Oncology Grand Rounds

New Agents and Strategies in Gynecologic Cancers

Tuesday, June 9, 2020

5:00 PM – 6:30 PM ET

Faculty

Paula J Anastasia, RN, MN, AOCN
Jennifer Filipi, MSN, NP
David M O'Malley, MD
Shannon N Westin, MD, MPH

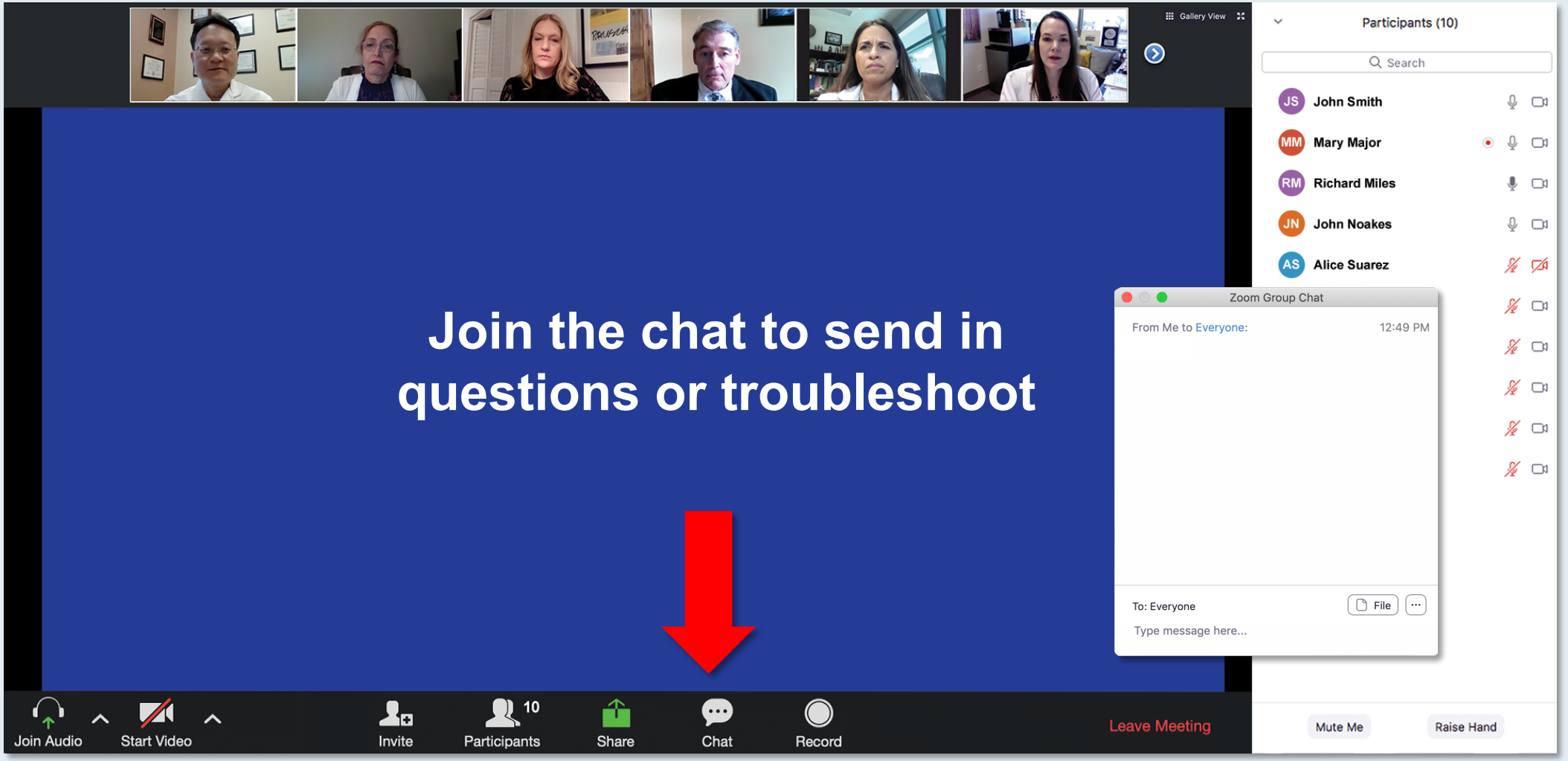
Moderator

Neil Love, MD

Research To Practice®

Familiarizing yourself with the Zoom interface

How to participate in the chat



RTP Live Webinar Nursing Series

Monday	Tuesday	Wednesday	Thursday	Friday
25	26 **Breast Ca** **5:00 PM**	27	28 **GI Ca** **5:00 PM**	29
Jun 1	2 **Lymphoma** **5:00 PM**	3	4 **CLL** **5:00 PM**	5
8	9 **GYN** **5:00 PM**	10	11 **Metastatic Lung Ca** **5:00 PM**	12
15	16 **Locally Advanced Lung Ca** **5:00 PM**	17	18 **Bladder Ca** **5:00 PM**	19
22	23 **CAR-T** **5:00 PM**	24	25 **PARP** **5:00 PM**	26
29	30 **Prostate Ca** **5:00 PM**	Jul 1 9 AM	2	3
6	7	8	9	10

Oncology Grand Rounds

New Agents and Strategies in Metastatic Lung Cancer

Thursday, June 11, 2020

5:00 PM – 6:30 PM ET

Faculty

Kelly EH Goodwin, MSN, RN, ANP-BC
Wendi S Lee, MSN, RN, NP-C
Suresh S Ramalingam, MD
Gregory J Riely, MD, PhD

Moderator

Neil Love, MD

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Oncology Grand Rounds

New Agents and Strategies in Gynecologic Cancers

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About the Enduring Program

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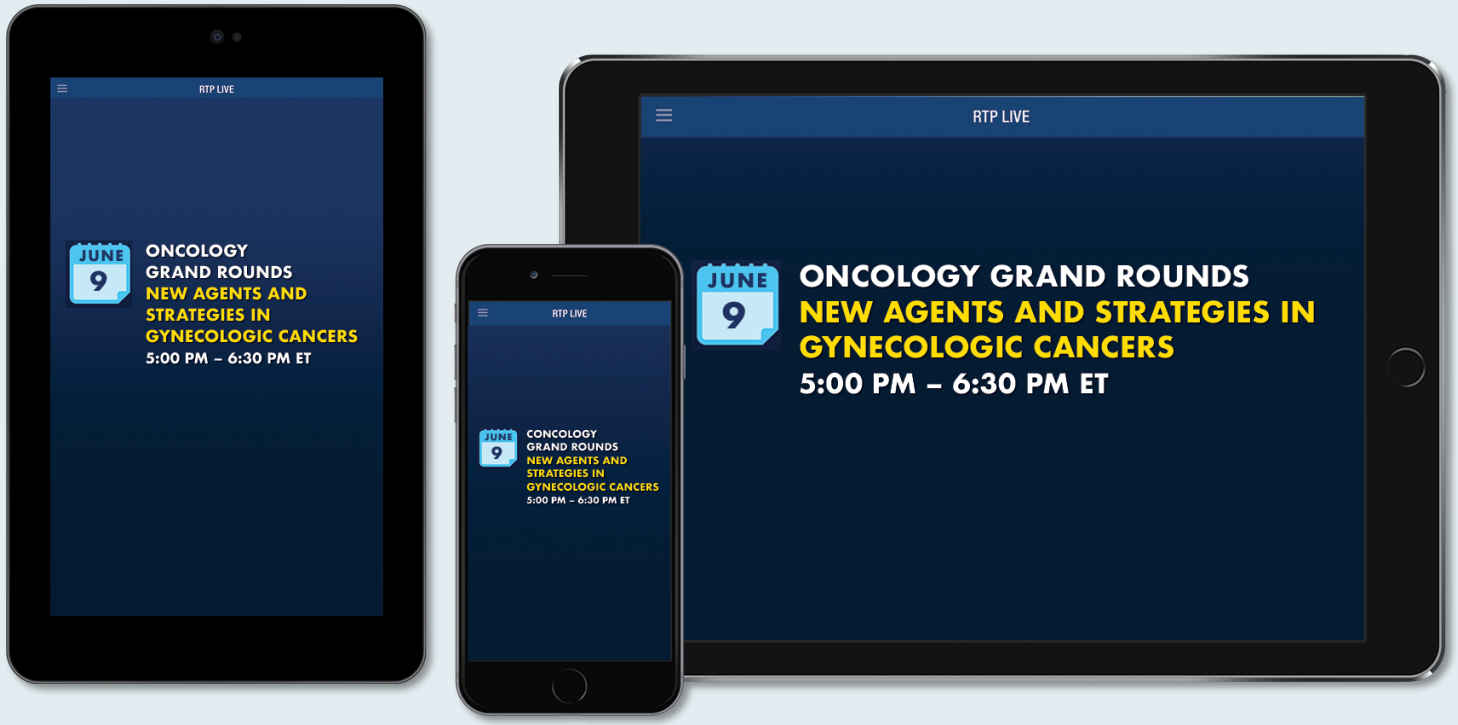

ONCOLOGY TODAY

WITH DR NEIL LOVE

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Agenda

Module 1: PARP Inhibitors in Ovarian Cancer — Biology, Clinical Benefit; Managing Side Effects, Optimizing Adherence

- Case Presentation: Ms Filipi — 72-year-old retired nurse
- Case Presentation: Ms Anastasia — 63-year-old music conductor

Module 2: Risks and Benefits of Immune Checkpoint Inhibitors (ICIs) in Endometrial Cancer

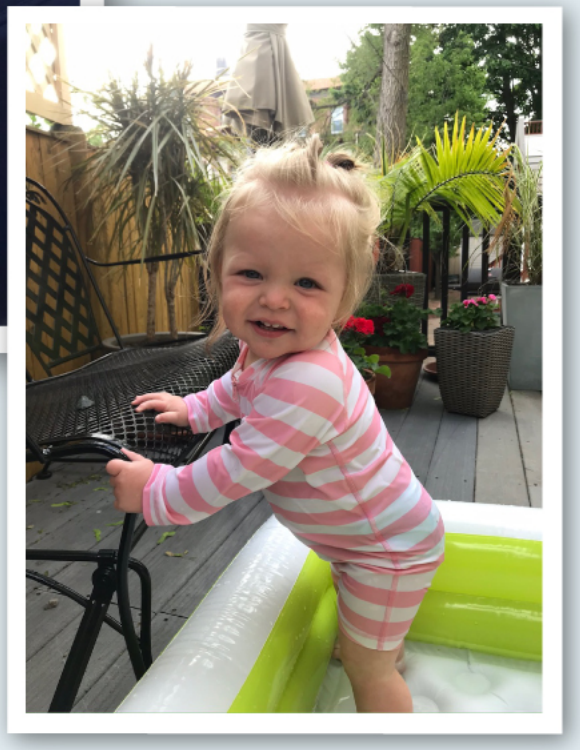
- Case Presentation: Ms Filipi — 68-year-old non-profit manager
- Case Presentation: Ms Anastasia — 67-year-old widow and grandmother

Module 3: Risks and Benefits of ICIs in Cervical Cancer

- Case Presentation: Ms Filipi — 35-year-old personal trainer

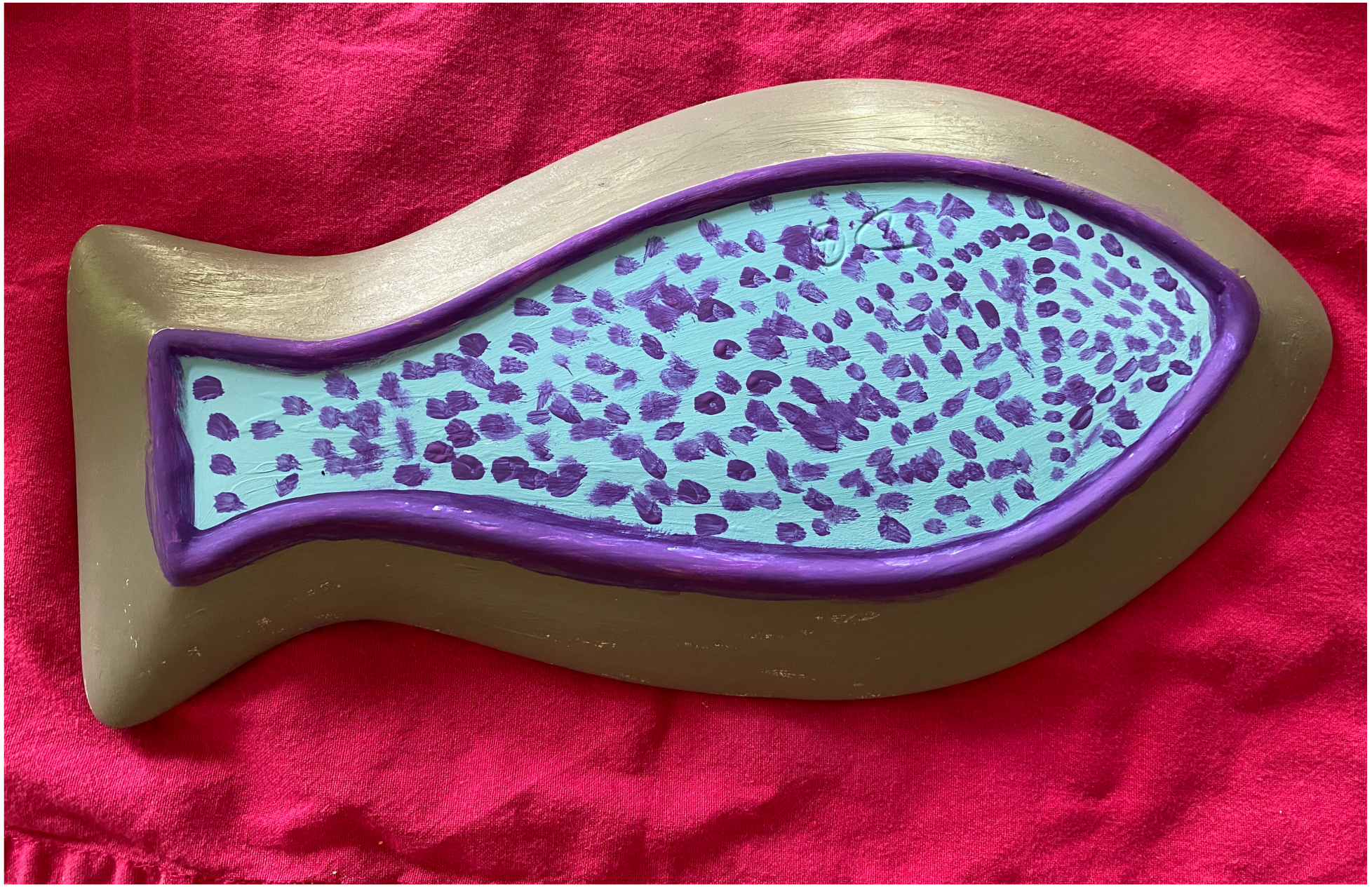
Paula J Anastasia, RN, MN, AOCN
David Geffen School of Medicine
Los Angeles, California

Jennifer Filipi, MSN, NP
Massachusetts General Hospital
Center for Gynecologic Oncology
Boston, Massachusetts



David M O'Malley, MD
The Ohio State University and The James Cancer Center
Columbus, Ohio

Shannon N Westin, MD, MPH
University of Texas
MD Anderson Cancer Center
Houston, Texas



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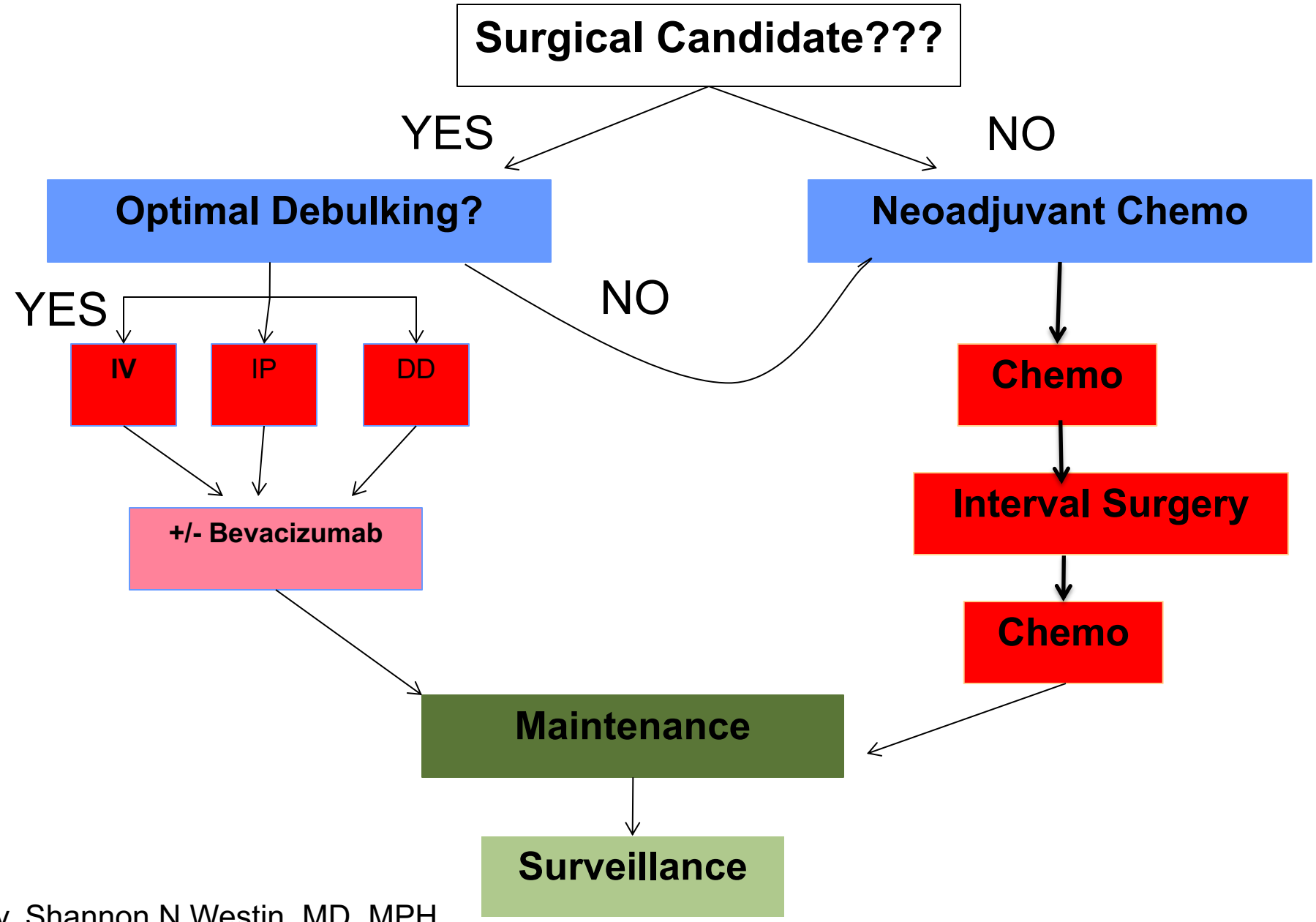
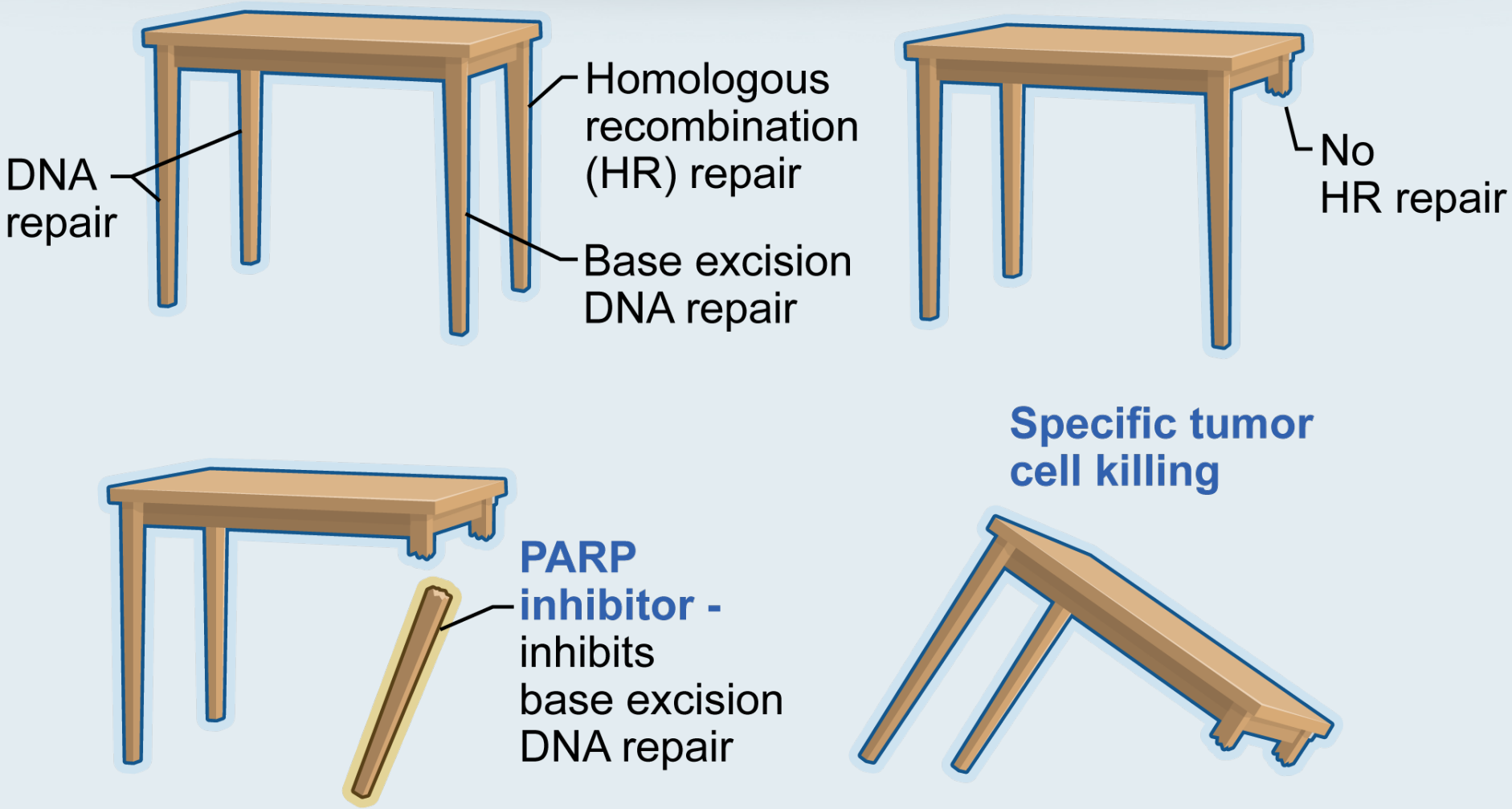
Module 1: PARP Inhibitors in Ovarian Cancer — Biology, Clinical Benefit; Managing Side Effects, Optimizing Adherence

New Advanced Ovarian Cancer



Courtesy, Shannon N Westin, MD, MPH

Mechanism of Cell Death from Synthetic Lethality Induced by PARP Inhibition

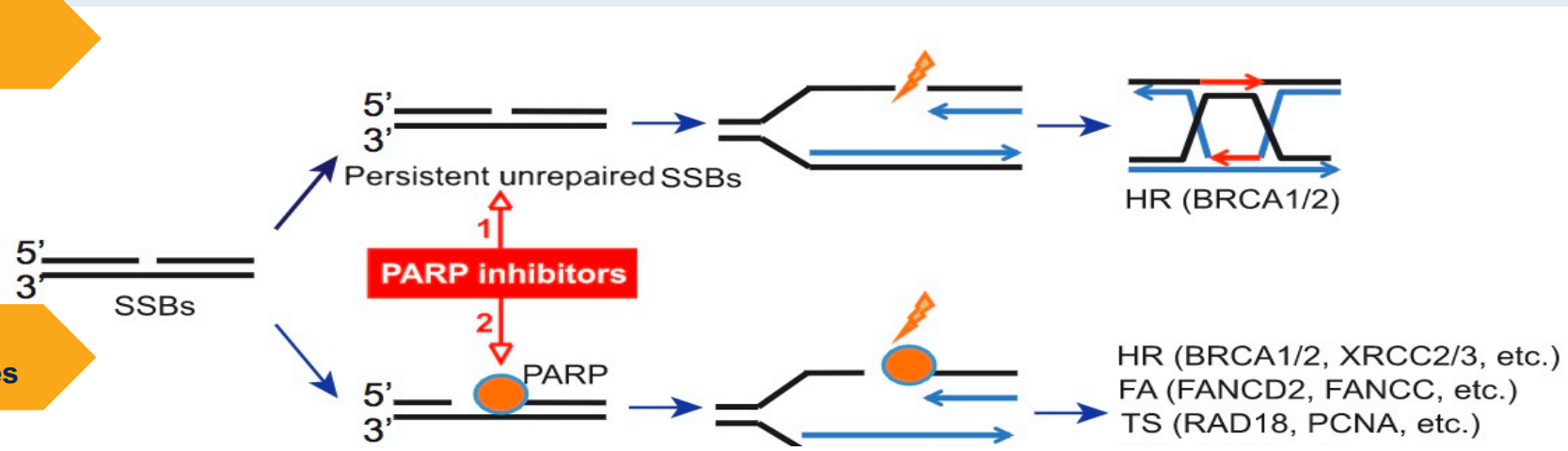


Courtesy of Jenny C Chang, MD

Dual Mechanisms of Action of PARP Inhibitors

Catalytic inhibition

Trapping of PARP-DNA complexes



	Catalytic inhibition IC_{50} in wild-type DT40 cells (nM)	Catalytic inhibition IC_{50} in wild-type DT40 cells (μM)	PARP-trapping potency (relative to olaparib)	Class
Veliparib	30	>50	<0.2	Type 1
Olaparib	6	4.5	1	Type 2
Rucaparib	21	3	1	Type 2
Niraparib	60	2.3	~2	Type 2
Talazoparib	4	0.04	~100	Type 2

Murai J, Pommier Y. Classification of PARP Inhibitors Based on PARP Trapping and Catalytic Inhibition, and Rationale for Combinations with Topoisomerase I Inhibitors and Alkylating Agents. In: Curtin NJ, Sharma RA, eds. *PARP Inhibitors for Cancer Therapy*. New York: Springer International Publishing;2015:261-74.

Phase 3 1L Maintenance Trials

Study Design		GOG-0218 (N=1873)	SOLO-1 (N=451)	PAOLA-1 (N=612)	PRIMA (N=620)	VELIA (N=1140)
Treatment arms vs placebo		Bevacizumab (n=625)	Olaparib (n=260)	Bevacizumab ± Olaparib	Niraparib	Veliparib
Key Patient Population		All comers	*BRCA* mutation	All comers	All comers	*All comers*
Undergo tumor testing		HRR (post-hoc)	*BRCA*	*BRCA*	HRD	*BRCA*
Stage	III	73.8%	84.6%	Eligible	Eligible: Attempt upfront debulking	Eligible
	IV	26.2%	15.4%	Eligible	Eligible: Any debulking attempts	Eligible
Surgery	Residual disease after surgery	Stage III incomplete • Macroscopic: 32.8% • >1 cm: 41.0%	Macroscopic[a] • Primary: 23.0% • Interval: 19.1%	NR[b]	Required for Stage III	Primary or Interval
	Inoperable disease	0	1.5%	NR[b]	Eligible	
Treatment Duration		15 months	24 months	15 months for Bev 24 months for Olaparib	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

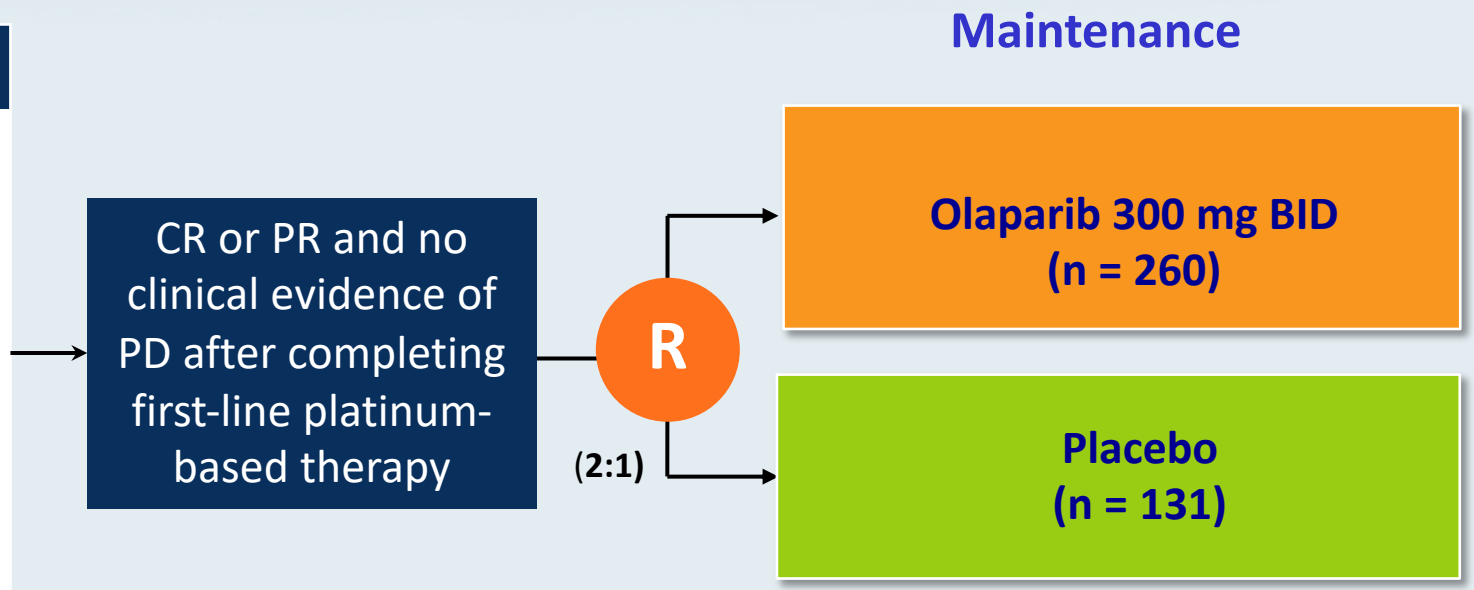
Courtesy, Shannon N Westin, MD, MPH

SOLO-1: A Phase III Trial of Maintenance Olaparib in OC with BRCA Mutation

NCT01844986

Eligibility

- Newly diagnosed ovarian, fallopian tube or primary peritoneal cancer
- FIGO Stage III-IV
- High-grade serous or endometrioid histology
- Deleterious or suspected deleterious BRCA1 or BRCA2 mutation-positive



Primary endpoint: Investigator-assessed progression-free survival

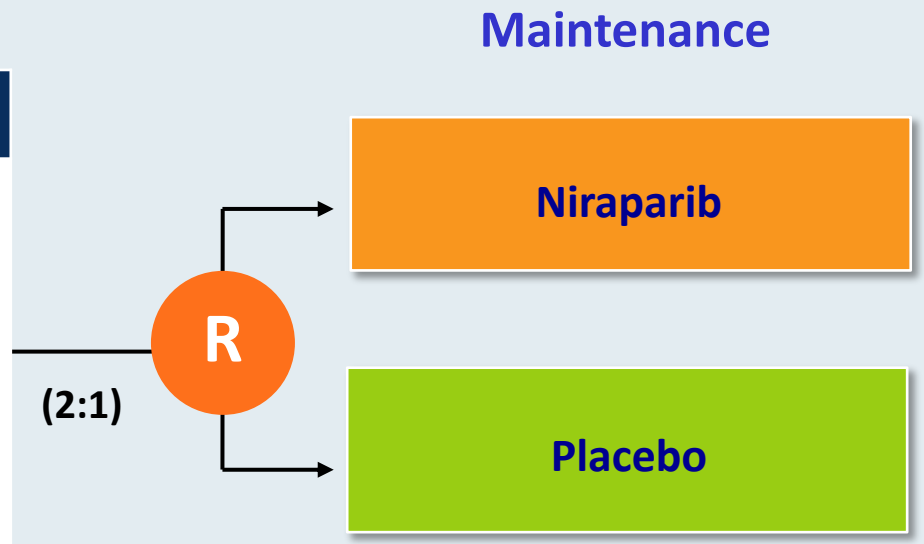
www.clinicaltrials.gov; Moore KN et al. *Proc ASCO* 2014;Abstract TPS5616; Moore K et al. *N Engl J Med* 2018;[Epub ahead of print].

PRIMA Trial: A Phase III Trial of Maintenance Niraparib in OC

NCT02655016

Eligibility (N = 620)

- Newly diagnosed ovarian cancer
- Advanced-stage (FIGO III or IV) disease
- Completion of first-line platinum-based therapy
- CR or PR to most recent platinum chemotherapy



Primary endpoint: Progression-free survival

Gonzalez-Martin A et al. *Proc ESMO* 2018;Abstract 941PD.

Phase III PAOLA-1/ENGOT-OV25 Study Design

Eligibility

- Newly diagnosed Stage III-IV high-grade serous/endometroid ovarian, fallopian tube or primary peritoneal cancer
- Surgery (upfront or interval)
- Platinum-taxane based chemo
- ≥ cycles of bevacizumab

NED/CR/PR

R

(2:1; N = 806)

Maintenance Therapy

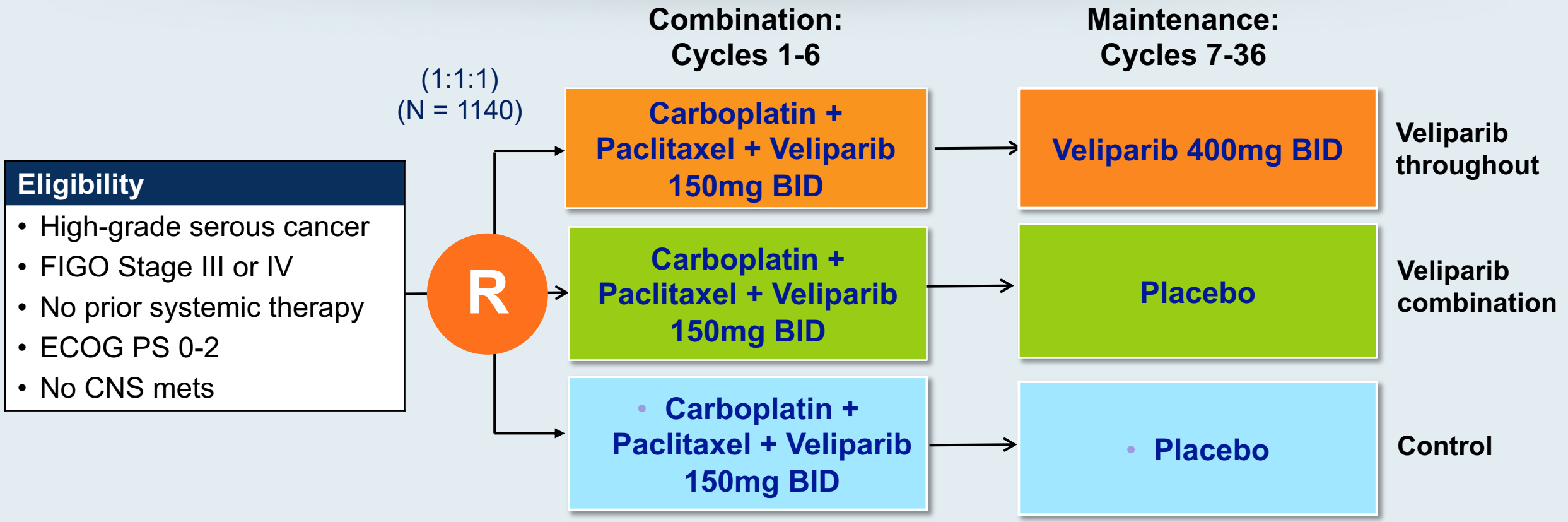
Olaparib (300 mg BID) x 2 yrs
+
Bevacizumab

Placebo x 2 yrs
+
Bevacizumab

Primary endpoint: Investigator-assessed PFS
Secondary endpoints: TFST, PFS2, TSST, OS, HRQoL, Safety and tolerability

Ray-Coquard IL et al. ESMO 2019; Abstract 3955.

Phase III VELIA/GOG-3005 Study Design



Primary endpoint: Progression-free survival (PFS) for veliparib-throughout vs control, including the combination and maintenance phase

Coleman RL et al. ESMO 2019; Abstract 2772.

FDA approves niraparib for first-line maintenance of advanced ovarian cancer

Press Release – April 29, 2020

"The Food and Drug Administration approved niraparib for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.

Efficacy was investigated in PRIMA (NCT02655016), a double-blind, placebo-controlled trial that randomized 733 patients to niraparib or matched placebo. Patients were in a complete or partial response to first-line platinum-based chemotherapy."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-niraparib-first-line-maintenance-advanced-ovarian-cancer

FDA approves olaparib plus bevacizumab as maintenance treatment for ovarian, fallopian tube, or primary peritoneal cancers

Press Release – May 28, 2020

The Food and Drug Administration expanded the indication of olaparib to include its combination with bevacizumab for first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency positive status defined by either a deleterious or suspected deleterious *BRCA* mutation, and/or genomic instability.

FDA also approved the Myriad myChoice® CDx (Myriad Genetic Laboratories, Inc.) as a companion diagnostic for olaparib.

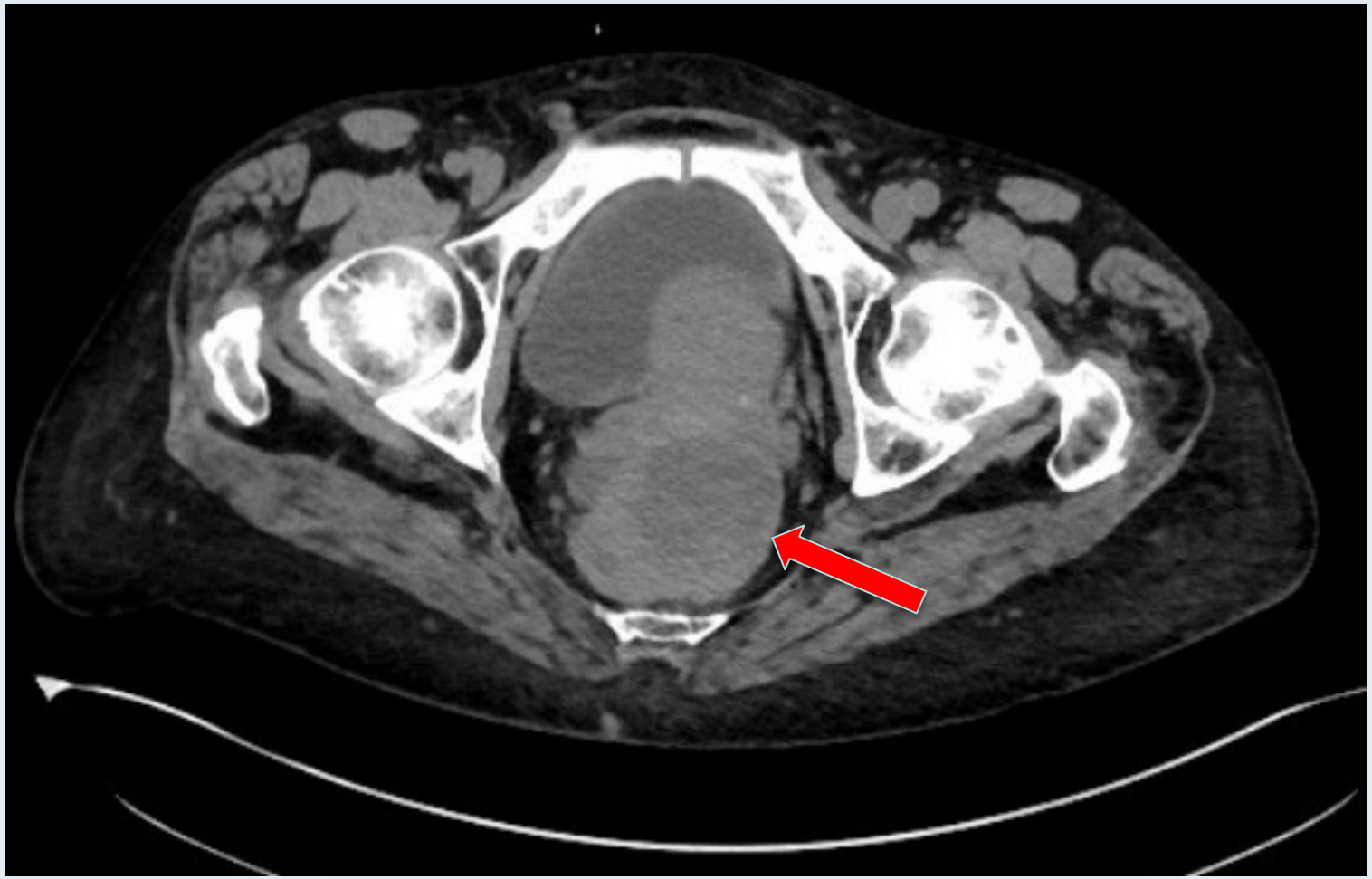
Efficacy of this new indication was investigated in PAOLA-1 (NCT03737643), a randomized, double-blind, placebo-controlled, multi-center trial comparing olaparib with bevacizumab versus placebo plus bevacizumab in patients with advanced high-grade epithelial ovarian cancer, fallopian tube, or primary peritoneal cancer following first-line platinum-based chemotherapy and bevacizumab.

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-olaparib-plus-bevacizumab-maintenance-treatment-ovarian-fallopian-tube-or-primary

72-year-old retired nurse and grandmother (from the practice of Ms Filipi)

- 7/2019: Present to ER with BRBPR
  - CA125: 1754
  - Biopsy confirmed ovarian origin
- Cytoreductive surgery
- Carboplatin and paclitaxel x 6
  - Thrombocytopenia
- Genetic testing: Negative germline, somatic BRCA mutation
- Maintenance olaparib

72-year-old retired nurse and grandmother (from the practice of Ms Filipi)



At a minimum, all patients with ovarian cancer should have the following assay(s) conducted at diagnosis regardless of family history of cancer.

a. BRCA germline testing

b. BRCA somatic testing

c. Multiplex germline testing

d. Multiplex somatic testing

e. Both a and b

f. Both c and d

g. I don’t know

Bevacizumab is often added to chemotherapy for patients presenting with ovarian cancer and…

a. Optimal debulking surgery

b. Ascites

c. Both a and b

d. Neither a nor b

e. I don’t know

In order to receive PARP inhibitor maintenance treatment after debulking surgery and first-line platinum-based chemotherapy, a patient with ovarian cancer…

a. Must have evidence of residual disease

b. Must not have experienced disease progression

c. Both a and b

d. Neither a nor b

e. I don’t know

In which of the following situations is the use of primary maintenance PARP inhibitors (postoperative, postchemotherapy) standard?

a. Patients with ovarian cancer and homologous recombinant proficiency

b. Patients with ovarian cancer and BRCA germline mutations

c. Both a and b

d. Neither a nor b

e. I don’t know

Which of the following PARP inhibitors is approved for use as primary maintenance therapy for patients with BRCA wild-type ovarian cancer?

a. Olaparib

b. Niraparib

c. Rucaparib

d. Veliparib

e. Both a and b

f. All of the above

g. I don’t know

Which of the following PARP inhibitors is approved in combination with bevacizumab for use as primary maintenance therapy after first-line platinum-based chemotherapy?

a. Olaparib

b. Niraparib

c. Rucaparib

d. Veliparib

e. Both a and b

f. All of the above

g. I don’t know

Which of the following PARP inhibitors has demonstrated benefit in combination with chemotherapy after debulking surgery and then continued as maintenance treatment?

a. Olaparib

b. Niraparib

c. Rucaparib

d. Veliparib

e. Both a and b

f. All of the above

g. I don’t know

What was the duration of treatment with olaparib and niraparib in the Phase III trials evaluating maintenance therapy with PARP inhibitors after debulking surgery and first-line platinum-based chemotherapy?

a. 2 years for both

b. 3 years for both

c. 2 years for olaparib, 3 years for niraparib

d. 2 years for niraparib, 3 years for olaparib

e. I don’t know

63-year-old Ashkenazi Jewish woman, mother, violinist and music conductor (from the practice of Ms Anastasia)

- 2-4/2018: Abdominal distension/bloating, early satiety; CT scan: solid pelvic mass14 x 7.6 cm, extensive omental caking, irregular nodularity at both lung bases
- Baseline CA-125: 2247
- Paracentesis: 2.3L removed, cytology c/w adenocarcinoma favor OC
- Multigene hereditary cancer panel: Negative for pathogenic variant
- 7/2018: Completes neoadjuvant carboplatin and paclitaxel x 3 (CA-125: 68)
- 8/2018: Interval cytoreductive surgery → R0 (Stage 3C HGS ovarian cancer)
- 11/2018: Completes adjuvant carboplatin and paclitaxel x 3 (CA-125: 9)
  - Thrombocytopenia post-surgery (nadir: 64K), Grade 1 neuropathy, fatigue, anemia, constipation
- Genomic tumor testing: Somatic mutation HRD-positive
- 2/2019: Maintenance olaparib 300mg BID

Patient Education for Olaparib

- Reinforce common side effects: fatigue and nausea, but short lived
- Obtain Baseline CBC, Plt, Diff, Comprehensive Metabolic Panel, CA 125; Then monthly After 3 months may continue q 3 month labs and physical exam
- *Our practice* monitors **weekly** CBC, Plt, Diff x 4 weeks
- We hold dose one week if Plts < 75K, Hgb < 9.0g/dl, ANC < 1500/mm3
- If blood counts are held a week and return to less than grade 1, package insert recommends dose reduction. We dose 150mg q am and 300mg at hs. PI recommends 150mg and 100mg in am and pm
- We provide blood transfusion if Hgb < 9.0g/dl and or symptomatic
- Consider daily folate, and monthly Vitamin B12 injection, especially if elevated MCV
- For fatigue (r/o anemia, hypothyroid, dehydration) encourage exercise and mobility. Fatigue can be due to deconditioning.
- Nausea may occur in form of queasiness: recommend prophylactic antiemetic initially then may taper If not needed
- Small frequent meals and grazing
- May benefit from PPI or anti-acid which can mimic nausea
- Alternative options include behavior modification, acupuncture, CBD oil
- If significant nausea where patient is not adequately hydrating or losing weight, hold drug one week; if improvement then consider dose reduction
- Recommended guidelines: Discontinue PARP inhibitor maintenance therapy after 2 years (or recurrence)

63-year-old Ashkenazi Jewish woman -- Younger Years Before Her Cancer Diagnosis

Performing at Disneyland and Adventureland During Treatment

Remission

Completion of Chemo

Photo:

95 yr old Mother (who she drives 2hrs weekly to visit)

Dr Beth Karlan

Conducting Orchestra 2019

Palm Springs Tram
Elevation 8500 ft

Girls Trip to Las Vegas 2019

How often should complete blood counts be monitored in patients with ovarian cancer who are receiving niraparib?

a. Weekly for the duration of treatment

b. Monthly for the duration of treatment

c. Weekly for the first month, monthly for the next 11 months and periodically thereafter

d. Weekly for the first 6 months and monthly thereafter

e. I don’t know

Which PARP inhibitor has been associated with increased serum creatinine levels and normal renal function?

a. Olaparib

b. Niraparib

c. Rucaparib

d. Veliparib

e. None of the above

f. I don’t know

Hematologic Toxicity

Toxicity	Grade	Olaparib[1]	Rucaparib[2]	Niraparib[3]
Anemia (%)	All Grades	90	67	50.1
	Grade 3 and 4	15	23	25.3
Thrombocytopenia (%)	All	30	39	61.3
	Grades 3 and 4	3	6	33.8
Neutropenia (%)	All	25	35	30.2
	Grades 3 and 4	7	10	19.6

- At maximum administered dose of olaparib (600 mg BID), G4 thrombocytopenia was observed[4]

Courtesy, Shannon N Westin, MD, MPH

[1]FDA package insert, [2]FDA package insert, [3]NOVA NEJM 2016, [4]Fong NEJM 2009

Gastrointestinal Toxicity

Toxicity	Grade	Olaparib [1]	Rucaparib[2]	Niraparib[3]
Nausea (%)	All Grades	64	77	74
	Grade 3 and 4	3	5	3.0
Constipation (%)	All	21[5]	40	40
	Grades 3 and 4	0	2	0.5
Vomiting (%)	All	43	46	34
	Grades 3 and 4	4	4	2
Decreased appetite (%)	All	22	39	25
	Grades 3 and 4	1	3	0.3
Abdominal pain (%)	All	43	32	23
	Grades 3 and 4	8	3	1
Diarrhea (%)	All	31	34	19
	Grades 3 and 4	1	2	0.3
Dyspepsia (%)	All	25	10[4]	11
	Grades 3 and 4	0	<1	0

Courtesy, Shannon N Westin, MD, MPH

[1]FDA insert, [2]FDA insert, [3]NOVA NEJM 2016, [4]Swisher Lancet Onc 2016, [5]Ledermann Lancet Oncology 2014

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

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

Niraparib Dose Reductions	Dose
Starting Dose	• 300 mg daily
First Dose Reduction	• 200 mg daily
Second Dose Reduction	• 100 mg daily

Courtesy, Shannon N Westin, MD, MPH

FDA Prescribing Information.

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Module 2: Risks and Benefits of Immune Checkpoint Inhibitors (ICIs) in Endometrial Cancer

Checkpoint inhibitors are approved for and commonly used in cervical and endometrial cancer but not ovarian cancer.

a. I am aware of this

b. I was not aware of this

What is the usual sequence of treatment for patients with MSI-high metastatic endometrial cancer?

a. Chemotherapy first line; pembrolizumab second line

b. Chemotherapy first line; pembrolizumab second line for increased PD-L1 levels

c. Chemotherapy first line; pembrolizumab/lenvatinib second line

d. Pembrolizumab first line; chemotherapy second line

e. I don’t know

What is the usual sequence of treatment for patients with MS-stable metastatic endometrial cancer?

a. Chemotherapy first line; pembrolizumab second line

b. Chemotherapy first line; pembrolizumab second line for increased PD-L1 levels

c. Chemotherapy first line; pembrolizumab/lenvatinib second line

d. Pembrolizumab first line; chemotherapy second line

e. I don’t know

Have you encountered a patient with endometrial cancer who received pembrolizumab/lenvatinib?

a. No

b. Yes, but I did not observe loss of appetite and/or weight loss

c. Yes, and I observed loss of appetite and/or weight loss in at least 1 patient

The rapidity of onset and severity of hypertension associated with lenvatinib is greater than that with bevacizumab.

a. I am aware of this

b. I was not aware of this

BARCELONA 2019 ESMO congress

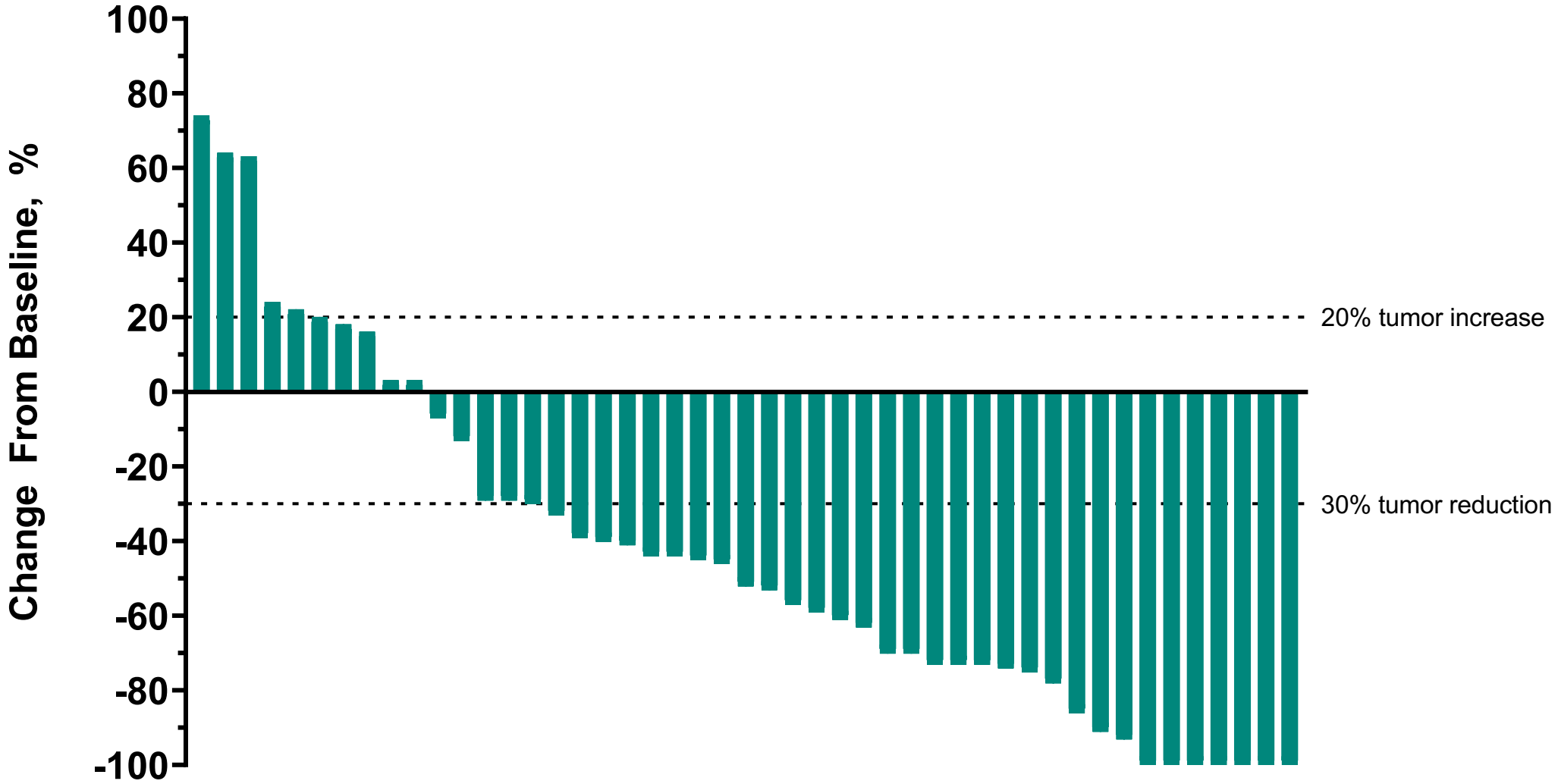
Pembrolizumab in Patients with MSI-H Advanced Endometrial Cancer from the KEYNOTE-158 Study

David M. O'Malley,[1] Aurelien Marabelle,[2] Ana De Jesus Acosta,[3] Sarina A. Piha-Paul,[4] Alexander Arkhipov,[5] Federico Longo,[6] Daniel Motola-Kuba,[7] Ronnie Shapira Frommer,[8] Ravit Geva,[9] Bobbie J. Rimel,[10] Jose A. Lopez-Martin,[11] Aaron R. Hansen,[12] Janice M. Mehnert,[13] Xinqun Chen,[14] Fan Jin,[14] Kevin Norwood,[14] Patrick A. Ott[15]

[1]The Ohio State University Wexner Medical Center and The Ohio State University James Comprehensive Cancer Center, Columbus, OH, USA; [2]Gustave Roussy Cancer Campus, Villejuif, France; [3]Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [4]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]Federal State Autonomous Institution "Treatment and Rehabilitation Center" of the Ministry of Health of the Russian Federation, Moscow, Russia; [6]Hospital Universitario Ramón y Cajal, Instituto Ramón y Cajal de Investigación Sanitaria (IRICYS), CIBERONC, Madrid, Spain; [7]COMOP A.C., Clinical Investigation, Mexico City, Mexico; [8]Sheba Medical Center, Ramat-Gan, Israel; [9]Division of Oncology, Tel Aviv Sourasky Medical Center, Tel-Aviv University, Tel Aviv, Israel; [10]Cedars-Sinai Medical Center, Los Angeles, CA, USA; [11]Medical Oncology, 12 de Octubre University Hospital & Research Institute (i+12), Madrid, Spain; [12]University of Toronto, Princess Margaret Cancer Centre, Toronto, ON, Canada; [13]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; [14]Merck & Co., Inc., Kenilworth, NJ, USA; [15]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Best Percentage Change From Baseline in Target Lesion Size

MSI-H Endometrial Cancer; per RECIST v1.1 by Central Review



Includes patients who had ≥1 evaluable postbaseline tumor assessment. Changes from baseline >100% were truncated at 100%.
Data cutoff date: Dec 6, 2018.

O'Malley DM et al. ESMO 2019.

Lenvatinib and Pembrolizumab in Patients With Advanced Endometrial Cancer

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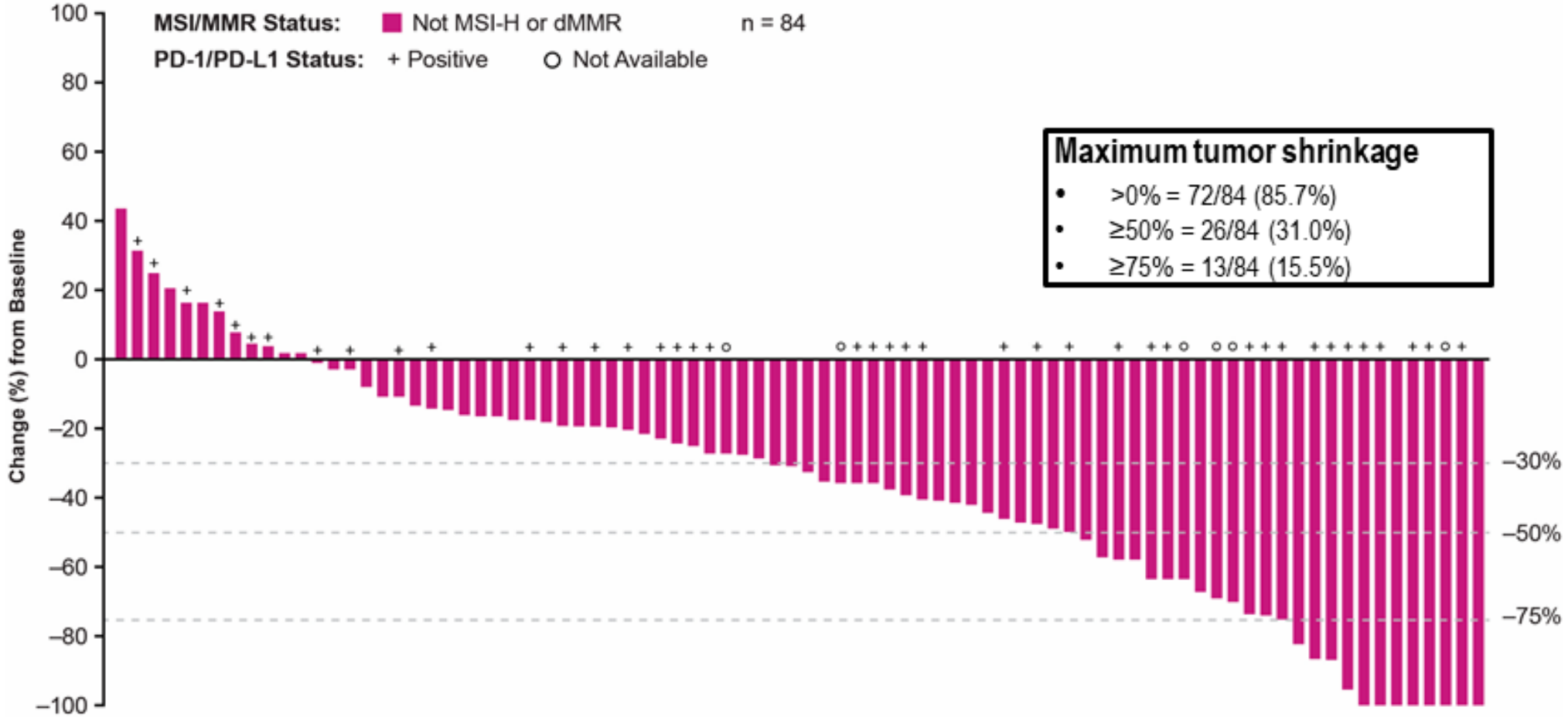
Percentage Change in Sum of Diameters of Target Lesions at Postbaseline Nadir (Independent Imaging Review; RECIST version 1.1)



n = the number of previously treated not MSI-H or dMMR patients with both baseline and at least 1 postbaseline target lesion assessment.

Courtesy, David M O'Malley, MD

Makker V et al. ESMO 2019.

68-year-old non-profit manager (from the practice of Ms Filipi)

- 2016: Endometrial cancer → surgery → carboplatin/paclitaxel x 6 → pelvic XRT
- 2019: Recurrence
- Clinical trial (16-322): Avelumab + talazoparib in MSS endometrial cancer
  - 2020: PD (small volume disease and asymptomatic)
- Pembrolizumab and lenvatinib (10mg → 14mg after a week)
  - BP: 180/116 (asymptomatic)
    - Held lenvatinib, 100mg losartan
  - BP still high → added 25mg HCTZ
  - BP still high → took another 25mg HCTZ
  - BP finally stabilized
- Restarted lenvatinib 14mg the following day with no further issues

I’m not feeling well….

Hi.

Good news: BP is still stable.
Not so good news: I'm feeling awful. I have no energy, no interest in doing ANYTHING, much less exercise, have no appetite and am in almost constant abdominal discomfort and mild nausea. And every once in while I get a localized pain in the area which I assume is where my cancer is. My mouth is also sore which doesn't make eating much fun. I also need to see a dentist for a broken tooth which should have been dealt with earlier, but then COVID-19.

- This isn’t compatible with her goals
- We gave her 5 days off and decreased her lenvatinib dose to 10mg
  - » Be careful about hypotension
- Check thyroid studies (on pembrolizumab)
- Change dose time from morning to nighttime


Studio

“I’m old and short and sometimes feel invisible. That’s why I dyed my hair purple. Thank you for making me feel seen and heard”

67-year-old widow and grandmother (from the practice of Ms Anastasia)

- 2018: High-grade Stage 3C endometrial cancer s/p TAH/BSO, PP ALND: 1 node+, MSI-stable, ER+ → Pelvic RT + weekly cisplatin → vaginal brachytherapy
- 1/2019-4/2019: Carboplatin + paclitaxel x 4
- 5/2019: Letrozole
- 8/2019-10/2019: Recurrent disease 1st relapse
- Liposomal doxorubicin + bevacizumab x 3 → PD (liver and peritoneal mets)
- 10/2019: Pembrolizumab 200mg + Lenvatinib 20mg
  - Dose hold and reduction of lenvatinib to 10mg (Gr 2 fatigue, nausea, diarrhea and wt loss)
- 2020: Relocates from East coast to California to be with 4 adult offspring, grandchildren
- New bone mets, enlargement of peritoneal disease after 6 months of stable disease on pembrolizumab/lenvatinib

Lessons Learned from Cancer Survivors

- *~Being cancer free does not mean being free of cancer*
- *~Transitioning to recovery is stressful*
- *~Despite risk, survivors manifest remarkable resilience with respect to the cancer experience and even the potential to find benefit from the experience*
- *~Cancer for many may provide a "teachable moment"*

Rowland, J. What cancer survivors are telling us. New Haven, CT:
Defining Excellence in Cancer Survivorship, Yale Cancer Center; January 14-15, 2008.

Agenda

Module 1: PARP Inhibitors in Ovarian Cancer — Biology, Clinical Benefit; Managing Side Effects, Optimizing Adherence

- Case Presentation: Ms Filipi — 72-year-old retired nurse
- Case Presentation: Ms Anastasia — 63-year-old music conductor

Module 2: Risks and Benefits of Immune Checkpoint Inhibitors (ICIs) in Endometrial Cancer

- Case Presentation: Ms Filipi — 68-year-old non-profit manager
- Case Presentation: Ms Anastasia — 67-year-old widow and grandmother

Module 3: Risks and Benefits of ICIs in Cervical Cancer

- Case Presentation: Ms Filipi — 35-year-old personal trainer

Module 3: Risks and Benefits of ICIs in Cervical Cancer

Pembrolizumab is approved as second-line treatment for metastatic cervical cancer…

a. In all patients

b. In patients with elevated PD-L1 levels

c. In combination with chemotherapy

d. All of the above

e. I don’t know

KEYNOTE-158

- Multicenter, non-randomized, open- label, **multi-cohort** trial
- **Pembrolizumab** 200 mg every 3 weeks until toxicity or progression
- Among the 98 cervical cancer patients
  - 77 (79%) had tumors that expressed PD-L1 with a CPS ≥ 1 and
  - Received at least one line of chemotherapy in the metastatic setting

Pembrolizumab [prescribing information]. Whitehouse Station,NJ:Merck & Co., Inc.;2018.
Chung HC et al J Clin Oncol. 2019 Jun 10;37(17):1470-1478.

Courtesy, David M O'Malley, MD

Efficacy Results in Patients with Recurrent or Metastatic Cervical Cancer (CPS ≥1) in KEYNOTE-158

Endpoint	n=77*
Objective response rate	
ORR (95% CI)	14.3% (7.4, 24.1)
Complete response rate	2.6%
Partial response rate	11.7%
Response duration	
Median in months (range)	NR (4.1, 18.6+)†
% with duration ≥6 months	91%

* Median follow-up time of 11.7 months (range 0.6 to 22.7 months)

† Based on patients (n=11) with a response by independent review

\+ Denotes ongoing

NR = not reached

Pembrolizumab [prescribing information]. Whitehouse Station,NJ:Merck & Co., Inc.;2018.
Chung HC et al J Clin Oncol. 2019 Jun 10;37(17):1470-1478.

Courtesy, David M O'Malley, MD

Checkpoint inhibitors frequently cause low-grade rash or other dermatologic side effects.

a. I am aware of this

b. I was not aware of this

Checkpoint inhibitors frequently cause thyroid dysfunction.

a. I am aware of this

b. I was not aware of this

The clinical and imaging presentation of checkpoint inhibitor-related autoimmune pneumonitis may be similar to the presentation of pneumonitis caused by COVID-19.

a. Agree

b. Disagree

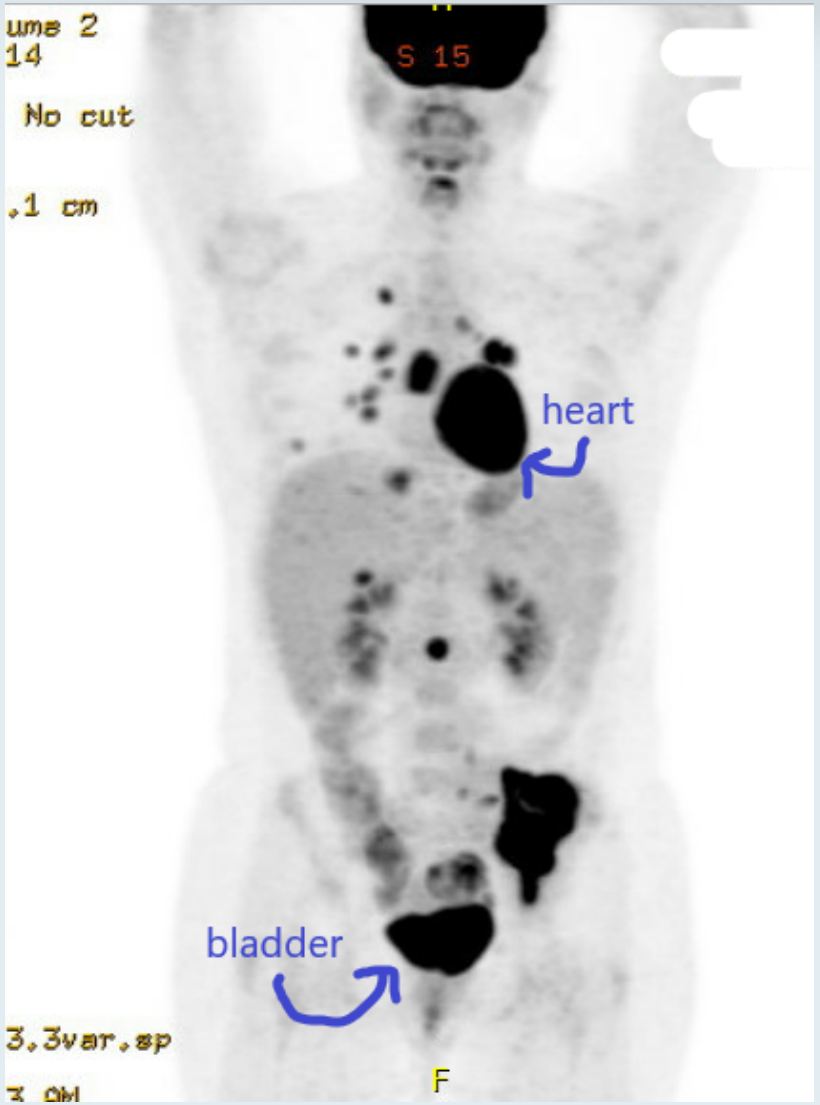
c. I don’t know

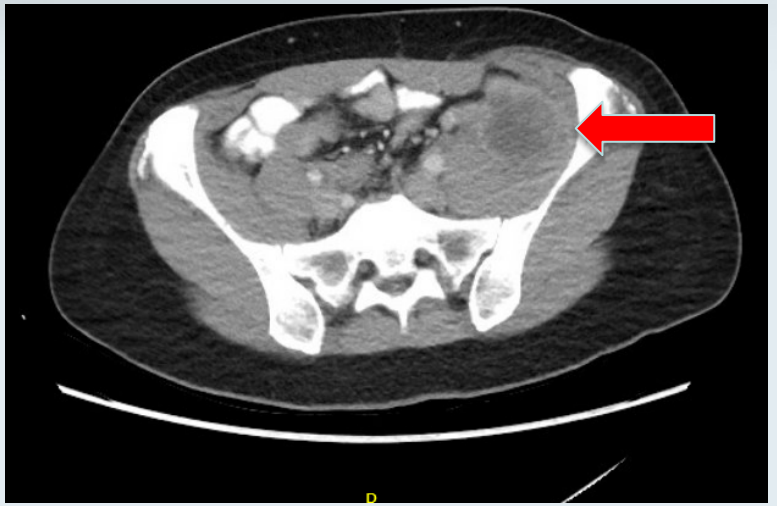
35-year-old mom and personal trainer (from the practice of Ms Filipi)

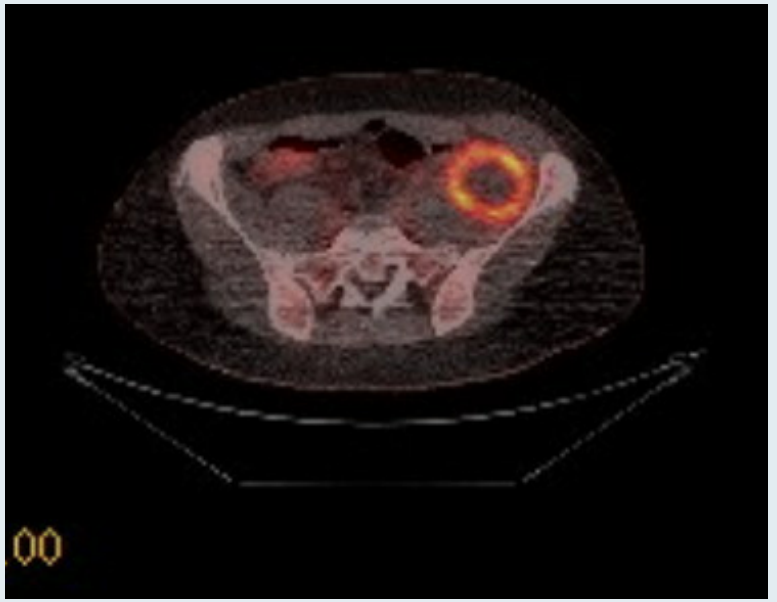
- 8/2014: postcoital bleeding → 10/14 PAP: AIS but could not exclude invasive adenocarcinoma (HPV+ 18 and 45)
- 11/2014: Stage 1B cervical cancer, no distant mets → Hysterectomy, pelvic LN dissection → Chemo + XRT
- 1.5 years later, presents with pelvic and back pain
- 3/2018: Completes cisplatin, paclitaxel and bevacizumab x 8 → refractory disease
  - Pain requiring narcotic, paclitaxel hypersensitivity reaction, febrile neutropenia, neuropathy
- 5/2018: Phase 1 trial of nivolumab and ipilimumab → Stable disease x 5 months
  - Rash, fatigue, cough
- 10/2018: New mental status changes, headaches; Brain metastases (came off clinical trial)
  - WBRT
- PD-L1 positive staining; Pembrolizumab x 6
- 3/2019: Patient passes away

35-year-old woman (from the practice of Ms Filipi)

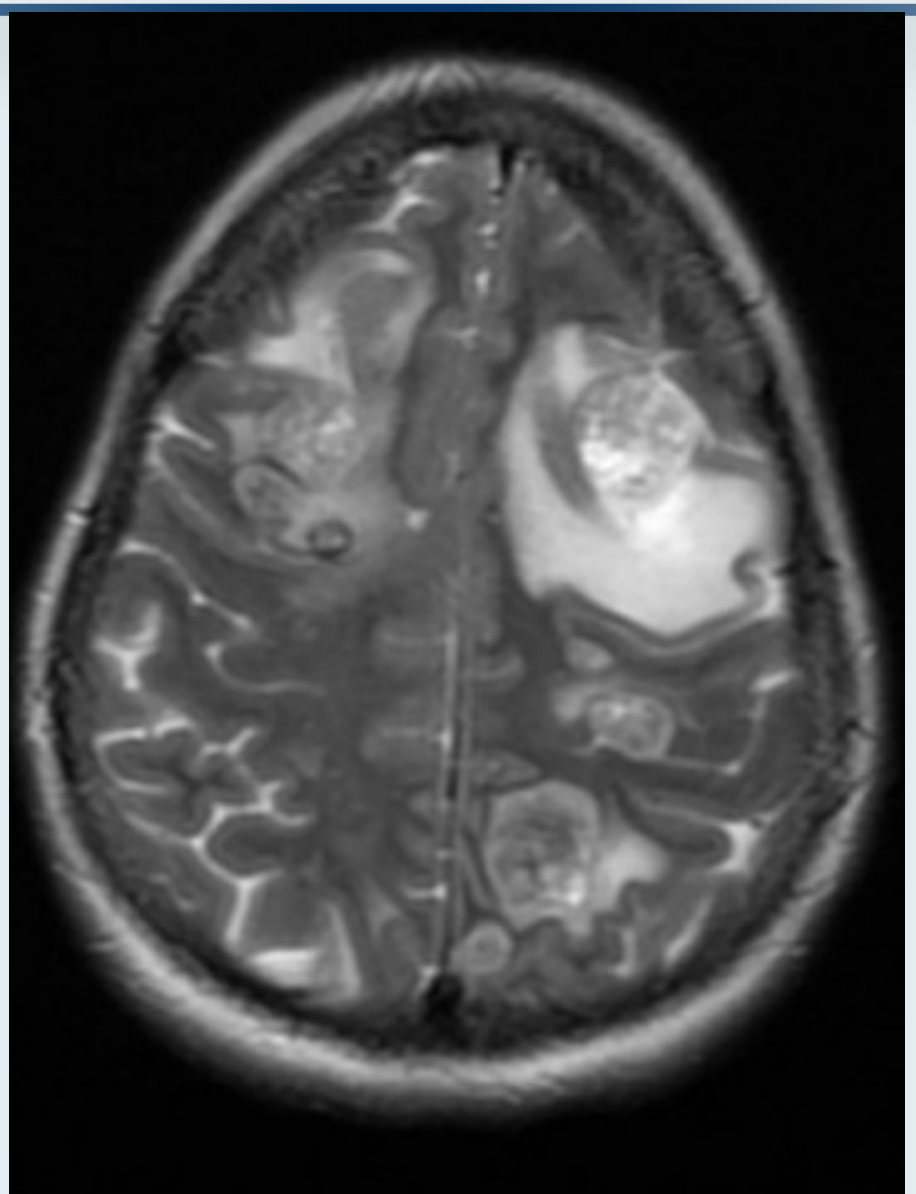
35-year-old woman (from the practice of Ms Filipi)







35-year-old woman (from the practice of Ms Filipi)
October 2018 Brain MRI: Numerous Metastases



Thank you for joining us!

CNE (NCPD) credit information will be emailed to each participant tomorrow morning.