Meet The Professor
Management of Ovarian Cancer

Susana Banerjee, MBBS, MA, PhD
Consultant Medical Oncologist
Research Lead, Gynecological Cancers
Reader in Women's Cancers
The Institute of Cancer Research
The Royal Marsden NHS Foundation Trust
London, United Kingdom

Commercial Support

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Dr Love — Disclosures

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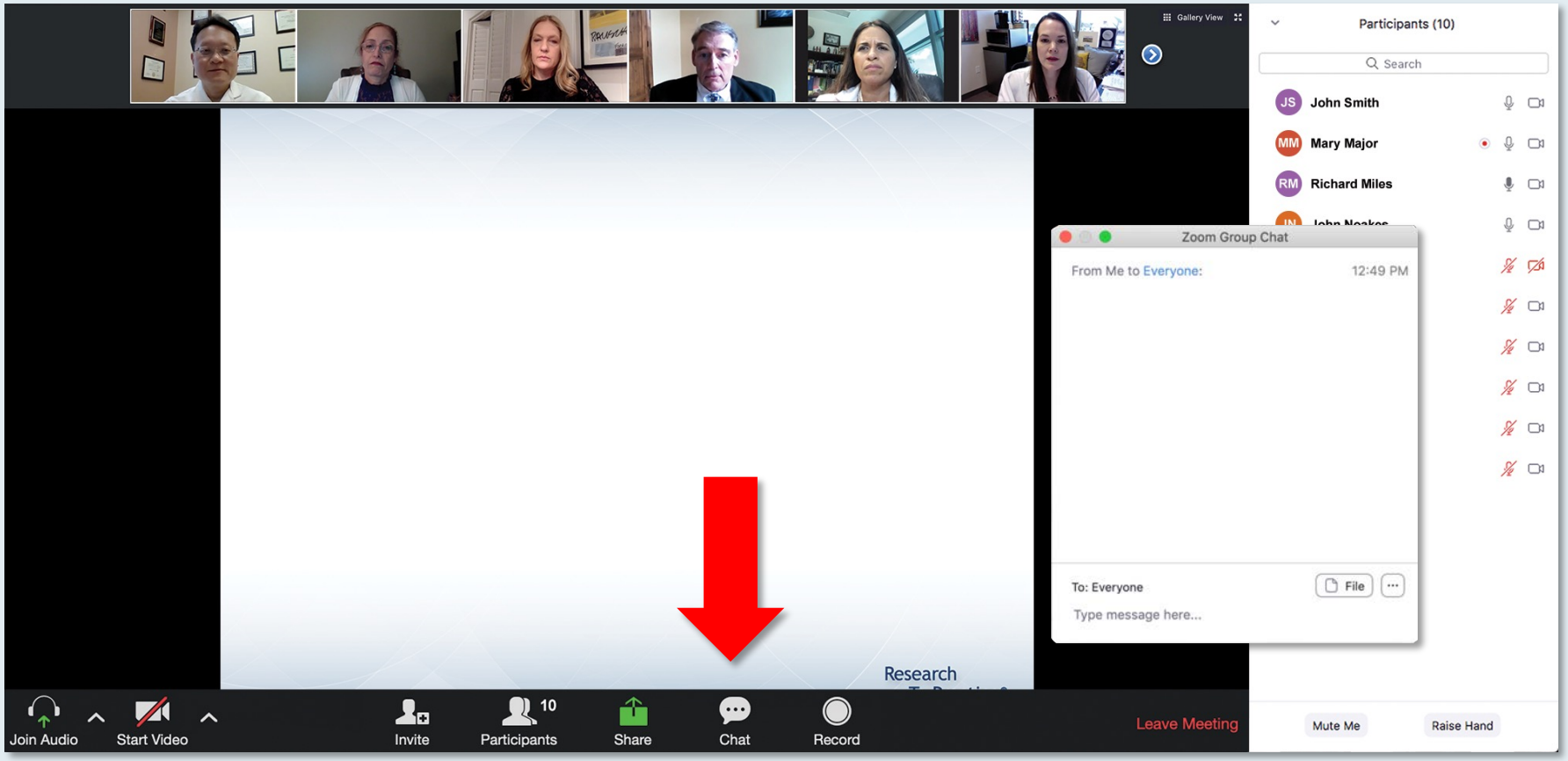

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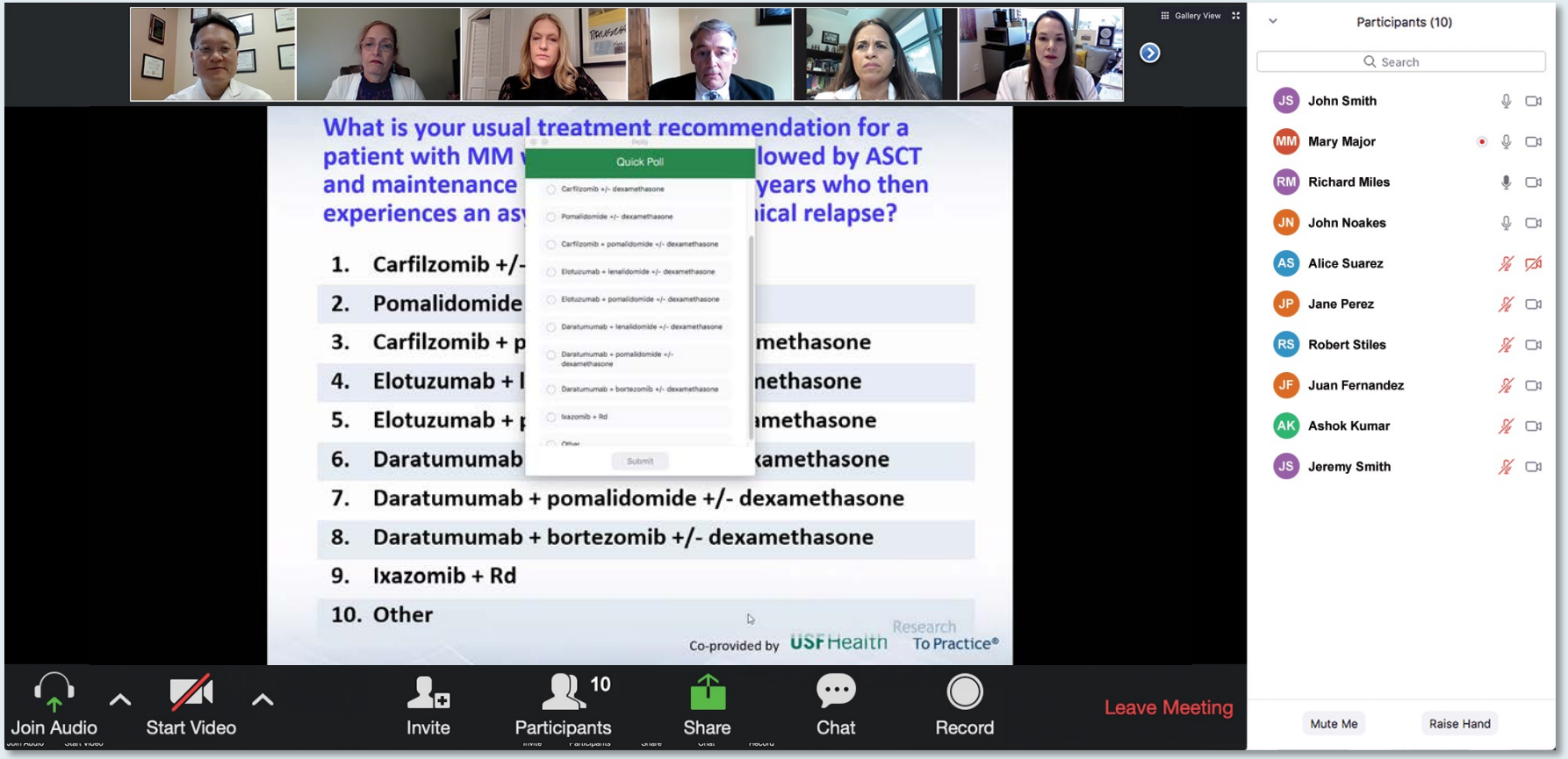

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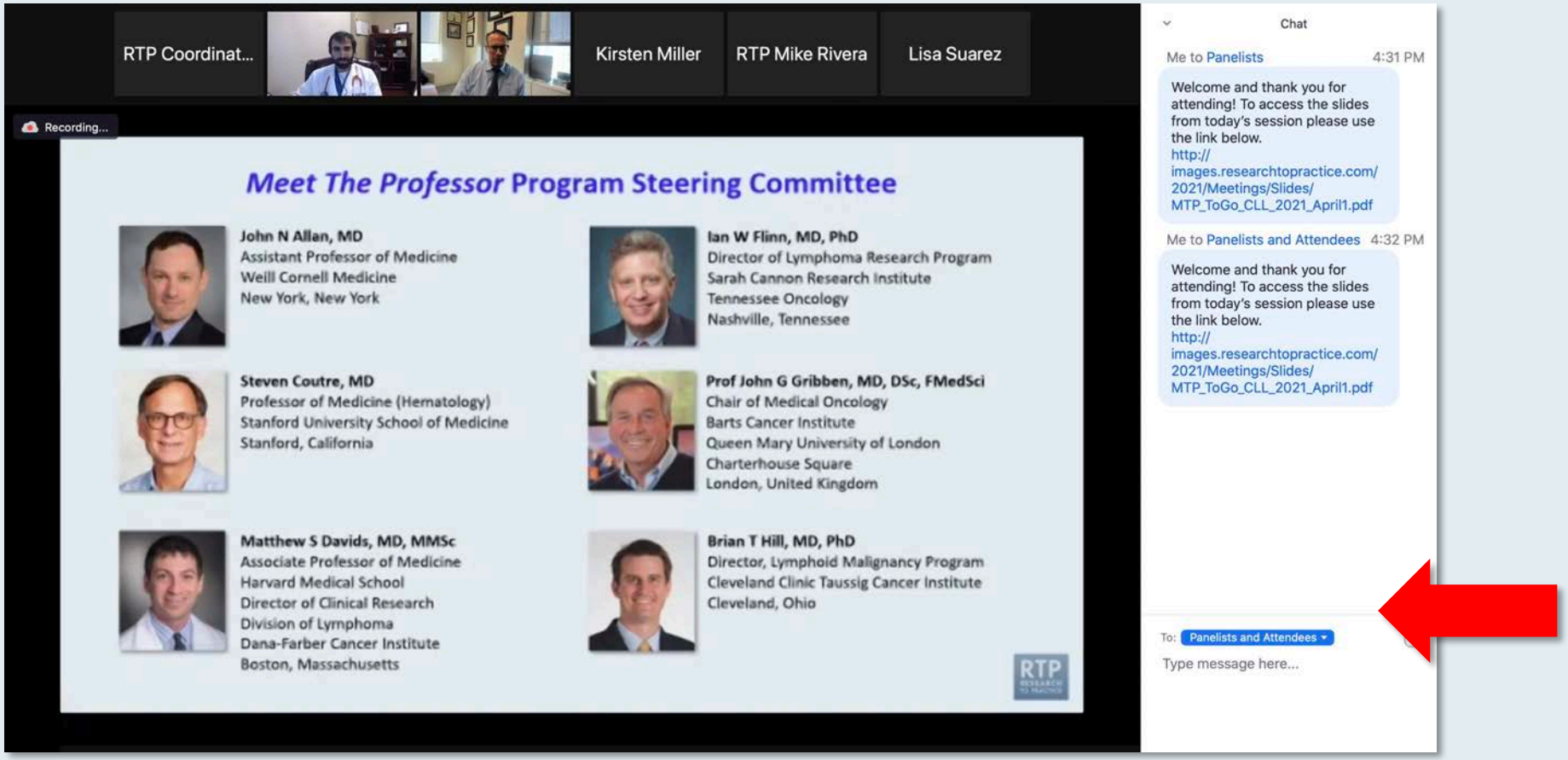

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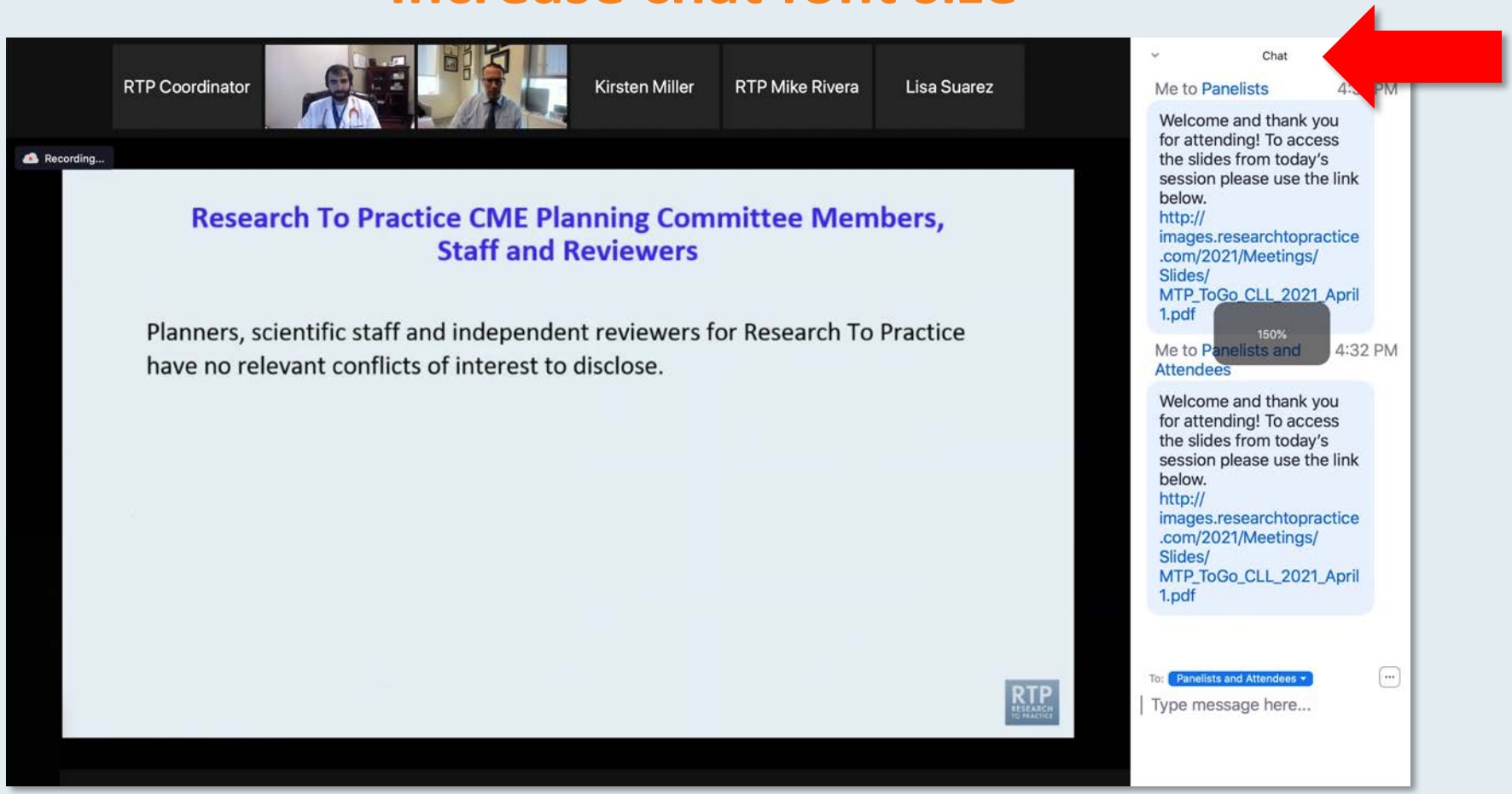

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Current and Future Treatment Strategies for Advanced Ovarian Cancer

DR KATHLEEN MOORE

UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

OKLAHOMA CITY, OKLAHOMA

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Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

In Partnership with Project Echo® and Florida Cancer Specialists

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Moderator

Neil Love, MD

Thank you for joining us!

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

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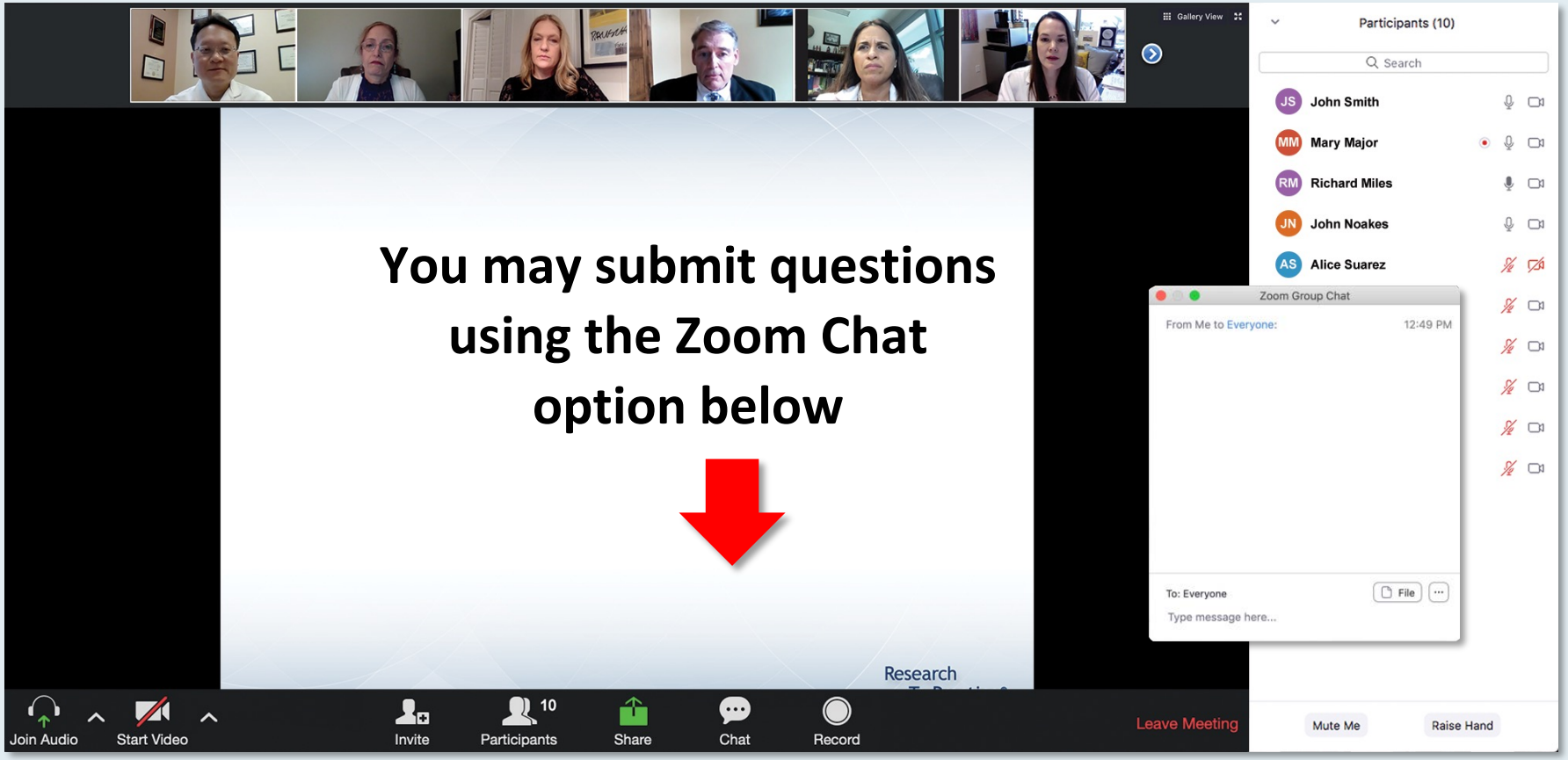

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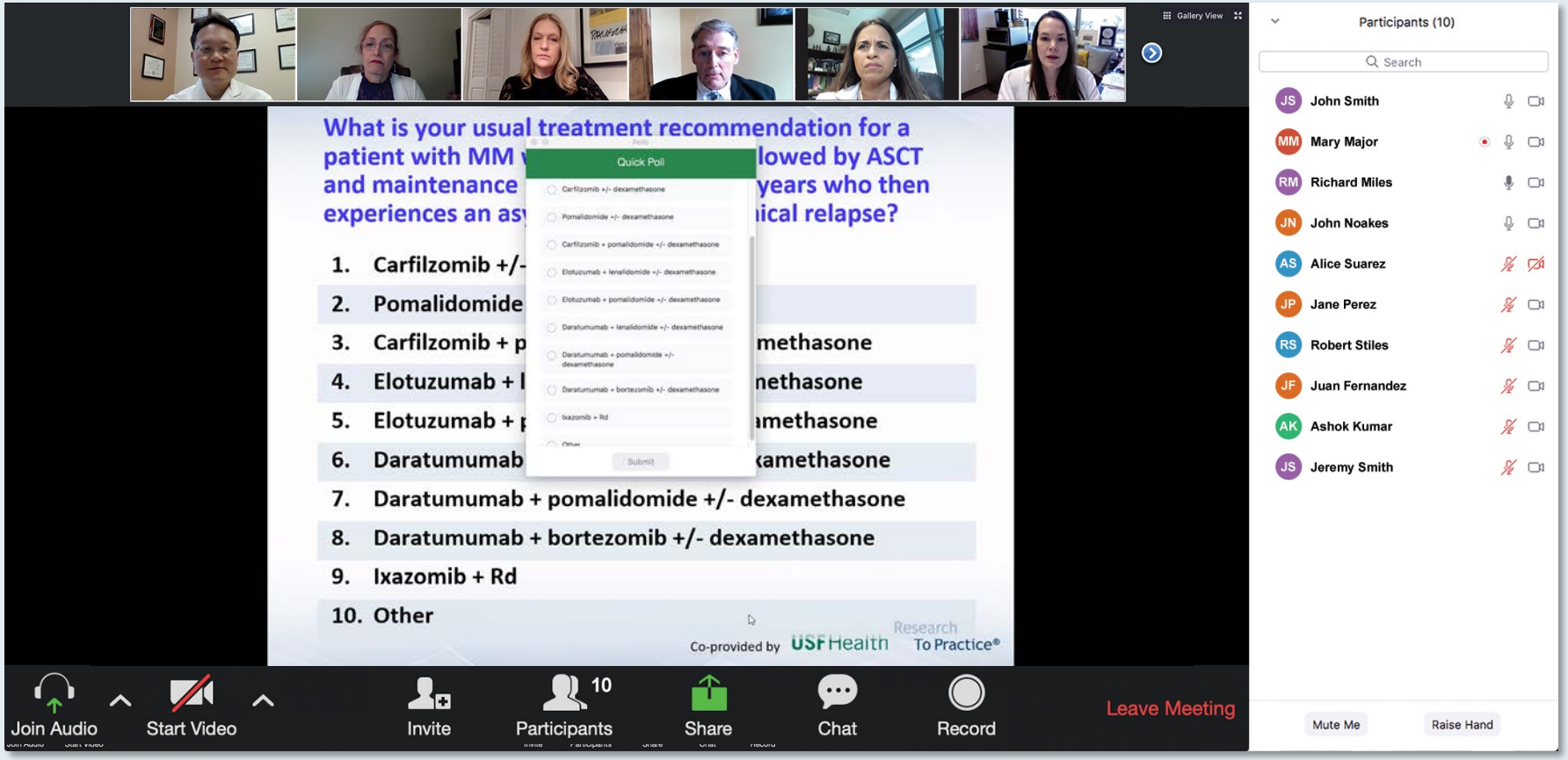

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Dana M Chase, MD
Gynecologic Oncologist, Arizona Oncology (US Oncology Network)
Associate Professor, Creighton University School of Medicine
Assistant Professor, University of Arizona College of Medicine
Phoenix, Arizona

Maria Regina Flores
Advent Health Orlando
Orlando Regional Hospital
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Florida Cancer Specialists and Research Institute
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Florida Cancer Specialists and Research Institute
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Richmond, Indiana

William Robert Mitchell, MD
Southern Oncology Specialists
Charlotte, North Carolina

Yanjun Ma, MD
Tennessee Oncology
Murfreesboro, Tennessee

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Meet The Professor with Dr Banerjee

MODULE 1: Cases from Community Practice

- Dr Choksi: A 68-year-old woman with BRCA wild-type high-grade serous ovarian cancer (HGSOC)
- Dr Ibrahim: A 77-year-old woman with Stage IIIC ovarian cancer with a germline BRCA mutation who develops severe anemia on olaparib
- Dr Mitchell: A 67-year-old woman with Stage M1C high-grade serous carcinoma of the peritoneum – Somatic BRCA1 mutation, PD-L1 overexpression
- Dr Ma: A 47-year-old woman with recurrent serous/papillary ovarian cancer and a somatic BRCA1 mutation
- Dr Chase: A 63-year-old woman with recurrent high-grade fallopian tube carcinoma
- Dr Flores: A 72-year-old woman with relapsed BRCA wild-type HGSOC
- Dr Hart: A 46-year-old woman with Stage IIB clear cell ovarian cancer

MODULE 2: Journal Club with Dr Banerjee

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

MODULE 4: Key Recent Papers

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THE CANCER HOSPITAL, BROMPTON.—Messrs. John Young & Son, Architects.

Karamanou M et al. *JBUON* 2017;22(5):1367-71.

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Royal Marsden Annual Review 2019 - 2020.

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Case Presentation – Dr Choksi: A 68-year-old woman with BRCA wild-type HGSOC

Dr Mamta Choksi

- 5/2018 Hospitalized with abdominal pain, nausea/vomiting
- 6/2018 Underwent 2200 mL of paracentesis: Adenocarcinoma, CA-125 847
- Staging Bilateral adnexal lesions, multiple peritoneal nodules, omental metastases, abdomen/pelvic ascites
- 8/2018 Neoadjuvant carboplatin/paclitaxel x 3, with good response → Hysterectomy, BSO, debulking, omentectomy and mini-laparotomy (R0) → Carboplatin/paclitaxel x 3 plus bevacizumab on cycle 5

Questions

- After completion of adjuvant chemotherapy, what would be your preference for maintenance therapy – single-agent bevacizumab, single-agent PARP inhibitor, or bevacizumab in combination with a PARP inhibitor? If a PARP inhibitor is used, which one would you prefer?

Case Presentation – Dr Ibrahim: A 77-year-old woman with Stage IIIC ovarian cancer with a gBRCA mutation who develops severe anemia on olaparib

Dr Sulfi Ibrahim

- Diagnosed with Stage IIIC ovarian cancer
- Neoadjuvant carboplatin/paclitaxel x 3 cycles → optimal debulking surgery → adjuvant carboplatin/paclitaxel x 3 cycles
- Olaparib maintenance therapy is initiated, but the patient develops significant anemia (Hb 5 g/dL)
- Blood transfusion accompanied by olaparib dose reduction from 300 mg BID to 300 mg in the morning and 150 mg in the evening
- Repeat CBC shows Hb at 7 g/dL → second blood transfusion

Question

- What would be the best way to manage this patient who is extremely motivated to stay on the olaparib and complete the 2 years of adjuvant therapy, but obviously does have significant anemia with the olaparib? Should I dose reduce the olaparib further or would you advocate for the use of erythropoietin-stimulating agents to manage her anemia and keep her on a higher dose of olaparib?

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Case Presentation – Dr Mitchell: A 67-year-old woman with Stage M1C high-grade serous carcinoma of the peritoneum – sBRCA1m

Dr William Mitchell

- 5/2020 Presented with diarrhea x 10 days → CT scan: Multiple peritoneal implants (CA125: 325 U/mL)
- CT-guided biopsy: High-grade carcinoma
- Neoadjuvant carboplatin/paclitaxel → TAH/BSO (R0)
  - Pathology: Stage M1C, high-grade serous carcinoma of the peritoneum
- NGS: Somatic BRCA1 mutation, PD-L1 overexpression
- Adjuvant carboplatin/paclitaxel (CA125: 30 U/mL)
- Gynecologist started her on olaparib as part of her adjuvant therapy

Questions

- What is our strategy for these patients? What's the likelihood of survival? What is the role of olaparib in this situation? What is the risk-benefit analysis in a patient who's been rendered disease-free after effective front-line therapy? Is the olaparib being used for active disease or adjuvant therapy?
- Is the use of olaparib a cost-effective option in terms of value-based medicine contracting?

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Case Presentation – Dr Ma: A 47-year-old woman with recurrent serous/papillary ovarian cancer and a somatic BRCA1 mutation

Dr Yanjun Ma

- 9/2017: Diagnosed with Stage IIIB serous/papillary ovarian cancer, s/p debulking surgery
- Adjuvant carboplatin/paclitaxel
- Genetic testing: Somatic BRCA1 mutation
- 12/2019: Pelvic recurrence with 2nd debulking surgery
- NGS after 2nd surgery: No BRCA1 somatic mutation
- 1/2020: Liposomal doxorubicin/carboplatin → Maintenance niraparib
  - Severe marrow suppression and anemia → Switched to olaparib
- 1/2021: Radiographic PD → Gemcitabine/bevacizumab

Questions

- Was the change in her somatic BRCA1 mutation due to clonal selection or a discrepancy in the technology between genetic testing and NGS?
- Is the more recent practice to do debulking surgery first rather than neoadjuvant therapy first a data-based decision?

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Case Presentation – Dr Chase: A 63-year-old woman with recurrent high-grade fallopian tube carcinoma

Dr Dana Chase

- 12/2018: Diagnosed with high-grade serous carcinoma with elevated CA 125 (742), left supraclavicular lymphadenopathy
  - Neoadjuvant carbo/taxol for 3 cycles
  - 3/2019: Exploratory laparotomy, TAH-BSO, omentectomy and debulking; pathology shows high-grade fallopian tube cancer
  - 5/2019: Completed additional adjuvant chemotherapy
- 2020: Platinum-sensitive recurrence and paclitaxel/carboplatin initiated
- Genetic testing: Somatic BRCA mutation, HRD-positive

Question

- Would you incorporate the PAOLA regimen for this patient? Would you add bevacizumab alone?

Case Presentation – Dr Flores: A 72-year-old woman with relapsed BRCA wild-type HGSOC

Dr Regina Flores

- PMH: CAD s/p CABG
- Diagnosed with Stage IIIC HGSOC of the left ovary
- 2016: Neoadjuvant carboplatin/paclitaxel → R0 resection
- 2020: Relapsed in the urothelial bladder (refused second-look surgery)
- Carboplatin/paclitaxel x 6, with CR

Questions

- What would you do next? Which PARP inhibitor would you use and why?
- When and what is the role of a second-look operation?

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Case Presentation – Dr Hart: A 46-year-old woman with Stage IIB clear cell ovarian cancer

Dr Lowell Hart

- 2016: Diagnosed with Stage IIB clear cell ovarian cancer, s/p TAH-BSO and debulking
- 6/2016: Carboplatin/paclitaxel → PD
- Liposomal doxorubicin/bevacizumab, with mixed response
- Gemcitabine/bevacizumab, with improved response (PE treated with enoxaparin then apixaban)
- 2017 NGS: MSI-high; Genetic testing: BRCA wildtype
- Late 2017: Pembrolizumab, with mixed response → Added ipilimumab x 4, with PD
- 8/2018: Bevacizumab added to pembrolizumab, with improvement in response
- 7/2019: Olaparib added but discontinued due to hematochezia and colitis
- 9/2029: Niraparib added, with excellent tolerability and stable disease

Questions

- Do you believe we will be using these non-chemotherapy triplet regimens frequently in the future?
- In patients like her, who are reasonably stable on pembrolizumab, would you continue it indefinitely or stop after a couple of years?

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MODULE 1: Cases from Medical Oncologists

MODULE 2: Journal Club with Dr Banerjee

- PARP inhibitors in OC: An overview of the practice-changing trials
- SOLO-1: Patient-centered outcomes and effect of disease progression on health status
- SOLO-2: Olaparib tablets as maintenance therapy for platinum-sensitive relapsed OC with a BRCA1/2 mutation
- ARIEL3: Effect of age on efficacy, safety and patient-centered outcomes with maintenance rucaparib in OC
- MEDIOLA: Olaparib with durvalumab and bevacizumab in nongermline BRCA-mutated platinum-sensitive relapsed OC
- Undertreatment of older patients with newly diagnosed epithelial OC
- Exploring older women's attitudes to and experience of treatment for advanced OC
- Professional burnout in European young oncologists
- Impact of COVID-19 on oncology professionals: Results of the ESMO Resilience Task Force survey collaboration

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

MODULE 4: Key Recent Papers

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REVIEW ARTICLE

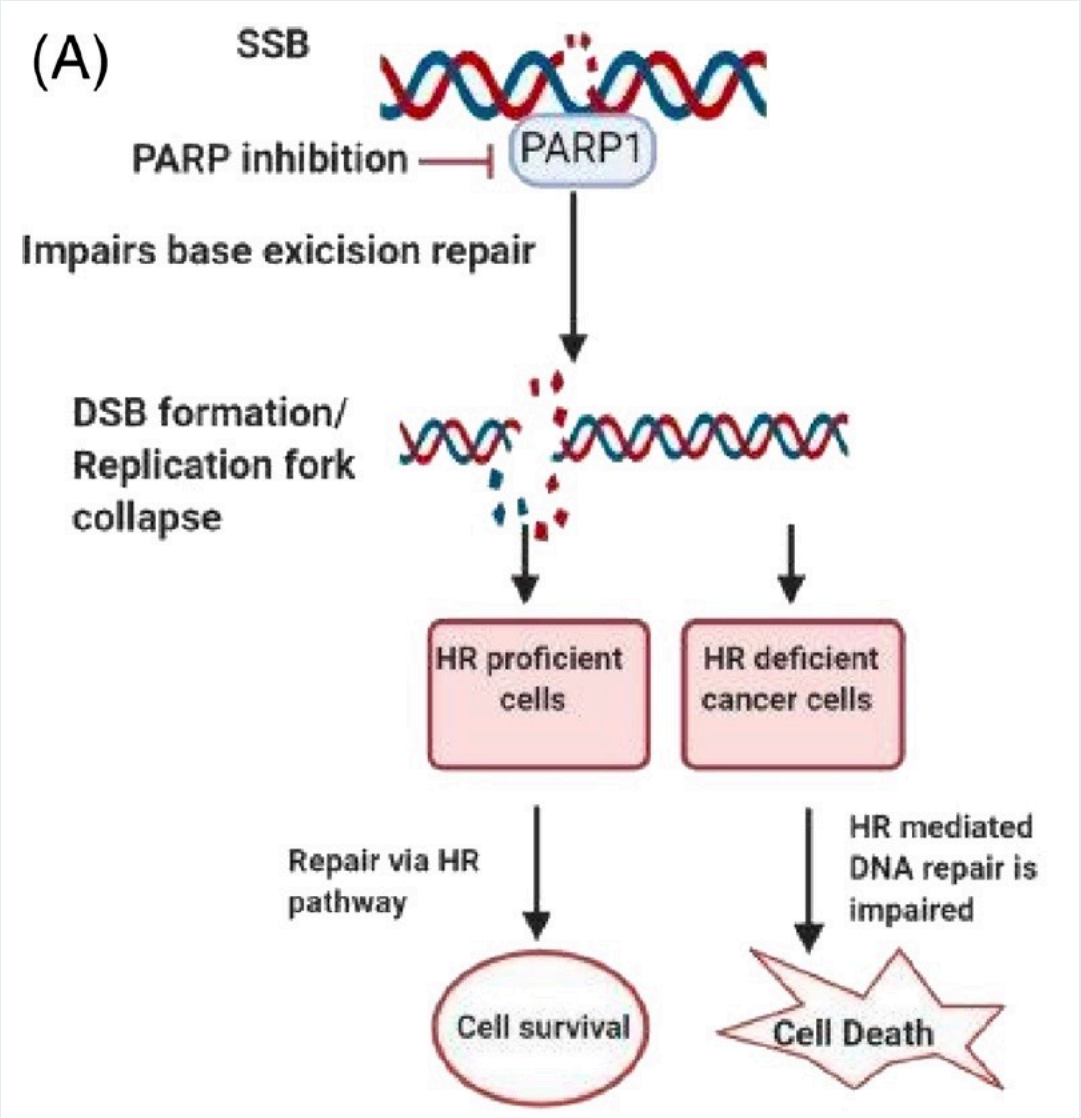
Genes Chromosomes Cancer 2021;60(5):385-97

WILEY

PARP inhibitors in ovarian cancer: An overview of the practice-changing trials

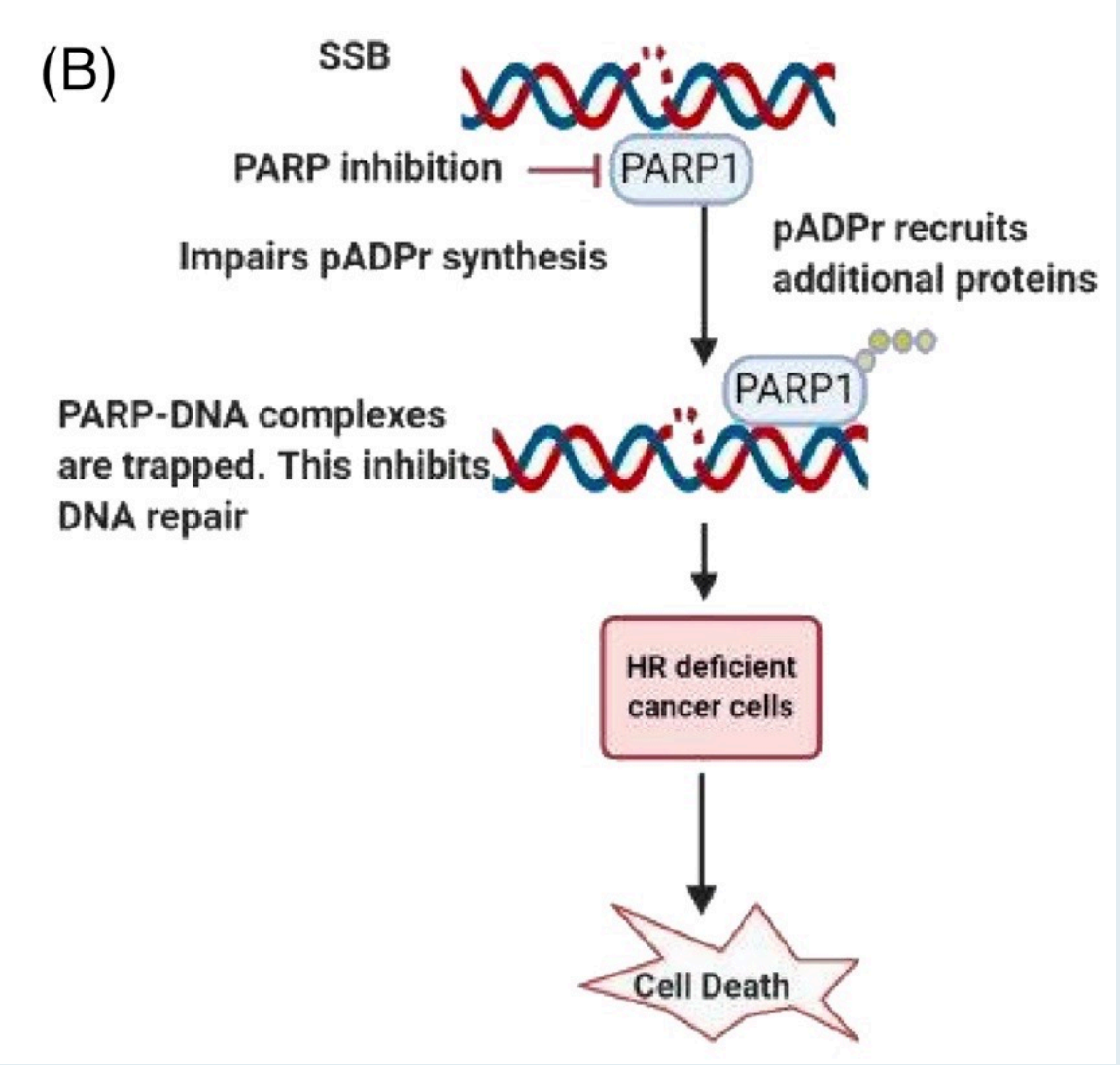
Tiffany Foo[1,2] | Angela George[1,2] | Susana Banerjee[1,3]

Mechanism of Action of PARP Inhibitors: (A) Impaired Base-Excision Repair



Foo T et al. *Genes Chromosomes Cancer* 2021;60(5):385-97.

Mechanism of Action of PARP Inhibitors: (B) PARP Trapping



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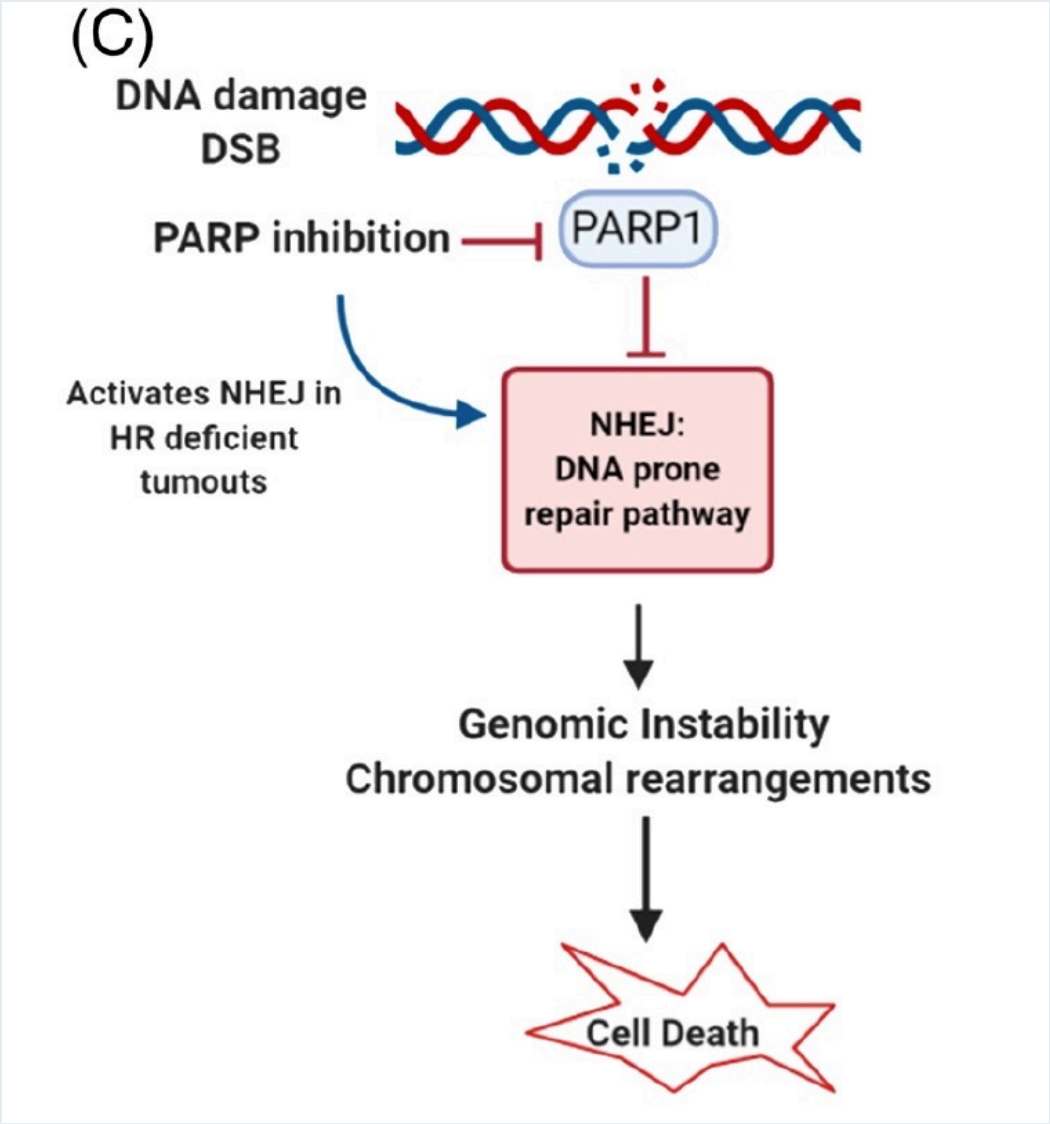
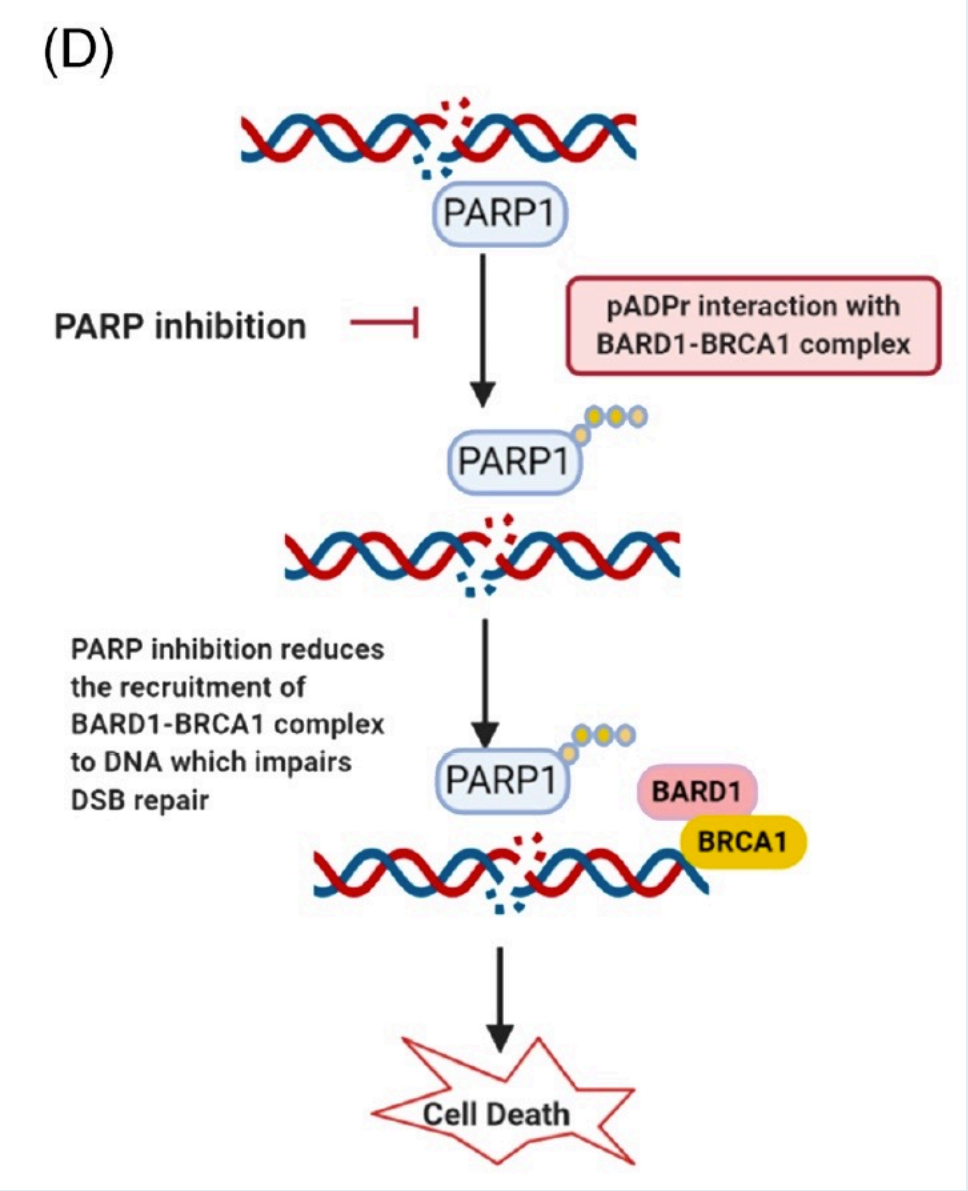
Mechanism of Action of PARP Inhibitors: (C) Nonhomologous End-Joining (NHEJ)



Foo T et al. *Genes Chromosomes Cancer* 2021;60(5):385-97.

Mechanism of Action of PARP Inhibitors: (D) Impaired BRCA1 Recruitment



Foo T et al. *Genes Chromosomes Cancer* 2021;60(5):385-97.

Lancet Oncol 2021;22:632-42

Patient-centred outcomes and effect of disease progression on health status in patients with newly diagnosed advanced ovarian cancer and a *BRCA* mutation receiving maintenance olaparib or placebo (SOLO1): a randomised, phase 3 trial

Michael Friedlander, Kathleen N Moore, Nicoletta Colombo, Giovanni Scambia, Byoung-Gie Kim, Ana Oaknin, Alla Lisyanskaya, Gabe S Sonke, Charlie Gourley, Susana Banerjee, Amit Oza, Antonio González-Martín, Carol Aghajanian, William H Bradley, Joyce Liu, Cara Mathews, Frédéric Selle, Alain Lortholary, Elizabeth S Lowe, Robert Hettle, Emuella Flood, Elena Parkhomenko, Paul DiSilvestro

Lancet Oncol 2021;22:620-31

Olaparib tablets as maintenance therapy in patients with platinum-sensitive relapsed ovarian cancer and a *BRCA1/2* mutation (SOLO2/ENGOT-Ov21): a final analysis of a double-blind, randomised, placebo-controlled, phase 3 trial

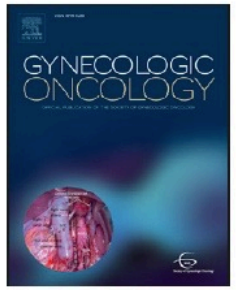
*Andrés Poveda, Anne Floquet, Jonathan A Ledermann, Rebecca Asher, Richard T Penson, Amit M Oza, Jacob Korach, Tomasz Huzarski, Sandro Pignata, Michael Friedlander, Alessandra Baldoni, Tjoung-Won Park-Simon, Kenji Tamura, Gabe S Sonke, Alla Lisyanskaya, Jae-Hoon Kim, Elias Abdo Filho, Tsveta Milenkova, Elizabeth S Lowe, Phil Rowe, Ignace Vergote, Eric Pujade-Lauraine, the SOLO2/ENGOT-Ov21 investigators**

Gynecologic Oncology 159 (2020) 101–111

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno



The effect of age on efficacy, safety and patient-centered outcomes with rucaparib: A post hoc exploratory analysis of ARIEL3, a phase 3, randomized, maintenance study in patients with recurrent ovarian carcinoma

Nicoletta Colombo [a,*], Amit M. Oza [b], Domenica Lorusso [c], Carol Aghajanian [d], Ana Oaknin [e], Andrew Dean [f], Johanne I. Weberpals [g], Andrew R. Clamp [h], Giovanni Scambia [c], Alexandra Leary [i], Robert W. Holloway [j], Margarita Amenedo Gancedo [k], Peter C. Fong [l], Jeffrey C. Goh [m], David M. O'Malley [n], Deborah K. Armstrong [o], Susana Banerjee [p], Jesus García-Donas [q], Elizabeth M. Swisher [r], Juliette Meunier [s], Terri Cameron [t], Lara Maloney [u], Sandra Goble [v], Josh Bedel [w], Jonathan A. Ledermann [x], Robert L. Coleman [y]

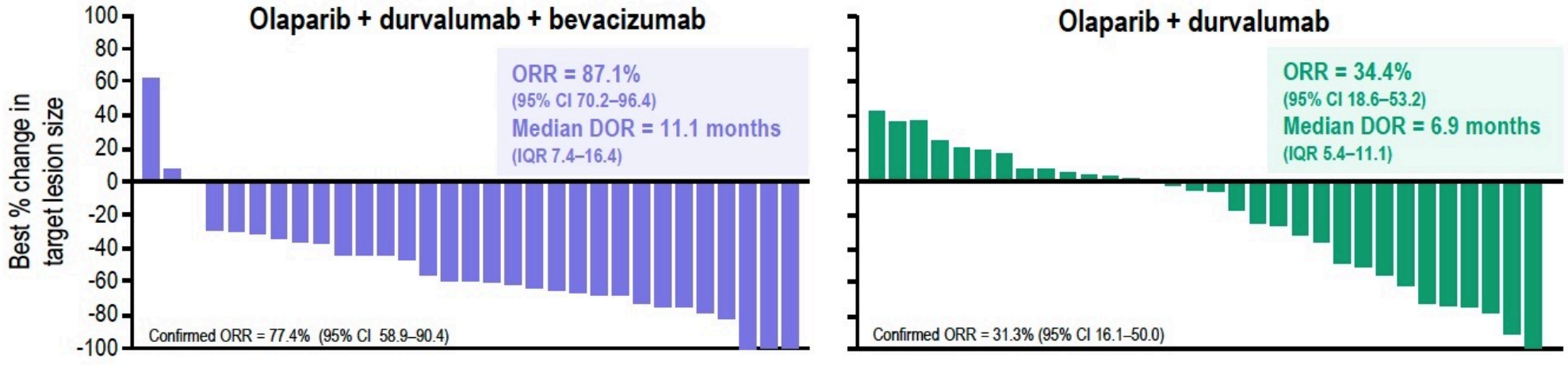
VIRTUAL 2020 ESMO congress

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]

Triplet cohort demonstrates high ORR



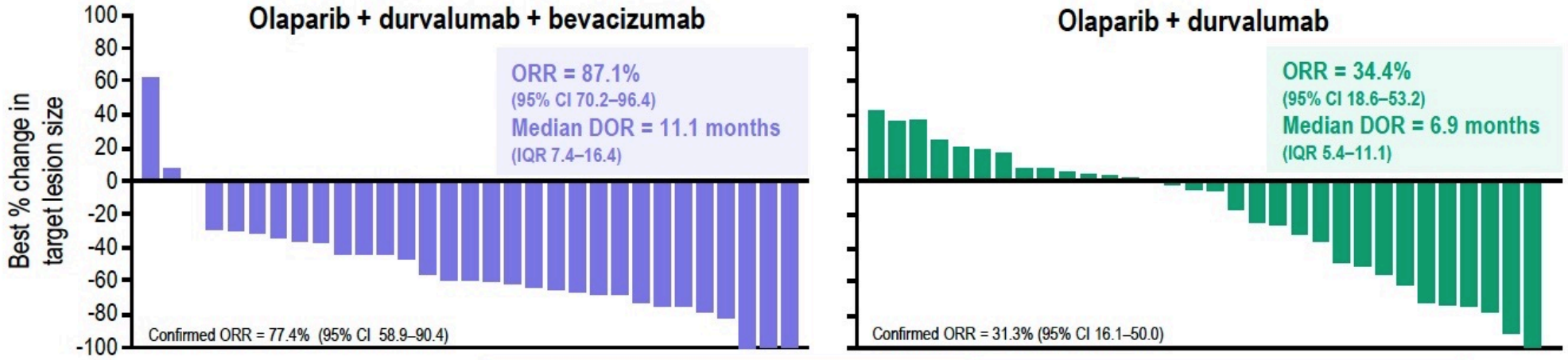
IQR, interquartile range

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

VIRTUAL 2020 ESMO congress

Triplet cohort demonstrates high ORR

Exploratory analysis suggests triplet cohort ORR is not GIS-dependent



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

RTP RESEARCH TO PRACTICE

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

Cancers (Basel) 2021;13(5):952

MDPI

Article

Under-Treatment of Older Patients with Newly Diagnosed Epithelial Ovarian Cancer Remains an Issue

Lucy Dumas [1,2], Rebecca Bowen [3], John Butler [1] and Susana Banerjee [1,2,*]

Cancers (Basel) 2021;13(6):1207

cancers

MDPI

Article

Exploring Older Women's Attitudes to and Experience of Treatment for Advanced Ovarian Cancer: A Qualitative Phenomenological Study

Lucy Dumas [1,2,†], Emma Lidington [3,†], Laura Appadu [1], Philippa Jupp [1], Olga Husson [2,4] and Susana Banerjee [1,2,*]

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 28: 1590–1596, 2017
doi:10.1093/annonc/mdx196
Published online 25 April 2017

ORIGINAL ARTICLE

Professional burnout in European young oncologists: results of the European Society for Medical Oncology (ESMO) Young Oncologists Committee Burnout Survey

S. Banerjee[1,*], R. Califano[2], J. Corral[3], E. de Azambuja[4], L. De Mattos-Arruda[5], V. Guarneri[6], M. Hutka[7], K. Jordan[8], E. Martinelli[9], G. Mountzios[10], M. A. Ozturk[11], M. Petrova[12], S. Postel-Vinay[13], M. Preusser[14], C. Qvortrup[15], M. N. M. Volkov[16], J. Tabernero[5], D. Olmos[17,18] & M. H. Strijbos[19]

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

ESMO OPEN | CANCER HORIZONS

ORIGINAL RESEARCH

The impact of COVID-19 on oncology professionals: results of the ESMO Resilience Task Force survey collaboration

S. Banerjee[1,2*], K. H. J. Lim[3,4], K. Murali[5], K. Kamposioras[3], K. Punie[6], C. Oing[7], M. O'Connor[8], E. Thorne[9], B. Devnani[10], M. Lambertini[11,12], C. B. Westphalen[13], P. Garrido[14], T. Amaral[15,16], G. Morgan[17], J. B. A. G. Haanen[18] & C. Hardy[9]

ESMO Open 2021;6(2):100058.

Meet The Professor with Dr Banerjee

MODULE 1: Cases from Medical Oncologists

MODULE 2: Journal Club with Dr Banerjee

- PARP inhibitors in OC: An overview of the practice-changing trials
- SOLO-1: Patient-centered outcomes and effect of disease progression on health status
- SOLO-2: Olaparib tablets as maintenance therapy for platinum-sensitive relapsed OC with a BRCA1/2 mutation
- ARIEL3: Effect of age on efficacy, safety and patient-centered outcomes with maintenance rucaparib in OC
- MEDIOLA: Olaparib with durvalumab and bevacizumab in nongermline BRCA-mutated platinum-sensitive relapsed OC
- Undertreatment of older patients with newly diagnosed epithelial OC
- Exploring older women's attitudes to and experience of treatment for advanced OC
- Professional burnout in European young oncologists
- Impact of COVID-19 on oncology professionals: Results of the ESMO Resilience Task Force survey collaboration

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

MODULE 4: Key Recent Papers

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In general, what is the optimal approach to mutation testing for possible use of a PARP inhibitor for a patient with newly diagnosed ovarian cancer?

 Dr Armstrong	Multigene germline and somatic/NGS	 Dr Matulonis	Multigene germline and somatic/NGS
 Dr Coleman	Multigene germline and somatic/NGS	 Dr Mirza	Multigene germline and somatic/NGS
 Dr Dizon	Germline BRCA; if negative, multigene somatic (eg, NGS)	 Dr Moore	Multigene germline and somatic/NGS
 Prof Ledermann	Multigene germline and somatic/NGS	 Dr Westin	Germline BRCA; if negative, multigene somatic (eg, NGS)

NGS = next-generation sequencing

Do you routinely assess homologous recombination deficiency (HRD) status in your patients with advanced ovarian cancer?

 Dr Armstrong	No	 Dr Matulonis	No
 Dr Coleman	Yes	 Dr Mirza	No
 Dr Dizon	Yes	 Dr Moore	Yes
 Prof Ledermann	No	 Dr Westin	Yes

NGS = next-generation sequencing

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

 Dr Armstrong	Carboplatin/paclitaxel → olaparib	 Dr Matulonis	Carboplatin/paclitaxel → olaparib
 Dr Coleman	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib	 Dr Mirza	Carboplatin/paclitaxel → niraparib
 Dr Dizon	Carboplatin/paclitaxel → olaparib	 Dr Moore	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 Prof Ledermann	Carboplatin/paclitaxel → olaparib	 Dr Westin	Carboplatin/paclitaxel → olaparib or niraparib

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

 Dr Armstrong	Carboplatin/paclitaxel → olaparib	 Dr Matulonis	Carboplatin/paclitaxel → olaparib
 Dr Coleman	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib	 Dr Mirza	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 Dr Dizon	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib	 Dr Moore	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 Prof Ledermann	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib	 Dr Westin	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib

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

 Dr Armstrong	Carboplatin/paclitaxel → olaparib	 Dr Matulonis	Carboplatin/paclitaxel → olaparib
 Dr Coleman	Carboplatin/paclitaxel + bevacizumab → bevacizumab + niraparib	 Dr Mirza	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 Dr Dizon	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib	 Dr Moore	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib
 Prof Ledermann	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib	 Dr Westin	Carboplatin/paclitaxel + bevacizumab → bevacizumab + olaparib

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

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

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

 Dr Armstrong	Carboplatin/paclitaxel OR carboplatin/paclitaxel → niraparib	 Dr Matulonis	Discuss several options with patient
 Dr Coleman	Carboplatin/paclitaxel + bevacizumab → bevacizumab	 Dr Mirza	Carboplatin/paclitaxel → niraparib
 Dr Dizon	Carboplatin/paclitaxel → niraparib	 Dr Moore	Carboplatin/paclitaxel + bevacizumab → bevacizumab
 Prof Ledermann	Carboplatin/paclitaxel	 Dr Westin	Carboplatin/paclitaxel OR carboplatin/paclitaxel → niraparib

A 60-year-old woman with Stage IIIC ovarian cancer (BRCA wild type) is s/p suboptimal debulking surgery with an elevated CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy if her disease was HRD-positive

 Dr Armstrong	Carbo/pac → niraparib	 Dr Matulonis	Discuss several options with patient
 Dr Coleman	Carbo/pac + bev → bev + olaparib	 Dr Mirza	Carbo/pac + bev → bev + olaparib
 Dr Dizon	Carbo/pac + bev → bev + olaparib	 Dr Moore	Carbo/pac + bev → bev + olaparib
 Prof Ledermann	Carbo/pac + bev → bev + olaparib	 Dr Westin	Carbo/pac + bev → bev + olaparib

Carbo/pac = carboplatin/paclitaxel; bev = bevacizumab

A 60-year-old woman with Stage IIIC ovarian cancer (BRCA wild type) is s/p suboptimal debulking surgery with an elevated CA-125 level. Regulatory and reimbursement issues aside, what would you recommend as postoperative systemic therapy if her disease was HRD-negative

 Dr Armstrong	Carbo/pac OR carbo/pac → niraparib	 Dr Matulonis	Discuss several options with patient
 Dr Coleman	Carbo/pac + bev → bev	 Dr Mirza	Carbo/pac → niraparib
 Dr Dizon	Carbo/pac + bev → niraparib	 Dr Moore	Carbo/pac + bev → bev
 Prof Ledermann	Carbo/pac + bev → bev	 Dr Westin	Carbo/pac + bev → bev

Carbo/pac = carboplatin/paclitaxel; bev = bevacizumab

A 60-year-old woman with Stage IIIC ovarian cancer and a germline BRCA mutation undergoes suboptimal debulking surgery and receives carboplatin/paclitaxel followed by olaparib. For how long would you typically continue the olaparib if the patient is tolerating it well?

 Dr Armstrong	2 years (depends on disease status at completion of chemotherapy)	 Dr Matulonis	2 years
 Dr Coleman	2 years	 Dr Mirza	2 years
 Dr Dizon	Indefinitely	 Dr Moore	2 years
 Prof Ledermann	2 years	 Dr Westin	2 years

A 60-year-old woman with Stage IIIC ovarian cancer (BRCA wild type, HRD-positive) undergoes suboptimal debulking surgery and receives carboplatin/paclitaxel followed by niraparib. For how long would you typically continue the niraparib if the patient is tolerating it well?

 Dr Armstrong	3 years	 Dr Matulonis	3 years
 Dr Coleman	3 years	 Dr Mirza	3 years
 Dr Dizon	Indefinitely	 Dr Moore	3 years
 Prof Ledermann	3 years	 Dr Westin	3 years

Regulatory and reimbursement issues aside, which starting dose of niraparib would you use for a 125-lb patient with advanced ovarian cancer and a platelet count of 200,000 after a response to front-line platinum-based chemotherapy?

1. 300 mg daily
2. 200 mg daily
3. 100 mg daily
4. Other

What starting dose of niraparib would you use for a 125-lb patient with advanced ovarian cancer after response to front-line platinum-based chemotherapy with a platelet count of 200,000 for whom you are about to initiate maintenance niraparib?

 Dr Armstrong	200 mg daily	 Dr Matulonis	200 mg daily
 Dr Coleman	200 mg daily	 Dr Mirza	200 mg daily
 Dr Dizon	300 mg daily	 Dr Moore	200 mg daily
 Prof Ledermann	200 mg daily	 Dr Westin	200 mg daily

A woman in her mid-60s with recurrent high-grade serous ovarian cancer begins rucaparib monotherapy (600 mg BID). Within a few weeks her serum creatinine increases from 0.86 mg/dL to 1.6 mg/dL. What would be the optimal management approach?

 Dr Armstrong	Continue rucaparib at same dose	 Dr Matulonis	Continue rucaparib at the same dose
 Dr Coleman	Continue rucaparib at the same dose	 Dr Mirza	Hold rucaparib until creatinine returns to normal, then restart at the same dose
 Dr Dizon	Hold rucaparib until creatinine returns to normal, then restart at reduced dose	 Dr Moore	Continue rucaparib at the same dose
 Prof Ledermann	Hold rucaparib until creatinine returns to normal, then restart at the same dose	 Dr Westin	Continue rucaparib at the same dose

In general, what is your approach to antiemetic therapy for a patient with ovarian cancer who is starting treatment on a PARP inhibitor?

 Dr Armstrong	Recommend antiemetic if pt has nausea
 Dr Coleman	Recommend antiemetic if pt has nausea
 Dr Dizon	Prophylactic antiemetic prior to PARPi
 Prof Ledermann	Recommend antiemetic if pt has nausea
 Dr Matulonis	Recommend antiemetic if pt has nausea
 Dr Mirza	Reduce PARPi dose if pt has nausea
 Dr Moore	Prophylactic antiemetic prior to PARPi for the first 2 months
 Dr Westin	Recommend antiemetic if pt has nausea

Does your approach to antiemetic therapy differ according to which PARP inhibitor is administered?

 Dr Armstrong	No	 Dr Matulonis	Yes (cautious use of ondansetron w/niraparib as niraparib may also cause constipation)
 Dr Coleman	No	 Dr Mirza	No
 Dr Dizon	No	 Dr Moore	No
 Prof Ledermann	No	 Dr Westin	No

According to your clinical experience, do PARP inhibitors cause insomnia?

 Dr Armstrong	No	 Dr Matulonis	Yes
 Dr Coleman	Yes	 Dr Mirza	No
 Dr Dizon	No	 Dr Moore	Yes
 Prof Ledermann	Yes	 Dr Westin	Yes

Meet The Professor with Dr Banerjee

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Current FDA-Approved and Investigational PARP Inhibitors: Differences

PARP inhibitor	IC_{50}	PARP trapping potency	PARPi target selectivity (strength of binding)	Half life	Dose
Olaparib	6 nM	1	Potent PARP1 inhibitor, less selective	11.9 hours	400 mg BID
Rucaparib	21 nM	1	Potent PARP1 inhibitor, less selective	18 hours	600 mg BID
Niraparib	60 nM	~2	Selective inhibitor of PARP1 and 2	36 hours	300 mg qd
Veliparib	30 nM	<0.2	Potent PARP1 inhibitor, less selective	5 hours	400 mg BID
Talazoparib	4 nM	~100	Potent PARP1 inhibitor, less selective	50 hours	1 mg qd

Lim JSJ, Tan DSP. *Cancers* 2017;9(8):pii:E109.

Phase III First-Line PARP Maintenance Trials

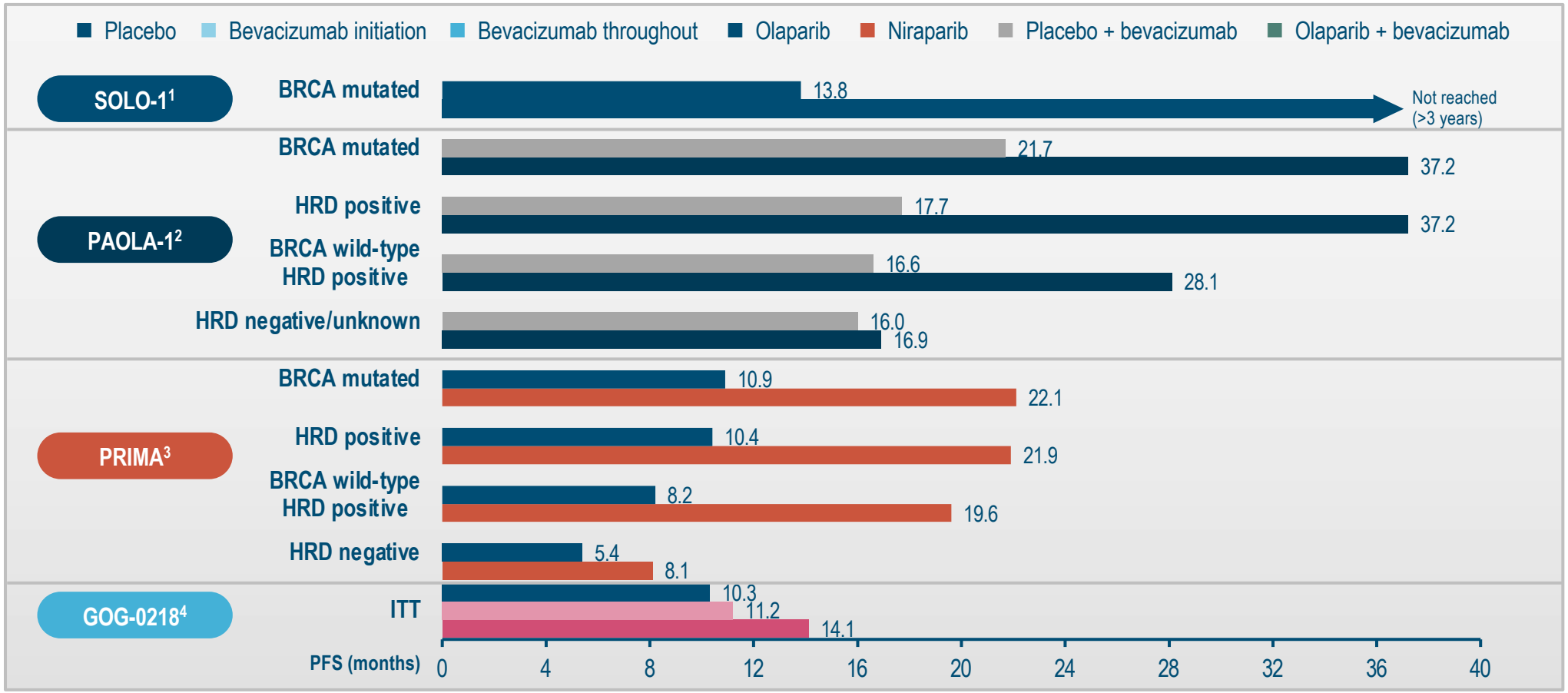
Study Design	SOLO-1 (N=451)	PAOLA-1 (N=612)	PRIMA (N=620)	VELIA (N=1140)
Treatment arms vs placebo	**Olaparib (n=260)**	**Bevacizumab ± Olaparib**	**Niraparib**	**Veliparib**
Patient Population	*BRCA* mutation	All comers	All comers	*All comers*
Treatment Duration	24 months	15 months for Bev 24 months for Olaparib	36 months or until PD	24 months

[a]Residual disease based on stage was not reported. [b]Stage III and IV eligible, but requirements for prior surgery not reported (NR) on clinicaltrials.gov

Burger RA, *N Engl J Med* 2011; Norquist B *Clin Cancer Res* 2018*; Bevacizumab* prescribing information;
Moore K, NEJM 2018; Gonzalez-Martin NEJM 2019; Ray-Coquard NEJM 2019; Coleman NEJM 2019

Courtesy of Shannon N Westin, MD, MPH

SUMMARY OF APPROVED MAINTENANCE STUDIES IN THE FIRST-LINE



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

BRCA, breast cancer gene; HRD, homologous recombination deficiency; ITT, intent-to-treat; PFS, progression-free survival

1. Moore K, et al. N Engl J Med 2018;379:2495–2505; 2. Ray-Coquard IL, et al. N Engl J Med 2019; 381:2416–2428; 3. Gonzalez-Martin A, et al. N Engl J Med 2019;381:2391–2402; 4. Burger RA, et al. N Engl J Med 2011;365:2473–2483

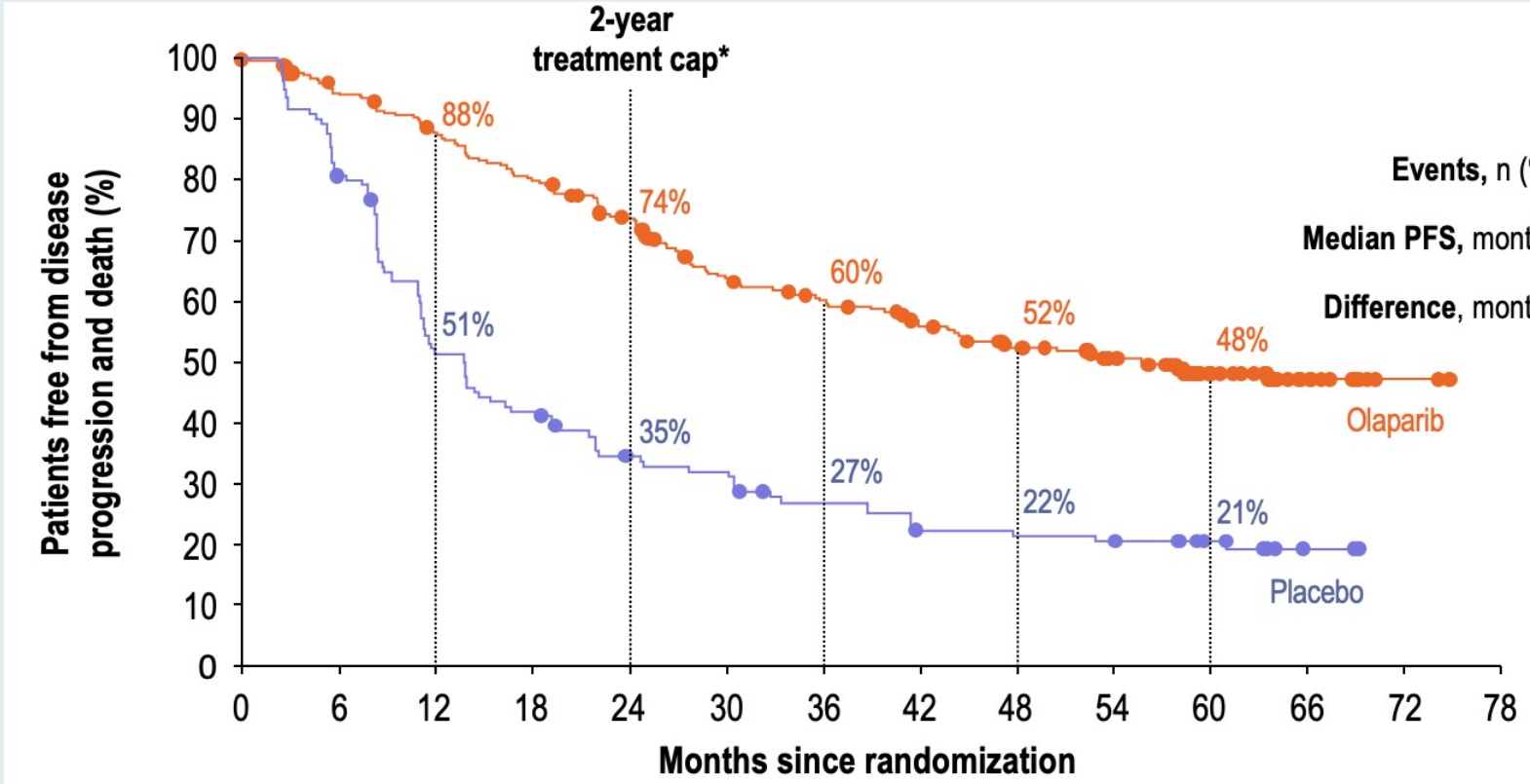
Courtesy of Robert L Coleman, MD

Maintenance Olaparib for Patients (pts) with Newly Diagnosed, Advanced Ovarian Cancer (OC) and a BRCA Mutation (BRCAm): 5-Year (y) Follow-Up (f/u) from SOLO1

Banerjee S et al.

ESMO 2020;Abstract 811MO.

SOLO-1: PFS Benefit of Maintenance Olaparib Was Sustained Beyond the End of Treatment



	Olaparib (N=260)	Placebo (N=131)
Events, n (%)	118 (45)	100 (76)
Median PFS, months	**56.0**	**13.8**
Difference, months	42.2	
	HR 0.33 (95% CI 0.25–0.43)	

Median treatment duration:
Olaparib, 24.6 months
Placebo†, 13.9 months

No. at risk														
Olaparib	260	229	212	194	173	140	129	115	101	91	58	30	2	0
Placebo	131	103	65	53	41	38	30	24	23	22	16	3	0	

*13 patients, all in the olaparib arm, continued study treatment past 2 years; †n=130 (safety analysis set)
Investigator-assessed by modified RECIST v1.1. DCO: 5 March 2020

Banerjee S et al. ESMO 2020;Abstract 811MO.

RTP RESEARCH TO PRACTICE

Secondary efficacy outcomes* support the observed PFS benefit

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

Safety profile remained consistent with the primary DCO

n (%)	Olaparib (n=260)	Placebo (n=130)
Any AE	256 (98)	120 (92)
Grade ≥3 AE	103 (40)	25 (19)
Serious AE	55 (21)	17 (13)
AE leading to dose interruption	136 (52)	22 (17)
AE leading to dose reduction	75 (29)	4 (3)
AE leading to treatment discontinuation	30 (12)	4 (3)
MDS/AML	3 (1)	0 (0)
New primary malignancy	7 (3)	5 (4)

No additional cases of MDS/AML reported; incidence remained <1.5%

Follow-up for MDS/AML continued until death due to any cause

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

Banerjee S et al. ESMO 2020;Abstract 811MO.

Maintenance Olaparib for Patients (pts) with Newly Diagnosed, Advanced Ovarian Cancer and a BRCA Mutation: 5-Year Follow-Up from SOLO-1

Bradley WH et al.

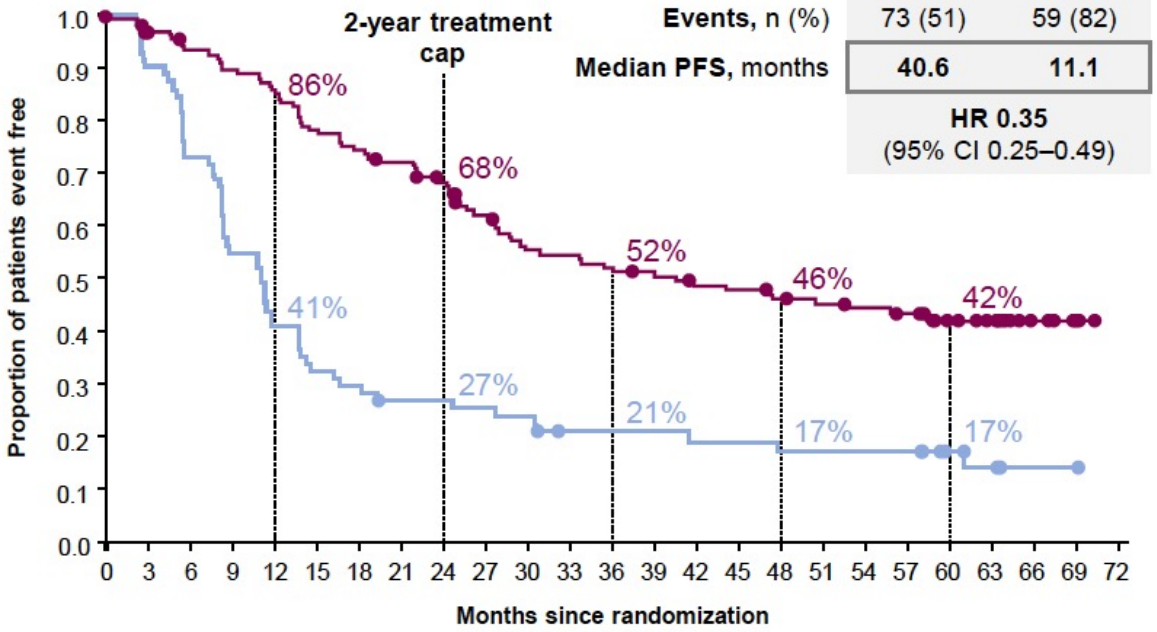
SGO 2021;Abstract 10520.

SOLO-1: Updated PFS by Risk Group

Higher-risk

Baseline characteristic, n (%)	Olaparib (N=146)	Placebo (N=73)
Interval debulking surgery	94 (64)	43 (59)
CR to prior chemotherapy*	107 (73)	54 (74)
*BRCA1*m	109 (75)	43 (59)
*BRCA2*m	36 (25)	30 (41)
*BRCA1*m and *BRCA2*m	1 (1)	0

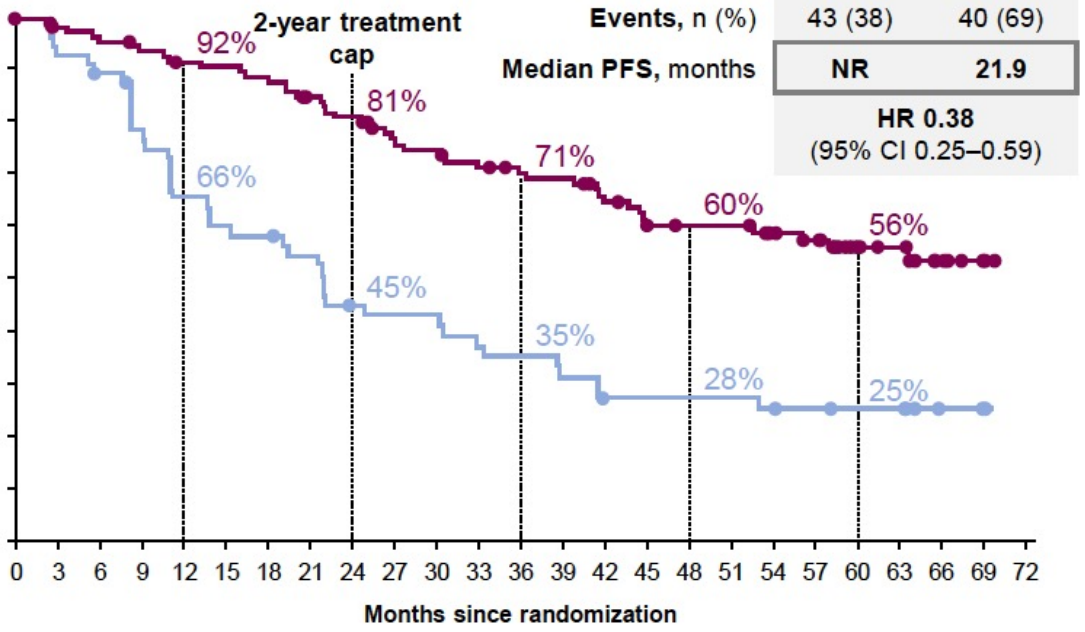
	(N=142)†	(N=72)†
Events, n (%)	73 (51)	59 (82)
Median PFS, months	40.6	11.1
	HR 0.35 (95% CI 0.25–0.49)	



Lower-risk

Baseline characteristic, n (%)	Olaparib (N=114)	Placebo (N=58)
Interval debulking surgery	0	0
CR to prior chemotherapy*	106 (93)	53 (91)
*BRCA1*m	82 (72)	48 (83)
*BRCA2*m	30 (26)	10 (17)
*BRCA1*m and *BRCA2*m	2 (2)	0

	(N=114)	(N=58)
Events, n (%)	43 (38)	40 (69)
Median PFS, months	NR	21.9
	HR 0.38 (95% CI 0.25–0.59)	



Bradley WH et al. SGO 2021;Abstract 10520.

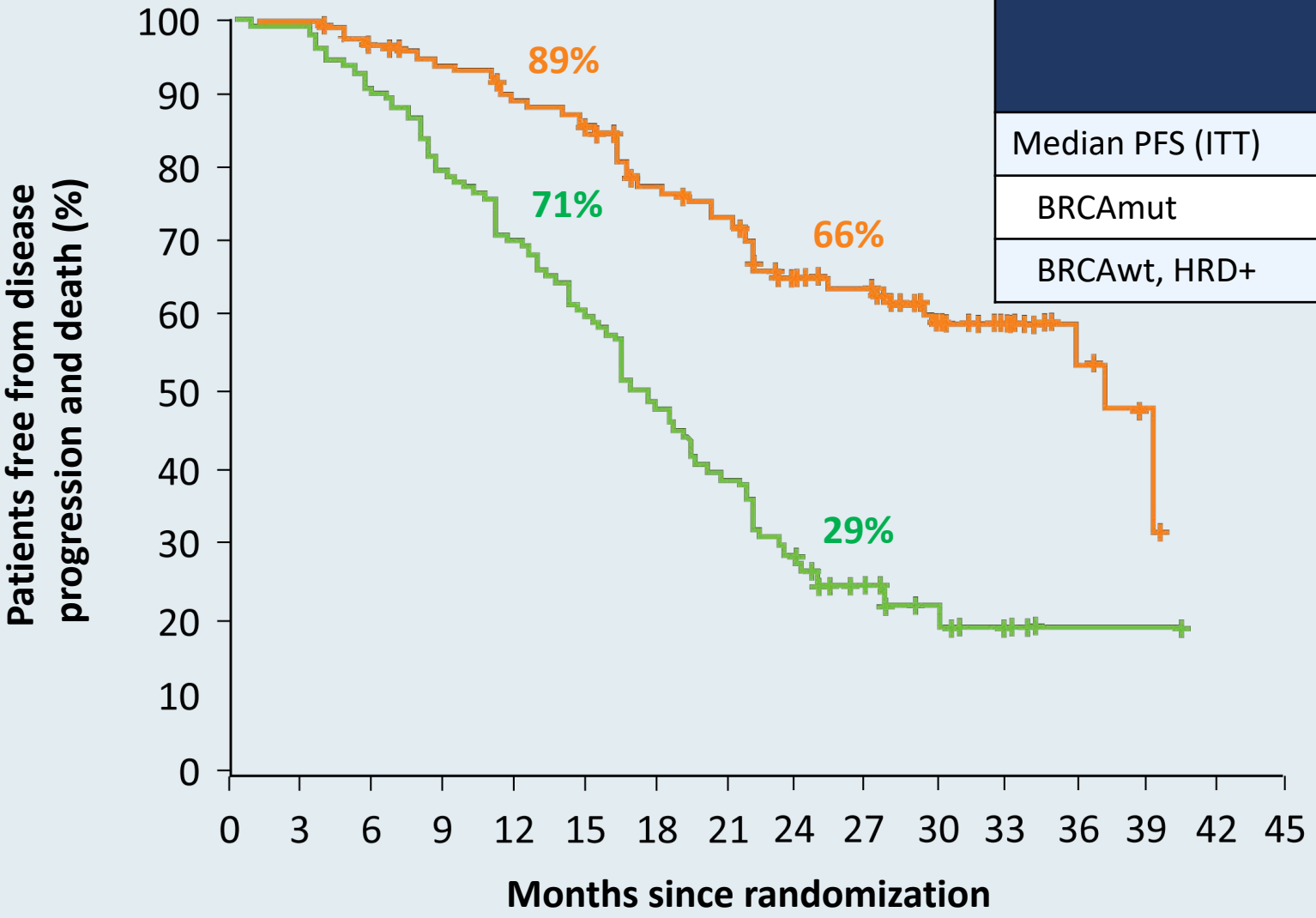
RTP RESEARCH TO PRACTICE

Maintenance Olaparib plus Bevacizumab (bev) in Patients (pts) with Newly Diagnosed Advanced High-grade Ovarian Carcinoma (HGOC): Final Analysis of Second Progression-Free Survival (PFS2) in the Phase III PAOLA-1/ENGOT-ov25 Trial

Gonzalez Martin A et al.

ESMO 2020;Abstract LBA33.

PAOLA-1: Progression-Free Survival (ITT)



	Olaparib + bevacizumab (n = 537)	Placebo + bevacizumab (n = 269)	Hazard ratio
Median PFS (ITT)	22.1 mo	16.6 mo	0.59
BRCAmut	37.2 mo	17.7 mo	0.33
BRCAwt, HRD+	28.1 mo	16.6 mo	0.43

Gonzalez Martin A et al. ESMO 2020;Abstract LBA33.

RTP RESEARCH TO PRACTICE

Niraparib Efficacy and Safety in Patients with BRCA Mutated (BRCAm) Ovarian Cancer: Results from Three Phase 3 Niraparib Trials

Gonzalez Martin A et al.

ASCO 2021;Abstract 5518.

Patients with BRCA-Mutated Ovarian Cancer in the PRIMA, NOVA and NORA Trials

- Overall, 526 patients in PRIMA, NOVA, and NORA had *BRCA*m ovarian cancer
- Mutations in *BRCA*1 were most common (60.6%–80.0%)

*BRCA*m Patient Characteristics and Baseline Demographics[a]						
	PRIMA (1L maintenance)		NOVA (2L maintenance)		NORA (2L maintenance)	
Characteristic	Niraparib (n=152)	Placebo (n=71)	Niraparib (n=138)	Placebo (n=65)	Niraparib (n=65)	Placebo (n=35)
Age, median (range), years	56.5 (32–83)	57 (33–82)	57 (36–83)	58 (38–73)	NA	NA
*BRCA*m status, n (%)[b]						
BRCA1 only	105 (69.1)	43 (60.6)	85 (61.6)	43 (66.2)	50 (76.9)	28 (80.0)
BRCA2 only	47 (30.9)	28 (39.4)	51 (37.0)	18 (27.7)	14 (21.5)	7 (20.0)
BRCA1 and *BRCA2*	0	0	9 (6.5)	4 (6.2)	1 (1.5)	0

Gonzalez Martin A et al. ASCO 2021;Abstract 5188.

Adverse Events: Class Effects and Specific Drug Differences

	Notes	Olaparib	Niraparib	Rucaparib	Talazoparib	Veliparib
Fatigue	50%-70%, mainly Gr1-2	✓	✓	✓	✓	✓
Hematologic AEs						
Anemia	40%-60%	✓	✓	✓	✓	✓ --
Thrombocytopenia	Niraparib dose adjustment, based on platelet counts	✓	✓ ++	✓	✓	✓
Neutropenia	~20%	✓	✓	✓	✓	✓
Gastrointestinal AEs						
Nausea/vomiting	Moderately emetic >30%	✓	✓	✓	✓	✓
Diarrhea	~33%	✓	✓	✓	✓	✓
Laboratory abnormalities						
ALT/AST elevation	5%-10% olaparib, niraparib; 34% rucaparib	✓ --	✓ --	✓ ++	✓ ++	?
Creatinine elevation	10%-12%	✓	✓	✓	NR	NR

NR = not reported

Olaparib PI, rev 5/2020; Niraparib PI, rev 4/2020; Rucaparib PI, rev 5/2020; Talazoparib PI, rev 3/2020;
Madariaga A et al. *Int J Gyn Cancer* 2020 April 9;[Online ahead of print]; Litton JK et al. *NEJM* 2018;379:753-63.

Adverse Events: Class Effects and Specific Drug Differences

	Notes	Olaparib	Niraparib	Rucaparib	Talazoparib	Veliparib
Respiratory disorders						
Dyspnea +/- cough	10%-20%, usually Gr 1-2	✓	✓	✓	✓	NR
Nasopharyngitis	~10%	✓	✓	✓	✓	NR
Nervous system and psychiatric disorders						
Insomnia/headache	10%-25%, usually Gr 1-2	✓	✓	✓	✓	✓
Dermatologic toxicity						
Rash, photosensitivity		<1%	✓	✓++	NR	NR
Cardiovascular toxicity						
Hypertension, tachycardia, palpitation		1%	✓++	NR	NR	NR
Rare AEs						
MDS/AML	~1% of pts	✓	✓	✓	✓	✓

NR = not reported

Olaparib PI, rev 5/2020; Niraparib PI, rev 4/2020; Rucaparib PI, rev 5/2020; Talazoparib PI, rev 3/2020; Madariaga A et al. *Int J Gyn Cancer* 2020 April 9;[Online ahead of print]; Litton JK et al. *NEJM* 2018;379:753-63.

Dose Adjustments for Adverse Events

Olaparib dose reductions	Dose (tablet)
Starting dose	• 300 mg BID
First dose reduction	• 250 mg BID
Second dose reduction	• 200 mg BID

Niraparib dose reductions	Dose
Starting dose	• 300 mg daily
First dose reduction	• 200 mg daily
Second dose reduction	• 100 mg daily

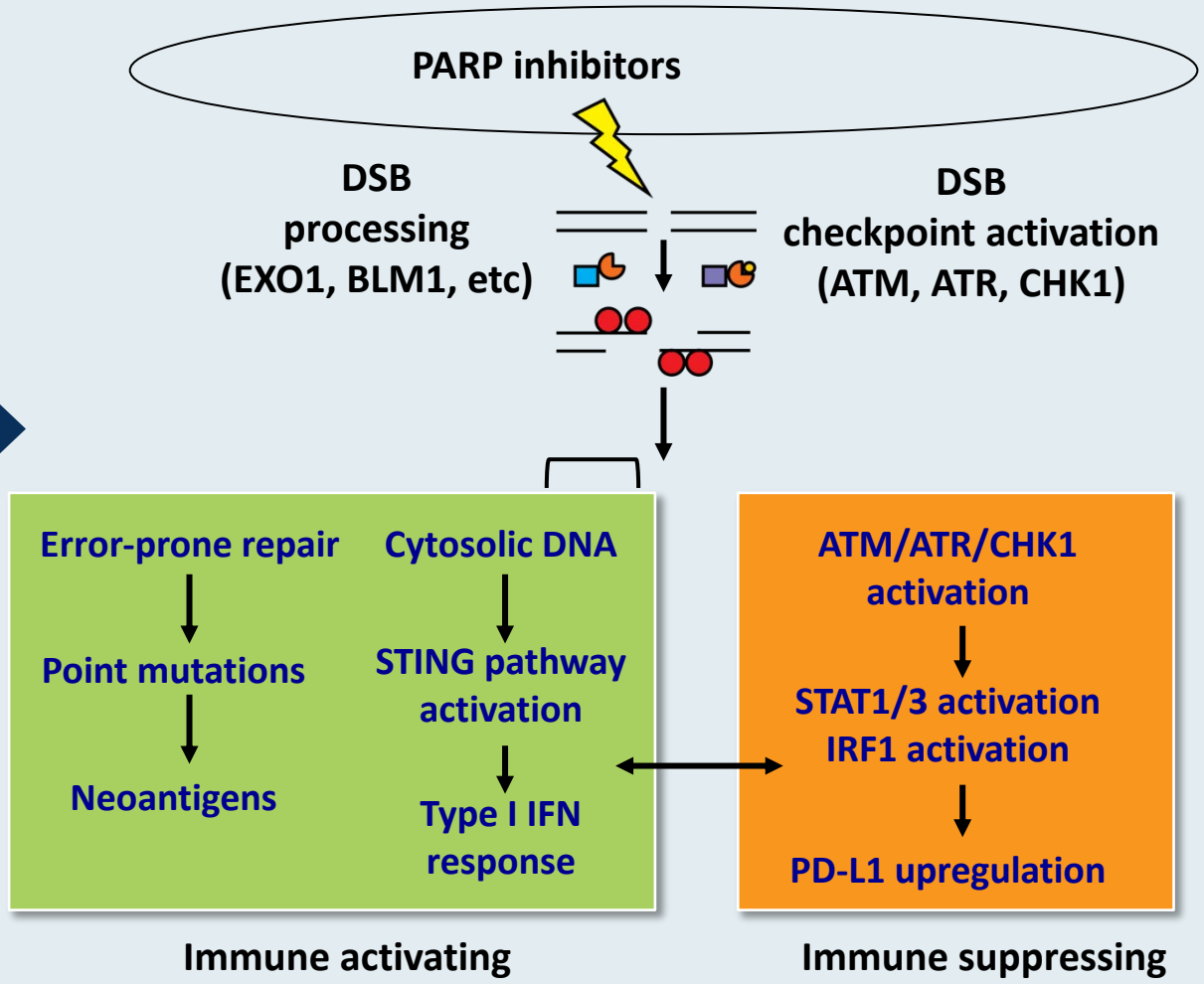
Rucaparib dose reductions	Dose
Starting dose	• 600 mg twice daily
First dose reduction	• 500 mg twice daily
Second dose reduction	• 400 mg twice daily
Third dose reduction	• 300 mg twice daily

Courtesy, Shannon N Westin, MD, MPH

FDA Prescribing Information.

Biologic Rationale for the Combination of a PARP Inhibitor with an Immune Checkpoint Inhibitor

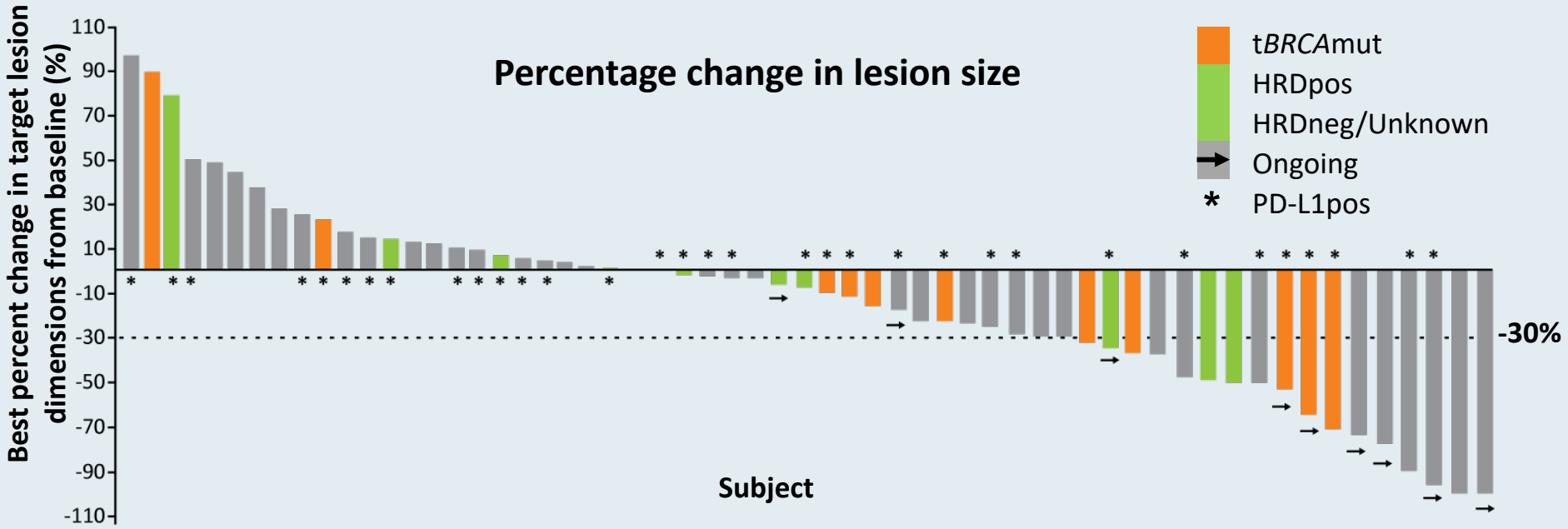
Preclinical models indicate synergy between PARPi + anti-PD-1 agents regardless of *BRCA* mutation status or PD-L1 status



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

Konstantinopoulos P et al. ASCO 2018;Abstract 106.

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



Response	All patients	tBRCAmut	HRD-pos	tBRCAwt	HRD-neg
ORR	11/47 (23%)	2/8 (25%)	4/16 (25%)	9/37 (24%)	7/26 (27%)
DCR	30/47 (64%)	5/8 (63%)	11/16 (69%)	24/37 (65%)	15/26 (58%)

Konstantinopoulos P et al. ASCO 2018;Abstract 106.

Select Ongoing or Planned Phase III Trials of PARP Inhibitors in Combination Therapy

Trial name (Trial identifier)	N	Setting	Treatment arms
ATHENA (NCT03522246)	1,012	Maintenance therapy after 1L platinum-based chemo	• **Rucaparib** + Nivolumab • **Rucaparib** + Placebo • Nivolumab + Placebo • Placebo
DUO-O (NCT03737643)	1,056	Maintenance therapy after 1L platinum-based chemo/Bev ± Durvalumab	• Bev • Bev + Durvalumab • Bev + Durvalumab + **Olaparib**
ANITA (NCT03598270)	414	Recurrent, platinum-sensitive	• Placebo + Platinum-based chemo → **Niraparib** • ATEZO + Platinum-based chemo → **Niraparib** + ATEZO

Bev = bevacizumab; ATEZO = atezolizumab

www.clinicaltrials.gov. Accessed December 2018.

FDA-Approved PARP Inhibitors as Maintenance Therapy for Recurrent, Platinum-Sensitive Disease

Niraparib

Indications:
- **Maintenance following response to platinum-based therapy**
- **Irrespective of BRCA status**

Pivotal study: ENGOT-OV16/NOVA

Approved: 3/2017

Rucaparib

Indications:
- **Maintenance following response to platinum-based therapy**
- **Irrespective of BRCA status**

Pivotal study: ARIEL3

Approved: 4/2018

Olaparib

Indications:
- **Maintenance following response to platinum-based therapy**
- **Irrespective of BRCA status**

Pivotal studies: SOLO-2, Study 19

Approved: 8/2017

Niraparib FDA insert, revised 3/2017; Rucaparib FDA insert, revised 4/2018; Olaparib FDA insert, revised 1/2018; Pujade-Lauraine E et al. *Lancet* 2017;18(9):1274-84; Mirza MR et al. *N Engl J Med* 2016;375(22):2154-64; Coleman RL et al. *Lancet* 2017;390(10106):1949-61; Ledermann J et al. *N Engl J Med* 2012;366:1382-92.

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

	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.

Efficacy Summary of PARP Inhibitors for Recurrent, Platinum-Sensitive OC

	PARPi	Control	HR
NOVA[1] — 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[2] — Olaparib			
gBRCA mutation	19.1 mo	5.5 mo	0.30
ARIEL3[3-4] — 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] Pujade-Lauraine E et al. *Lancet* 2017;18(9):1274-84; [3] Coleman RL et al. *Lancet* 2017;390(10106):1949-61; [4] Ledermann JA et al. *Lancet Oncol* 2020;21(5):710-722.

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Wednesday, June 16, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas E Hutson, DO, PharmD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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