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New Directions in the Management of Ovarian Cancer

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No disclosures

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Objectives

- To discuss molecular testing in ovarian cancer
- To summarize the use of PARP inhibitors and antiangiogenic agents in ovarian cancer
- To outline the emerging role of immunotherapy in advanced ovarian cancer

Molecular and Clinical Characteristics of Ovarian Cancer Subtypes

	High-Grade Serous or Endometrioid	Low-Grade Endometrioid	Low-Grade Serous	Clear Cell	Mucinous
Genetic	Up to 50% with alterations in HR Associated with TP53 and BRCA mutations	PTEN, ARID1A, PIK3CA alterations May have MSI	KRAS, BRAF mutations	PIK3CA, ARID1A, PTEN	KRAS
Clinical	Increased platinum sensitivity PARP inhibitors with potential activity in HRD tumors	Potentially more responsive to hormonal therapy, although not established	Hormonal therapies Potentially MEK inhibitors	Often resistant to initial plat-based therapy; Targeted or immuno-oncology agents being explored	Often chemotherap y-insensitive

MSI = microsatellite instability; MEK = mitogren-activated protein Prat, 2021; Konstantinopoulos et al, 2015

Germline Mutation Testing in Ovarian Cancer

- gBRAC mutations*:15 to 18%
  BRCA1 mutations: 40 to 60% cumulative risk of OC (mostly HGSC)
  BRCA2 mutations: 16 to 18% risk of OC (HGSC)

- Lynch syndrome**: 0.4 to 2%
  6 to 24% cumulative risk of OC (non-serous; mostly endometrioid or clear cell histologies). Higher risk for colorectal and uterine CA
  .
- Other genes have been identified as high risk: PALB2, BARD1, RAD51C, RAD51D and BRIP1

- Variants of unknown clinical significance (VUS)

*Pal T, Cancer. 2005; Mavaddat N, J Natl Cancer Inst. 2013
**Watson P, Int J Cancer. 2008; Bonadona V, JAMA. 2011

Clinical Utility of Multigene Panel Testing

- Traditional test: targeted sequencing of each candidate gene
- Multigene cancer panels use next-generation sequencing (NGS) to assess multiple genes simultaneously: BRAC1/2, PALB2, BARD1, BRIP1, RAD51C, RAD51D, MSH2, MLH1, PMS2, and MSH6

Decreases:

- Resource use (efficient use of funds and time)
- Number of patient visits
- Number of tests sent

Increases:

- Complexity of results
- Likelihood of identifying results of uncertain clinical significance
- Potential for misinterpretation of results

Norquist et al, 2016; SGO, 2014

Somatic Testing In Ovarian Cancer

- Somatic BRCA (sBRCA) mutations less common than gBRCA mutations: approx. 7% (higher in HGSC)
- Homologous recombination deficiency (HRD) is a potential target for PARP inhibition. Genomic loss of heterozygosity (LOH) was explored as a marker for HRD (offered by FoundationFocus CDxBRCA LOH, as a companion diagnostic for rucaparib)
- MSI-H ovarian cancer: 12% of unselected OC. A meta-analysis of 18 studies with 977 OC cases. MSI-H OC are more likely to have non-serous, including clear cell, mucinous, and endometrioid histologies, rather than serous pathology

Molecular Testing NCCN Guidelines

- Testing should be performed by a validated molecular testing in a CLIA-approved facility
- Testing to include at least: **BRCA1/2** (newly dg OC and/or recurrent) and **MSI or MMRP** (recurrent OC)
- Evaluation of homologous recombination deficiency (**HRD**) pathway genes can be considered
- The NCCN recognizes the value of identifying molecular alterations in the **less common ovarian histologies**: clear cell, mucinous (KRAS mutations in 50%; HER2 overexpression or amplification in up to 18%), borderline, and low grade serous tumors (KRAS mutations in 53%) to identify potential therapeutic targets

What Is the Standard Systemic Tx for Newly Diagnosed Advanced Epithelial Ovarian Cancer?

IV Carboplatin/Paclitaxel Q3W has been SOC > 20 years

- For stage IV or large volume residual disease (suboptimal): carboplatin/paclitaxel Q3W + bevacizumab is preferred[1]
  - Based on GOG 218,[2] ICON7[3]

- Alternative treatment is weekly chemotherapy
  - Dose-dense paclitaxel in fittest pts (JGOG 3016: GOG 262)[4,5]
  - Fractionated paclitaxel in infirm/weak pts (MITO- 7)[6]
- IP chemo is an option in the when the vol. of residual disease is < 1cm [7,8]

1. Ledermann JA, et al. Ann Oncol. 2013;24(suppl 6):vi24-vi32. 2. Burger RA, et al N Engl J Med. 2011;365:2473-2483. 3. Oza A, et al. Lancet Oncol. 2015;16:928-936. 4. Katsumata N, et al. Lancet Oncol. 2013;14:1020-1026.
5. Chan JK, et al. N Engl J Med. 2016;374:738-748. 6. Pignata S, et al Lancet Oncol. 2014;15:396-405. 7. Armstrong D, et al. N Engl J Med. 2006;354:34-43. 8. Chan JK, et al. N Engl J Med. 2016;374:738-748

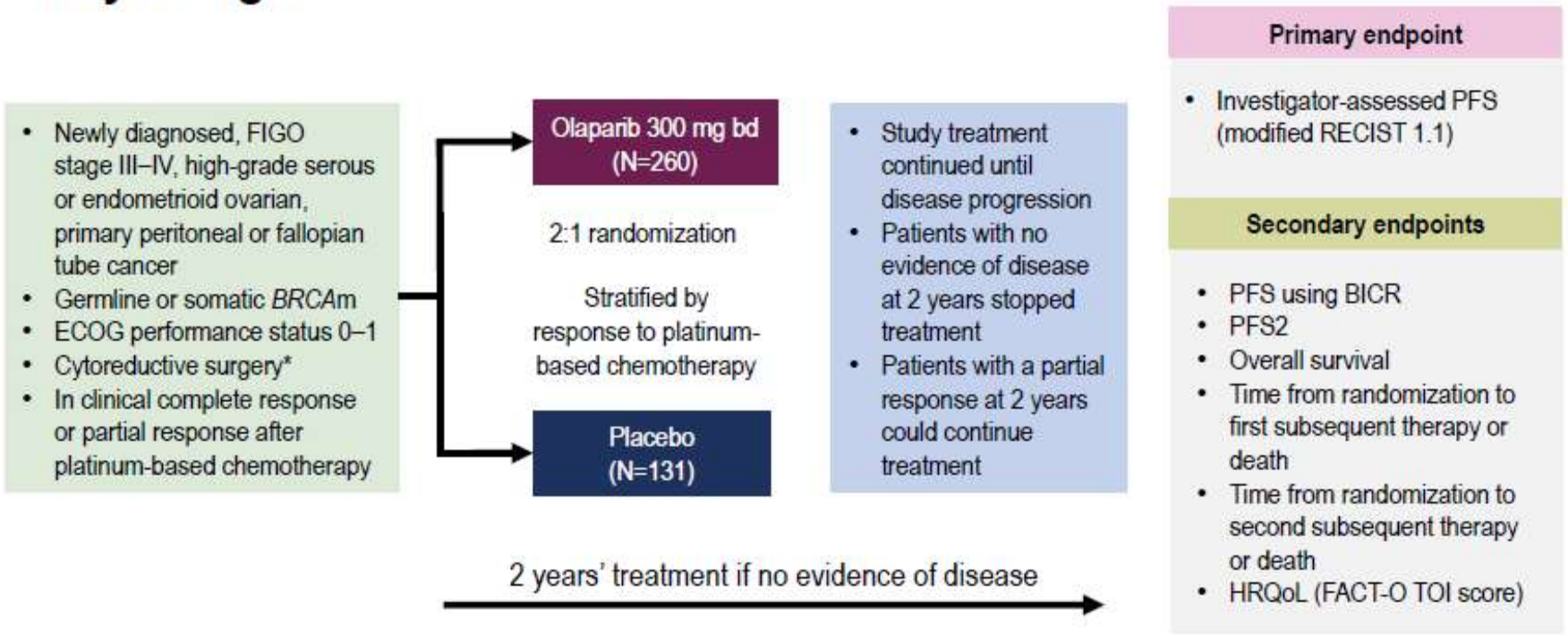
Antiangiogenic Agents Improve PFS but Not OS

Study	Study Arms	Median PFS, Mos	Median OS, Mos
GOG 218[1]	Carboplatin/paclitaxel/bevacizumab + bevacizumab maintenance	14.1	39.7
	Carboplatin/paclitaxel/bevacizumab	11.2	38.7
	Carboplatin/paclitaxel	10.3	39.3
ICON7[2]	Carboplatin/paclitaxel/bevacizumab + bevacizumab maintenance	21.8	NR
	Carboplatin/paclitaxel	20.3	NR

1. Burger RA, et al. N Engl J Med. 2011;365:2473-2483. 2. Perren TJ, et al. N Engl J Med. 2011;365:2484-2496. 3. du Bois A, et al. J Clin Oncol. 2014;32:3374-3382.

Maintenance olaparib in g/s BRCA+ ovarian CA SOLO-1

Study design



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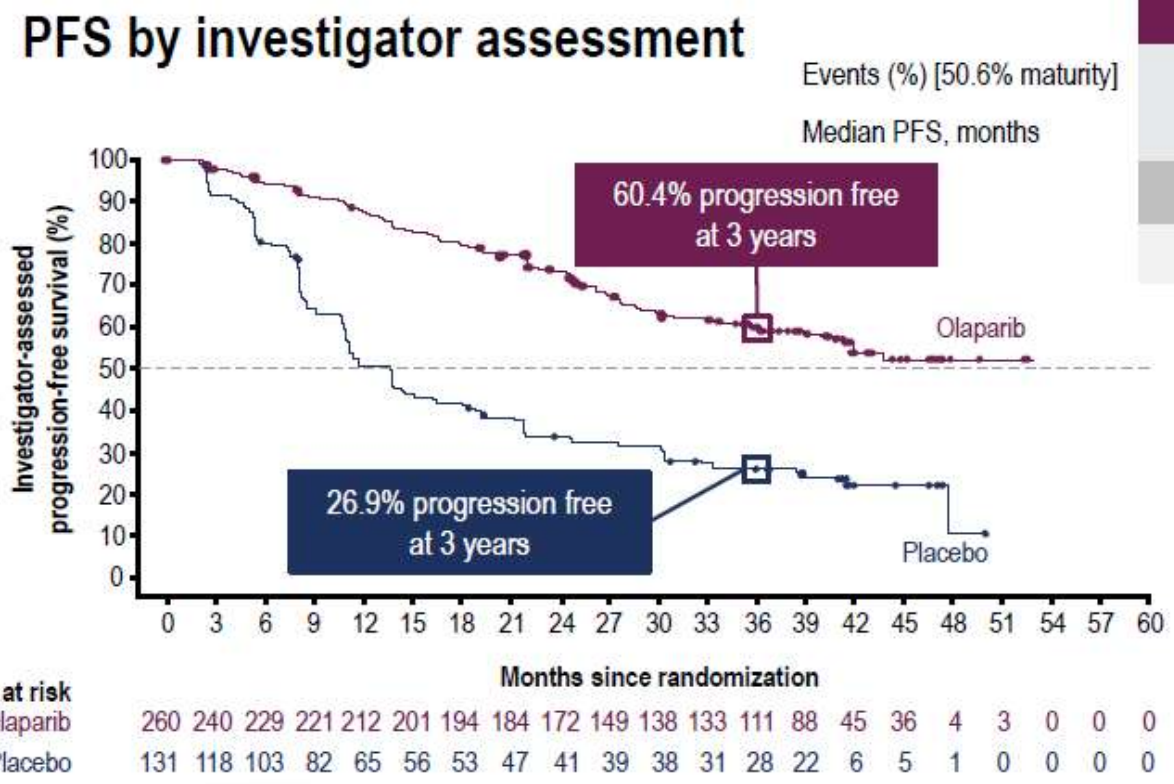
Moore K et al: N Engl J Med. 2018 Dec 27;379(26):2495-2505

SOLO-1



	Olaparib (N=260)	Placebo (N=131)
Events (%) [50.6% maturity]	102 (39.2)	96 (73.3)
Median PFS, months	NR	13.8
HR 0.30		
95% CI 0.23, 0.41; *P*<0.0001		

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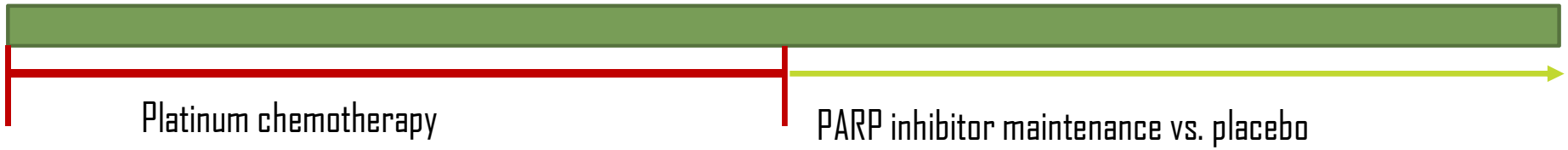
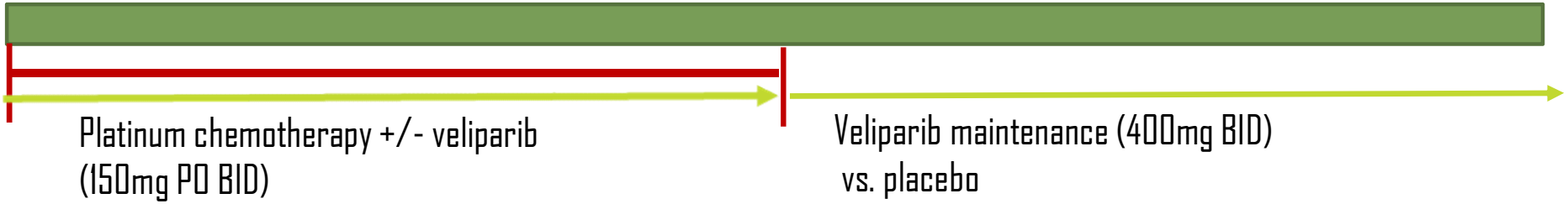
Frontline Maintenance Strategies for Ovarian Cancer

1. Chemo followed by PARP inhibitor maintenance: SOLO-1, PRIMA (niraparib)

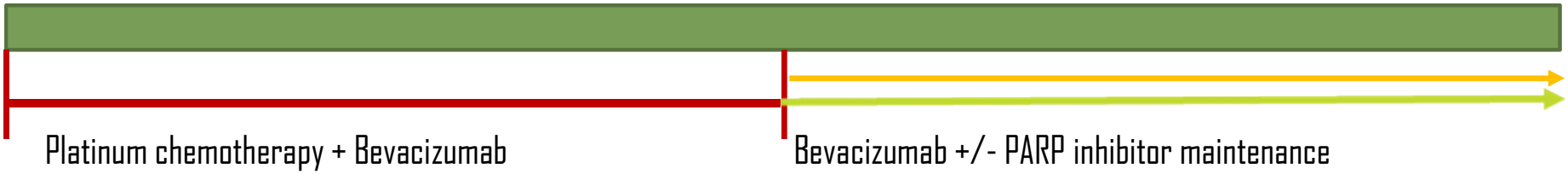


2. Chemo +/- PARP followed by +/- maintenance PARP : GOG3005 (veliparib)

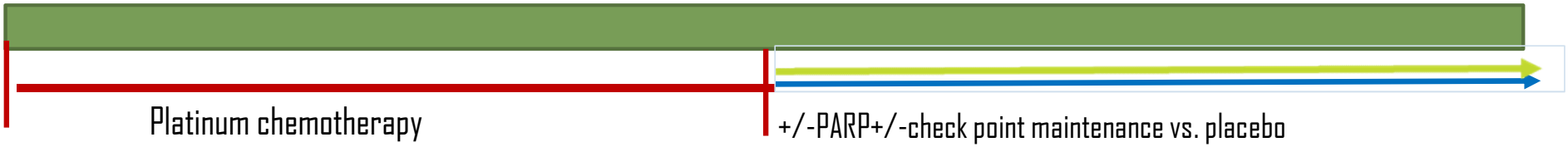


Frontline Maintenance Strategies for Ovarian Cancer

3. Chemo + upfront Bevacizumab followed by Bevacizumab +/- PARP inhibitor maintenance (olaparib) : PAOLA-1



4. Chemo followed by maintenance PARP vs. placebo +maintenance check point maintenance vs placebo : Athena (rucaparib/nivolumab)



Management Options for Patients With Recurrent Ovarian Cancer

Fifth GCIG Consensus Ovarian Cancer Recurrent Disease [1]

- There is no proven effective therapy for pts with asymptomatic CA 125 relapse
- Platinum sensitive: **platinum combination** (carboplatin/paclitaxel; carboplatin/pegylated doxorubicin; carboplatin/gemcitabine) +/- concurrent and maintenance bevacizumab; platinum combination +/- maintenance PARP inhibitor
- Platinum resistant: **single agent chemotherapy** (PLD, topotecan or weekly paclitaxel) +/-concurrent and maintenance bevacizumab (Aurelia trial)
- PFS is an acceptable end point if expected median OS > 12 mo; if < 12 mo OS is preferable

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1) Ann Oncol. 2017 Apr 1;28(4):727-732.

Bevacizumab for Recurrent Ovarian Cancer: Clinical Data Summary

Trial	Treatment	ORR, %	PFS, Mos	PFS HR *P* Value	OS, Mos	OS HR
Platinum-sensitive recurrent ovarian cancer						
GOG 213[1] (N = 673)	Paclitaxel/carboplatin	59	10.4	**0.628** ***P* < .0001**	37.3	0.829 *P* = .056
	Paclitaxel/carboplatin + bevacizumab	78	13.8		42.2	
OCEANS[2,3] (N = 484)	Gem/carboplatin	57	8.4		32.9	0.952 *P* = .65
	Gem/carboplatin + bevacizumab	79	12.4		33.6	
Platinum-resistant recurrent ovarian cancer						
AURELIA[4] (N =361)	Weekly Taxol vs.Doxil vs. Topotecan	11.8	3.4	0.48 p<0·0001	13.3	0·85 P < .174
	Chemo + bevacizumab	27.3	6.7		16.6	

1) Coleman RL, et al. Lancet Oncol. 2017;18:779-791. 2) Aghajanian C, et al. J Clin Oncol. 2012;30:2039-2045. 3) Aghajanian C, et al. Gynecol Oncol. 2015;139:10-16. 4) Pujade-Lauraine E et al, JCO 2014

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PARP Inhibitor Summary: Current Indications

	Olaparib[1]	Niraparib[2]	Rucaparib[3]
Approval date	December 2014, August 2017, December 2018	March 2017	December 2016, April 2018
Current indication	**Maintenance Frontline tx and maintenance tx for recurrent disease in CR or PR to platinum tx** **g*BRCA*+ pts with ≥ 3 lines of tx**	**Maintenance tx for recurrent disease in CR or PR to platinum tx**	**Maintenance tx for recurrent disease in CR or PR to platinum tx** **Somatic or g*BRCA*+ pts with ≥ 2 lines of tx**
Dose and schedule	300 mg (two 150-mg tablets) PO BID	300 mg (three 100-mg capsules) PO QD	600 mg (two 300-mg tablets) PO BID
Safety	**MDS/AML** confirmed in 2% **Pneumonitis**, including fatal cases, occurred in < 1%	**Thrombocytopenia** (61%; 29% grade ≥ 3) **Neutropenia** (30%; 20% grade ≥ 3) **Hypertension** (20%; 9% grade ≥ 3)	**Elevated AST/ALT** (75%; 5%-13% grade ≥ 3) **Dysgeusia** (39%)
	Most common tx-related AEs include fatigue (60% to 80%); GI symptoms: nausea (65% to 75%), vomiting (35% to 45%), diarrhea (20% to 35%), pain (30% to 40%); and anemia (35% to 50%)		

1) Olaparib [package insert]. 2017, 2019. 2) Niraparib [package insert]. 2017. 3) Rucaparib [package insert]. 2017, 2018.

Phase 3 PARP Inhibitor Maintenance Studies Show Strikingly Similar Results

Trial	ITT		BRCAm		HRD Positive		BRCAwt and HRD HRD Negative	
	PFS	OS	PFS	OS	PFS	OS	PFS	OS
NOVA (BICR)								
Niraparib	Pts were separated into gBRCA and non-BRCA groups		21.0	NR	12.9	NR	6.9	NR
Placebo			5.5	NR	3.8	NR	3.8	NR
Hazard ratio			0.27		0.38		0.58	
SOLO2 (Investigator-Assessed)								
Olaparib	Only patients with BRCAm cancers eligible		19.1	NR	NA		NA	
Placebo			5.5	NR				
Hazard ratio			0.30					
ARIEL3 (Investigator-Assessed)								
Rucaparib	10.8	NR	16.6	NR	13.6	NR	6.7	NR
Placebo	5.4	NR	5.4	NR	5.4	NR	5.4	NR
Hazard ratio	0.36		0.23		0.32		0.58	

BICR = blind independent central review; NR = not reached; NA = not applicable.
Pujade-Lauraine et al, 2017; Coleman, Oza et al, 2017; Mirza et al, 2016.

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PARP Inhibitor Characteristics Inform Treatment Choices

- Given comparable efficacy of the 3 agents available for ovarian cancer treatment, other characteristics will need to inform choice:
  - Toxicities
  - Drug-drug interactions
  - Schedule
  - Price
  - Special clinical situations

(eg, treatment of central nervous system disease: Olaparib, niraparib, and veliparib all cross the blood-brain barrier; Rucaparib has limited penetration across the blood-brain barrier)

Important Differences Between PARP Inhibitor and Bevacizumab Maintenance Trials

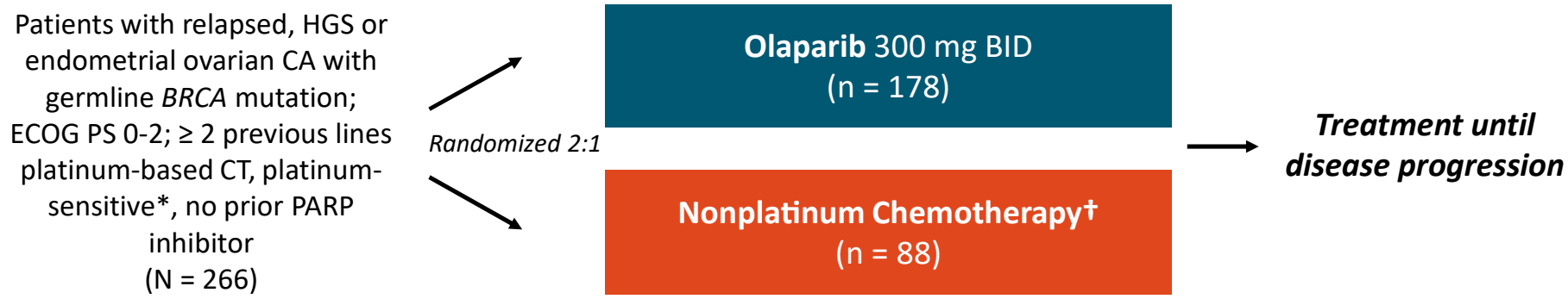
- Maintenance schedule and timing:
  - For OCEANS and GOG213, bevacizumab initiated with chemotherapy and used as maintenance post-chemotherapy
  - PARP inhibitor maintenance studies: PARP inhibitor started after chemotherapy has been completed (aka “switch maintenance”) in a documented platinum-sensitive population
- Histology:
  - All PARP inhibitor studies required high-grade serous carcinoma
  - Bevacizumab studies allowed all histologies
- # of prior lines of treatment:
  - Both bevacizumab trials only enrolled first recurrence
  - For PARP inhibitor studies, no limit on # of prior platinum treatments, but patients needed to be continuously sensitive
- Trial maturity:
  - No OS yet on PARP inhibitor trials; OS available on bevacizumab studies

OS = overall survival.

Aghajanian et al, 2012; Aghajanian et al, 2015; Coleman, Brady et al, 2017; Ledermann et al, 2012; Mirza et al, 2016; Pujade-Lauraine et al, 2017.

SOLO3: Phase III Trial of Olaparib vs. Chemotherapy in Patients With Platinum-Sensitive Relapsed Ovarian Cancer and Germline BRCA Mutation

- Multicenter, randomized, open-label, confirmatory phase III trial



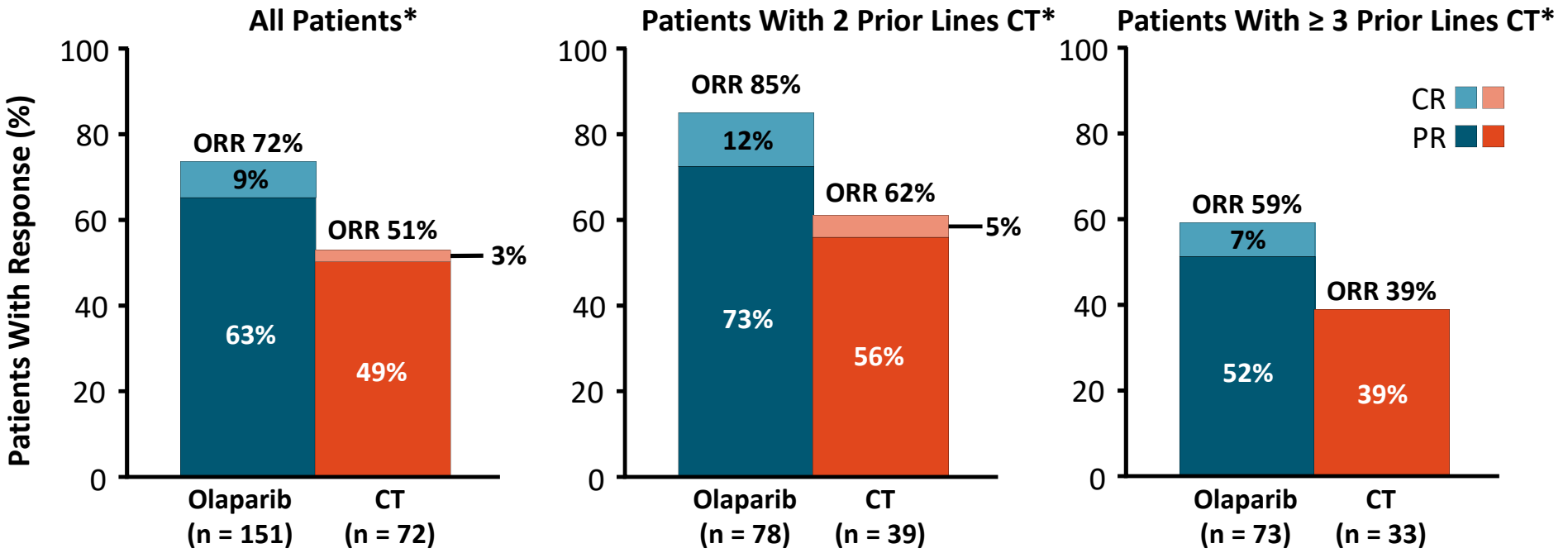
*Fully platinum sensitive: PD > 12 mos after platinum-based CT; partially platinum sensitive: PD 6-12 mos after platinum-based CT

†Investigator's choice of PLD 50 mg/m^2 on Day 1 of 28-day cycle (n = 47); paclitaxel 80 mg/m^2 on Days 1, 8, 15, and 22 of 28-day cycle (n = 20); gemcitabine 1000 mg/m^2 on Days 1, 8, and 15 of 28-day cycle (n = 13); topotecan 4 mg/m^2 on Days 1, 8, and 15 of 28-day cycle (n = 8)

- Primary endpoint: ORR by BICR (RECIST v1.1); original planned N of 411 patients with 90% power (2-sided α = .05); protocol amended Sept 2017 to N of 250 patients with > 80% power (2-sided α = .05)
- Secondary endpoints: PFS, PFS2, OS, TFST, TSST, HRQoL, safety

Penson. ASCO 2019. Abstr 5506.

SOLO3: ORR by Blinded Independent Central Review

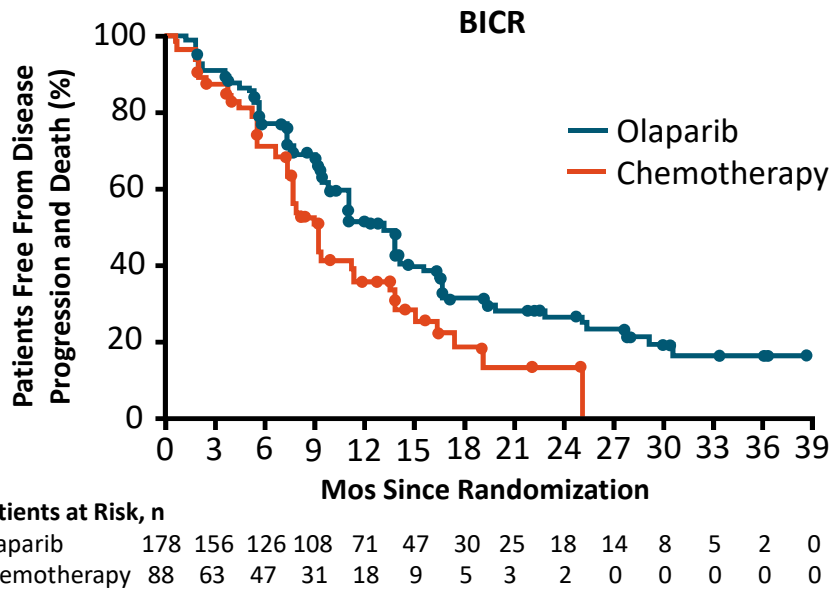


All Patients			Patients With 2 Prior Lines CT		Patients With ≥ 3 Prior Lines CT	
OR	95% CI	*P* Value	OR	95% CI	OR	95% CI
2.53	1.40-4.58	.002	3.44	1.42-8.54	2.21	0.96-5.20

*Patients with measurable disease at baseline.

Penson. ASCO 2019. Abstr 5506. Reproduced with permission.

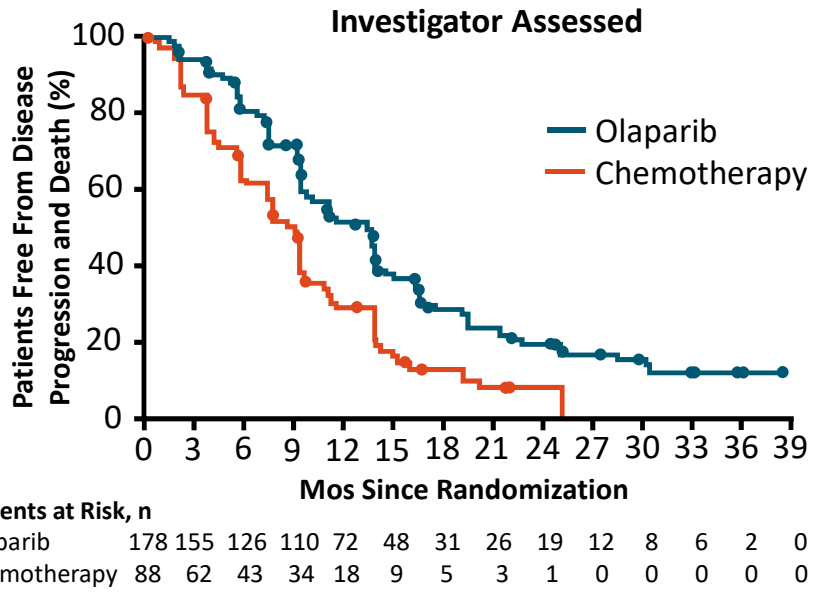
SOLO3: PFS in ITT Population



Patients at Risk, n

Olaparib	178	156	126	108	71	47	30	25	18	14	8	5	2	0
Chemotherapy	88	63	47	31	18	9	5	3	2	0	0	0	0	0

	Olaparib (n = 178)	Chemotherapy (n = 88)
PFS events, n (%)	110 (62)	49 (56)
Median PFS, mos	13.4	9.2
HR (95% CI; *P* value)	0.62 (0.43-0.91; *P* = .013)	



Patients at Risk, n

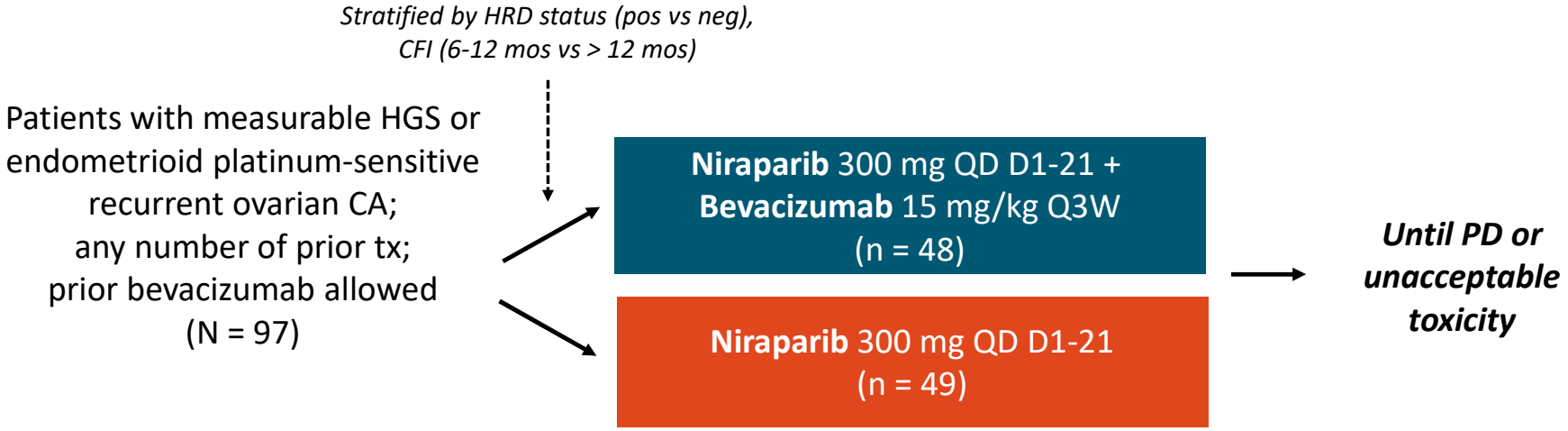
Olaparib	178	155	126	110	72	48	31	26	19	12	8	6	2	0
Chemotherapy	88	62	43	34	18	9	5	3	1	0	0	0	0	0

	Olaparib (n = 178)	Chemotherapy (n = 88)
PFS events, n (%)	123 (69)	63 (72)
Median PFS, mos	13.2	8.5
HR (95% CI; *P* value)	0.49 (0.35-0.70; *P* < .001)	

Penson. ASCO 2019. Abstr 5506. Reproduced with permission.

Phase II AVANOVA2: Niraparib + Bevacizumab vs Niraparib Alone in Platinum-Sensitive Recurrent Ovarian Cancer [1]

- Prospective, randomized, open-label phase II trial



- Primary endpoint: PFS in ITT population (investigator assessed)
- Secondary endpoint: DCR

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(1) Mirza. ASCO 2019. Abstr 5505. NCT02354131.

AVANOVA2

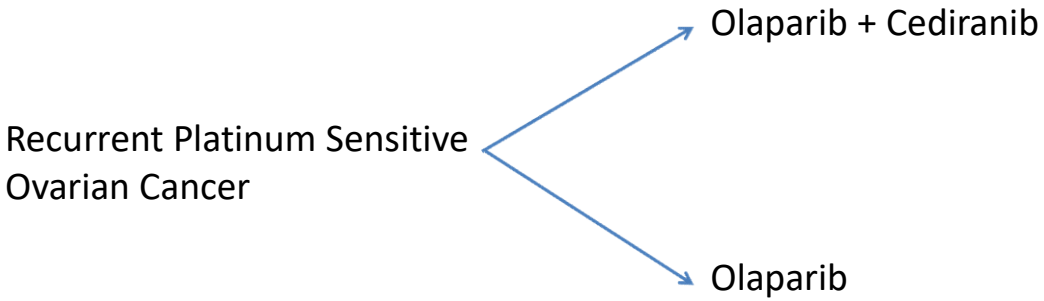
PFS in ITT Population (Primary Endpoint)

Median PFS, Mos	Niraparib + Bevacizumab (n = 48)	Niraparib (n = 49)	HR (95% CI)	*P* Value
ITT	11.9	5.5	0.35 (0.21-0.57)	< .0001

ORR and DCR

Outcome, %	Niraparib + Bevacizumab (n = 48)	Niraparib (n = 49)	Odds Ratio (95% CI)	*P* Value
ORR	60	27	4.23 (1.79-9.97)	.001
DCR	79	53	3.36 (1.37-8.22)	.008

Randomized phase 2 trial comparing the combination of olaparib and cediranib against olaparib alone in recurrent platinum-sensitive ovarian cancer[(1)]. NCT0111648.



	Olaparib + Cediranib	Olaparib
Median PFS	16.5 mos	8.2 mos
	(HR 0.50, 95% CI 0.30-0.83, p=0.007)	
Median OS	44.2 mos	33.3 mos
	(HR 0.64, 95% CI 0.36-1.11, p=0.11)	

- **gBRCA mut carriers**: PFS was 16.5 vs 16.4 mos (HR 0.75, p=0.42), and OS was 40.1 vs 44.2 mos (HR 0.79, p=0.55) for Olap and Ced/Olap, respectively.
- **Pts without known gBRCA mut**: PFS was 5.7 vs 23.7 mos (HR 0.32, p=0.002), and OS was 23.0 vs 37.8 mos (HR 0.48, p=0.074).

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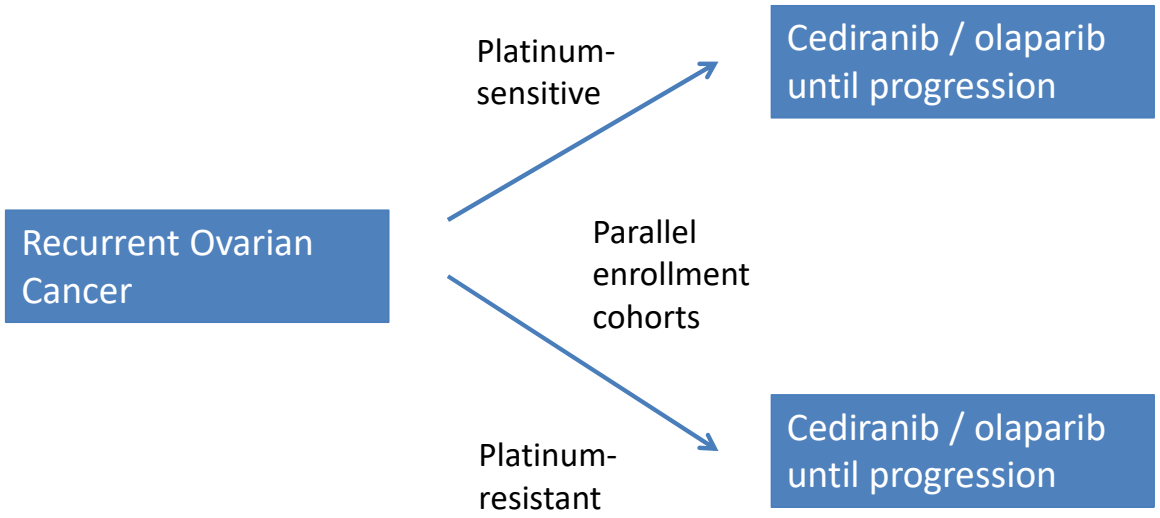
(1) J. Liu et al Lancet VOLUME 15, ISSUE 11, P1207-1214, OCTOBER 01, 2014 Updated J. Liu et al 2017 ASCO abstract 5535

CCC, PHII-139: A Phase 2 Study of Olaparib and Cediranib for the Treatment of Recurrent Ovarian Cancer (1)



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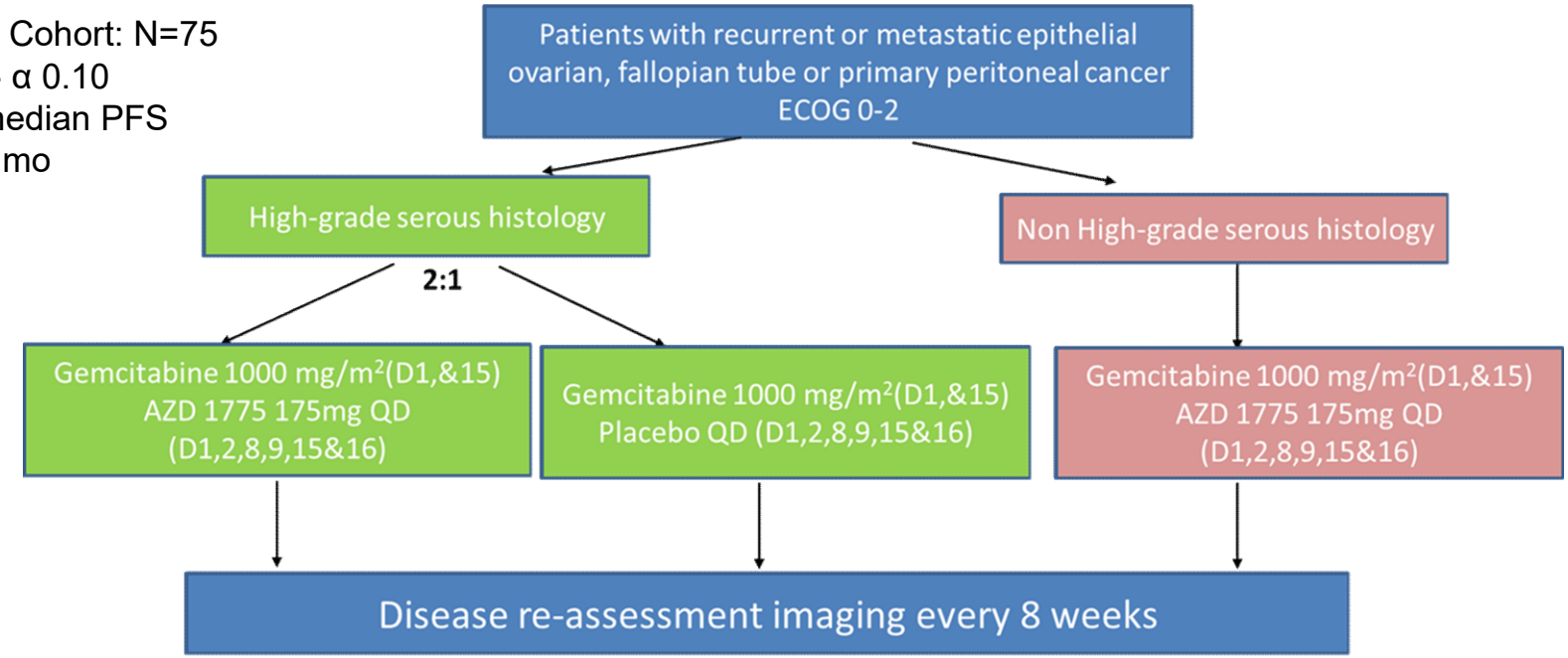
(1) PI: Joyce F Liu, NCT02345265

CCC: A Randomized Phase II Trial of Gemcitabine vs. Gemcitabine + Adavosertib (AZD1775) in Women with Recurrent, Platinum Resistant Epithelial Ovarian Cancer [1]

Experimental Cohort: N=75
90% power - α 0.10
Increase in median PFS
from 3.5 to 7 mo



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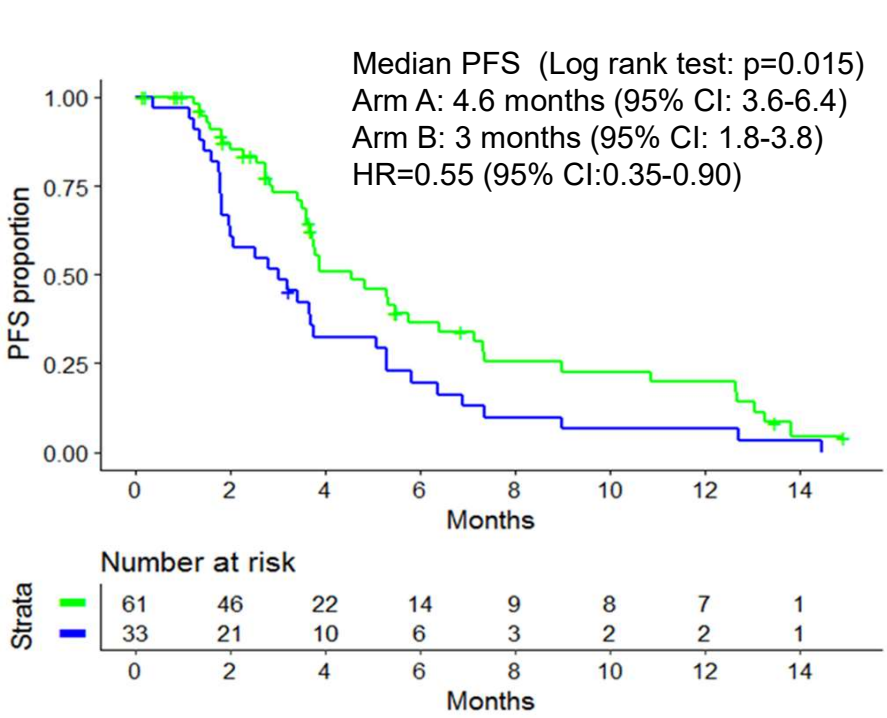
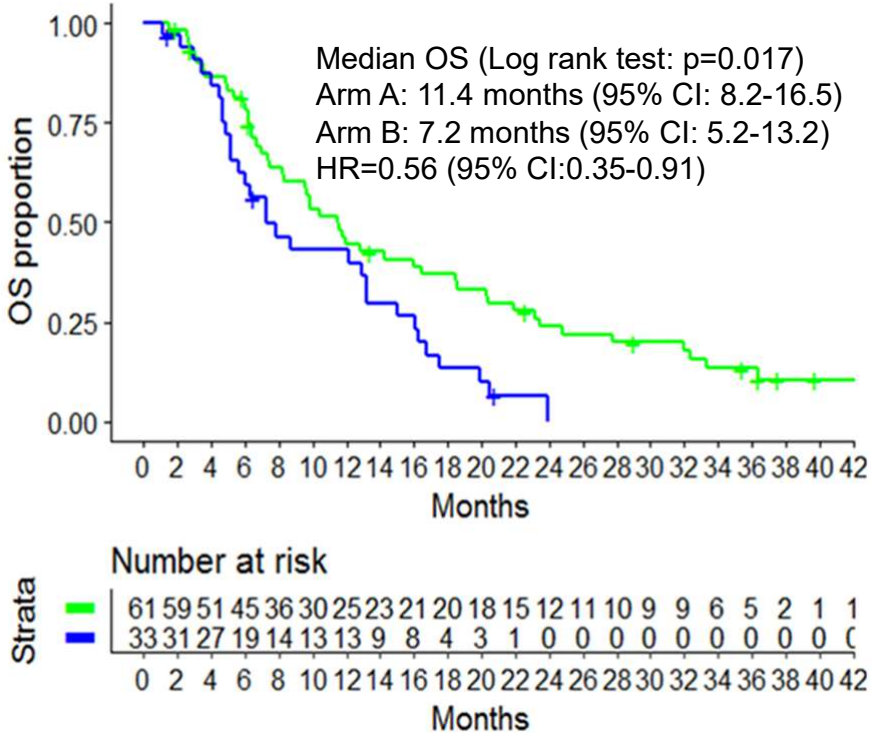
(1) Stephanie Lheureux et al. ASCO 2019

Phase II Trial of Gemcitabine vs. Gemcitabine + Adavosertib (AZD1775) in Recurrent Platinum Resistant Ovarian Cancer





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(1) Stephanie Lheureux et al. ASCO 2019

Immunotherapy Options for Patients With Recurrent Ovarian Cancer

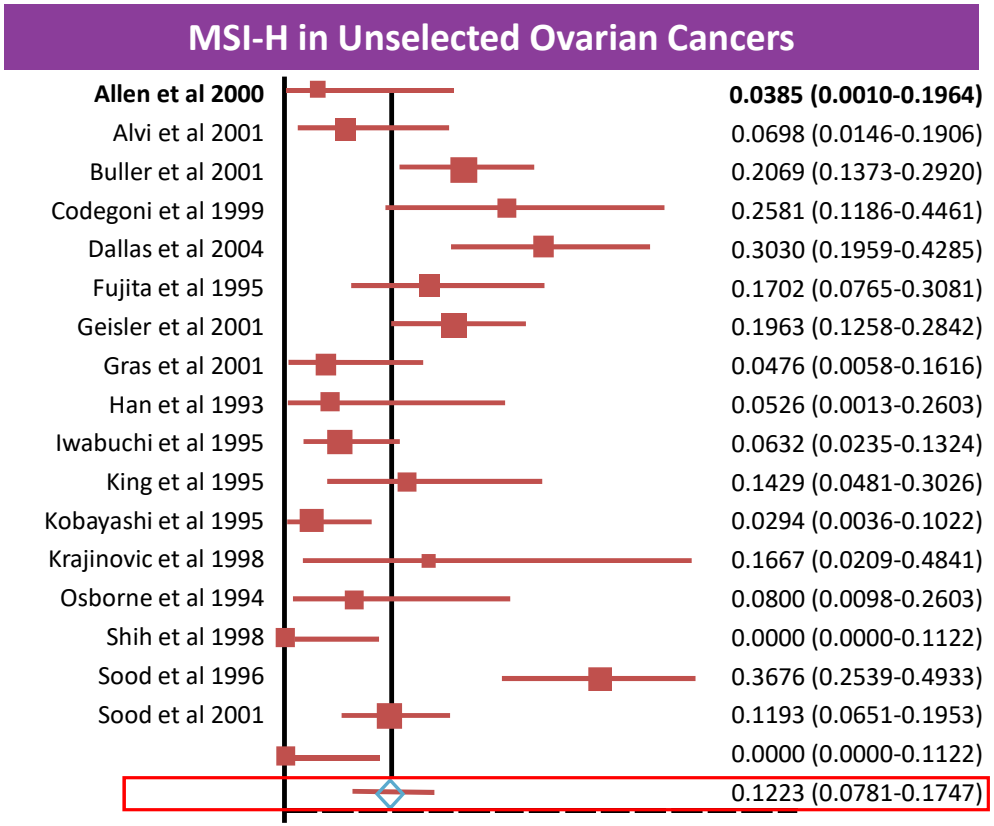
Pembrolizumab in Pts With Metastatic MSI-High or dMMR Tumors After PD on Prior Tx

- Included data from KEYNOTE-016, -164, -012, -028, and -158 for total of 149 pts
- MMR testing using standard PCR-based assay for detection of MSI

Tumor Type	n	ORR, % (95% CI)	DoR Range, Mos
CRC	90	36 (26-46)	1.6+ to 22.7+
Non-CRC	59	46 (33-59)	1.9+, 22.1+
Endometrial cancer	14	36(13-65)	4.2+ to 17.3+
Biliary cancer	11	27 (6-61)	11.6+ to 19.6+
Gastric or GEJ cancer	9	56 (21-86)	5.8+ to 22.1+
Pancreatic cancer	6	83 (36-100)	2.6+ to 9.2+
Small intestinal cancer	8	38 (9-76)	1.9+ to 9.1+)

- Additional pts not listed in table included 2 each of breast and prostate cancer; 1 each of bladder, esophageal, sarcoma, thyroid, retroperitoneal adenocarcinoma, SCLC, and RCC with 6 pts achieving CR or PR

MSI-HIGH AND DMMR IN OVARIAN CANCER (1)



Histologic Subtype	HNPCC	MSI-High	dMMR	Pooled
	Proportion (95% CI)	Proportion (95% CI)	Proportion (95% CI)	Proportion (95% CI)
Serous	0.42 (0.29-0.55)	0.36 (0.18-0.57)	0	0.32 (0.20-0.44)
Nonserous	0.57 (0.44-0.70)	0.063 (0.42-0.81)	0.95 (0.81-0.99)	0.68 (0.56-0.80)
Mucinous	0.16 (0.08-0.25)	0.22 (0.07-0.42)	0.26 (0.05-0.55)	0.19 (0.12-0.27)
Endometrioid	0.25 (0.17-0.35)	0.32 (0.21-0.45)	0.34 (0.10-0.64)	0.29 (0.22-0.36)
Clear cell	0.17 (0.07-0.30)	0.10 (0.009-0.27)	0.35 (0.15-0.58)	0.18 (0.09-0.28)
Undifferentiated	1 study	1 study	1 study	0.24 (0.07-0.47)

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(1) Pal T, et al. Clin Cancer Res. 2008;14:6847-6854.

Immune Checkpoint Inhibitors in OC

	Nivolumab[1]	Pembrolizumab Keynote 28 [2]	Avelumab[3]	Atezolizumab[4]	Durvalumab[5]
N	20	26	124	12	20*
Prior therapies	≥4: 55%	≥5: 38.5%	≥3: 65.3%	≥6: 58%	Median: 4*
PD-L1+ prevalence	80% (IC 2/3)	100% (≥1% TC)	77% (≥1% TC)	83% (IC 2/3)	>5% TC: 73% (11/15)*
Overall Response Rate	15%	11.5%	9.7%	25%	Not reported
Duration	4 (20%) >24 wks	7 (30%) >24 wks	16.1% @24 wks	mPFS ~12 wks	Not reported

* Includes ovarian cancer (n = 15), triple-negative breast cancer (n = 2), cervical cancer (n = 2), and uterine leiomyosarcoma patients (n = 1)

CI, confidence interval; DCR, disease-control rate; IC, immune cell; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; TC, tumor cell; TRAE, treatment-related adverse event, Tx, treatment

1. Hamanishi J, et al. *J Clin Oncol.* 2015;33(34):4015-4022. 2. Varga A, et al. *J Clin Oncol.* 2015;33(suppl): Abstract 5510. 3. Disis ML, et al. *J Clin Oncol.* 2016;34(suppl): Abstract 5533. 4. Infante JR, et al. *Ann Oncol.* 2016;27(Suppl 6): Abstract 871P. 5. Lee J-M, et al. *J Clin Oncol.* 2016;34(suppl): Abstract 3015.

TOPACIO: A Phase 1/2 study of niraparib + pembrolizumab in patients with advanced triple-negative breast cancer or recurrent ovarian cancer

Phase 1

- n=9 evaluable OC patients
- RP2D: niraparib 200 mg PO QD + pembrolizumab 200 mg IV every 21 days

Phase 2

- n=53 (51 evaluable + 2 discontinued the study <9 wks with no post-baseline scan)
- 83% comprehensive biomarker profile

RP2D: recommended phase 2 dose; PO = orally; QD = once daily; ; IV = intravenous.
Konstantinopoulos et al, 2018.

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Clinical Activity Is Observed Across Biomarker Populations in Patients with Ovarian Platinum-Resistant/Refractory

Response	All (%)	BRCAm (%)	HRDpos[a] (%)	BRCAwt (%)	HRDneg (%)
ORR	**11/47 (23%) (23%)**	**2/8 (25%)**	**4/16 (25%) (25%)**	**9/37 (24%) (24%)**	**7/26 (27%) (27%)**
DCR	30/47 (64%)	5/8 (63%)	11/16 (69%)	24/37 (65%)	15/26 (58%)

- The addition of pembrolizumab to niraparib in BRCAwt and HRDneg led to ORR similar to PARPi efficacy in the BRCAm population
- HRD status does not correlate with response to this combination in platinum-resistant/refractory disease

[a]HRDpos includes *BRCA* mutation or HRD score ≥42 per Myriad assay. Patients with inconclusive biomarker results were not included in the biomarker subpopulations. Responses include confirmed and unconfirmed responses.
DCR = disease control rate.
Konstantinopoulos et al, 2018.

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CCC: Randomized Phase I/IIb Trial of Atezolizumab (MPDL3280A), SGI-110 and NY-ESO-1 Vaccine (CDX-1401) in Recurrent Ovarian Cancer

- **Cohort 1:** Atezolizumab IV on days 1 and 15, every 28 days for up to 24 courses
- **Cohort 2:** Guadecitabine SC on days 1-5, every 28 days for up to 6 + Atezolizumab IV on days 8 and 22, every 28 days for up to 24 courses
- **Cohort 3:** Guadecitabine + atezolizumab as in Cohort II. Patients also receive CDX-1401 vaccine IV on day 15 and poly ICLC SC on days 15-16, every 28 days for up to 6 courses

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Conclusions

- Molecular testing has become a standard approach for patients with ovarian CA
- Cytotoxic chemotherapy still has a role in ovarian cancer
  - Differences in dose and schedule may be important
  - Role of IP therapy becoming clearer
- Angiogenesis is an established target
  - Bevacizumab now FDA approved in various scenarios
- PARP inhibitors have emerged as important therapy
  - Olaparib, rucaparib, and niraparib now FDA approved
  - Labels are expanding based on recently reported positive trials
- Role of immunotherapy promising in ovarian cancer

Thank you!

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