Therapeutic Advances in Gynecologic Oncology

- **Rebecca A. Brooks, MD**
- **UC Davis Comprehensive Cancer Center**
- **November 16, 2024**

Themes by Disease Site

- Cervix
  - IO with upfront treatment – Keynote 826, BEATcc, A 18
  - Induction chemo prior to RT - INTERLACE
- Endometrial
  - Upfront IO – RUBY, NRG GY018, Keynote B21
  - PARP + IO maintenance –DUO- E & RUBY 2
  - Selenexor
- Ovary
  - Mirvetuximab
- Gyn cancers
  - HER2 – Destiny

Keynote 826: IO with Chemo Becomes Standard of Care for PDL1+ Metastatic Cervical Cancer

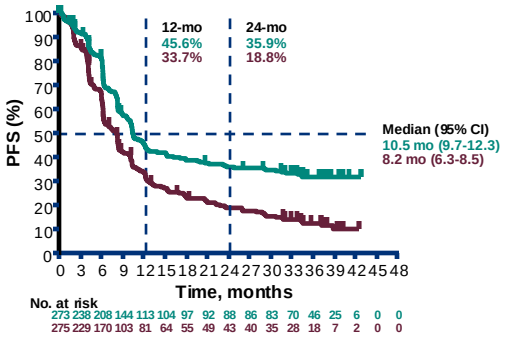
Key Eligibility Criteria:

- Persistent, recurrent, or metastatic cervical cancer not amenable to curative treatment
- No prior systemic chemotherapy (prior radiotherapy and chemoradiotherapy permitted)
- ECOG PS 0 or 1

R 1:1

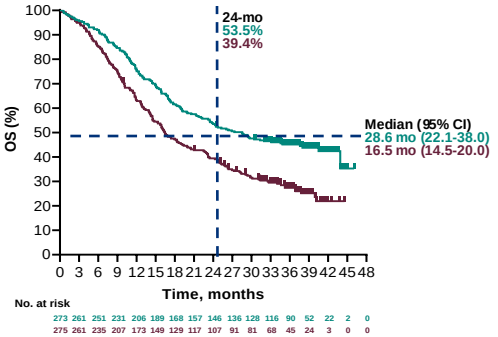
- Pembrolizumab 200 mg IV Q3W for up to 35 cycles + Paclitaxel + Cisplatin or Carboplatin IV Q3W for up to 6 cycles[a] ± Bevacizumab 15 mg/kg IV Q3W
- Placebo IV Q3W for up to 35 cycles + Paclitaxel + Cisplatin or Carboplatin IV Q3W for up to 6 cycles[a]± Bevacizumab 15 mg/kg IV Q3W

PFS: PD-L1 CPS ≥1 Population



	Pembro arm	Placebo arm
n/N	171/273	220/275
Events	62.6%	80.0%
HR (95% CI)	0.58 (0.47-0.71)	

OS: PD-L1 CPS ≥1 Population



	Pembro arm	Placebo arm
n/N	153/273	201/275
Events	56.0%	73.1%
HR (95% CI)	0.60 (0.49-0.74)	

Primary Endpoints: PFS (per RECIST v1.1 by investigator), OS
Secondary Endpoints: ORR, DOR, 12-mo PFS, safety

Columbo et al, N Engl J Med 2021

OS by Bevacizumab use - Keynote 826

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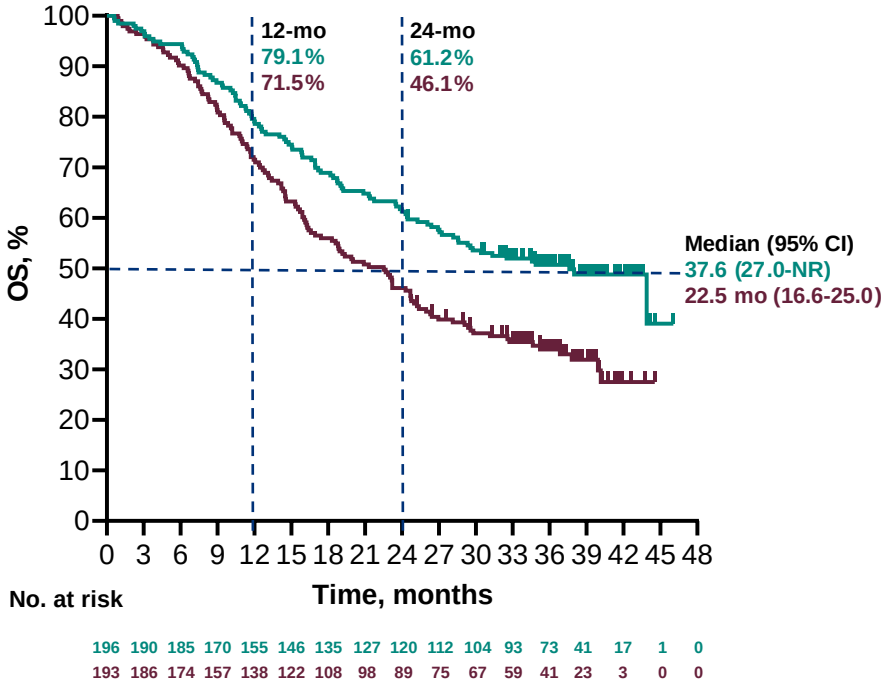
With Bevacizumab (N=389)

	n/N	Events	HR (95% CI)
Pembro arm	99/196	50.5%	0.61 (0.47-0.80)
Placebo arm	130/193	67.4%	

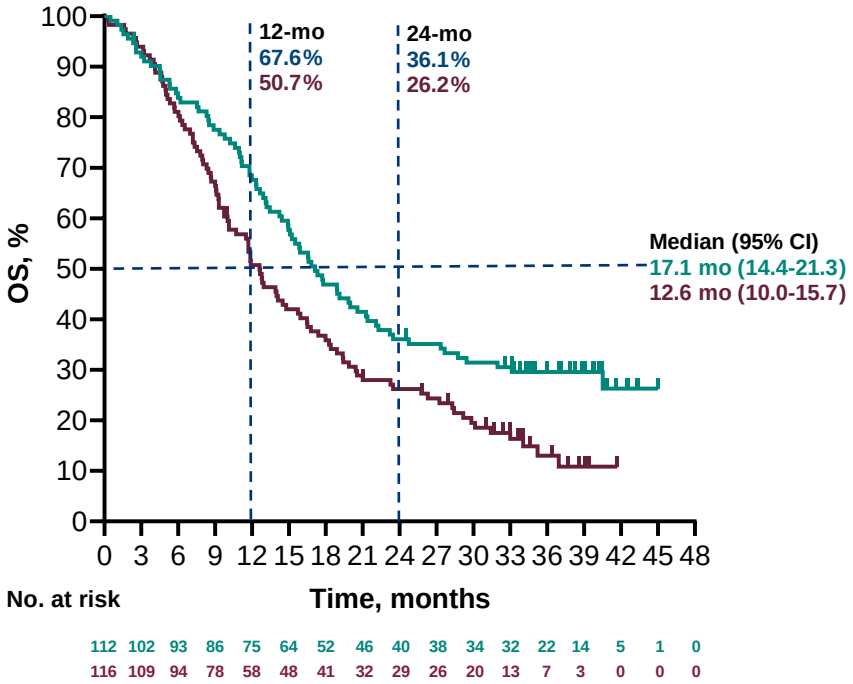


No. at risk

196	190	185	170	155	146	135	127	120	112	104	93	73	41	17	1	0
193	186	174	157	138	122	108	98	89	75	67	59	41	23	3	0	0

Without Bevacizumab (N=228)

	n/N	Events	HR (95% CI)
Pembro arm	79/112	70.5%	0.67 (0.49-0.91)
Placebo arm	98/116	84.5%	



No. at risk

112	102	93	86	75	64	52	46	40	38	34	32	22	14	5	1	0
116	109	94	78	58	48	41	32	29	26	20	13	7	3	0	0	0

Adapted from Duska Winter SGO 2024, Lorusso Annals Oncol In Press

BEATcc (ENGOT-Cx10-GEICO 68C/JGOG1084/GOG-3030)

Metastatic, persistent or recurrent cervical cancer not amenable to curative therapy

GOG/ECOG PS

No prior systemic anti-cancer therapy for R/M CC

In patients with pelvic disease, no bladder or rectal mucosa involvement

Available archival or fresh tumor sample for PD-L1 expression

R 1:1

N=410

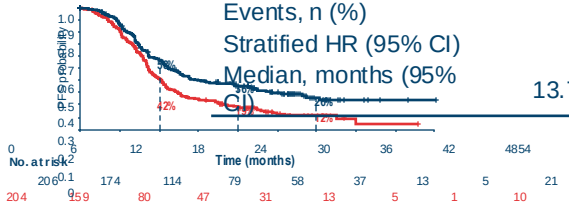
Atezolizumab 1200 mg + Bevacizumab 15 mg/kg + Paclitaxel+ cis/carboplatin[a] all IV Q3W

Continued until disease progression/unacceptable toxicity

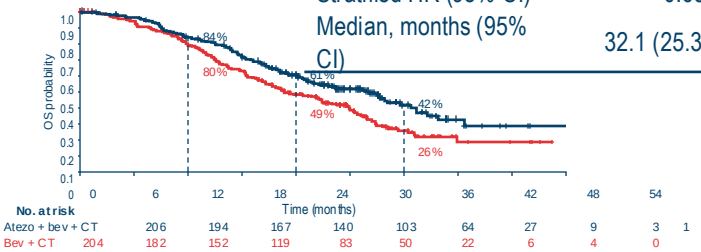
Bevacizumab 15 mg/kg + Paclitaxel + cis/carboplatin[a] all IV Q3W

Stratified by:

- Prior concurrent chemoradiation (Y/N)
- Histology (squamous cell carcinoma vs adenocarcinoma including adenosquamous carcinoma)
- Chemotherapy backbone



PFS	Atezo + bev + CT	Bev + CT
Events, n (%)	138 (67)	166 (81)
Stratified HR (95% CI)	0.62 (0.49–0.78); p<0.0001	
Median, months (95% CI)	13.7 (12.3–16.6)	10.4 (9.7–11.7)

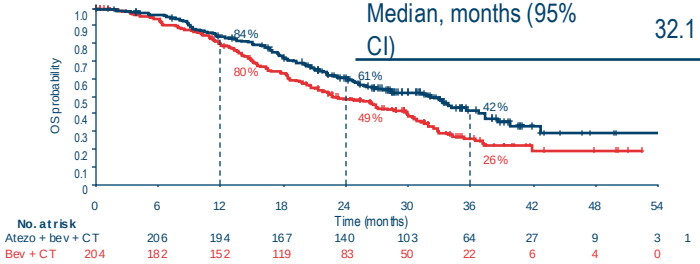


OS	Atezo + bev + CT	Bev + CT
Events, n (%)	105 (51)	129 (63)
Stratified HR (95% CI)	0.68 (0.52–0.88); p=0.0046[a]	
Median, months (95% CI)	32.1 (25.3–36.8)	22.8 (20.3–28.0)

Adapted Oaknin, virtual ESMO 2023

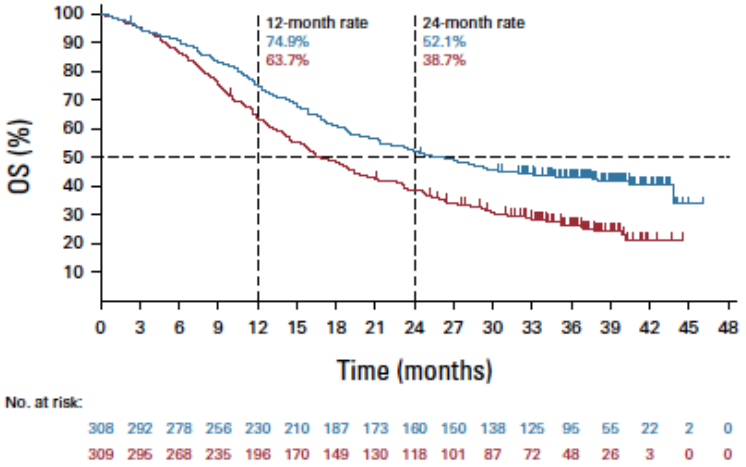
BEATcc compared to Keynote 826 - OS

OS	Atezo + bev + CT	Bev
Events, n (%)	105 (51)	129
Stratified HR (95% CI)	0.68 (0.52–0.88); p=0.004	
Median, months (95% CI)	32.1 (25.3–36.8)	22.8 (20



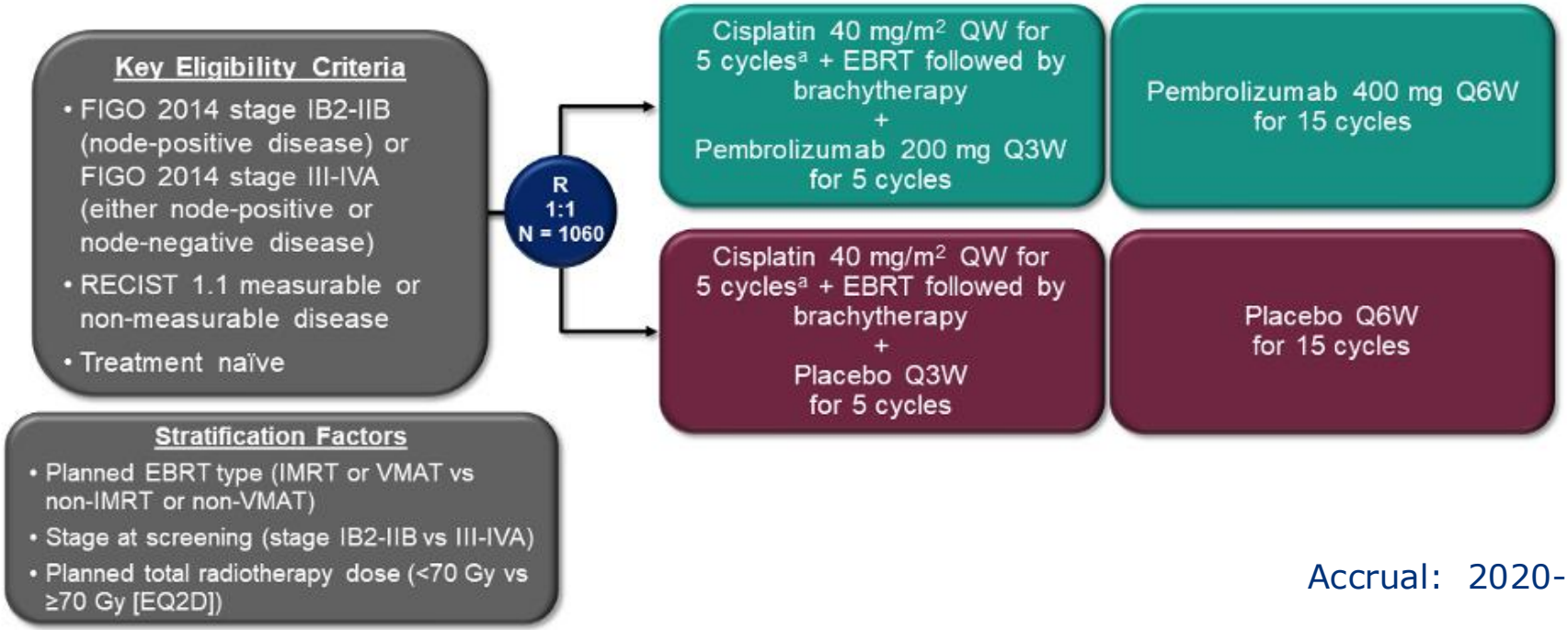
OS: All-Comer Population

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)	



J Clin Oncol 41:5505-5511

Upfront IO with chemoRT: ENGOT-cx11/GOG-3047/KEYNOTE-A18



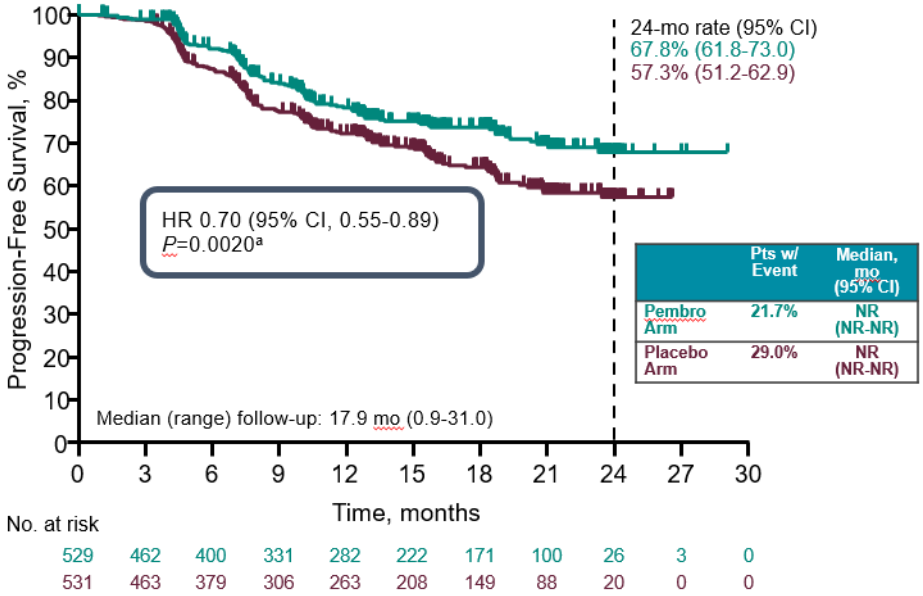
Accrual: 2020-2022

Adapted Lorusso, ESMO 2023

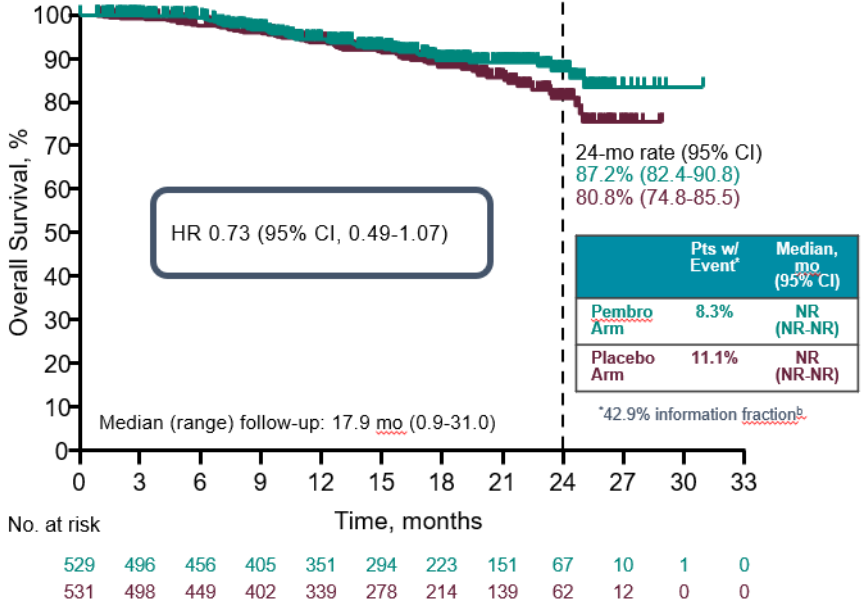
KEYNOTE A18: Progression Free and Overall Survival

Protocol specified first interim analysis: triggered at the completion of enrollment and when 237 events (PD or death) had occurred.

PFS



OS



At the time of this analysis, 58% on pembro arm and 55% of CRT arm are still on treatment.

Lorusso, ESMO 2023

PFS: Protocol-specified subgroups

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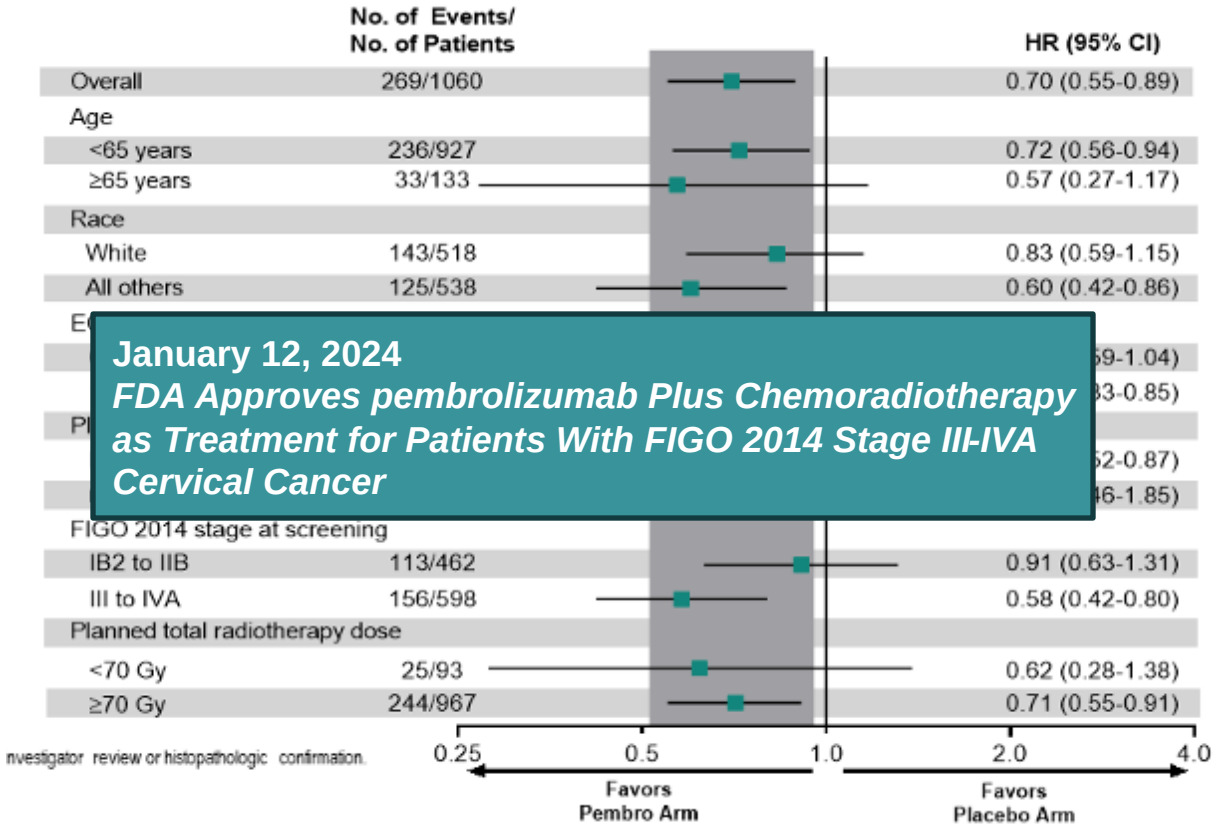

January 12, 2024

FDA Approves pembrolizumab Plus Chemoradiotherapy as Treatment for Patients With FIGO 2014 Stage III-IVA Cervical Cancer

Lorusso, ESMO 2023

Induction Chemotherapy: Interlace trial

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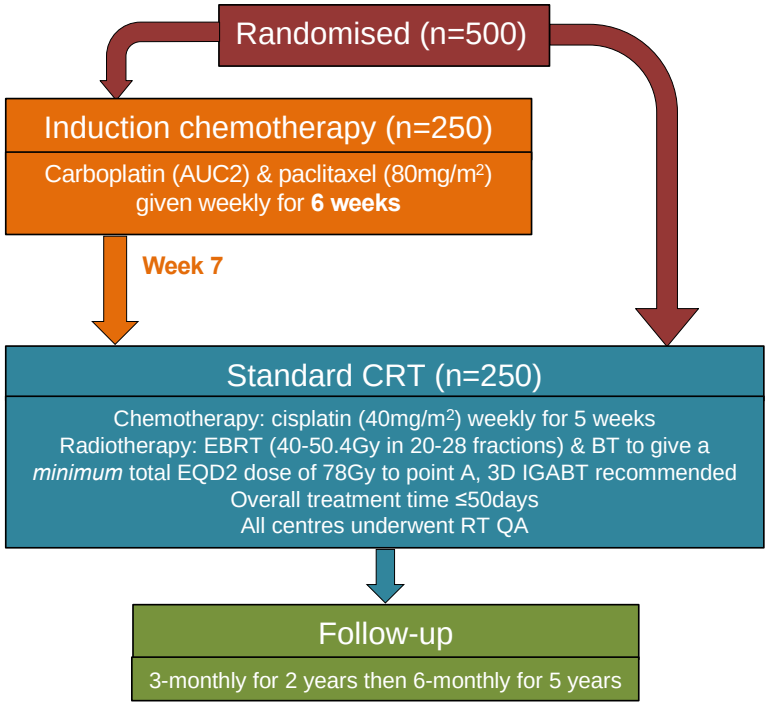
Key eligibility criteria

- Newly diagnosed histologically confirmed FIGO (2008) stages IB1 node+,IB2, II, IIIB, IVA squamous, adeno, adenosquamous cervical cancer
- No nodes above aortic bifurcation on imaging
- Adequate renal, liver & bone marrow function
- Fit for chemotherapy & radical RT
- No prior pelvic RT

RT = Radiotherapy
3D-Conformal = 3D conformal radiotherapy
IMRT = Intensity modulated radiotherapy
EBRT = External beam radiotherapy
BT = Brachytherapy
IGABT = Image-guided adaptive brachytherapy
RT QA = Radiotherapy quality assurance



Stratified by

- Site
- Stage
- Nodal status
- 3D-Conformal v IMRT EBRT
- 2D v 3D BT
- Tumour size
- SCC v other

Primary endpoints

- PFS
- OS

- Adverse events
- Pattern of relapse
- QOL
- Time to subsequent treatment

Accrual: 2012-2022

McCormack, ESMO 2023

Interlace: Progression-free and overall survival

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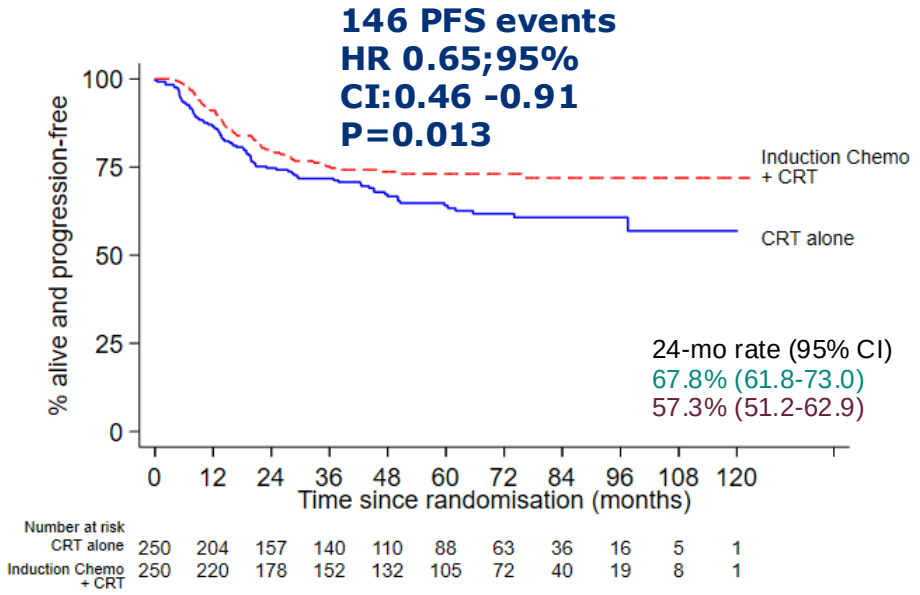
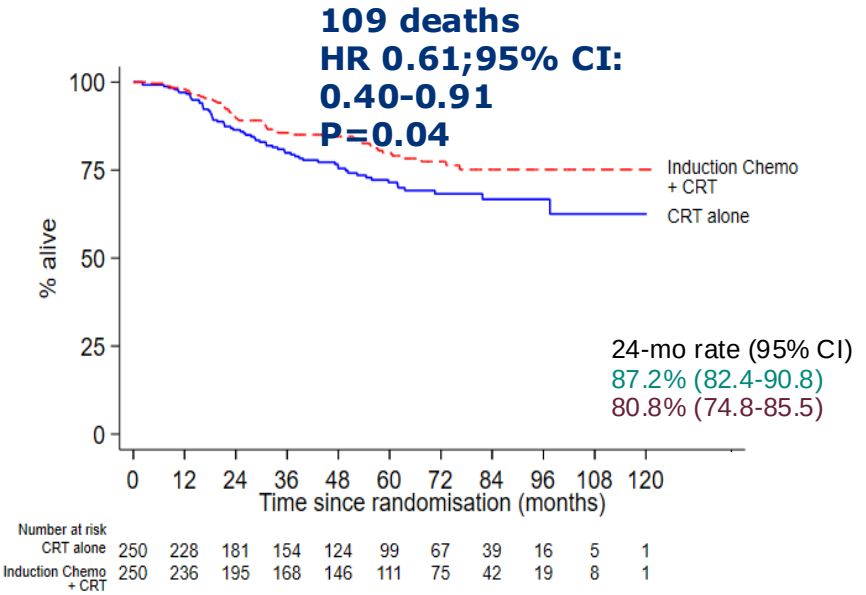
PFS (median f/u: 64 months)



	Induction Chemo+ CRT (n=250)	CRT alone (n=250)
3yr PFS	**75%**	**72%**
5yr PFS	**73%**	**64%**

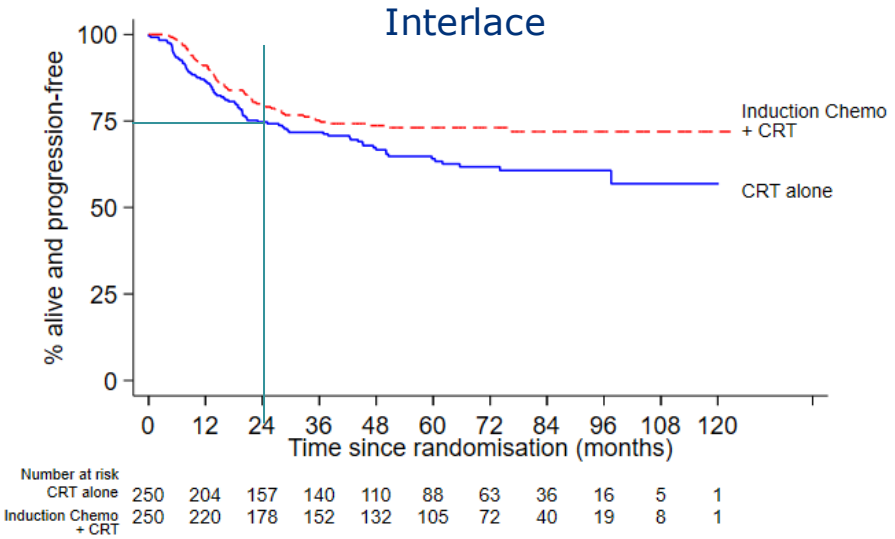
OS (median f/u: 64 months)

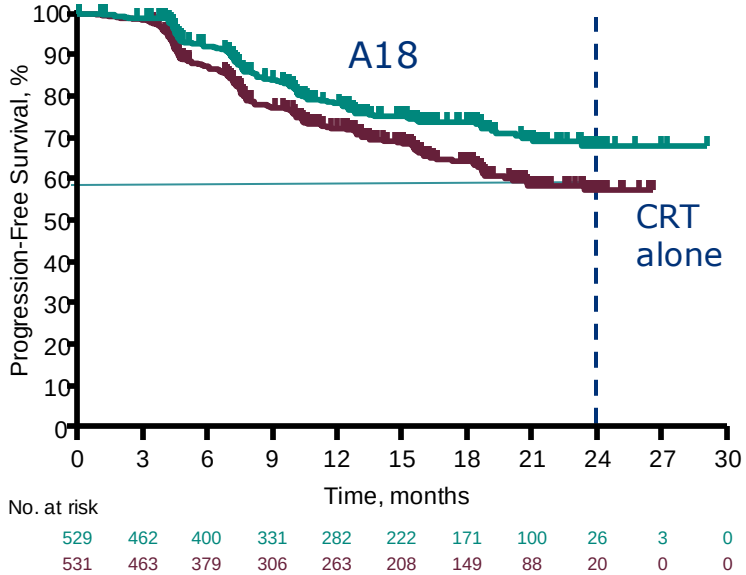


	Induction Chemo+ CRT (n=250)	CRT alone (n=250)
3yr OS	**86%**	**80%**
5yr OS	**80%**	**72%**

McCormack, ESMO 2023

Comparison of Interlace vs A18





	CRT alone (n=250)
3yr PFS	**72%**
5yr PFS	**64%**

24-mo rate (95% CI)
57.3% (51.2-62.9)

Adapted from Duska Winter SGO 2024

Interlace Participant Disease Characteristics

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	CRT alone (N=250)	Induction Chemo + CRT (N=250)
FIGO stage (2008)	**No.**	
IB1	2 (<1)	
IB2	23 (9)	
IIA	14 (6)	
IIB	176 (70)	
IIIB	30 (12)	
IVA	5 (2)	
Cell type		
Non-squamous	45 (18)	
Squamous	205 (82)	
Nodal status		
Negative	142 (57)	
Positive	108 (43)	
Longest tumour diameter, cm median (range)	4.9 (1.8-12.8)	4.8 (1.3-13.5)

	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Stage at screening (FIGO 2014 criteria)		
IB2-IIB	235 (44.4%)	227 (42.7%)
III-IVA	294 (55.6%)	304 (57.3%)
Lymph node involvement[b]		
Positive pelvic only	326 (61.6%)	324 (61.0%)
Positive para-aortic only	14 (2.6%)	10 (1.9%)
Positive pelvic and para-aortic	105 (19.8%)	104 (19.6%)
No positive pelvic or para-aortic	84 (15.9%)	93 (17.5%)
Planned type of EBRT		
IMRT or VMAT	469 (88.7%)	470 (88.5%)
Non-IMRT and non-VMAT	60 (11.3%)	61 (11.5%)
Planned total radiotherapy dose (EQD2)		
<70 Gy	47 (8.9)	46 (8.7)
≥70 Gy	482 (91.1)	485 (91.3)

Adapted from McCormack, ESMO 202

But will Interlace change SOC?

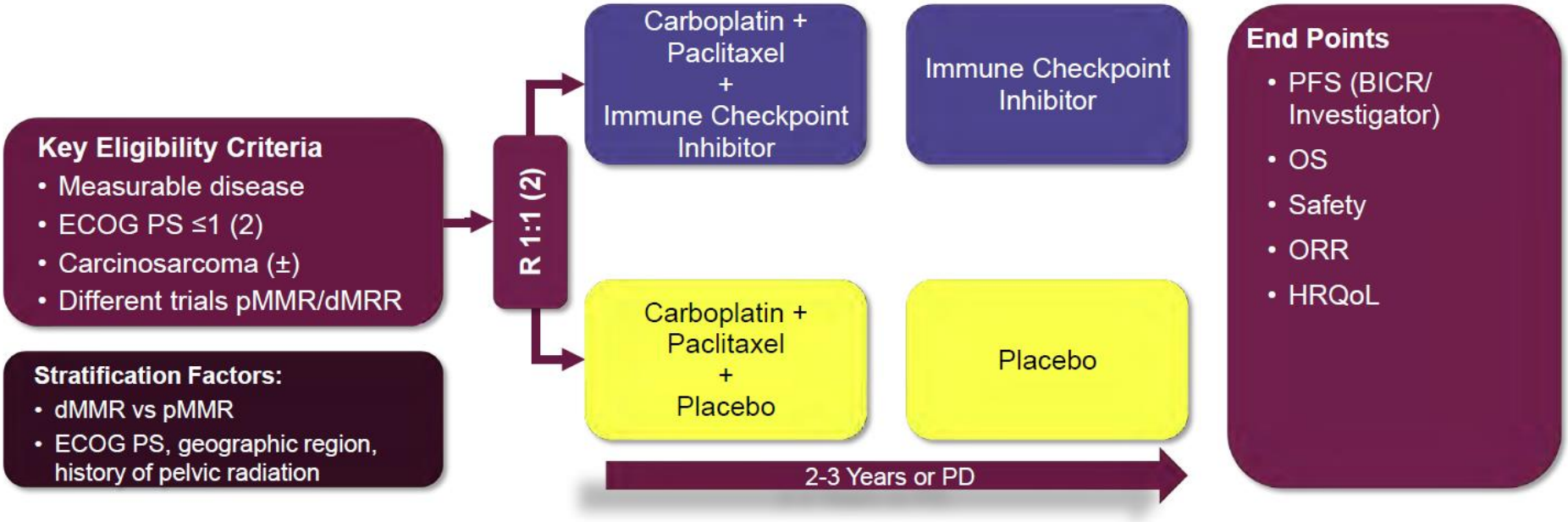
- Higher toxicity
- More complexity
- Bone marrow reserve for definitive RT?
- No incorporation of IO

Exciting Time for Endometrial Cancer!

FDA drug approvals

- **July 13, 2023**: *Dostarlimab-gxly* with chemotherapy and maintenance for dMMR and/or MSI-H advance/recurrent endometrial cancer
- **April 5, 2024:** Accelerated approval for *Fam-trastuzumab deruxtecan-nxki* for HER2 IHC 3+ recurrent solid tumors
- **June 14, 2024**: *Durvalumab* with chemotherapy followed by maintenance for advanced or recurrent dMMR endometrial cancer
- **June 17 2024**: *Pembrolizumab* with chemotherapy followed by maintenance for advance/recurrent endometrial cancer (dMMR/MSI-H or pMMR)
- **August 1 2024**: *Dostarlimab-gxly* with chemotherapy and maintenance for adults with advance/recurrent endometrial cancer

Benefits of IO in upfront EMCA Treatment: Core Study Designs



BICR=blinded independent central review; dMMR=deficient mismatch repair; ECOG PS=Eastern Cooperative Oncology Group Performance Status; HRQoL=health-related quality of life; ORR=overall response rate; OS=overall survival; pMMR=proficient mismatch repair; PD=progressive disease; PFS=progression-free survival; R=randomized.

Mirza M et al. NEJM March 2023
Eskander et al. NEJM March 2023
Colombo N, et al. Lancet Oncol Sept 2024
Marth C, et al. SGO 2024 Annual Meeting

Adapted from Eskander UC5 2024

PFS Benefit of IO + Chemo in the dMMR EC Population

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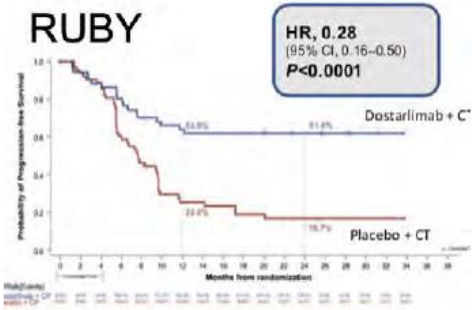
GY018

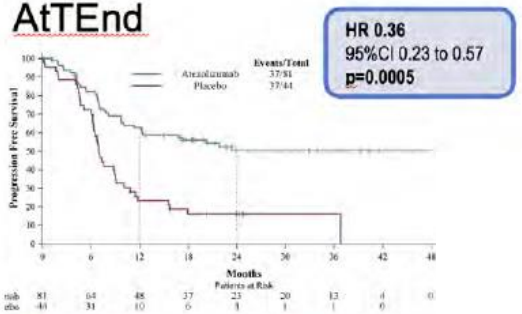
	No with events%	Median
Pembro + CT	23.2	NR (30.6-NR)
Placebo + CT	52.2	7.6 (6.4-9.9)

RUBY



	No with events%	Median
Dorsta + CT	35.8	NR (11.8-NR)
Placebo + CT	72.3	7.7 (5.6-9.7)

AtTEnd



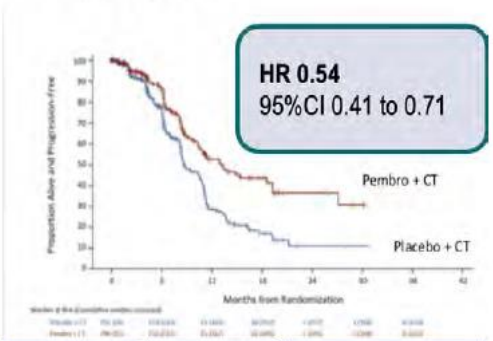
	No with events%	Median
Atezo + CT	45.7	NR (12.3-NR)
Placebo + CT	84.1	6.9 (6.2-9.0)

Adapted from Eskander UC5 2024

PFS Benefit of IO + Chemo in the pMMR EC Population

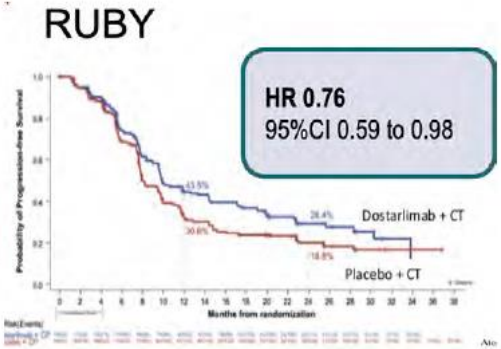
UC DAVIS HEALTH

GY018



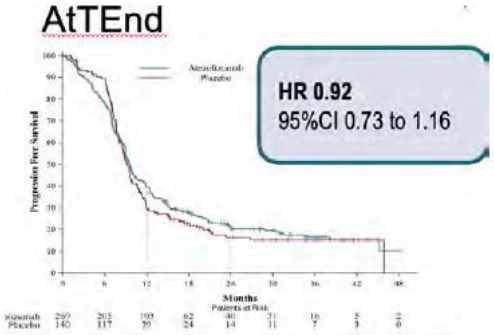
	No with events%	Median
Pembro + CT	30.6	13.1 (10.5-18.8)
Placebo + CT	45.5	8.7 (8.4-10.7)
Maturity	38.1%	

RUBY



	No with events%	Median
Dorsta + CT	60.4	9.9 (9.0-13.3)
Placebo + CT	70.7	7.9 (7.6-9.8)
Maturity	65.4%	

AtTEnd



	No with events%	Median
Atezo + CT	78	9.5 (9.0-10.4)
Placebo + CT	77	9.2 (8.5-9.9)
Maturity	78%	

Adapted from Eskander UC5 2024

Comparison: GY018 vs RUBY Part 1

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	GY018 Pembro	RUBY Dostarlimab
Measurable stage III/IVA	X	X
Non-measurable stage IVB	X	X
Non-measurable clear cell, carcinosarcoma, serous, mixed, IIIC2-IVA		X
Recurrent EMCA	X	X
Carcinosarcoma		X
PS 0-1	X	X
PS 2	X	
Time since completion of adjuvant chemo	≥12 mo	≥6 mo

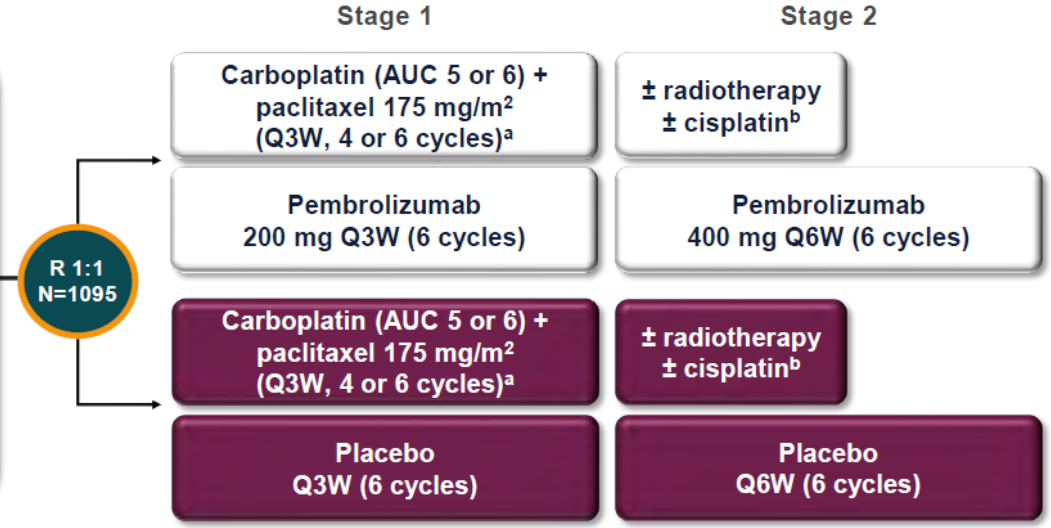
What about IO in early stage completely resected Endometrial cancer? (ENGOT-E11/GOG-3053-KEYNOTE- B21)

Key Eligibility Criteria

- Newly diagnosed EC or carcinosarcoma
- Curative surgery with no residual disease
- At high risk for recurrence:
  - FIGO (2009) surgical stage I/II, non-endometrioid with myometrial invasion
  - FIGO (2009) surgical stage I/II of any histology with known aberrant p53 expression or *TP53* mutation with myometrial invasion
  - FIGO (2009) surgical stage III/IVA of any histology
- No prior radiation or systemic therapy (including neoadjuvant) for EC

Stratification Factors

- **MMR status (pMMR vs dMMR)**, and within pMMR stratum:
  - Planned radiation (chemo-EBRT vs EBRT vs no EBRT)
  - Histology (endometrioid vs non-endometrioid)
  - FIGO (2009) surgical stage (I/II vs III/IVA)



Dual primary endpoints

- DFS as assessed radiographically by the investigator or by histopathologic confirmation
- OS

Van Gorp et al. ESMO 2024

What about IO in early stage completely resected Endometrial cancer? (ENGOT-E11/GOG-3053-KEYNOTE- B21)

Characteristic	Pembro + Chemo (n = 545)	Placebo + Chemo (n = 550)
Age, median (range), y	62 (29–95)	62 (27–89)
ECOG PS 0	409 (75%)	416 (76%)
Race		
White	315 (58%)	362 (66%)
Asian	189 (35%)	157 (29%)
Multiple	23 (4%)	10 (2%)
Black or African American	11 (2%)	13 (2%)
American Indian or Alaska Native	2 (<1%)	3 (<1%)
Missing	5 (<1%)	5 (<1%)
Lymph node dissection	483 (89%)	502 (91%)
Lymph node status		
Lymph node involvement	223 (41%)	250 (45%)
No lymph node involvement	300 (55%)	284 (52%)
Not evaluable	22 (4%)	16 (3%)
MMR status at study entry		
dMMR	141 (26%)	140 (25%)
pMMR	404 (74%)	410 (75%)

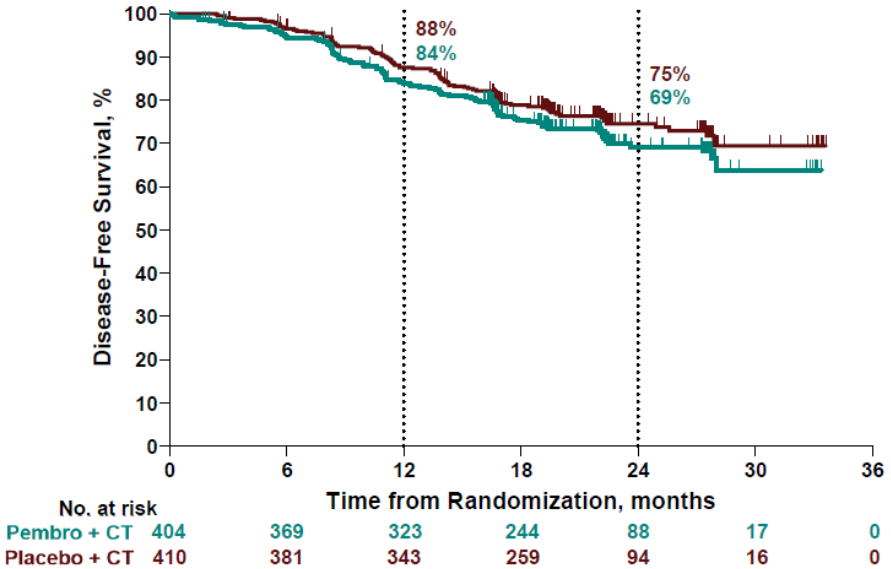
Characteristic	Pembro + Chemo (n = 545)	Placebo + Chemo (n = 550)
FIGO 2009 stage at study entry		
IA/B	146 (27%)	144 (26%)
II	40 (7%)	41 (7%)
IIIA	109 (20%)	94 (17%)
IIIB	20 (4%)	19 (3%)
IIIC1	144 (26%)	169 (31%)
IIIC2	78 (14%)	81 (15%)
IVA/B[a]	8 (1%)	2 (<1%)
Planned radiation therapy at study entry		
EBRT[b] with cisplatin	94 (17%)	95 (17%)
EBRT[b] without cisplatin	256 (47%)	246 (45%)
Brachytherapy only	49 (9%)	52 (9%)
No EBRT or brachytherapy	146 (27%)	157 (29%)
Histology subtype		
Endometrioid	297 (54%)	297 (54%)
Non-endometrioid	248 (46%)	253 (46%)

Adapted from Eskander UC5 2024

What about IO in early stage completely resected Endometrial cancer? (ENGOT-E11/GOG-3053-KEYNOTE- B21)

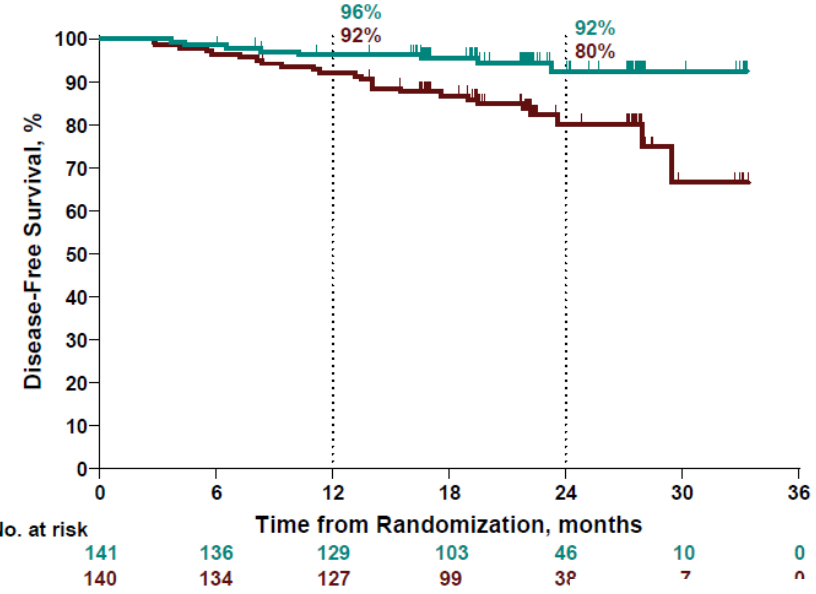
pMMR Subgroup

	Events, n (%)	Median (95% CI), mo	HR (95% CI)
Pembro + CT	111 (27)	NR (NR–NR)	1.20 (0.91–1.57)
Placebo + CT	96 (23)	NR (NR–NR)	



dMMR Subgroup

	Events, n (%)	Median (95% CI), mo	HR (95% CI)
Pembro + CT	8 (6)	NR (NR–NR)	0.31 (0.14–0.69)
Placebo + CT	25 (18)	NR (29.5–NR)	



Adapted from Van Gorp et al ESMO 2024

What Lies Ahead: Will Immunotherapy be moved to the Frontline as a Chemotherapy Replacement?

GOG 3064 KN-C93

R → Pembrolizumab
R → Chemo

Primary endpoints:
PFS, OS

Key secondary endpoints:
ORR, DCR, DOR

Recruitment ongoing

dMMR patient population

ENGOT-en13 DOMENICA

R → Dostarlimab
R → Chemo

Primary endpoint:
PFS

Key secondary endpoints:
OS, PROs, ORR, DOR

Recruitment ongoing

dMMR patient population

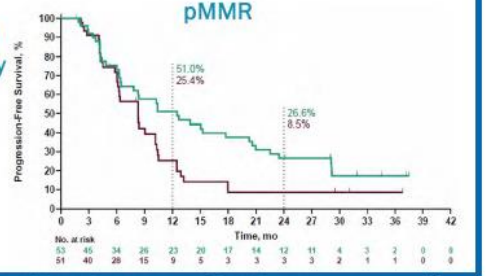
ENGOT-en9 LEAP-001

R → Lenvatinib + pembrolizumab

Pembrolizumab/Lenvatinib Miss OS, PFS in Endometrial Cancer

December 8, 2023
Sabrina Serani

PFS in Prior Neo/Adjuvant Chemotherapy Subgroup



patient populations

Adapted from Eskander UC5 2024

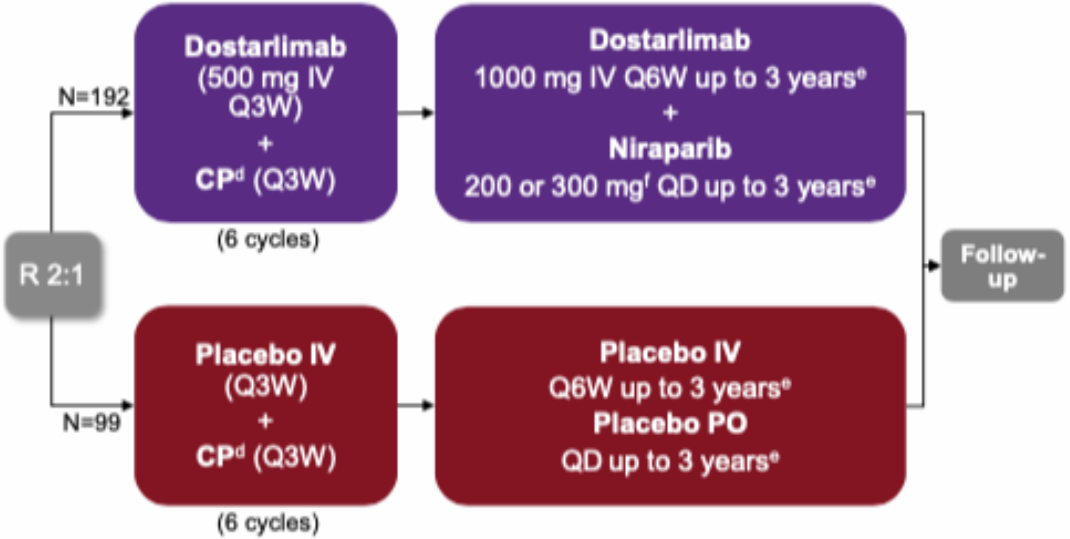
Chemo with IO followed by PARP IO maintenance: ENGOT/EN6-NSGO/GOG-3031/RUBY Part 2

Eligible patients

- Stage III/IV disease or first recurrent EC[a]
  - All histologies except sarcomas[b]
- Naive to systemic anticancer therapy or had a recurrence or PD ≥6 months after completing systemic anticancer therapy
- Naive to PARP inhibitor therapy

Stratification

- MMR/MSI status[c]
  - 25% dMMR/MSI-H
  - 75% MMRp/MSS
- Prior external pelvic radiotherapy
- Disease status



Primary endpoint

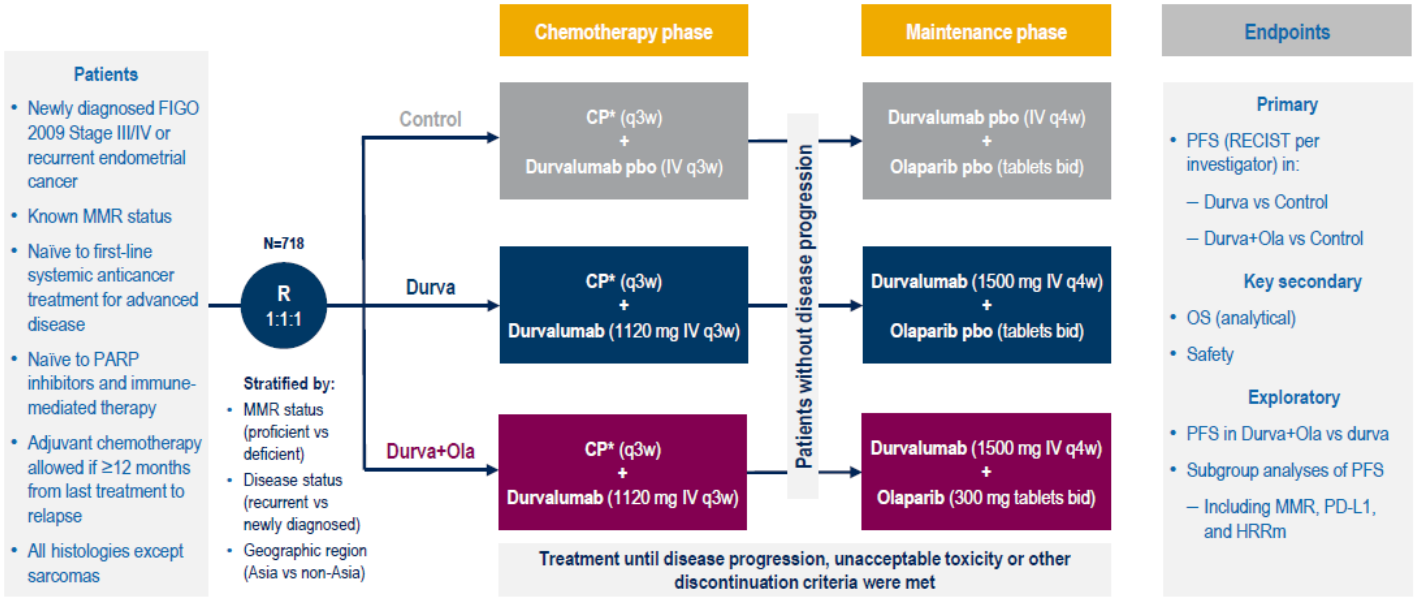
- PFS by INV per RECIST v1.1
  - Overall
  - MMRp/MSS

Secondary endpoints

- OS
- PFS by BICR
- ORR
- DOR
- DCR (BOR of CR, PR, or SD)
- PFS2
- HRQOL/PRO
- PK

Mirza RM. SGO 2024

Chemo with IO followed by PARP IO maintenance: DUO-E/GOG-3014/ENGOT-en10



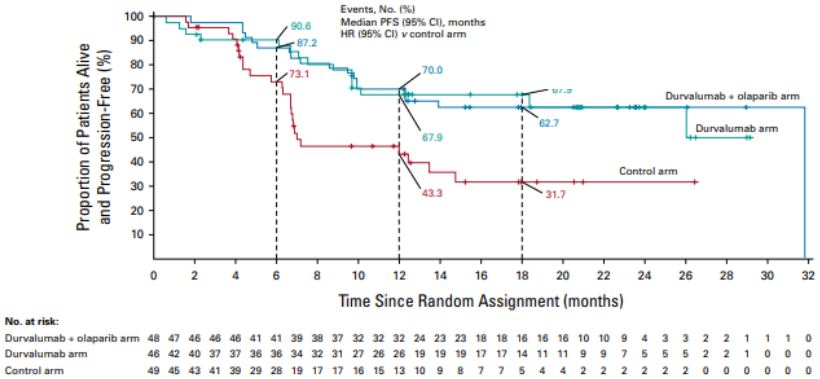
*Six cycles of carboplatin at an area under the concentration–time curve of 5 or 6 mg per mL/min and paclitaxel 175 mg/m².
bid, twice daily; CP, carboplatin/paclitaxel; durva, durvalumab; FIGO, International Federation of Gynaecology and Obstetrics; HRRm, homologous recombination repair mutation; IV, intravenously; ola, olaparib; pbo, placebo; q3(4)w, every 3(4) weeks; R, randomisation; RECIST, Response Evaluation Criteria for Solid Tumours.

Westin S et al, ESMO 2023

Chemo with IO followed PARP+ IO maintenance – dMMR

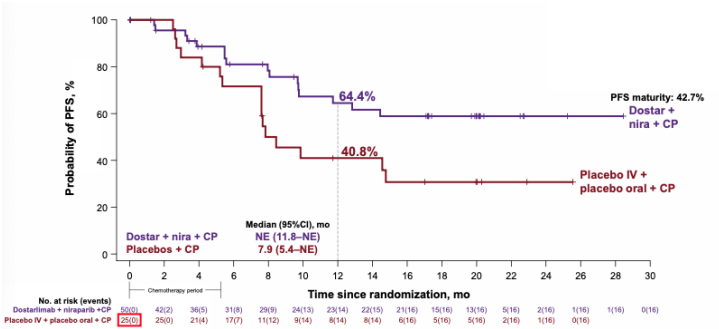
Stage III-IV or recurrent endometrial cancer, PARPi and IO naive

DUO-E



	PFS (mo)	HR vs control
Durvalumab + Olaparib	31.8	0.41 (0.21-0.75)
Durvalumab	NR	0.42 (0.22-0.80)
Control	7	

RUBY Part 2



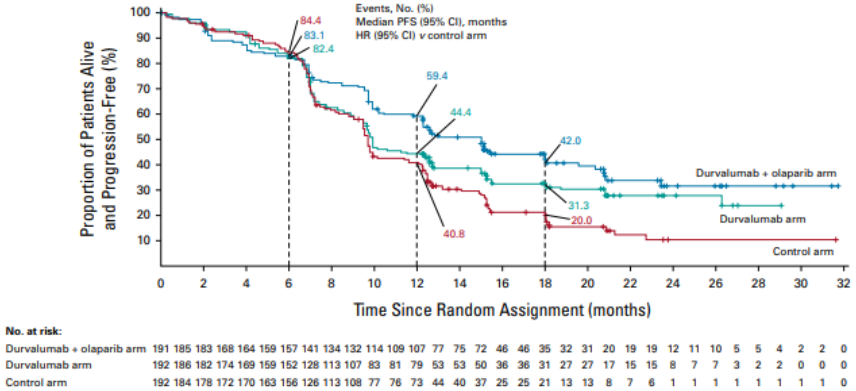
	PFS (mo)	HR vs control
Dostarlimab + Niraparib	NR	0.48 (0.24-0.96)
-		
Control	7.9	

Westin et al, 2023 Mirza et al, SGO 2024

Chemo with IO followed PARP+ IO maintenance – pMMR

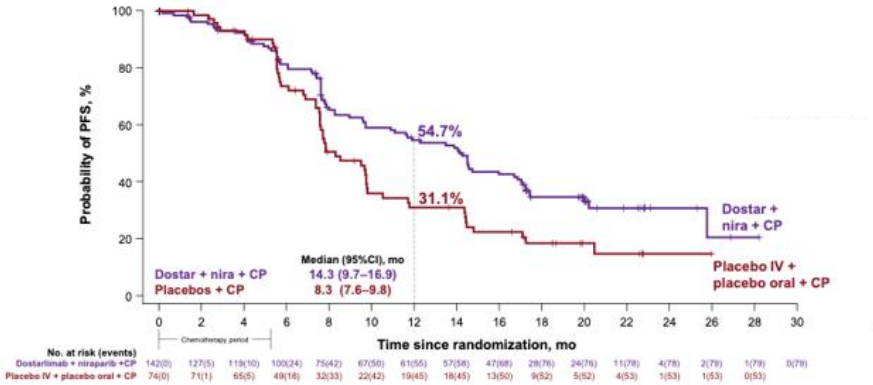
Stage III-IV or recurrent endometrial cancer, PARPi and IO naive

DUO-E



	PFS (mo)	HR vs control
Durvalumab + Olaparib	15	0.57 (0.44-0.73)
Durvalumab	9.9	0.77 (0.6-0.97)
Control	9.7	

RUBY Part 2

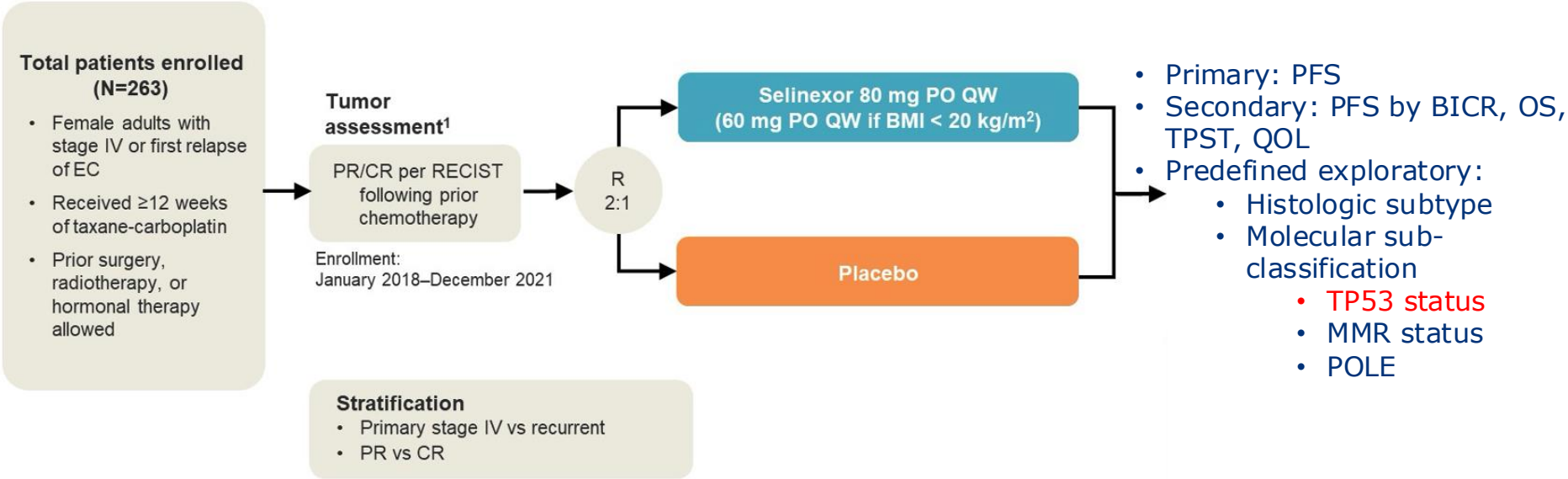


	PFS (mo)	HR vs control
Dostarlimab + Niraparib	14.3	0.63 (0.44-0.91)
-		
Control	8.3	

Westin et al, 2023 Mirza et al, SGO 2024

What else is up and coming? ENGOT-EN5/GOG-3055/SIENDO

- Selinexor - novel oral maintenance therapy targeting TP53wt endometrial cancer
- Prevents XPO1-mediated export of tumor suppressor genes, including p53wt



Makker V et al. ASCO 2024
Vergote et al. J Clin Oncol 2023

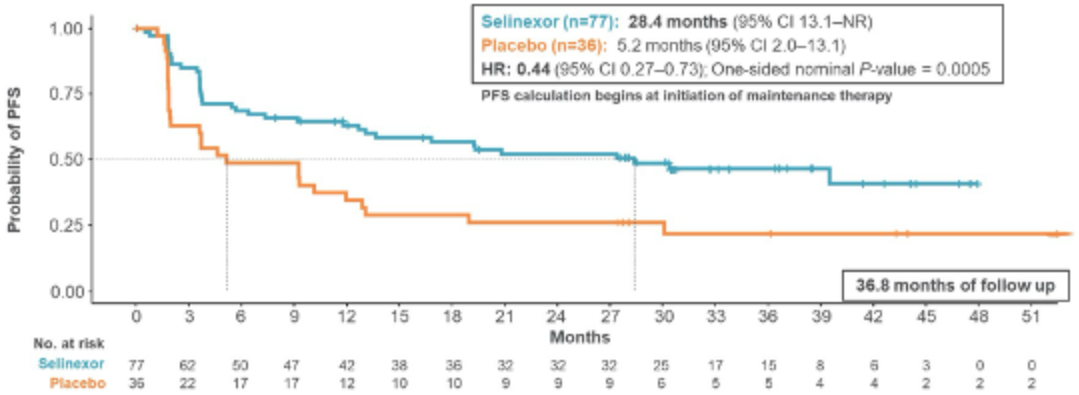
SIENDO

- Selinexor maintenance did not show clinically meaningful PFS
- Exploratory analysis showed promising PFS benefit in TP53wt subpopulation

	Selinexor	Placebo	P-value	Hazard Ratio (95% CI)
mPFS in Overall (months)	5.7	3.8	.126	0.76 (0.54 to 1.08)
mPFS in TP53 wild-type (months)	13.7	3.7	.002	0.41 (0.23 to 0.72)

Vergote et al. J Clin Oncol 2023

SIENDO sub-analysis: Long term mPFS in TP53wt Subgroup



TP53wt mPFS of 28.4 months with Selinexor vs 5.2 months months in placebo

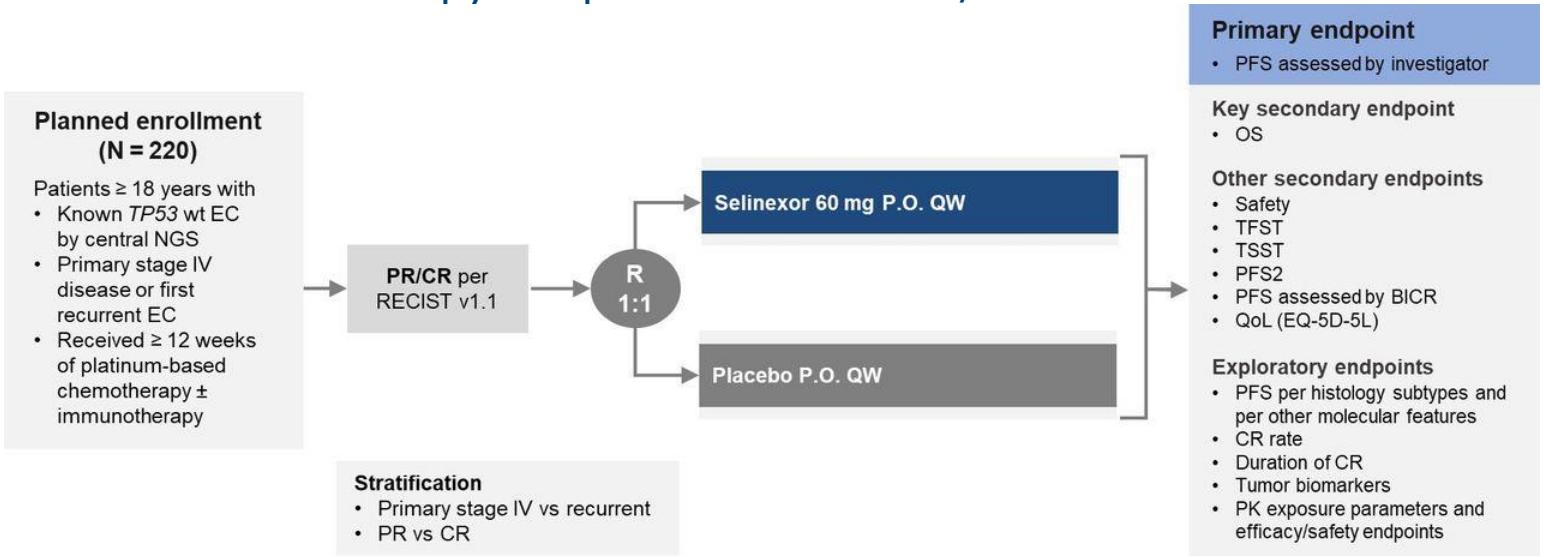
- TP53wt/pMMR subgroup mPFS 39.5 months with Selinexor
- TP53wt/dMMR subgroup mPFS 13.1 months with Selinexor

Makker V et al. ASCO 2024

Next steps in Selinexor

UC DAVIS HEALTH

- ENGOT-EN20/GOG-3083/XPORT-EC-042: Selinexor maintenance after chemotherapy for p53wt in advance/recurrent endometrial



Vergote et al, Int J Gynecol Cancer 2024

Mirasol: Mirvetuximab Soravtansine vs Investigators Choice of Chemo in FRα PROC

- Randomized, open-label phase III study using PS2+ scoring in patients with FRα-high PROC

Stratified by chemotherapy choice, no. of prior tx (1 vs 2 vs 3)

Patients with platinum-resistant (<6 mo PFI), advanced, high-grade ovarian cancer; prior bevacizumab and PARP inhibitor allowed; *BRCA*m (N = 430)

Mirvetuximab Soravtansine 6 mg/kg IV Q3W

Mirvetuximab dosing adjusted per ideal body weight

Investigator's Choice of Chemotherapy

Paclitaxel: 80 mg/m² QW
PLD: 40 mg/m² Q4W
Topotecan: 4 mg/m² Days 1, 8, and 15 Q4W or 1.25 mg/m² Days 1-5 Q3W

Statistical Assumptions

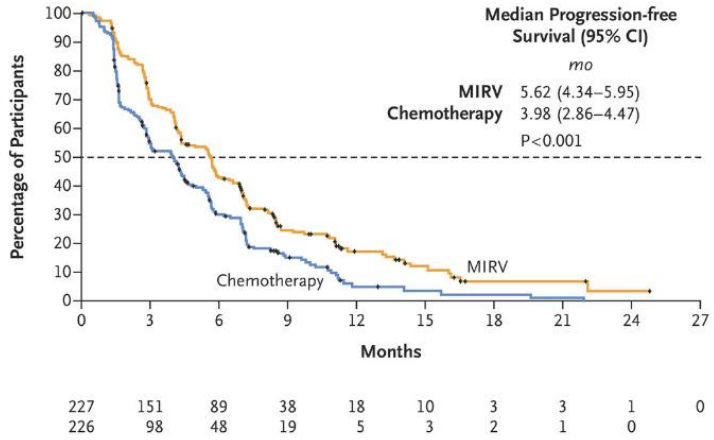
- 2 sided α = .05; power = 90%; HR: 0.7; control arm median PFS: 3.5 mo

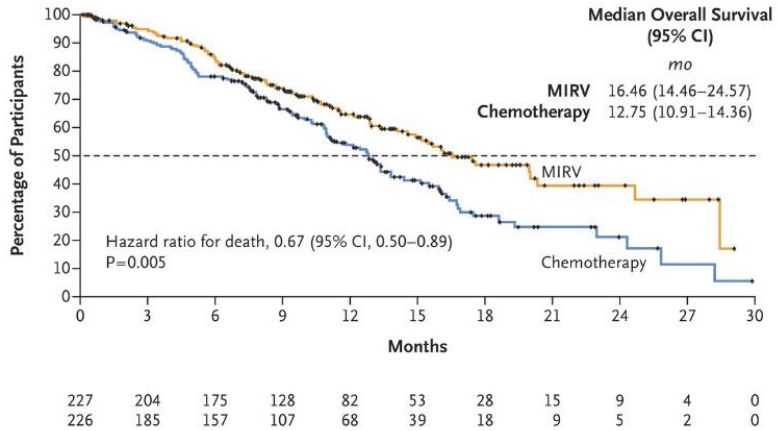
- **Primary endpoints**: PFS by investigator (BICR for sensitivity analysis)
- **Secondary endpoints**: ORR by investigator, OS, and PROs

NCT04209855

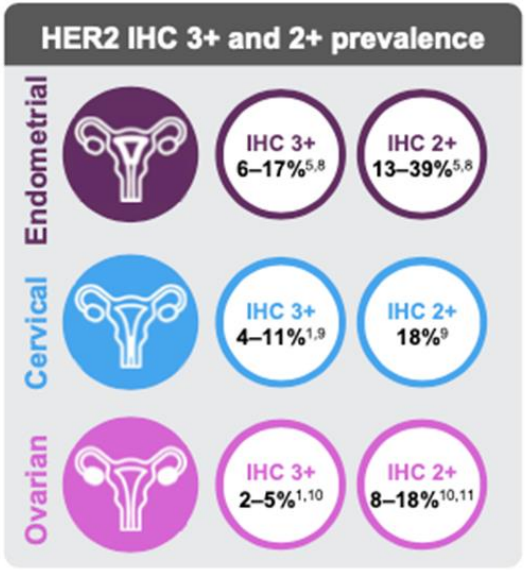
Mirvetuximab vs Chemo in PROC: Outcomes

Efficacy Endpoints	MIRV (n=227)	IC (n=226)	Hazard Ratio	P-value
mPFS (INV) (months, 95% CI)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)	0.65 (0.52, 0.81)	<0.0001
mPFS (BICR) (months, 95% CI)	5.91 (4.93, 6.97)	4.34 (3.52, 4.99)	0.72 (0.56, 0.92)	0.0082
ORR (INV) (95% CI)	42.3 (35.8, 49.0)	15.9 (11.4, 21.4)	NA	<0.0001
Complete response % (n)	5.3 (12)	0	NA	NA
Partial response % (n)	37.0 (84)	15.9 (36)	NA	NA
ORR (BICR) (95% CI)	36.1 (29.9, 42.7)	14.6 (10.3, 19.9)	NA	<0.0001
mOS (months, 95% CI)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)	0.67 (0.50, 0.88)	0.0046





Moore K et al, N Engl J Med December 6, 2023



DESTINY-PanTumor02: T-DXd for HER2-expressing solid tumors

A Phase 2, open-label, multicenter study (NCT04482309)

Key eligibility criteria

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)*
  - Cervical cohort was expanded to include five IHC 1+ patients†
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1

T-DXd 5.4 mg/kg Q3W

n≈40 per cohort‡

Primary endpoint

- Confirmed ORR (investigator)

Secondary endpoints

- DOR, DCR, PFS, OS
- Safety

Exploratory analyses

- Subgroup analyses by HER2 status§
- Subgroup analyses by biomarkers§

Primary analysis DCO

- June 8, 2023

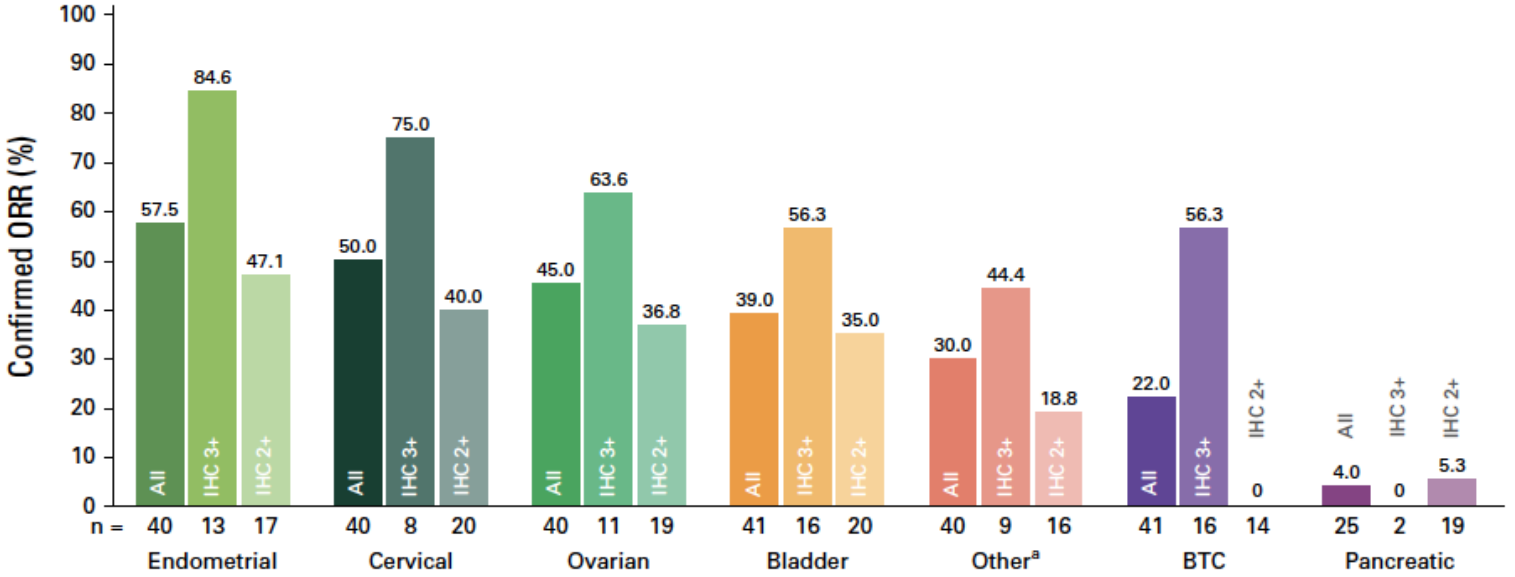
- Endometrial
- Cervical
- Ovarian
- Bladder
- Other tumors¶
- Biliary tract
- Pancreatic

- FDA approved for HER2 IHC 3+ recurrent solid tumors after prior systemic chemotherapy

Makker et al. SGO 2024

Meric-Bernstam F et al. J Clin Oncol. 2024;42:47–58;

DESTINY-PanTumor02



Meric-Bernstam, J Clin Oncol, 2024

Conclusions

- Cervical cancer
  - IO upfront – recurrent/metastatic PDL1+, stage III-IVA with chemoRT
  - Induction chemo prior to RT – INTERLACE – role TBD
- Endometrial
  - Upfront IO – all comers advanced/recurrent RUBY, NRG GY018, Keynote B21
  - PARP + IO maintenance –DUO- E & RUBY 2 – role TBD
  - P53 Wt maintenance - Selinexor promising initial data, trial ongoing
- Ovary
  - Mirvetuximab – FOLRα positive
- Gyn cancers
  - HER2 – Destiny – promising results in EMCA, OVCA, cervix

Thank you and Questions?