



# HIGHLIGHTS OF GYNECOLOGIC MALIGNANCIES

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### **Disclosures**

I have nothing to disclose.



### **Objectives**

- Review practice changing publications and drug approvals impacting Gynecologic Oncology practice
- PARPi in high grade epithelial ovarian cancer as maintenance following initial therapy
- Chemoradiation versus chemotherapy in high risk endometrial cancer
- Checkpoint inhibitor therapy in MSI-H gynecologic cancers
- Adjuvant chemotherapy following definitive chemoradiation in cervical cancer
- ADC in advanced cervical cancer
- Second line therapy in metastatic endometrial cancer
- Tissue agnostic, biomarker driven NTRK therapy in gynecologic malignancies

### **Consensus Approach to Initial Therapy of High Grade EOC**



Lindsay Kuroki, and Saketh R Guntupalli BMJ 2020;371:bmj.m3773

### **Olaparib Maintenance Therapy: SOLO-1**

#### Phase III SOLO1 Trial of Olaparib vs Placebo as First-line Maintenance Therapy in Ovarian Cancer With BRCA Mutation

Randomized, double-blind, placebo-controlled, multicenter phase III trial



### **Olaparib Maintenance Therapy: SOLO-1**



### **Olaparib Maintenance Therapy: SOLO-1**

#### Final analysis of OS

#### Median OS improved by 12.9 months with maintenance olaparib vs placebo\*



\*Median durations of follow-up were 65.7 months for placebo; "FAS includes all patients randomly assigned to a treatment group; "eCRF stratification variables were used to correct for any patients who were mis-stratified at randomization in a past hoc analysis C1. confidence interval; EAS, full analysis set



### **Olaparib Maintenance Therapy: PAOLA-1**

#### PAOLA-1: Maintenance Olaparib + Bevacizumab After Initial Therapy for Ovarian Cancer

 Randomized, placebo-controlled phase III trial for patients with newly diagnosed, FIGO stage III-IV, high-grade serous/endometrioid ovarian, fallopian tube or primary peritoneal cancer

Patients with newly diagnosed ovarian cancer and PR or CR after upfront or interval surgery, standard platinum/taxane-based CT, and ≥ 3 cycles of bevacizumab (N = 806)



Slide credit: clinicaloptions.com

- Primary endpoint: investigator assessed PFS (RECIST v1.1)
- Secondary endpoints: TFST, PFS2, TSST, OS, HRQoL, AE
- Sensitivity analysis: PFS by BICR

Ray-Coguard. ESMO 2019. Abstr. LBA2.

### **Olaparib Maintenance: PAOLA-1**



### **OLAPARIB** maintenance

#### Table 3. Efficacy results from SOLO-1 and PAOLA-1 trials

Trial name	Patient population	Maintenance treatment arms	PFS in indicated population	Companion diagnostic
SOLO-1	BRCAm newly diagnosed advanced ovarian cancer	Olaparib vs. placebo	<i>BRCA</i> m population PFS NR vs. 13.8 months HR: 0.30 (0.23, 0.41)	BRACAnalysis CDx and FoundationOne CDx
PAOLA-1	Newly diagnosed advanced ovarian cancer	O+B vs. P+B	HRD-positive population PFS 37.2 vs. 17.7 months HR: 0.33 (0.25, 0.45)	Myriad myChoice CDx

Abbreviations: *BRCAm, BRCA* mutated; CDx, companion diagnostic; HR, hazard ratio; HRD, homologous recombination deficient; NR, not reached; O+B, olaparib plus bevacizumab; P+B, placebo plus bevacizumab; PFS, progression-free survival.

Both trials demonstrated that BRCAm patients treated with Olaparib monotherapy and HRD positive patients Treated with O+B had a clinically meaningful improvement in PFS.

### **Olaparib Maintenance: Safety**

#### Table 4. Safety results from SOLO-1 and PAOLA-1 trials

Trial name	Patient population	Maintenance treatment arms	Median time on therapy (months)	Discontinuations because of AE	All grade AEs	Grade 3–4 AEs	On treatment deaths
SOLO-1 (n = 391)	BRCAm newly diagnosed advanced ovarian cancer	Olaparib vs. placebo	O: 24.6 P: 13.9	O: 12% P: 2%	O: 99% P: 92%	O: 30% P: 5%	No deaths because of AEs while on study drug or within 30 days after last dose in either arm
PAOLA-1 ( <i>n</i> = 806)	Newly diagnosed advanced ovarian cancer	O+B vs. P+B	O+B: 17.3 P+B: 15.6	O+B: 20% P+B: 6%	O+B: 99% P+B: 96%	O+B: 57% P+B: 50%	O+B: 1 death because of aplastic anemia/ pneumonia P+B: 4 deaths (2 myocardial infarction, 1 intestinal perforation, 1 cardiovascular failure)

Abbreviations: AE, adverse event; B, bevacizumab; BRCAm, BRCA mutated; O, olaparib; O+B, olaparib plus bevacizumab; P, placebo; P+B, placebo plus bevacizumab.

### **NIRAPARIB Maintenance: PRIMA**

#### PRIMA: Maintenance Niraparib vs Placebo in Ovarian Cancer at High Risk of Recurrence After 1L Platinum

Randomized, double-blind, placebo-controlled phase III trial (active, not recruiting, as of 10/2020)



### **Niraparib Maintenance: PRIMA**



#### PRIMA: PFS in Patients With HRD and HRP (by BICR)



### **Niraparib Maintenance: PRIMA**

Subgroup	Niraparib	Placebo	Hazard Ratio for Dis	ease Progression or De	eath (95% CI)
	no. of patients with or death/to	disease progression tal no. (%)			
All patients	232/487 (47.6)	155/246 (63.0)			0.62 (0.50-0.76)
Age					
<65 yr	136/297 (45.8)	86/147 (58.5)			0.61 (0.47-0.81)
≥65 yr	96/190 (50.5)	69/99 (69.7)	•		0.53 (0.38-0.74)
ECOG score					
0	146/337 (43.3)	107/174 (61.5)			0.60 (0.46-0.77)
1	86/150 (57.3)	48/72 (66.7)		-	0.69 (0.48-1.00)
Stage of disease at initial diagnosis					
111	143/318 (45.0)	103/158 (65.2)			0.54 (0.42-0.70)
IV	89/169 (52.7)	52/88 (59.1)			0.79 (0.55-1.12)
Neoadjuvant chemotherapy					
Yes	151/322 (46.9)	107/167 (64.1)			0.59 (0.46-0.76)
No	81/165 (49.1)	48/79 (60.8)			0.66 (0.46-0.94)
Best response to platinum therapy					
Complete response	146/337 (43.3)	100/172 (58.1)			0.60 (0.46-0.77)
Partial response	86/150 (57.3)	55/74 (74.3)			0.60 (0.43-0.85)
Geographic region					
North America	104/218 (47.7)	82/115 (71.3)			0.50 (0.37-0.68)
All other regions	128/269 (47.6)	73/131 (55.7)		-	0.72 (0.54-0.96)
Homologous-recombination status					
BRCA mutation	49/152 (32.2)	40/71 (56.3) -			0.40 (0.27-0.62)
No BRCA mutation, homologous- recombination deficiency	32/95 (33.7)	33/55 (60.0)			0.50 (0.31-0.83)
Homologous-recombination proficiency	111/169 (65.7)	56/80 (70.0)	•	-	0.68 (0.49-0.94)
Not determined	40/71 (56.3)	26/40 (65.0)		<u> </u>	0.85 (0.51-1.43)
				+	
		0.25	0.50	1.00 2.00	
			Niraparib Better	Placebo Better	

#### Figure 3. Disease Progression or Death, According to Prespecified Subgroups.

Shown is the incidence of disease progression or death, according to the listed subgroups, in the two trial groups. On the Eastern Cooperative Oncology Group (ECOG) performance-status evaluation, a score of 0 indicates that the patient is fully active and able to carry on all predisease performance without restriction, and a score of 1 indicates that the patient is restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. The vertical shading indicates the 95% confidence interval for the overall population.

### **PARPi Approved for Maintenance After Initial Therapy**

Agent	FDA Approved	Indication	Biomarker	Dose
Olaparib	12/19/18	Maintenance in tBRCA positive patients after response to initial therapy	Germline or somatic BRCA mutation	300 mg BID for 2 years
Olaparib	5/8/20	Maintenance in combination with bevacizumab after response to initial therapy including bevacizumab	tBRCA or HRD positive	300 mg BID for 2 years, Bevaciumab 15 mg/kg every 21 days x 15 cycles
Niraparib	4/29/20	Maintenance after response to initial therapy	None	200 mg per day if <77 kg OR platelets <150; 300 mg per day if >77kg AND platelets>150

# ENDOMETRIAL CANCER, CERVICAL CANCER



### **Does Adjuvant Chemoradiotherapy Extend Relapse-Free Survival in Stage III or IV Endometrial Cancer?**

#### The NEW ENGLAND JOURNAL of MEDICINE

#### ORIGINAL ARTICLE

#### Adjuvant Chemotherapy plus Radiation for Locally Advanced Endometrial Cancer

Daniela Matei, M.D., Virginia Filiaci, Ph.D., Marcus E. Randall, M.D., David Mutch, M.D., Margaret M. Steinhoff, M.D., Paul A. DiSilvestro, M.D., Katherine M. Moxley, M.D., Yong M. Kim, M.D., Ph.D., Matthew A. Powell, M.D., David M. O'Malley, M.D., Nick M. Spirtos, M.D., William Small, Jr., M.D., Krishnansu S. Tewari, M.D., William E. Richards, M.D., John Nakayama, M.D., Ursula A. Matulonis, M.D., Helen Q. Huang, M.S., and David S. Miller, M.D. Phase III GOG 258

• Open label trial of 736 patients, 6/09-6/14

- Adjuvant chemoradiotherapy: cisplatin 50 mg/m2 days 1 and 29 with volume-directed EBRT (4500 cGy in 25 fractions) followed by carboplatin AUC 5-6 plus paclitaxel 175 mg/m2 every 3 weeks for 4 cycles with growth factor support
- Versus adjuvant carboplatin AUC 6 plus placlitaxel 175 mg/m2 every 3 weeks for 6 cycles.

### Adjuvant CRT versus CT: GOG 258



Subgroup I	No. of Events	Total No.	Hazard Ratio (95% CI)	
FIGO stage				
I, II, or IIIA	52	167	<b>⊢≣</b> ;;	0.76 (0.43-1.32)
IIIB	15	25	II	1.65 (0.59-4.65)
IIIC or IIIC1	113	355	<u>⊢ ; ∎</u>	1.21 (0.83-1.76)
IIIC2 or IVA	91	189	<b>⊢</b> ∎	0.73 (0.48-1.10)
Age at entry				
≤65 yr	165	532	<b>⊢</b>	0.98 (0.72-1.33)
>65 yr	106	204		0.81 (0.55-1.19)
Gross residual disease				
Absent	260	719	<b>■</b> ,1	0.93 (0.73-1.19)
Present	11	17		0.81 (0.23-2.87)
Histology				
Endometrioid, grade 1	32	166	<b>⊢</b>	0.98 (0.49-1.96)
Endometrioid, grade 2	67	221	⊢ <b></b>	1.05 (0.65-1.70)
Endometrioid, grade 3	48	129	<b>⊢</b>	1.09 (0.62-1.92)
Serous	74	131	<b>⊢≣</b> ;;	0.85 (0.54-1.34)
Other	50	89		0.68 (0.39-1.19)
BMI category				
Normal or underweight	53	143	<b>⊢</b>	1.09 (0.64-1.87)
Overweight	74	165	<b>⊢</b>	0.92 (0.58-1.45)
Obesity class I, II, or III	144	428	<b>⊢</b> ∎ <mark></mark>	0.92 (0.67-1.28)
Primary analysis population	271	736		0.90 (0.71-1.15)

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### dMMR in Gynecologic Malignancies

Mismatch repair proteins correct genetic errors.

dMMR leads to genomic instability, with accumulation of errors and a high tumor mutation burden associated with infiltrating lymphocytes that are sensitive to PD-1/PD-L1 blockade

dMMR common in endometrial cancer: 25-30% of endometrioid endometrial carcinoma



Latham A, J Clin Oncol 2018

### **Pembrolizumab in dMMR/MSI-H**

Cancer type <sup>11</sup>	n (%)	Overall response rate (% (95% CI))	Duration of response (range, months)
Total	149 (100%)	39.6% (31.7-47.9)	1.6 <sup>a</sup> -22.7 <sup>a</sup>
Colorectal	90 (60.4%)	36% (26–46%)	1.6 <sup>a</sup> -22.7 <sup>a</sup>
Noncolorectal	59 (39.6%)	46% (33–59%)	1.9 <sup>a</sup> –22.1 <sup>a</sup>
Endometrial	14 (9.4%)	36% (13-65%)	4.2 <sup>a</sup> –17.3 <sup>a</sup>
Dillory	11 (7.4%)	27% (0-61%)	11.6ª 10.6ª
Gastric or GE junction	9 (6.0%)	56% (21-86%)	5.8 <sup>a</sup> -22.1 <sup>a</sup>
Pancreatic	6 (4.0%)	83% (36–100%)	2.6 <sup>a</sup> -9.2 <sup>a</sup>
Small intestinal	8 (5.4%)	38% (9–76%)	1.9 <sup>a</sup> –9.1 <sup>a</sup>
Breast	2 (1.3%)	PR, PR	7.6–15.9
Prostate	2 (1.3%)	PR, SD	9.8 <sup>a</sup>
Bladder	1 (0.7%)	NE	NA
Esophageal	1 (0.7%)	PR	18.2 <sup>a</sup>
Sarcoma	1 (0.7%)	PD	NA
Thyroid	1 (0.7%)	NE	NA
Retroperitoneal adenocarcinoma	1 (0.7%)	PR	7.5 <sup>a</sup>
Small cell lung	1 (0.7%)	CR	8.9 <sup>a</sup>
Renal cell	1 (0.7%)	PD	NA

Table 1 Clinical response to pembrolizumab in microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancers

CI, confidence interval; CR, complete response; GE, gastroesophageal; NA, not applicable; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

<sup>a</sup>Ongoing response.

Keytruda package insert, 2019

### **Endometrial Cancer: Molecular Classification**



### dMMR Endometrial Cancer: Pembrolizumab



### **Pembrolizumab in Advanced Cervical Cancer**

Approved for patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1, CPS >=1

KEYNOTE-158, Chung H, JCO 2019

N= 98 patients with advanced cervical cancer

ORR 12%, CR 3 PR 9

All responses seen in patients with PD-L1 positive tumors, ORR 4 14.6%



### **Approved Checkpoint Inhibitors in dMMR/MSI-H Tumors**

- Pembrolizumab: approved 4/2017
  - Indication: adult and pediatric patients with unresectable of metastatic solid tumors that are MSI-high or mismatch repair deficient (dMMR) that have progressed following prior treatment and who have no satisfactory alternatives
  - Targets PD-1/PD-L1 pathway: pooled analysis of 5 independent trials, each with different eligibility criteria, n = 149, 15 cancer types
    - ORR 39%, duration of response 6 months in 78%
    - ARs: fatigue, pruritis, diarrhea, decreased appetite, rash, fevers, cough, dyspnea, musculoskeletal pain, constipation, nausea, IRAEs
- Dostarlimab: approved 8/17/21
  - o Indication: adult patients with dMMR recurrent or advanced solid tumors that have progressed on or following prior treatment
  - GARNET trial: n = 209 patients with dMMR recurrent or advanced solid tumors
    - ORR 41.6%, CR 9%, duration of response longer than 6 months in 95% of patients, median response duration 34.7 months
- Pembrolizumab: approved 6/16/20: Indication: unresectable or metastatic solid tumors, TMB>= 10mut/Mb
  - KEYNOTE 158: cohort of 102 patients with TMB-H: ORR 29%, 50% of responses lasted greater than 2 years

### **Endometrial Cancer: Second Line Therapy**

- Advanced endometrial cancer that is not MSI-H or dMMR
- Disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

### **Endometrial Cancer, 2<sup>nd</sup> line: KEYNOTE 775**



<sup>a</sup>Patients may have received up to 2 prior platinum-based CT regimens if 1 is given in the neoadjuvant or adjuvant treatment setting. <sup>b</sup>Maximum of 35 doses. <sup>c</sup>Maximum cumulative dose of 500 mg/m<sup>2</sup>.

BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IV, intravenous; PFS, progression-free survival; pMMR, mismatch repair-proficient; ORR, objective response rate; PO, per os (by mouth); QD, once daily; Q3W, every 3 weeks; QW, once weekly.

SGO VIRTUAL ANNUAL MEETING 2021 ON WOMEN'S CANCER®



### **Endometrial Cancer**, 2<sup>nd</sup> line: **KEYNOTE 775**



#### **Progression-free Survival**<sup>a</sup>







### **Cervical Cancer: Adjuvant Chemotherapy to Improve Cure?**



Mileskin, L ASCO 2021

### **Cervical Cancer: OUTBACK trial**



Mileshkin L et al, JCO 2021.

- PFS at 5 years 63 v 61%
- Similar pattern of recurrence in both arms

- Questions that remain:
  - Would different drugs be better, less toxic?
  - Should only higher risk patients receive extra treatment?

### **Cervical cancer: Tisotumab vedotin**

- Antibody drug conjugate directed at Tissue Factor, covalently linked to MMAE (microtubule disrupter).
- Approved after phase 2, single arm innovaTV 204 trial
  - Tisotumab vedotin monotherapy in patients with progression on or after carboplatin/taxol/bevacizumab therapy
  - N = 102
  - $\circ$  2 mg/kg iv every 3 weeks
- FDA approved 9/21/21.



### **Cervical cancer: Tisotumab vedotin**

- ORR 24%
  - CR 7%, PR 17%, 49% SD
  - Median DoR 8.3 months; ongoing response after 6 months 62%
  - Median time to response 1.4 months
- Tolerable: most toxicities grade 1/2
  - Alopecia, epistaxis, nausea, fatigue, arthralgias, conjunctivitis, dry eye
  - Neuropathy gr 3 in 7%, gr 1-2 26%
  - $\circ$  1 death due to septic shock



Coleman RL, Lancet 2021



## RARE MOLECULAR BIOMARKERS

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### **NTRK Fusion**

- Larotrectinib: accelerated approval 11/26/18
  - o 3 multicenter, open-label, single-arm trials: LOXO-TRK-14001, SCOUT, and NAVIGATE
  - o ORR 75%, CR 22% PR 53%, duration of response exceeded 6 months in 73%, 12 months in 39%
  - ARs >+20%: fatigue, nausea, dizziness, vomiting, increased AST/ALT, cough, constipation, diarrhea
  - $\circ~$  Approved dose: 100 mg BID
- Entrectinib: approved 8/15/2019
  - Tissue agnostic, NTRK 1,2,3 fusion
  - o 3 trials: ALKA-372-001, STARTRK-1, STARTRK-2
  - ORR 57%, CR 7%, duration of response 6 months 68%
  - ARs: CHF, CNS effects, skeletal fractures, hepatotoxicity, hyperuricemia, QT prolongation, vision disorders.

### **NTRK Fusion Frequency**



### **NTRK Fusions in Gynecologic Malignancy**

<u>Am J Surg Pathol.</u> Author manuscript; available in PMC 2019 Sep 27. Published in final edited form as:

<u>Am J Surg Pathol. 2018 Jun; 42(6): 791–798.</u>

doi: 10.1097/PAS.000000000001055

PMCID: PMC6764747 NIHMSID: NIHMS945057 PMID: <u>29553955</u>

#### NTRK Fusions Define a Novel Uterine Sarcoma Subtype with Features of Fibrosarcoma

 Sarah Chiang, MD,<sup>1,\*</sup> Paolo Cotzia, MD <sup>1</sup> Devid M, Uhanan, MD <sup>2</sup> Alevender Deler, MD <sup>3</sup> Müllers D, Ter, MD <sup>4</sup>
 PMCID: PMC6506462

 Lei Zhang, MD,<sup>1</sup> Jaclyn F. Hechtman, Gynecol Oncol Rep. 2019 May; 28: 141–144.
 PMCID: PMC6506462

 MBBS, MD, FRCPA,<sup>1</sup> Kay J. Park, ME
 Published online 2019 Apr 23. doi: 10.1016/j.gore.2019.04.006
 PMID: 31080864

 Ryma Benayed, PhD,<sup>1</sup> Marc Ladanyi,
 PMCID: PMC6506462
 PMID: 31080864

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NTRK-1 fusion in endocervical fibroblastic malignant peripheral nerve sheath tumor marking eligibility for larotrectinib therapy: A case report

A.E. Wells,<sup>a</sup> A.M. Mallen,<sup>b</sup> M.M. Bui,<sup>c</sup> D.R. Reed,<sup>d</sup> and S.M. Apte<sup>e,\*</sup>

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### **NTRK Inhibitor Response**

		Larotrectinit	22	Entrectinib <sup>24</sup>		
Cancer type	n (%)	Overall response rate (% (95% Cl))	Duration of response (range, months)	n (%)	Overall response rate (% (95% Cl))	Duration of response (range, months)
Total	55 (100%)	75% (61–85%)	1.6 <sup>a</sup> -33.2 <sup>a</sup>	54 (100%)	57% (43–71%)	2.8-26.0 <sup>a</sup>
Appendix	1 (1.8%)	SD	NA		NA	
Breast	1 (1.8%)	PD	NA	6 (11.1%)	83% (36–100%)	4.2-14.8 <sup>b</sup>
Cholangiocarcinoma	2 (3.6%)	SD, NE	NA	1 (1.9%)	PR	9.3
Colorectal	4 (7.3%)	25% (NA)	5.6 <sup>b</sup>	4 (7.4%)	25% (NA)	4.8 <sup>b</sup>
Gastrointestinal stromal tumor	3 (5.5%)	100% (29–100%)	9.5–17.3 <sup>a,b</sup>		NA	
Gynecologic	NA			2 (3.7%)	PR	20.3 <sup>b</sup>
Infantile fibrosarcoma	7 (12.7%)	100% (59-100%)	1.4ª-10.2ª		NA	
Lung	4 (7.3%)	75% (19–99%)	8.2-20.3ª	10 (18.5%)	70% (35–93%)	1.9 <sup>b</sup> -20.1 <sup>b</sup>
Melanoma	4 (7.3%)	50% (NA)	1.9–17.5 <sup>ª</sup>		NA	
Neuroendocrine		NA		3 (5.6%)	PR	5.6 <sup>b</sup>
Pancreas	1 (1.8%)	0% (NA)	NA	3 (5.6%)	PR, PR	7.1-12.9
Salivary gland	12 (21.8%)	83% (52–98%)	7.7–27.9 <sup>a</sup>	7 (13.0%)	86% (42-100%)	2.8-16.5 <sup>b</sup>
Soft tissue sarcoma	11 (20.0%)	91% (59–100%)	3.6-33.2ª	13 (24.1%)	46% (19–75%)	2.8-15.1
Thyroid	5 (9.1%)	100% (48-100%)	3.7-27.0 <sup>a</sup>	5 (9.3%)	20% (NA)	7.9

CI, confidence interval; NA, not applicable; NE, not evaluable; *NTRK*, neurotrophic receptor tyrosine kinase gene; PD, progressive disease; PR, partial response; SD, stable disease; TRK, tropomyosin receptor kinase.

<sup>a</sup>Ongoing response. <sup>b</sup>Value at data cutoff.

Doebele RC, Lancet Oncol 2020.

Drilon A. Cancer Discov 2017

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### **Future Directions**

#### Combination Checkpoint Inhibitor Studies in Advanced/Recurrent Endometrial Cancer

Checkpoint Inhibitors Plus Antiangiogenic Agents

KEYNOTE-146<sup>[1]</sup> KEYNOTE-775 (phase III)<sup>[2]</sup> ENGOT-en9/LEAP-001 (phase III)<sup>[3]</sup> Pembrolizumab + Lenvatinib

> NCT03367741<sup>[4]</sup>: Nivolumab + Cabozantinib

Checkpoint Inhibitors Plus Chemotherapy

NRG-GY018<sup>[5]</sup>: Pembrolizumab + Paclitaxel/Carboplatin

AtTEnd/ENGOT-en7<sup>[6]</sup>: Atezolizumab + Paclitaxel/Carboplatin

RUBY (ENGOT-EN6; GOG-3031)<sup>[7]</sup>: Dostarlimab + Chemotherapy

1. Makker. JCO. 2020; 38: 2981. 2. NCT03517449. 3. NCT03884101. 4. NCT03367741. 5. NCT03914612. 6. NCT03603184. 7. NCT03981796.

### **Future Directions**

- Overcome PARPi resistance in ovarian cancer
- Later line role of her2 targeted therapies in high grade serous endometrial cancer after Herceptin-based regimens
- PARPi in high grade serous endometrial carcinoma
- Targeting HPV driven GYN malignancies
- Novel ADCs





