Mass General Brigham
Mass General Cancer Center

Immunotherapy for GYN malignancies; slowly but surely

Oladapo Yeku, MD, PhD, FACP
Assistant Professor, Harvard Medical School
Director of Translational research,
Gynecologic Oncology Program, Massachusetts General Hospital

13th Annual Winter Cancer Symposium
March 1-3, 2024

Agenda

1. Cervical Cancer

- Definitive chemo-immunotherapy with radiation
- Combination immunotherapy with platinum-based chemotherapy for advanced/metastatic disease disease and CPS >1
- PD-1 inhibitor for CPS >1 in the post-platinum setting
- Antibody drug conjugates

2. Endometrial Cancer

- Combination immunotherapy with platinum-based chemotherapy for advanced/metastatic disease disease and dMMR/MSI-H
- PD-1 inhibitor with or without lenvatinib based on mismatch repair status in the post-platinum setting

3. Ovarian Cancer

- PD-1 inhibitor for TMB-H or dMMR
- ADC

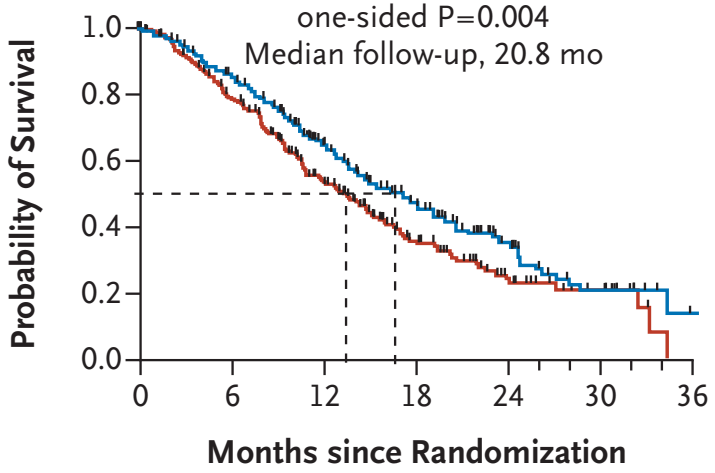
Cervical Cancer

Incorporation of bevacizumab into frontline therapy for recurrent, metastatic cervical cancer

A

	Events *no. (%)*	Median Overall Survival *mo*
Chemotherapy (N=225)	140 (62)	13.3
Chemotherapy+Bev (N=227)	131 (58)	17.0

Hazard ratio, 0.71 (98% CI, 0.54–0.95); one-sided P=0.004
Median follow-up, 20.8 mo

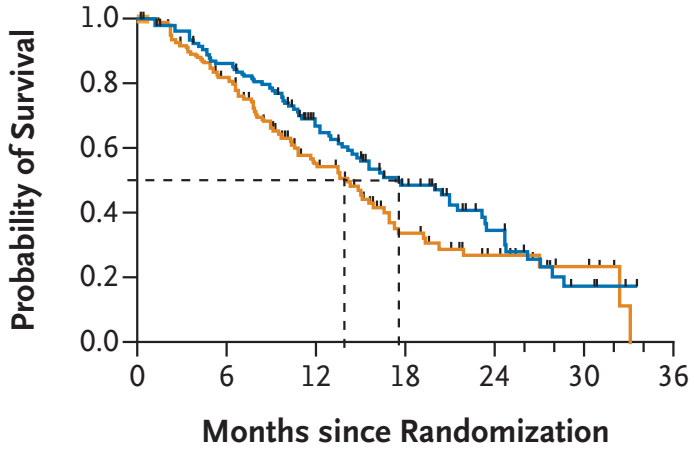


No. at Risk						
Chemotherapy	225	167	94	45	17	8
Chemotherapy +bev	227	184	121	69	30	10

B

	Events *no. (%)*	Median Overall Survival *mo*
CP (N=114)	69 (61)	14.3
CP+Bev (N=115)	66 (58)	17.5

Hazard ratio, 0.68 (95% CI, 0.48–0.97); one-sided P=0.04

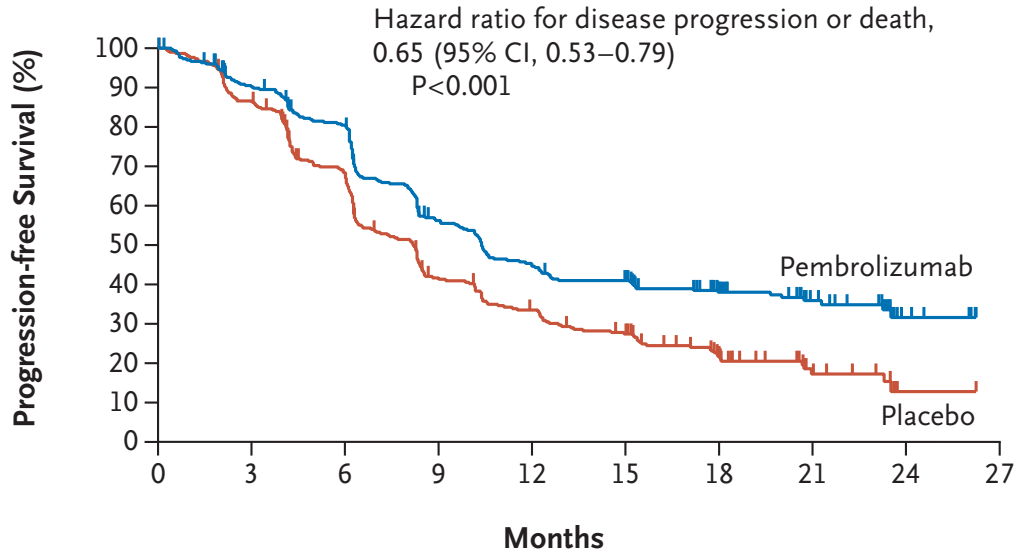


No. at Risk						
CP	114	89	50	22	12	5
CP+bev	115	94	63	37	17	5

K. Tewari et al. Improved Survival with Bevacizumab in Advanced Cervical Cancer. NEJM. 2014

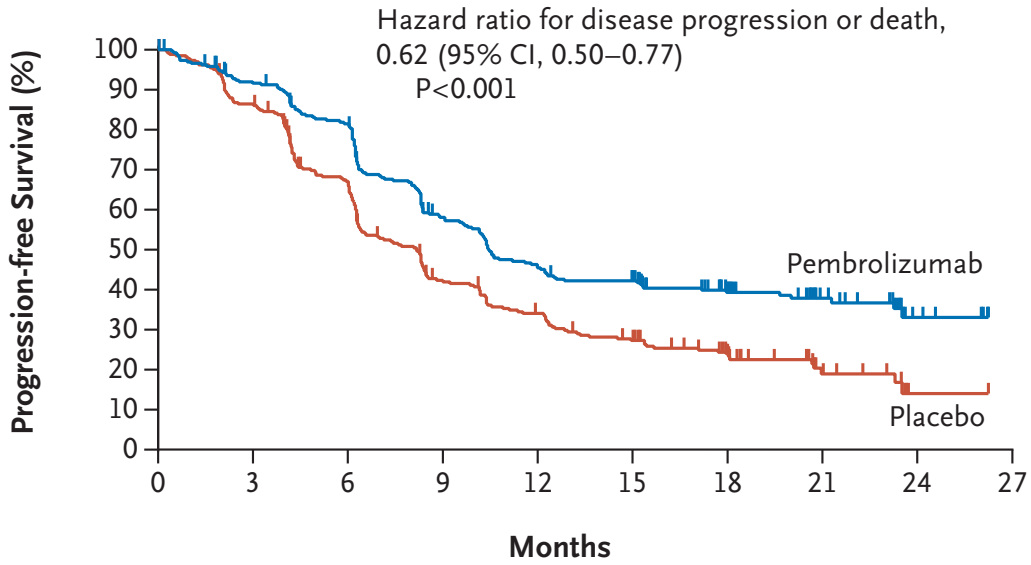
Chemo-immunotherapy for persistent, recurrent or metastatic disease

B **Intention-to-Treat Population**



No. at Risk										
Pembrolizumab	308	263	229	155	123	110	70	35	10	0
Placebo	309	259	195	113	89	71	39	13	1	0

B **Patients with a PD-L1 Combined Positive Score of ≥1**



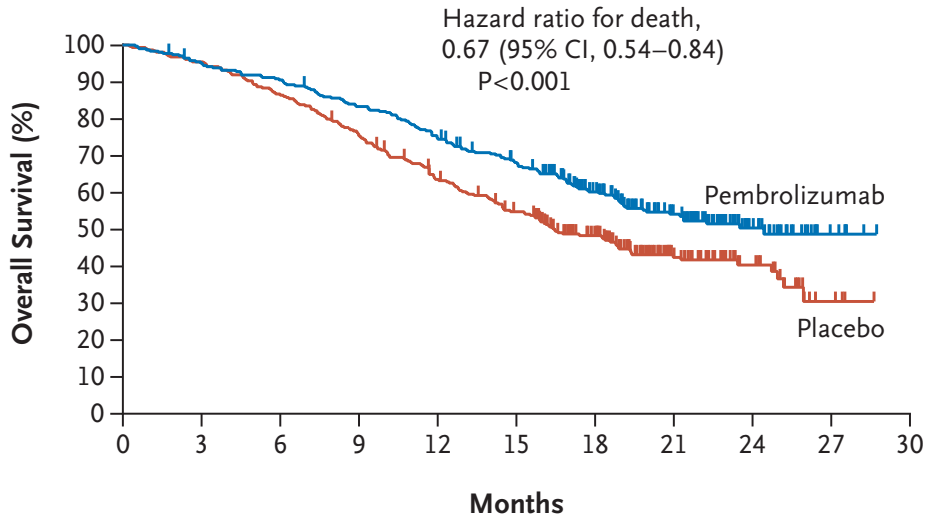
No. at Risk										
Pembrolizumab	273	238	208	143	112	101	66	34	10	0
Placebo	275	229	170	103	81	63	38	13	1	0

PFS

N. Colombo et al. Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. NEJM. 2021

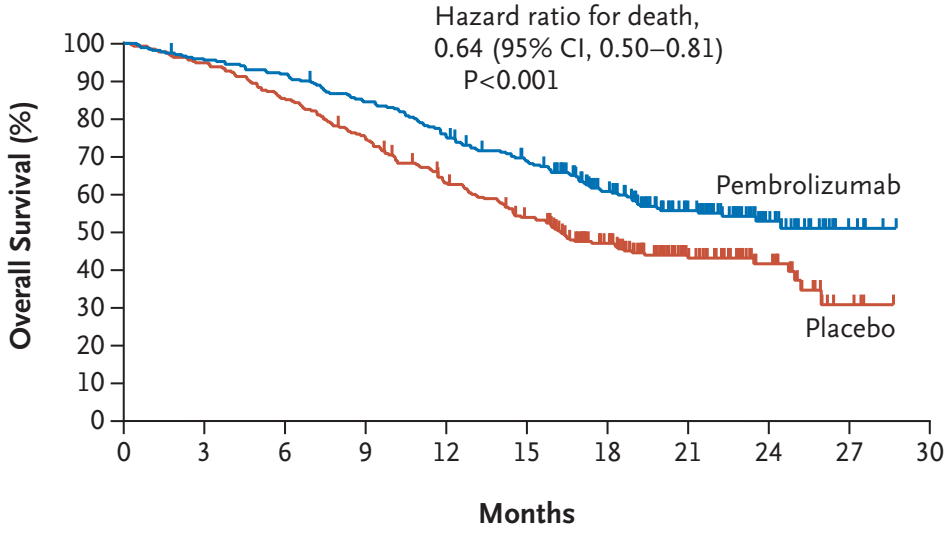
Chemo-immunotherapy for persistent, recurrent or metastatic disease

A **Intention-to-Treat Population**



No. at Risk											
Pembrolizumab	308	291	277	254	228	201	145	89	36	6	0
Placebo	309	295	268	234	191	160	116	60	28	4	0

B **Patients with a PD-L1 Combined Positive Score of ≥1**



No. at Risk											
Pembrolizumab	273	260	250	229	204	181	132	82	34	6	0
Placebo	275	261	235	206	168	140	100	55	25	4	0

OS

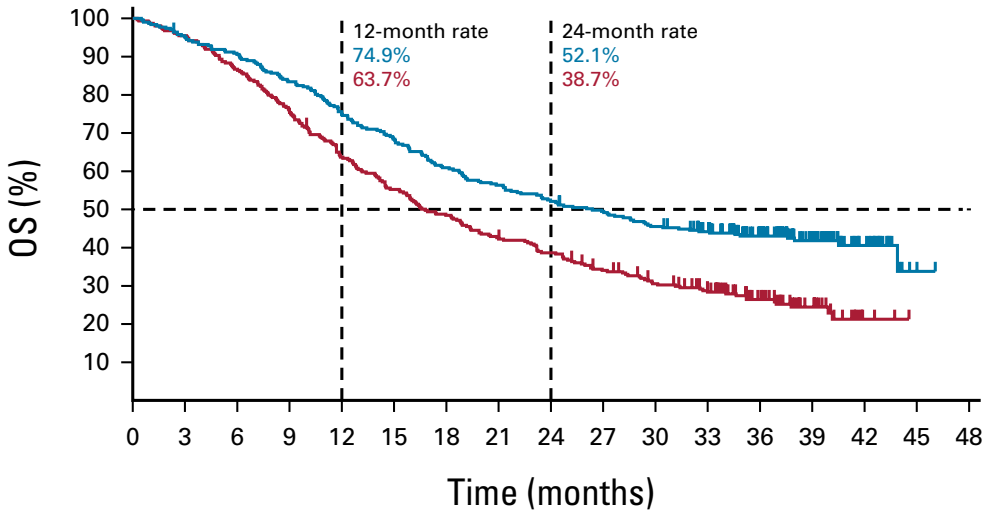
N. Colombo et al. Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. NEJM. 2021

Final results of KEYNOTE-826: Final-line pembrolizumab and chemotherapy v.s. placebo and chemotherapy

A

OS: All-Comer Population

Treatment Group	No. of Events/ No. of Patients (%)	Median OS, Months (95% CI)	HR (95% CI)
Pembro + chemo ± bev	178/308 (57.8)	26.4 (21.3 to 32.5)	0.63 (0.52 to 0.77)
Placebo + chemo ± bev	228/309 (73.8)	16.8 (14.6 to 19.4)	



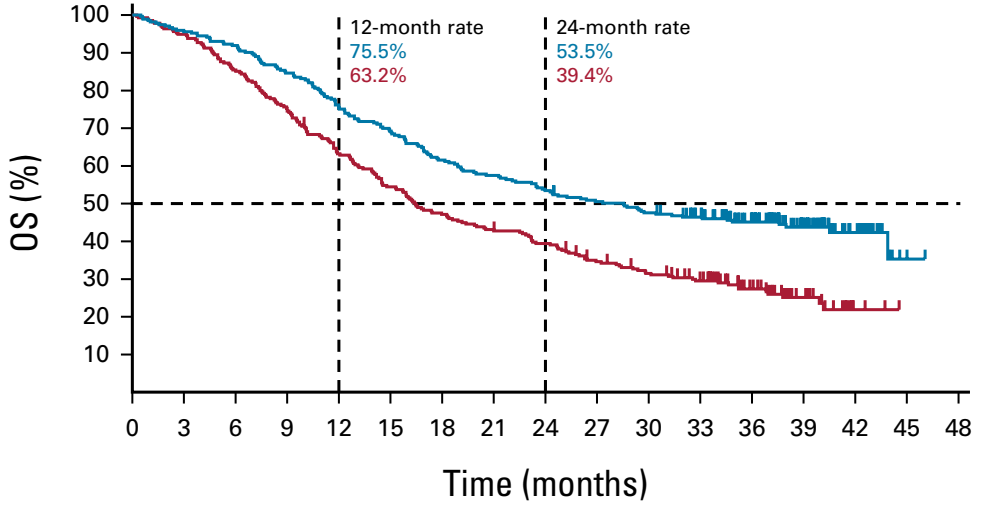
No. at risk:

308	292	278	256	230	210	187	173	160	150	138	125	95	55	22	2	0
309	295	268	235	196	170	149	130	118	101	87	72	48	26	3	0	0

B

OS: PD-L1 CPS ≥1 Population

Treatment Group	No. of Events/ No. of Patients (%)	Median OS, Months (95% CI)	HR (95% CI)
Pembro + chemo ± bev	153/273 (56.0)	28.6 (22.1 to 38.0)	0.60 (0.49 to 0.74)
Placebo + chemo ± bev	201/275 (73.1)	16.5 (14.5 to 20.0)	

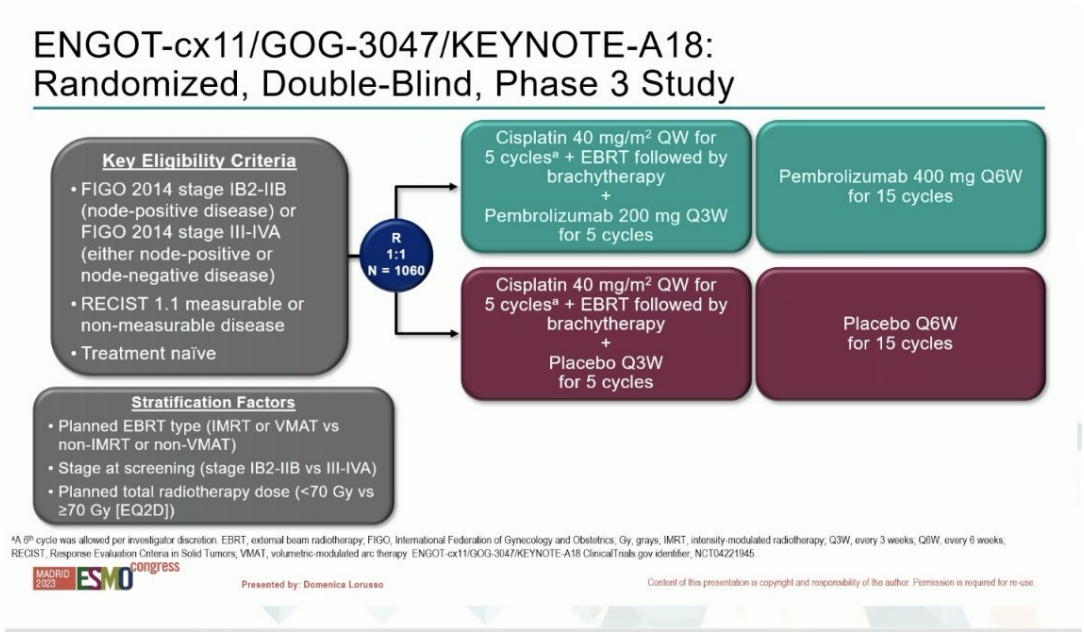


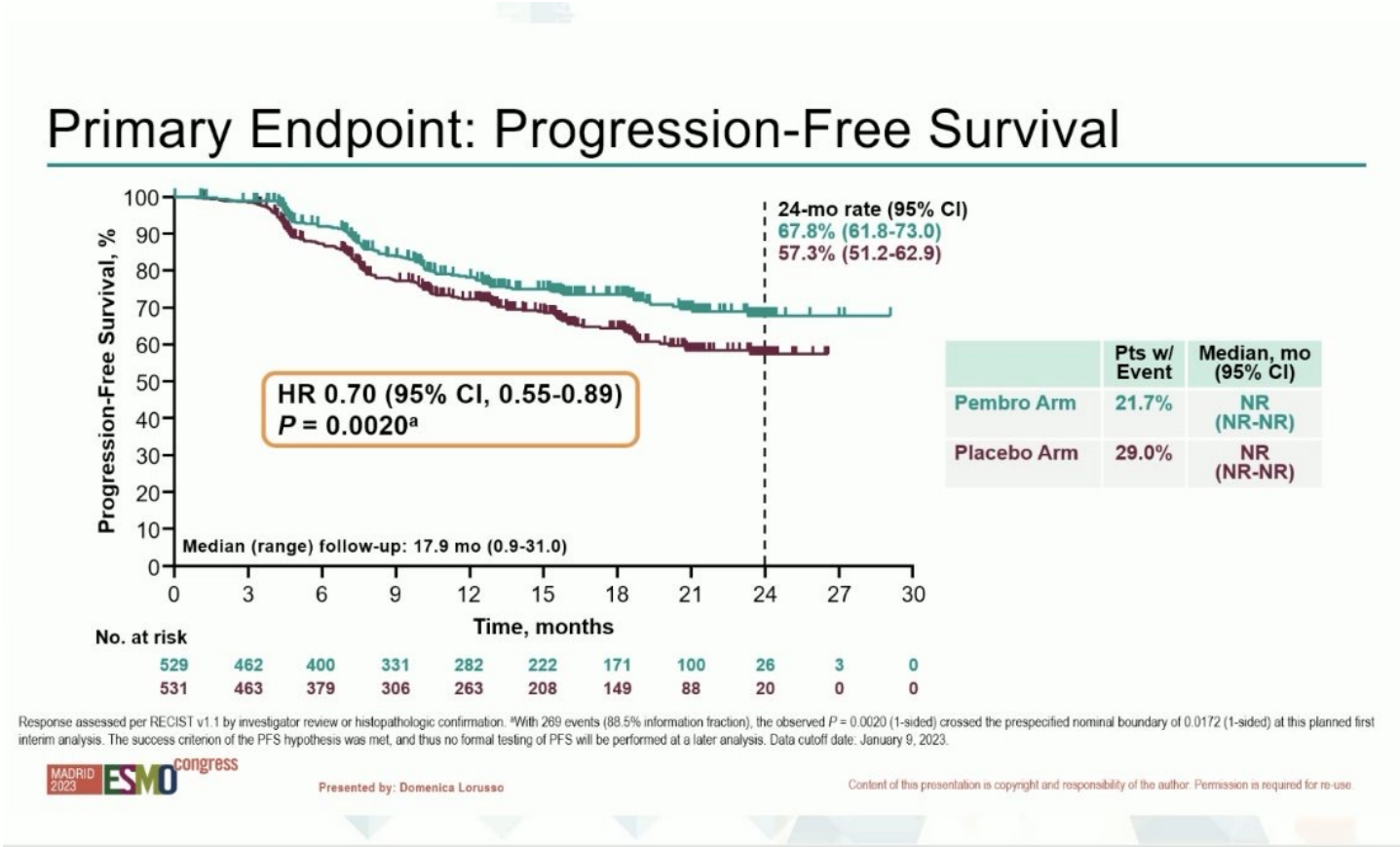
No. at risk:

273	261	251	231	206	189	168	157	146	136	128	116	90	52	22	2	0
275	261	235	207	173	149	129	117	107	91	81	68	45	24	3	0	0

B. Monk et al. First-Line Pembrolizumab + Chemotherapy Versus Placebo + Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Final Overall Survival Results of KEYNOTE-826. J Clin Oncol. 2023

Frontline immunotherapy with cisplatin-sensitized radiation

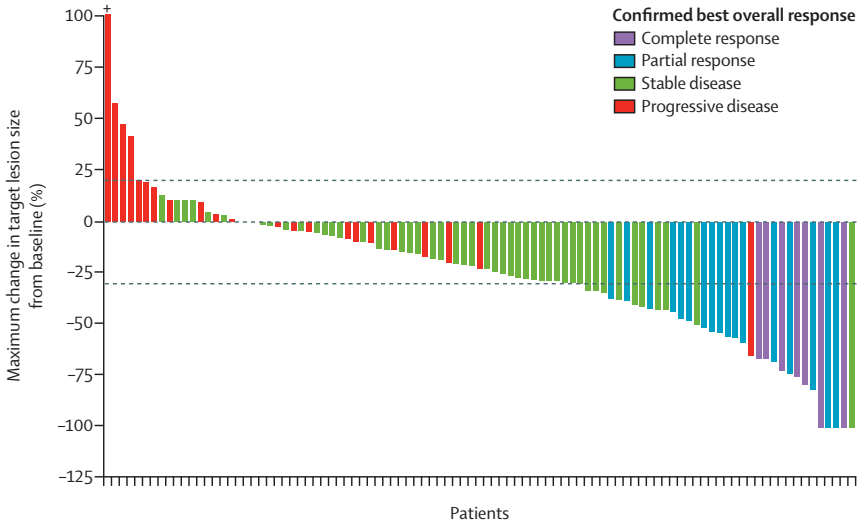




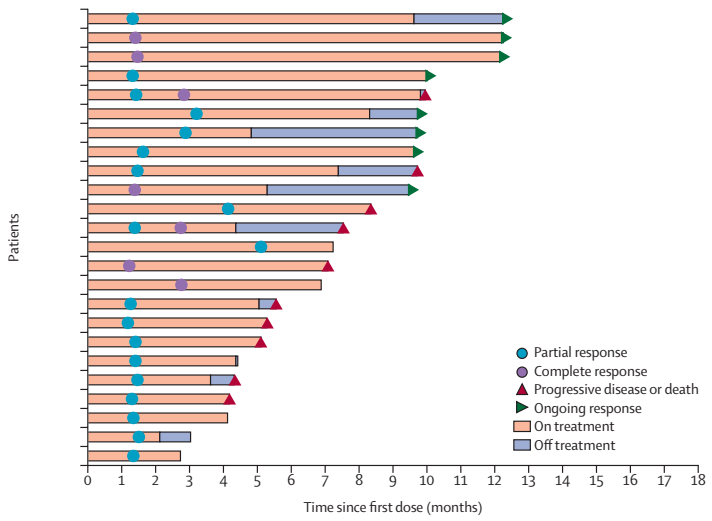
Stratification	PFS
FIGO (2014) IB2-IIB **(n= 462)**	0.91 (95% CI: 0.63, 1.31)
FIGO (2014) III-IVA **(n= 596)**	0.59 (95% CI: 0.43, 0.82)

ADC for Cervical Cancer: Tisotumab Vidotin

A



B



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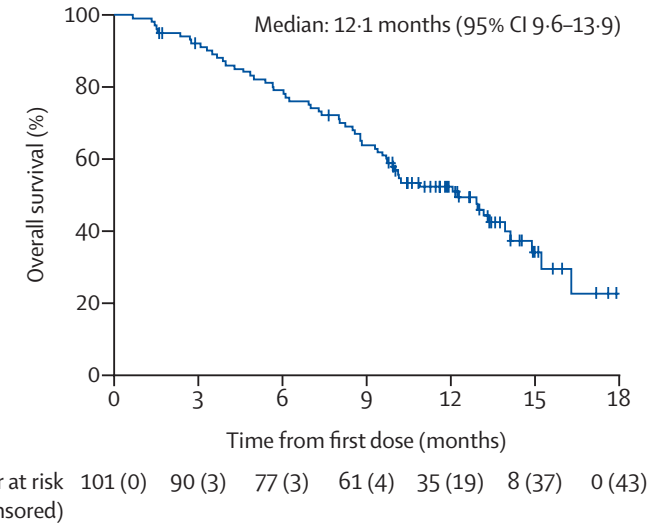


ORR: 24%

DCR: 72%
mPFS: 4.2 m

mOS: 12.1 m

R. Coleman et al. Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer. Lancet Oncol. 2021

Summary

Pembrolizumab in combination with cisplatin and radiation is FDA-approved for FIGO (2014) III-IVA Cervical cancer.

PD1-inhibitors are approved in combination with platinum-based chemotherapy, paclitaxel with or without bevacizumab in the advanced, persistent, or metastatic setting.

PD-1 inhibitor monotherapy is approved for recurrent metastatic cervical cancer with CPS > 1

Tisotumab, and antibody drug conjugate is approved in the post-chemo-immunotherapy setting.

With the incorporation of immunotherapy in the definitive setting, how will this impact downstream therapy?

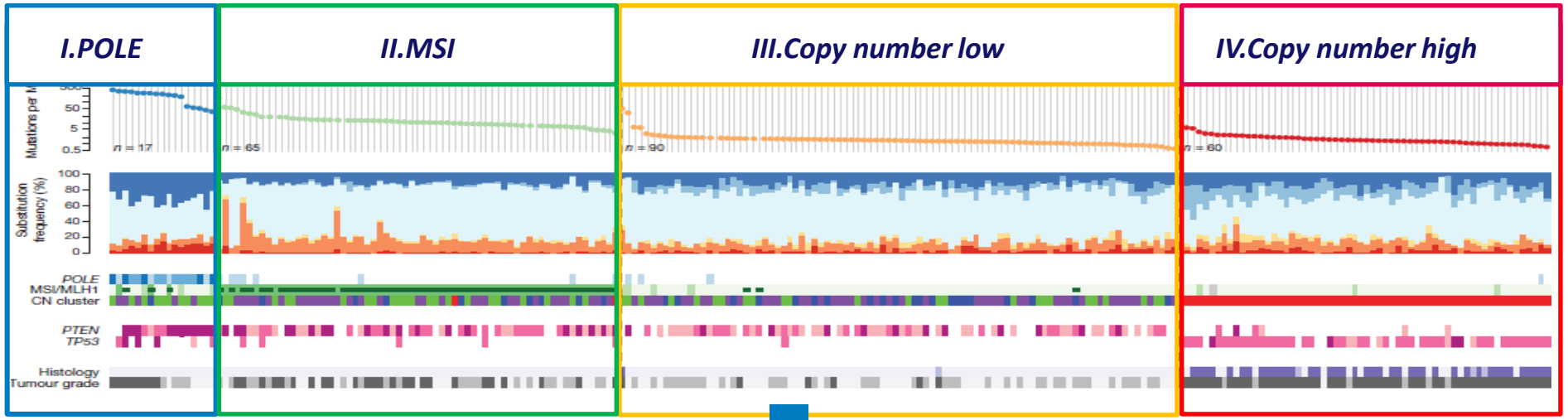
How will this affect the efficacy of Tumor Infiltrating Lymphocyte therapy?

Is there a role for bispecific T-cell engagers or chimeric antigen receptor T-cell therapy?

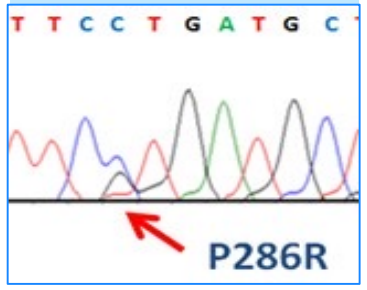
Endometrial Cancer

Endometrial Cancer Subgroups

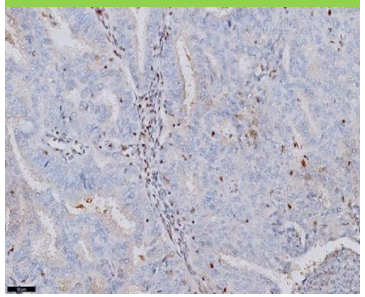
[a,b]



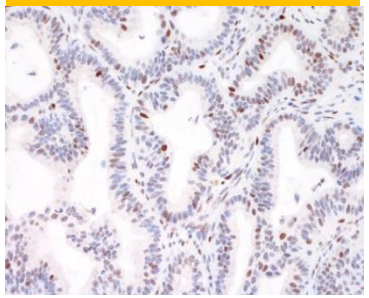
Mol Class 1
***POLE mut*[c]**



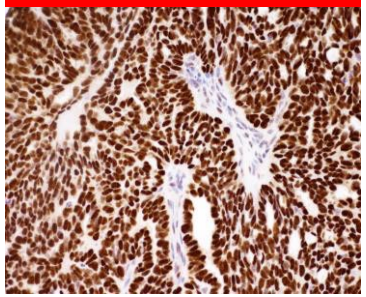
Mol Class 2
dMMR[c]



Mol Class 3
NSMP[c]



Mol Class 4
p53*abn*[c]



Images courtesy of Nicoletta Colombo, MD, PhD.

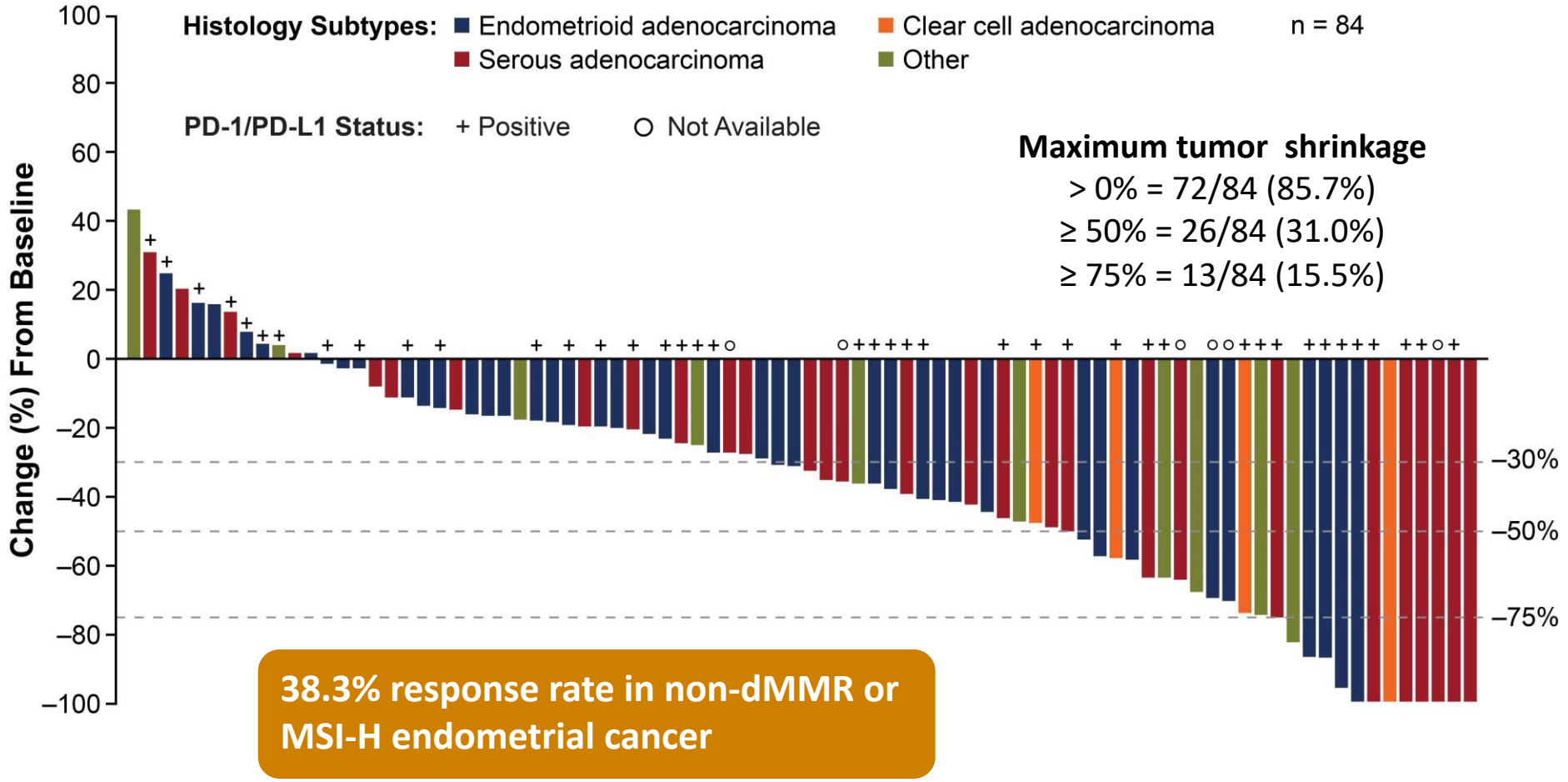
a. Cancer Genome Atlas Res Network. *Nature.* 2013;497:67-73; b. Stelloo E, et al. *Clin Cancer Res.* 2016;22:4215-4224.

Single-Agent Immunotherapy Efficacy in Biomarker-Selected Endometrial Cancer

Study	Drug	N	Patient Selection	ORR, %
KEYNOTE-158[a]	Pembrolizumab	49	Advanced/metastatic dMMR	57
GARNET[b]	Dostarlimab	126	Previously treated recurrent/advanced dMMR	45
PHAEDRA[c]	Durvalumab	35	Advanced/metastatic dMMR	43
Konstantinopoulos[d]	Avelumab	15	Advanced/metastatic dMMR	26.7

a. Marabelle A, et al. *J Clin Oncol*. 2019;38:1-10; b. Oaknin A, et al. ESMO 2020. Presentation LBA36; c. Antill Y, et al. ASCO® 2019. Presentation 5501; d. Konstantinopoulos PA, et al. ASCO® 2019. Presentation 5502.

Pembrolizumab and Lenvatinib for MSS endometrial cancer

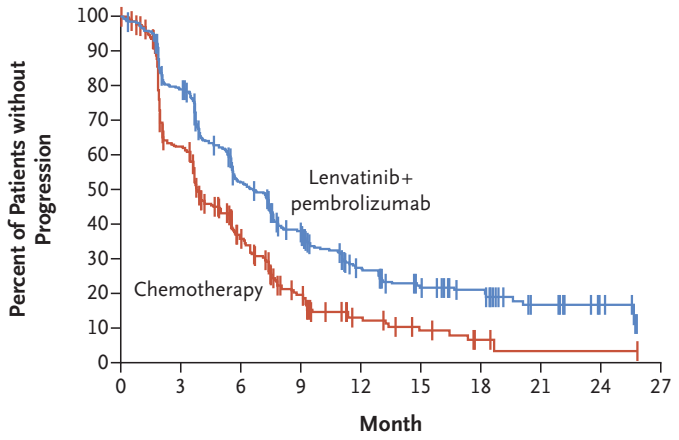


38.3% response rate in non-dMMR or MSI-H endometrial cancer

Makker V, et al. SGO 2020. Abstract 10.

Pembrolizumab and Lenvatinib for MSS endometrial cancer

A pMMR Population

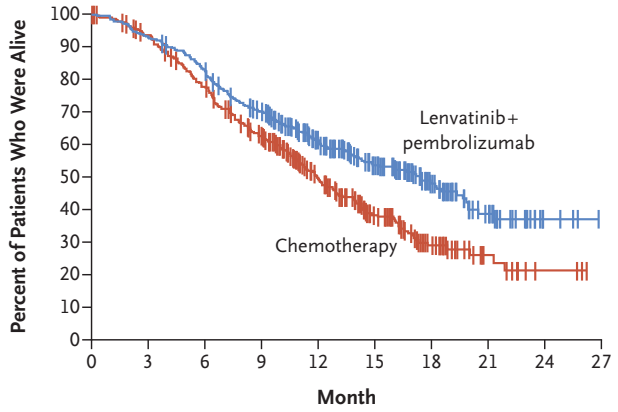


	Median Progression-free Survival (95% CI) *mo*
Lenvatinib+ Pembrolizumab	6.6 (5.6–7.4)
Chemotherapy	3.8 (3.6–5.0)

Hazard ratio for progression or death, 0.60 (95% CI, 0.50–0.72)
P<0.001

No. at Risk										
Lenvatinib+pembrolizumab	346	264	165	112	60	39	30	12	5	0
Chemotherapy	351	177	83	37	15	8	3	1	1	0

B pMMR Population



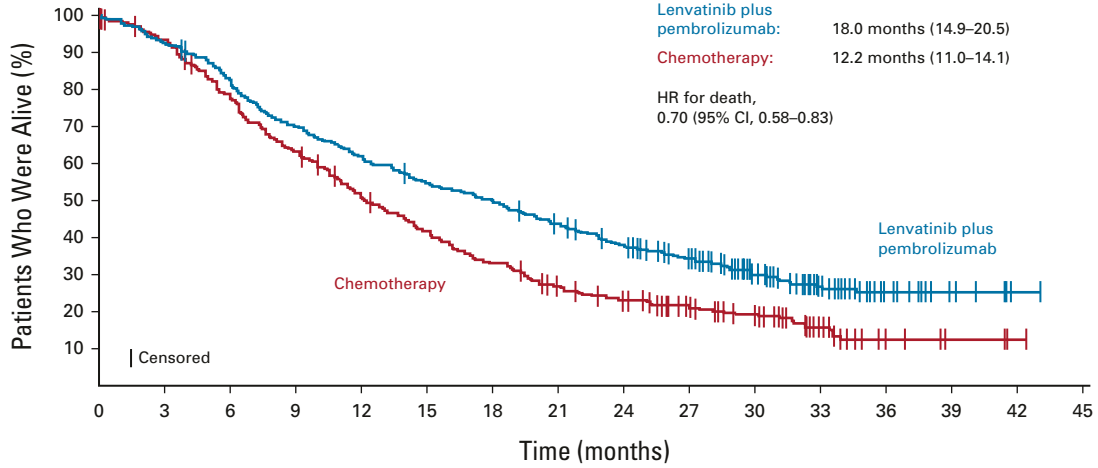
	Median Overall Survival (95% CI) *mo*
Lenvatinib+ Pembrolizumab	17.4 (14.2–19.9)
Chemotherapy	12.0 (10.8–13.3)

Hazard ratio for death, 0.68 (95% CI, 0.56–0.84)
P<0.001

No. at Risk										
Lenvatinib+pembrolizumab	346	322	285	232	160	109	62	28	5	0
Chemotherapy	351	319	262	201	120	70	33	11	3	0

V. Makker et al. Lenvatinib plus pembrolizumab for advanced endometrial cancer. NEJM. 2022

C



No. at risk:															
Lenvatinib plus pembrolizumab	346	322	285	242	214	188	171	148	124	95	65	41	20	7	2
Chemotherapy	351	324	267	217	171	138	111	86	71	53	40	21	6	3	1

V. Makker et al. Lenvatinib plus pembrolizumab in previously treated endometrial cancer. JCO. 2023

Incorporation of immunotherapy with chemotherapy in the first-line setting

RUBY Study

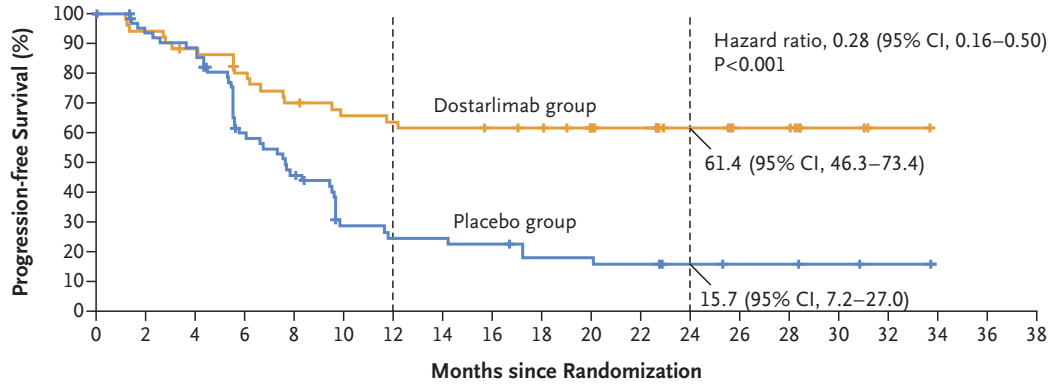
- Carboplatin + paclitaxel ± dostarlimab
- Primary endpoint: PFS
- Stratified by
  - Prior pelvic RT (Y/N)
  - Disease status (recurrent, primary III or IV)
  - MSI instability status (I,S)

NRG-GY018

- Carboplatin + paclitaxel ± pembrolizumab
- Primary endpoint: PFS
- Stratified by
  - pMMR vs dMMR
  - Performance status
  - Measurable disease

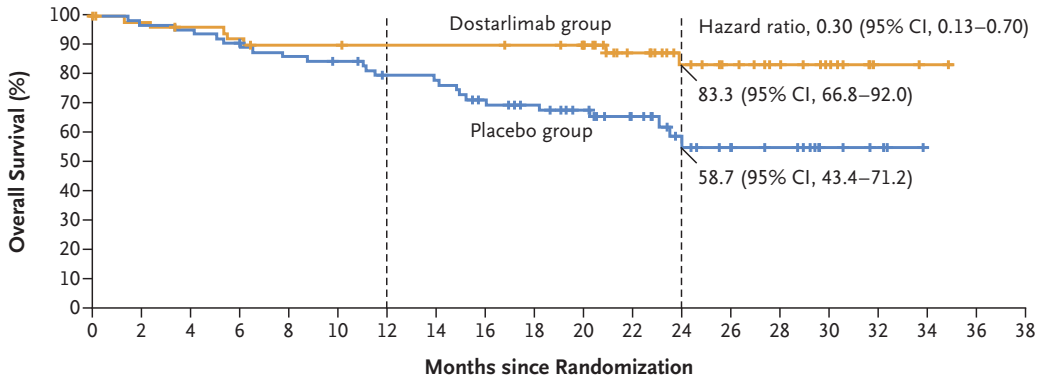
Incorporation of immunotherapy with chemotherapy in the first-line setting: RUBY

A dMMR–MSI-H Population



No. at Risk																			
Dostarlimab group	53	48	44	39	34	31	30	29	28	27	25	19	13	9	9	4	1	0	
Placebo group	65	57	54	34	26	14	12	12	11	8	8	7	4	3	3	2	1	0	
No. of Events																			
Dostarlimab group	0	3	6	10	15	17	18	19	19	19	19	19	19	19	19	19	19	19	
Placebo group	0	4	7	24	32	41	43	43	44	46	46	47	47	47	47	47	47	47	

B dMMR–MSI-H Population

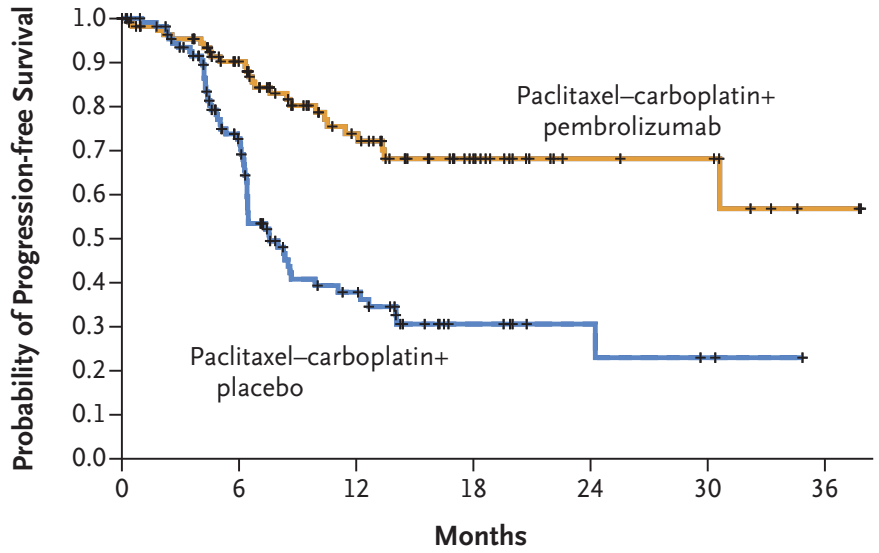


No. at Risk																			
Dostarlimab group	53	50	48	46	44	44	43	43	43	42	41	29	20	16	12	8	2	1	0
Placebo group	65	63	62	59	55	53	48	47	41	37	32	25	16	12	10	5	3	0	
No. of Events																			
Dostarlimab group	0	1	2	4	5	5	5	5	5	5	5	6	7	7	7	7	7	7	7
Placebo group	0	2	3	6	9	10	13	14	18	19	20	21	23	24	24	24	24	24	

MR. Mirza et al. Dostarlimab for primary advanced or recurrent endometrial cancer. NEJM. 2023

Incorporation of immunotherapy with chemotherapy in the first-line setting: NRG-GY018

A dMMR Cohort



No. at Risk							
Paclitaxel–carboplatin+ pembrolizumab	112	80	44	22	9	8	2
Paclitaxel–carboplatin+ placebo	113	62	24	8	4	2	0

	No. of Events	No. of Patients	Median Progression-free Survival (95% CI)
			mo
Paclitaxel–Carboplatin+ Pembrolizumab	26	112	NR (30.6–NR)
Paclitaxel–Carboplatin+ Placebo	59	113	7.6 (6.4–9.9)

Hazard ratio for disease progression or death, 0.30 (95% CI, 0.19–0.48)

R. Eskander et al. Pembrolizumab plus chemotherapy in advanced endometrial cancer. NEJM. 2023

Summary

Pembrolizumab or Dorstalimab in combination with carboplatin and paclitaxel is FDA approved for treatment of dMMR endometrial cancer in the first-line metastatic setting.

Pembrolizumab or Dorstalimab is approved for dMMR endometrial carcinoma in the recurrent setting.
Pembrolizumab and lenvatinib is approved for pMMR endometrial carcinoma in the recurrent setting.

With the incorporation of immunotherapy in the first-line setting with chemotherapy, what happens with dMMR in the recurrent setting?

There is an emerging role for Antibody Drug Conjugates in the post-immunotherapy setting.

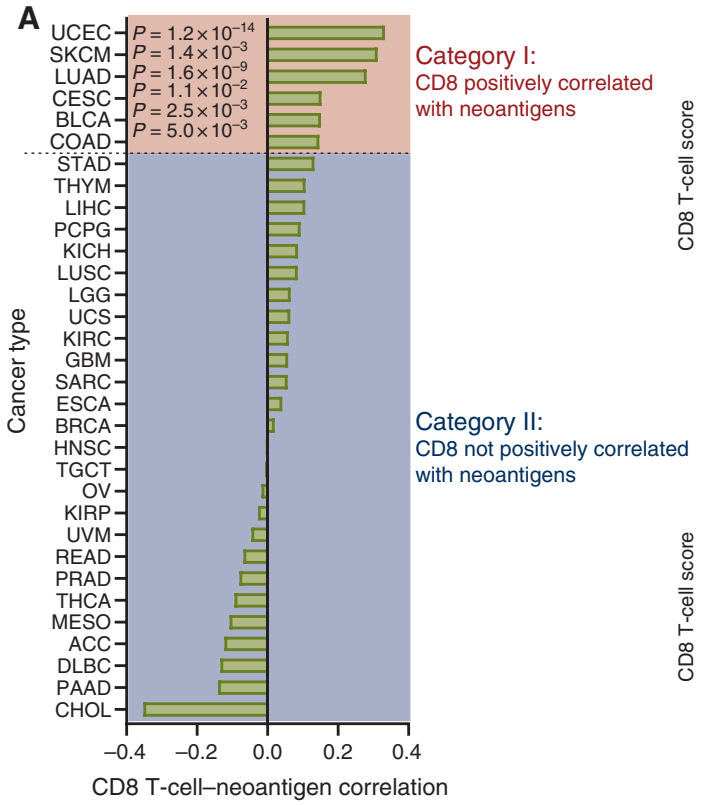
Will immunotherapy be included with adjuvant radiation? How will this affect downstream therapy.

Will there be a role for other types of immunotherapy such as bispecific T-cell engagers?

Ovarian Cancer

Immune checkpoint inhibitors for ovarian cancer

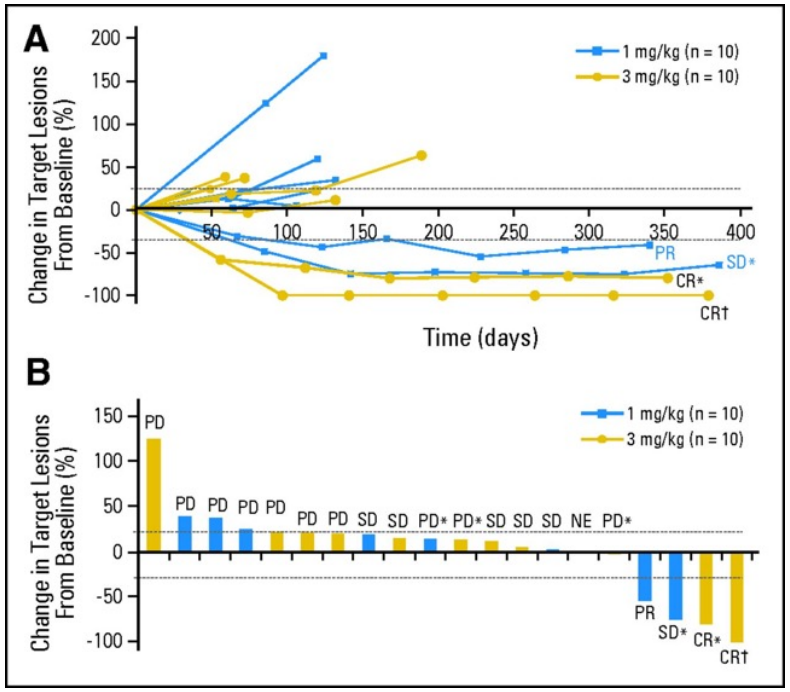
- Approved indication for immune checkpoint inhibitor in Ovarian cancer is for TMB high (≥10 mutations/megabase) solid tumors who have progressed following prior treatment and have no satisfactory alternative treatment options
- Incidence of TMB^{high} OC is still low
- Other studies suggest that TMB^{high} in tumors with low neoantigen load (category II), such as OC, are unlikely to respond[a]



a. McGrail, et al. JCO Precis Oncol. 2020;4.

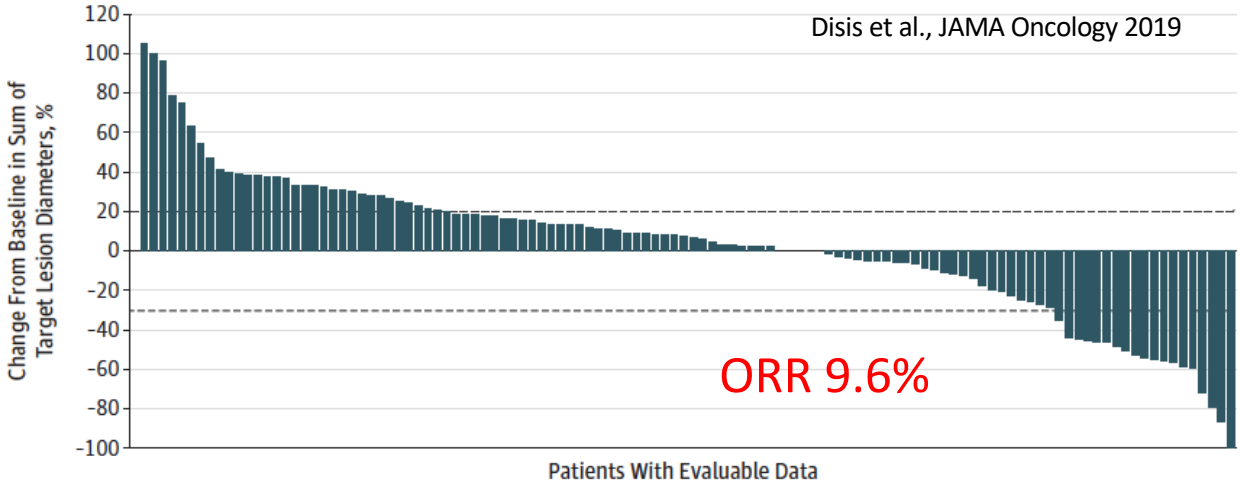
Immune checkpoint inhibitors for ovarian cancer

A



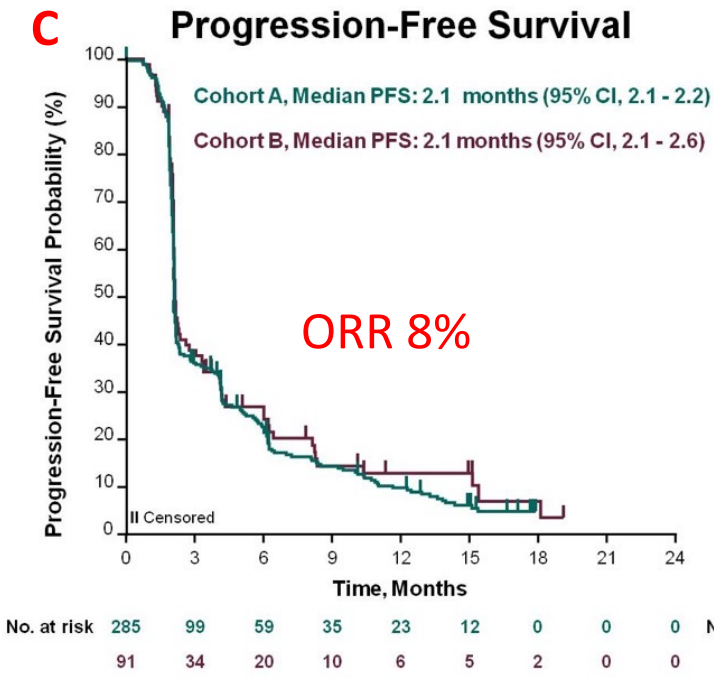
Hamanishi et al., JCO 2015

B



Disis et al., JAMA Oncology 2019

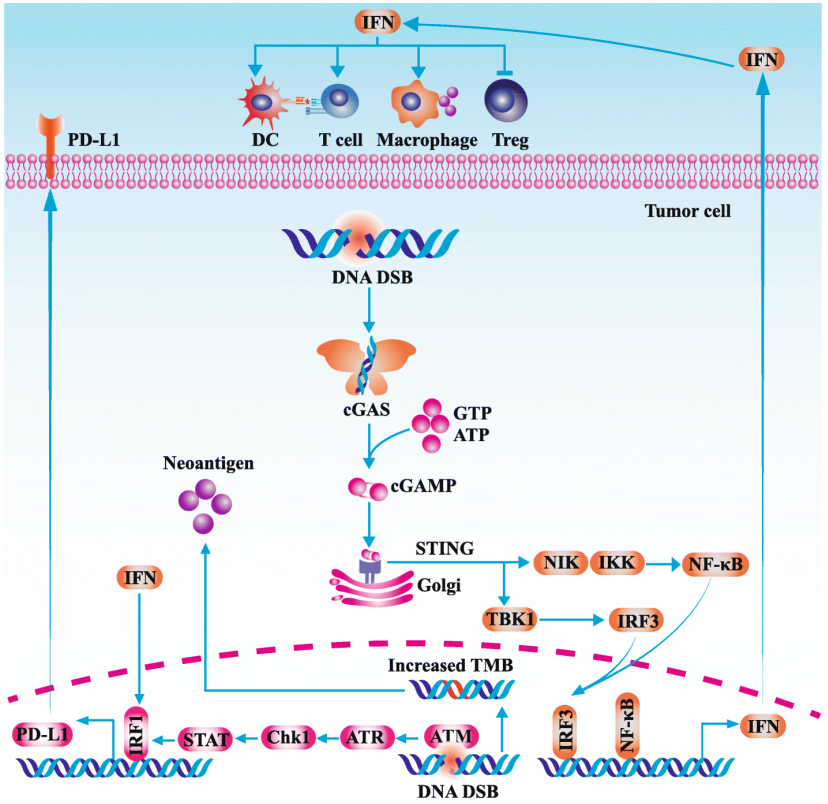
C



Matulonis et al., 2018

Rationale for immunotherapy combinations in OC

- PARPi-mediated double-strand DNA breaks upregulate PD-L1 expression
- Generated neoantigens increase immunogenicity and TMB
- Potential to increase sensitivity to ICI therapy



PARP inhibitor combinations

	Durvalumab in recurrent ovarian cancer[a]	MEDIOLA[b]	TOPACIO/KEYNOTE-162[c]
Regimen	Olaparib (300 mg BID) + Durvalumab (PD-L1) (1500 mg Q4wks)	Olaparib (300 mg BID) + Durvalumab (1500 mg Q4wks) +/- Bevacizumab (10 mg/Kg Q2weeks)	Niraparib (200 mg QD) + Pembrolizumab (200 mg Q3wks)
Patient population	Phase II Platinum Res, Platinum Sens	Phase II Platinum sensitive (non-gBRCAm)	Phase I/II Platinum Res
N	35	O+D (32) ; O+D+B (31)	62
ORR, %	14	31.3% ; 77.4%	18
Disease Control Rate (PR, SD) or (CR, PR, SD, %	71	-	65
Median PFS, mos	-	5.5 ; 14.7	3.4
6-month PFS, %	-		31
12-month OS, %			12

a. Lampert et al, CCR 2020. b. Drew et al, b. Konstantinopoulos et al, Anals Onc, 2020. c. JAMA Oncl, 2019

Immune checkpoint inhibitors in combination with chemotherapy and biologic (VEGF) therapy

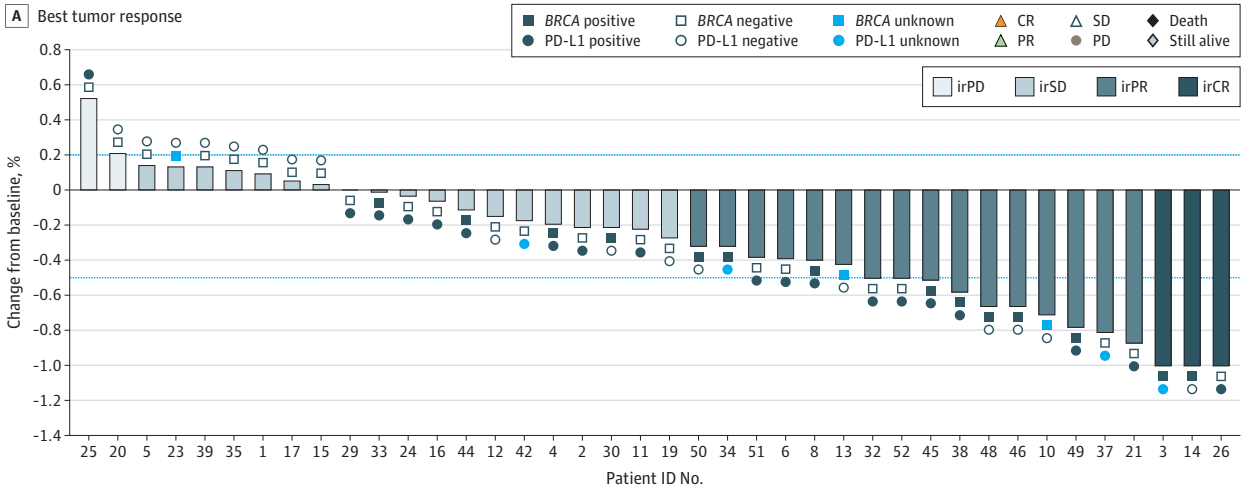
Trial	Phase	ICI	Combination with	Disease Setting	Primary Endpoint	Results
Lee et al[a]	2	Pembrolizumab	PLD	Platinum-resistant	CBR	CBR: 52.2% ORR: 26.1%
Walsh et al[b]	2	Pembrolizumab	Cisplatin, gemcitabine	Platinum-resistant	ORR	ORR: 57% CBR: 86% mDOR: 3.5 months mPFS: 5.35 months
Liu et al[c]	2	Nivolumab	Bevacizumab	Platinum-sensitive Platinum- resistant	ORR	ORR: 28.9% (O) ORR: 40% (S) ORR: 16.7% (R) mPFS: 9.7 months (O) mPFS: 12.1 month (S) mPFS: 7.7 months (R)
Zsiros et al[d]	2	Pembrolizumab	Oral cyclophosphamide Bevacizumab	Platinum-resistant Platinum-sensitive	ORR PFS	ORR: 47.5% PFS: 10 months CBR: 95%

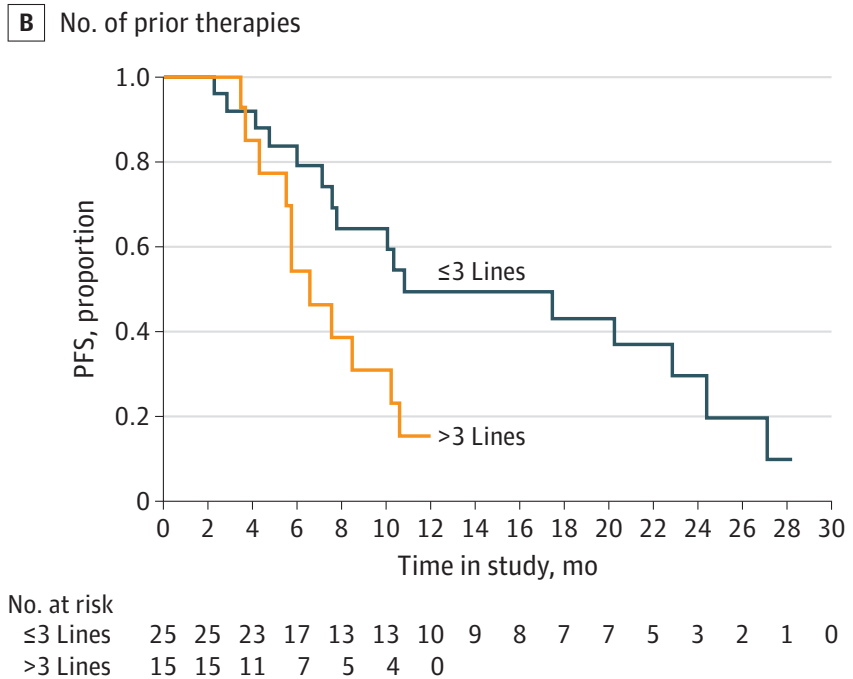
a. Lee et al. Gynecol Oncol 2020. b. Walsh et al. SGO. Abs 2019. c. Liu et al. Jama Oncl 2019. d. Zsiros et al. JAMA Oncol 2021

Cyclophosphamide, bevacizumab, pembrolizumab

Table. Best Responses to Efficacy Measures

Best response	Patient group[a] Platinum-sensitive disease (n = 10)	Platinum-resistant disease (n = 30)	All (n = 40)
Unevaluable	0	0	0
Complete response	0	3 (10.0)	3 (7.5)
Partial response	6 (60.0)	10 (33.3)	16 (40.0)
Stable disease only, wk			
≥24	3 (30.0)	8 (26.7)	11 (27.5)
<24	1 (10.0)	7 (23.3)	8 (20.0)
Progressive disease	0	2 (6.7)	2 (5.0)
Objective response rate (complete plus partial responses)	6 (60.0)	13 (43.3)	19 (47.5)
Total clinical benefit rate (complete plus partial responses plus stable disease)	10 (100)	28 (93.3)	38 (95.0)
DOR, median (IQR) [range], mo[b]	11.5 (4.1-16.3) [1.6-21.3]	5.5 (2.4-8.7) [0-26.4]	5.8 (3.1-10.7) [0-26.4]





Zsiros et al. JAMA Oncol 2021

Cyclophosphamide, bevacizumab, pembrolizumab

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

NCCN Guidelines Index
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Discussion

PRINCIPLES OF SYSTEMIC THERAPY
Acceptable Recurrence Therapies for Epithelial Ovarian (including LCOC)[p]/Fallopian Tube/Primary Peritoneal Cancer[q]

Recurrence Therapy for Platinum-Resistant Disease (alphabetical order)

Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Cytotoxic Therapy Cyclophosphamide (oral)/ bevacizumab[k,39] Docetaxel[40] Etoposide (oral)[41] Gemcitabine[42,43] Liposomal doxorubicin[42,43] Liposomal doxorubicin/ bevacizumab[k,s,44] Paclitaxel (weekly)[g,45] Paclitaxel (weekly)/ bevacizumab[g,k,s,44] Topotecan[46,47] Topotecan/bevacizumab[k,s,44] Targeted Therapy (single agents) Bevacizumab[k,s,21,22] Mirvetuximab soravtansine-gynx (for FRα-expressing tumors)[z,48]	Cytotoxic Therapy[u] Capecitabine Carboplatin[*] Carboplatin/docetaxel[*] Carboplatin/paclitaxel (weekly)[g,*] Carboplatin/gemcitabine[14] ± bevacizumab[k,s,t,15,*] Carboplatin/liposomal doxorubicin[16] ± bevacizumab[k,s,17,*] Carboplatin/paclitaxel[g,18] ± bevacizumab[k,s,t,19,*] Cyclophosphamide Cyclophosphamide (oral)/pembrolizumab/bevacizumab[k,50,51] Doxorubicin Gemcitabine/bevacizumab[k,52] Gemcitabine/cisplatin[20,*] Ifosfamide Irinotecan Ixabepilone/bevacizumab (category 2B)[k,aa,53] Melphalan Oxaliplatin Paclitaxel Paclitaxel, albumin bound Pemetrexed Sorafenib/topotecan[49] Vinorelbine Targeted Therapy (single agents) Niraparib (category 3)[v,27] Olaparib (category 3)[w,28] Pazopanib (category 2B)[29] Rucaparib (category 3)[x,30]	Carboplatin/paclitaxel (for age >70)[g,y,*] Carboplatin/paclitaxel, albumin bound (for confirmed taxane hypersensitivity)[*] Immunotherapy Dostarlimab-gxly (for dMMR/MSI-H recurrent or advanced tumors)[z,37] Pembrolizumab (for patients with MSI-H or dMMR solid tumors, or TMB-H tumors ≥10 mutations/ megabase)[z,38] Hormone Therapy Fulvestrant (for low-grade serous carcinoma) Targeted Therapy Dabrafenib + trametinib (for *BRAF* V600E-positive tumors)[z,32] Entrectinib or larotrectinib (for *NTRK* gene fusion-positive tumors)[z] Fam-trastuzumab deruxtecan-nxki (for HER2-positive tumors [IHC 3+ or 2+])[54] Mirvetuximab soravtansine-gynx/bevacizumab (for FRα-expressing tumors)[k,z,55,56] Selpercatinib (for *RET* gene fusion-positive tumors)[z,33] For low-grade serous carcinoma: • Trametinib[34] • Binimetinib (category 2B)[35,36]

Other interesting combinations with chemotherapy and a cautionary tale

Trial	Phase	ICI	Combination with	Disease Setting	Primary Endpoint	Results
Pujade-Lauraine et al[a]	3	Avelumab	Monotherapy (M) PLD Combo (C) PLD alone (P)	Platinum-resistant Platinum-refractory	ORR	ORR: 3.7% (M) ORR: 13.3% (C) ORR: 4.2% (P)
Zamarin et al[b]	2	Nivolumab	Monotherapy (M) Ipilimumab Combo (C)	Platinum-sensitive Platinum-resistant	ORR	ORR: 12.2% (M) ORR: 31.4% (C) mPFS: 2 months (M) mPFS: 3.9 months (C)
Omatsu et al[c]	**3**	**Nivolumab**	**PLD Gemcitabine**	**Platinum-resistant**	**OS**	**PFS: 2.04 (N) vs 3.84**

a. Pujade-Lauraine et al. Gynecol Oncol. Abs LBA1 2019. b. Zamarin et al. J Clin Oncol 2020. c. Omatsu et al. Annals Oncol. Abs. Vol 31, supp4, S611 2020.

Is there a role for immunotherapy in the upfront setting?

Trial	Phase	ICI	Combination with	Disease Setting	Primary Endpoint	Status
IMAGYN050/GOG 3015/ENGOT-ov39[a]	3	Atezolizumab	Bevacizumab, carboplatin, paclitaxel	Newly-diagnosed stage 3-4 OC/TC/ PPC	PFS, OS	Active, not recruiting
JAVELIN OVARIAN PARP-100[c]	3	Avelumab	Carboplatin Paclitaxel	Newly-diagnosed stage 3-4 OC	PFS	Active, not recruiting

IMagyn050: Addition of Atezolizumab to Bevacizumab, Paclitaxel, and Carboplatin

Trial Design:

- Pts with stage III or IV OC with either primary cytoreductive surgery and gross residual disease or patients who underwent neoadjuvant chemo
- 1:1 randomization: atezolizumab 1200 mg or placebo for cycles 1-22 in combination with carboplatin, paclitaxel and bevacizumab
- Stratification by: PD-L1 staining (< 1% or ≥ 1%), stage III vs IV, treatment strategy (PCS vs NCT) or PS (ECOG 0 vs 1-2)
- Endpoints: Co-primary PFS and OS in the intent-to-treat population (ITT) and PD-L1+ population

IMagyn050	Carboplatin, paclitaxel, bevacizumab, atezolizumab	Carboplatin, paclitaxel, bevacizumab, placebo	HR (95% CI)
Median PFS, mos	19.5	18.4	HR 0.92, 95% CI 0.79-1.07
Median PFS in PD-L1-positive, mos	20.8	18.5	HR 0.80, 95% CI 0.65-0.99
Discontinuation, %	26	22	

JAVELIN ovarian PARP 100: Avelumab + Chemotherapy Followed by Avelumab Maintenance

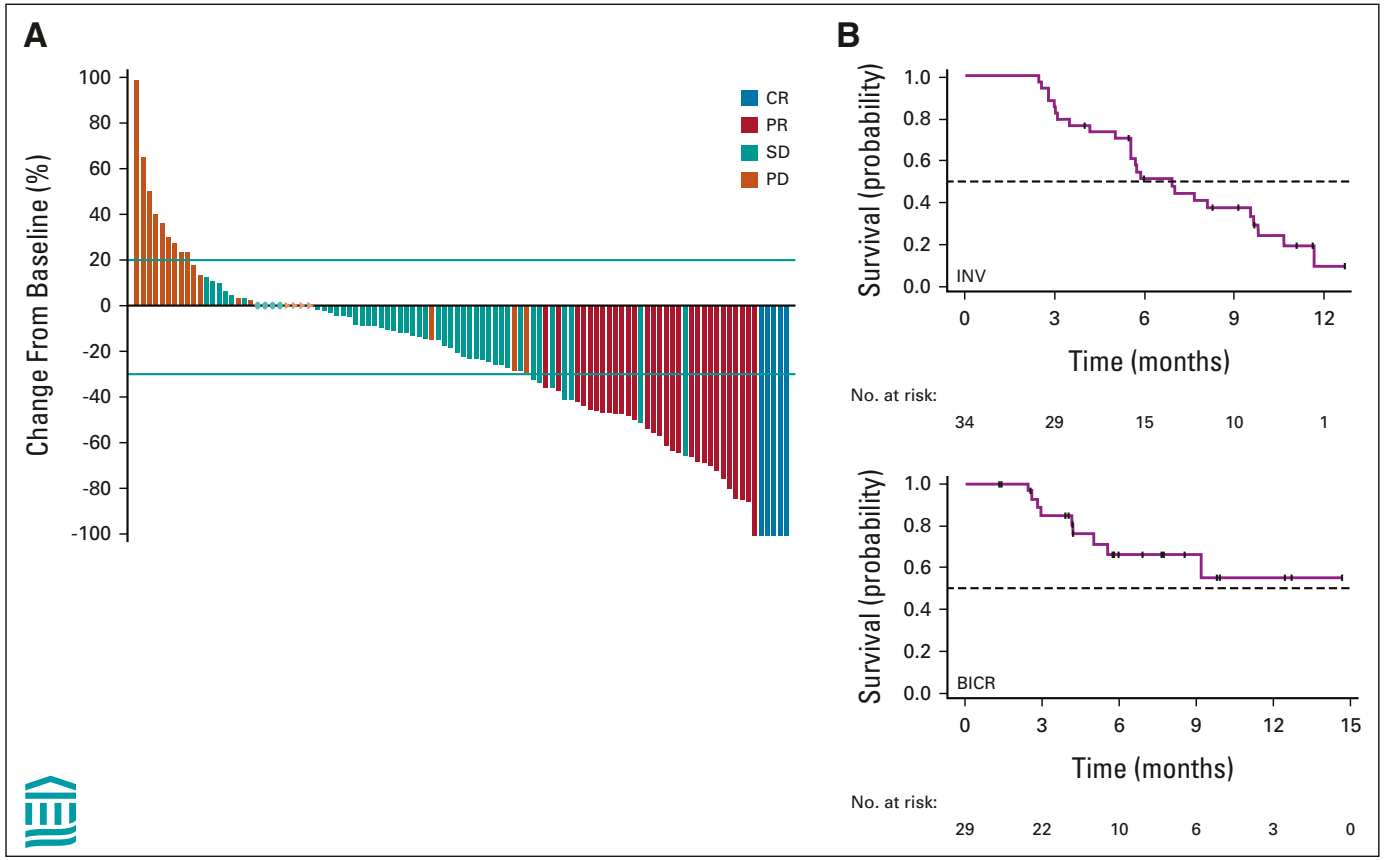
Trial Design:

- Patients with stage III or IV OC with either primary cytoreductive surgery or patients who underwent neoadjuvant chemotherapy
- 1:1:1 randomization: receive carboplatin, paclitaxel, followed by avelumab maintenance, chemotherapy with avelumab with avelumab maintenance or chemotherapy followed by observation
- Endpoints: PFS

Javelin 100 (998 patients randomized)	Carboplatin, paclitaxel, avelumab and avelumab maintenance	Carboplatin, paclitaxel, followed by avelumab maintenance	Carboplatin + paclitaxel
Patient population	Advanced disease, PD-L1 positive	Advanced disease, PST	
Median PFS, mos	18.1	16.8	NE
ORR	36.0	30.4	30.0

Antibody Drug Conjugates: Mirvatuximab Soravtansine

- Platinum Resistant Ovarian Cancer
- 1-3 lines of prior therapy
- Prior bevacizumab, PARP allowed
- High FRα expression ≥ 75% (≥ 2+ IHC)
- 6 mg/kg every 3 weeks



Endpoint	Total N = 106
ORR (95% CI)	32.4% (23.6, 42.2)
ORR (1-2 prior lines)	35%
ORR (3 prior lines)	30%
Median DOR (months) 95% CI	5.9 (5.6, 7.7)

Matulonis UA et al. Efficacy and Safety of Mirvetuximab Soravtansine in Patients With Platinum-Resistant Ovarian Cancer With High Folate Receptor Alpha Expression: Results From the SORAYA Study. J Clin Oncol. 2023 May 1;41(13):2436-2445.

Antibody Drug Conjugates Mirvatuximab Soravtansine

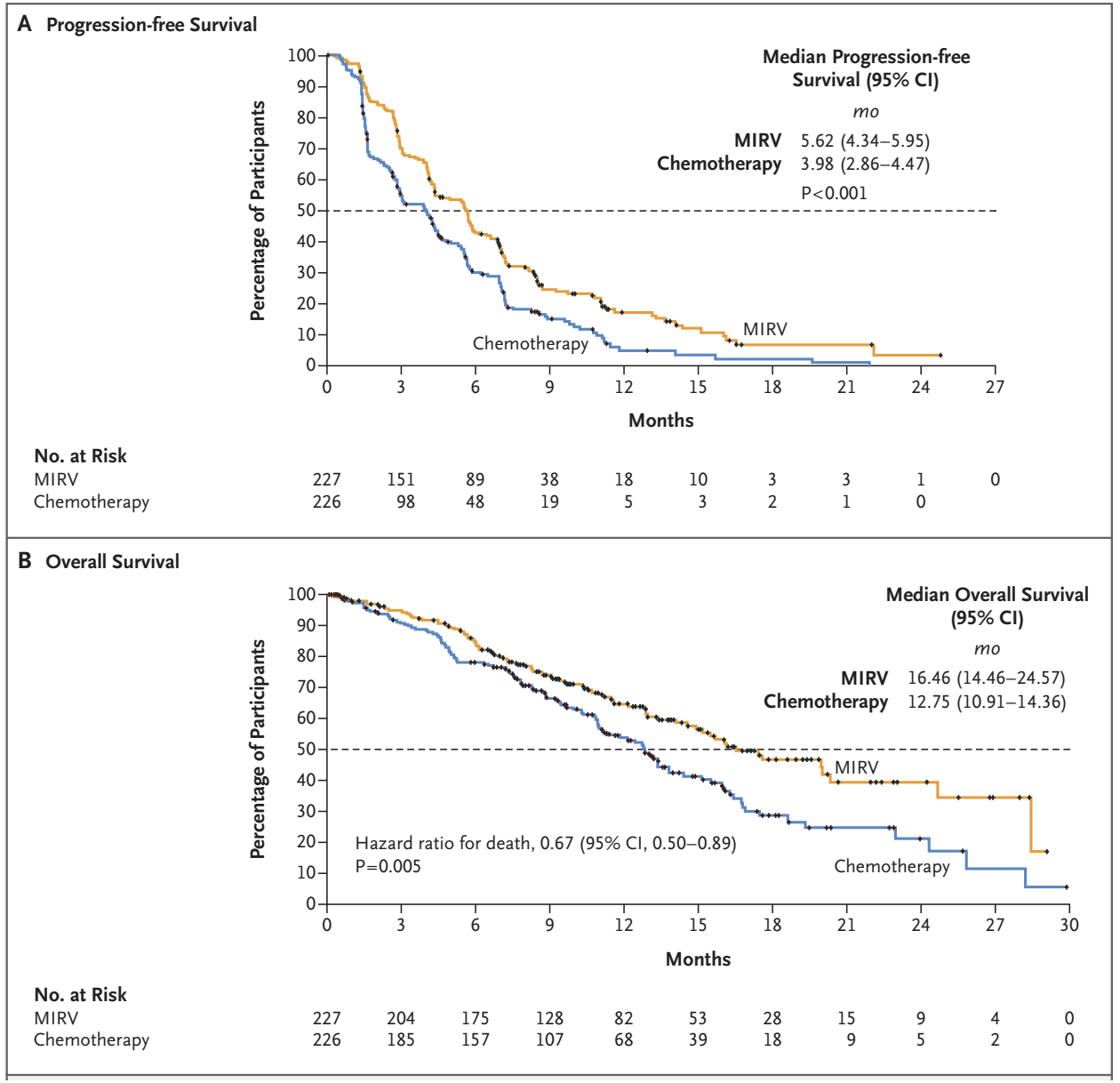
Enrollment and Key Eligibility
Platinum Resistant disease
Prior Bevacizumab and PARP allowed
1-3 Prior lines
BRCA mutations allowed
High FRα expression ≥ 75% (≥ 2+ IHC)

1:1

ARM 1
Mirvetuximab soravtansine
6 mg/kg every 3 weeks

ARM 2
Investigators choice chemotherapy
Paclitaxel Liposomal Doxorubicin Topotecan

Endpoints
Primary: Progression Free Survival
Secondary:
ORR
Patient Reported Outcomes



Moore KN et al. Mirvetuximab Soravtansine in FRα-Positive, Platinum-Resistant Ovarian Cancer. N Engl J Med. 2023 Dec 7;389(23):2162-2174.

A word on other forms of immunotherapy

Bispecific T-cell engagers

Chimeric Antigen Receptor (CAR) T-cells

Vaccines?

Summary

Immune checkpoint inhibitors, especially as monotherapy, have no role in the management of platinum resistant ovarian cancer

With checkpoint immunotherapy, the earlier the exposure during a patient's treatment, the better

Other checkpoints, like CD47, have not proven to be better than PD-L1 and CTLA4

Second generation (Fc-modified) immune checkpoint inhibitors might have improved responses in ovarian cancer

Antibody Drug Conjugates have an established role in the management of platinum resistant ovarian cancer

Sequencing and movement upstream toward the adjuvant setting are in progress

What about the others? Platinum refractory disease, clear cell, carcinosarcoma, mucinous carcinoma


Mass General Brigham