Breakfast with the Investigators: Ovarian Cancer

A CME Hybrid Symposium Held in Conjunction with the 2022 ASCO Annual Meeting

Sunday, June 5, 2022

6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty

Antonio González-Martín, MD, PhD

Joyce F Liu, MD, MPH

Kathleen N Moore, MD, MS

Moderator

Neil Love, MD

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Faculty

Antonio González-Martín, MD, PhD
Co-Director, Oncology Department
Cancer Center Director, Clínica Universidad de Navarra
Madrid, Spain

Kathleen N Moore, MD, MS
Virginia Kerley Cade Chair in Developmental Therapeutics
Associate Director for Clinical Research
Director, Early Phase Drug Development
Stephenson Cancer Center at the University of Oklahoma HSC
Professor, Section of Gynecologic Oncology
Associate Program Director, Gynecologic Oncology Fellowship
University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma

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

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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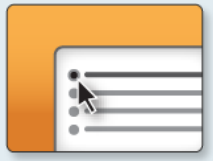
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

Complete Your Evaluation: Tap the CME Evaluation button to complete your evaluation electronically to receive credit for your participation.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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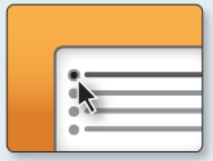
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A CME credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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Friday June 3	**Acute Myeloid Leukemia and Myelodysplastic Syndromes** 11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)
	Lung Cancer 6:30 PM – 9:00 PM CT (7:30 PM – 10:00 PM ET)
Saturday June 4	**Prostate Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Gastrointestinal Cancers 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Sunday June 5	**Ovarian Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Chronic Lymphocytic Leukemia and Non-Hodgkin Lymphoma 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Monday June 6	**Urothelial Bladder Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Breast Cancer 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Tuesday June 7	**Multiple Myeloma** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

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Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2022 ASCO Annual Meeting

Ovarian Cancer

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6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty
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Joyce F Liu, MD, MPH
Kathleen N Moore, MD, MS

Urothelial Bladder Cancer

Monday, June 6, 2022
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty
Yohann Loriot, MD, PhD
Elizabeth R Plimack, MD, MS
Jonathan E Rosenberg, MD

Chronic Lymphocytic Leukemia and Non-Hodgkin Lymphoma

Sunday, June 5, 2022
7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)

Faculty
Ian W Flinn, MD, PhD
Brian T Hill, MD, PhD
John P Leonard, MD
Matthew Lunning, DO
Laurie H Sehn, MD, MPH
Mitchell R Smith, MD, PhD

Breast Cancer

Monday, June 6, 2022
7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)

Faculty
Javier Cortés, MD, PhD
Matthew P Goetz, MD
Erika Hamilton, MD
Ian E Krop, MD, PhD
Hope S Rugo, MD
Sara M Tolaney, MD, MPH

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2022 ASCO Annual Meeting

Multiple Myeloma

Tuesday, June 7, 2022
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty
Ajai Chari, MD
Elizabeth O'Donnell, MD
Robert Z Orlowski, MD, PhD

Spencer H Bachow, MD
Lynn Cancer Institute
Boca Raton, Florida

Shaachi Gupta, MD, MPH
Florida Cancer Specialists
Lake Worth, Florida

Philip L Brooks, MD
Northern Light Eastern Maine Medical Center and Lafayette Family Cancer Institute
Brewer, Maine

Zanetta S Lamar, MD
Florida Cancer Specialists
Naples, Florida

Shams Bufalino, MD
Advocate Aurora Health
Park Ridge, Illinois

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

Lionel A Kankeu Fonkoua, MD
Mayo Clinic
Rochester, Minnesota

Vignesh Narayanan, MD
Colorado Permanente Medical Group (CPMG)
Lone Tree, Colorado

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Namrata I Peswani, MD
Harold C Simmons
Comprehensive Cancer Center
Richardson, Texas

Matthew R Strickland, MD
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts

Erik Rupard, MD
The Reading Hospital
West Reading, Pennsylvania

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Commercial Support

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

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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, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, 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, Mersana Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

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Dr González-Martín — Disclosures

Advisory Committee and Consulting Agreements	Alkermes, Amgen Inc, AstraZeneca Pharmaceuticals LP, Clovis Oncology, Genmab, GlaxoSmithKline, ImmunoGen Inc, MacroGenics Inc, Merck, Merck Sharp & Dohme LLC, Mersana Therapeutics Inc, Novartis, Oncoinvent, Pfizer Inc, PharmaMar, Roche Laboratories Inc, SOTIO LLC, Sutro Biopharma
Contracted Research	GlaxoSmithKline, Roche Laboratories Inc
Speakers Bureau	AstraZeneca Pharmaceuticals LP, Clovis Oncology, GlaxoSmithKline, Merck Sharp & Dohme LLC, PharmaMar, Roche Laboratories Inc

Dr Liu — Disclosures

Advisory Committee	AstraZeneca Pharmaceuticals LP, Clovis Oncology, Eisai Inc, Epsila Bio, Genentech, a member of the Roche Group, GlaxoSmithKline, Regeneron Pharmaceuticals Inc
Trial Support to Institution for Study Conduct	2X Oncology, Aravive Inc, Arch Oncology, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Clovis Oncology, CytomX Therapeutics, GlaxoSmithKline, Regeneron Pharmaceuticals Inc, Surface Oncology, Tesaro, A GSK Company, Vigeo Therapeutics, Zentalis Pharmaceuticals

Dr Moore — Disclosures

Advisory Committee	Alkermes, Aravive Inc, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Eisai Inc, Elevar Therapeutics, EMD Serono Inc, Genentech, a member of the Roche Group, Hengrui Therapeutics Inc, I-Mab Biopharma, ImmunoGen Inc, IMXmed, Lilly, Merck, Mereo BioPharma, Mersana Therapeutics Inc, Novartis, Onconova Therapeutics Inc, OncXerna Therapeutics Inc, Tarveda Therapeutics, Tesaro, A GSK Company, VBL Therapeutics
Consulting Agreement	AstraZeneca Pharmaceuticals LP
Contracted Research	Lilly, Merck, PTC Therapeutics
Data and Safety Monitoring Board/Committee	SQZ Biotech

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Agenda

Module 1 – Current Management of Advanced Ovarian Cancer

Module 2 – Novel Agents and Strategies Under Investigation

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Agenda

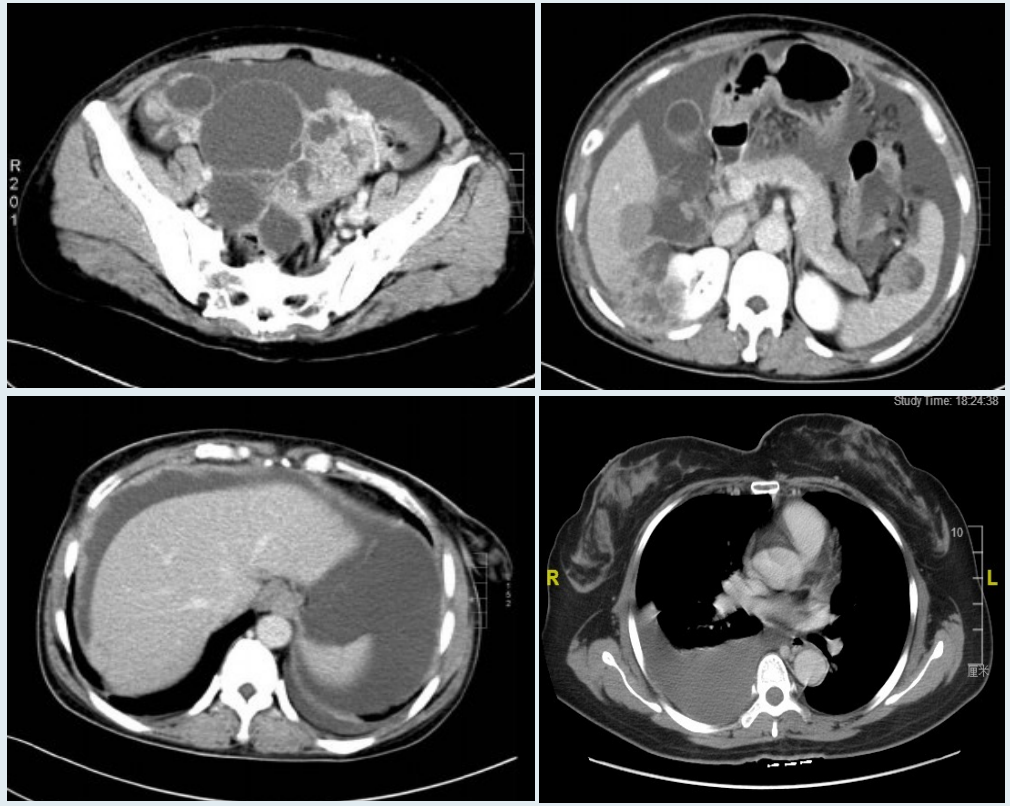
Module 1 – Current Management of Advanced Ovarian Cancer

Module 2 – Novel Agents and Strategies Under Investigation

Case 1 — Kathleen N Moore, MD, MS

- 67-yr-old woman presents with chief complaint of abdominal distension, cough, and pain for >1 mo
- Patient has history of mild hypertension, but negative for diabetes, coronary heart disease, depression
- Family history: sister with AML
- Exam significant for decreased breath sounds in right-side of chest
- Abdominal distension with fluid wave and ballotable mass; pelvic exam shows nodularity in cul-de-sac and fixed pelvic mass
- Labs: CA-125, 231 U/mL; albumin, 3.3 g/dL

Imaging



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Case 1 — Kathleen N Moore, MD, MS

- **Tissue biopsy of omentum confirmed high-grade mixed endometrioid/ serous cancer**
- **Patient started on neoadjuvant paclitaxel/carboplatin + bevacizumab**
- **During first cycle of therapy, her germline panel showed no deleterious mutations in *BRCA1/2***
- **Bevacizumab given with cycles 1-2 with good response to fluid collection and tumor volume, but significant disease still present after cycle 3 (no bevacizumab)**
- **IDS had near-complete gross resection with MRD**
- **FM tumor testing for HRD test was 19% and she had a somatic *BRCA2*m**

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Case 1 — Kathleen N Moore, MD, MS

- **Restarted bevacizumab cycle 5 and 6 with paclitaxel and carboplatin but at time the patient was treated, PAOLA-1 was not reported and her only option for front line PARPi was monotherapy olaparib**
- **Olaparib started approximately 7 weeks after completing chemotherapy. CA-125 at the start had normalized to 15 U/mL**
- **Olaparib continued for 2 years and then discontinued**

Case 2 — Joyce F Liu, MD, MPH

- 52yo woman presenting with pelvic discomfort
  - CT scan with multiple large solid and cystic pelvic masses concerning for malignancy. 3.5-cm metastatic peritoneal implant within L paracolic region, possible 1.2-cm hepatic implant, retroperitoneal lymphadenopathy.
  - CA125 2,800
  - Recommended for neoadjuvant chemotherapy
- Neoadjuvant carboplatin/paclitaxel x 3 cycles. CA125 fall from 3,719 to 159; good radiographic response.
- Optimal IDS to no residual disease.
  - Path: High-grade serous carcinoma, involving bilateral ovaries, FTs, and uterine serosa. Complete chemotherapy response in omentum. CRS 3.
- Completed adjuvant chemotherapy with 3 cycles of carboplatin/paclitaxel
  - Treatment complicated by severe fatigue, neuropathy limiting ADLs, thrombocytopenia (nadir 46K)
- Offered but declined participation in ATHENA trial

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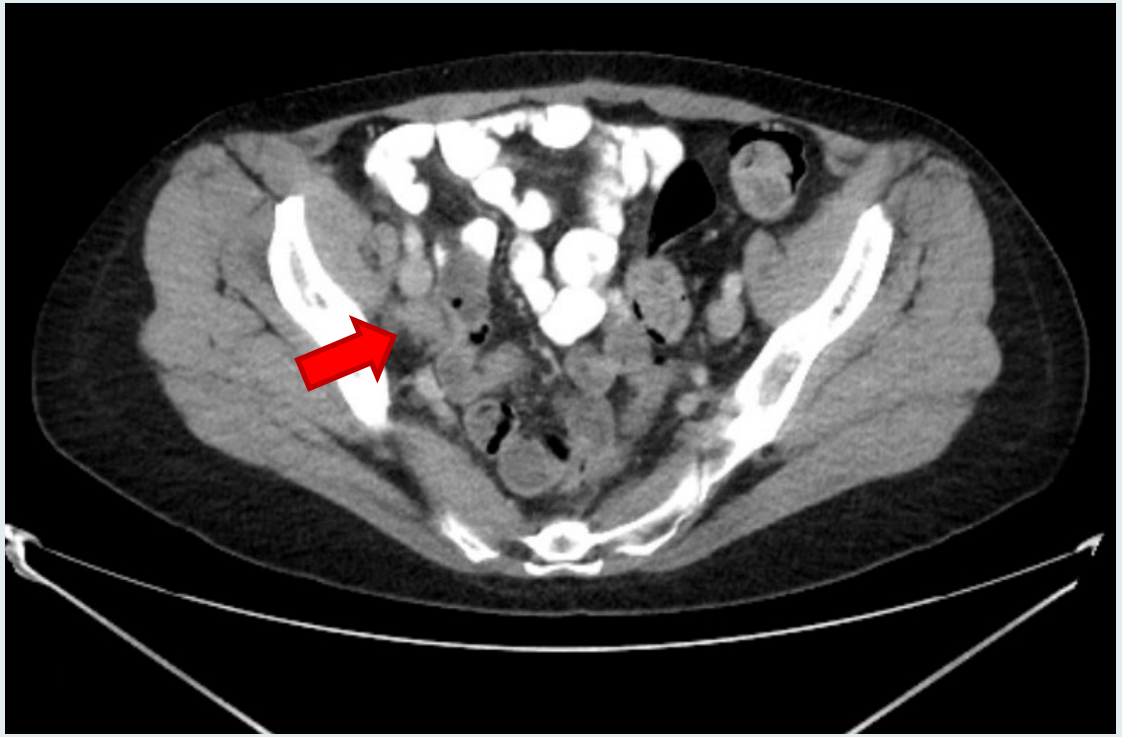
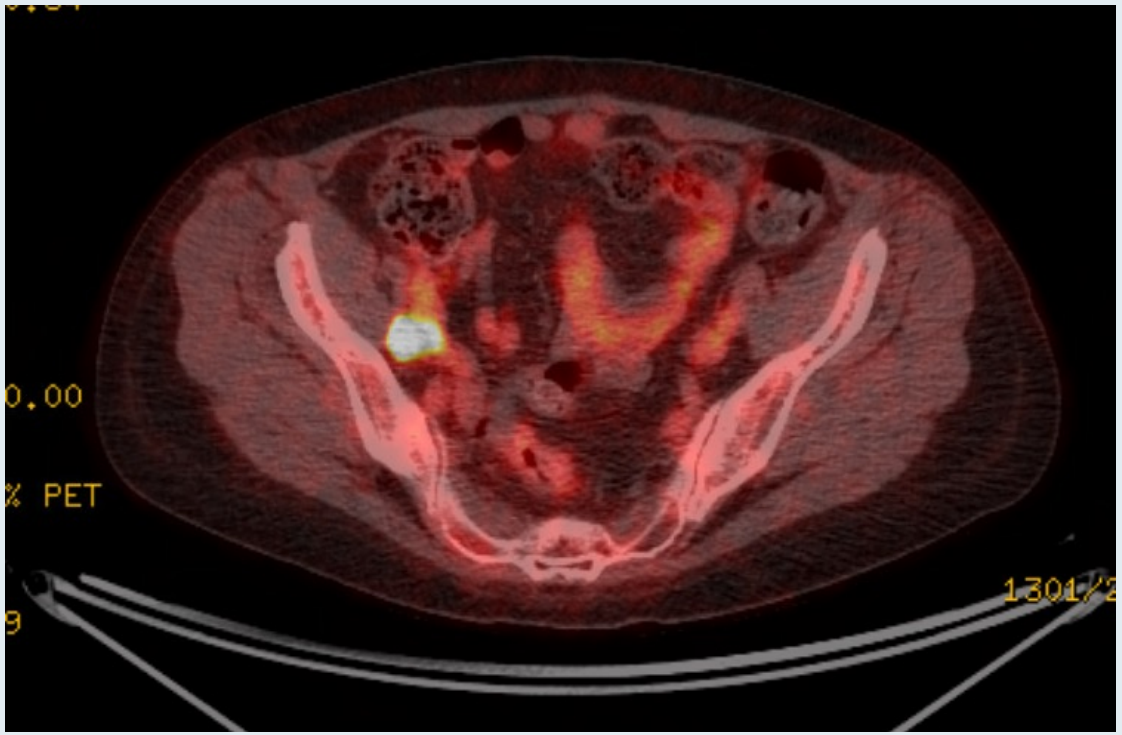
Case 2 — Joyce F Liu, MD, MPH

- **NOVA, PAOLA-1 and VELIA data publicly reported**
- **Myriad MyChoice assay returned as HR deficient**
- **Started on niraparib maintenance 200 mg daily per weight and platelet-based dosing (weight 68 kg, platelets 174K)**
  - **Tolerated well with Grade 1 fatigue**
  - **Intermittent Grade 1 neutropenia, normal Hgb and platelets**
- **20 months after starting maintenance therapy, slow rise in CA125 (8 → 10 → 31 → 43)**
  - **CT with slight increase in R external iliac node**
  - **PET-CT with FDG-uptake in enlarged R external iliac LN, concerning for nodal metastasis**

Case 2 — Joyce F Liu, MD, MPH

CT Scan and PET Scan





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Case 2 — Joyce F Liu, MD, MPH

- **Given oligometastatic platinum-sensitive recurrence, discussed secondary cytoreductive surgery**
- **At time of surgery, external iliac LN fixed to underlying iliac vein with no safe plane for resection.**
  - **Decision made to coordinate resection with vascular surgery**
- **Niraparib restarted at 200 mg daily as anticipated coordination could take weeks**
  - **3 weeks after restarting, reports petechiae along shins**
  - **Sent for CBCD – platelet count 1K, Hgb 9.4 (baseline 12.4), ANC 1,340**
  - **Niraparib held, supportive transfusion, platelets fully recover to normal after 3 weeks**
- **Surgery coordinated 5 weeks later**
  - **Right external iliac LN area dissected completely. Path: HGSOC involve 1 of 3 LNs. Rind resected from vein with necrotic tumor surrounded by dense fibrosis without viable tumor.**
- **Patient did not want to consider repeated chemotherapy at this time**
  - **Local EBRT performed to lymph node bed**
  - **Restarted on niraparib at 100 mg daily with close CBCD monitoring**

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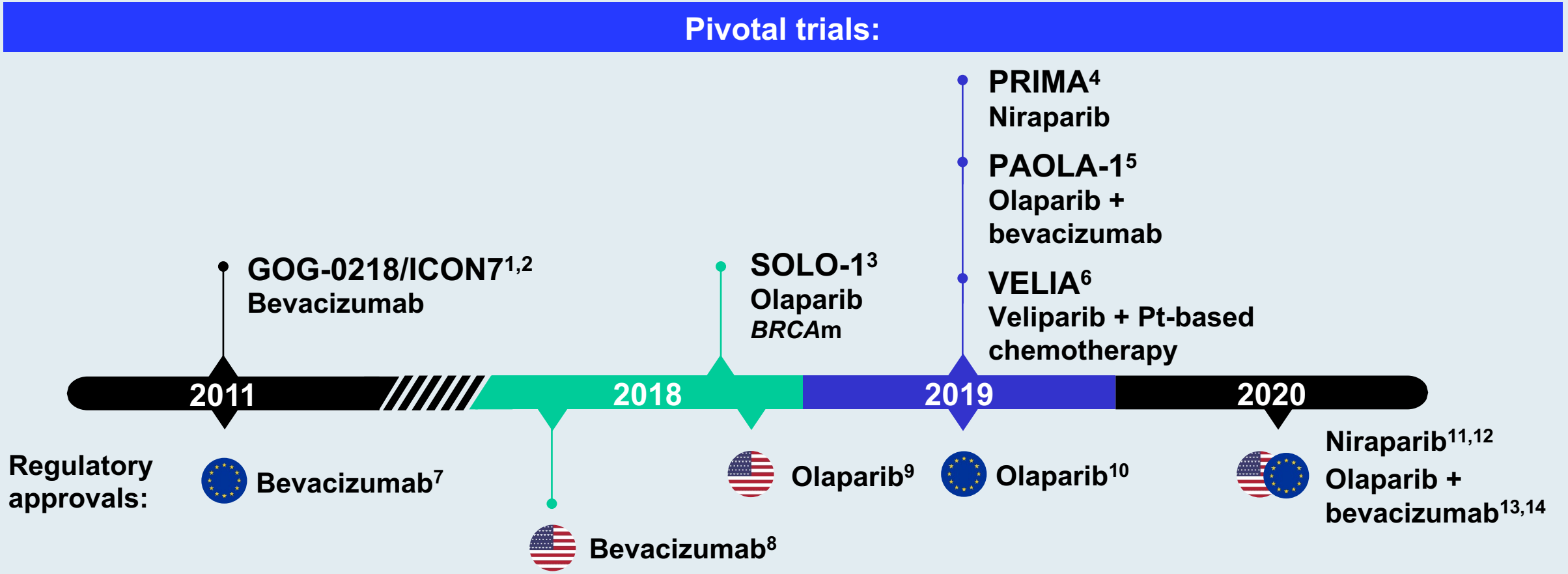
Pivotal Trials and Regulatory Milestones in 1L Maintenance Therapy of Advanced Ovarian Cancer



Dates shown indicate the year of the publication of the pivotal studies and regulatory approvals for these compounds.

1L, first line; *BRCA*m, breast cancer gene mutant; GOG, Gynecologic Oncology Group; Pt, platinum.

1. Burger RA et al. *N Engl J Med*. 2011;365(26):2473-2483. 2. Perren TJ et al. *N Engl J Med*. 2011;365(26):2484-2496. 3. Moore K et al. *N Engl J Med*. 2018;379(26):2495-2505. 4. González-Martín A et al. *N Engl J Med*. 2019;381(25):2391-2402. . Ray-Coquard I et al. *N Engl J Med*. 2019;381(25):2416-2428. 6. Coleman RL et al. *N Engl J Med*. 2019;381(25):2403-2415. 7. European Medicines Agency. Published September 22, 2011. Accessed June 7, 2021. 8. F. Hoffmann-La Roche Ltd. Published June 13, 2018. Accessed June 7, 2021. 9. US Food and Drug Administration. Published December 26, 2018. Accessed June 7, 2021. 10. European Medicines Agency. Published April 26, 2019. Accessed June 7, 2021. 11. GlaxoSmithKline. Published April 29, 2020. Accessed June 7, 2021. 12. GlaxoSmithKline. Published October 29, 2020. Accessed June 7, 2021. 13. US Food and Drug Administration. Published May 11, 2020. Accessed June 7, 2021. 14. European Medicines Agency. Published September 17, 2020. Accessed June 7, 2021.

Courtesy, Kathleen Moore, MD

Phase III First-Line PARP Inhibitor Maintenance Trials

Study design	SOLO-1[1] (N = 391)	PAOLA-1[2] (N = 612)	PRIMA[3] (N = 620)	VELIA[4] (N = 1,140)
Treatment arms vs placebo	**Olaparib (n = 260)**	**Bevacizumab ± olaparib**	**Niraparib**	**Veliparib**
Patient population	*BRCA* mutation	All comers	All comers	All comers
Treatment duration	24 months	15 months for bev 24 months for olaparib	36 months or until PD	24 months
Median PFS	56 vs 14 months HR: 0.33	22.1 vs 16.6 months HR: 0.59	22.1 vs 10.9 months HR 0.40	23.5 vs 17.3 months HR: 0.68

PD = disease progression; PFS = progression-free survival

[1] Banerjee *Lancet Oncol* 2021;22(12):1721-31. [2] Ray-Coquard et al. SGO 2020;Abstract 33; [3] González-Martín A et al. ASCO 2021;Abstract 5518; [4] Aghajanian C et al. *Gyn Oncol* 2021;162(2):375-81.

Phase 2 OVARIO Study of Niraparib + Bevacizumab Therapy in Advanced Ovarian Cancer Following Frontline Platinum-Based Chemotherapy with Bevacizumab

Melissa M. Hardesty,[1] Thomas Krivak,[2] Gail S. Wright,[3] Erika Hamilton,[4] Evelyn L. Fleming,[5] Jimmy Belotte,[6] Erika Keeton,[6] Ping Wang,[6] Aine Clements,[7] Heidi J. Gray,[8] Gottfried E. Konecny,[9] Richard G. Moore,[10] Debra L. Richardson[11]

[1]Alaska Women's Cancer Care, Anchorage, AK, USA; [2]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, The Western Pennsylvania Hospital, Pittsburgh, PA, USA; [3]Florida Cancer Specialists and Research Institute, New Port Richey, FL, USA; [4]Sarah Cannon Research Institute; Tennessee Oncology, Nashville, TN, USA; [5]Division of Gynecologic Oncology, Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; [6]GlaxoSmithKline, Waltham, MA, USA; [7]Department of Gynecologic Oncology, Riverside Methodist Hospital, Columbus, OH, USA; [8]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Washington, Seattle, WA, USA; [9]University of California Los Angeles, Los Angeles, CA, USA; [10]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY, USA; [11]Division of Gynecologic Oncology, Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

ANNUAL MEETING ON WOMENS' CANCER
BUILDING BRIDGES // BREAKING BARRIERS

Society of Gynecologic Oncology

SGO 2022;Abstract 40.

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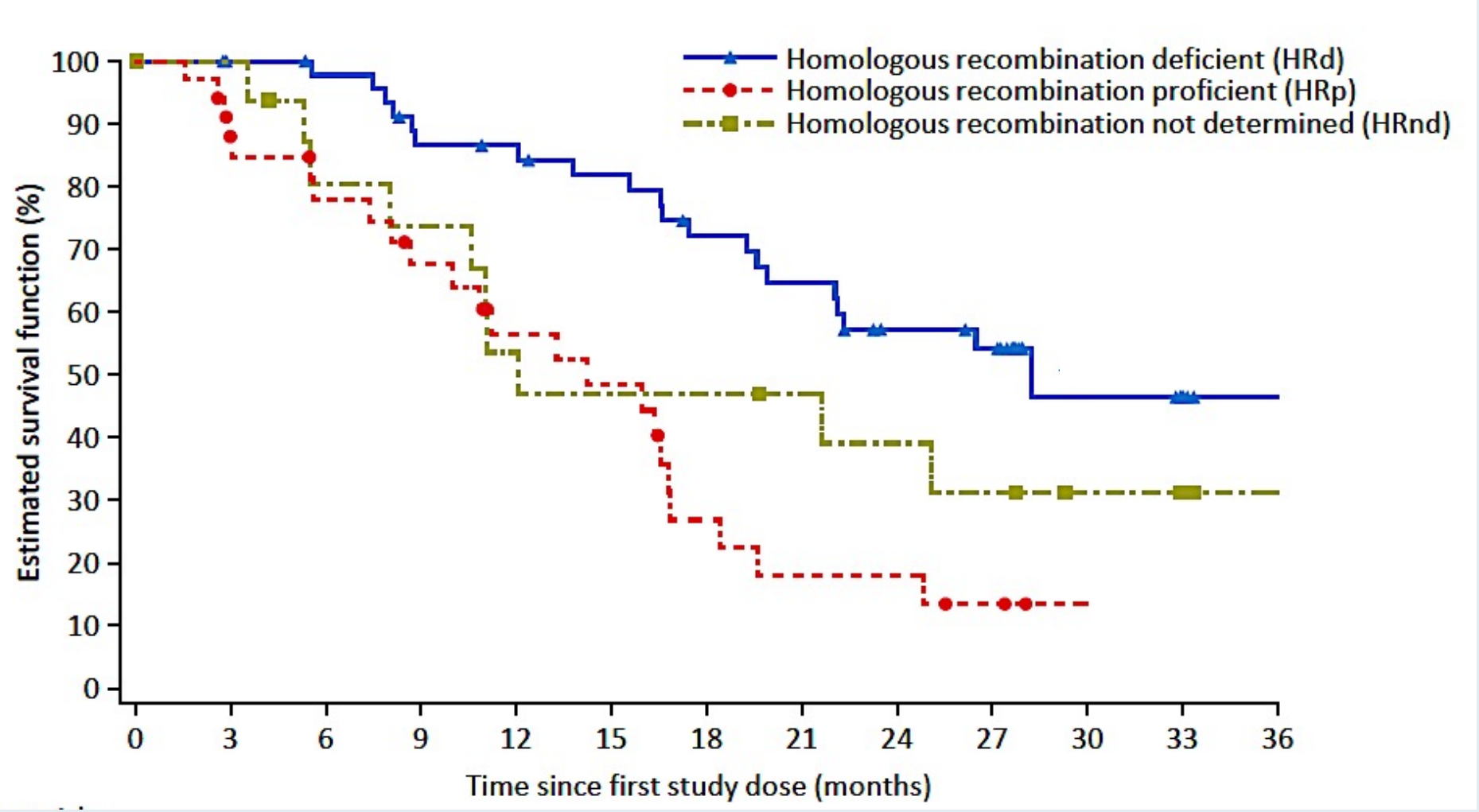
OVARIO: PFS by Homologous Recombination Deficiency Status



Overall (n = 105)	
18-mo PFS rate	62
24-mo PFS rate	53

HRd (n = 49)	
18-mo PFS rate	76
24-mo PFS rate	63

HRp (n = 38)	
18-mo PFS rate	47
24-mo PFS rate	42

HRnd (n = 18)	
18-mo PFS rate	56
24-mo PFS rate	50

Hardesty et al. SGO 2022;Abstract 40.

Efficacy and Safety of Niraparib as Maintenance Treatment in Patients with Newly Diagnosed Advanced Ovarian Cancer Using an Individualized Starting Dose (PRIME Study): A Randomized, Double-blind, Placebo-controlled, Phase 3 Trial

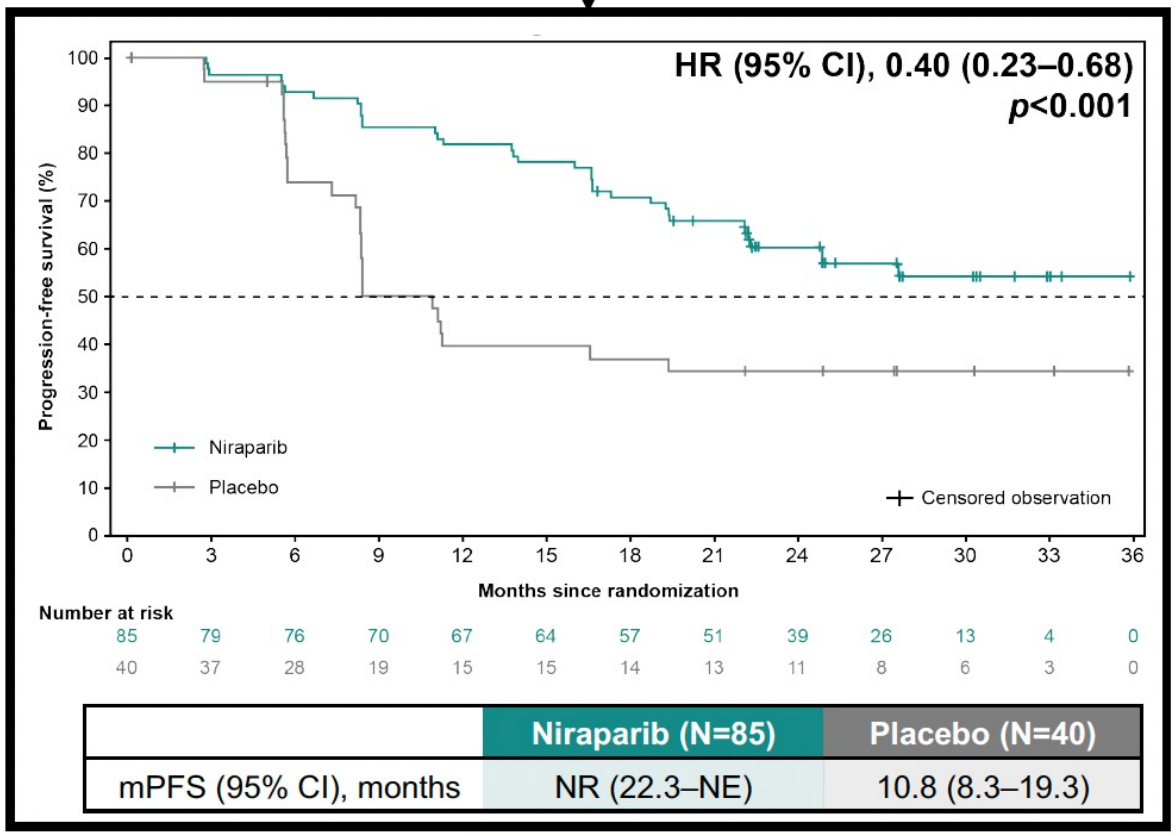
Ning Li*, Jianqing Zhu, Rutie Yin, Jing Wang, Lingya Pan, Beihua Kong, Hong Zheng, Jihong Liu, Xiaohua Wu, Li Wang, Yi Huang, Ke Wang, Dongling Zou, Hongqin Zhao, Chunyan Wang, Weiguo Lu, An Lin, Ge Lou, Guiling Li, Pengpeng Qu, Hongying Yang, Xiaoa Zhen, Wenzhao Hang, Jianmei Hou, Lingying Wu*

* National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

SGO 2022;Abstract LBA5.

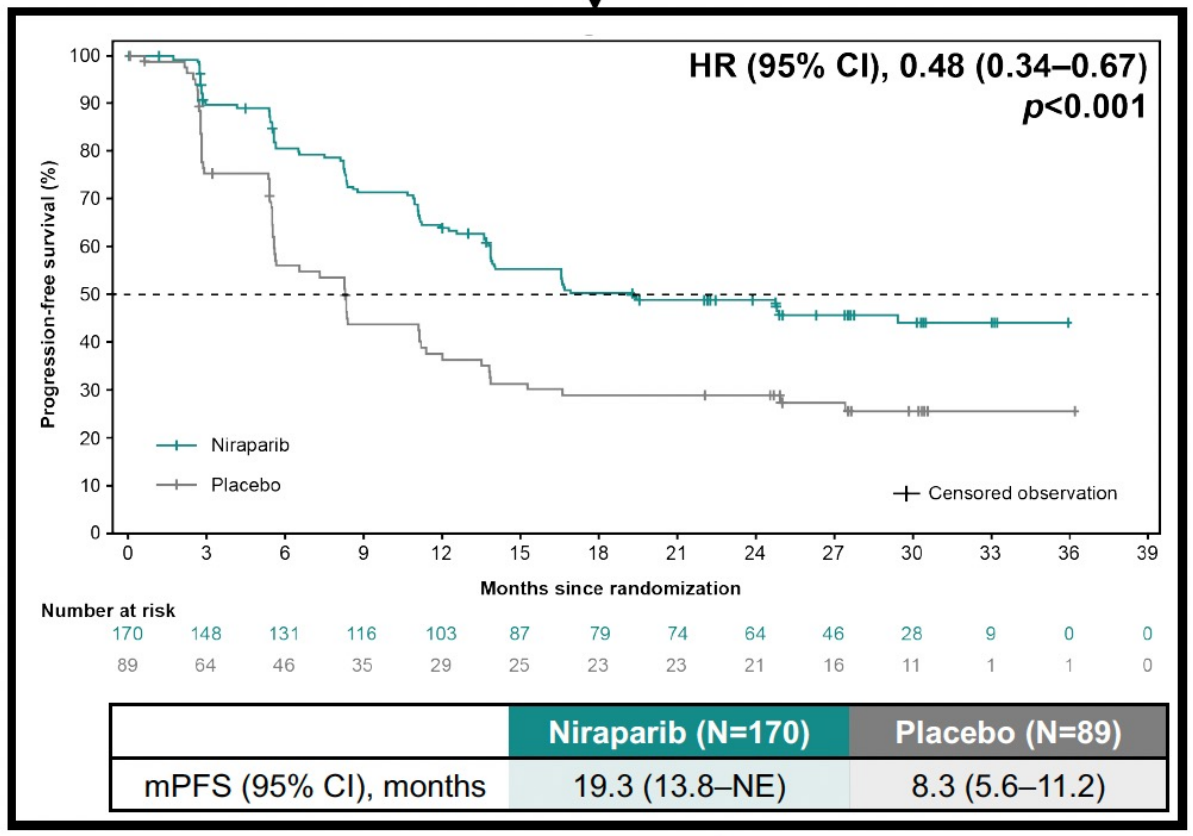
PRIME: PFS Benefit by g*BRCA*mut Status

g*BRCA*mut



	Niraparib (N=85)	Placebo (N=40)
mPFS (95% CI), months	NR (22.3–NE)	10.8 (8.3–19.3)

Non-g*BRCA*mut



	Niraparib (N=170)	Placebo (N=89)
mPFS (95% CI), months	19.3 (13.8–NE)	8.3 (5.6–11.2)

- Median PFS has not been yet reached for the g*BRCA*mut population.
- The benefit of niraparib in the non-g*BRCA*mut population is confirmed.

Li et al. SGO 2022;Abstract LBA5.

Bevacizumab in First-Line Chemotherapy to Improve the Survival Outcome for Advanced Ovarian Clear Cell Carcinoma: A Multicenter, Retrospective Analysis

Seki T et al.

ASCO 2022;Abstract 5502.

Track: Gynecologic Oral Session
June 6, 2022; 9:00 AM

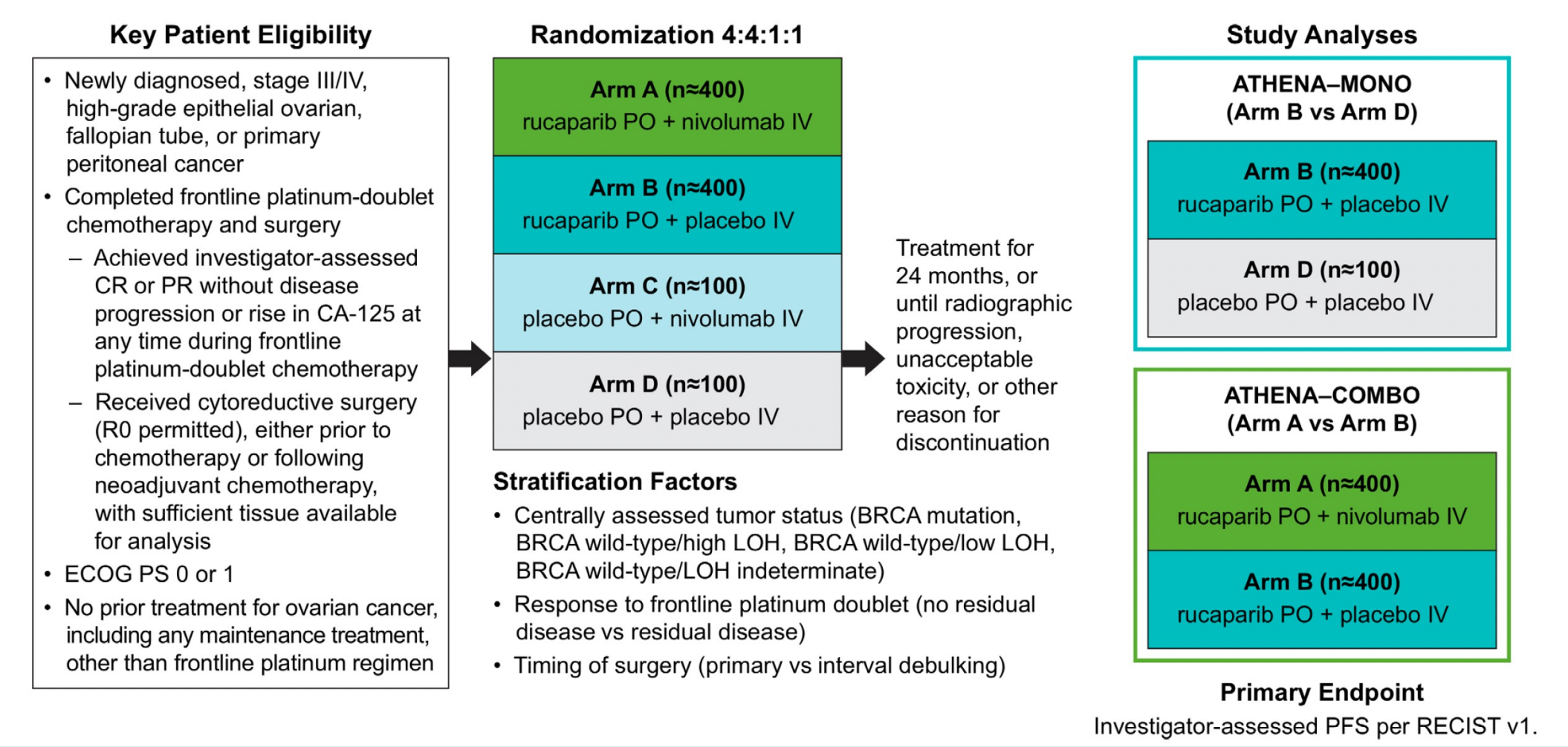
Efficacy of Maintenance Olaparib plus Bevacizumab in Patients with Newly Diagnosed Advanced Ovarian Cancer According to BRCA Mutation Genotype in the Phase III PAOLA-1/ENGOT-ov25 Trial

Labidi-Galy SI et al.

ASCO 2022;Abstract 5571.

Track: Gynecologic Poster Session

ATHENA-MONO and ATHENA-COMBO Study Design



Monk BJ et al. *Int J Gynecol Cancer* 2021;31(12):1589-94.

Rucaparib Significantly Improves PFS in First-Line Maintenance Treatment for Women with Ovarian Cancer Regardless of Their Biomarker Status in the Phase III ATHENA-MONO Trial

Press Release – March 31, 2022

- ATHENA study evaluating rucaparib monotherapy versus placebo (ATHENA-MONO) successfully achieved the primary endpoint of improved PFS in both populations in the primary efficacy analyses: HRD-positive and all patients randomized (ITT)
  - Median PFS of 20.2 months for rucaparib vs 9.2 months for placebo in the ITT population
- The exploratory PFS endpoints were also achieved in both HRD-negative and BRCA mutant subgroups of patients
- Safety of rucaparib observed in ATHENA-MONO was consistent with both the current US and European labels
- ATHENA-MONO results will serve as the basis of a supplemental NDA for US label expansion to be submitted during Q2 2022; European submission to follow during Q3 2022
- These data, including additional analyses, have been submitted for presentation at the American Society of Clinical Oncology Annual Meeting in June 2022

https://ir.clovisoncology.com/investors-and-news/news-releases/press-release-details/2022/Clovis-Oncologys-Rubraca-Rucaparib-Significantly-Improves-Progression-Free-Survival-in-First-line-Maintenance-Treatment-in-Women-with-Ovarian-Cancer-Regardless-of-Their-Biomarker-Status-in-Phase-3-ATHENA-MONO-Trial/default.aspx

ATHENA–MONO (GOG-3020/ENGOT-ov45): A Randomized, Double-Blind, Phase 3 Trial Evaluating Rucaparib Monotherapy versus Placebo as Maintenance Treatment Following Response to First-Line Platinum-Based Chemotherapy in Ovarian Cancer

Monk BJ et al.

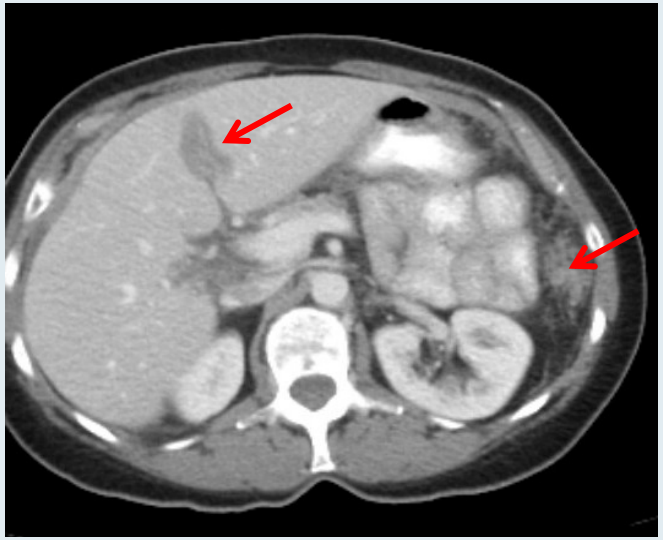
ASCO 2022;Abstract LBA5500.

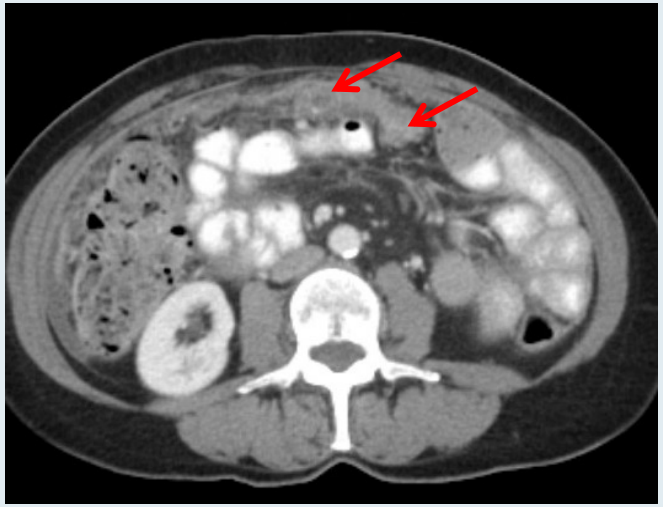
Track: Gynecologic Oral Session
June 6, 2022; 9:00 AM

Case 3 — Kathleen N Moore, MD, MS

- 71-yr-old with sBRCA2 ovarian cancer
- Received 6 cycles of IV carboplatin + paclitaxel, normalized her CA-125 and CT scan followed by 2 years of olaparib maintenance, tolerated well
- At conclusion of olaparib maintenance, CA-125 was 12 U/mL and CT was normal
- She has been in 3 month surveillance for two years and presented with an elevated CA-125 to 150 U/mL and her CT is shown

Imaging





RTP RESEARCH TO PRACTICE

Case 3 — Kathleen N Moore, MD, MS

- **2 yr after completing olaparib maintenance (24 months from completion of chemotherapy), she was diagnosed with recurrent ovarian cancer**
- **She receives 6 cycles of carboplatin and PLD, and CT scan after 6 cycles showed decreasing peritoneal carcinomatosis. CA-125 is down to 32**
- **She has completed carboplatin and PLD**
- **She was counseled during chemotherapy regarding the OReO results and options for maintenance to include adding in bevacizumab now and to follow or repeat use of a PARPi per OReO**
- **She was started on olaparib following cycle 6 and remains on treatment x 6 months with SD and stable CA-125**

Case 4 — Antonio González-Martín, MD, PhD

- **67 y/o at diagnosis**
- **She complained of abdominal distention and constipation in January 2016**
- **Due to worsening of abdominal distention the patient went to emergency on March 23rd, 2016 where an ultrasound showed bilateral adnexal masses and ascites.**
- **A PET-CT on March 31st, 2016 confirmed peritoneal carcinomatosis, retropritoneal lymphadenopathies and bilateral adnexal masses.**
- **CA 125 467 U/mL**

Case 4 — Antonio González-Martín, MD, PhD

First Treatment and Pathology Report

- **After evaluation in MDT a primary cytoreductive surgery (PCS) was proposed**
- **PCS on April 4th, 2016**
  - **Basal PCI: 30**
  - **Omentectomy, left hemicolectomy, hysterectomy with bilateral oophorectomy, bilateral diaphragmatic peritonectomy, splenectomy, pelvic and para-aortic lymphadenectomy, resection of multiple nodules in the small bowel and colon.**
  - **Surgical outcome: Residual tumour of 5 mm in bowel serosa**
- **Pathology: HGSC. FIGO Stage IIIC**
- **BRCA testing: gBRCA2 mutated**

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Case 4 — Antonio González-Martín, MD, PhD

Front-Line Systemic Therapy

- **Patient was included in PAOLA-1 study**
- **She received 6 cycles of paclitaxel-carboplatin with bevacizumab from the 2nd cycle**
- **Last platinum dose was mid October 2016**
- **She started olaparib 300 mg tid in November 2016**
- **Olaparib was discontinued in April 2017 due to anaemia despite dose interruption/ dose reduction**
- **She completed 15 months of bevacizumab and then she started F/U**

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Case 4 — Antonio González-Martín, MD, PhD

First Relapse: Diagnosis and Treatment

- **In October 2019 she started vespertine fever and asthenia**
- **A PET-CT on January 28th, 2020 showed pelvic lymph node relapse and presacral disease (TFIp 39 months)**
- **After discussion at the MDT a secondary cytoreductive surgery (SCS) was proposed**
- **SCS was conducted on February 10th, 2020 achieveing complete cytoreduction**
- **She received 6 cycles of post-operative carboplatin-PLD.**
- **Last platinum dose in October 2020 with NED in the post-Cht imaging assessment.**

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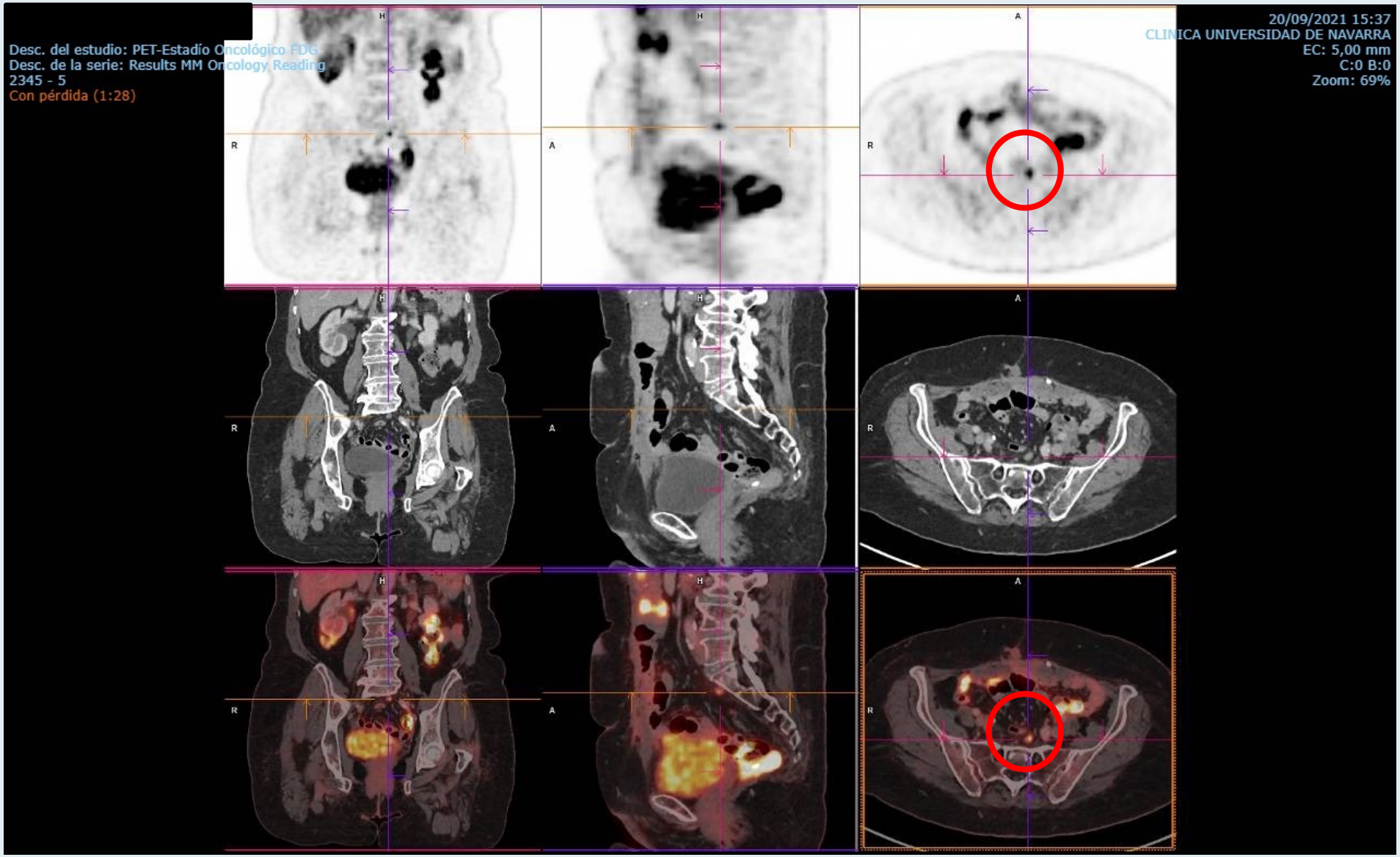
Case 4 — Antonio González-Martín, MD, PhD

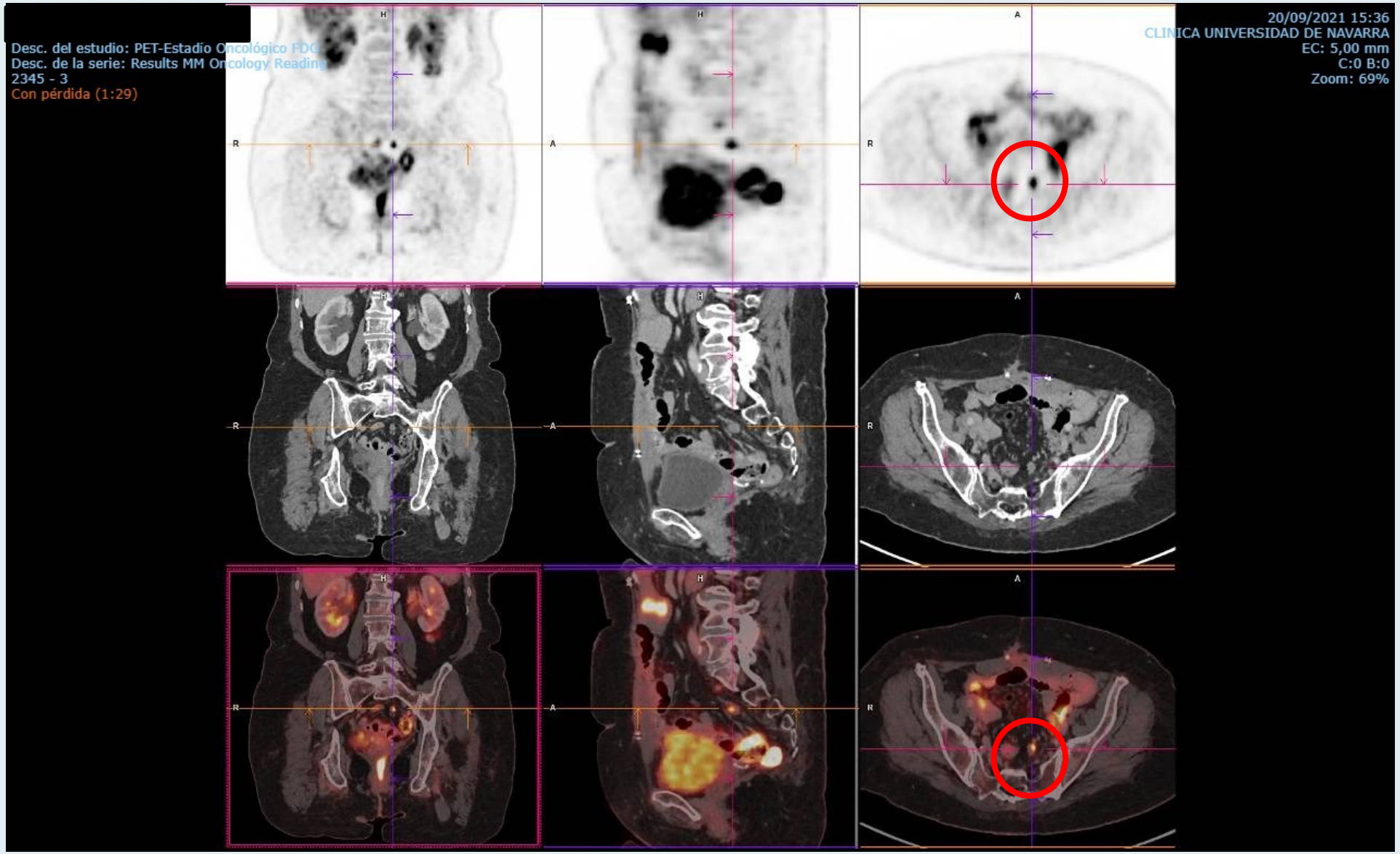
Second Progression: Diagnosis

- **A PET-CT on September 20th, 2021 showed 3 new pelvic lesions of small volume in different sites from prior relapse (platinum-free interval 11 months).**
- **Patient was asymptomatic**

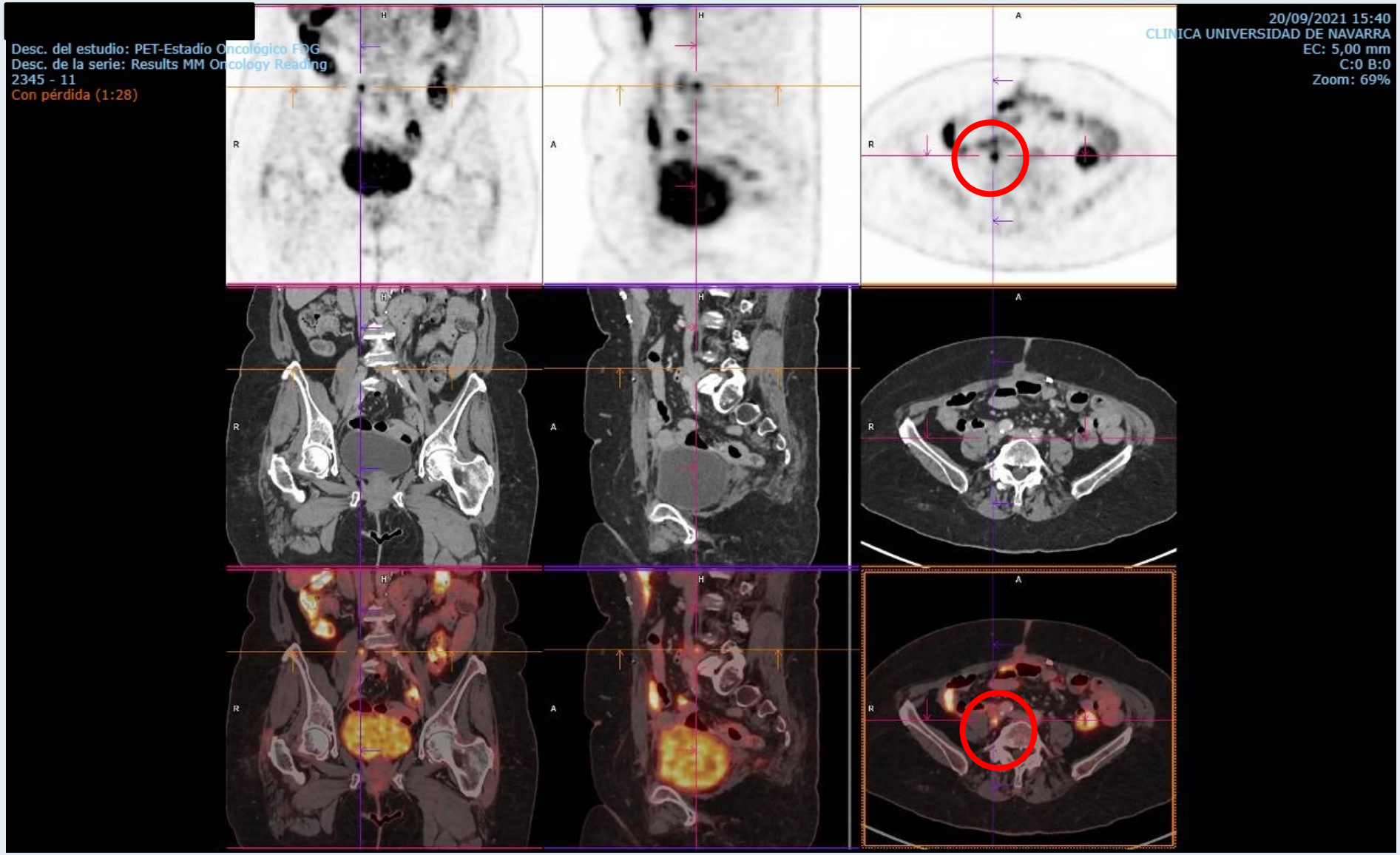
Case 4 — Antonio González-Martín, MD, PhD



Case 4 — Antonio González-Martín, MD, PhD



Case 4 — Antonio González-Martín, MD, PhD



Case 4 — Antonio González-Martín, MD, PhD

Second Progression: Treatment

- **Options**
  - **Tertiary cytoreductive surgery**
  - **Platinum based chemotherapy +/- bevacizumab**
  - **PARPi monotherapy**
- **Rucaparib 600 mg tid was started on October 1st, 2021 based on:**
  - **Low volume disease**
  - **No progression on prior PARPi**
  - **Patient did not accept a new platinum chemotherapy line**
- **Since January 19th, 2022 a dose reduction to 500 mg tid and a schedule of 6 days on 1 day off per week was required in order to control asthenia**
- **A PET-CT on January 13, 2022 showed CR that is maintatined**

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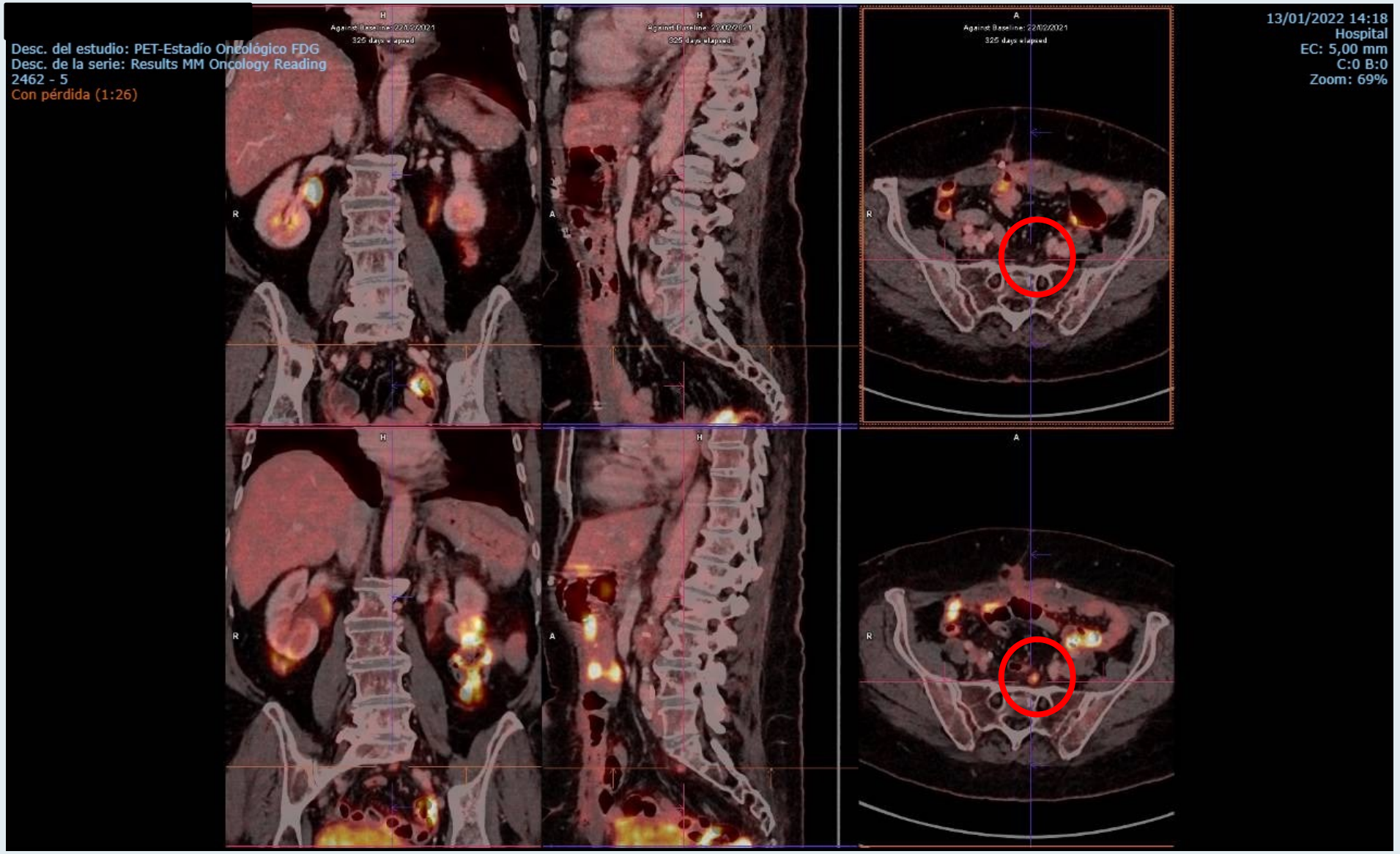
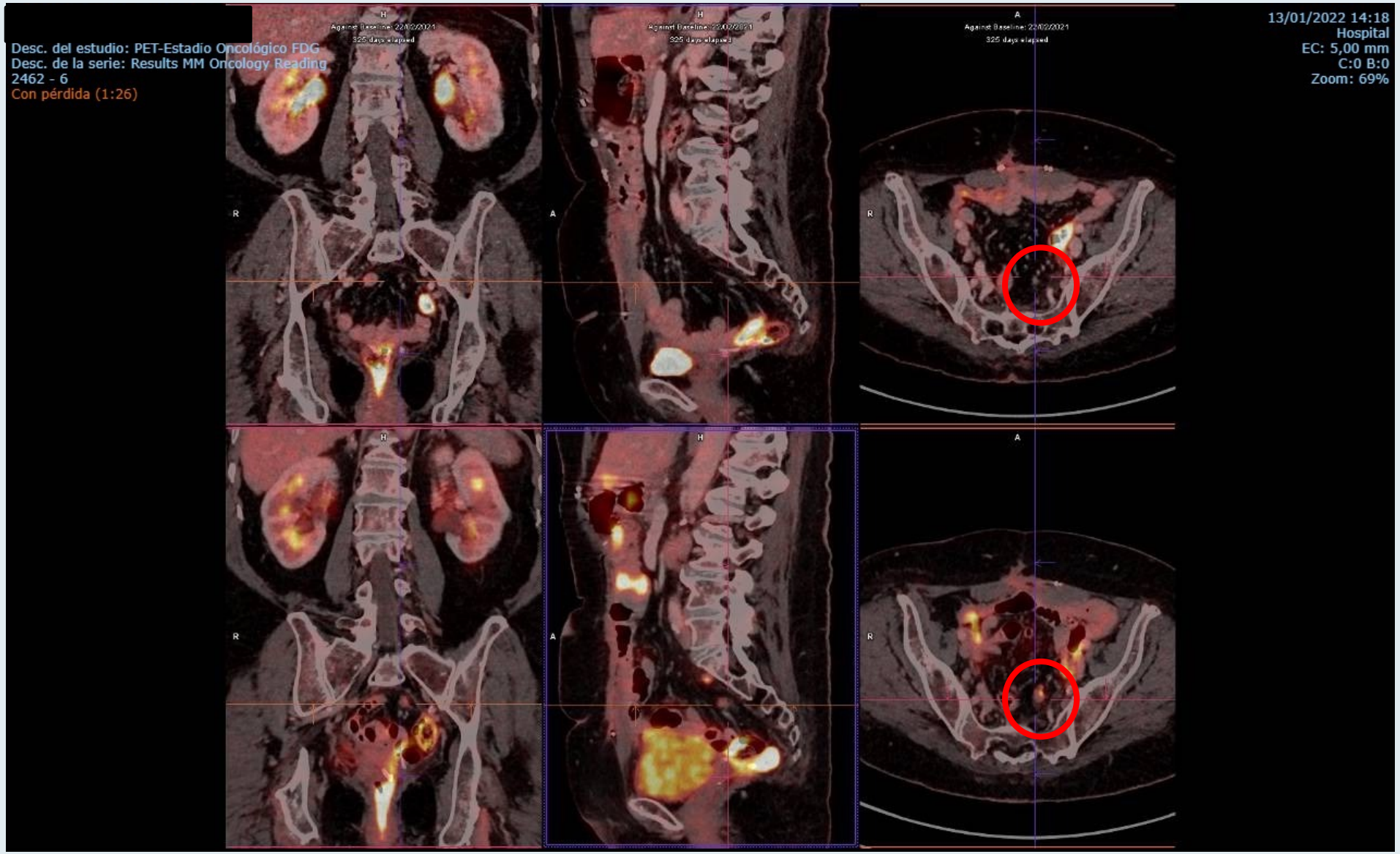
Case 4 — Antonio González-Martín, MD, PhD



Case 4 — Antonio González-Martín, MD, PhD



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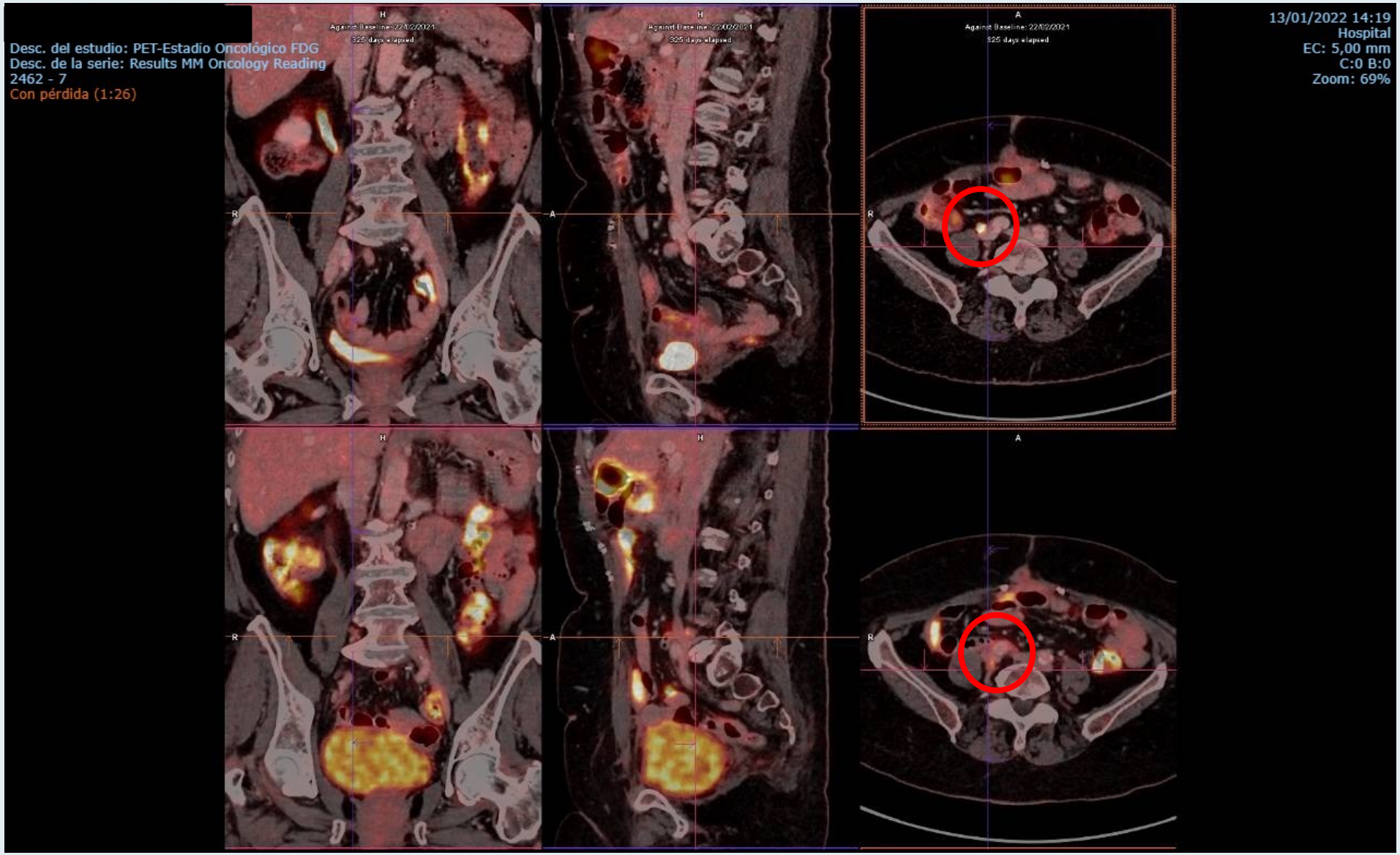
Case 4 — Antonio González-Martín, MD, PhD



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2021 ESMO congress

Abstract LBA33

ENGOT European Network of Gynaecological Oncological Trial groups

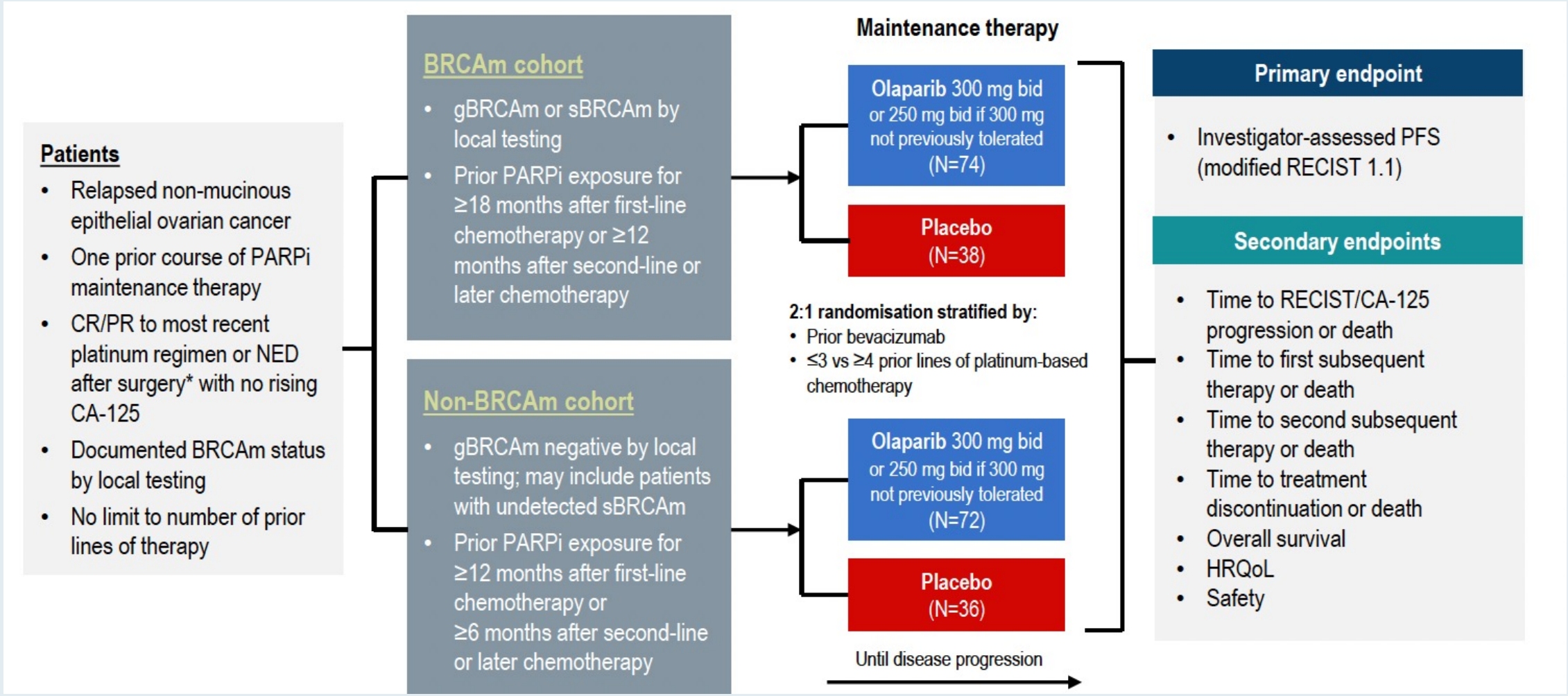
GINECO

Maintenance olaparib rechallenge in patients with ovarian carcinoma previously treated with a PARP inhibitor: Phase IIIb OReO/ENGOT Ov-38 trial

Eric Pujade-Lauraine,[1] Frédéric Selle,[2] Giovanni Scambia,[3] Bernard Asselain,[4] Frederik Marmé,[5] Kristina Lindemann,[6] Nicoletta Colombo,[7] Radoslaw Madry,[8] Rosalind Glasspool,[9] Coraline Dubot,[10] Ana Oaknin,[11] Claudio Zamagni,[12] Florian Heitz,[13] Laurence Gladieff,[14] Maria Jesús Rubio-Pérez,[15] Paolo Scollo,[16] Christopher Blakeley,[17] Bob Shaw,[17] Isabelle Ray-Coquard,[18] Andrés Redondo[19]

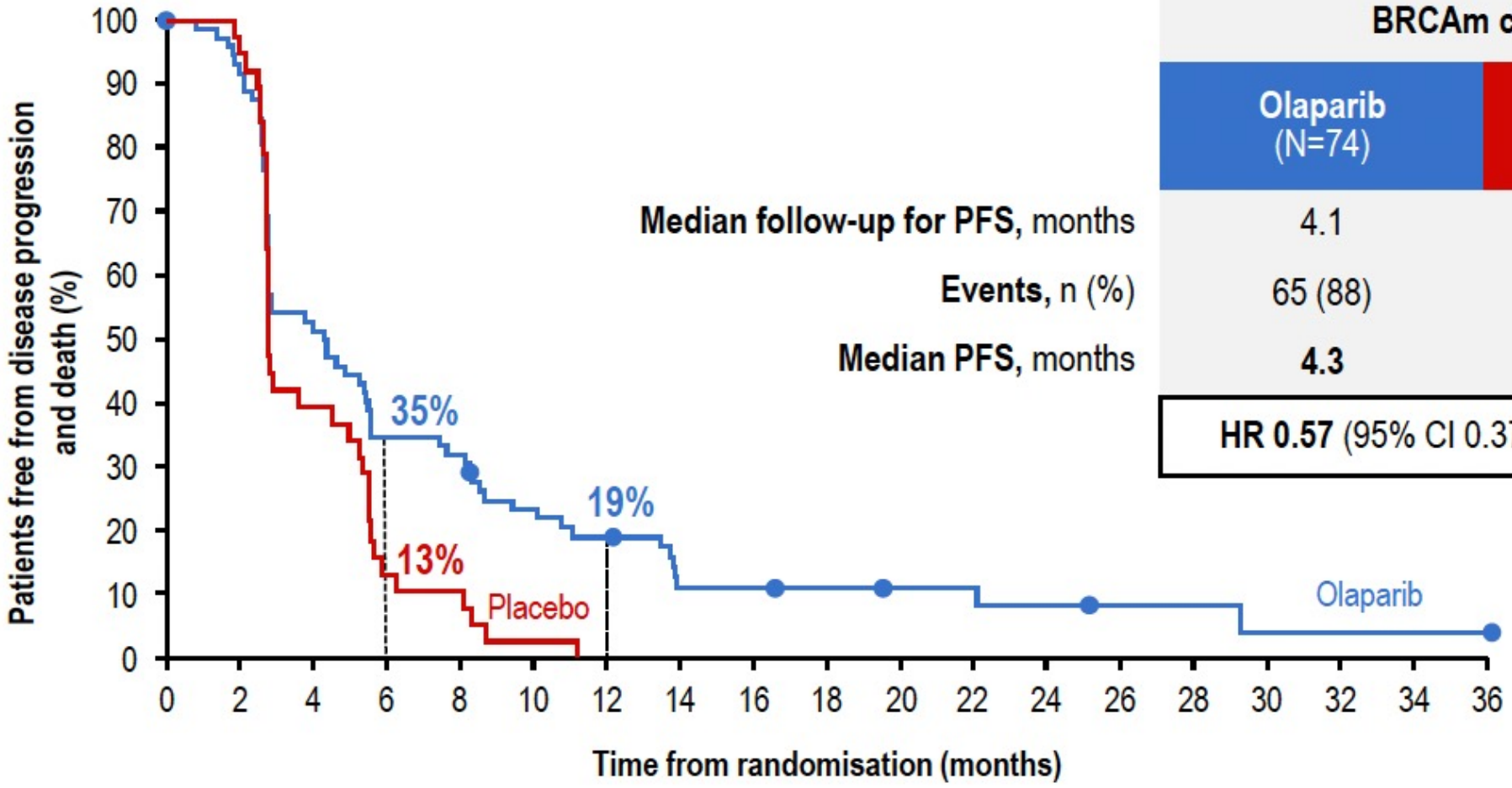
RTP RESEARCH TO PRACTICE

OReO Phase IIIB Study Schema



Pujade-Lauraine E et al. ESMO 2021;Abstract LBA33.

OReO: Progression-Free Survival in the BRCAm Cohort

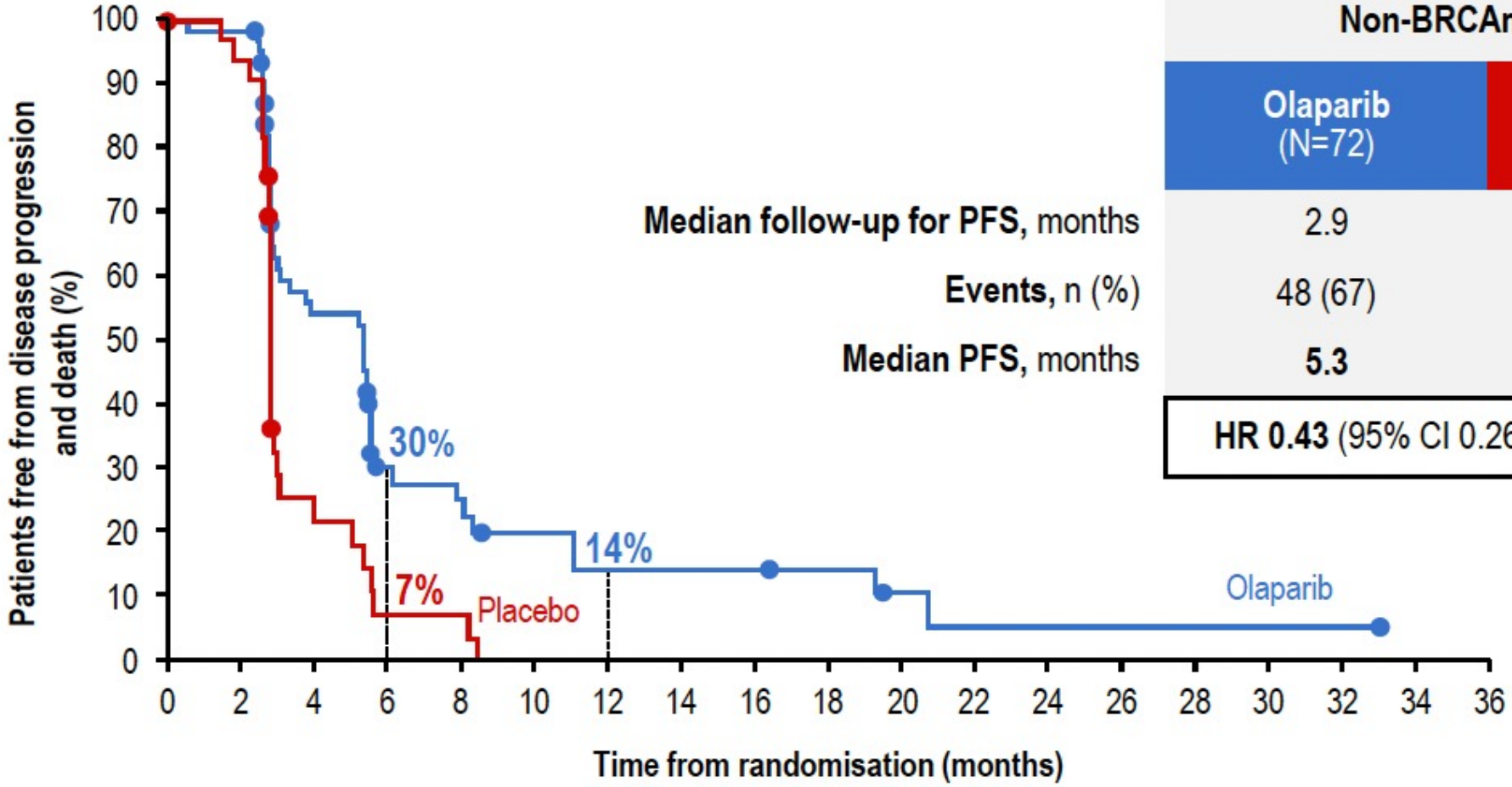


BRCAm cohort	Olaparib (N=74)	Placebo (N=38)
Median follow-up for PFS, months	4.1	2.8
Events, n (%)	65 (88)	38 (100)
Median PFS, months	**4.3**	**2.8**

HR 0.57 (95% CI 0.37–0.87); *P*=0.022

Pujade-Lauraine E et al. ESMO 2021;Abstract LBA33.

OReO: Progression-Free Survival in the Non-BRCAm Cohort

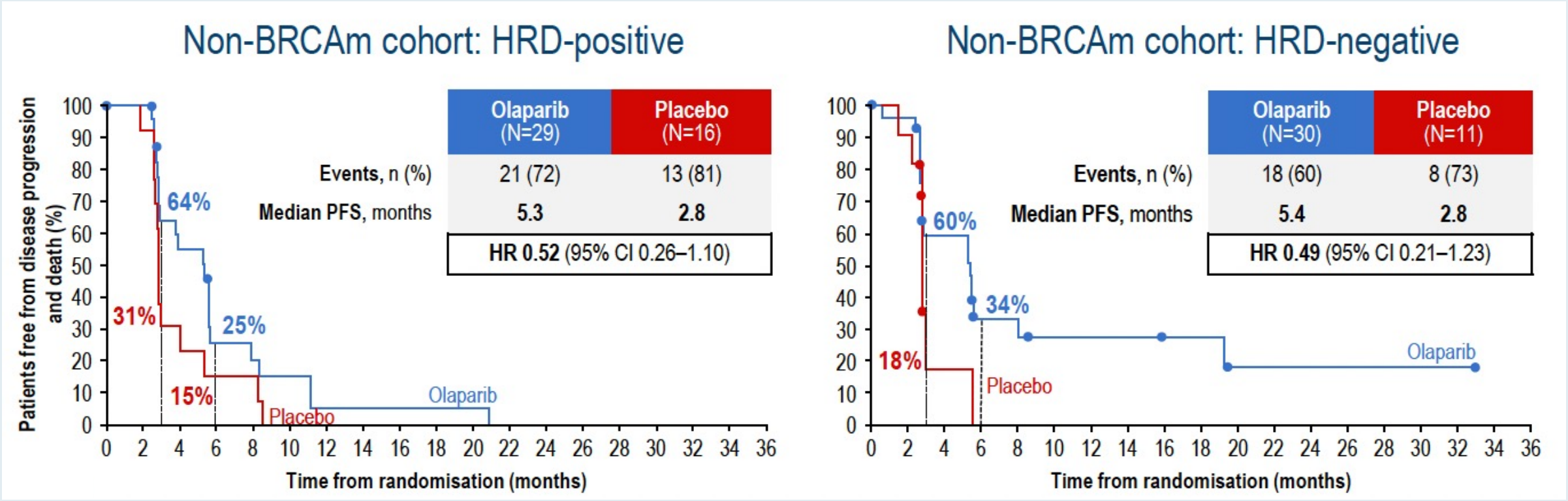


Non-BRCAm cohort	Olaparib (N=72)	Placebo (N=36)
Median follow-up for PFS, months	2.9	2.8
Events, n (%)	48 (67)	30 (83)
Median PFS, months	**5.3**	**2.8**

HR 0.43 (95% CI 0.26–0.71); *P*=0.0023

Pujade-Lauraine E et al. ESMO 2021;Abstract LBA33.

OReO: Progression-Free Survival in the Non-BRCAm Cohort by HRD Status



Pujade-Lauraine E et al. ESMO 2021;Abstract LBA33.

OReO/ENGOT Ov-38 Trial: Impact of Maintenance Olaparib Rechallenge According to Ovarian Cancer Patient Prognosis—An Exploratory Joint Analysis of the BRCA and Non-BRCA Cohorts

Selle F et al.

ASCO 2022;Abstract 5558.

Track: Gynecologic Poster Session

Agenda

Module 1 – Current Management of Advanced Ovarian Cancer

Module 2 – Novel Agents and Strategies Under Investigation

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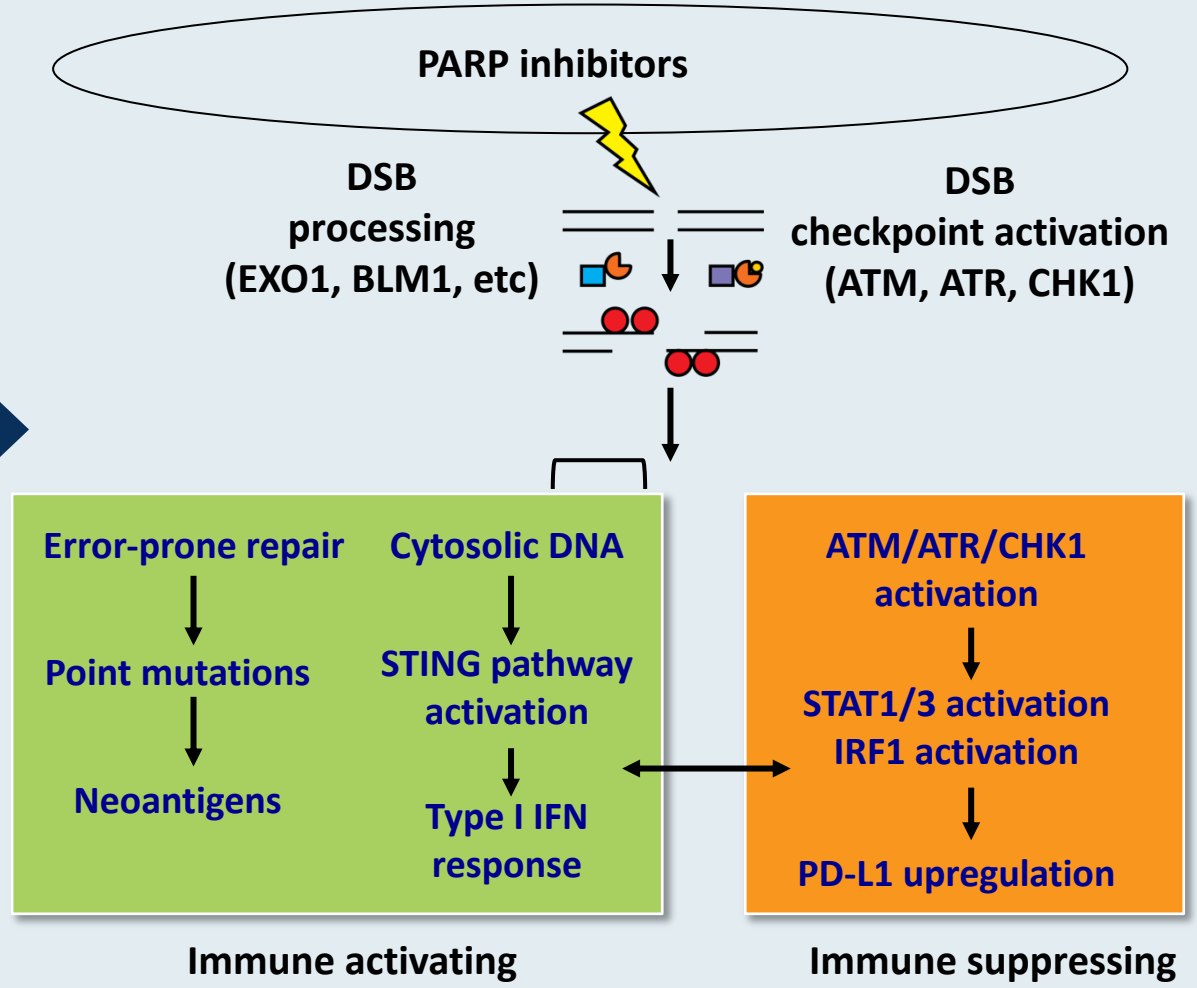
TO PRACTICE

Biologic Rationale for Combining a PARP Inhibitor with an Immune Checkpoint Inhibitor

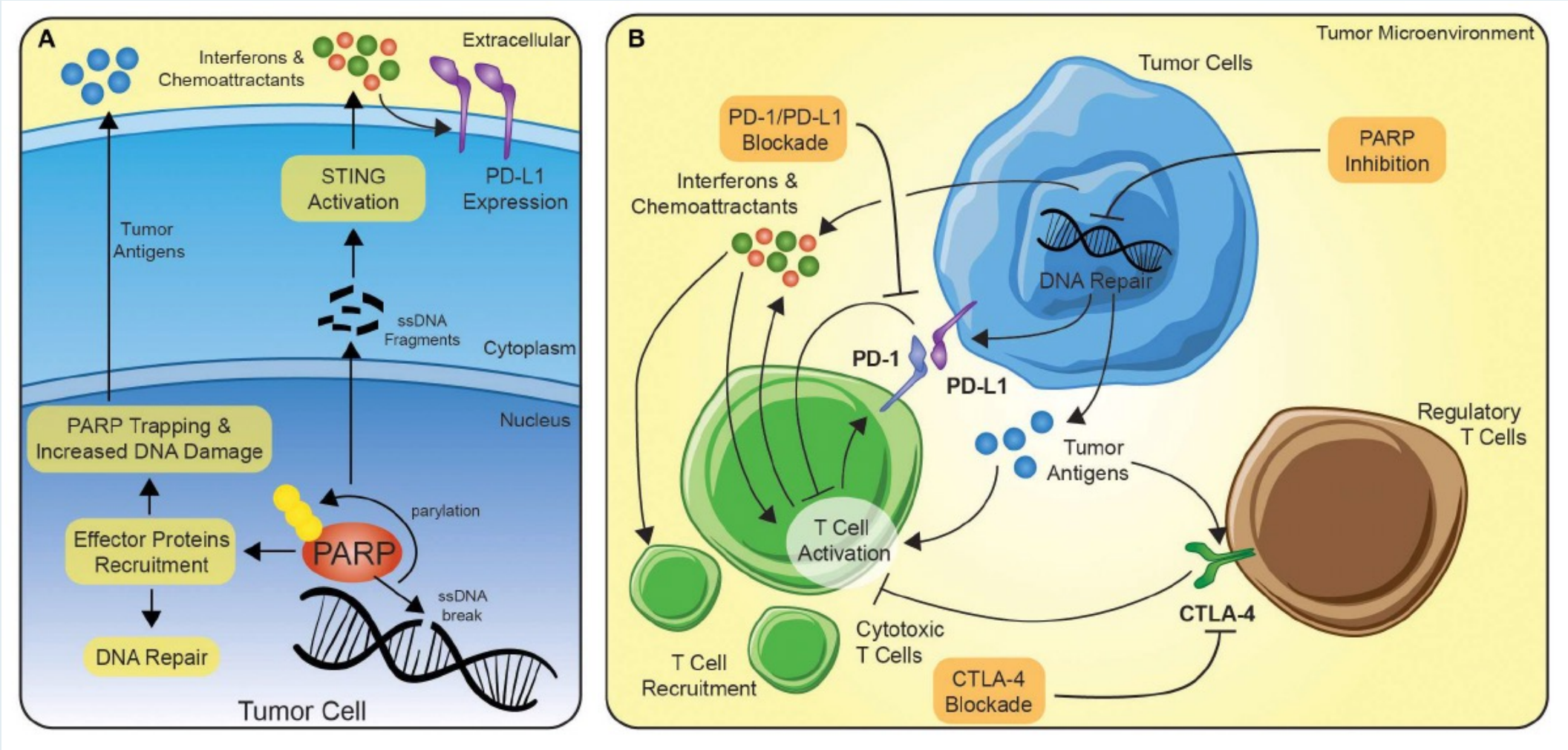
Preclinical models indicate synergy between PARPi + anti-PD-1 agents regardless of *BRCA* mutation status or PD-L1 status



Preclinical data demonstrate synergy with PARPi and anti-PD-1 combinations.

Konstantinopoulos P et al. ASCO 2018;Abstract 106.

The Potential Synergy Between PARP Inhibition and Immune Checkpoint Blockade



Vikas P et al. *Front Oncol* 2020;10:570.

Research

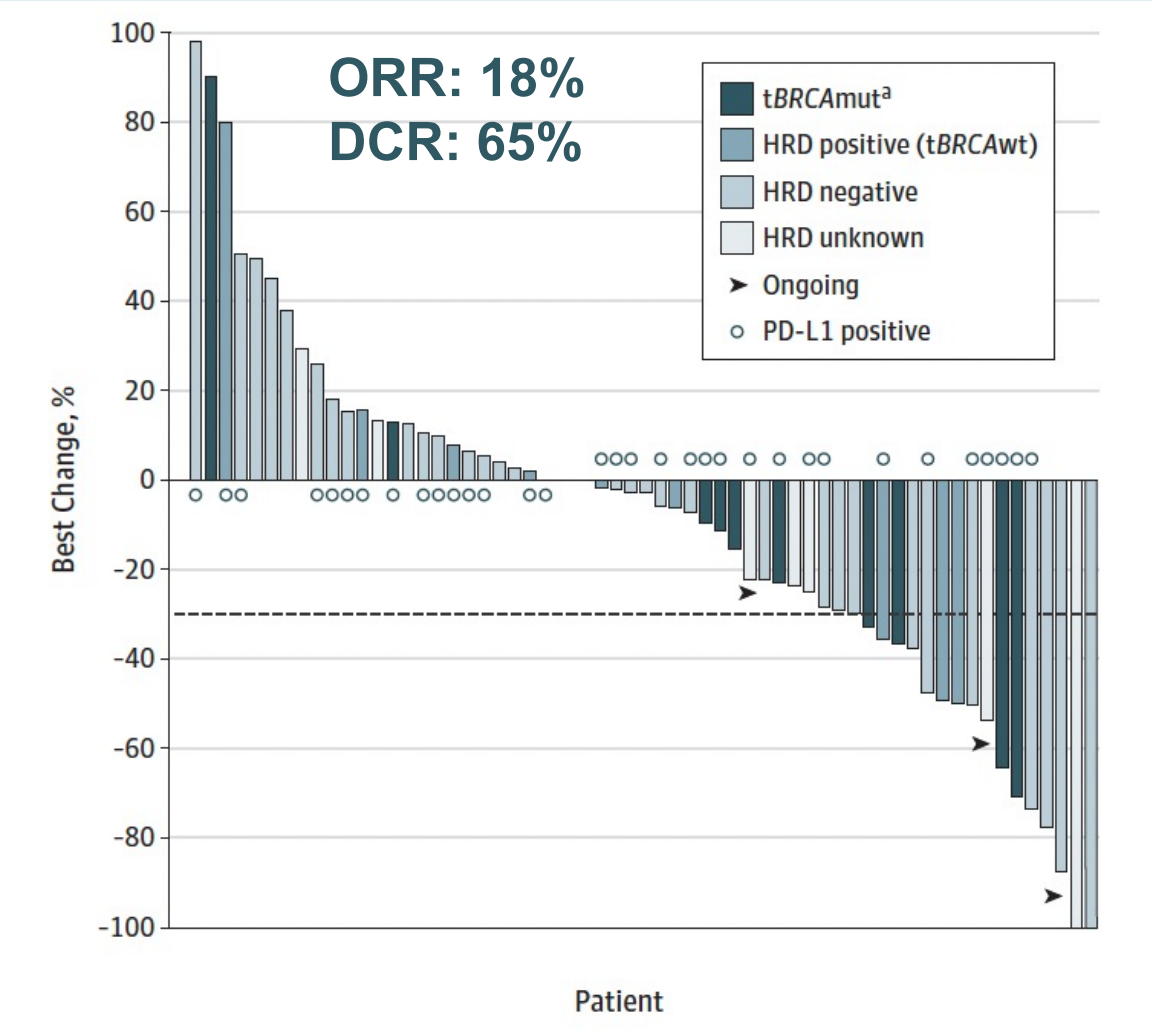
JAMA Oncol 2019;5(8):1141-9.

JAMA Oncology | Original Investigation

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

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

TOPACIO/KEYNOTE-162: Antitumor Activity of Niraparib in Combination with Pembrolizumab



DCR = disease control rate

Konstantinopoulos PA et al. *JAMA Oncol* 2019;5(8):1141-9.

RTP RESEARCH TO PRACTICE

VIRTUAL 2020 ESMO congress

Abstract 814MO.

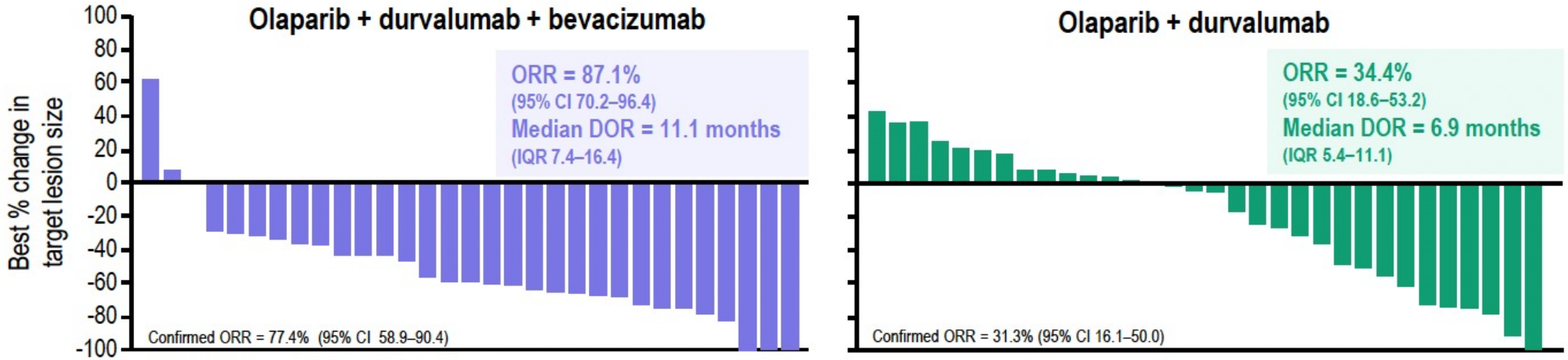
Phase II study of olaparib plus durvalumab and bevacizumab (MEDIOLA): initial results in patients with non-germline BRCA-mutated platinum sensitive relapsed ovarian cancer

Yvette Drew,[1] Richard Penson,[2] David M O'Malley,[3] Jae-Weon Kim,[4] Stefan Zimmermann,[5] Patricia Roxburgh,[6] Joohyuk Sohn,[7] Salomon M Stemmer,[8] Sara Bastian,[9] Michelle Ferguson,[10] Benoit You,[11] Susan Domchek,[12] Haiyan Gao,[13] Helen K Angell,[13] Kassondra Meyer,[14] Laura Opincar,[14] Lone Ottesen,[13] Susana Banerjee[15]

[1]Northern Centre for Cancer Care, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Newcastle University, Newcastle upon Tyne, UK; [2]Massachusetts General Hospital, Boston, MA, USA; [3]The Ohio State University – James Comprehensive Cancer Center, Columbus, OH, USA; [4]Seoul National University Hospital, Seoul, Republic of Korea; [5]Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland; [6]Beatson West of Scotland Cancer Centre, and Institute of Cancer Sciences, University of Glasgow, Glasgow, UK, [7]Yonsei Cancer Centre, Yonsei University, Sinchon-dong, Republic of Korea; [8]Rabin Medical Center-Beilinson Campus, Petach Tikva and Tel-Aviv University, Tel-Aviv, Israel; [9]Kantonsspital Graubuenden, Chur, Switzerland; [10]NHS Tayside, Dundee, UK; [11]Institut de Cancérologie des Hospices Civils de Lyon, CITOHL, GINECO, Université Claude Bernard Lyon 1, Lyon, France; [12]Basser Center for BRCA University of Pennsylvania, Philadelphia, PA, USA; [13]AstraZeneca, Cambridge, UK; [14]AstraZeneca, Gaithersburg, MD, USA; [15]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK

ClinicalTrials.gov identifier: NCT02734004
This study was sponsored by AstraZeneca

MEDIOLA Non-gBRCA Mutated: Antitumor Activity



Genomic instability status* subgroup	Olaparib + durvalumab + bevacizumab		Olaparib + durvalumab	
	ORR (95% CI), %	n/N patients	ORR (95% CI), %	n/N patients
GIS-positive	100.0 (69.2–100.0)	10/10	50.0 (18.7–81.3)	5/10
GIS-negative	75.0 (34.9–96.8)	6/8	16.7 (0.4–64.1)	1/6
GIS-unknown	84.6 (54.6–98.1)	11/13	31.3 (11.0–58.7)	5/16

*GIS, as determined by Foundation Medicine tumour analysis; must have genome-wide LOH ≥14, a somatic *BRCA1* and/or *BRCA2* mutation, or a mutation in *ATM*, *BRIP1*, *PALB2*, *RAD51C*, *BARD1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PPP2R2A*, *RAD51B*, *RAD51D* or *RAD54L* to be considered positive. At the time of the DCO, the prespecified cut-off for genome-wide LOH of 14% was used[1]; GIS, genomic instability status; IQR, interquartile range; LOH, loss of heterozygosity. [1]Swisher *et al. Lancet Oncol* 2017;18:75–87

Drew Y et al. ESMO 2020;Abstract 814MO.

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

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

Poster #23

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

SGO 2021 VIRTUAL ANNUAL MEETING ON WOMEN'S CANCER®

Abstract 10415

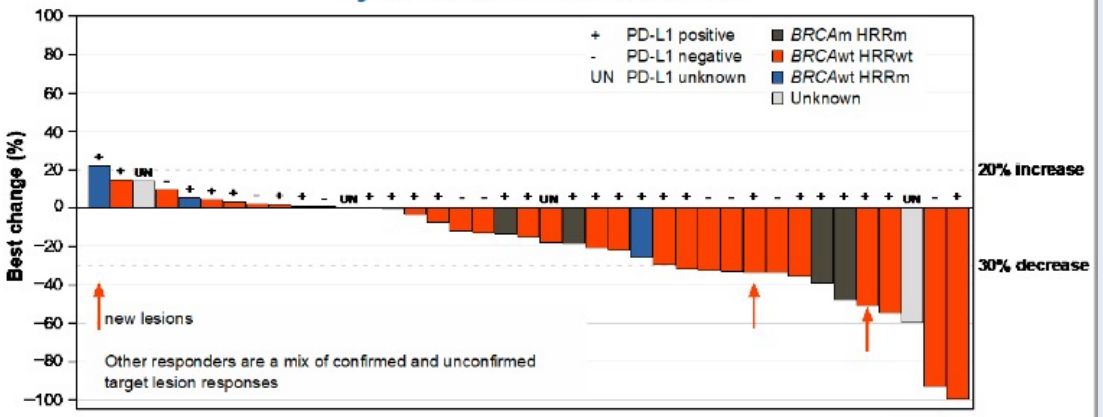
Society of Gynecologic Oncology

Antitumor Activity

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

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

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



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

SGO 2021 VIRTUAL ANNUAL MEETING ON WOMEN'S CANCER®

Society of Gynecologic Oncology

Liu JF et al. SGO 2021;Abstract 10415.

RTP RESEARCH TO PRACTICE

MOONSTONE/GOG-3032: Interim Analysis of a Phase 2 Study of Niraparib + Dostarlimab in Patients (pts) with Platinum-Resistant Ovarian Cancer (PROC)

Randall LM et al.

ASCO 2022;Abstract 5573.

Poster Session: Gynecologic Cancer

Updated Results From the Phase 1b Expansion Study of Upifitamab Rilsodotin (UpRi; XMT-1536), a NaPi2b-directed Dolaflexin Antibody Drug Conjugate (ADC) in Ovarian Cancer

Richardson, Debra L[1]; Hamilton, Erika P[2]; Barve, Minal[3]; Anderson, Charles K[4]; Taylor, Sara K[5]; Lakhani, Nehal[6]; Buscema, Joseph[7]; Tolcher, Anthony W[8]; Zarwan, Corrine[9]; Werner, Theresa L[10]; Hays, John L[11]; Richards, Paul[12]; Arend, Rebecca[13]; Edenfield, Jeffery[14]; Putiri, Emily[15]; Bernardo, Patricia[15]; Burger, Robert A[15]; Matulonis, Ursula A[16]

[1]Stephenson Cancer Center, University of Oklahoma Health Sciences Center and the Sarah Cannon Research Institute, Oklahoma City, OK; [2]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [3]Mary Crowley Cancer Research, Dallas, TX; [4]Willamette Valley Cancer Institute and Research Center, Eugene, OR; [5]BC Cancer - Kelowna, Kelowna BC, Canada; [6]START Midwest, Grand Rapids, MI; [7]Arizona Oncology, Tucson, AZ; [8]NEXT Oncology, San Antonio, TX; [9]Lahey Clinic, Burlington, MA; [10]Huntsman Cancer Institute, University of Utah,
Salt Lake City, UT; [11]Arthur James Cancer Hospital, Ohio State University, Columbus, OH; [12]US Oncology, Oncology and Hematology Assoc. of Southwest VA, Salem, VA; [13]University of Alabama at Birmingham, Birmingham, AL; [14]Prisma Health Cancer Institute, Greenville, SC; [15]Mersana Therapeutics, Inc, Cambridge, MA; [16]Dana-Farber Cancer Institute, Boston, MA

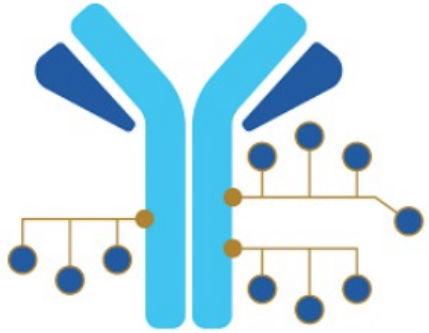
Abstract 76

ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 18 – 21, 2022

SGO 2022;Abstract 76.

Society of Gynecologic Oncology

Upifitamab Rilsodotin (UpRi): First-in-Class ADC Targeting NaPi2b



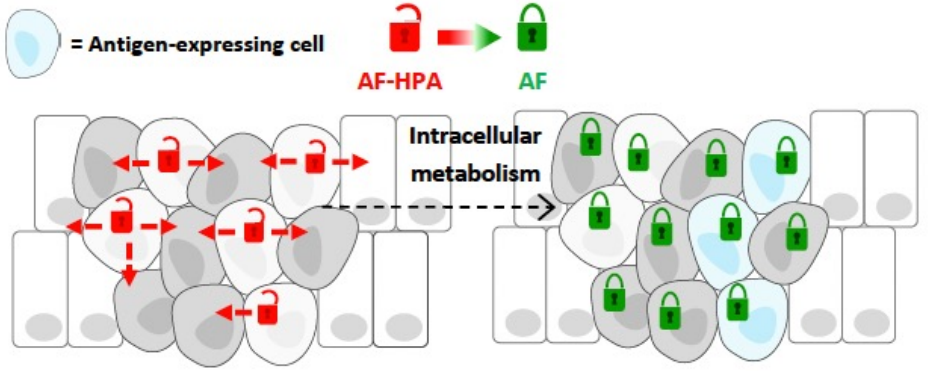
UpRi

Antibody: Humanized monoclonal anti-NaPi2b[1]

Linker: Polymer scaffold; cleavable ester linker[2]

Payload: AF-HPA (DolaLock-controlled bystander effect)[1]

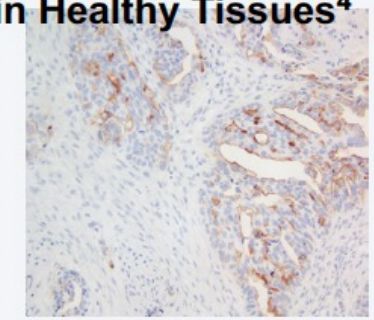
Drug-to-Antibody Ratio: ~10



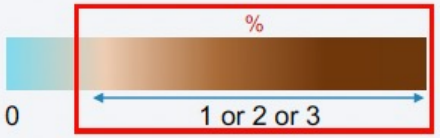
Upon ADC internalization into tumor cells and efficient release of payload, AF-HPA payload is metabolized to AF that remains highly potent but loses the ability to cross the cell membrane, locking it in the tumor, controlling the bystander effect, and consequently limiting impact on adjacent healthy cells[2,3]

NaPi2b Is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer With Limited Expression in Healthy Tissues[4]

- NaPi2b expressed by tumor cells in two-thirds of patients with high-grade serous ovarian cancer[2]
- NaPi2b is a lineage antigen (not an oncogene)[1]



NaPi2b IHC assay in development *– an optimal diagnostic assay would be robust, predictive, reproducible, easily able to distinguish a wide range of expression using* ***TPS scoring method***[2]



Richardson DL et al. SGO 2022;Abstract 76.

RTP RESEARCH TO PRACTICE

UpRi Phase Ib Study Schema

Patient Population: HGSOC[a] progressing after standard treatments; measurable disease per RECIST v1.1; ECOG PS 0 or 1

Ovarian Cancer Cohort
- 1–3 prior lines in platinum-resistant
- 4 prior lines regardless of platinum status
- High-grade serous histology
- Archived tumor and fresh biopsy (if medically feasible) for NaPi2b
- Exclusion: Primary platinum-refractory disease

UpRi IV Q4W until disease progression or unacceptable toxicity

36 mg/m² cohort initiated in August 2019

43 mg/m² to a max of ~80 mg cohort initiated in December 2019

Primary Objectives
- Evaluate safety and tolerability of MTD or RP2D
- Assess preliminary efficacy (ORR, DCR)

Secondary Objectives
- Association of tumor NaPi2b expression and objective tumor response using an IHC assay with a broad dynamic range to distinguish tumors with high and low NaPi2b expression
- Further assessment of preliminary anti-neoplastic activity (DoR)

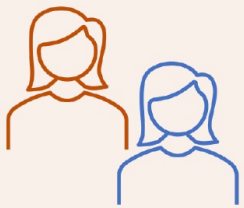
Assessment: Tumor imaging (MRI or CT) at baseline and every 2nd cycle; response assessed per RECIST v1.1

Richardson DL et al. SGO 2022;Abstract 76.

Expansion Cohort Experience Across a Range of Doses Allowed for Further Optimization of UpRi Profile

Updated Analysis of Phase 1b PROC Expansion Cohort to Evaluate Safety and ORR Based on UpRi Dose Levels[a]

Dose Group 36 (33–38 mg/m^2) (n=29)

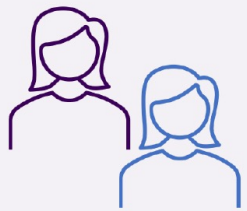


12 patients at **36 mg/m^2** starting dose (all BSA levels)

+

17 patients at ~80 mg starting dose with BSA ≥1.8 who received an actual dose of **33 to 38 mg/m^2**

Dose Group 43 (>38–43 mg/m^2) (n=66)



39 patients at **43 mg/m^2** starting dose with BSA <1.8

+

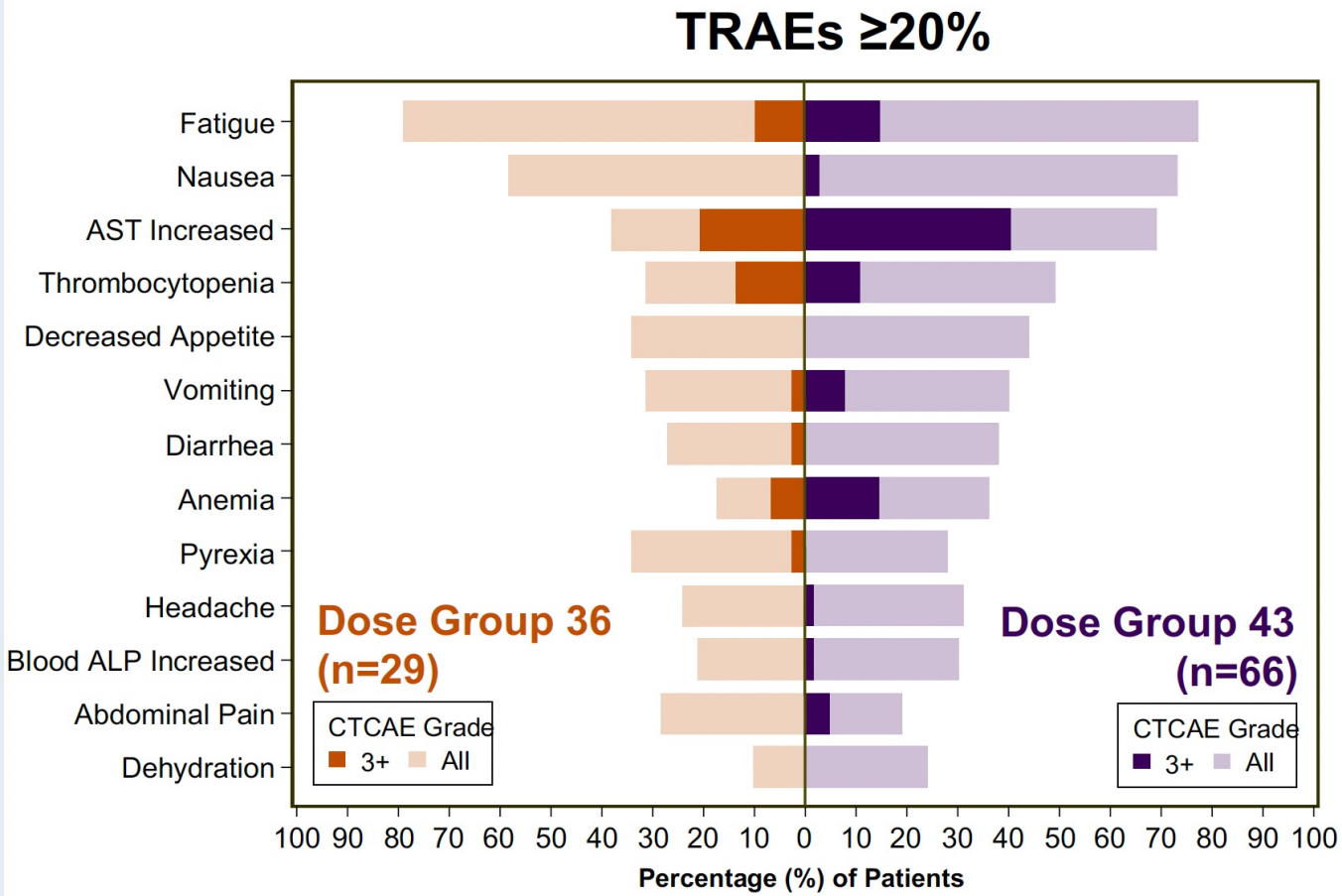
27 patients at ~80 mg starting dose with BSA ≥1.8 who received an actual dose of **>38 mg/m^2**

Richardson DL et al. SGO 2022;Abstract 76.

RTP RESEARCH TO PRACTICE

TRAEs by UpRi Dose Group

Dose Group 36 Had a More Favorable Safety Profile Compared to Dose Group 43



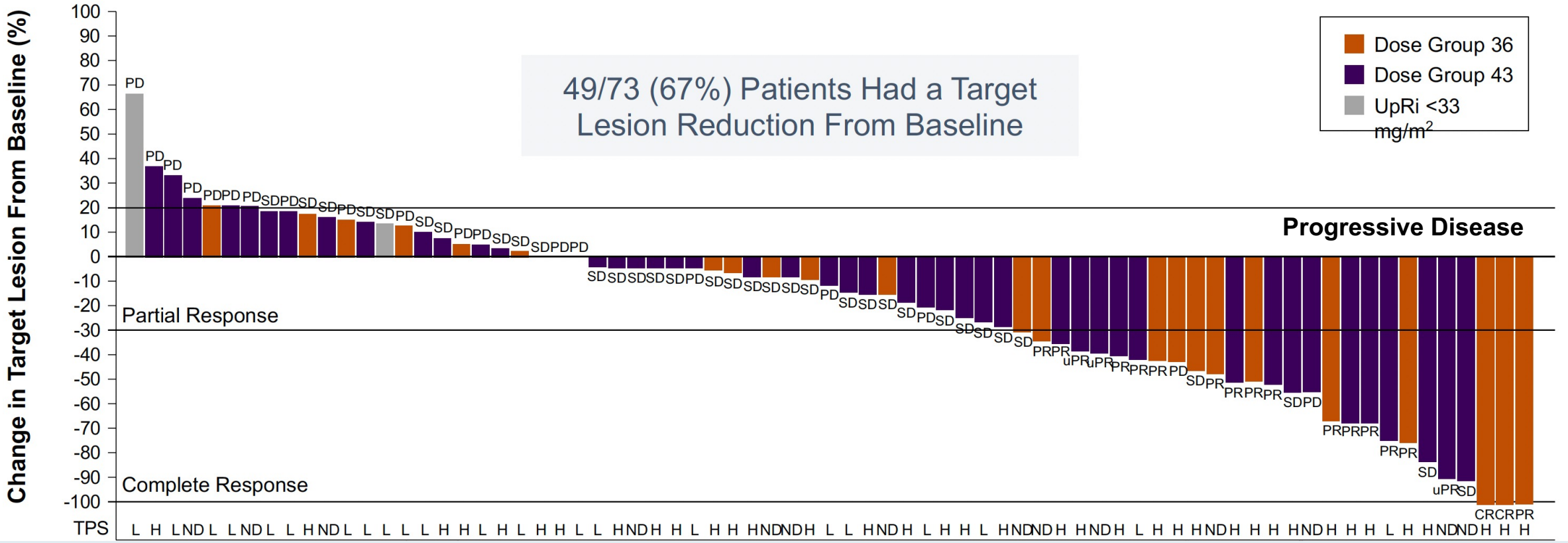
- No severe ocular toxicity, neutropenia, or peripheral neuropathy in either dose group
- 4 (14%) patients had treatment-related SAEs in Dose Group 36 vs 18 (27%) in Dose Group 43
- Lower frequencies and lower grade pneumonitis occurred in Dose Group 36 (with no Grade 3+) vs Dose Group 43[a]

Richardson DL et al. SGO 2022;Abstract 76.

RTP RESEARCH TO PRACTICE

Best Response by UpRi Dose Group

Similar Tumor Reduction in Both Dose Groups: Two-thirds of Patients Had Reductions in Target Tumor Lesions by RECIST 1.1



Richardson DL et al. SGO 2022;Abstract 76.

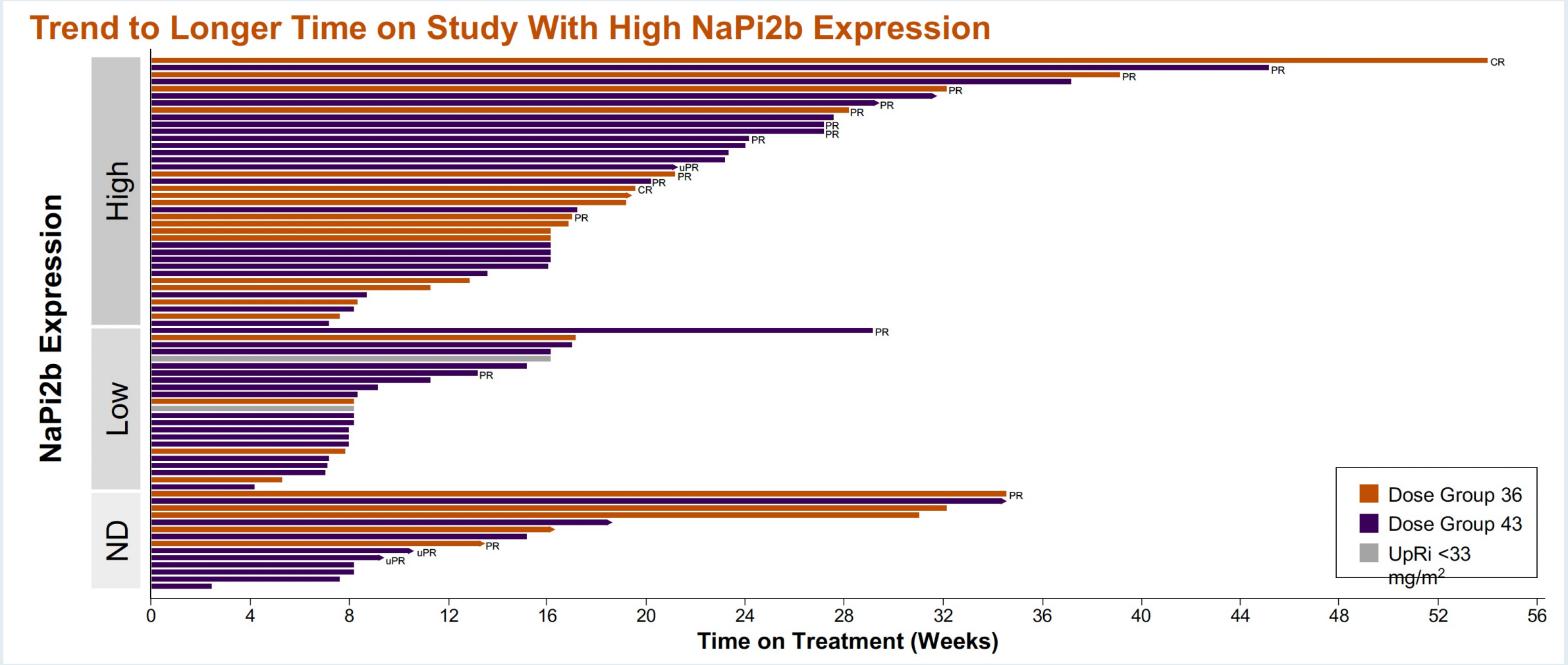
Confirmed ORR by UpRi Dose Group, NaPi2b Level and Duration of Response

		All Dose Levels	Dose Group 36	Dose Group 43
NaPi2b-High (TPS ≥75)	N	38	16	22
	ORR, n (%)	**13 (34)**	**7 (44)**	**6 (27)**
	CR, n (%)	2 (5)	2 (13)	0
	PR, n (%)	11 (29)	5 (31)	6 (27)
	DCR, n (%)	33 (87)	12 (75)	21 (95)
All NaPi2b Levels	N	75	25	48
	ORR, n (%)	**17 (23)**	**9 (36)**	**8 (17)**
	CR, n (%)	2 (3)	2 (8)	0
	PR, n (%)	15 (20)	7 (28)	8 (17)
	DCR, n (%)	54 (72)	18 (72)	35 (73)

- **Median DoR in patients (all dose levels) with NaPi2b-high ovarian cancer (n=13): 5 months**
- No obvious difference in median DoR observed between Dose Groups 36 and 43

Richardson DL et al. SGO 2022;Abstract 76.

Time on UpRi Study in Evaluable Patients



Richardson DL et al. SGO 2022;Abstract 76.

Ongoing UPLIFT (ENGOT-OV67/GOG-3048) Study Schema

Patient Population: HGSOC[a] progressing after standard treatments; measurable disease per RECIST v1.1; ECOG PS 0 or 1; enrolling regardless of NaPi2b expression

Key Inclusion Criteria

- Platinum-resistant ovarian cancer (PROC)
- 1–4 prior lines of therapy
- Grade ≤2 peripheral neuropathy
- Archival or fresh tissue required for biomarker evaluation

Key Exclusion Criteria

- 1–2 prior lines bevacizumab-naive
- Primary platinum-refractory disease

UpRi 36 mg/m^2 up to max 80 mg; IV Q4W

Primary Endpoint

- Confirmed ORR in NaPi2b-high (N = ~100)

Secondary Endpoint

- Confirmed ORR in overall population (N = up to ~180 including 100 NaPi2b-high)

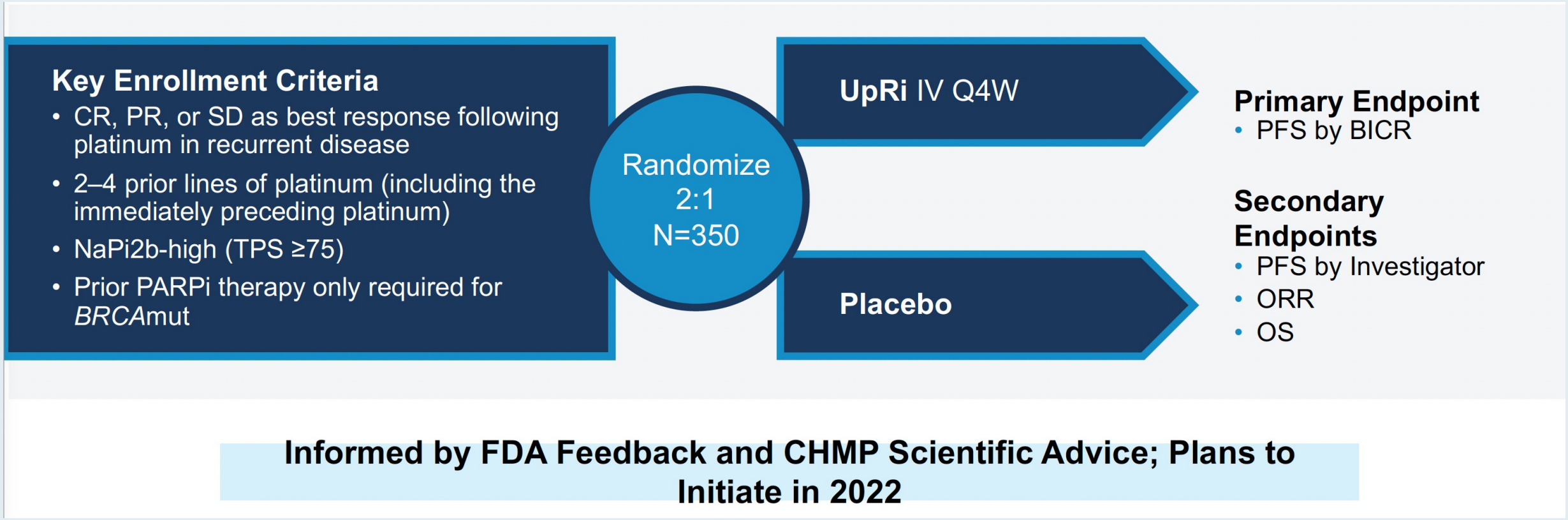
Other Secondary Endpoints

- DoR
- Safety

Prospectively-defined retrospective analysis to validate NaPi2b biomarker cutoff

Richardson DL et al. SGO 2022;Abstract 76.

Ongoing UP-NEXT Phase III (ENGOT-OV71-NSGO-CTU/GOG-3049) Study Schema



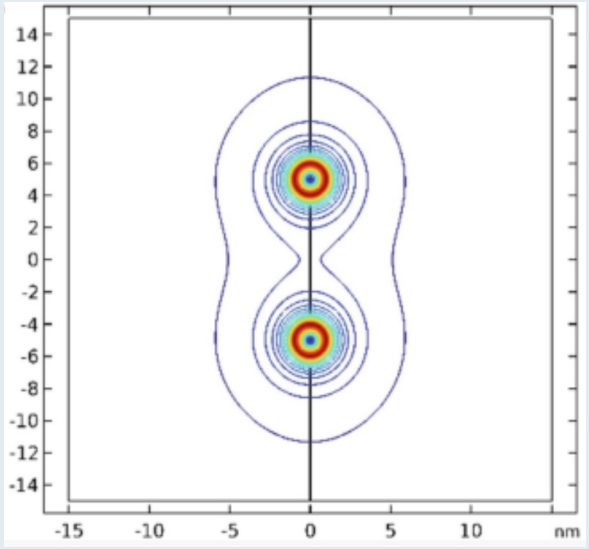
Informed by FDA Feedback and CHMP Scientific Advice; Plans to Initiate in 2022

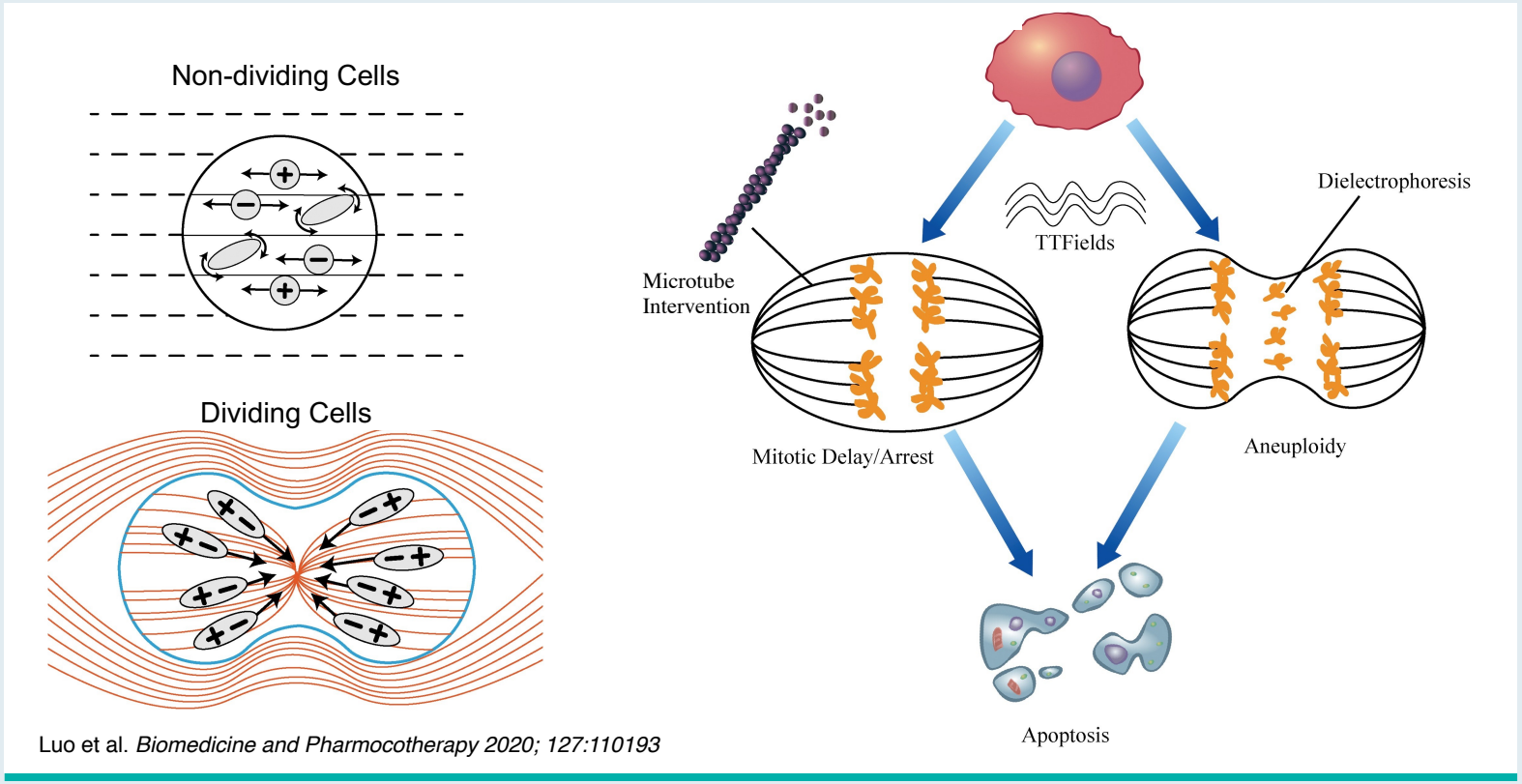
Richardson DL et al. SGO 2022;Abstract 76.

RTP RESEARCH TO PRACTICE

Tumor Treating Fields (TTF)

Dividing Cell under TTF
Selective Electric Field Sensitivity



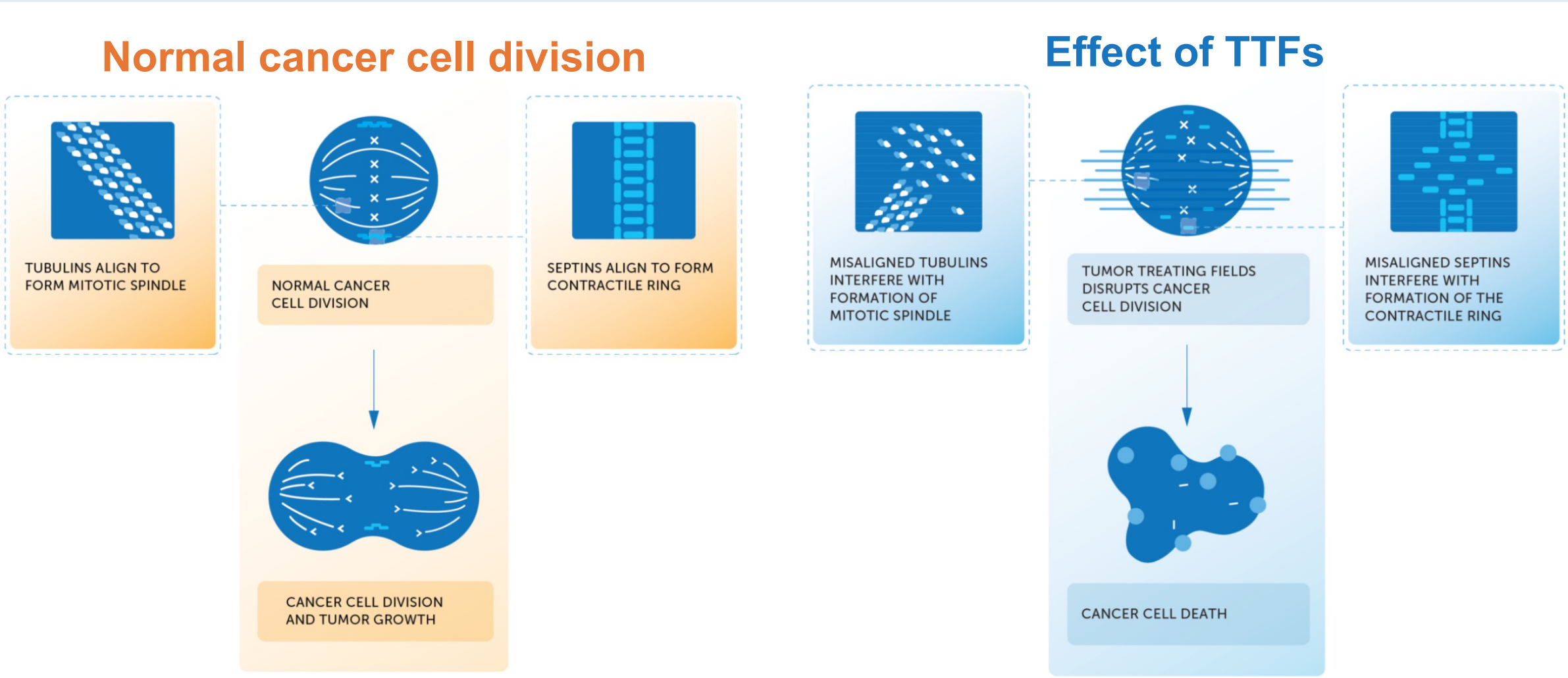


Luo et al. *Biomedicine and Pharmocotherapy 2020; 127:110193*

Luo et al. *Biomed Pharmacother* 2020;127:11013.

RTP RESEARCH TO PRACTICE

Effect of TTFs on Dividing Cancer Cells



www.novocure.com/our-therapy/

RTP RESEARCH TO PRACTICE

NovoTTF-100L™(O) System: A Portable Medical Device That Allows Normal Daily Activities

Vergote I et al. *Gynecol Oncol* 2018;150(3):471-7.

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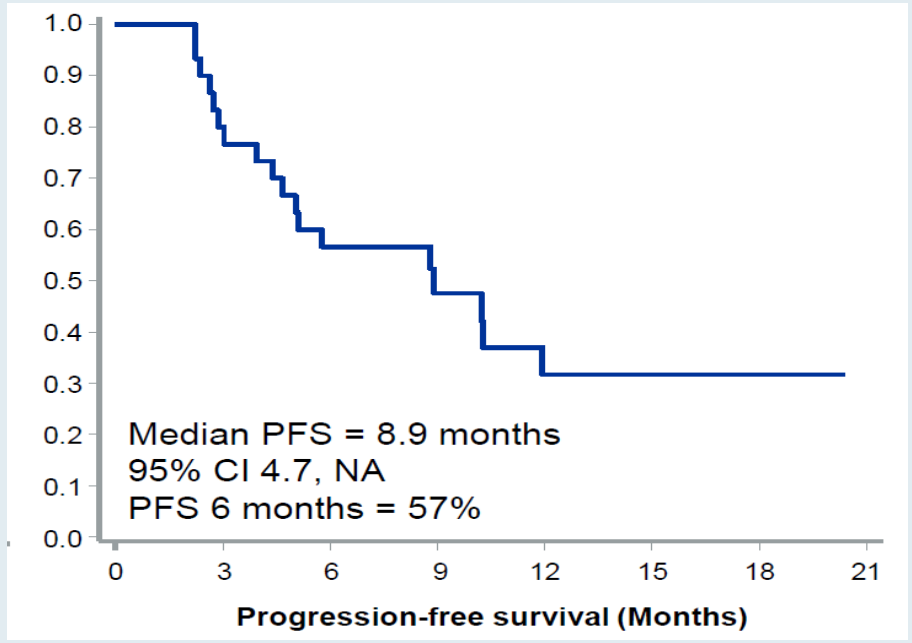
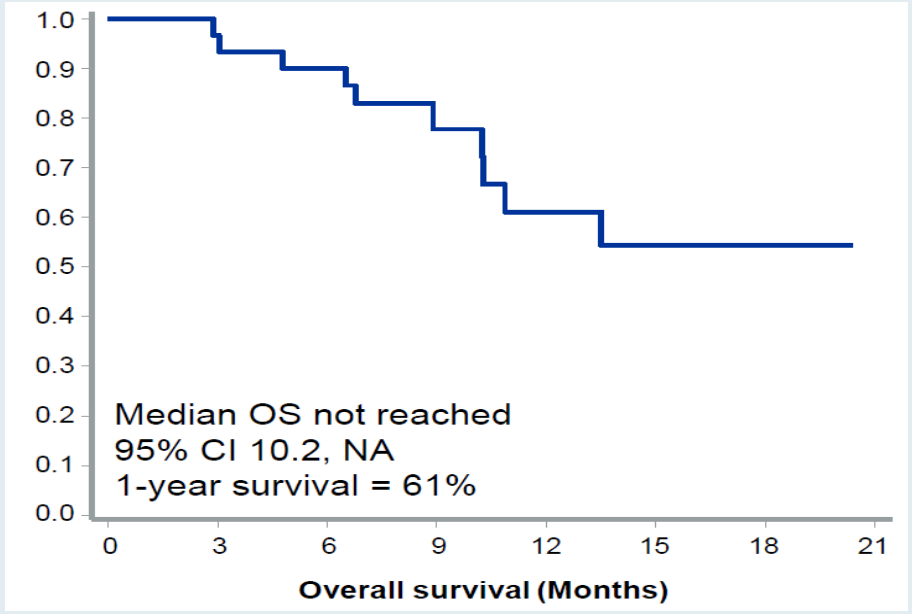
INNOVATE: TTFs + Paclitaxel

Outcomes (PROC)	TTFields + paclitaxel (n = 31)
Median OS in months (95% CI)	NR
Survival rates, % (95% CI) 6 months 12 months	 90 (72-97) 61 (37-78)
Median PFS in months (95% CI)	8.9 (4.7-NA)
PFS rates, % (95% CI) 6 months	 57 (37-72)
Best response in patients w/ available radiologic data,* n (%) CR PR SD PD CBR	28 (90%) 0 (0) 7 (25%) 13 (46%) 8 (29%) 20 (71%)





Vergote I et al. *Gynecol Oncol* 2018;150(3):471-7.

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INNOVATE: Select Adverse Events

Adverse event	TTFields + paclitaxel (N = 31)	
	Grade 1-2	Grade 3-4
Skin irritation	26 (84%)	2 (6%)
Abdominal pain	13 (42%)	0
Constipation	8 (26%)	0
Diarrhea	15 (48%)	2 (6%)
Nausea	13 (42%)	0
Vomiting	7 (23%)	0
Fatigue	10 (32%)	0
Edema	14 (45%)	0
Dysgeusia	8 (26%)	0
Neuropathy	14 (45%)	0

Vergote I et al. *Gynecol Oncol* 2018;150(3):471-7.

Recommendation Announced to Continue the Phase III Pivotal INNOVATE-3 Study of Tumor Treating Fields for Ovarian Cancer

Press Release — March 23, 2022

"The results of a pre-specified interim analysis for the phase 3 pivotal INNOVATE-3 study evaluating the safety and efficacy of Tumor Treating Fields (TTFields) together with paclitaxel for the treatment of patients with platinum-resistant ovarian cancer were announced today.

An independent data monitoring committee (DMC) reviewed the safety data for all platinum-resistant ovarian cancer patients enrolled on the trial. In addition, an analysis of overall survival was performed on the first 540 patients randomized. The interim analysis did not indicate a need to increase the sample size and the DMC recommended that the study should continue to final analysis as planned."

www.yahoo.com/now/novocure-announces-favorable-recommendation-continue-120000088.html

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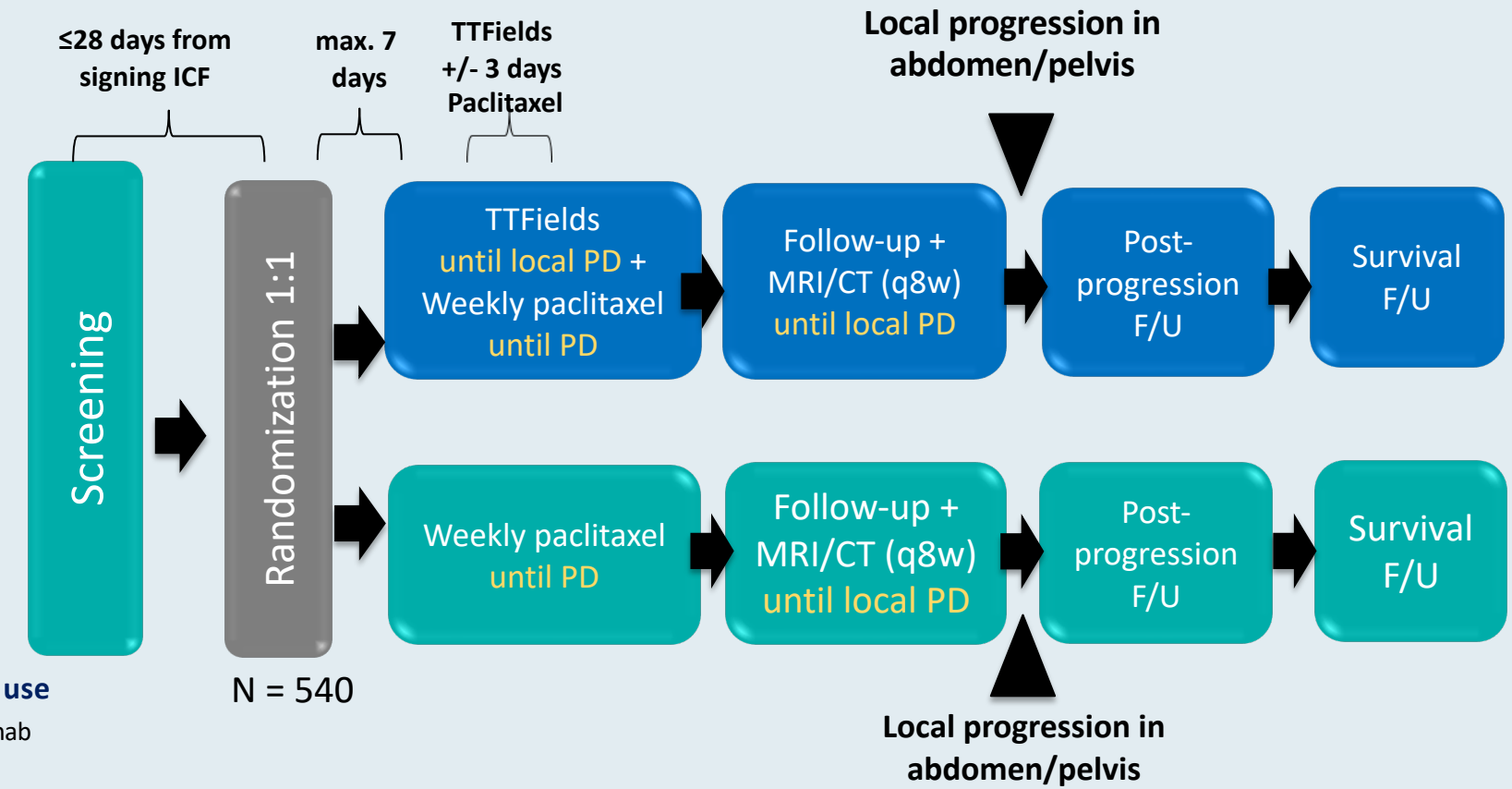
INNOVATE-3 (ENGOT-OV50/GOG-3029) (TTFields, 200 kHz)

Enrollment target (n = 540)

Number of sites (n = 110)

- ENGOT enrollment began March 2019
- GOG enrollment began February 2020

Enrollment closed October 2020



Stratification

- **Prior therapy**
  - no prior systemic therapy following PROC
  - one prior line
  - two prior lines
- **Prior bevacizumab use**
  - prior bevacizumab use
  - no prior bevacizumab
- **BRCA status**
  - mutated BRCA
  - wild type BRCA/ unknown

https://clinicaltrials.gov/ct2/show/NCT03940196

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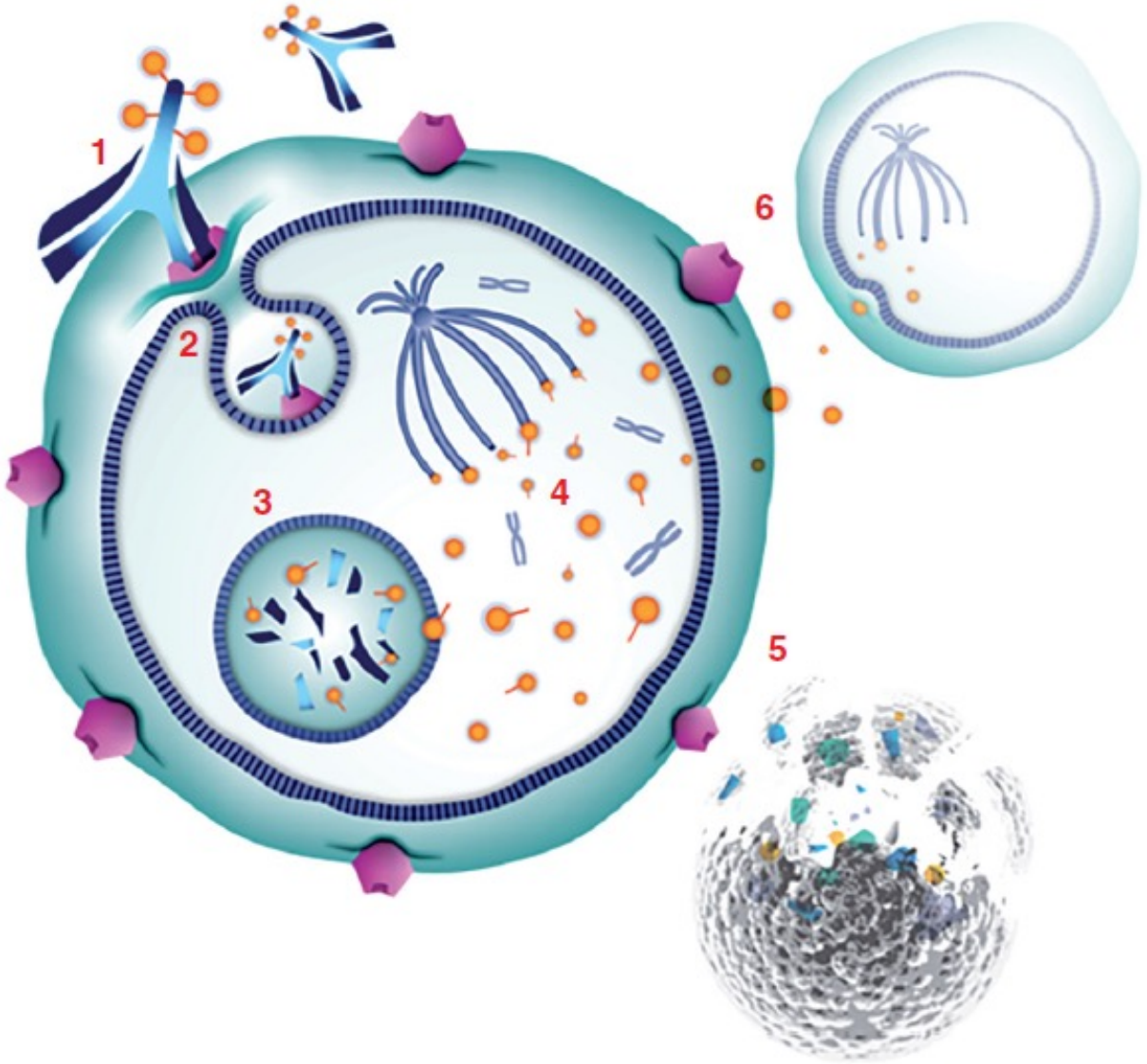
Mirvetuximab Soravtansine: Mechanism of Action



(1) Mirvetuximab soravtansine binds with high affinity to FRα expressed on the tumor cell surface

(2) The antibody-drug conjugate (ADC)/receptor complex becomes internalized via antigen-mediated endocytosis

(3) Lysosomal processing releases active DM4 catabolites from the ADC molecule

(4) These maytansinoid derivatives inhibit tubulin polymerization and microtubule assembly

(5) The potent antimitotic effects result in cell-cycle arrest and apoptosis

(6) Active metabolites can also diffuse into neighboring cells and induce further cell death — in other words, bystander killing

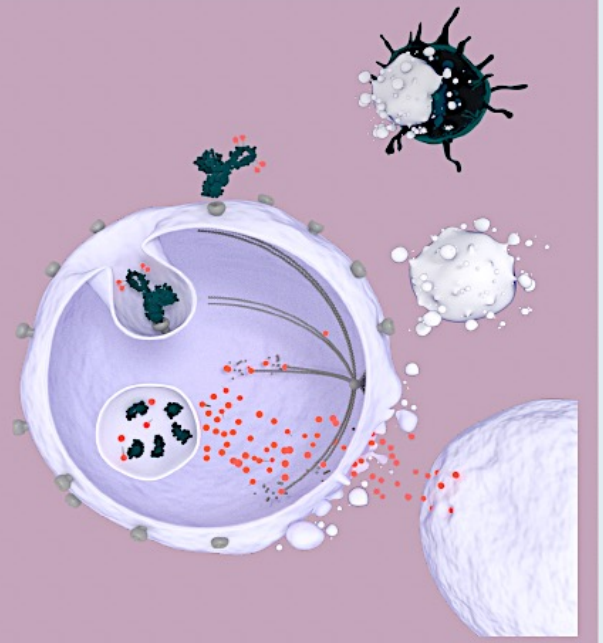
Moore K et al. *Future Oncol* 2018:14(2);123-36.

RTP RESEARCH TO PRACTICE

Efficacy and Safety of Mirvetuximab Soravtansine in Patients With Platinum-Resistant Ovarian Cancer With High Folate Receptor Alpha Expression: Results From the SORAYA Study

Ursula A. Matulonis,[1] Domenica Lorusso,[2] Ana Oaknin,[3] Sandro Pignata,[4] Hannelore Denys,[5] Nicoletta Colombo,[6] Toon Van Gorp,[7] Jason A. Konner,[8] Margarita Romeo Marin,[9] Philipp Harter,[10] Conleth G. Murphy,[11] Jiuzhou Wang,[12] Elizabeth Noble,[12] Brooke Esteves,[12] Michael Method,[12] Robert L. Coleman[13]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Fondazione Policlinico Universitario A. Gemelli, IRCCS and Catholic University of Sacred Heart, Rome, Italy; [3]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [4]Istituto Nazionale Tumori di Napoli Fondazione G Pascale IRCCS, Naples, Italy; [5]Ghent University Hospital, Ghent, Belgium; [6]European Institute of Oncology IRCCS, Milan, Italy and University of Milan-Bicocca, Milan, Italy; [7]University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium; [8]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [9]Institut Català d'Oncologia, Badalona, Spain; [10]Ev. Kliniken Essen-Mitte, Essen, Germany; [11]Bon Secours Hospital and Cancer Trials, Cork, Ireland; [12]ImmunoGen, Inc., Waltham, MA, USA; [13]US Oncology Research, Texas Oncology, The Woodlands, TX, USA



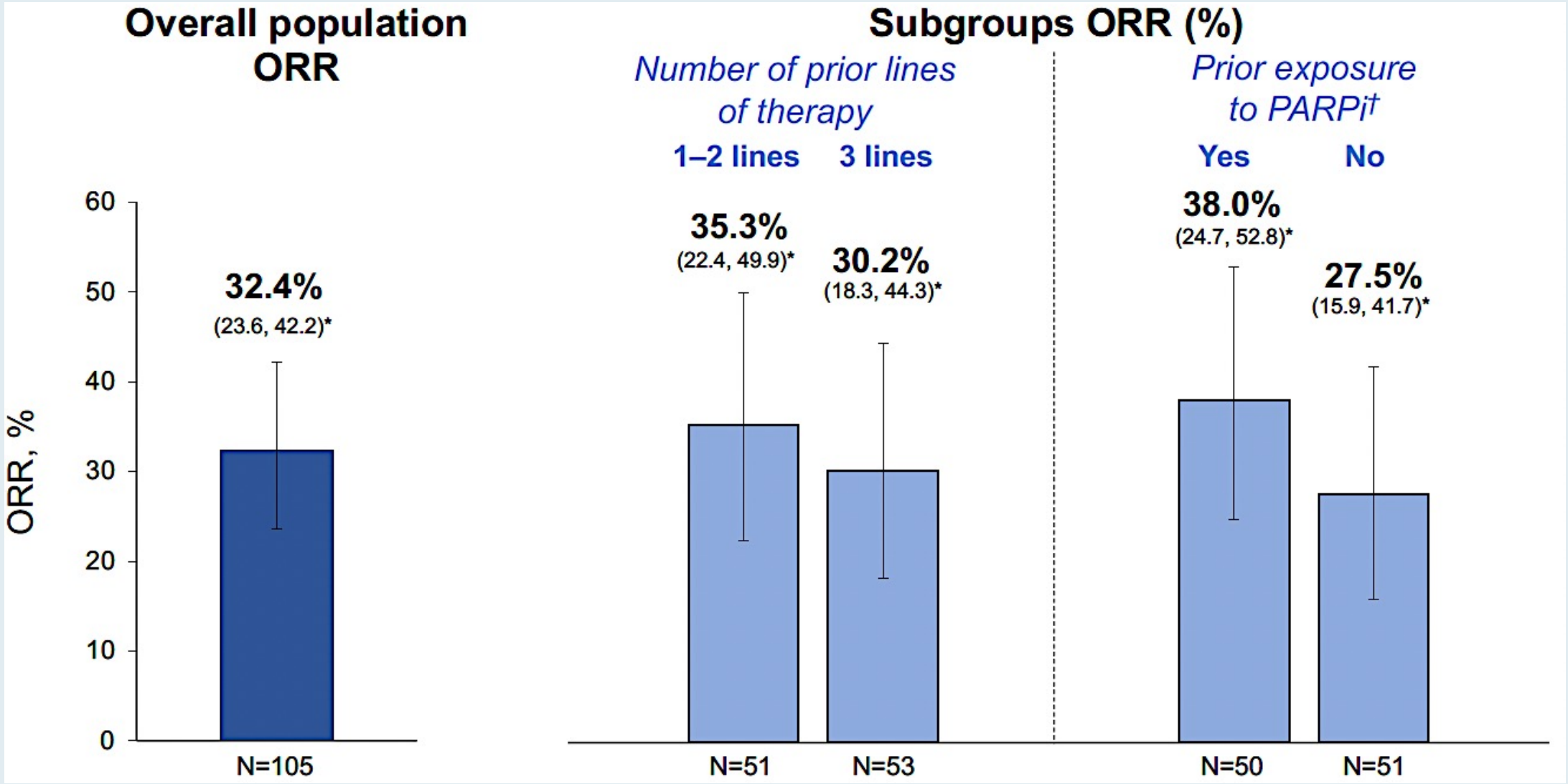
SORAYA

ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 18 - 21, 2022

SGO 2022;Abstract LBA4.

Society of Gynecologic Oncology

SORAYA: Investigator-Assessed Objective Response Rate by Prior Therapy



Matulonis UA et al. SGO 2022;Abstract LBA4.

SORAYA: Treatment-Related Adverse Events (≥10%)

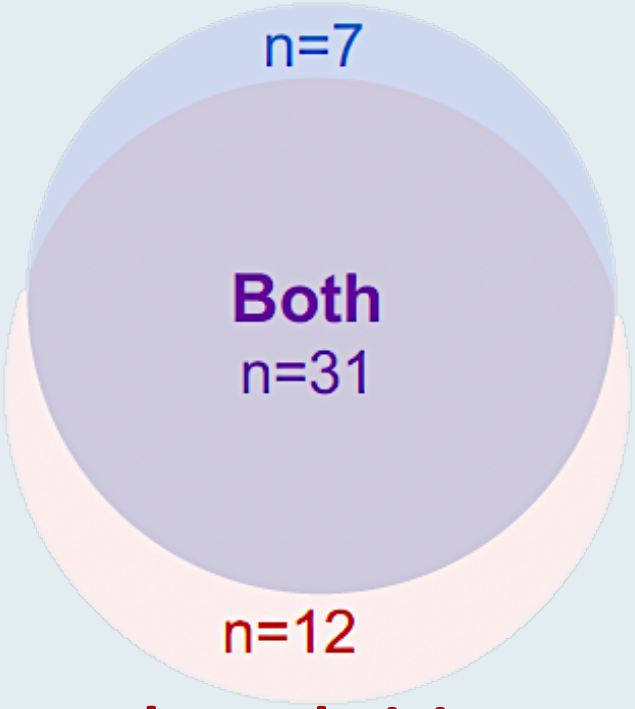
TRAEs, n (%)	All Grades	Grade 3	Grade 4
Patients with any event	91 (86)	29 (27)	1 (1)
Blurred vision	43 (41)	6 (6)	0 (0)
Keratopathy*†	38 (36)	8 (8)	1 (1)
Nausea	31 (29)	0 (0)	0 (0)
Dry eye	24 (23)	2 (2)	0 (0)
Fatigue	24 (23)	1 (1)	0 (0)
Diarrhea	23 (22)	2 (2)	0 (0)
Asthenia	16 (15)	1 (1)	0 (0)
Photophobia	15 (14)	0 (0)	0 (0)
Peripheral neuropathy	13 (12)	0 (0)	0 (0)
Decreased appetite	13 (12)	1 (1)	0 (0)
Vomiting	12 (11)	0 (0)	0 (0)
Neutropenia	11 (10)	1 (1)	0 (0)

- Most AEs were low-grade, reversible ocular and GI events
- Serious Grade ≥3 TRAEs were reported in 8% of patients
- TRAEs led to dose delay in 32% and dose reduction in 19%
- 7 patients (7%) discontinued treatment due to TRAEs
- 1 death was recorded as possibly related to study drug
  - Respiratory failure
  - Autopsy: No evidence of drug reaction; lung metastases

Matulonis UA et al. SGO 2022;Abstract LBA4.

Unique Events Associated with Mirvetuximab Soravtansine: Keratopathy and Blurred Vision

Events developed in 50/106 (47%) patients: mostly low grade



Proactive supportive care
– Lubricating artificial tears
– Corticosteroid eye drops

Predictable
– Median time to onset: cycle 2 (~1.5 months)

Manageable with dose modifications, if needed
– 22% of patients (23/106) had dose delay and/or reduction

Reversible
– At data cutoff: >80% of Grade 2-3 events had resolved to Grade 0-1
– 9 patients still receiving mirvetuximab soravtansine or being followed up for resolution

<1% discontinuation due to ocular events
– 1 of 106 patients discontinued due to Grade 4 keratopathy, which resolved within 15 days

Matulonis UA et al. SGO 2022;Abstract LBA4.

Mirvetuximab Soravtansine (MIRV) in Patients with Platinum-Resistant Ovarian Cancer with High Folate Receptor Alpha (FRα) Expression: Characterization of Antitumor Activity in the SORAYA Study

Matulonis UA et al.

ASCO 2022;Abstract 5512.

Track: Gynecologic Poster Session

Case 5 — Joyce F Liu, MD, MPH

- 55yo woman
- History of triple-negative cancer 15 years prior, treated with R-sided lumpectomy, adjuvant chemo and RT
  - Local recurrence 3 years later, treated with neoadjuvant cisplatin/docetaxel with complete remission, followed by mastectomy
  - Germline testing negative for *BRCA* mutation
- Begins to develop rising CA27-29
  - Imaging: Extensive omental caking. +Pleural effusion. CA125 421
  - Path: Metastatic adenocarcinoma most c/w high grade serous ovarian cancer
- Neoadjuvant carboplatin/paclitaxel → CA125 1,017 to 82, response on scan. Interval cytoreductive surgery, followed by carboplatin/paclitaxel/bevacizumab
  - Repeat genetic testing demonstrates *BRCA1* mutation (del exon 17)
- Enrolls to OVARIO trial and receives bevacizumab/niraparib maintenance (1 year bevacizumab), niraparib continued for 1.5 years, then develops disease progression
- Receives repeat carboplatin/paclitaxel chemotherapy with stable disease and goes on treatment holiday after 6 cycles
  - Disease progression 3 months later

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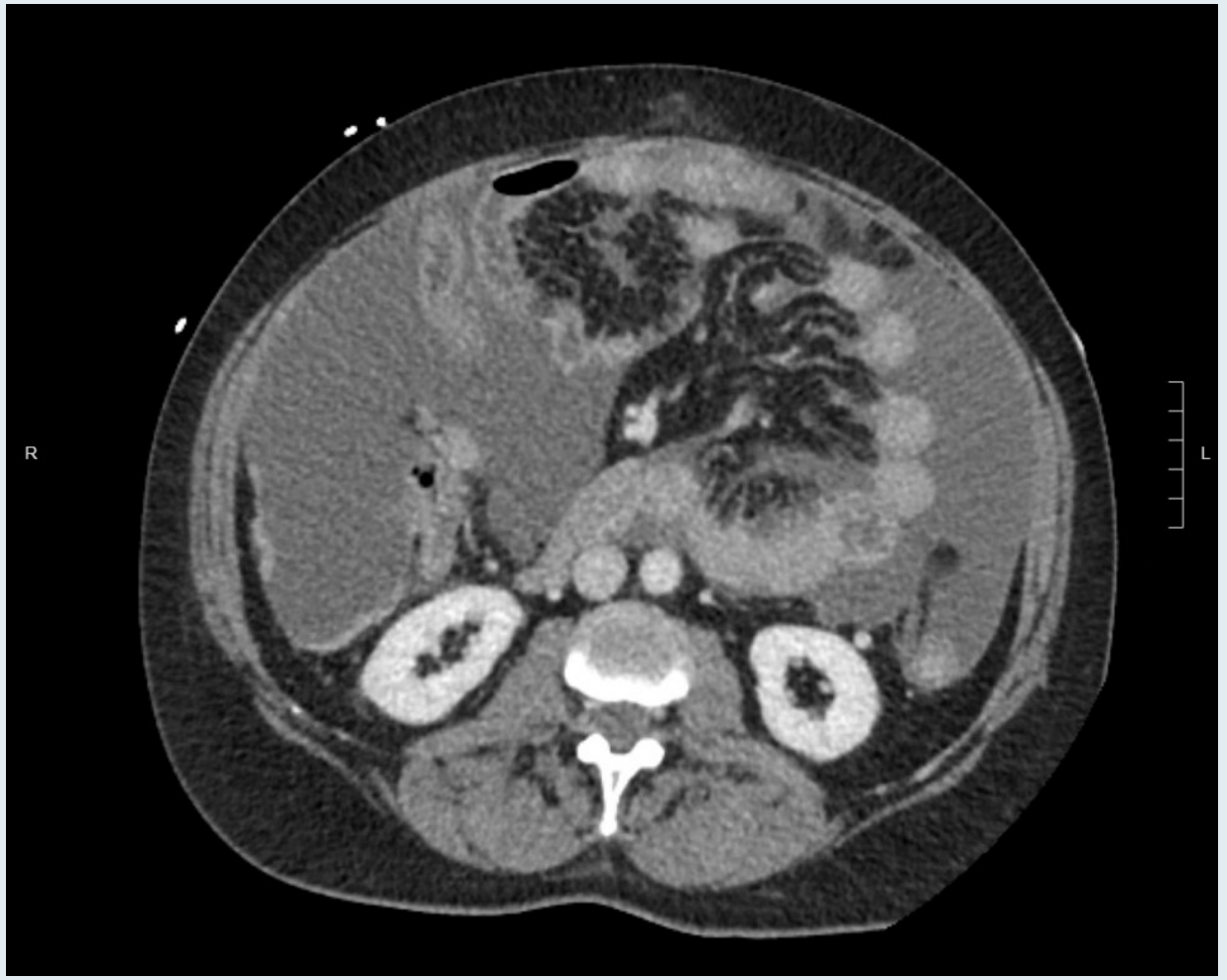
Case 5 — Joyce F Liu, MD, MPH

CT Scan at Progression; CA125 522



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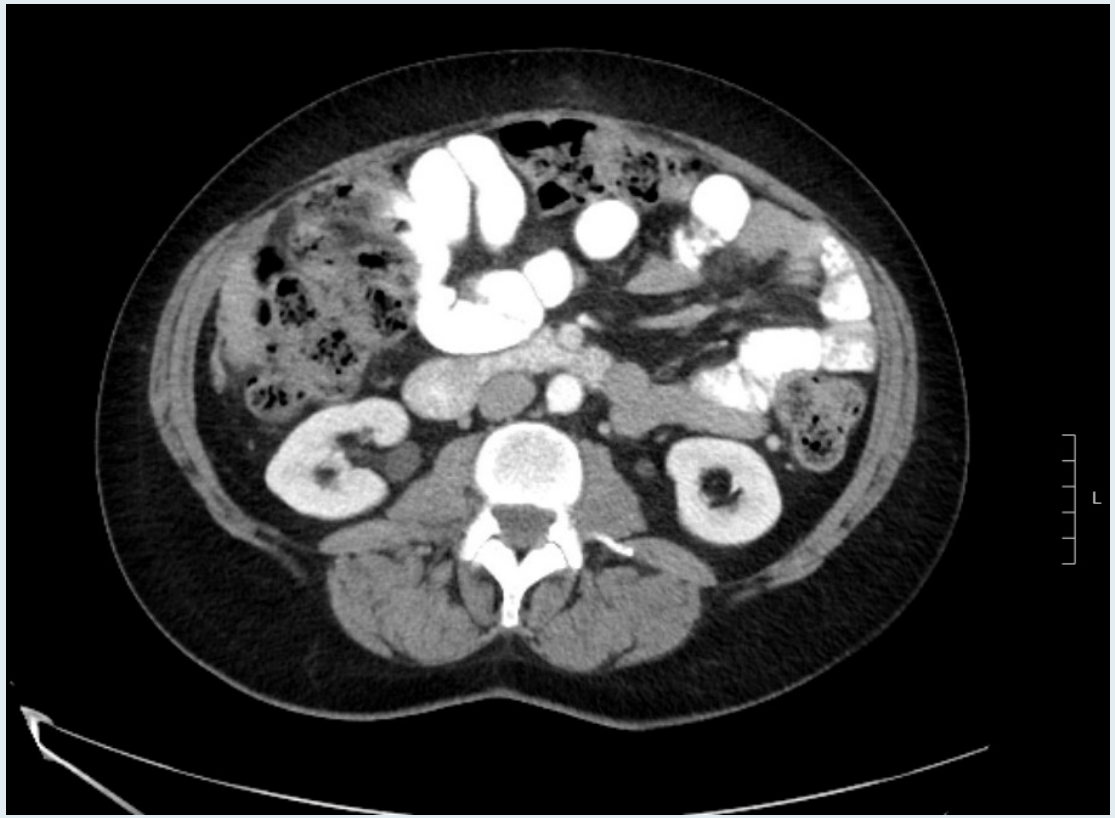
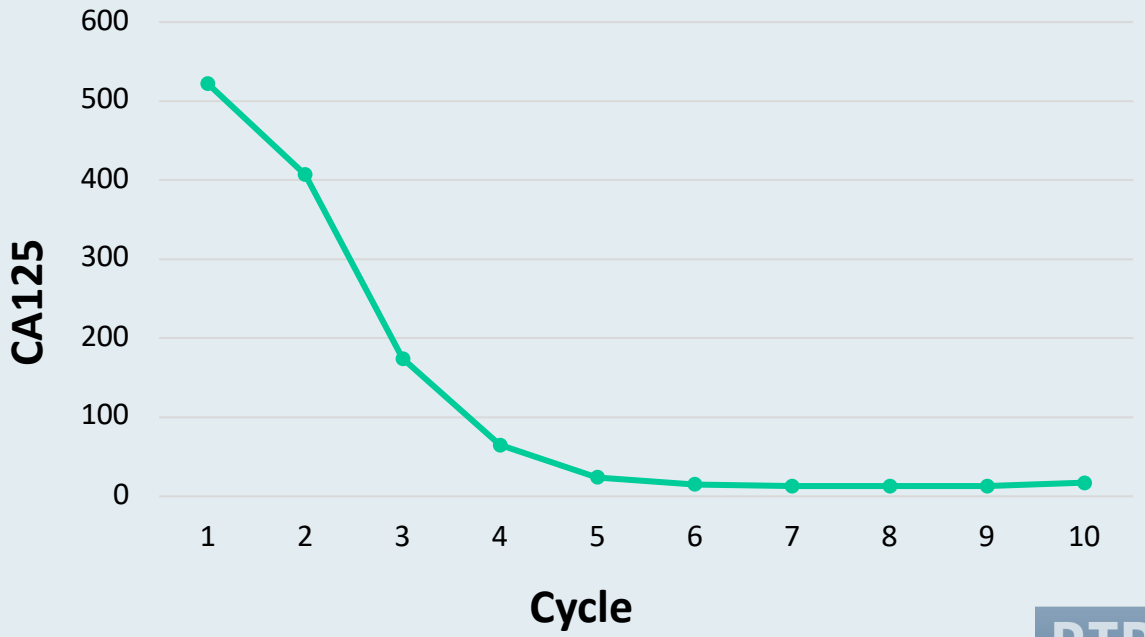
Case 5 — Joyce F Liu, MD, MPH

- **Tumor testing positive for FR alpha**
- **Enrolled to SORAYA trial with mirvetuximab soravtansine**

Imaging after 2 cycles:



CA125 trend on study



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Case 5 — Joyce F Liu, MD, MPH

- **Complete resolution of ascites and all symptoms**
- **Bought a chainsaw for herself as a Christmas gift and had a friend teach her how to use it**
  - **Cutting up tree trunks and wood in her backyard**
- **Did notice some slightly dry eyes bilaterally**
  - **Treated with lubricating drops and stable**

Case 6 — Antonio González-Martín, MD, PhD

- **Diagnosed at 68 y/o with HGSC FIGO Stage IIIC tBRCAwt HRDuk**
- **She received PCS in January 2018 with outcome of complete cytoreduction**
- **1st line systemic therapy: paclitaxel-carboplatin-bevacizumab**
- **Last platinum in June 2018**
- **1st relapse detected by increment of CA 125 to 51 U/mL (previously normal). A PET-CT showed no extra-abdominal locations and disease was considered suitable for complete resection by the MDT**
- **SCS in February 2020 with outcome of complete cytoreduction**
- **2nd line systemic therapy: 4 cycles of carboplatin-PLD (last in July 2020) followed by niraparib maintenance started in August 2020.**

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Case 6 — Antonio González-Martín, MD, PhD

Second Progression and Treatment

- **In November a CT showed perihepatic implant and mesenteric nodules.**

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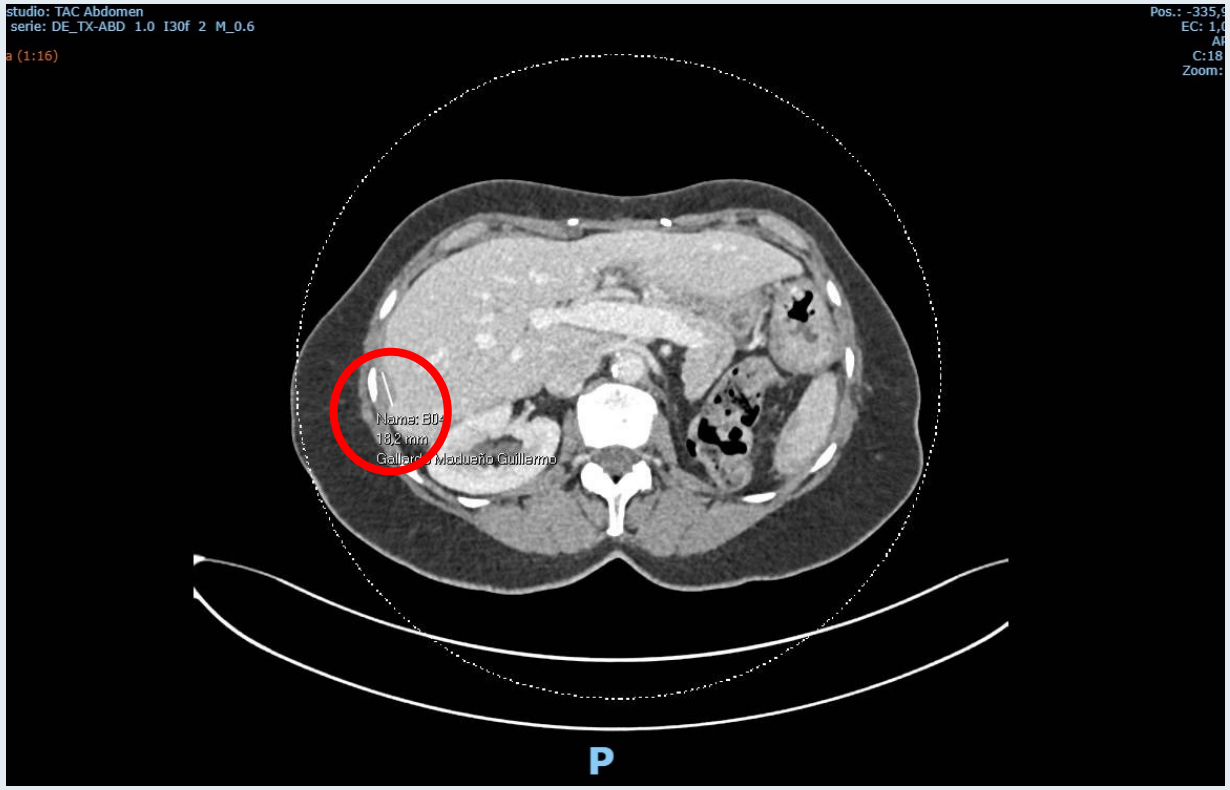
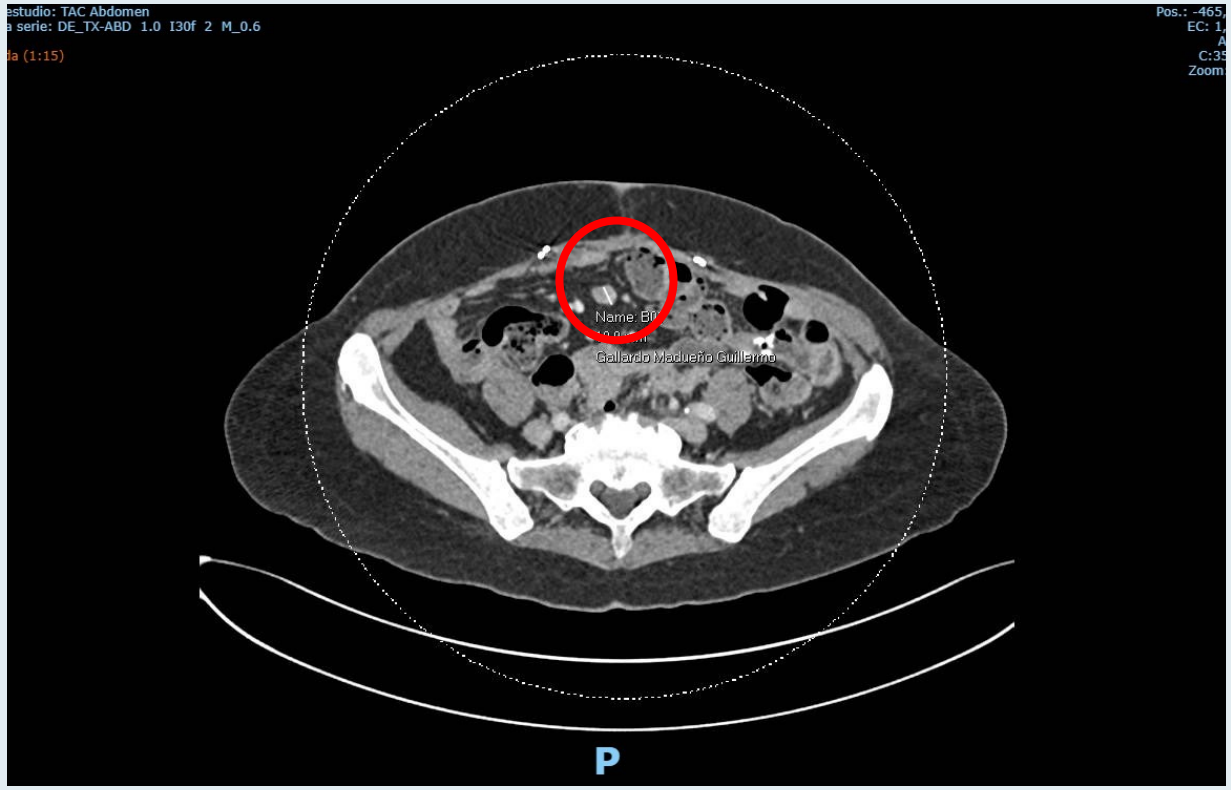
Case 6 — Antonio González-Martín, MD, PhD

Basal CT Scan





Case 6 — Antonio González-Martín, MD, PhD

Second Progression and Treatment

- **In November a PET-CT showed perihepatic implant and mesenteric nodules.**
- **Patient signed pre-screening for SORAYA trial and resulted eligible.**
- **She started on December 17th, 2020 mirvetuximab soravtansine 6 mg/kg.**

Case 6 — Antonio González-Martín, MD, PhD

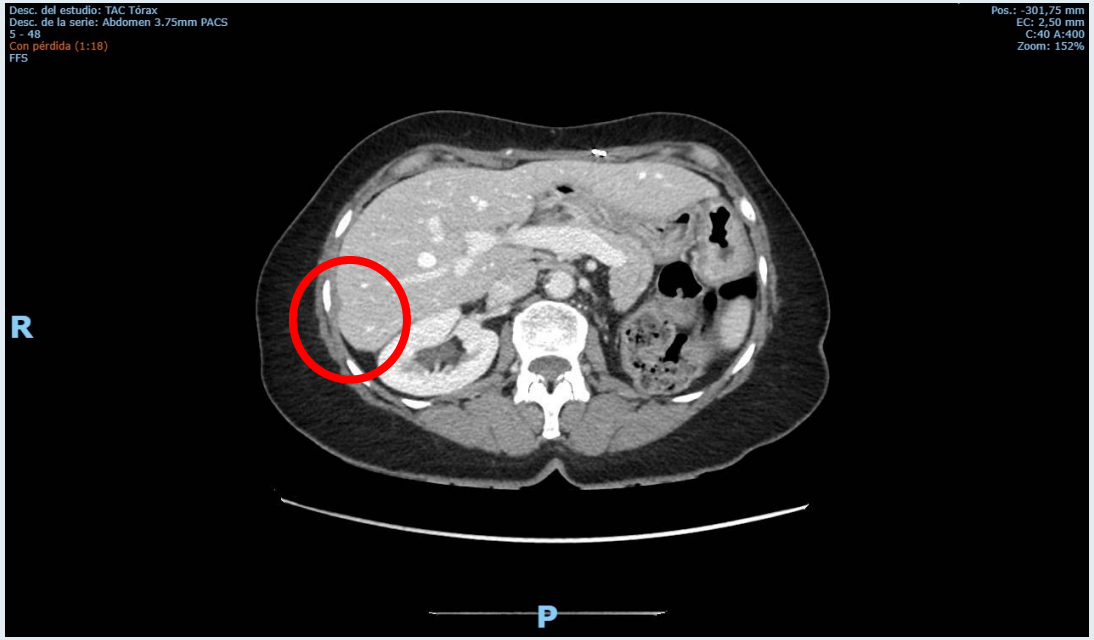
Second Progression and Treatment

- **Safety**
  - **Grade 3 diarrhoea after cycle 1, that required one dose reduction to 5 mg/kg**
  - **Grade 3 keratitis and Grade 3 blurred vision after cycle 4, that decreased to Grade 1 with topic corticosteroids, and continued mirve with new dose reduction**
- **She got PR after 4th cycle and CR after cycle 8**

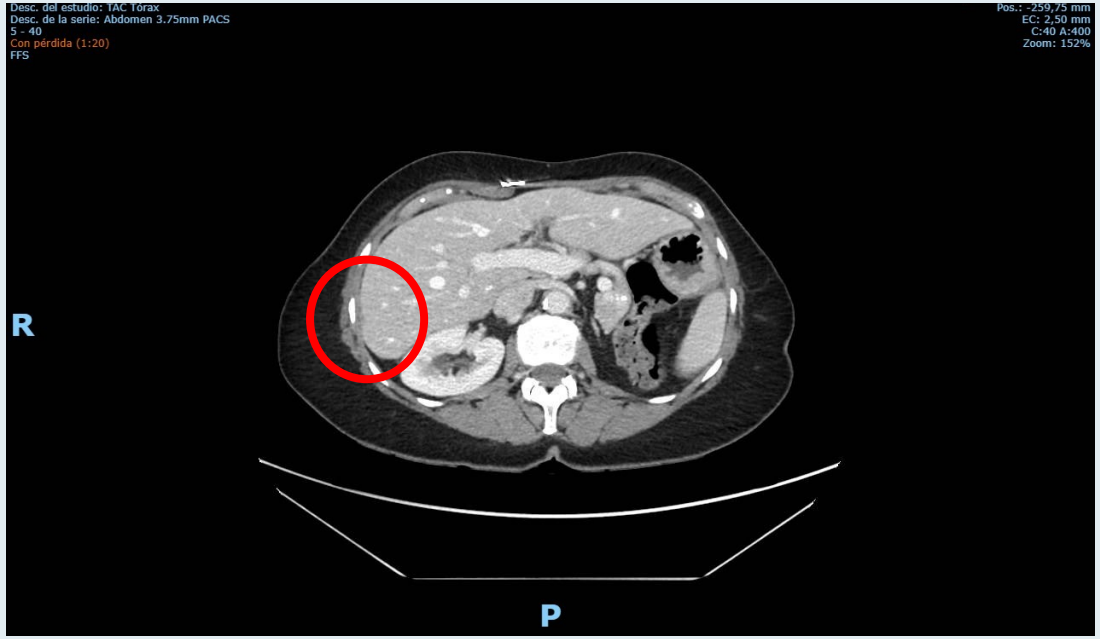
Case 6 — Antonio González-Martín, MD, PhD

Best Response

After cycle 4



After Cycle 8



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Case 6 — Antonio González-Martín, MD, PhD

Second Progression and Treatment

- **Patient continued treatment for 15 cycles and progressed on November 19th, 2021**
- **The PFS on mirvetuximab was 11 months and prior PFS after platinum-based therapy and niraparib maintenance was 4 months**

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Appendix of Key Data Sets

Phase 2 OVARIO Study of Niraparib + Bevacizumab Therapy in Advanced Ovarian Cancer Following Frontline Platinum-Based Chemotherapy with Bevacizumab

Melissa M. Hardesty,[1] Thomas Krivak,[2] Gail S. Wright,[3] Erika Hamilton,[4] Evelyn L. Fleming,[5] Jimmy Belotte,[6] Erika Keeton,[6] Ping Wang,[6] Aine Clements,[7] Heidi J. Gray,[8] Gottfried E. Konecny,[9] Richard G. Moore,[10] Debra L. Richardson[11]

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ANNUAL MEETING ON WOMENS' CANCER
BUILDING BRIDGES // BREAKING BARRIERS

Society of Gynecologic Oncology

SGO 2022;Abstract 40.

RTP RESEARCH TO PRACTICE

OVARIO Study Design

Patients with newly diagnosed high-grade serous or endometrioid stage IIIB to IV epithelial ovarian, fallopian tube, or peritoneal cancer who achieved a CR, PR, or NED result after front-line platinum-based chemotherapy + bevacizumab

All patients underwent tissue testing for HRd at enrollment

Niraparib (200 or 300 mg QD) + bevacizumab (15 mg/kg Q3W)

Starting niraparib dose, n (%)	N=105
200 mg (<77 kg and/or platelet count <150,000/µL)	82 (78)
300 mg (all others)	23 (22)

Endpoint assessment	
Primary endpoint	• PFS rate at 18 months (PFS18)
Secondary endpoints	• PFS • Overall survival • RECIST or CA-125 PFS • Time to first subsequent therapy • Time to second subsequent therapy • Safety and tolerability • Patient-reported outcome
Exploratory endpoints	• PFS rate at 6 months (PFS6) and 12 months (PFS12)
Statistical analysis plan	• Efficacy: PFS18 and PFS24 will be estimated by frequency analysis, with corresponding 95% exact CI will be reported • The time to event endpoints (PFS, TFST, TSST) will be analyzed using Kaplan-Meier methodology • Progression will be assessed by RECIST v1.1 per investigator

Hardesty et al. SGO 2022;Abstract 40.

OVARIO: Treatment Related Adverse Events (TRAEs)

Parameter, n (%)	N=105		
	Related to nira or bev	Related to nira	Related to bev
Any TRAE	105 (100)	104 (99)	96 (91)
Any Grade ≥3 TRAE	84 (80)	81 (77)	54 (51)
Any serious TRAE	21 (20)	19 (18)	7 (7)
TRAE leading to treatment discontinuation	42 (40)	32 (30)	23 (22)
TRAE leading to dose reduction	78 (74)	77 (73)	27 (26)
TRAE leading to treatment interruption	93 (88)	90 (86)	58 (55)

TRAEs in ≥20% of patients (N=105) Related to niraparib or bevacizumab		
Preferred term, n (%)	Any Grade	Grade ≥3
Thrombocytopenia[a]	74 (70)	41 (39)
Fatigue	60 (57)	9 (9)
Anemia[b]	55 (52)	36 (34)
Nausea	55 (52)	1 (1)
Hypertension[c]	53 (50)	28 (27)
Proteinuria	41 (39)	5 (5)
Headache	32 (30)	6 (6)
Neutropenia[d]	28 (27)	13 (12)
Leukopenia[e]	24 (23)	0

Hardesty et al. SGO 2022;Abstract 40.

OVARIO: Conclusions

- **OVARIO enrolled a high-risk population**
  - 63% received NACT/IDS; 42% had partial response after first-line platinum-based therapy in combination with bevacizumab
- **In the overall population, more than half (53%) of patients remained progression free at 24 months**
  - 63% remained progression free in the homologous recombination deficient (HRd) group, and 42% in the homologous recombination proficient (HRp) group
  - Median time to first subsequent therapy was 17.5 months, and median time to second subsequent therapy was not reached in the overall population
- **Progression-free survival (PFS) analysis suggests that the maintenance combination of niraparib and bevacizumab is efficacious;** clinical benefit was observed in the overall population, and across biomarker subgroups in a continuum
  - **Overall:** Median PFS (mPFS) of 19.6 months (95% CI 16.5-25.1)
  - **HRd subgroup:** mPFS of 28.3 months (95% CI 19.9-NE) and not yet reached in the BRCAm subgroup
  - **HRp subgroup:** mPFS of 14.2 months (95% CI 8.6-16.8)
- **Safety of niraparib in combination with bevacizumab was consistent with the known side effects** of each treatment as monotherapy, and no new safety signals were observed
  - Rate of treatment discontinuation is higher for combination therapy than for monotherapy alone, consistent with other PARPi+ bevacizumab studies

Hardesty et al. SGO 2022;Abstract 40.

Efficacy and Safety of Niraparib as Maintenance Treatment in Patients with Newly Diagnosed Advanced Ovarian Cancer Using an Individualized Starting Dose (PRIME Study): A Randomized, Double-blind, Placebo-controlled, Phase 3 Trial

Ning Li*, Jianqing Zhu, Rutie Yin, Jing Wang, Lingya Pan, Beihua Kong, Hong Zheng, Jihong Liu, Xiaohua Wu, Li Wang, Yi Huang, Ke Wang, Dongling Zou, Hongqin Zhao, Chunyan Wang, Weiguo Lu, An Lin, Ge Lou, Guiling Li, Pengpeng Qu, Hongying Yang, Xiaoa Zhen, Wenzhao Hang, Jianmei Hou, Lingying Wu*

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SGO 2022;Abstract LBA5.

PRIME: Demographics and Baseline Characteristics

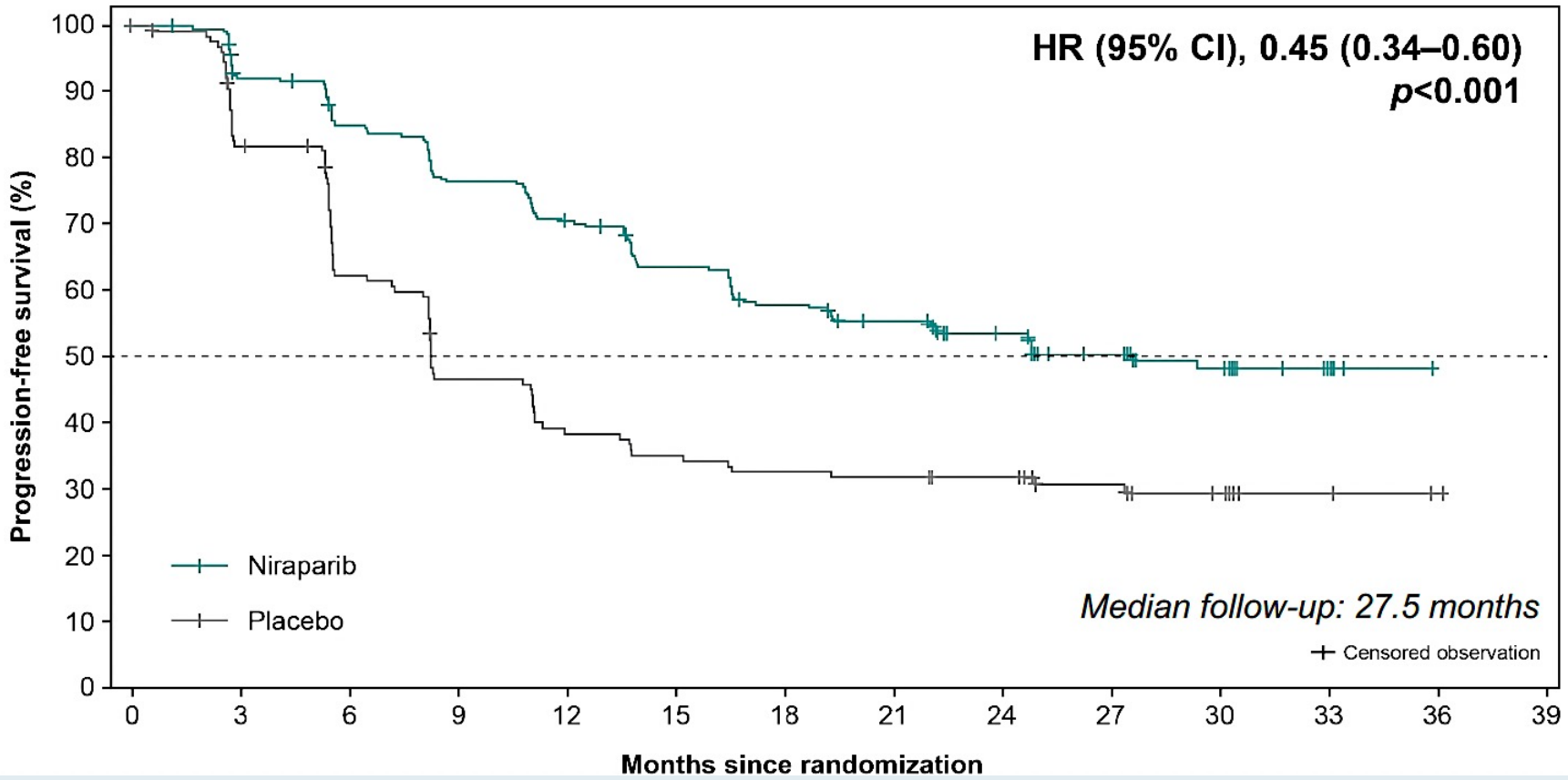
Characteristic	Niraparib (N=255)	Placebo (N=129)
Median age (range), years	53.0 (32–77)	54.0 (33–77)
Median weight (range), kg	59.0 (39.5–100.0)	57.0 (37.0–97.0)
ECOG performance status, n (%)		
0	98 (38.4)	52 (40.3)
1	157 (61.6)	77 (59.7)
FIGO stage, n (%)		
III	182 (71.4)	94 (72.9)
IV	73 (28.6)	35 (27.1)
Primary tumor location, n (%)		
Ovary	229 (89.8)	117 (90.7)
Fallopian tube	19 (7.5)	9 (7.0)
Peritoneum	7 (2.7)	3 (2.3)
Histologic subtype, n (%)		
Serous ovarian cancer	253 (99.2)	128 (99.2)
Endometrioid carcinoma	2 (0.8)	0
Other	0	1 (0.8)

Characteristic	Niraparib (N=255)	Placebo (N=129)
Neoadjuvant chemotherapy, n (%)		
Yes	121 (47.5)	59 (45.7)
No	134 (52.5)	70 (54.3)
Response to Pt-based CT, n (%)		
CR	212 (83.1)	103 (79.8)
PR	43 (16.9)	26 (20.2)
g*BRCA* mutation status, n (%)		
g*BRCA*mut	85 (33.3)	40 (31.0)
Non-g*BRCA*mut	170 (66.7)	89 (69.0)
Homologous recombination[a], n (%)		
Deficient	170 (66.7)	87 (67.4)
Proficient	85 (33.3)	42 (32.6)
Postoperative residual disease status, n (%)		
Optimal (R0/R1)	193 (75.7)	105 (81.4)
Suboptimal (R2) or missing	52 (24.3)	24 (18.6)

- The niraparib and placebo groups were well-balanced.

Li et al. SGO 2022;Abstract LBA5.

PRIME: PFS (by Blinded Independent Central Review) in the ITT Population



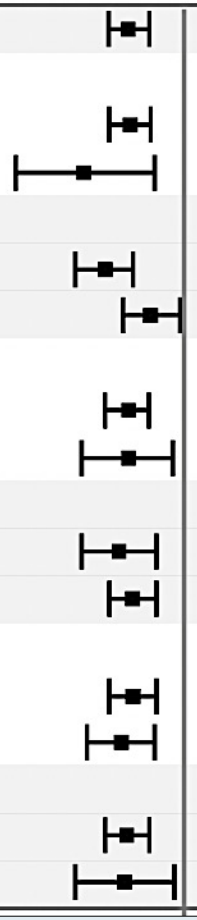
16.5 months longer median PFS with niraparib versus placebo

	Niraparib (N=255)	Placebo (N=129)
PFS (54.4% data maturity)		
Events, n (%)	123 (48.2)	86 (66.7)
mPFS (95% CI), months	24.8 (19.2–NE)	8.3 (7.3–11.1)
Patients without PD or death (%)		
24 months	52.6	30.4

Li et al. SGO 2022;Abstract LBA5.

PRIME: PFS Benefit in Prespecified Subgroups

Subgroup	Events/patients (%)		Hazard ratio for PFS (95% CI)
	Niraparib	Placebo	
Overall	123/255 (48.2)	86/129 (66.7)	0.45 (0.34–0.60)
Age			
<65 years	108/229 (47.2)	73/114 (64.0)	0.47 (0.34–0.63)
≥65 years	15/26 (57.7)	13/15 (86.7)	0.24 (0.09–0.66)
Neoadjuvant chemotherapy			
Yes	62/121 (51.2)	46/59 (78.0)	0.32 (0.21–0.48)
No	61/134 (45.5)	40/70 (57.1)	0.63 (0.42–0.94)
Response to Pt-based chemotherapy			
Complete response	98/212 (46.2)	66/103 (64.1)	0.45 (0.32–0.61)
Partial response	25/43 (58.1)	20/26 (76.9)	0.45 (0.23–0.86)
***gBRCA* mutation status**			
*gBRCA*mut	35/85 (41.2)	25/40 (62.5)	0.40 (0.23–0.68)
Non-g*BRCA*mut	88/170 (51.8)	61/89 (68.5)	0.48 (0.34–0.67)
Homologous recombination			
Deficient	75/170 (44.1)	57/87 (65.5)	0.48 (0.34–0.68)
Proficient	48/85 (56.5)	29/42 (69.0)	0.41 (0.25–0.65)
Postoperative residual disease status			
Optimal	94/193 (48.7)	71/105 (67.6)	0.44 (0.32–0.61)
Suboptimal or missing	29/62 (46.8)	15/24 (62.5)	0.43 (0.21–0.87)



Li et al. SGO 2022;Abstract LBA5.

A Phase I/II Study of Ruxolitinib with Frontline Neoadjuvant and Post-Surgical Therapy in Patients with Advanced Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

Landen CN et al.

ASCO 2022;Abstract 5501.

Track: Gynecologic Oral Session
June 6, 2022; 9:00 AM

Eligibility and Dosing in Pivotal Studies of PARP Inhibitors for Recurrent, Platinum-Sensitive Ovarian Cancer

	NOVA[1] (Niraparib)	SOLO-2[2] (Olaparib)	ARIEL3[3] (Rucaparib)
BRCA status	With or without gBRCA mutation	gBRCA mutation (Study 19: +/- gBRCA mutation)	With or without gBRCA mutation
HRD testing	Yes	No	Yes
Tumor assessment schedule	Every 8 wk to C14 → every 12 wk	Every 12 wk until wk 72 → every 24 wk	Every 8 wk to C14 → every 12 wk
Dosing/formulation	300 mg qd	300 mg BID	600 mg BID
No. of prior lines of chemo	2 or more	2 or more	2 or more

[1] Mirza MR et al. *N Engl J Med* 2016;375(22):2154-64; [2] Pujade-Lauraine E et al. *Lancet* 2017;18(9):1274-84; [3] Coleman RL et al. *Lancet* 2017;390(10106):1949-61.

Progression-Free Survival with PARP Inhibitors for Recurrent, Platinum-Sensitive Ovarian Cancer

	PARPi	Control	HR
NOVA[1-2] — Niraparib			
gBRCA mutation	21.0 mo	5.5 mo	0.27
No gBRCA mutation, HRD+	12.9 mo	3.8 mo	0.38
No gBRCA mutation	9.3 mo	3.9 mo	0.45
SOLO-2[3-4] — Olaparib			
gBRCA mutation	19.1 mo	5.5 mo	0.30
Overall survival	51.7 mo	38.8 mo	0.74
ARIEL3[5-6] — Rucaparib			
ITT (All comers)	10.8 mo	5.4 mo	0.36
g or sBRCA mutation	16.6 mo	5.4 mo	0.23
HRD+	13.6 mo	5.4 mo	0.32
$BRCA^{WT}$/High LOH	13.6 mo	5.4 mo	0.32
$BRCA^{WT}$/Low LOH	6.7 mo	5.4 mo	0.58

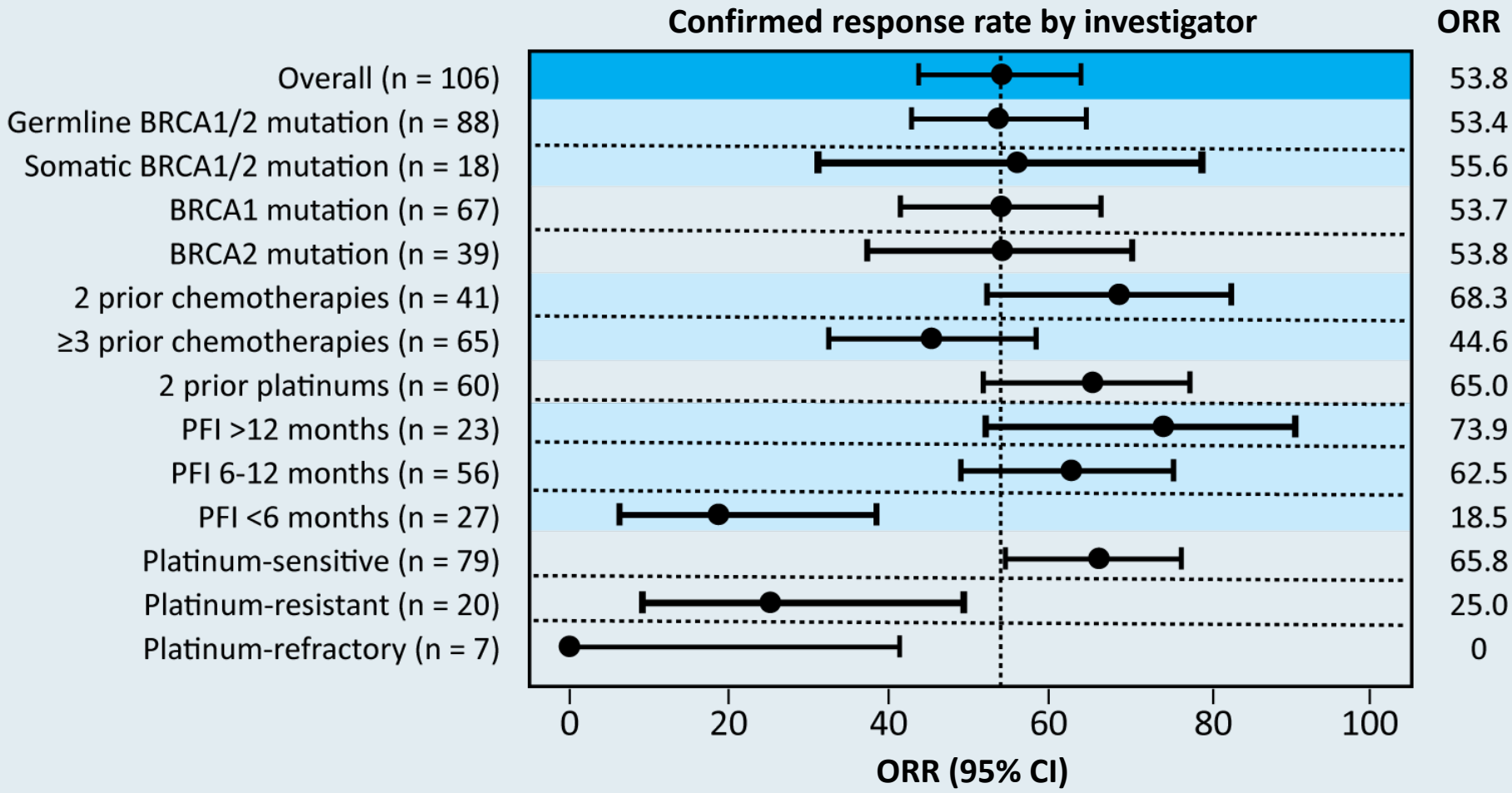
[1] Mirza MR et al. *N Engl J Med* 2016;375(22):2154-64; [2] Del Campo JM et al. *J Clin Oncol* 2019 Nov;37(32):2968-73. [3] Poveda A et al. *Lancet Oncol* 2021;22:620-31. [4] Pujade-Lauraine E et al. *Lancet* 2017;18(9):1274-84; [5] Coleman RL et al. *Lancet* 2017;390(10106):1949-61; [6] Ledermann JA et al. *Lancet Oncol* 2020;21(5):710-22.

Study 42: Olaparib Monotherapy in Patients with Relapsed Ovarian Cancer and gBRCA Mutations Who Received 3 or More Lines of Prior Chemotherapy

Platinum sensitivity	ORR	Median DoR
Total (N = 137)	34%	7.9 mo
Platinum sensitive (n = 39)	46%	8.2 mo
Platinum resistant (n = 81)	30%	8.0 mo
Platinum refractory (n = 14)	14%	6.4 mo
Unknown (n = 3)	67%	6.3 mo

Domchek SM et al. *Gynecol Oncol* 2016;140(2):199-203.

Study 10/ARIEL2: Rucaparib in Patients with Relapsed Ovarian Cancer with Germline or Somatic BRCA Mutations Who Received 2 or More Lines of Prior Chemotherapy



Oza AM et al. *Gynecol Oncol* 2017;147:267-75.

Lancet Oncol 2022;23(4):465-78.

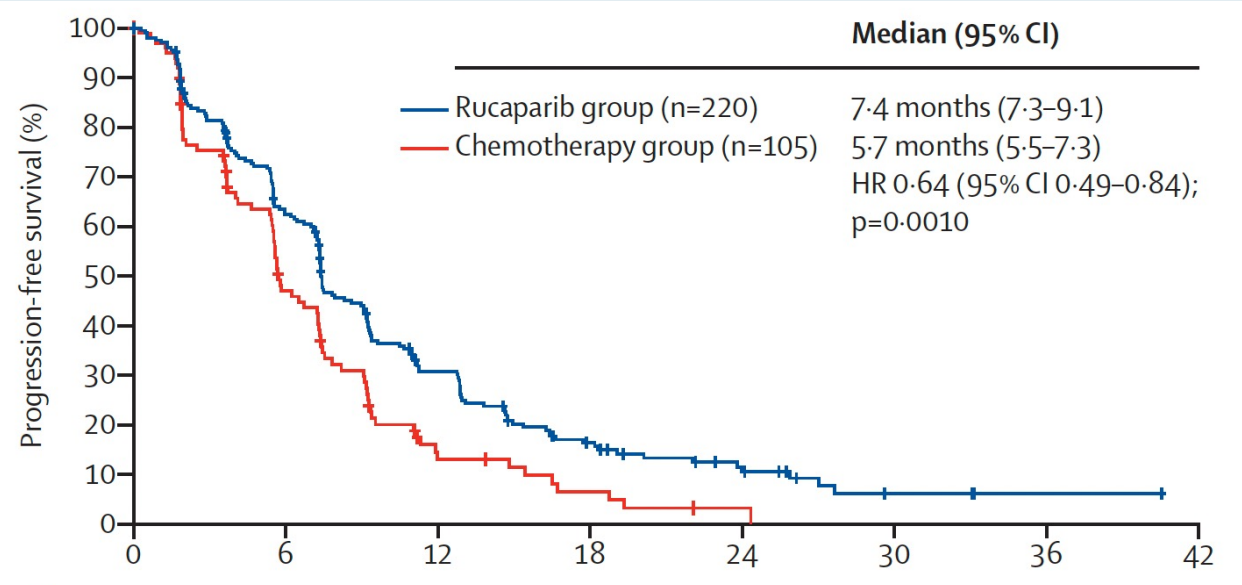
Articles

Rucaparib versus standard-of-care chemotherapy in patients with relapsed ovarian cancer and a deleterious *BRCA1* or *BRCA2* mutation (ARIEL4): an international, open-label, randomised, phase 3 trial

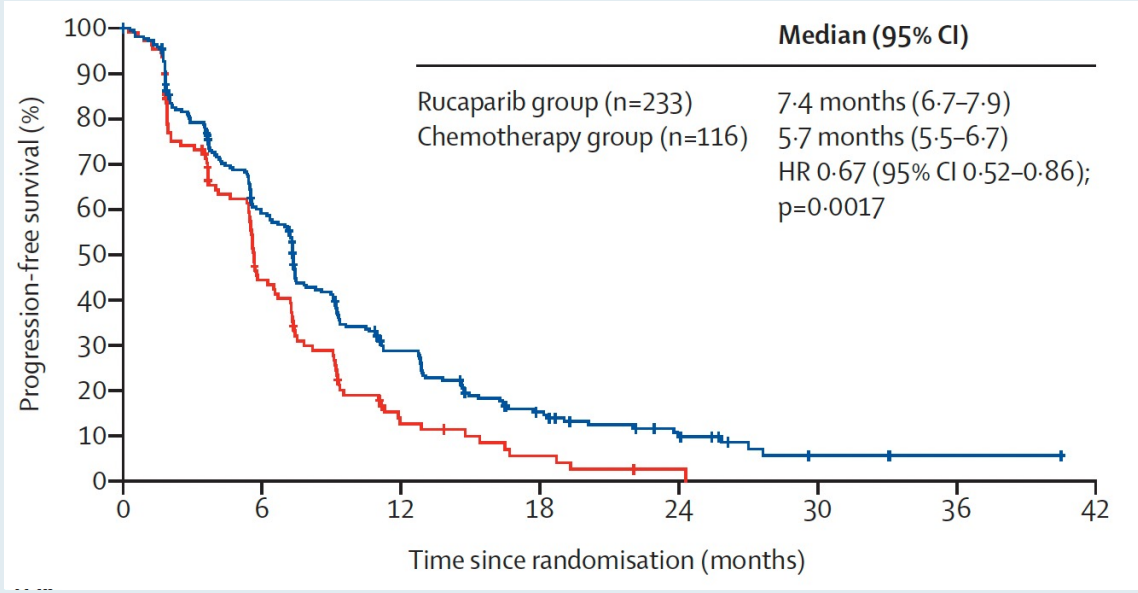
Rebecca Kristeleit, Alla Lisyanskaya, Alexander Fedenko, Mikhail Dvorkin, Andreia Cristina de Melo, Yaroslav Shparyk, Irina Rakhmatullina, Igor Bondarenko, Nicoletta Colombo, Valentyn Svintsitskiy, Luciano Biela, Marina Nechaeva, Domenica Lorusso, Giovanni Scambia, David Cibula, Róbert Póka, Ana Oaknin, Tamar Safra, Beata Mackowiak-Matejczyk, Ling Ma, Daleen Thomas, Kevin K Lin, Karen McLachlan, Sandra Goble, Amit M Oza

ARIEL4: Progression-Free Survival in the Efficacy and ITT Populations

Efficacy population (BRCA1 or BRCA2 mutations with reversion mutations)



Intent to treat population



Kristeleit et al. *Lancet Oncol* 2022;23(4):465-78.

RTP RESEARCH TO PRACTICE

ARIEL4: Overall Response Rate and Duration of Response

	Efficacy population			ITT population		
Endpoint	Rucaparib (n = 220)	Chemotherapy (n = 105)	*p*-value	Rucaparib (n = 233)	Chemotherapy (n = 116)	*p*-value
ORR	40%	32%	0.13	38%	30%	0.13
DoR, median	9.4 mo	7.2 mo	—	9.4 mo	7.2 mo	—

Kristeleit et al. *Lancet Oncol* 2022;23(4):465-78.

Research

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

JAMA Oncology | Original Investigation

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

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

TOPACIO/KEYNOTE-162: Patient Characteristics at Baseline

Characteristic	Combined Phases 1 and 2 Patients With Ovarian Carcinoma (n = 62)
Age, median (range), y	60 (46-83)
ECOG performance status, No. (%)[a]	
0	44 (71)
1	18 (29)
Prior lines of therapy, median (range)	3 (1-5)
Prior bevacizumab, No. (%)	39 (63)
Prior chemotherapy, No. (%)[b]	
Anthracycline	40 (65)
Cyclophosphamide	5 (8)
Gemcitabine hydrochloride	29 (47)
Paclitaxel	61 (98)
Platinum	62 (100)
Topotecan hydrochloride	3 (5)
Platinum status, No. (%)	
Resistant	30 (48)
Refractory	17 (27)
Not applicable[c]	15 (24)

Characteristic	Combined Phases 1 and 2 Patients With Ovarian Carcinoma (n = 62)
t*BRCA* status, No. (%)	
BRCA1 mutation	9 (15)
BRCA2 mutation	2 (3)
BRCA wild type	49 (79)
Unknown	2 (3)
HRD status, No. (%)	
HRD positive	22 (35)
HRD negative	33 (53)
HRD unknown	7 (11)
PD-L1 status, No. (%)[d]	
Positive	35 (56)
Negative	21 (34)
Unknown	6 (10)

Konstantinopoulos PA et al. *JAMA Oncol* 2019;5(8):1141-9.

RTP RESEARCH TO PRACTICE

VIRTUAL 2020 ESMO congress

Abstract 814MO.

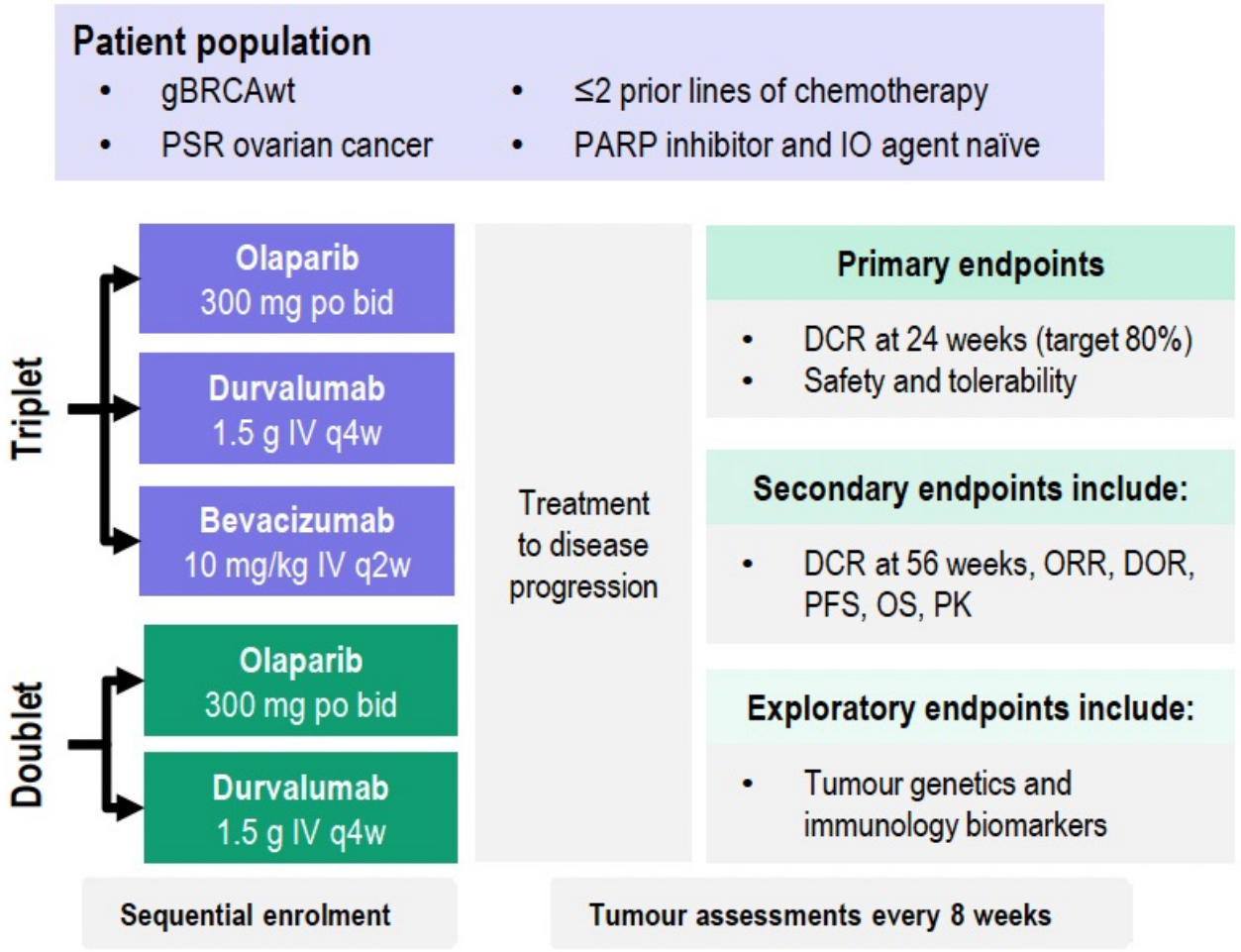
Phase II study of olaparib plus durvalumab and bevacizumab (MEDIOLA): initial results in patients with non-germline BRCA-mutated platinum sensitive relapsed ovarian cancer

Yvette Drew,[1] Richard Penson,[2] David M O'Malley,[3] Jae-Weon Kim,[4] Stefan Zimmermann,[5] Patricia Roxburgh,[6] Joohyuk Sohn,[7] Salomon M Stemmer,[8] Sara Bastian,[9] Michelle Ferguson,[10] Benoit You,[11] Susan Domchek,[12] Haiyan Gao,[13] Helen K Angell,[13] Kassondra Meyer,[14] Laura Opincar,[14] Lone Ottesen,[13] Susana Banerjee[15]

[1]Northern Centre for Cancer Care, Newcastle upon Tyne Hospitals NHS Foundation Trust, and Newcastle University, Newcastle upon Tyne, UK; [2]Massachusetts General Hospital, Boston, MA, USA; [3]The Ohio State University – James Comprehensive Cancer Center, Columbus, OH, USA; [4]Seoul National University Hospital, Seoul, Republic of Korea; [5]Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland; [6]Beatson West of Scotland Cancer Centre, and Institute of Cancer Sciences, University of Glasgow, Glasgow, UK, [7]Yonsei Cancer Centre, Yonsei University, Sinchon-dong, Republic of Korea; [8]Rabin Medical Center-Beilinson Campus, Petach Tikva and Tel-Aviv University, Tel-Aviv, Israel; [9]Kantonsspital Graubuenden, Chur, Switzerland; [10]NHS Tayside, Dundee, UK; [11]Institut de Cancérologie des Hospices Civils de Lyon, CITOHL, GINECO, Université Claude Bernard Lyon 1, Lyon, France; [12]Basser Center for BRCA University of Pennsylvania, Philadelphia, PA, USA; [13]AstraZeneca, Cambridge, UK; [14]AstraZeneca, Gaithersburg, MD, USA; [15]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK

ClinicalTrials.gov identifier: NCT02734004
This study was sponsored by AstraZeneca

MEDIOLA Non-gBRCA Mutated Study Schema



	Olap + durva + bev (N=31)	Olap + durva (N=32)
Median age, years	64.0	68.5
Age group (years), n (%)		
<50	3 (9.7)	4 (12.5)
≥50–<65	14 (45.2)	8 (25.0)
≥65	14 (45.2)	20 (62.5)
Race, n (%)		
White	20 (64.5)	24 (75.0)
Asian	10 (32.3)	3 (9.4)
Other	1 (3.2)	5 (15.6)
Platinum sensitivity, n (%)		
>6–12 months	18 (58.1)	14 (43.8)
>12 months	13 (41.9)	18 (56.3)
Number of prior lines of chemotherapy, n (%)		
1 prior line	20 (64.5)	23 (71.9)
2 prior lines	11 (35.5)	9 (28.1)
Enrolment completed	January 2019	February 2019
Patients on study treatment at DCO, n (%) (13 February 2020)		
Olap; durva; bev	13 (41.9); 13 (41.9); 12 (38.7)	7 (21.9); 6 (18.8); NA

Drew Y et al. ESMO 2020;Abstract 814MO.

RTP RESEARCH TO PRACTICE

BARCELONA 2019 ESMO congress

Poster board number: 1190PD

Phase II study of olaparib + durvalumab (MEDIOLA): Updated results in the germline BRCA-mutated platinum-sensitive relapsed ovarian cancer cohort

Yvette Drew,[1] Bella Kaufman,[2] Susana Banerjee,[3] Alain Lortholary,[4] Sook Hee Hong,[5] Yeon Hee Park,[6] Stefan Zimmermann,[7] Patricia Roxburgh,[8] Michelle Ferguson,[9] Ricardo H Alvarez,[10] Susan Domchek,[11] Christopher Gresty,[12] Helen K Angell,[12] Vidalba Rocher Ros,[13] Kassondra Meyer,[13] Mark Lanasa,[13] Pia Herbolsheimer,[13] Maja de Jonge[14]

[1]Northern Centre for Cancer Care, Newcastle upon Tyne Hospitals NHS Foundation Trust Newcastle upon Tyne, UK; [2]Chaim Sheba Medical Center, Tel Hashomer, Israel; [3]The Royal Marsden Hospital, London, UK; [4]Centre Catherine de Sienne, Nantes, France; [5]Seoul St Mary's Hospital, Catholic University of Korea, Seoul, South Korea; [6]Samsung Medical Center, Seoul, Republic of Korea; [7]Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland; [8]University of Glasgow and Beatson West of Scotland Cancer Centre, Glasgow, UK; [9]NHS Tayside, Dundee, UK; [10]Cancer Treatment Centers of America-Atlanta and Augusta University, Augusta, GA, USA; [11]Basser Center for BRCA University of Pennsylvania, Philadelphia, PA, USA; [12]AstraZeneca, Cambridge, UK; [13]AstraZeneca, Gaithersburg, MD, USA and [14]Erasmus MC Daniel den Hoed Cancer Center, Rotterdam, Netherlands

esmo.org

MEDIOLA mBRCA Cohort Study Schema

- MEDIOLA is a multi-cohort, Phase I/II study
- The design of the BRCAm ovarian cohort is presented below; other ovarian cancer cohorts are ongoing

N=34*

- Platinum-sensitive relapsed ovarian cancer†
- Germline mutation in *BRCA1* or *BRCA2*
- ≥1 previous platinum-based therapy
- PARP inhibitor and immunotherapy naïve

Olaparib monotherapy 300 mg bid PO for 4 weeks

then

Olaparib 300 mg bid PO plus **durvalumab** IV 1.5 g every 4 weeks

Treatment until disease progression or intolerable toxicity

Primary endpoints

- Disease control rate at 12 weeks
- Safety and tolerability

Secondary endpoints

- Disease control rate at 28 weeks
- Objective response rate
- Duration of response
- Progression-free survival
- Overall survival
- PD-L1 expression in tumour samples

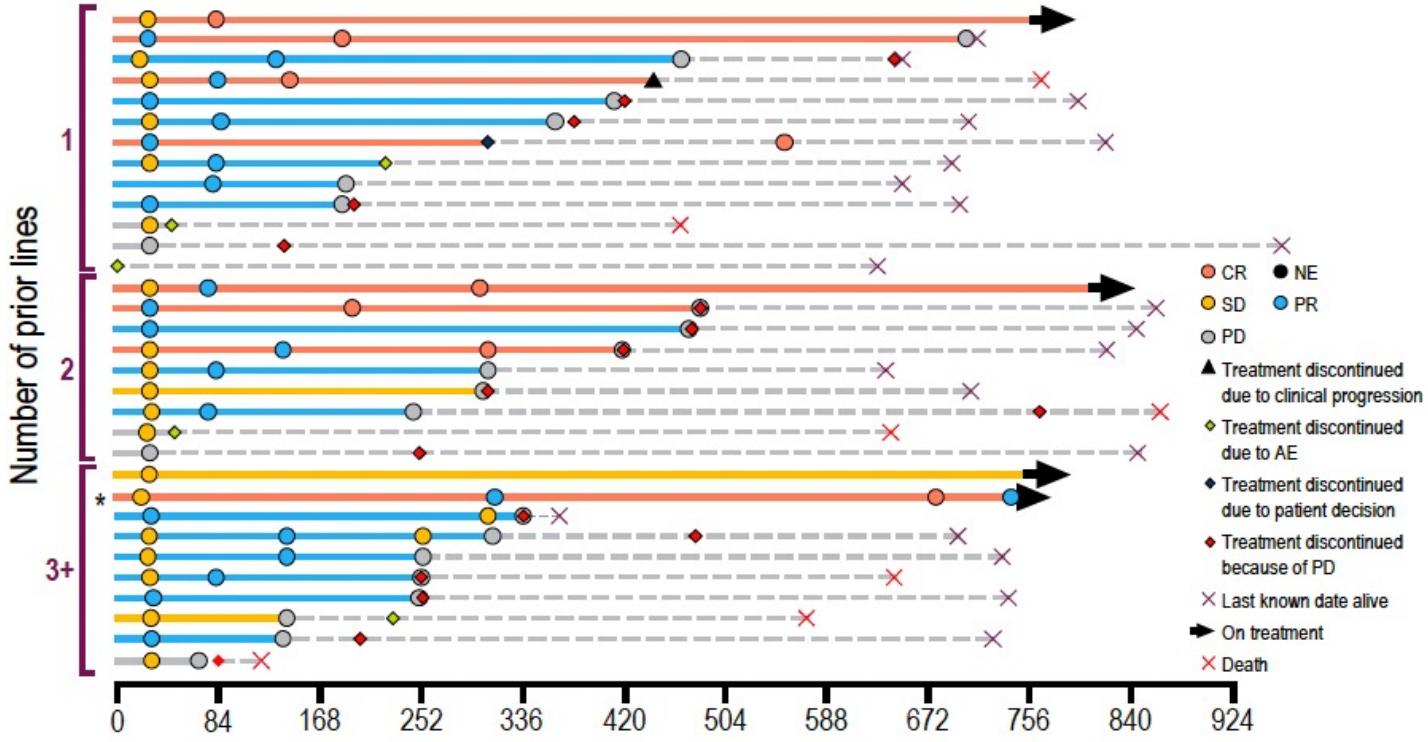
Drew Y et al. ESMO 2019;Abstract 1190PD.

MEDIOLA mBRCA Cohort: Efficacy

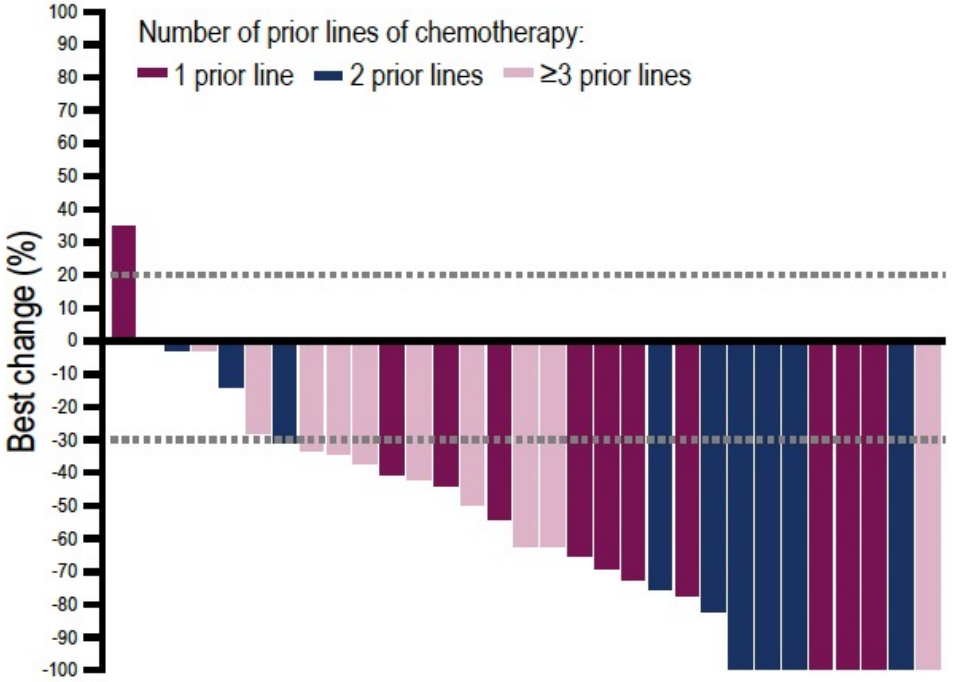
- DCR at 12 weeks: 81.3% (90% CI 66.3, 91.5)
- DCR at 28 weeks: 65.6% (90% CI 49.6, 79.4)
- Unconfirmed ORR: 71.9% (95% CI 53.3, 86.3)
- mPFS: 11.1 months (95% CI 8.2, 15.6)

Greater clinical activity was seen in earlier- versus later-line patients

Time to progression or treatment discontinuation



Best percentage change in target lesion size†



Drew Y et al. ESMO 2019;Abstract 1190PD.

RTP RESEARCH TO PRACTICE

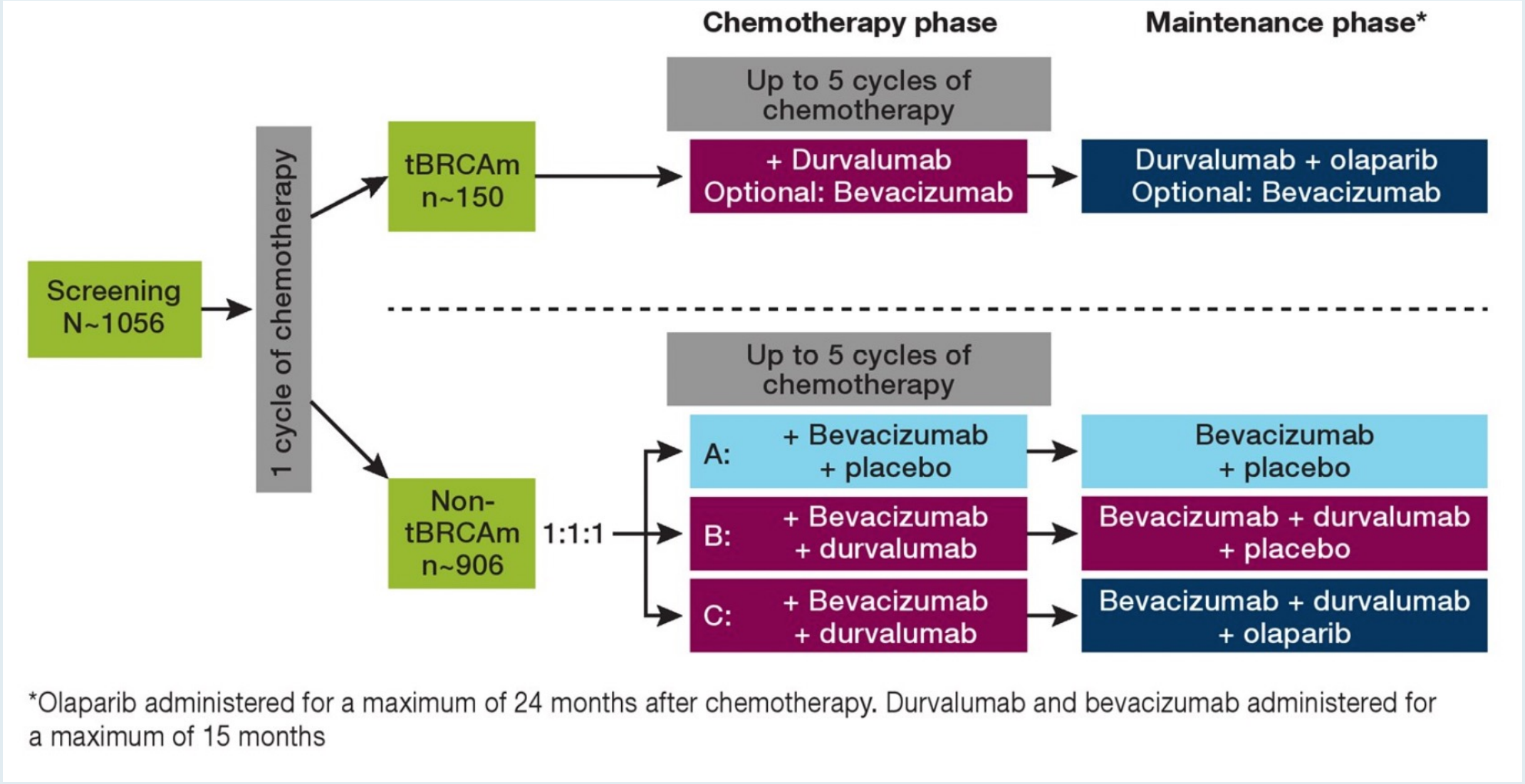
MOONSTONE/GOG-3032: Interim Analysis of a Phase 2 Study of Niraparib + Dostarlimab in Patients (pts) with Platinum-Resistant Ovarian Cancer (PROC)

Randall LM et al.

ASCO 2022;Abstract 5573.

Poster Session: Gynecologic Cancer

DUO-O Study Design

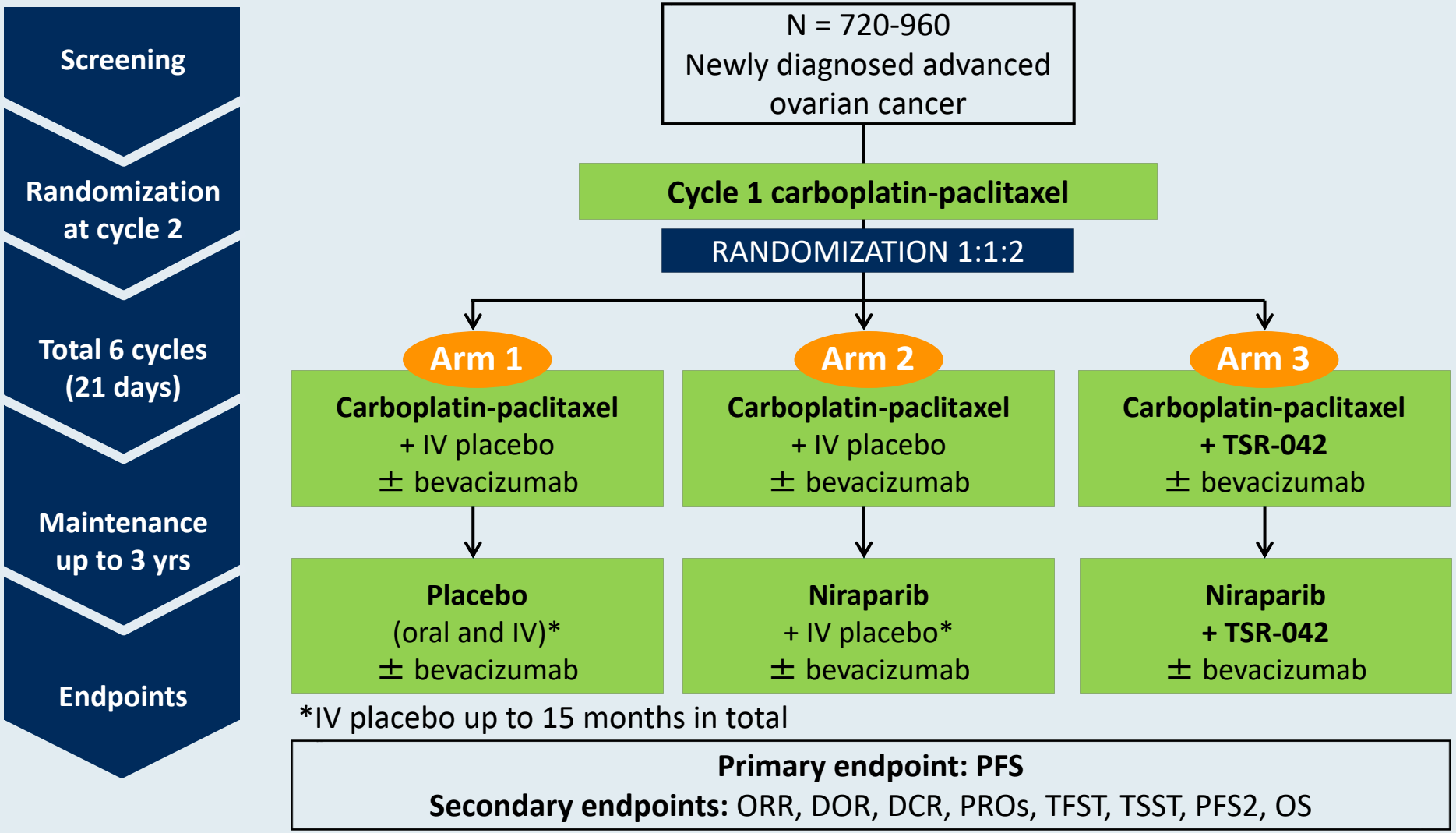


*Olaparib administered for a maximum of 24 months after chemotherapy. Durvalumab and bevacizumab administered for a maximum of 15 months

Harter P et al. ASCO 2019;Abstract TPS5598.

RTP RESEARCH TO PRACTICE

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



www.clinicaltrials.gov/ct2/show/NCT03602859

Courtesy of Ursula Matulonis, MD

RTP RESEARCH TO PRACTICE

Overall Survival Data from a 3-Arm, Randomized, Open-label, Phase 2 Study of Relacorilant, a Selective Glucocorticoid Receptor Modulator, Combined with Nab-Paclitaxel in Patients with Recurrent Platinum-Resistant Ovarian Cancer

Colombo N et al.

ASCO 2022;Abstract LBA5503.

Track: Gynecologic Oral Session
June 6, 2022; 9:00 AM

Randomized Phase III Trial on Trabectedin (ET-743) Single Agent versus Clinician's Choice Chemotherapy in Recurrent Ovarian, Primary Peritoneal, or Fallopian Tube Cancers of BRCA-Mutated or BRCAness Phenotype Patients (MITO23)

Scambia G et al.

ASCO 2022;Abstract LBA5504.

Track: Gynecologic Oral Session
June 6, 2022; 9:00 AM

MIRASOL Phase III Study Schema

MIRASOL

Enrollment and Key Eligibility

- Platinum-resistant disease (PFI ≤ 6 mo)
  - 1° platinum refractory disease excluded (primary PFI < 3 mo)
- Prior bevacizumab and PARPi allowed
- 1-3 prior lines of therapy
- Patients with BRCA mutations allowed
- FRα-high by PS2+ scoring (≥75% PS2+)

Statistical Assumptions

- 430 patients/ 330 events for PFS by INV
- α=0.05 (two-sided)
- Power=90%; HR=0.7; control arm mPFS 3.5 mo

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

1:1 Randomization
STRATIFICATION FACTORS
Investigator's Choice (IC) Chemotherapy
(Paclitaxel, PLD, Topotecan)
Prior Therapies
(1 vs 2 vs 3)

Investigator's Choice (IC) Chemotherapy
Paclitaxel, PLD,† or Topotecan
Paclitaxel: 80 mg/m2 weekly; PLD: 40 mg/m² every 4 weeks;
Topotecan: 4 mg/m² on days 1, 8, and 15 every four weeks;
or 1.25 mg/m² on days 1-5 every 3 weeks

Moore KN et al. SGO 2022;Abstract 297.

PICCOLO Phase II Trial Schema

PICCOLO

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.

Case 7 — Joyce F Liu, MD, MPH

- **44yo woman, presenting with pelvic discomfort, found to have bilateral adnexal masses**
- **Primary debulking surgery with Stage II high-grade serous ovarian cancer**
- **Genetic testing negative. Somatic testing with *TP53* mutation, variants of uncertain significance in *CDK12* and *FANCI***
- **Treated with adjuvant carboplatin/paclitaxel x 6 cycles**
- **Recurrence 11 months after completion of therapy, with soft tissue nodularity in mesentery; mediastinal, para-aortic, and pelvic lymphadenopathy; diffuse sclerotic osseous lesions in thoracic and lumbosacral spine; low-attenuation lesion at R hepatic dome.**
  - **CA125 rise to 42 from nadir 6.**

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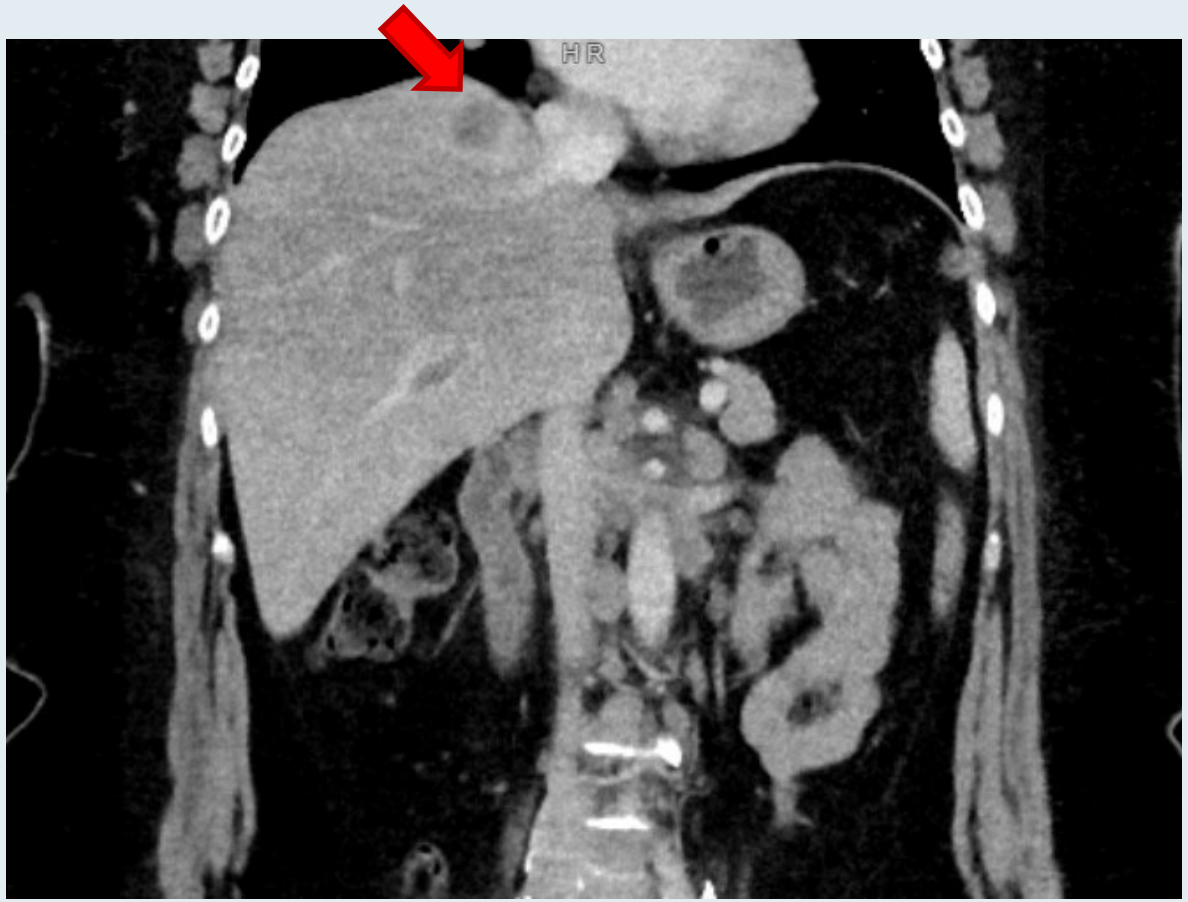
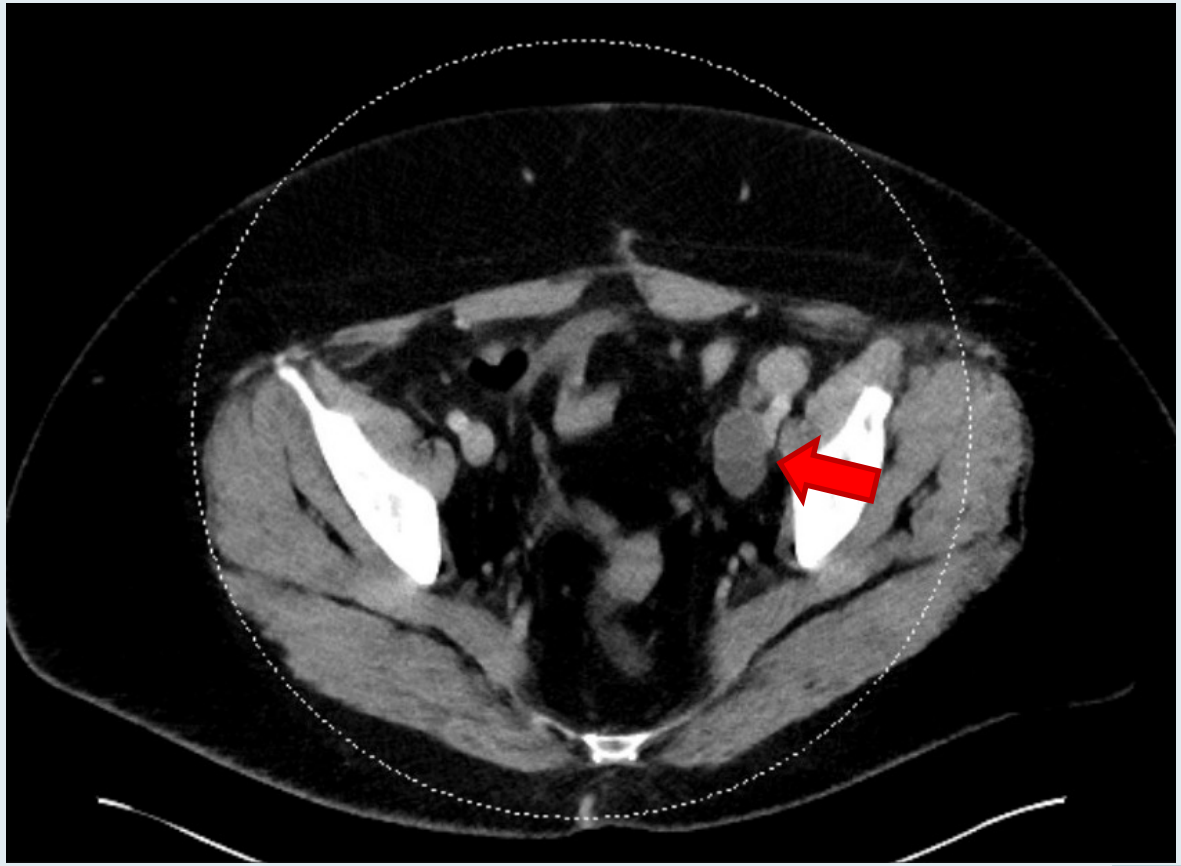
Case 7 — Joyce F Liu, MD, MPH

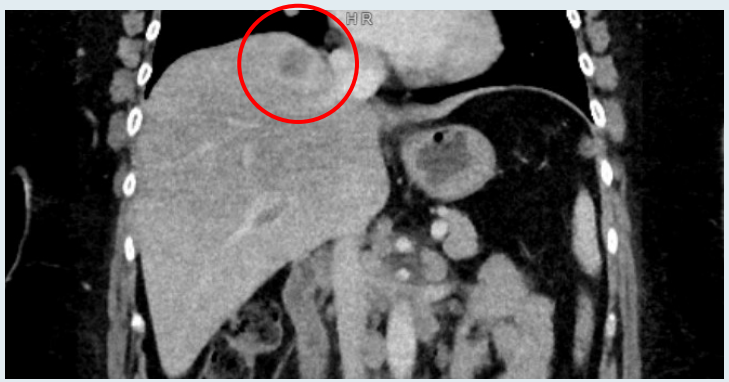
Scan at Recurrence

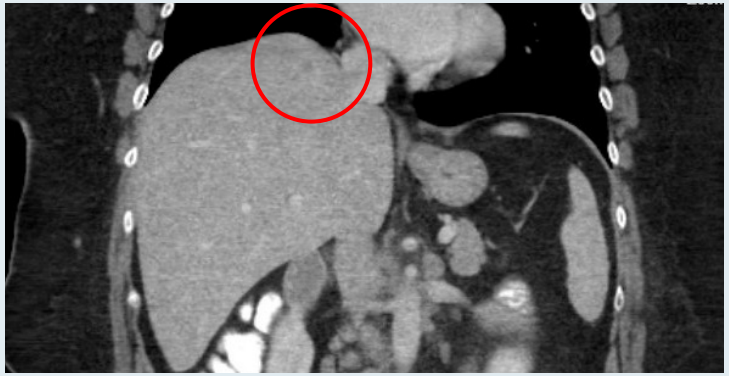


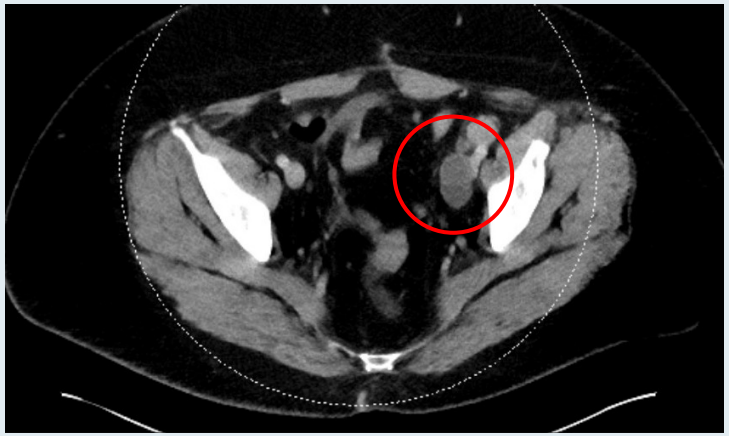


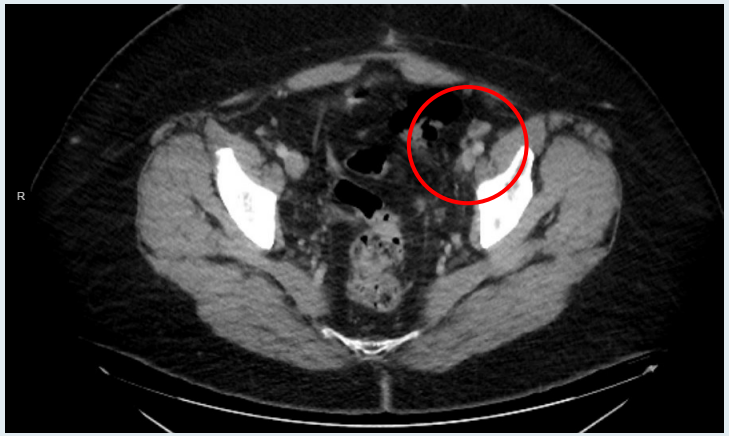
Case 7 — Joyce F Liu, MD, MPH

- **Enrolls to clinical trial of talazoparib + avelumab**
- **CA125 trend from 58 → 106 (4 weeks after starting) → nadir 19**









- **On trial for 7 months before developing RECIST progression**

RTP RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Chronic Lymphocytic Leukemia and Non-Hodgkin Lymphoma

A CME Hybrid Symposium Held in Conjunction with the 2022 ASCO Annual Meeting

Sunday, June 5, 2022
7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)

Faculty

Ian W Flinn, MD, PhD
Brian T Hill, MD, PhD
John P Leonard, MD
Matthew Lunning, DO
Laurie H Sehn, MD, MPH
Mitchell R Smith, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

CME links will be posted in the chat (Zoom participants only) and emailed to all participants within 24 hours of the program.

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