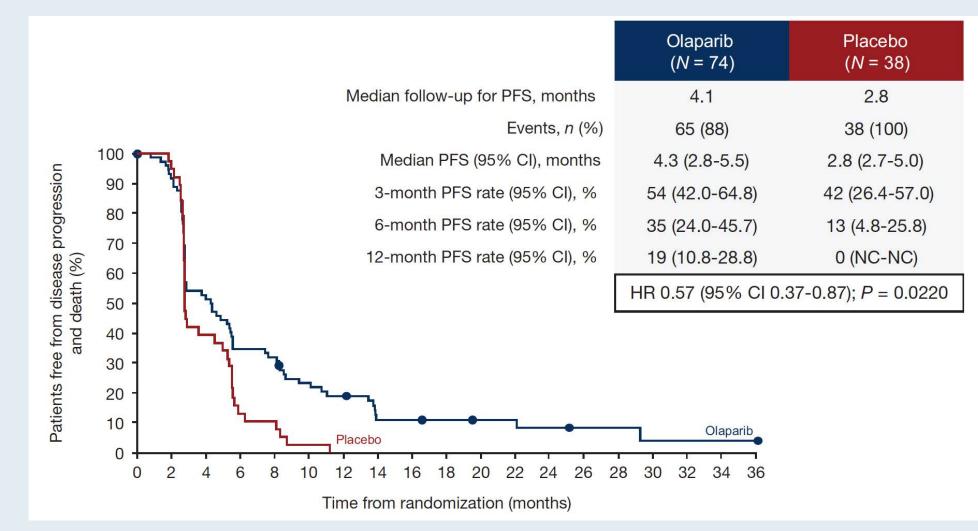
#### **ORIGINAL ARTICLE**

Maintenance olaparib rechallenge in patients with platinum-sensitive relapsed ovarian cancer previously treated with a PARP inhibitor (OReO/ ENGOT-ov38): a phase IIIb trial

E. Pujade-Lauraine<sup>1,2\*</sup>, F. Selle<sup>2,3</sup>, G. Scambia<sup>4,5</sup>, B. Asselain<sup>1,2</sup>, F. Marmé<sup>6,7</sup>, K. Lindemann<sup>8,9,10</sup>, N. Colombo<sup>11,12</sup>, R. Mądry<sup>13,14</sup>, R. Glasspool<sup>15,16,17</sup>, I. Vergote<sup>18,19</sup>, J. Korach<sup>20,21</sup>, S. Lheureux<sup>22,23</sup>, C. Dubot<sup>2,24</sup>, A. Oaknin<sup>25,26</sup>, C. Zamagni<sup>5,27</sup>, F. Heitz<sup>28,29,30,31</sup>, L. Gladieff<sup>2,32</sup>, M. J. Rubio-Pérez<sup>26,33</sup>, P. Scollo<sup>5,34,35</sup>, C. Blakeley<sup>36†</sup>, B. Shaw<sup>36</sup>, I. Ray-Coquard<sup>2,37</sup> & A. Redondo<sup>26,38</sup>, on behalf of the OReO/ENGOT-ov38 investigators

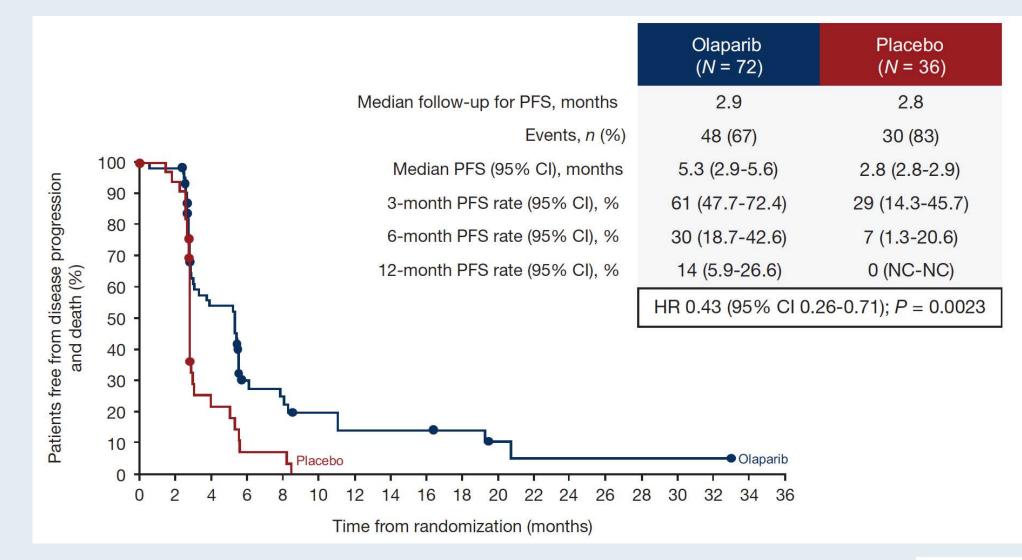


# **OReO: Investigator-Assessed PFS in the BRCA-Mutation Cohort**





# **OReO: Investigator-Assessed PFS in the Non-BRCA-Mutation Cohort**





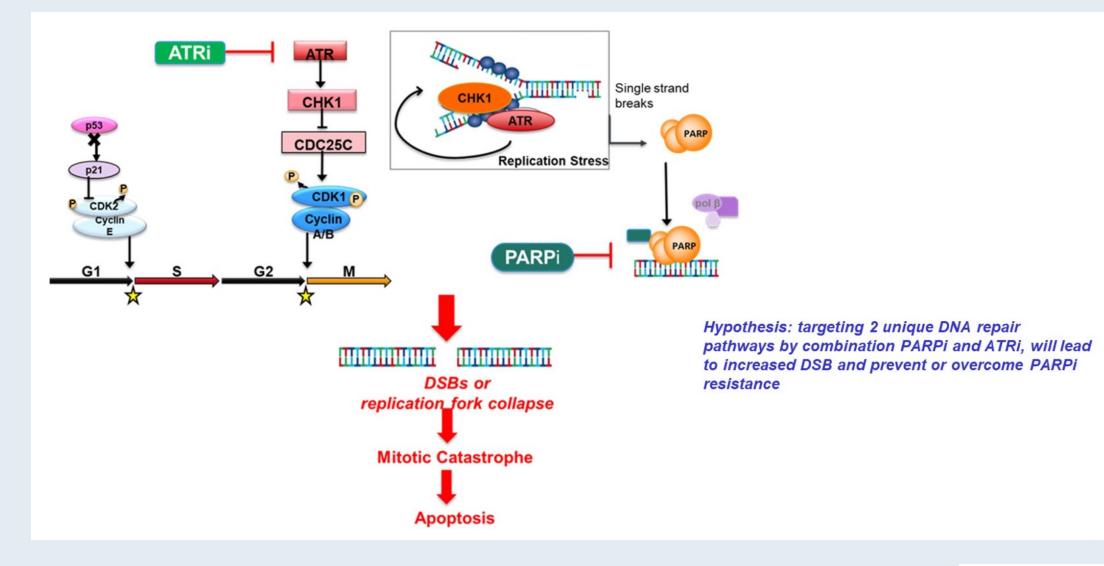
# <u>Combination ATR and PARP Inhibitor (CAPRI): A phase 2</u> study of ceralasertib plus olaparib in patients with recurrent, platinum-sensitive epithelial ovarian cancer (Cohort A).

Fiona Simpkins, Dimitrios Nasioudis, Stephanie L. Wethington, Lainie P. Martin, Janos L. Tanyi, Nawar A. Latif, Drew A. Torigian, Dalia K. Omran, Diego Rodriguez, Simon Smith, Emma Dean, Susan M. Domchek, Ronny Drapkin, Ie-Ming Shih, Eric J. Brown, Wei-Ting Hwang, Deborah K. Armstrong, Geoffrey Shapiro, Stephanie Gaillard, Robert L. Giuntoli II, Joyce F. Liu

ASCO 2024; Abstract 5510.



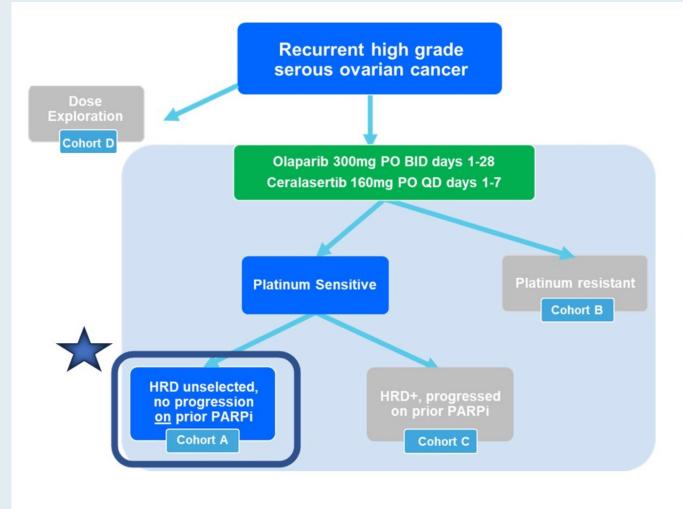
# Scientific Rationale for Combining a PARP Inhibitor with an ATR Inhibitor





Simpkins F et al. ASCO 2024; Abstract 5510.

# **CAPRI: A Phase II Study of Ceralasertib with Olaparib for Recurrent Platinum-Sensitive Ovarian Cancer (Cohort A)**



#### Specific Aim (Cohort A)

Safety and objective response rates (ORR) of combination of olaparib (PARPi) and ceralasertib (ATRi) in platinum sensitive recurrent HGSOC, HRD unselected, who had not progressed on prior PARPi

#### Study Endpoints:

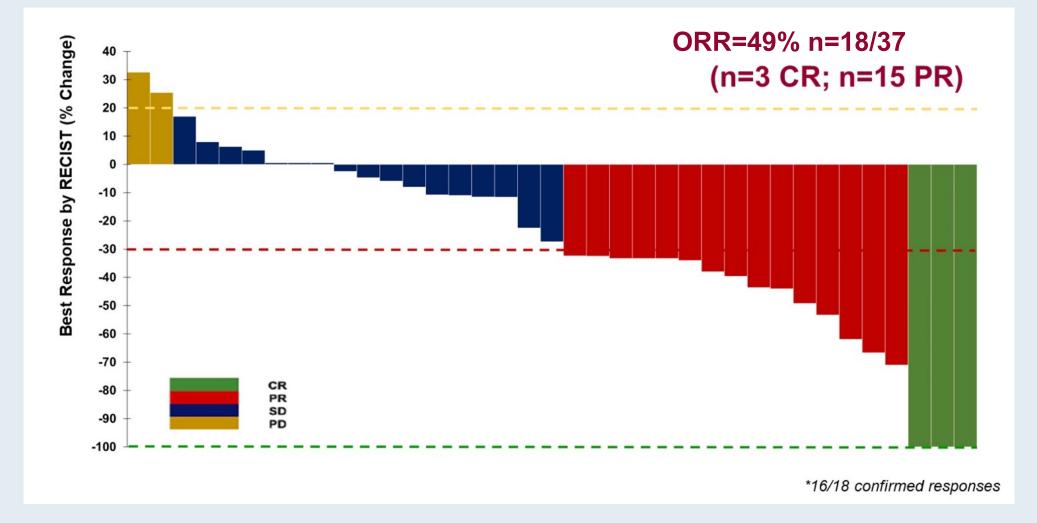
Primary endpoints: ORR, toxicity Secondary endpoint: PFS

Interim analysis after n=17, required an ORR of 40% to proceed to second stage with **total enrollment of 37 patients** 



Simpkins F et al. ASCO 2024; Abstract 5510.

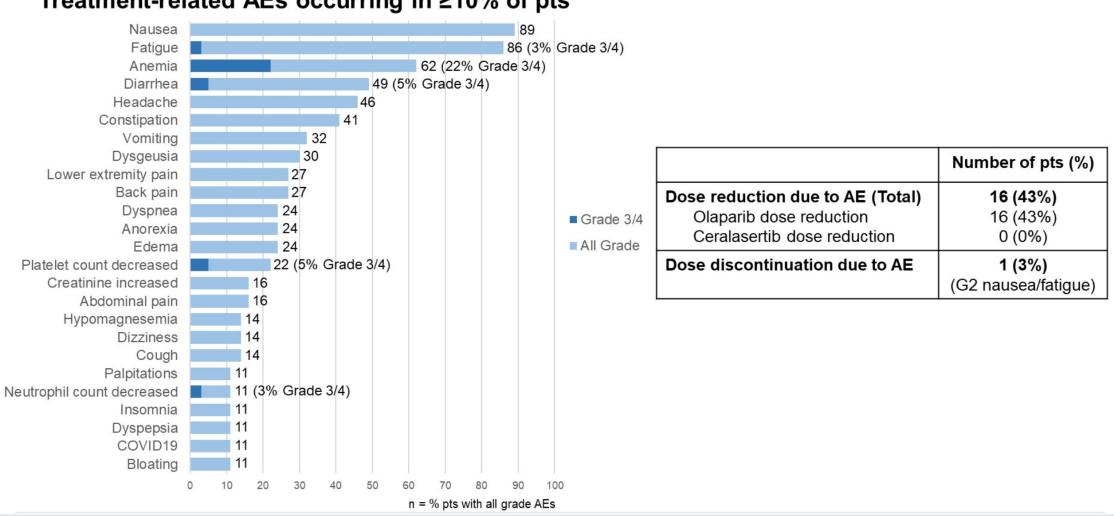
## **CAPRI: Ceralasertib and Olaparib – Response Data**





Simpkins F et al. ASCO 2024; Abstract 5510.

# **CAPRI: Ceralasertib and Olaparib – Safety Profile**



Year<sub>in</sub>

202

Treatment-related AEs occurring in ≥10% of pts

AE = adverse event

# **Antibody-Drug Conjugates for Ovarian Cancer**

Moore KN et al. Mirvetuximab soravtansine in FRα-positive, platinum-resistant ovarian cancer.
 N Engl J Med 2023;389(23):2162-74.



# **DISCUSSION QUESTION**

• What has been your clinical experience with efficacy and tolerability with mirvetuximab soravtansine?

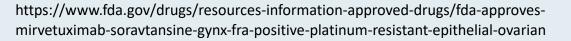


## FDA Approves Mirvetuximab Soravtansine-Gynx for FRα-Positive Platinum-Resistant Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer Press Release: March 22, 2024

"On March 22, 2024, the Food and Drug Administration approved mirvetuximab soravtansine-gynx for adult patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have **received** one to three prior systemic treatment regimens.

Efficacy was evaluated in Study 0416 (MIRASOL, NCT04209855), a multicenter, open-label, activecontrolled, randomized, two-arm trial in 453 patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer. Patients were permitted to receive up to three prior lines of systemic therapy. The trial enrolled patients whose tumors were positive for FRα expression as determined by the FOLR1 (FOLR1-2.1) RxDx Assay.

The major efficacy outcome measures were overall survival (OS), investigator-assessed progression-free survival (PFS) and confirmed overall response rate (ORR) per investigator assessment. PFS and ORR were evaluated according to RECIST, version 1.1."





#### ORIGINAL ARTICLE

# Mirvetuximab Soravtansine in FR $\alpha$ -Positive, Platinum-Resistant Ovarian Cancer

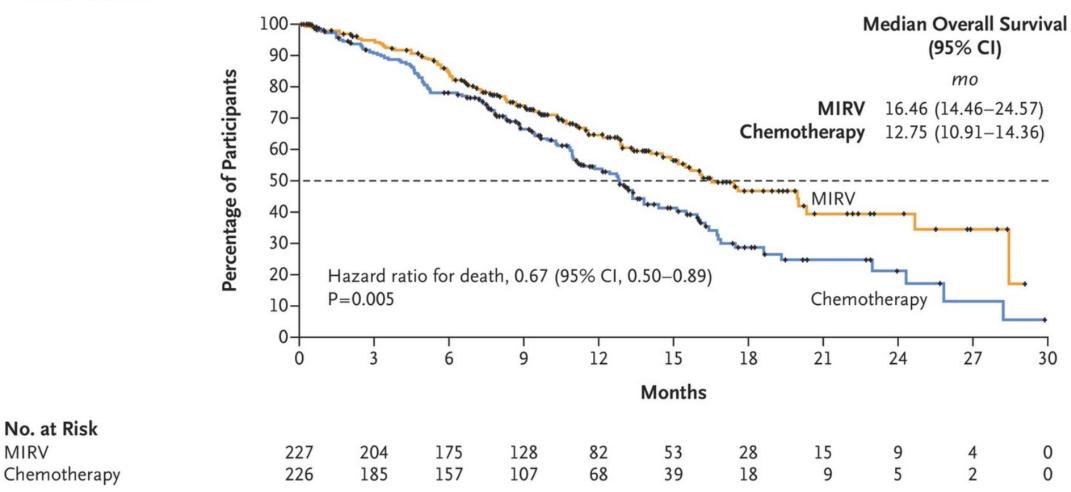
K.N. Moore, A. Angelergues, G.E. Konecny, Y. García, S. Banerjee, D. Lorusso,
J.-Y. Lee, J.W. Moroney, N. Colombo, A. Roszak, J. Tromp, T. Myers, J.-W. Lee,
M. Beiner, C.M. Cosgrove, D. Cibula, L.P. Martin, R. Sabatier, J. Buscema,
P. Estévez-García, L. Coffman, S. Nicum, L.R. Duska, S. Pignata, F. Gálvez,
Y. Wang, M. Method, A. Berkenblit, D. Bello Roufai, and T. Van Gorp,
for Gynecologic Oncology Group Partners and the European Network
of Gynaecological Oncological Trial Groups\*

N Engl J Med 2023;389(23):2162-74.



#### **MIRASOL: OS Outcomes**

**Overall Survival** 





Moore KN et al. N Engl J Med 2023;389(23):2162-74.

MIRV

### **PICCOLO Phase II Trial Schema**

## PICC<sup>1</sup>

#### **Enrollment and Key Eligibility**

- Platinum-sensitive disease (PFI >6 mo)
- At least 2 prior lines of platinum-based therapy
  - Patients with documented platinum allergy require only 1 prior line of platinum
- FRα-high by IHC scoring (≥75% PS2+)
- Appropriate for single agent therapy as next line of therapy as determined by investigator

#### **Statistical Assumptions**

- N=75
- Null hypothesis: ORR is ≤ 28% tested using an optimal
   Simon's two-stage design w/o pause in enrollment

#### Mirvetuximab Soravtansine

6 mg/kg AIBW (calculated using adjusted ideal body weight) intravenously once every 3 weeks



Alvarez Secord A et al. SGO 2022; Abstract 300.

#### Positive Topline Results from the Phase II PICCOLO Trial Evaluating Mirvetuximab Soravtansine for High Folate Receptor-Alpha (FRα)-Expressing Platinum-Sensitive Ovarian Cancer Press Release: June 6, 2024

"[The manufacturer] announced positive topline results from the Phase 2 PICCOLO trial evaluating investigational mirvetuximab soravtansine monotherapy in heavily pre-treated patients with folate receptor-alpha (FRα) positive, platinum-sensitive ovarian cancer (PSOC).

The study met its primary endpoint with an objective response rate (ORR) of 51.9% (95%CI 40.4 – 63.3%).

In addition, the median duration of response (DOR), a key secondary endpoint, was 8.25 months.

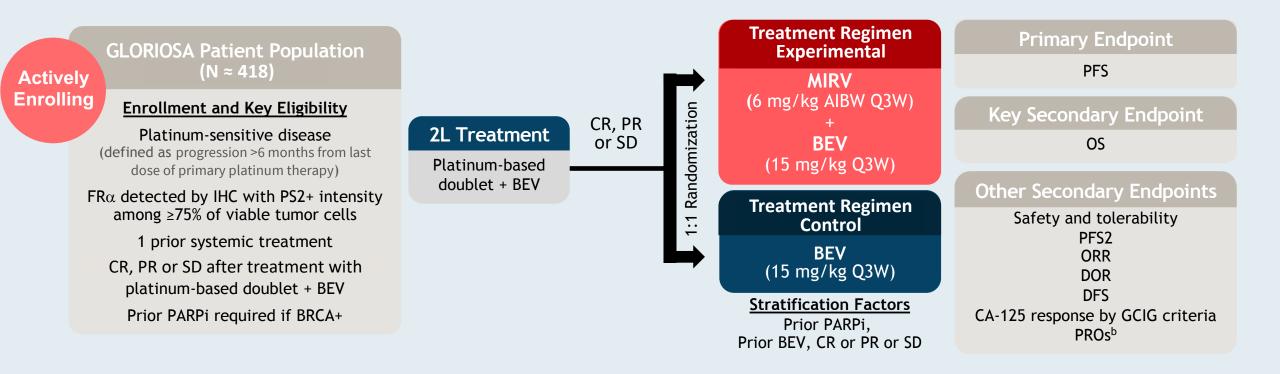
The safety profile of mirvetuximab soravtansine was consistent with findings from previous studies, and no new safety concerns were identified. Full data from the PICCOLO study will be presented at a future medical meeting."

https://news.abbvie.com/2024-06-06-AbbVie-Announces-Positive-Topline-Results-from-Phase-2-PICCOLO-Trial-Evaluating-Mirvetuximab-Soravtansine-ELAHERE-R-for-High-Folate-Receptor-Alpha-FR-Expressing-Platinum-Sensitive-Ovarian-Cancer



### **GLORIOSA Phase III Trial Schema**

#### An open-label, Phase III trial of MIRV + BEV maintenance for FRα-high platinum-sensitive ovarian cancer





O'Malley DM et al. ASCO 2023; Abstract TPS5622. www.clinicaltrials.gov. NCT05445778. Accessed September 2023.

### Agenda

**INTRODUCTION: ASCO 2024 Review** 

**MODULE 1: Ovarian Cancer** 

**MODULE 2: HER2** as a Therapeutic Target

**MODULE 3: Endometrial Cancer** 

**MODULE 4: Cervical Cancer** 



#### **HER2-Targeted Treatment Approaches**

- Meric-Bernstam F et al. Efficacy and safety of **trastuzumab deruxtecan** in patients with HER2-expressing solid tumors: Primary results from the **DESTINY-PanTumor02** phase II trial. *J Clin Oncol* 2024;42(1):47-58.
- Nishikawa T et al. Trastuzumab deruxtecan for human epidermal growth factor receptor 2-expressing advanced or recurrent uterine carcinosarcoma (NCCH1615): The STATICE trial. J Clin Oncol 2023; 41(15):2789-99.



## **DISCUSSION QUESTIONS**

- Where in the treatment course are you typically offering trastuzumab deruxtecan (T-DXd) to your patients with ovarian, endometrial and cervical cancer?
- Are you only offering T-DXd to patients with IHC 3+ disease per the indication, or would you consider it for a patient with no other options and lower levels of expression?



#### FDA Grants Accelerated Approval to Trastuzumab Deruxtecan for Unresectable or Metastatic HER2-Positive Solid Tumors Press Release: April 5, 2024

"On April 5, 2024, the Food and Drug Administration granted accelerated approval to fam-trastuzumab deruxtecan-nxki for adult patients with unresectable or metastatic HER2-positive (IHC3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options. Efficacy was evaluated in 192 adult patients with previously treated unresectable or metastatic HER2-positive (IHC 3+) solid tumors who were enrolled in one of three multicenter trials: DESTINY-PanTumor02 (NCT04482309), DESTINY-Lung01 (NCT03505710), and DESTINY-CRC02 (NCT04744831). All three trials excluded patients with a history of interstitial lung disease (ILD)/pneumonitis requiring treatment with steroids or ILD/pneumonitis at screening and clinically significant cardiac disease. Patients were also excluded for active brain metastases or ECOG performance status >1. Treatment was administered until disease progression, death, withdrawal of consent, or unacceptable toxicity.

The recommended fam-trastuzumab deruxtecan-nxki dosage for this indication is 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity. This tumor agnostic indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-fam-trastuzumab-deruxtecan-nxki-unresectable-or-metastatic-her2









#### Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: DESTINY-PanTumor02 interim results

#### Funda Meric-Bernstam

The University of Texas MD Anderson Cancer Center, Houston, TX, USA

June 5, 2023

Additional authors: Vicky Makker, Ana Oaknin, Do-Yo Kyung Hae Jung, Iwona Ługowska, Luis Manso, Arár Daniil Stroyakovskiy, Chiedozie Anoka, Yan Ma, Soha





Original Reports | Gynecologic Cancer

#### <sup>®</sup>Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial

Funda Meric-Bernstam, MD<sup>1</sup> (D); Vicky Makker, MD<sup>2,3</sup> (D); Ana Oaknin, MD<sup>4</sup> (D); Do-Youn Oh, MD<sup>5</sup> (D); Susana Banerjee, PhD<sup>6</sup> (D); Antonio González-Martín, MD<sup>7</sup> (D); Kyung Hae Jung, MD<sup>8</sup> (D); Iwona Ługowska, MD<sup>9</sup>; Luis Manso, MD<sup>10</sup> (D); Aránzazu Manzano, MD<sup>11</sup>; Bohuslav Melichar, MD<sup>12</sup>; Salvatore Siena, MD<sup>13</sup> (D); Daniil Stroyakovskiy, MD<sup>14</sup> (D); Anitra Fielding, MBChB<sup>15</sup>; Yan Ma, MSc<sup>16</sup>; Soham Puvvada, MD<sup>15</sup>; Norah Shire, PhD<sup>15</sup>; and Jung-Yun Lee, MD<sup>17</sup> (D)

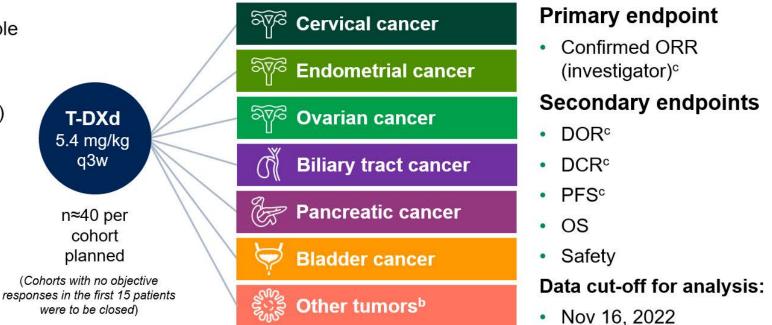


J Clin Oncol 2024;42(1):47-58

#### **DESTINY-PanTumor02** Phase II Basket Trial Schema

#### An open-label, multicenter study (NCT04482309)

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer guidelines<sup>1</sup>)<sup>a</sup>
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1

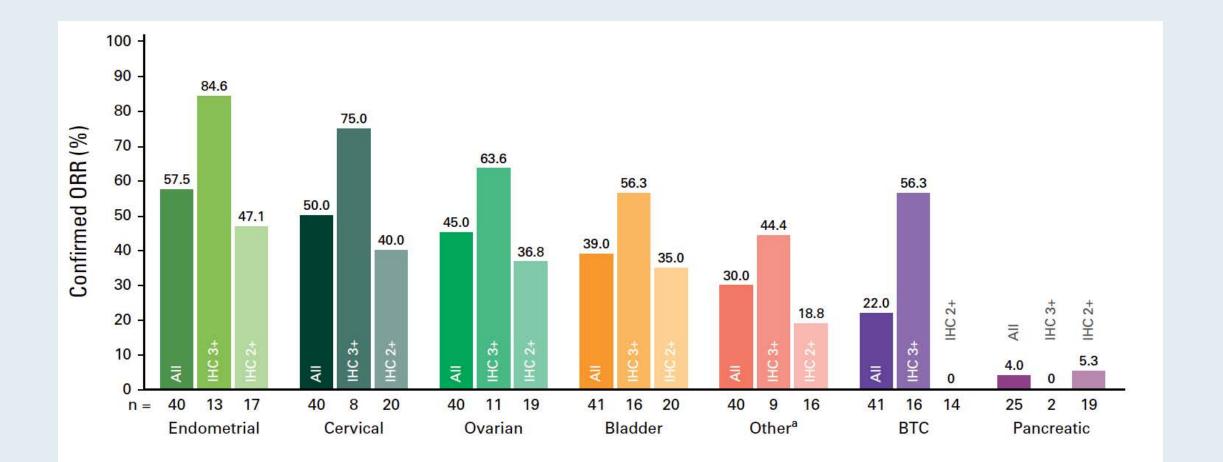


2L+ = second or later line of treatment



Meric-Bernstam F et al. ASCO 2023; Abstract LBA3000; J Clin Oncol 2024; 42(1): 47-58.

#### **DESTINY-PanTumor02: Objective Response Rate by HER2 Status**





Meric-Bernstam F et al. ASCO 2023; Abstract LBA3000; J Clin Oncol 2024; 42(1): 47-58.

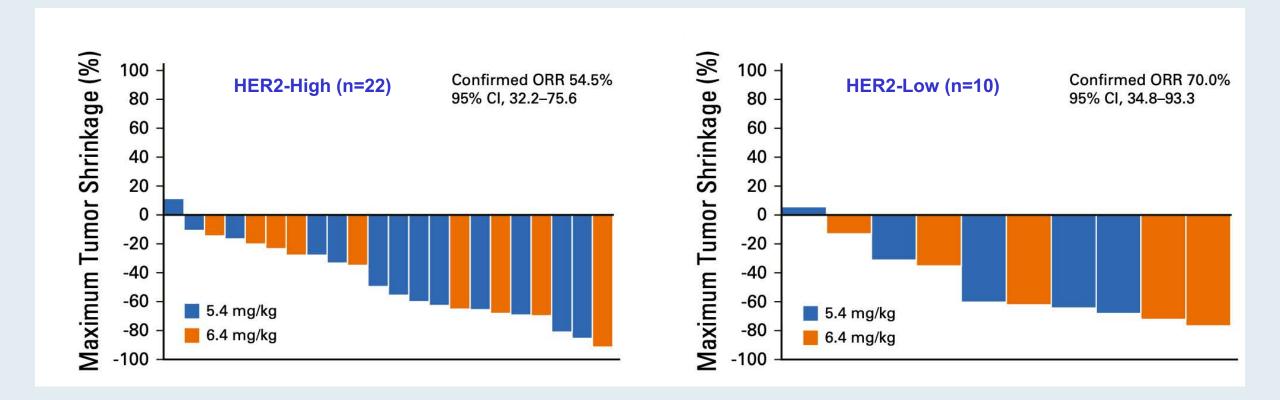
## Trastuzumab Deruxtecan for Human Epidermal Growth Factor Receptor 2–Expressing Advanced or Recurrent Uterine Carcinosarcoma (NCCH1615): The STATICE Trial Tadaaki Nishikawa, MD, PhD<sup>1</sup>; Kosei Hasegawa, MD, PhD<sup>2</sup>; Koji Matsumoto, MD<sup>3</sup>; Masahiko Mori, MD, PhD<sup>4</sup>; Yasuyuki Hirashima, MD, PhD<sup>5</sup>; Kazuhiro Takehara, MD, PhD<sup>6</sup>; Kazuya Ariyoshi, MD, PhD<sup>7</sup>; Tomoyasu Kato, MD, PhD<sup>8</sup>;

Tadaaki Nishikawa, MD, PhD<sup>1</sup>; Kosei Hasegawa, MD, PhD<sup>2</sup>; Koji Matsumoto, MD<sup>3</sup>; Masahiko Mori, MD, PhD<sup>4</sup>; Yasuyuki Hirashima, MD, PhD<sup>5</sup>; Kazuhiro Takehara, MD, PhD<sup>6</sup>; Kazuya Ariyoshi, MD, PhD<sup>7</sup>; Tomoyasu Kato, MD, PhD<sup>8</sup>; Shigehiro Yagishita, MD, PhD<sup>9</sup>; Akinobu Hamada, PhD<sup>9</sup>; Mamiko Kawasaki, MS<sup>10</sup>; Satoshi Kawashima, PhD<sup>10</sup>; Sawako Tomatsuri, MS<sup>10</sup>; Yukari Nagasaka, BS<sup>10</sup>; Hiroshi Yoshida, MD, PhD<sup>11</sup>; Ryunosuke Machida, ME<sup>12</sup>; Akihiro Hirakawa, PhD<sup>13</sup>; Kenichi Nakamura, MD, PhD<sup>10</sup>; and Kan Yonemori, MD, PhD<sup>1</sup>

J Clin Oncol 2023;41(15):2789-99.



#### **STATICE:** Trastuzumab Deruxtecan for Uterine Carcinosarcoma — Response





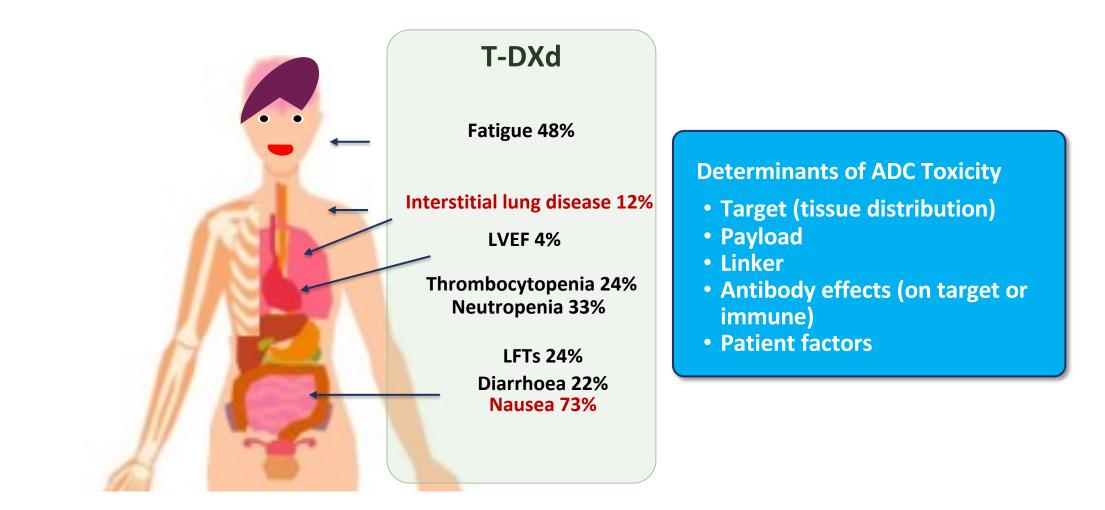
Nishikawa T et al. J Clin Oncol 2023;41(15):2789-99.

## **DISCUSSION QUESTIONS**

- How, specifically, are you monitoring for interstitial lung disease (ILD) in your patients receiving T-DXd?
- At what level of ILD are you permanently discontinuing treatment even after resolution of symptoms?



## Side Effects of Trastuzumab Deruxtecan (T-DXd)



## **T-DXd: Management of ILD**

#### **Routine Monitoring**

- 1. Monitor for symptoms (cough, dyspnea, pyrexia)
- 2. Review every 4-6 weeks
- 3. Monitor SpO2 (examine if drop by 2-4% for 1-3d)
- 4. CT scans every 9-12 weeks

#### **Diagnostic if ILD suspected**

- 1. Lung function test
- 2. CT chest scan (ideally high-resolution CT)
- 3. Possibly Bronchoscopy
- 4. Bloods, blood and sputum cultures

	Grade 1	Grade 2	Grade 3/4	
Description	Asymptomatic (diagnostic observations only)	Symptomatic; limiting instrument. ADL	Severe symptoms; limiting self-care ADL; oxygen (G3); Life-threatening (G4)	
T-DXd	Hold (restart if resolved within 49 days, otherwise discontinue)	Discontinue	Discontinue	
Dose reduction	Same dose if ≤28d, lower dose if > 28d	N/A	N/A	
Steroids	0.5 mg/kg/day	≥1 mg/kg/day	Methylprednisolone i.v. 500-1000 mg/d for 3d, followed by ≥1 mg/kg/d prednisolone for 14d	
Escalation	If worsens despite initiation of steroids, follow Grade 2 guidelines	if not better within 5d: Increase dose or switch to IV	if not better within 5d: Infliximab, IVIG or MMF	
Duration	Until improvement, followed by gradual taper over ≥4 weeks	For at least 14d or until complete resolution of clinical and chest CT findings then gradually taper (for at least 4wks)		

### Agenda

**INTRODUCTION: ASCO 2024 Review** 

**MODULE 1: Ovarian Cancer** 

**MODULE 2: HER2** as a Therapeutic Target

**MODULE 3: Endometrial Cancer** 

**MODULE 4: Cervical Cancer** 



#### **Immunotherapy for Endometrial Cancer**

- Van Nieuwenhuysen E et al. Durvalumab + carboplatin/paclitaxel (CP) followed by durvalumab ± olaparib as first-line treatment for newly diagnosed advanced or recurrent endometrial cancer (EC) in DUO-E: Results by BRCA1/BRCA2 mutation (BRCAm) status. ASCO 2024;Abstract 5595.
- Pepin JT et al. Safety and tolerability of durvalumab + carboplatin/paclitaxel followed by durvalumab
   + olaparib in patients with newly diagnosed advanced or recurrent endometrial cancer (EC) in the
   DUO-E/GOG-3041/ENGOT-EN10 trial. ASCO 2024; Abstract 5599.
- Westin SN et al. Durvalumab plus carboplatin/paclitaxel followed by maintenance durvalumab with or without olaparib as first-line treatment for advanced endometrial cancer: The phase III DUO-E trial. J Clin Oncol 2023;42;283-99.
- Eskander RN et al. **Overall survival** and **progression-free survival** by **PD-L1 status** among endometrial cancer patients treated with **pembrolizumab plus carboplatin/paclitaxel** as compared to carboplatin/paclitaxel plus placebo in the **NRG GY018** trial. SGO 2024; Late-breaking abstract.



## **DISCUSSION QUESTIONS**

- What is your preferred first-line therapy for metastatic microsatellite instability-high (MSI-H)/mismatch repair-deficient (dMMR) EC? Is your approach any different for a younger patient with no comorbidities? Does PD-L1 status matter?
- Do you have a preferred anti-PD-1/PD-L1 antibody for patients with MSI-H/dMMR EC?



## **DISCUSSION QUESTIONS**

- Regulatory and reimbursement issues aside, what would be your recommended first-line therapy for a patient with microsatellite-stable/mismatch repair-proficient metastatic EC?
- How frequently are BRCA and other HRD pathway abnormalities seen in patients with EC? Do you believe these are driving the benefit observed with PARP inhibitors?
- Based on findings from DUO-E and RUBY Part 2, are there any situations in which you would like to include a PARP inhibitor for any of your patients with EC? If yes, for which specific patient populations?



#### FDA Approves Durvalumab with Chemotherapy for Mismatch Repair-Deficient Primary Advanced or Recurrent Endometrial Cancer Press Release: June 14, 2024

"On June 14, 2024, the Food and Drug Administration approved durvalumab with carboplatin plus paclitaxel followed by single-agent durvalumab for adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR).

Efficacy was evaluated in DUO-E (NCT04269200), a randomized, multicenter, double-blind, placebo-controlled trial in patients with primary advanced or recurrent endometrial cancer. Tumor MMR status was a stratification factor and was assessed using an immunohistochemistry tumor tissue test. The major efficacy outcome measure was progression-free survival (PFS), determined by investigator assessment using RECIST v1.1.

The most common adverse reactions (>25%) with durvalumab in combination with carboplatin and paclitaxel were peripheral neuropathy, musculoskeletal pain, nausea, alopecia, fatigue, abdominal pain, constipation, rash, diarrhea, vomiting, and cough.

The recommended durvalumab dose for patients with a body weight  $\geq$  30 kg is 1,120 mg with carboplatin plus paclitaxel every 3 weeks for 6 cycles, followed by single-agent durvalumab 1,500 mg every 4 weeks. The recommended durvalumab dose for patients with a body weight of < 30 kg is 15 mg/kg with carboplatin and paclitaxel every 3 weeks for 6 cycles, followed by durvalumab 20 mg/kg every 4 weeks."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-durvalumab-chemotherapymismatch-repair-deficient-primary-advanced-or-recurrent



#### **ASCO 2024**

Durvalumab + carboplatin/paclitaxel followed by durvalumab ± olaparib as first-line treatment for newly diagnosed advanced or recurrent endometrial cancer in the DUO-E/GOG-3041/ENGOT-EN10 trial: results by *BRCA1* and/or *BRCA2* mutation status

Abstract: 5595

Poster: 466

Els Van Nieuwenhuysen,<sup>1</sup> Jean-Francois Baurain,<sup>2</sup> Hye Sook Chon,<sup>3</sup> Jessica Thomes Pepin,<sup>4</sup> Michael J. Sundborg,<sup>5</sup> Michael A. Gold,<sup>6</sup> Byoung Gie Kim,<sup>7</sup> Stephanie V. Blank,<sup>8</sup> Ji-Hong Liu,<sup>9</sup> Michael McCollum,<sup>10</sup> Masahiko Mori,<sup>11</sup> Goda Jonuškienė,<sup>12</sup> Kathleen Moore,<sup>13</sup> Zoltán Novák,<sup>14</sup> Pedro Luis Ramos Guette,<sup>15</sup> Charles Andreé Joseph de Pádua,<sup>16</sup> Marta Gil-Martin,<sup>17</sup> Matthew Kowgier,<sup>18</sup> Paula Michelle del Rosario,<sup>19</sup> Shannon N. Westin<sup>20</sup>



### **DUO-E: Progression-Free Survival by BRCA Mutation Status**

		CP arm	CP+D arm	CP+D+O arm
All patients	Events, n/N (%)	25/49 (51.0)	15/46 (32.6)	18/48 (37.5)
	Median, months (95% CI) <sup>†</sup>	7.0 (6.7-14.8)	NR (NR-NR)	31.8 (12.4-NR)
	HR (95% CI) vs CP*		0.42 (0.22-0.80)	0.41 (0.21-0.75)
BRCAm	Events, n/N (%)	6/9 (66.7)	6/14 (42.9)	6/16 (37.5)
	Median, months (95% CI) <sup>†</sup>	6.9 (1.7-NR)	26.0 (7.1-NR)	31.8 (9.9-NR)
	HR (95% CI) vs CP <sup>1</sup>		NC	NC
Non-BRCAm	Events, n/N (%)	15/32 (46.9)	7/24 (29.2)	11/30 (36.7)
	Median, months (95% CI) <sup>†</sup>	12.0 (6.7-NR)	NR (NR-NR)	NR (NR-NR)
	HR (95% CI) vs CP <sup>1</sup>		0.48 (0.18-1.15)	0.52 (0.23-1.13)
Unknown	Events, n/N (%)	4/8 (50.0)	2/8 (25.0)	1/2 (50.0)
	Median, months (95% CI) <sup>†</sup>	6.8 (4.2-NR)	NR (NR-NR)	7.2 (NR-NR)
	HR (95% CI) vs CP <sup>2</sup>		NC	NC

\*Aggregated ctDNA and tissue BRCAm status: \*Calculated using the Kaplan-Meier method: CI for median is derived based on the Brookmeyer-Crowley method; #HR and CI are estimated from an unstratified Cox proportional hazards model. NC, not calculable.

#### Table 4. PFS by BRCAm status\* (pMMR subpopulation)

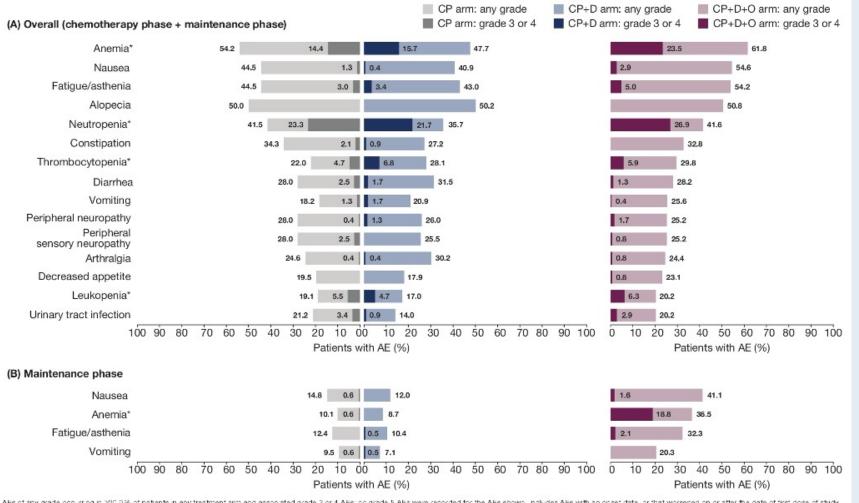
		CP arm	CP+D arm	CP+D+O arm
All patients	Events, n/N (%)	148/192 (77.1)	124/192 (64.6)	108/191 (56.6)
	Median, months (95% CI) <sup>+</sup>	9.7 (9.2–10.1)	9.9 (9.4–12.5)	15.0 (12.4–18.0)
	HR (95% CI) vs CP <sup>‡</sup>		0.77 (0.60–0.97)	0.57 (0.44–0.73)
BRCAm	Events, n/N (%)	11/13 (84.6)	4/10 (40.0)	7/14 (50.0)
	Median, months (95% CI) <sup>+</sup>	9.9 (4.2–12.5)	15.0 (8.7–NR)	15.2 (5.3–NR)
	HR (95% CI) vs CP <sup>‡</sup>		NC	NC
Non-BRCAm	Events, n/N (%)	116/149 (77.9)	101/156 (64.7)	87/152 (57.2)
	Median, months (95% CI) <sup>+</sup>	9.7 (8.8–12.0)	9.9 (9.5–12.6)	15.0 (12.4–19.4)
	HR (95% CI) vs CP⁺		0.77 (0.59–1.00)	0.57 (0.43-0.75)
Unknown	Events, n/N (%)	21/30 (70.0)	19/26 (73.1)	14/25 (56.0)
	Median, months (95% CI) <sup>+</sup>	9.5 (7.2–11.6)	8.2 (6.6–9.8)	9.9 (4.8–NR)
	HR (95% CI) vs CP <sup>‡</sup>		1.05 (0.56–1.96)	0.74 (0.37-1.45)

\*Aggregated ctDNA and tissue BRCAm status; \*Calculated using the Kaplan-Meier method. CI for median is derived based on the Brookmeyer-Crowley method; #R and CI are estimated from an unstratified Cox proportional hazards model.



Van Nieuwenhuysen E et al. ASCO 2024; Abstract 5595.

# DUO-E: Most Common Adverse Events (≥20% of Patients in Either Study Arm)



As of any grade occurring in 220.0% of patients in any treatment anniand associated grade 3 or 4 AEs; no grade 5 AEs were recorded for the AEs shown, includes AEs with an onset date, or that worsened on or after the date of tirst dose of study treatment (overall) or first dose of olaparib/placebo (maintenance phase) up until initiation of the tirst aubsequent anticemper therapy following discontinuation of study treatment or until the end of safety following discontinuation of study treatment or until the end of safety following discontinuation of target by following discontinuation of claparib/placebo or 90 days following discontinuation of tirst.



#### Pepin JT et al. et al. ASCO 2024; Abstract 5599.

**Original Reports** | Gynecologic Cancer

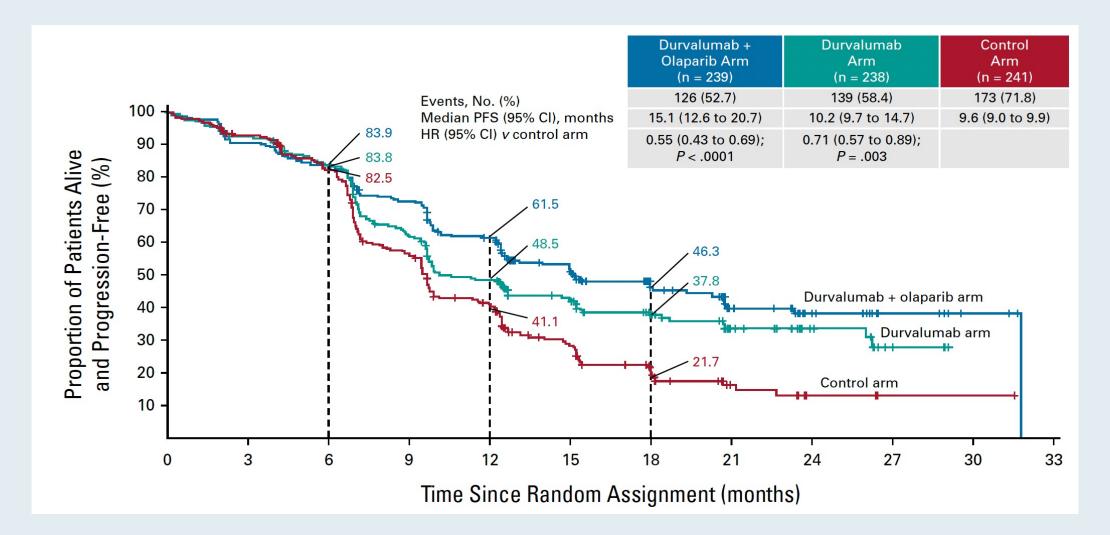
### <sup>®</sup>Durvalumab Plus Carboplatin/Paclitaxel Followed by Maintenance Durvalumab With or Without Olaparib as First-Line Treatment for Advanced Endometrial Cancer: The Phase III DUO-E Trial

Shannon N. Westin, MD, MPH<sup>1</sup> (D); Kathleen Moore, MD<sup>2</sup>; Hye Sook Chon, MD<sup>3</sup>; Jung-Yun Lee, MD<sup>4</sup> (D); Jessica Thomes Pepin, MD<sup>5</sup>; Michael Sundborg, MD<sup>6</sup>; Ayelet Shai, MD, PhD<sup>7</sup>; Joseph de la Garza, MD<sup>8</sup>; Shin Nishio, MD<sup>9</sup> (D); Michael A. Gold, MD<sup>10</sup>; Ke Wang, MD<sup>11</sup>; Kristi McIntyre, MD<sup>12</sup>; Todd D. Tillmanns, MD<sup>13</sup>; Stephanie V. Blank, MD<sup>14</sup> (D); Ji-Hong Liu, MD<sup>15</sup>; Michael McCollum, MD<sup>16</sup>; Fernando Contreras Mejia, MD<sup>17</sup> (D); Tadaaki Nishikawa, MD<sup>18</sup> (D); Kathryn Pennington, MD<sup>19</sup>; Zoltan Novak, MD, PhD<sup>20</sup>; Andreia Cristina De Melo, MD<sup>21</sup> (D); Jalid Sehouli, MD<sup>22</sup>; Dagmara Klasa-Mazurkiewicz, MD<sup>23</sup> (D); Christos Papadimitriou, MD<sup>24</sup>; Marta Gil-Martin, MD<sup>25</sup> (D); Birute Brasiuniene, MD, PhD<sup>26</sup> (D); Conor Donnelly, PhD<sup>27</sup>; Paula Michelle del Rosario, MD<sup>28</sup>; Xiaochun Liu, MD, PhD<sup>29</sup>; and Els Van Nieuwenhuysen, MD<sup>30</sup>; on behalf of the DUO-E Investigators

#### J Clin Oncol 2023;42;283-99.



### **DUO-E Primary Endpoint: Progression-Free Survival**



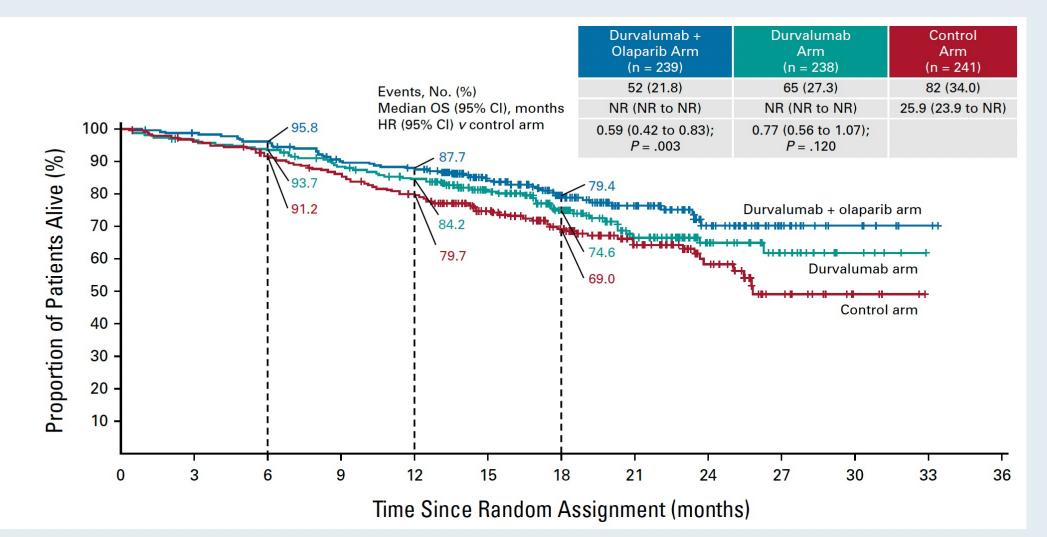


### **DUO-E: Progression-Free Survival in Key Subgroups**

Subgroup	Durvalumab + olaparib	Durvalumab	Control
MMR deficient (n = 48;46;49)	31.8 mo	Not reached	7.0 mo
PFS HR vs control	0.41	0.42	Reference
MMR proficient (n = 191;192;192)	15.0 mo	9.9 mo	9.7 mo
PFS HR vs control	0.57	0.77	Reference
PD-L1-positive (n = 150;170;163)	20.8 mo	11.3 mo	9.5 mo
PFS HR vs control	0.42	0.63	Reference
PD-L1-negative (n = 82;61;75)	10.1 mo	9.7 mo	9.9 mo
PFS HR vs control	0.80	0.89	Reference



### **DUO-E: Overall Survival**





## **DISCUSSION QUESTIONS**

- What is your preferred approach to the management of EC with a POLE mutation in the adjuvant and metastatic settings?
- Do you expect ongoing clinical trials evaluating anti-PD-1/PD-L1 antibody-based strategies in the adjuvant and neoadjuvant settings to be positive?
- In what situations, if any, are you currently employing adjuvant immunotherapy outside of a clinical trial setting?



#### FDA Approves Pembrolizumab with Chemotherapy for Primary Advanced or Recurrent Endometrial Carcinoma Press Release: June 17, 2024

"On June 17, 2024, the Food and Drug Administration approved pembrolizumab with carboplatin and paclitaxel, followed by single-agent pembrolizumab, for adult patients with primary advanced or recurrent endometrial carcinoma.

Efficacy was evaluated in KEYNOTE-868/NRG-GY018 (NCT03914612), a multicenter, randomized, double-blind, placebo-controlled trial enrolling 810 patients with advanced or recurrent endometrial carcinoma. The trial included two separate cohorts based on mismatch repair (MMR) status: 222 patients in the mismatch repair deficient (dMMR) cohort, and 588 patients in the mismatch repair (pMMR) proficient cohort.

The major efficacy outcome measure was progression-free survival (PFS), assessed by the investigator according to RECIST 1.1. In the dMMR cohort, median PFS was not reached (NR) (95% CI: 30.7, NR) in the pembrolizumab and chemotherapy arm and 6.5 months (95% CI: 6.4, 8.7) in the placebo and chemotherapy arm (Hazard ratio [HR] 0.30 [95% CI: 0.19, 0.48]; p-value <0.0001). In the pMMR cohort, median PFS was 11.1 months (95% CI: 8.7, 13.5) in the pembrolizumab and chemotherapy arm and 8.5 months (95% CI: 7.2, 8.8) for those receiving placebo and chemotherapy (HR 0.60 [95% CI: 0.46, 0.78; p-value <0.0001)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-chemotherapy-primary-advanced-or-recurrent-endometrial-carcinoma



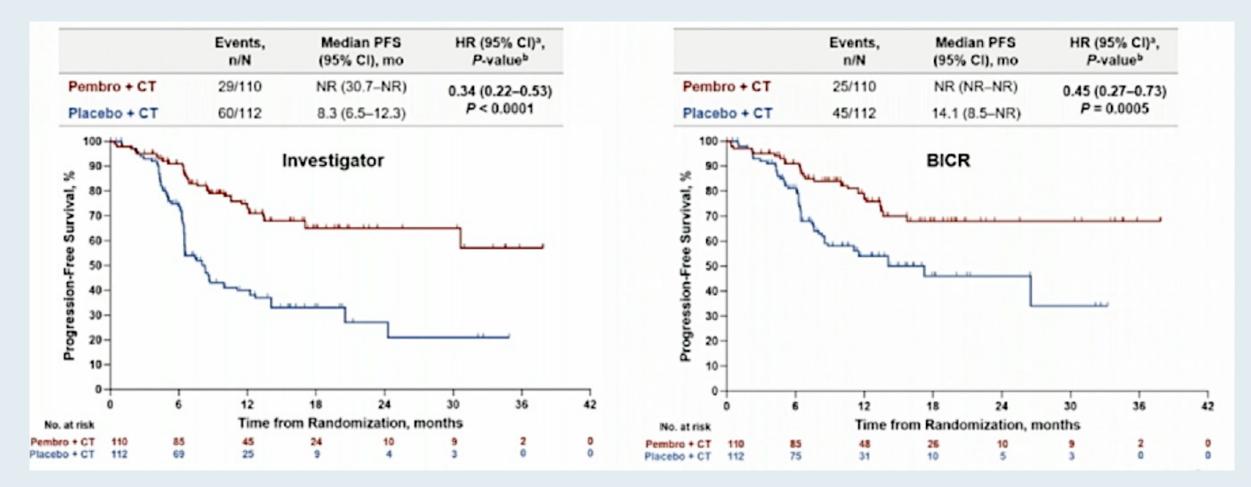
Overall Survival, Progression-Free Survival by PD-L1 Status, and Blinded Independent Central Review Results With Pembrolizumab Plus Carboplatin/Paclitaxel (CP) Versus Placebo Plus CP in Patients With Endometrial Cancer: Results From the NRG GY018 Trial

<u>R.N. Eskander</u>, M. Sill, A. Miller, L. Beffa, R. Moore, J. Hope, F. Musa, R. Mannel, M.S. Shahin, G. Canturia, E. Girda, C. Mathews, J. Kavecansky, C.A. Leath III, L. Gien, E. Hinchcliff, S. Lele, M.A. Powell, C. Aghajanian

SGO 2024; Plenary.



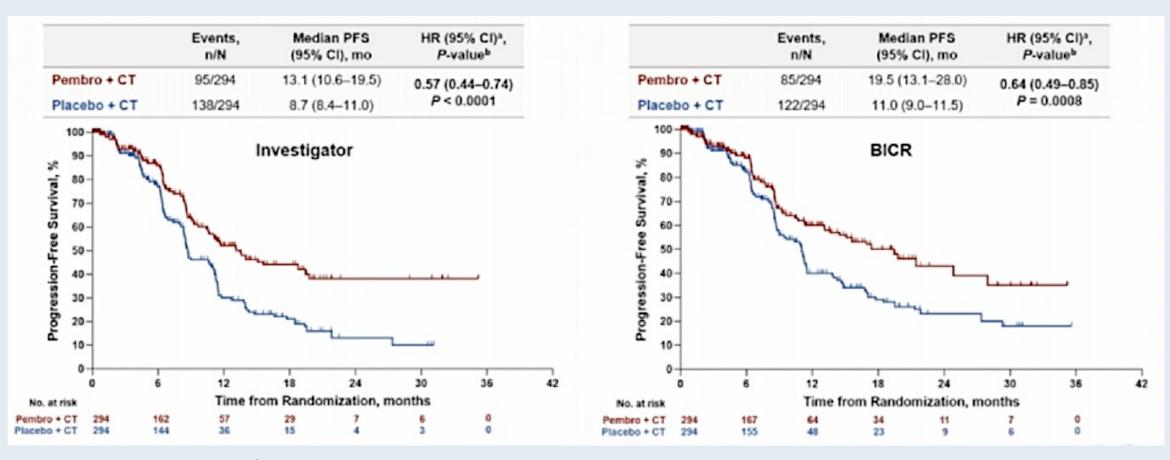
#### **NRG-GY018: PFS in the dMMR Population**





Eskander RN et al. SGO 2024; Plenary.

### **NRG-GY018: PFS in pMMR Population**



pMMR = mismatch repair proficient



Eskander RN et al. SGO 2024; Plenary.

#### **Selinexor for Endometrial Cancer**

- Makker V et al. Long-term follow-up of selinexor maintenance for patients with TP53wt advanced or recurrent endometrial cancer: A prespecified subgroup analysis from the phase 3 ENGOT-EN5/ GOG-3055/SIENDO study. ASCO 2024;Rapid Update.
- Makker V et al. Phase 3 **dose selection** for **selinexor** in **TP53wt endometrial cancer** based on exposure-response analysis. ASCO 2024;Abstract 5594.



## **DISCUSSION QUESTIONS**

- Do you believe the signal reported with the use of selinexor for patients with p53 wild-type disease is real?
- Would you currently consider using selinexor for EC outside of a trial under any circumstances?
- Are there any investigational agents like antibody-drug conjugates — for patients with progressive EC that may be more attractive than currently available therapeutic options?



Long-term Follow-up of Selinexor Maintenance for Patients With TP53wt Advanced or Recurrent Endometrial Cancer: A Prespecified Subgroup Analysis From the Phase 3 ENGOT-EN5/GOG-3055/SIENDO Study

Vicky Makker,<sup>1</sup> Brian Slomovitz<sup>2</sup>, Alejandro Pérez Fidalgo,<sup>3</sup> Erika Hamilton,<sup>4</sup> Giorgio Valabrega,<sup>5</sup> Toon Van Gorp,<sup>2</sup> Jalid Sehouli,<sup>6</sup> Jaroslav Klat,<sup>7</sup> Tally Levy,<sup>8</sup> Stephen Welch,<sup>9</sup> Debra L. Richardson,<sup>10</sup> Eva Maria Guerra Alia,<sup>11</sup> Giovanni Scambia,<sup>12</sup> Stéphanie Henry,<sup>13</sup> Pauline Wimberger,<sup>14</sup> Jerónimo Martinez,<sup>15</sup> Bradley J. Monk,<sup>16</sup> Pratheek Kalyanapu,<sup>17</sup> Mansoor Raza Mirza,<sup>18</sup> Ignace Vergote<sup>19</sup>

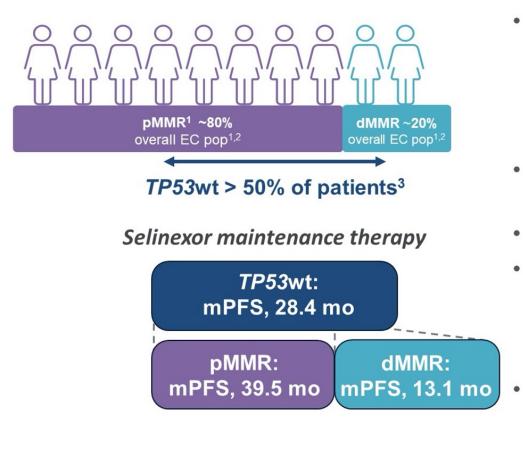
<sup>1</sup>Memorial Sloan Kettering Cancer Center; <sup>2</sup>Mount Sinai Medical Center and Florida International University, Miami, FL, USA; <sup>3</sup>GEICO. Hospital Clinico Universitario de Valencia. INCLIVA. CIBERONC. Spain; <sup>4</sup>Sarah Cannon Research Institute, Tennesee Oncology; <sup>5</sup>MITO and Department of Oncology, University of Torino, at Mauriziano Hospital, Turin, Italy; <sup>6</sup>NOGGO and Department of Gynecology, European Competence Center for Ovarian Cancer, Charité Comprehensive Cancer Center, Charité—Berlin University of Medicine; <sup>7</sup>CEEGOG and University Hospital Ostrava and University of Ostrava, Ostrava-Poruba, Czech Republic; <sup>8</sup>ISGO and Gynecologic Oncology Unit, Department of Obstetrics and Gynecology, Wolfson Medical Center, Holon, affiliated with Sackler Faculty of Medicine, Tel Aviv University; <sup>8</sup>London Health Sciences Centre; <sup>10</sup>Stephenson Cancer Center, University of Oklahoma Health Sciences Center; <sup>11</sup>GEICO and Hospital Universitario Ramón y Cajal; <sup>12</sup>MITO and Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; <sup>13</sup>BGOG and Université Catholique de Louvain, CHU UCL Namur Site Ste Elisabeth, Service d'onco-hématologie (SORMN), Place Louise Godin 15 B-5000 Namur; <sup>14</sup>NOGGO and Technische Universitat Dresden, University Hospital Carl Gustav Carus, Department of Obstetrics and Gynecology; <sup>15</sup>GEICO and Hospital Universitario Virgen de la Arrixaca, Department of Oncology, Murcia, Spain; <sup>16</sup>GOG Foundation, University of Arizona, Creighton University, Phoenix, AZ USA; <sup>17</sup>Karyopharm Therapeutics; <sup>18</sup>Rigshospitalet – Copenhagen University Hospital, Copenhagen, Denmark; <sup>19</sup>BGOG and Leuven Cancer Institute, University Hospitals Leuven, European Union

#### ASCO 2024; Rapid Update





### **SIENDO: Long-Term Follow-Up Summary**



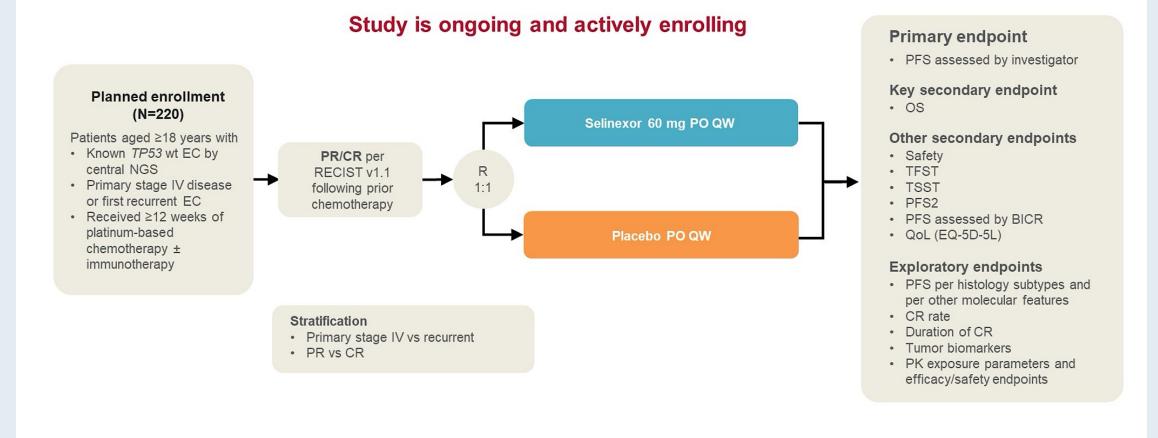
- A marked PFS benefit was observed with selinexor maintenance therapy in the novel *TP53*wt/pMMR subgroup (mPFS 39.5 mo), a patient population with limited effective therapeutic options
- Encouraging signals in overall survival analyses were also observed across all subgroups
- No new safety signals were identified
- The substantial signal of PFS improvement with selinexor in *TP53*wt EC is reinforced by the Q-TWiST analysis, which integrates both quality and quantity of life
- The data support the potential role of selinexor as a maintenance treatment option in advanced or recurrent *TP53*wt EC

1. Mirza M, et al. Presentation at: ESMO Congress Oct 20-24 2023, Abstract 740MO. 2. Vergote I, et al J Clin Oncol. 2023;41(35):5400-5410. 3. Leslie KK, et al. Gynecol Oncol. 2021;161(1):113-121.



Makker V et al. ASCO 2024; Rapid Abstract Update.

## ENGOT-EN20/GOG-3083/XPORT-EC-042 Phase III Trial Design



PK, pharmacokinetics; QoL, quality of life; TSST, time to second subsequent treatment. ClinicalTrials.gov identifier: NCT05611931. Updated Aug 14, 2023. Accessed Aug 18, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05611931



Makker V et al. ASCO 2024; Rapid Abstract Update.

## Agenda

**INTRODUCTION: ASCO 2024 Review** 

**MODULE 1: Ovarian Cancer** 

**MODULE 2: HER2** as a Therapeutic Target

**MODULE 3: Endometrial Cancer** 

**MODULE 4: Cervical Cancer** 



#### **Immune Checkpoint Inhibitors for Cervical Cancer**

- Lorusso D et al. **Pembrolizumab** or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): A randomised, double-blind, phase 3 clinical trial. *Lancet* 2024;403:1341-50.
- Oaknin A et al. Atezolizumab plus bevacizumab and chemotherapy for metastatic, persistent, or recurrent cervical cancer (BEATcc): A randomised, open-label, phase 3 trial. *Lancet* 2024;403:31-43.



## **DISCUSSION QUESTION**

• What is your current clinical approach for a patient with Stage III to IVA cervical cancer?



#### FDA Approves Pembrolizumab with Chemoradiation Therapy for FIGO 2014 Stage III to Stage IVA Cervical Cancer Press Release: January 12, 2024

"On January 12, 2024, the Food and Drug Administration approved pembrolizumab with chemoradiotherapy (CRT) for patients with FIGO 2014 Stage III-IVA cervical cancer.

Efficacy was evaluated in KEYNOTE-A18 (NCT04221945), a multicenter, randomized, double-blind, placebocontrolled trial enrolling 1060 patients with cervical cancer who had not previously received definitive surgery, radiation, or systemic therapy. The trial included 596 patients with FIGO 2014 Stage III-IVA disease and 462 patients with FIGO 2014 Stage IB2-IIB, node-positive disease.

The major efficacy outcome measures were progression- free survival (PFS) assessed by the investigator according to RECIST v1.1, or histopathologic confirmation, and overall survival (OS) ... The most common adverse reactions (≥10%) occurring in patients who received pembrolizumab with chemoradiotherapy were nausea, diarrhea, vomiting, urinary tract infection, fatigue, hypothyroidism, constipation, decreased appetite, weight loss, abdominal pain, pyrexia, hyperthyroidism, dysuria, rash, and pelvic pain.

The recommended dosing regimen for pembrolizumab is 200 mg IV every 3 weeks or 400 mg IV every 6 weeks until disease progression, unacceptable toxicity, or for up to 24 months. Pembrolizumab should be administered before chemoradiotherapy when given on the same day."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumabchemoradiotherapy-figo-2014-stage-iii-iva-cervical-cancer



#### Lancet 2024;403:1341-50.



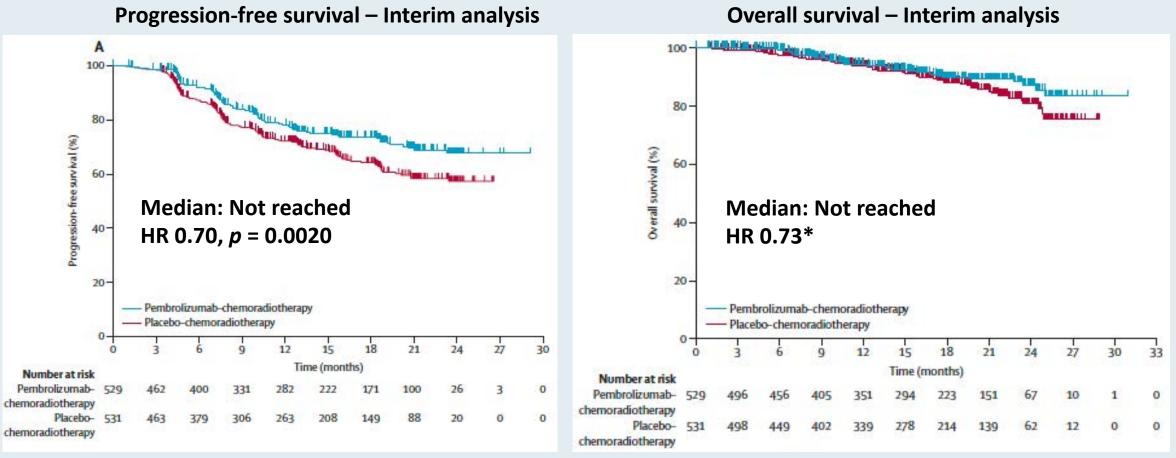
Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/ GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial

Domenica Lorusso, Yang Xiang, Kosei Hasegawa, Giovanni Scambia, Manuel Leiva, Pier Ramos-Elias, Alejandro Acevedo, Vladyslav Sukhin, Noelle Cloven, Andrea J Pereira de Santana Gomes, Fernando Contreras Mejía, Ari Reiss, Ali Ayhan, Jung-Yun Lee, Valeriya Saevets, Flora Zagouri, Lucy Gilbert, Jalid Sehouli, Ekkasit Tharavichitkul, Kristina Lindemann, Roberta Lazzari, Chih-Long Chang, Rudolf Lampé, Hong Zhu, Ana Oaknin, Melissa Christiaens, Stephan Polterauer, Tomoka Usami, Kan Li, Karin Yamada, Sarper Toker, Stephen M Keefe, Sandro Pignata\*, Linda R Duska\*, on behalf of the ENGOT-cx11/GOG-3047/KEYNOTE-A18 investigators†





## **KEYNOTE-A18: Progression-Free and Overall Survival**



\*p-value did not cross the pre-specified efficacy boundary



Lorusso D et al. Lancet 2024;403:1341-50.

#### **Tisotumab Vedotin for Recurrent or Metastatic Cervical Cancer**

- Sánchez LM et al. Tisotumab vedotin in 2L/3L recurrent or metastatic cervical cancer: Subsequent therapy data from ENGOT-cx12/GOG-3057/innovaTV 301. ASCO 2024;Abstract 5531.
- Vergote I et al. innovaTV 301/ENGOT-cx12/GOG-3057: A global, randomized, open-label, phase III study of tisotumab vedotin vs investigator's choice of chemotherapy in 2L or 3L recurrent or metastatic cervical cancer. ESMO 2023;Abstract LBA9.
- Vergote I et al. Tisotumab vedotin in combination with carboplatin, pembrolizumab, or bevacizumab in recurrent or metastatic cervical cancer: Results from the innovaTV 205/GOG-3024/ENGOT-cx8 study. *J Clin Oncol* 2023;41:5536-49.



## **DISCUSSION QUESTION**

• What has been your clinical experience with efficacy and tolerability with tisotumab vedotin?



#### FDA Approves Tisotumab Vedotin-tftv for Recurrent or Metastatic Cervical Cancer Press Release: April 29, 2024

"On April 29, 2024, the Food and Drug Administration granted traditional approval to tisotumab vedotintftv for recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. Tisotumab vedotin-tftv previously received accelerated approval for this indication.

Efficacy was evaluated in innovaTV 301 (NCT04697628), an open-label, active-controlled, multicenter, randomized trial that enrolled 502 patients with recurrent or metastatic cervical cancer who had received one or two prior systemic regimens, including chemotherapy with or without bevacizumab and/or an anti-PD-(L)-1 agent.

The major efficacy outcome measure was overall survival (OS) ... The most common adverse reactions (≥25%), including laboratory abnormalities, were decreased hemoglobin, peripheral neuropathy, conjunctival adverse reactions, increased aspartate aminotransferase, nausea, increased alanine aminotransferase, fatigue, decreased sodium, epistaxis, and constipation.

The recommended tisotumab vedotin dose is 2 mg/kg (maximum of 200 mg for patients ≥100 kg) administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tisotumab-vedotin-tftv-recurrent-or-metastatic-cervical-cancer



#### Abstract 5531

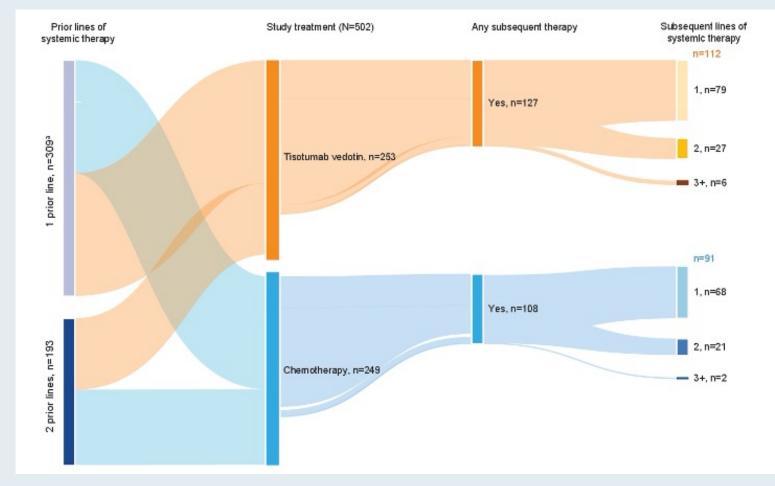
Tisotumab Vedotin in 2L/3L Recurrent or Metastatic Cervical Cancer: Subsequent Therapy Data From ENGOT-cx12/GOG-3057/innovaTV 301

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#### **ASCO 2024**



### innovaTV 301: Prior and Subsequent Therapies



- Cytotoxic chemotherapy and immunotherapy were the most common subsequent systemic anticancer therapies received in both treatment arms.
- Tisotumab vedotin did not prevent the initiation of subsequent therapies, including immunotherapy.



Sánchez LM et al. ASCO 2024; Abstract 5531.

# Year in Review: Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Tuesday, July 9, 2024 5:00 PM – 6:00 PM ET

Faculty Jesús G Berdeja, MD Thomas Martin, 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.

