Endometrial cancer: ASCO 2025

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Disclosures

- Advisory board participant: Merck, GSK, AstraZeneca, Tempus, Immunogen

- Master Yoda/The mandalorian is/are a bipartisan fictional characters.

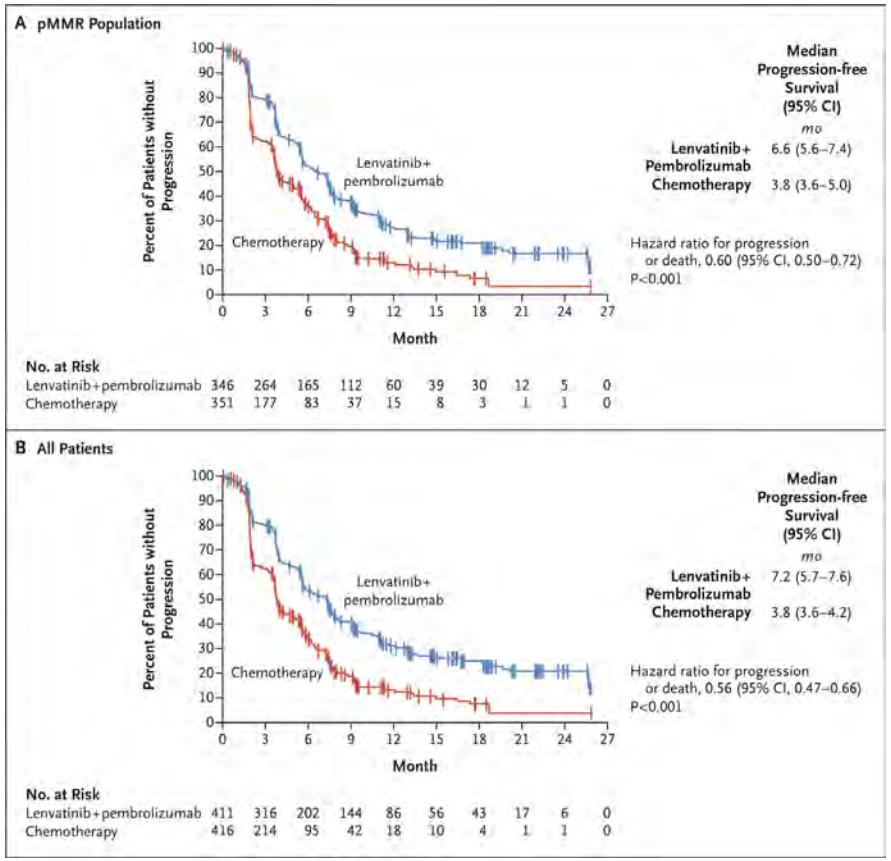
Key Takeaways

Not a big year for endometrial cancer

Adding multi-TKI to ICI+chemotherapy for first line endometrial cancer is tolerable and should be further studied

ctDNA is prognostic and longitidinal follow up is predictive of progression in endometrial cancer

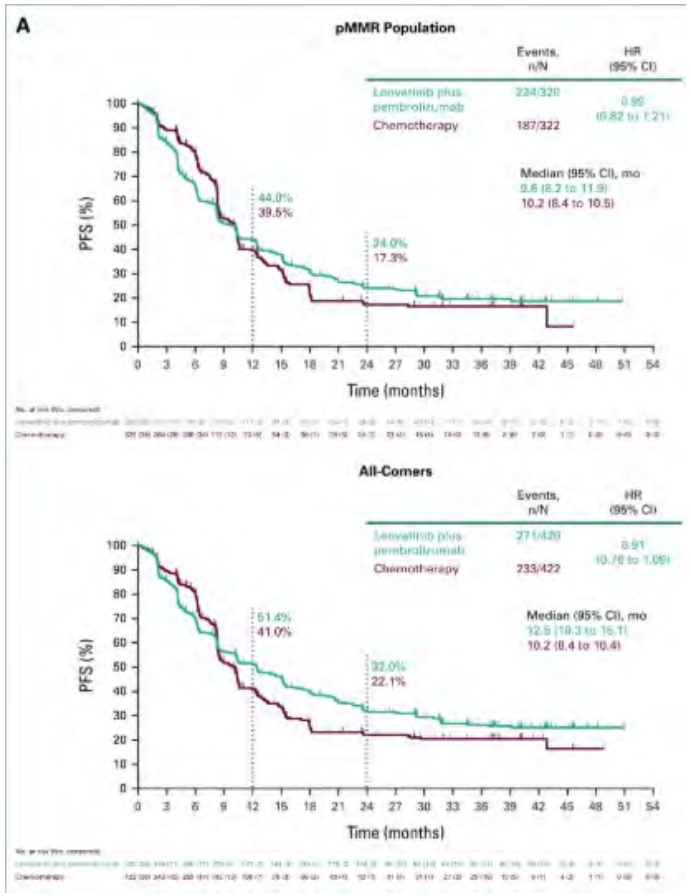
Multi-TKI
VEGFR/FGFR/PDGF + ICI
At recurrence=



KEYNOTE-775 Makker et al NEJM 2022

Improved PFS and OS in pMMR and dMMR

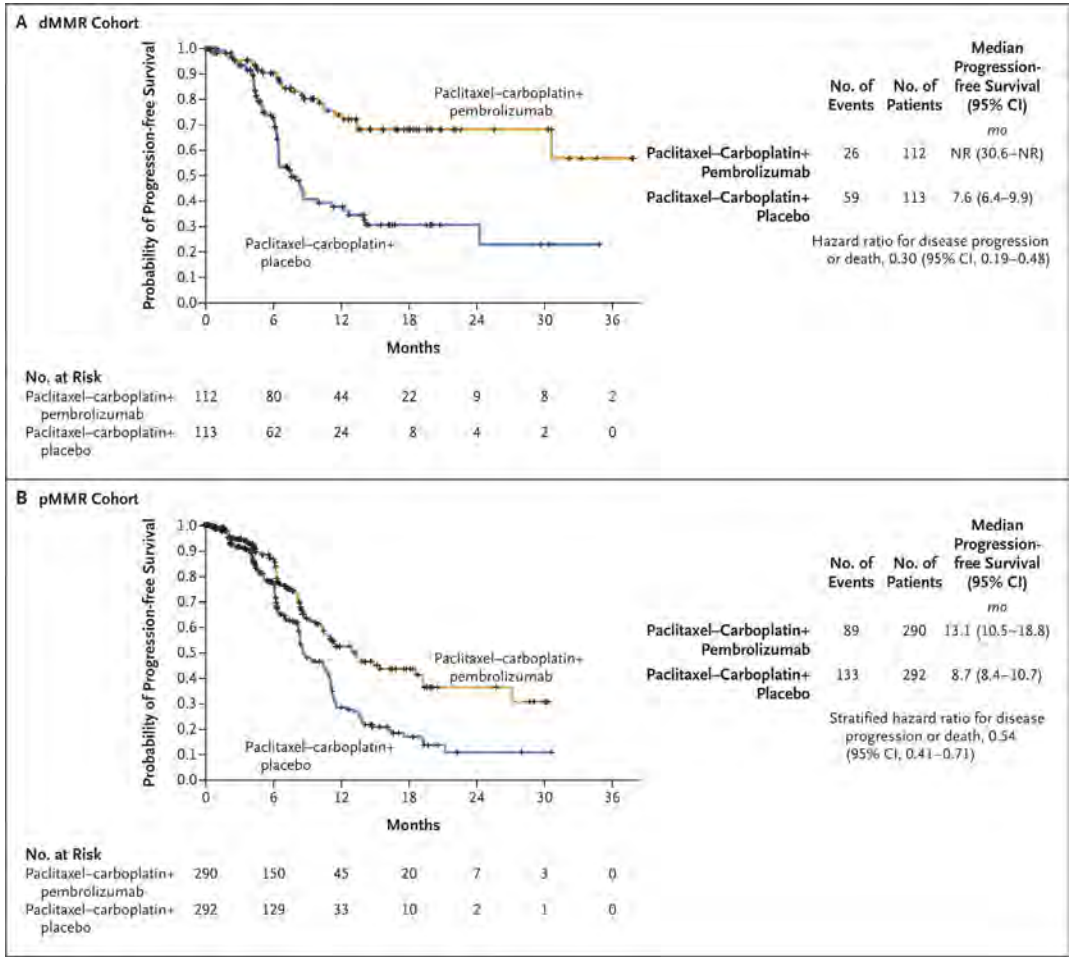
Multi-TKI VEGFR/FGFR/PDGF + ICI
Vs. carbo/taxol chemo
In first line therapy



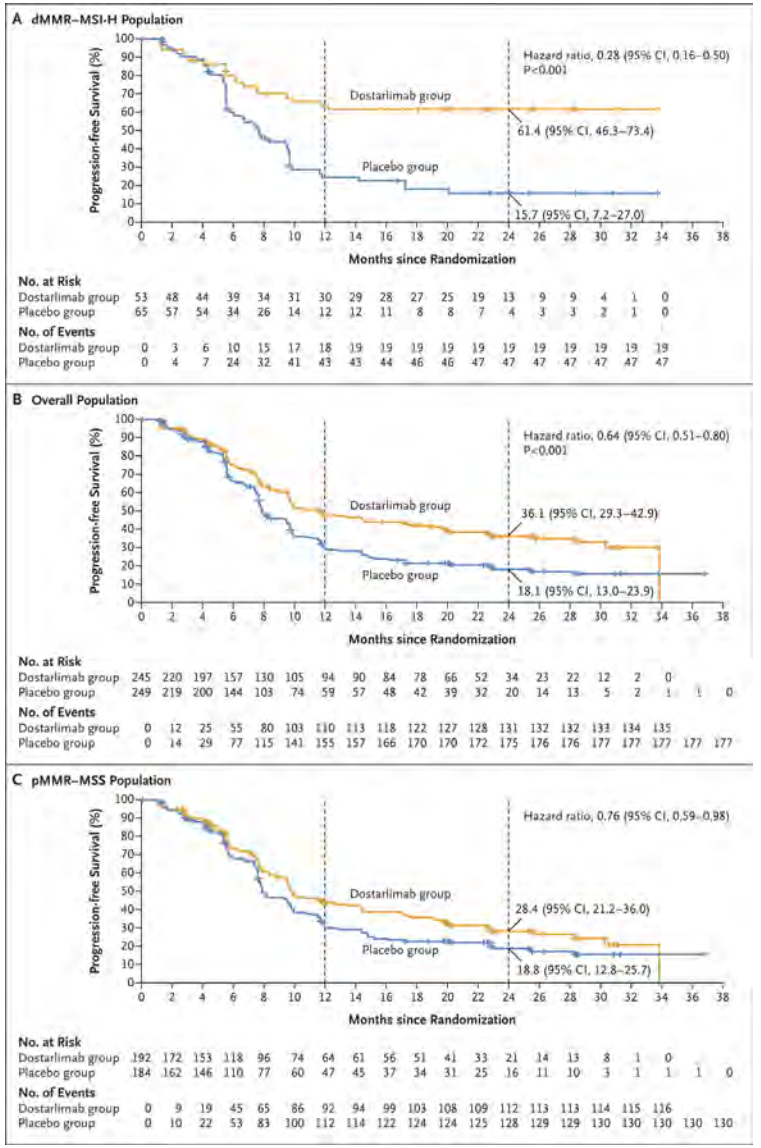
LEAP001 Marth et al JCO 2024

Improved PFS and in dMMR but not pMMR

Chemotherapy + ICI in First line/recurrent



Gy018 Eskander et al NEJM 2023



RUBY Mirza et al NEJM 2023

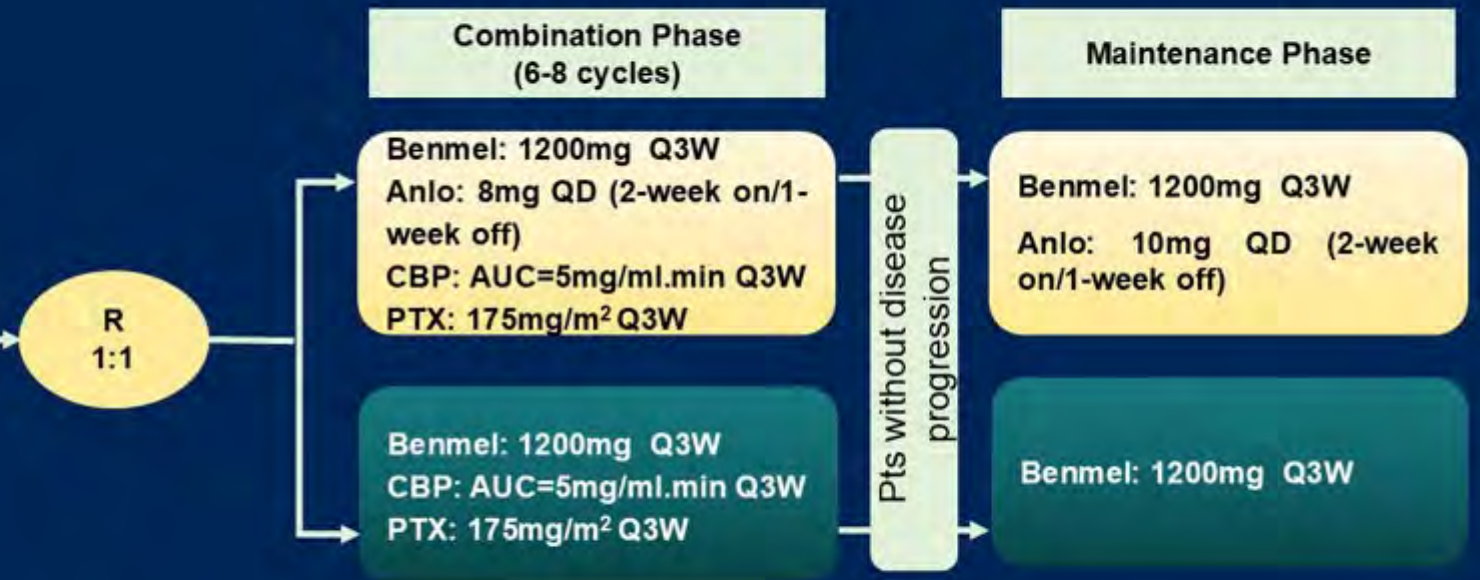
Improvement in PFS for both dMMR and pMMR

What happens if you add a multi-TKI and ICI to chemotherapy?

The only main plenary oral on endo rial cancer:

Methods

- Newly diagnosed FIGO 2009 stage III/IV or recurrent endometrial cancer (EC).
- Naïve to first-line systemic anticancer treatment.
- Including endometrioid, carcinosarcoma, and other histology type.
- Age：≥18 years old.
- ECOG PS: 0~1.
- Adequate organ function.



- Primary endpoint: ORR assessed by investigators according to RECIST v1.1.
- Secondary endpoint: OS, PFS, disease control rate (DCR) , duration of response (DOR) and safety.
- Stratified by: MMR status (dMMR/MSI-H or pMMR/MSS).

Baseline Characteristics were well balanced

	Benmel-Anlo (N=38)	Benmel(N=33)
Age, median(range), years	59.0 (37 - 73)	60.0 (43 - 74)
MMR status, n(%)		
dMMR/MSI-H	6 (15.79)	7 (21.21)
pMMR/MSS	32 (84.21)	26 (78.79)
Disease status, n(%)		
Newly diagnosed	11 (28.95)	11 (33.33)
III	1 (2.63)	1 (3.03)
IV	10 (26.32)	10 (30.30)
Recurrent	27 (71.05)	21 (63.64)
ECOG PS, n(%)		
0	12 (31.58)	13 (39.39)
1	25 (65.79)	20 (60.61)
Histology type, n(%)		
Endometrioid	38 (100.00)	31 (93.94)
Carcinosarcoma	0 (0.00)	1 (3.03)
Other	0 (0.00)	1 (3.03)
Previous chemotherapy, n(%)	20 (52.63)	13 (39.39)
Previous radiotherapy, n(%)	18 (47.37)	9 (27.27)
Prior surgery, n(%)	30 (78.95)	24 (72.73)

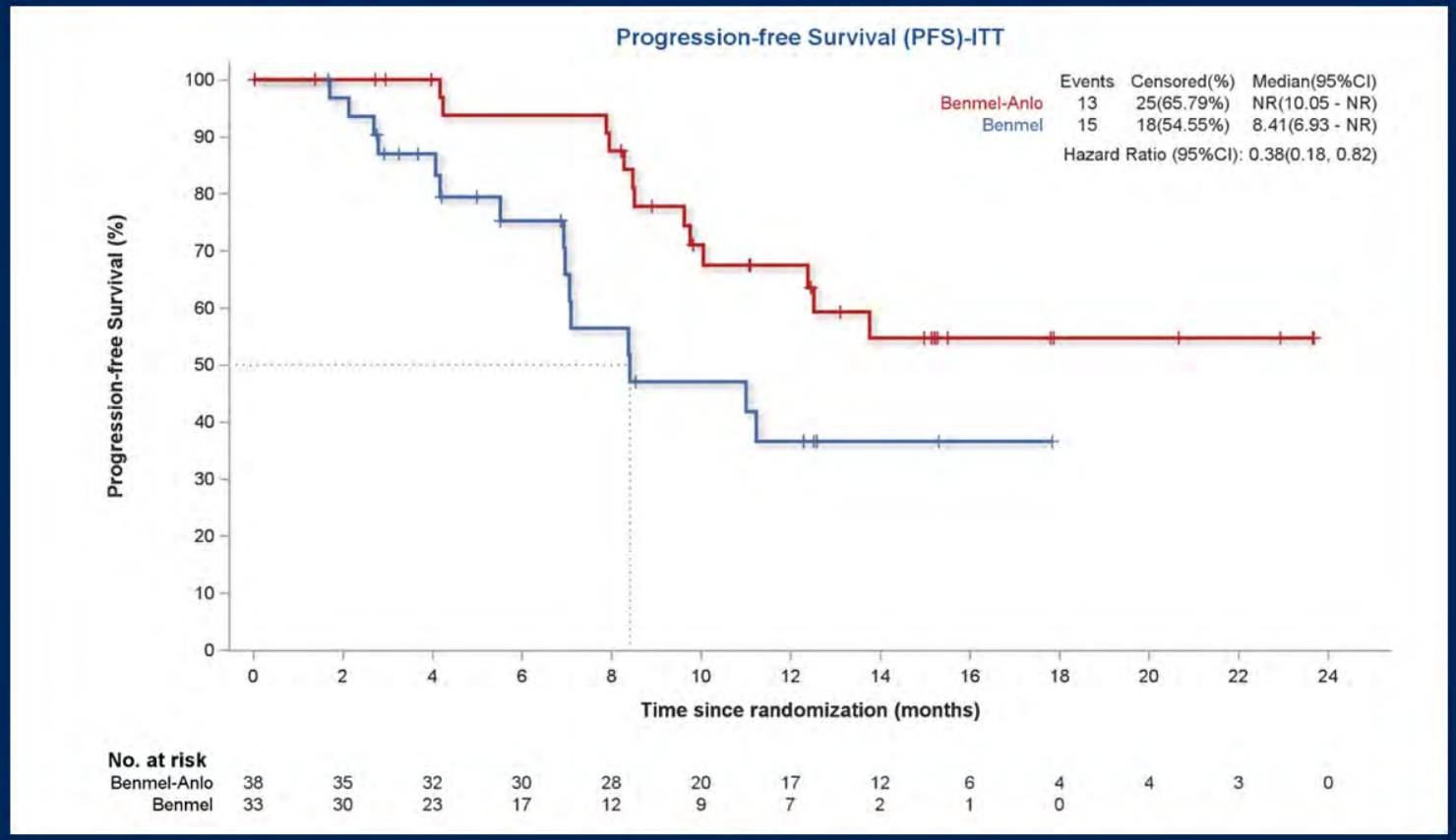
Efficacy: ORR/DCR/DOR

- **Data cutoff date**: November 1, 2024. There were 36 assessable cases in Benmel-Anlo arm and 31 in Benmel arm.
- **ITT population**:
  - **ORR:** 86.1% (Benmel-Anlo) vs 80.6% (Benmel)
  - DCR: 100% in both arms
  - Median DOR: Not reached (95% CI 8.71–NR) vs 6.97 months (95% CI 4.11–NR)
- **dMMR/MSI-H subpopulation**:
  - **ORR:** 100% (Benmel-Anlo) vs 85.7% (Benmel)
  - DCR: 100% in both arms
  - Median DOR: Not reached (95% CI 7.23–NR) vs Not reached (95% CI 2.69–NR)
- **pMMR/MSS subpopulation**:
  - **ORR:** 83.3% (Benmel-Anlo) vs 79.2% (Benmel)
  - DCR: 100% in both arms
  - Median DOR: Not reached (95% CI 6.93–NR) vs 5.75 months (95% CI 2.99–NR)

ORR/DCR/DOR compared between the two cohorts

	ITT		dMMR		pMMR	
	Benmel-Anlo (N=36)	Benmel(N=31)	Benmel-Anlo (N=6)	Benmel(N=7)	Benmel-Anlo (N=30)	Benmel(N=24)
ORR, n (%)	31 (86.1)	25(80.6)	6(100.0)	6(85.7)	25(83.3)	19(79.2)
95% CI	(70.50-95.33)	(62.53-92.55)	(54.07-100.00)	(42.13-99.64)	(65.28-94.36)	(57.85-92.87)
DCR, n (%)	36(100.0)	31(100.0)	6(100.0)	7(100.0)	30(100.0)	24(100.0)
95% CI	(90.26-100.00)	(88.78-100.00)	(54.07-100.00)	(59.04-100.00)	(88.43-100.00)	(85.75-100.00)
mDOR, (95%CI)	NR（8.71-NR）	6.97（4.11-NR）	NR(7.23-NR)	NR(2.69-NR)	NR(6.93-NR)	5.75(2.99-NR)

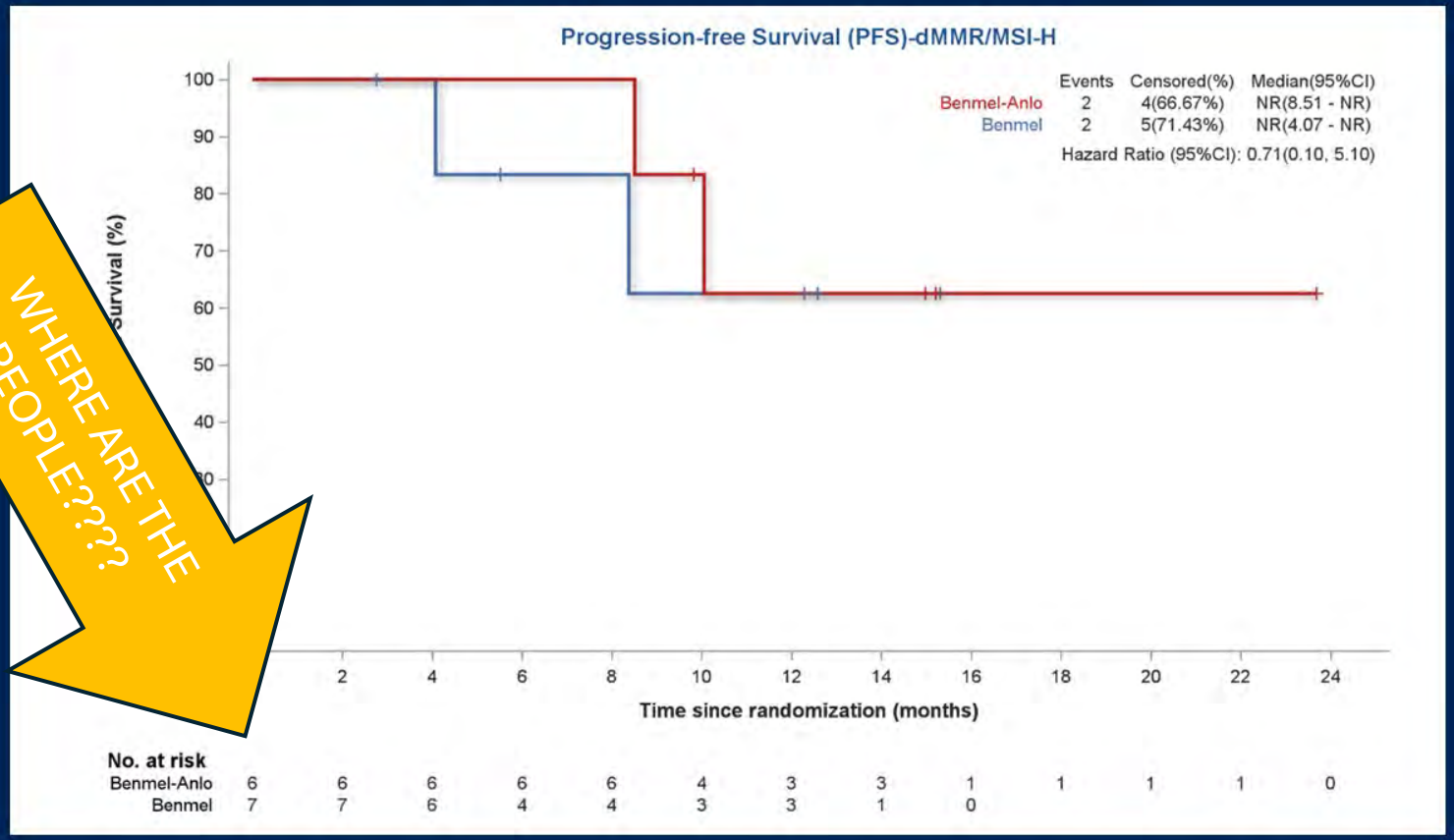
ITT population: PFS



PFS Kaplan-Meier survival curves-ITT

- **Median follow-up**:
  - 16.2 months (Benmel-Anlo, n=38)
  - 14.2 months (Benmel, n=33)
- **PFS Outcomes**:
  - **Event distribution**: 13/38 (34.2%) vs 15/33 (45.5%).
  - **Benmel-Anlo**: Median PFS **not reached** (95% CI 10.05–NR)
  - **Benmel**: Median PFS **8.41 months** (95% CI 6.93–NR)
  - HR 0.38 (95% CI 0.18-0.82)

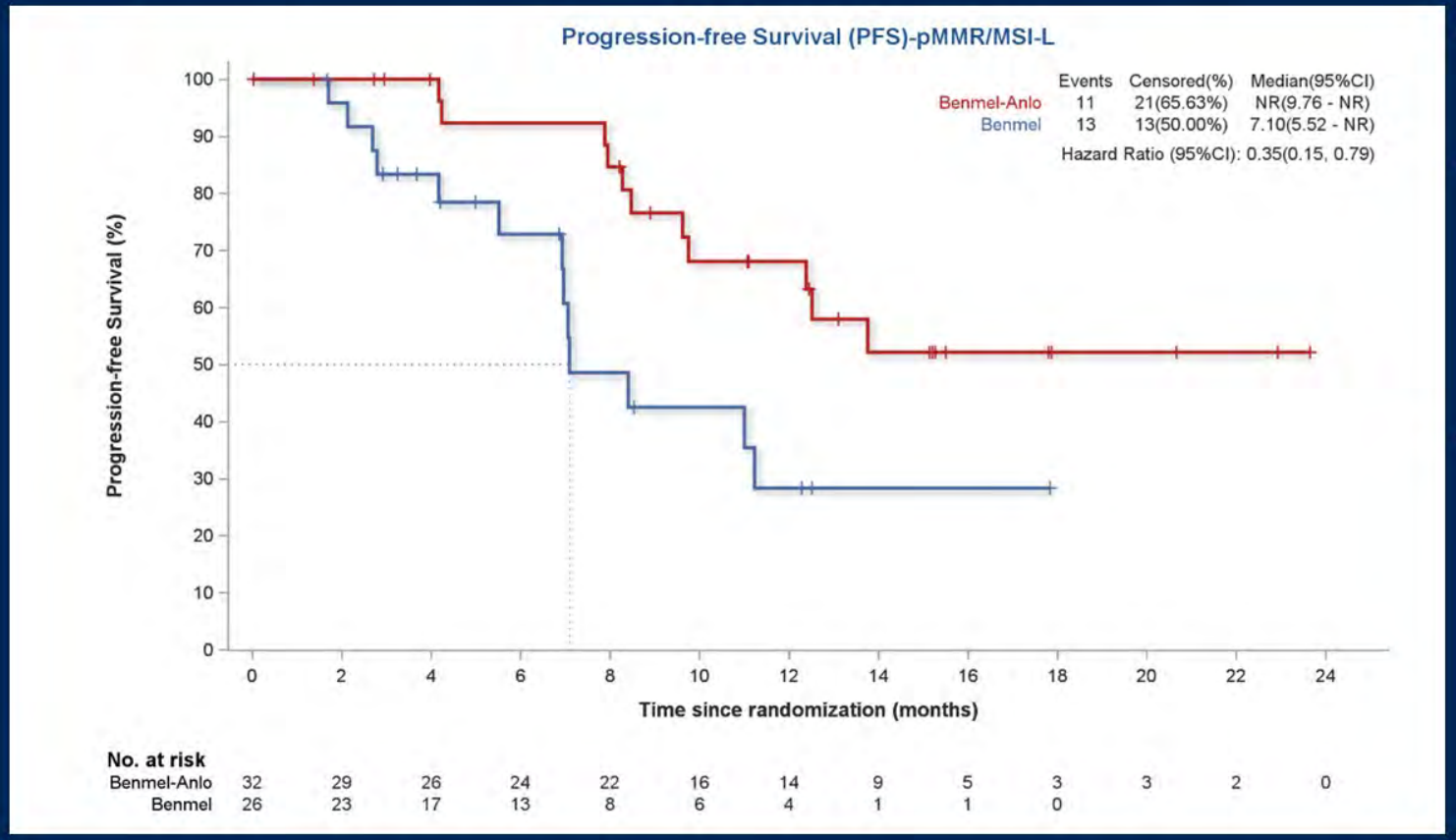
dMMR subpopulation: PFS



PFS Kaplan-Meier survival curves-dMMR subpopulation

- **dMMR/MSI-H Subpopulation Outcomes**
- **PFS events**: 4 total
  - **Benmel-Anlo**: 2/6 (33.3%)
  - **Benmel**: 2/7 (28.6%)
  - Median PFS not reached in either arm
- **Comparable PFS trends were shown in both cohorts.**

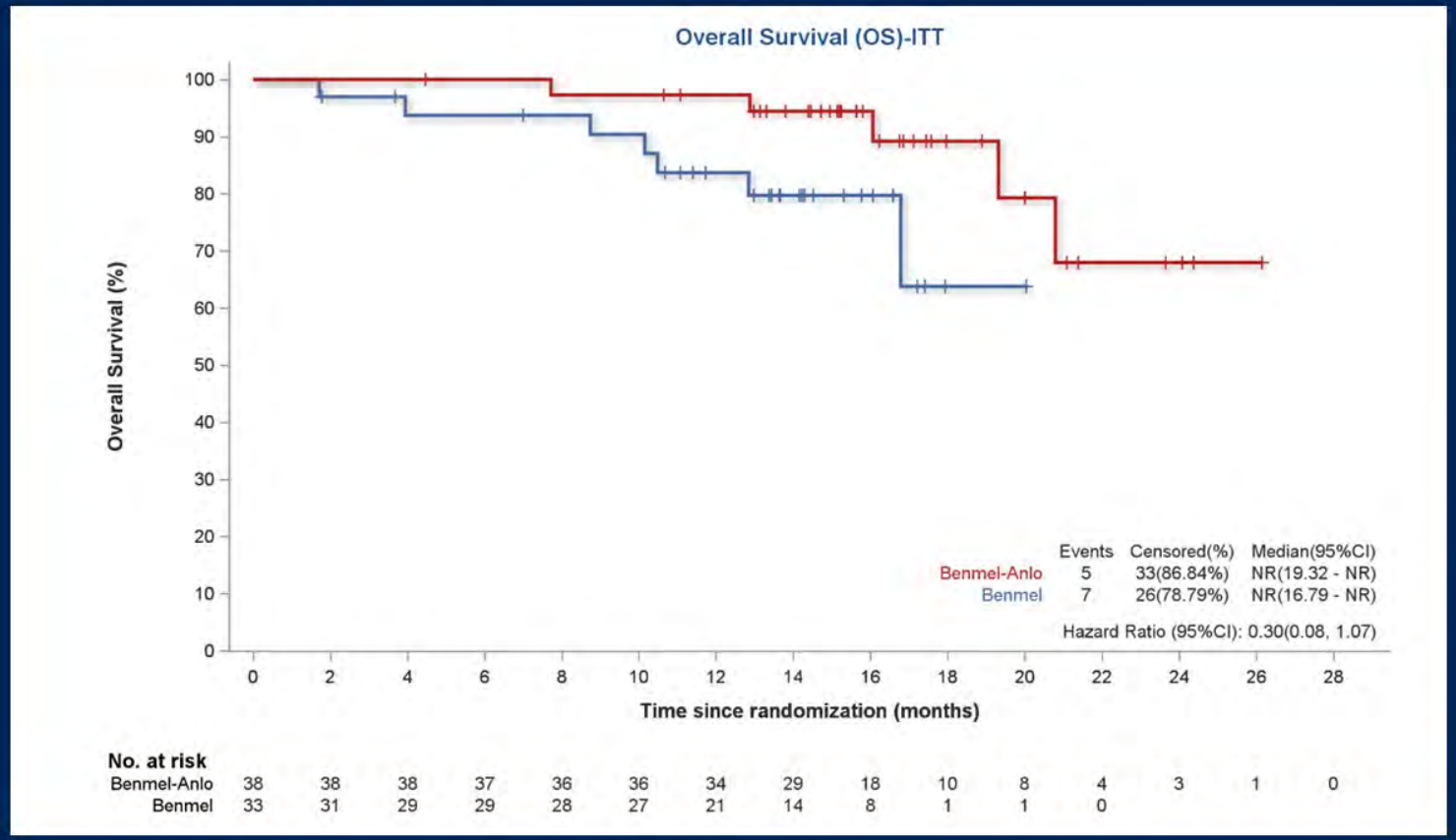
pMMR subpopulation: PFS



PFS Kaplan-Meier survival curves-pMMR subpopulation

- **pMMR/MSS Subpopulation Outcomes**
- **PFS events**: 24 total
  - **Benmel-Anlo**: 11/32 (28.9%)
  - **Benmel**: 13/26 (39.4%)
- **Median PFS**:
  - **Benmel-Anlo**: Median PFS not reached (95% CI 9.76–NR)
  - **Benmel**: 7.10 months (95% CI 5.52–NR)
  - **PFS**: Notable PFS extension trends were demonstrated, HR 0.35 (95% CI 0.15-0.79).

Efficacy: OS

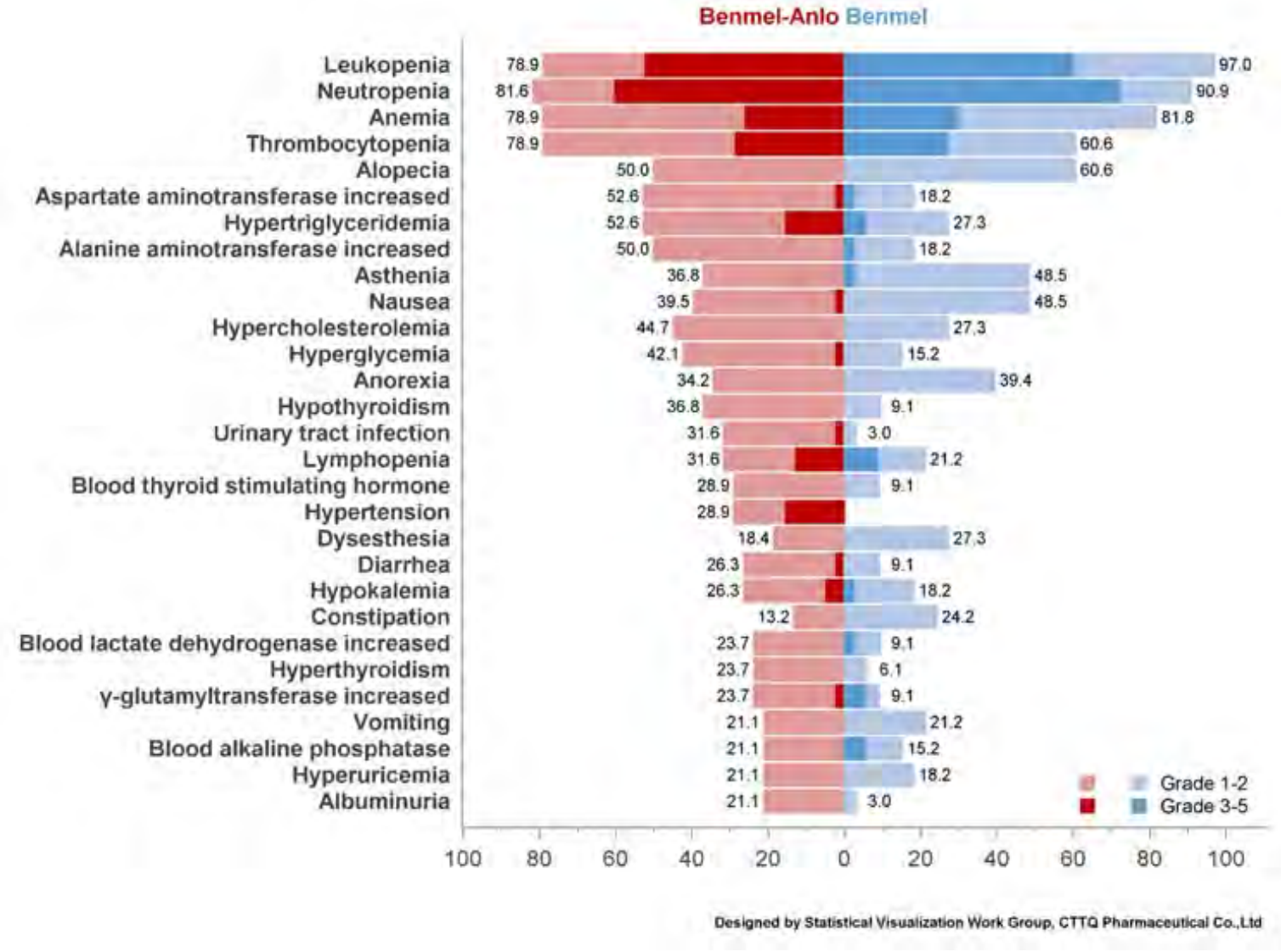


OS Kaplan-Meier survival curves

- **OS events (ITT)**: 10 total
  - **Benmel-Anlo**: 4/38 (10.5%)
  - **Benmel**: 6/33 (18.2%)
  - Median OS not reached in either arm
- **OS trend favored Benmel-Anlo, HR 0.30** (95% CI 0.08-1.07).

Safety:

Expected worsening of bone marrow toxicities and liver enzyme abnormalities




I WONDER WHAT'S NEXT?
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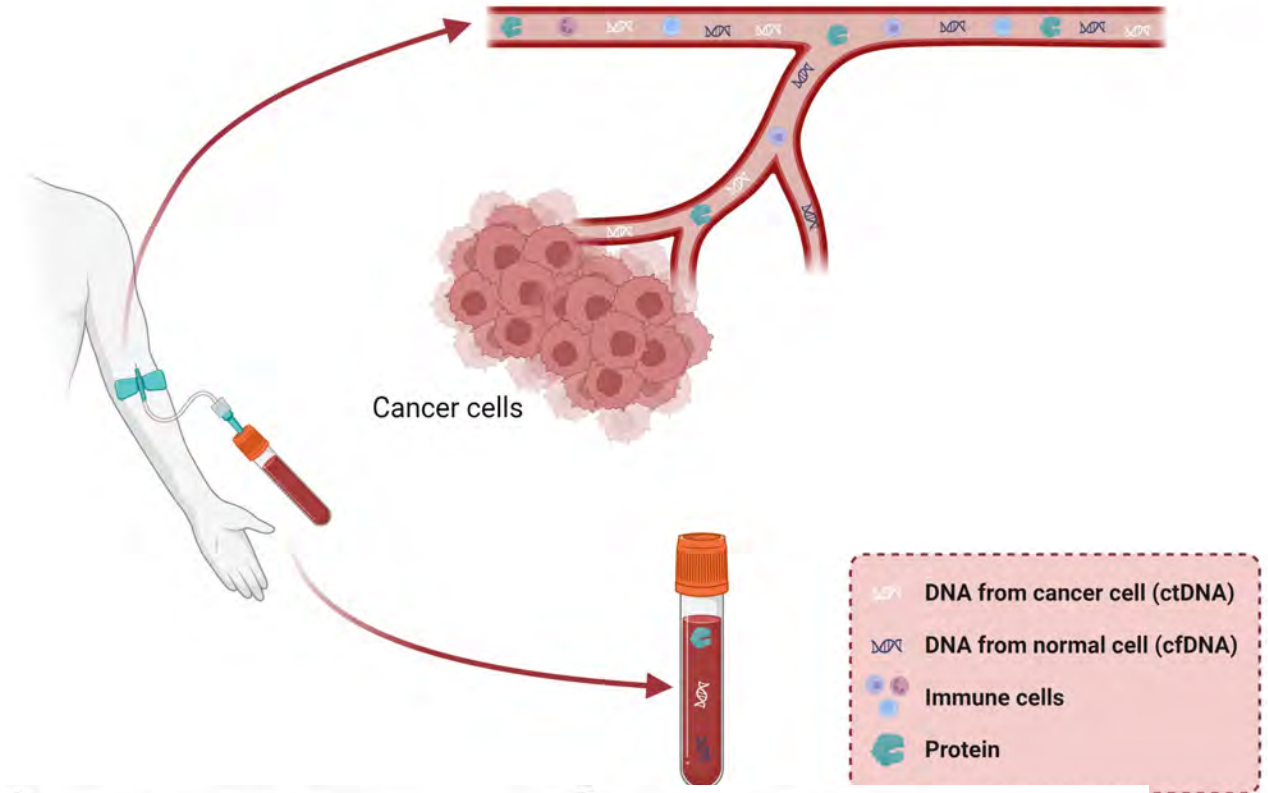
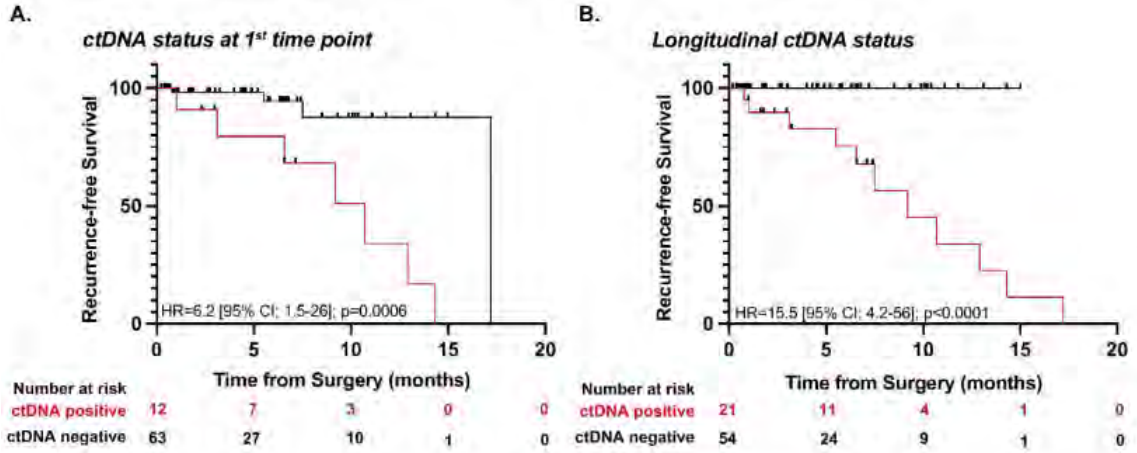




ORIGINAL ARTICLE

Circulating Tumor DNA Analysis Guiding Adjuvant Therapy in Stage II Colon Cancer

Authors: Jeanne Tie, M.D., Joshua D. Cohen, M.Phil., Kamel Lahouel, Ph.D., Serigne N. Lo, Ph.D., Yuxuan Wang, M.D., Ph.D., Suzanne Kosmider, M.B., B.S., Rachel Wong, M.B., B.S., +23, for the DYNAMIC Investigators* Author Info & Affiliations

Published June 4, 2022 | N Engl J Med 2022;386:2261-2272 | DOI: 10.1056/NEJMoa2200075 | VOL. 386 NO. 24

Does ctDNA collected longitudinally during endometrial cancer treatment predict prognosis?

Recio et al Gyn Onc 2024

DUO-E met its dual primary endpoints

Randomized, placebo-controlled, double-blind study[1]

Patients

- Newly diagnosed Stage III/IV or recurrent endometrial cancer
- Known MMR status
- Naïve to first-line systemic anticancer treatment
- Naïve to PARP inhibitors and immune-mediated therapy
- All histologies except sarcomas

N=718

R 1:1:1

Stratified by:

- MMR status (proficient vs deficient)
- Disease status (recurrent vs newly diagnosed)
- Geographic region (Asia vs non-Asia)

	Chemotherapy phase (six cycles)	Maintenance phase
CP	CP	Placebo
CP+D	CP + durvalumab	Durvalumab
CP+D+O	CP + durvalumab	Durvalumab + olaparib

Patients without disease progression

Treatment until disease progression, unacceptable toxicity, or other discontinuation criteria were met

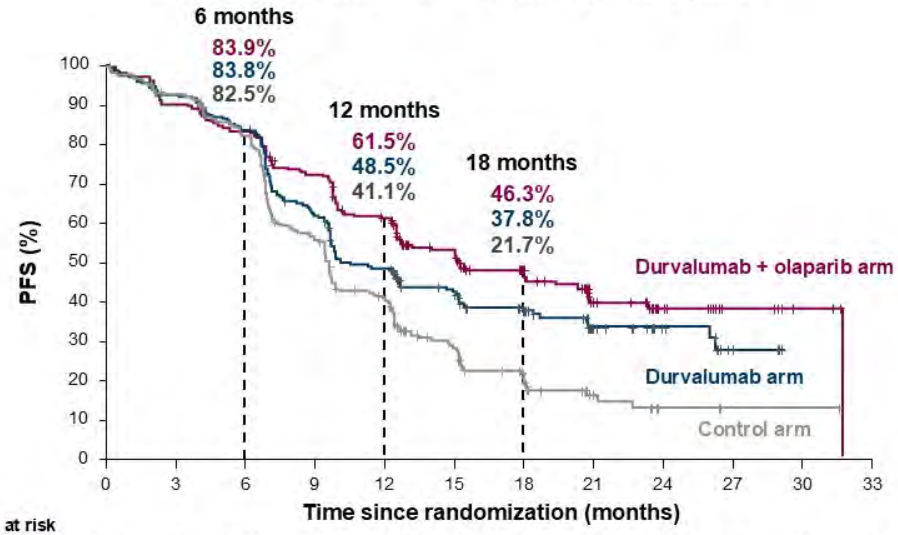
Endpoints

Primary (ITT): PFS (RECIST per investigator) in CP+D versus CP and CP+D+O versus CP

Secondary (ITT): OS (key secondary) and safety

Prespecified exploratory analyses: subpopulation analyses of PFS by MMR status

ITT population: PFS – primary endpoints



No. at risk												
Durvalumab + olaparib arm	239	214	198	169	139	95	51	30	16	7	3	0
Durvalumab arm	238	211	188	138	105	69	45	26	13	5	0	0
Control arm	241	213	184	125	86	45	26	10	3	1	1	0

	Control arm (N=241)	Durvalumab arm (N=238)	Durvalumab + olaparib arm (N=239)
Events, n (%)	173 (71.8)	139 (58.4)	126 (52.7)
Median PFS (95% CI), months	**9.6** (9.0–9.9)	**10.2** (9.7–14.7)	**15.1** (12.6–20.7)
HR (95% CI) vs control		**0.71** (0.57–0.89); **p=0.003**	**0.55** (0.43–0.69); **p<0.0001**

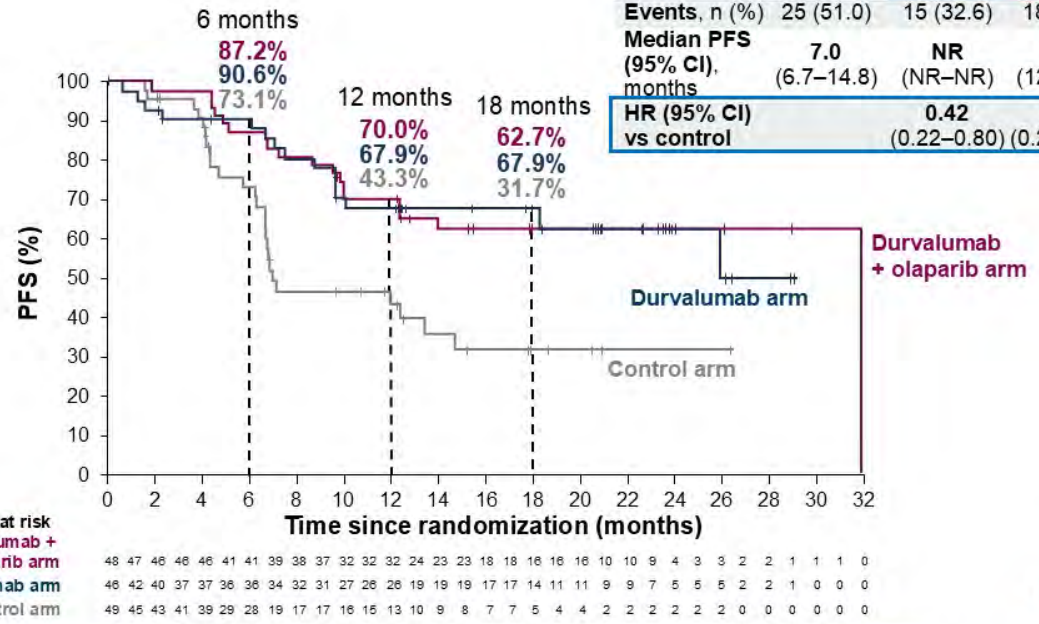
CI, confidence interval; CP, carboplatin + paclitaxel; D, durvalumab; HR, hazard ratio; ITT, intent to treat; MMR, mismatch repair; O, olaparib; OS, overall survival; PARP, poly(ADP-ribose) polymerase; PFS, progression-free survival; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.

1. Westin SN, et al. *J Clin Oncol* 2024;42:283–99. Kaplan–Meier figure borrowed with permission from Westin SN, et al. Durvalumab plus carboplatin/paclitaxel followed by maintenance durvalumab with or without olaparib as first-line treatment for advanced endometrial cancer: the phase III DUO-E trial. *J Clin Oncol* 2024;42:283–99: https://ascopubs.org/doi/full/10.1200/JCO.23.02132. © American Society of Clinical Oncology.

DUO-E: PFS based on mismatch repair status

PFS in the dMMR subpopulation

	Control (N=49)	D arm (N=46)	D+O arm (N=48)
Events, n (%)	25 (51.0)	15 (32.6)	18 (37.5)
Median PFS (95% CI), months	**7.0** (6.7–14.8)	**NR** (NR–NR)	31.8 (12.4–NR)
HR (95% CI) vs control		**0.42** (0.22–0.80)	0.41 (0.21–0.75)



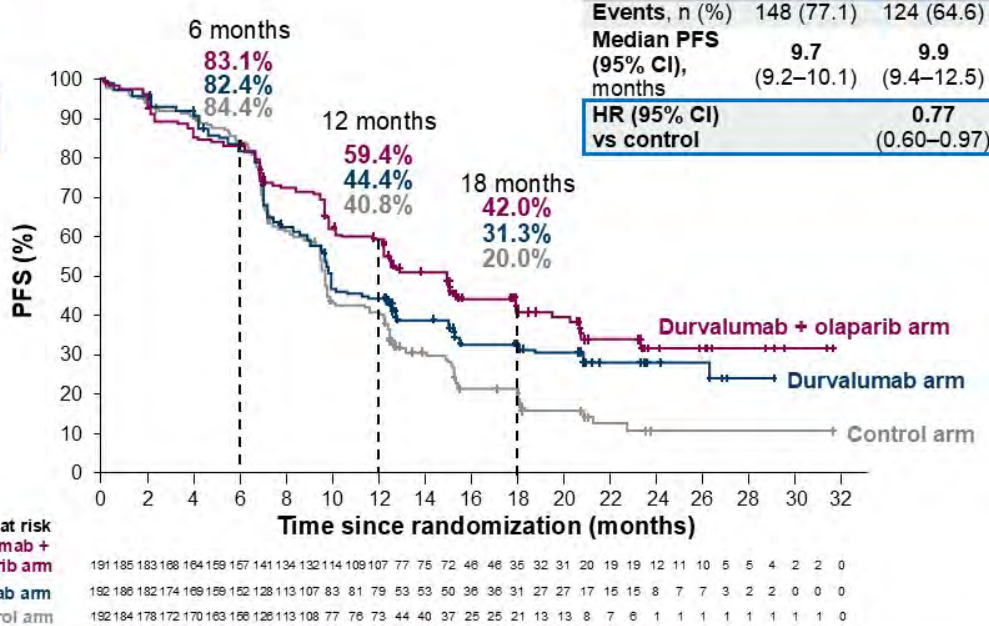
No. at risk

Durvalumab + olaparib arm	48	47	46	46	46	41	41	39	38	37	32	32	32	24	23	23	18	18	16	16	16	10	10	9	4	3	3	2	2	1	1	1	0
Durvalumab arm	46	42	40	37	37	36	36	34	32	31	27	26	26	19	19	19	17	17	14	11	11	9	9	7	5	5	5	2	2	1	0	0	0
Control arm	49	45	43	41	39	29	28	19	17	17	16	15	13	10	9	8	7	7	5	4	4	2	2	2	2	2	2	0	0	0	0	0	0

- The greatest benefit with CP + durvalumab versus CP was in the dMMR subpopulation[1]

PFS in the pMMR subpopulation

	Control (N=192)	D arm (N=192)	D+O arm (N=191)
Events, n (%)	148 (77.1)	124 (64.6)	108 (56.5)
Median PFS (95% CI), months	**9.7** (9.2–10.1)	**9.9** (9.4–12.5)	**15.0** (12.4–18.0)
HR (95% CI) vs control		**0.77** (0.60–0.97)	**0.57** (0.44–0.73)



No. at risk

Durvalumab + olaparib arm	191	185	183	168	164	159	157	141	134	132	114	109	107	77	75	72	46	46	35	32	31	20	19	19	12	11	10	5	5	4	2	2	0
Durvalumab arm	192	186	182	174	169	159	152	128	113	107	83	81	79	53	53	50	36	36	31	27	27	17	15	15	8	7	7	3	2	2	0	0	0
Control arm	192	184	178	172	170	163	156	126	113	108	77	76	73	44	40	37	25	25	21	13	13	8	7	6	1	1	1	1	1	1	1	0	

- In the pMMR subpopulation, the addition of olaparib further enhanced the PFS benefit[1]

Here, we present post hoc exploratory longitudinal circulating tumor (ct)DNA analyses

dMMR, mismatch repair deficient; NR, not reported; pMMR, mismatch repair proficient. 1. Westin SN, et al. *J Clin Oncol* 2024;42:283–99. Kaplan–Meier figure borrowed with permission from Westin SN, et al. Durvalumab plus carboplatin/paclitaxel followed by maintenance durvalumab with or without olaparib as first-line treatment for advanced endometrial cancer: the phase III DUO-E trial. *J Clin Oncol* 2024;42:283–99: https://ascopubs.org/doi/full/10.1200/JCO.23.02132. © American Society of Clinical Oncology.

DUO-E: sum[illegible] the biomarker-evaluable population (BEP)

Confusing

Summary of the BEP

718 pts in the ITT population

352 pts consented, with plasma samples evaluable for ctDNA testing **(total BEP)**

347 pts in the **baseline BEP (C1D1)**

349 pts had samples evaluable for ctDNA at **C3D1**

350 pts had samples evaluable for ctDNA at **C7D1**

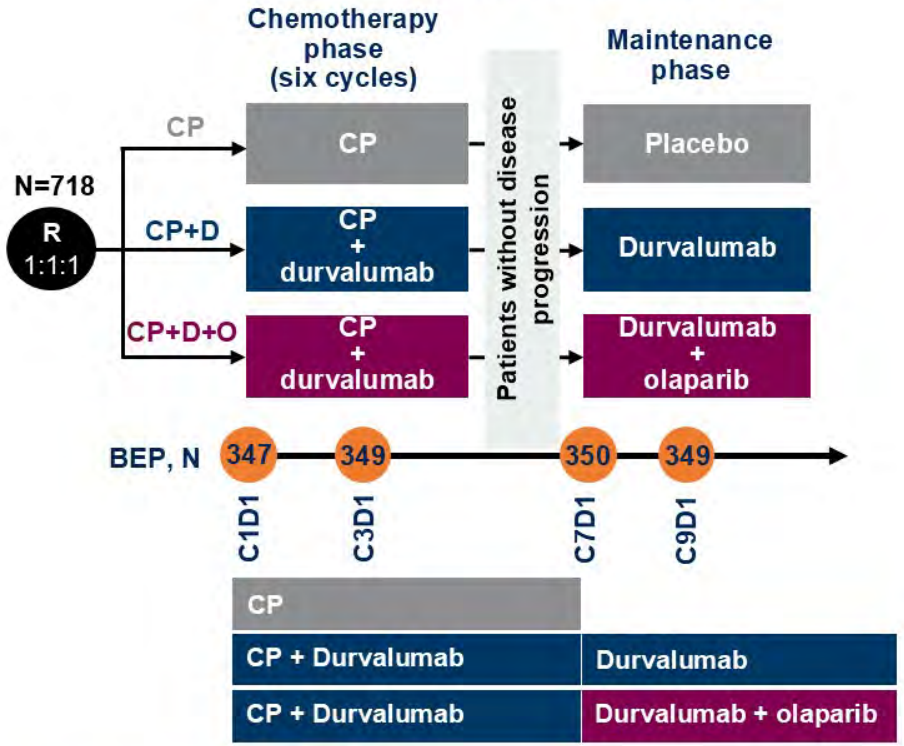
349 pts had samples evaluable for ctDNA at **C9D1**

341 patients had samples evaluable for ctDNA testing at all 4 timepoints

ctDNA analysis by treatment arm

CP arm	118 pts
CP+D arm	113 pts
CP+D+O arm	121 pts

Study design and ctDNA analysis



- Samples were collected at baseline (C1D1), during the chemotherapy phase (C3D1), prior to maintenance initiation (C7D1), and during the maintenance phase (C9D1)
- ctDNA was analyzed using the methylation-based Guardant Infinity™ assay (Guardant Health, Palo Alto, CA)

C, cycle; D, day; pts, patients.

PRESENTED BY: Prof. Shannon N. Westin

DUO-E ctDNA analysis: baseline characteristics

Characteristics were generally comparable between BEP and ITT populations

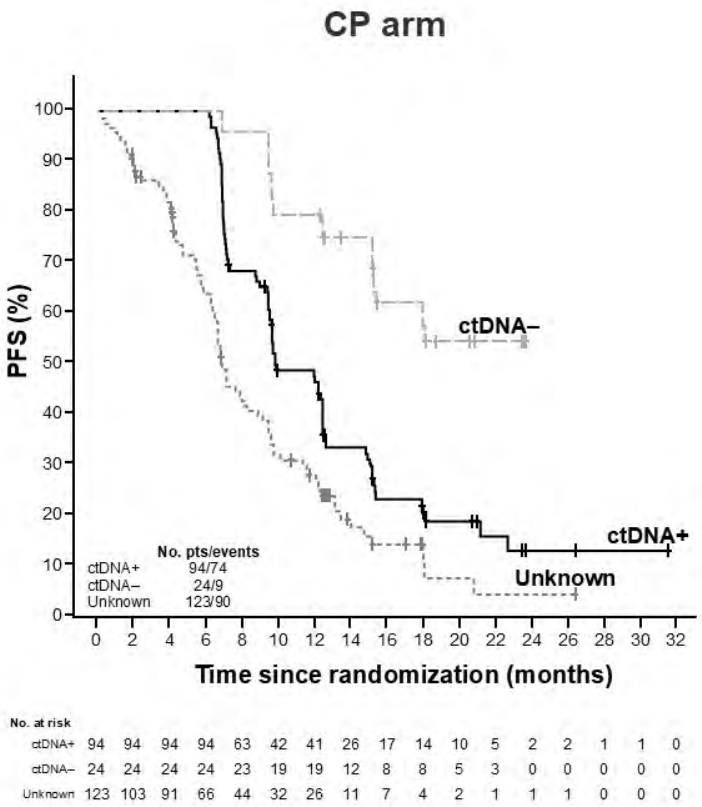
		ITT (N=718)			BEP (N=352)		
		CP (n=241)	CP+D (n=238)	CP+D+O (n=239)	CP (n=118)	CP+D (n=113)	CP+D+O (n=121)
Age, years	Median (range)	64 (31–85)	64 (22–84)	63 (27–86)	64 (36–85)	64 (28–78)	64 (29–84)
MMR status, n (%)	dMMR	49 (20)	46 (19)	48 (20)	14 (12)	23 (20)	28 (23)
	pMMR	192 (80)	192 (81)	191 (80)	104 (88)	90 (80)	93 (77)
ctDNA status, n (%)	ctDNA+	94 (39)	96 (40)	88 (37)	94 (80)	96 (85)	88 (73)
	ctDNA–	24 (10)	16 (7)	29 (12)	24 (20)	16 (14)	29 (24)
	Unknown	123 (51)	126 (53)	122 (51)	0 (0)	1 (1)	4 (3)
Disease type, n (%)	Newly diagnosed	115 (48)	113 (48)	114 (48)	56 (48)	60 (53)	65 (54)
	Recurrent	126 (52)	125 (53)	125 (52)	62 (53)	53 (47)	56 (46)
Region, n (%)	Asia	68 (28)	68 (29)	67 (28)	34 (29)	33 (29)	36 (30)
	Rest of the world	173 (72)	170 (71)	172 (72)	84 (71)	80 (71)	85 (70)
ECOG, n (%)	Normal activity	156 (65)	156 (66)	166 (70)	88 (75)	84 (74)	92 (76)
	Restricted activity	85 (35)	81 (34)	73 (31)	30 (25)	29 (26)	29 (24)

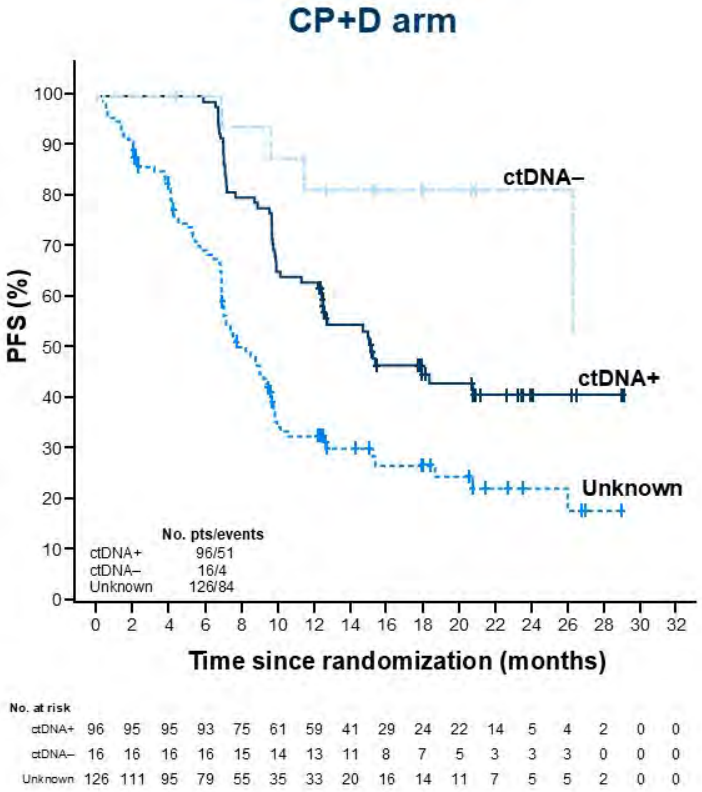
Proportions of patients for each characteristic may not sum to 100%, as percentages are presented rounded to whole numbers which may have resulted in rounding discrepancies

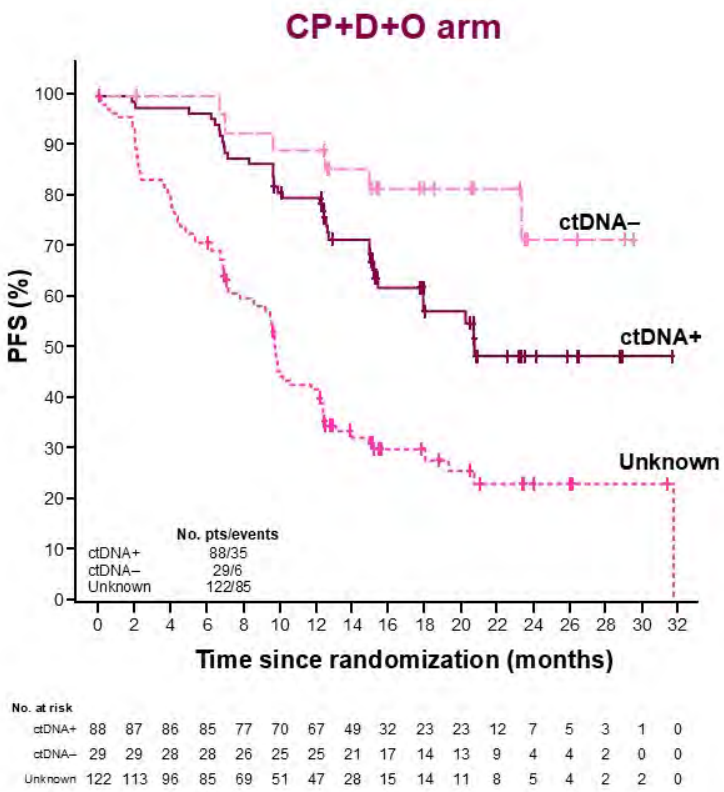
ECOG, Eastern Cooperative Oncology Group.

DUO-E: PFS rate by treatment and baseline ctDNA status in the ITT population

Baseline ctDNA positivity was associated with higher risk of progression across treatment arms







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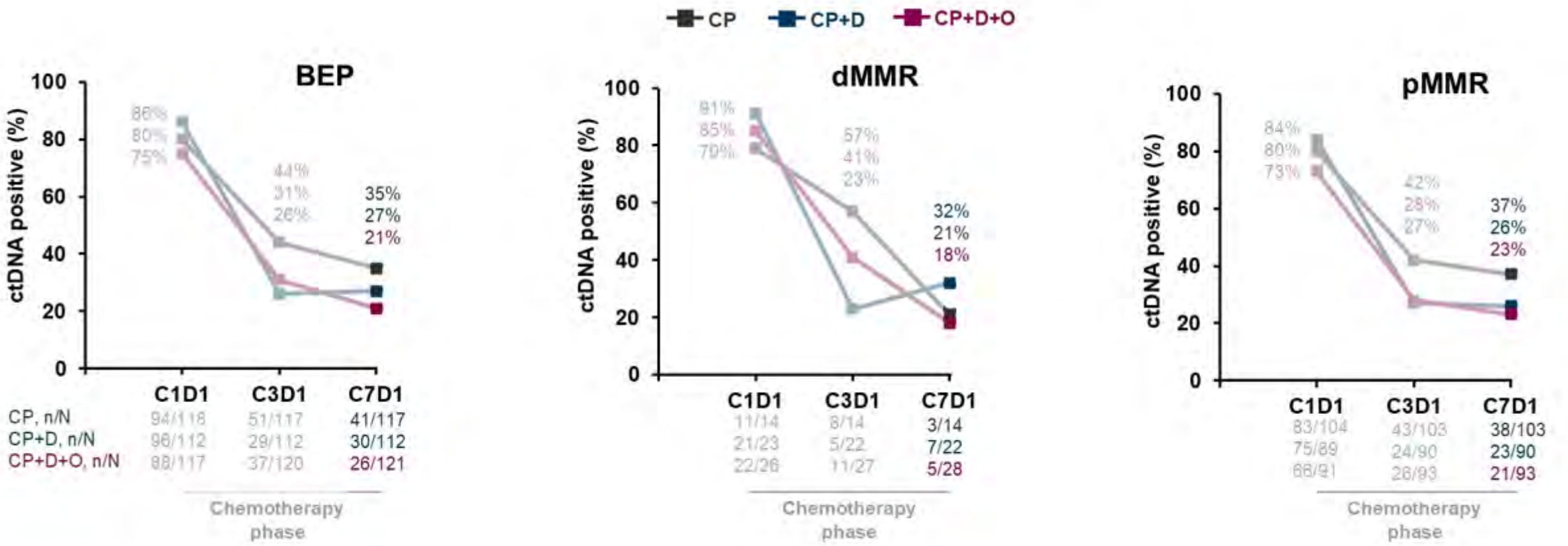
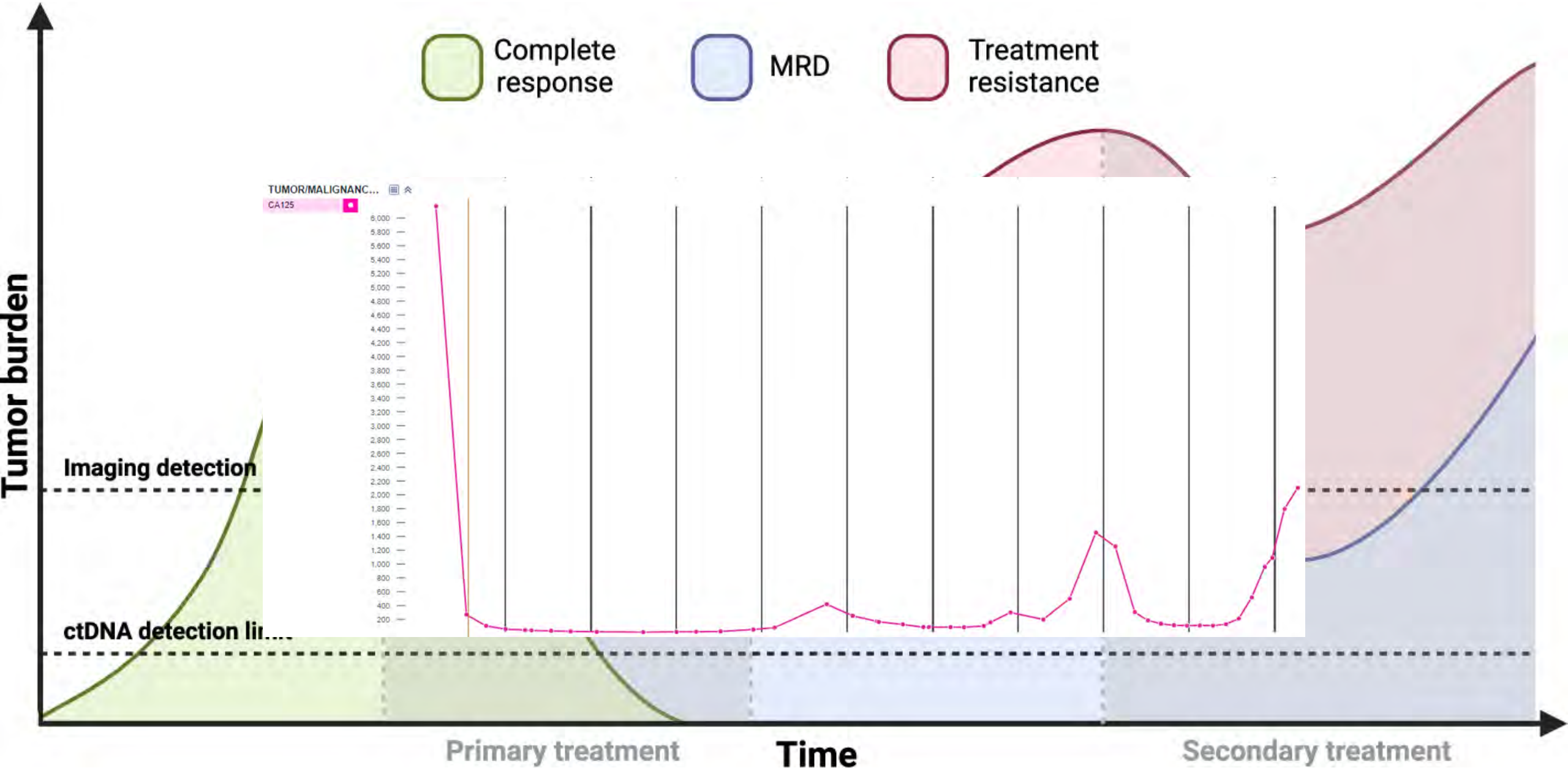
Treatment results in reduction of ctDNA in all groups and all types of therapy

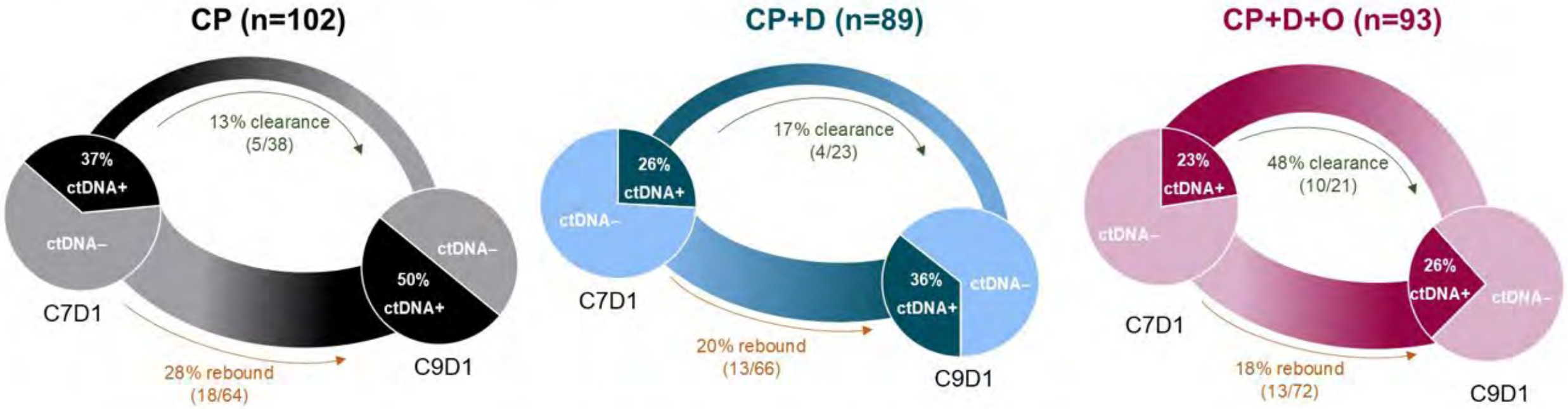




Bartolomucci, A., Nobrega, M., Ferrier, T. *et al.* Circulating tumor DNA to monitor treatment response in solid tumors and advance precision oncology. *npj Precis. Onc.* **9**, 84 (2025). https://doi.org/10.1038/s41698-025-00876-y

DUO-E: durvalumab and olaparib mediated ctDNA changes during the maintenance phase (C7D1–C9D1) in pMMR patients

Addition of olaparib may be driving novel anti-tumor activity in pMMR tumors not seen with durvalumab alone



- Durvalumab led to 4% more clearance of ctDNA and 8% less rebound, vs CP arm
- Addition of olaparib to durvalumab led to 35% more clearance of ctDNA and 10% less rebound, vs CP arm

Next step is to see the correlation between rebound and progression on imaging.

ME TRYING TO REMEMBER ALL THE NAMES OF THE DRUGS LIKE I DID WHEN I TOOK BOARDS

2025 ASCO ANNUAL MEETING

Phase 2 study of letrozole, abemaciclib and metformin in estrogen receptor (ER) positive, recurrent endometrial cancer (EC)

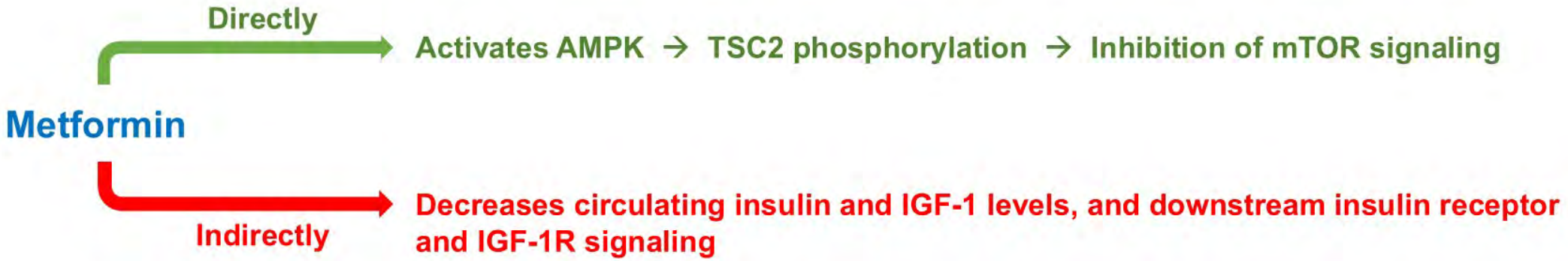
Panagiotis A. Konstantinopoulos, Ningxuan Zhou, Richard T. Penson, Susana Campos, Carolyn Krasner, Alexi A. Wright, Rebecca Porter, Neil Horowitz, Sara Bouberhan, Hannah Sawyer, Lani Koppermann, Martin Hayes, Madeline Polak, Meghan Shea, Page Widick, Su-Chun Cheng, Cesar Castro, Ursula A. Matulonis, Elizabeth K. Lee

Rationale for combined ER, CDK4/6 and PI3K inhibition in EC

- Previous studies have demonstrated promising activity of combined hormonal therapy and CDK4/6 inhibition in ER positive endometrioid EC*
- ctDNA sequencing at the time of progression through letrozole/abemaciclib demonstrated frequent acquired PI3K pathway alterations suggesting that there is a **strong selective pressure to activate the PI3K pathway upon exposure to combined aromatase and CDK4/6 inhibition** in EC**
- Preclinical studies have demonstrated **significant synergism with simultaneous inhibition** of the ER, CDK4/6 and PI3K pathways***

** Konstantinopoulos et al. JCO 2023, Green et al. Clin Can Res 2024, Mirza et al. Gyn Onc 2025*
*** Konstantinopoulos et al. JCO Precision Oncology 2025 *** Vora et al. Cancer Cell 2014, Herrera-Abreu et al. Cancer Res 2016*

Metformin inhibits PI3K pathway signaling



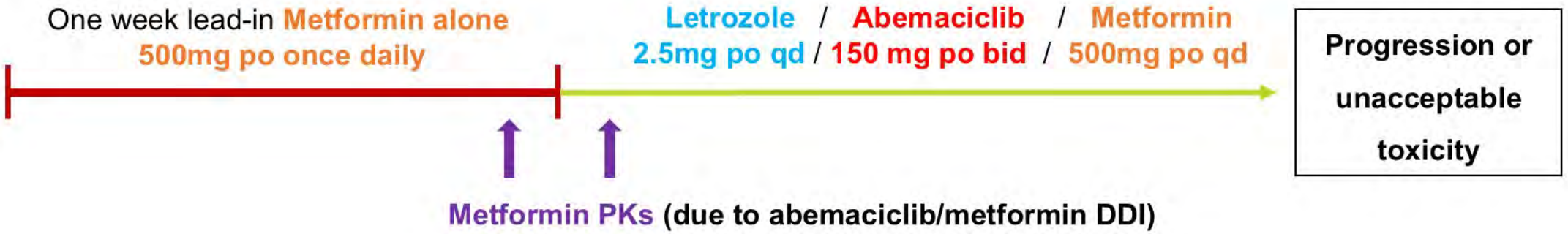
- Window of opportunity (WOO) studies in endometrial cancer have demonstrated that metformin **at a dose of 850mg orally daily** **decreases phospho-AKT and phospho-S6rp in endometrial cancer tissue samples** as well as **decreases circulating insulin and IGF-1 levels***

- Based on these considerations, **we hypothesized that PI3K inhibition using metformin may further enhance the activity of letrozole/abemaciclib in endometrial cancer**

PRESENTED BY: Panagiotis A. Konstantinopoulos

* *Schuler et al. Cancer Med 2015, Soliman et al. Gyn Onc 2016*

Treatment Schema / Trial Design



DESIGN: **Two Primary Endpoints (ORR and PFS6)**

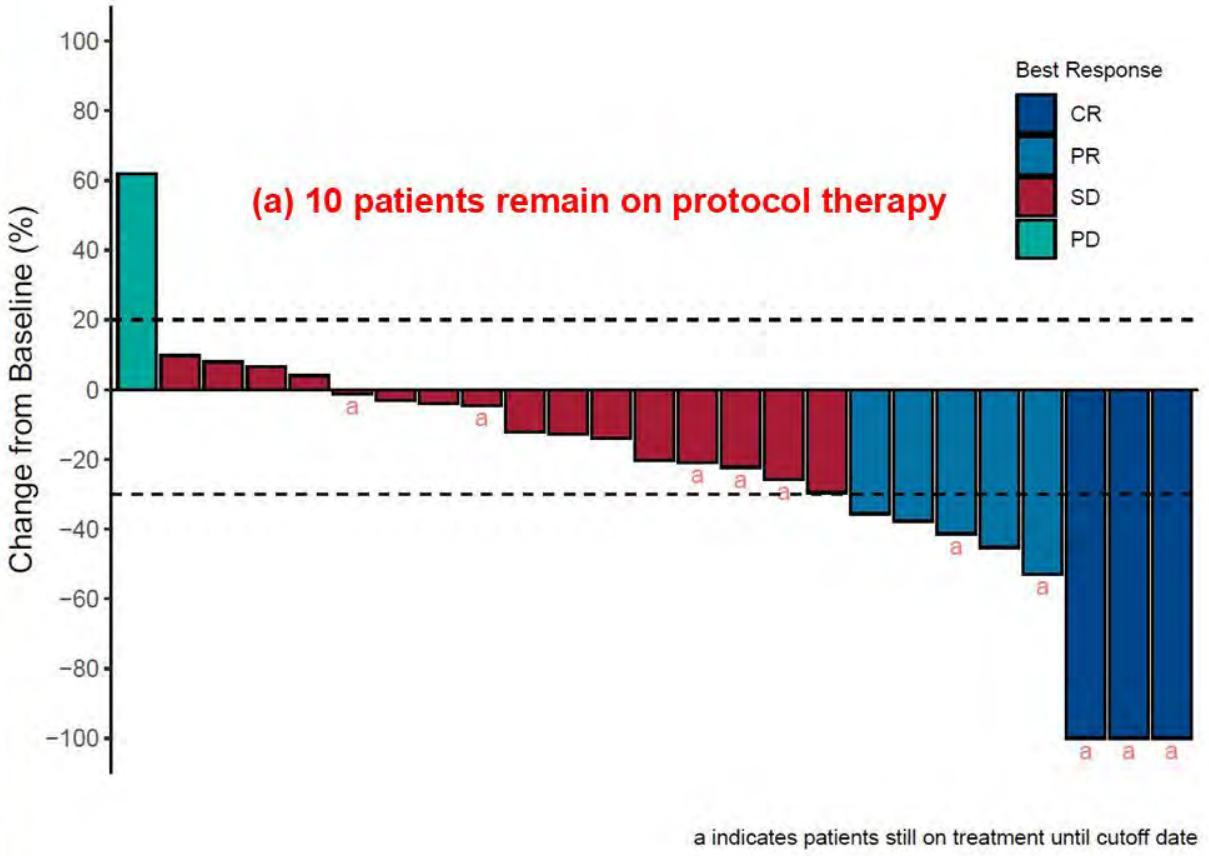
Target Accrual: **25 patients**

- **If ≥6 patients exhibit OR,** lower bound of binomial 90% CI exceeds 10%
- **If ≥9 patients exhibit PFS6,** lower bound of binomial 90% CI exceeds 20%

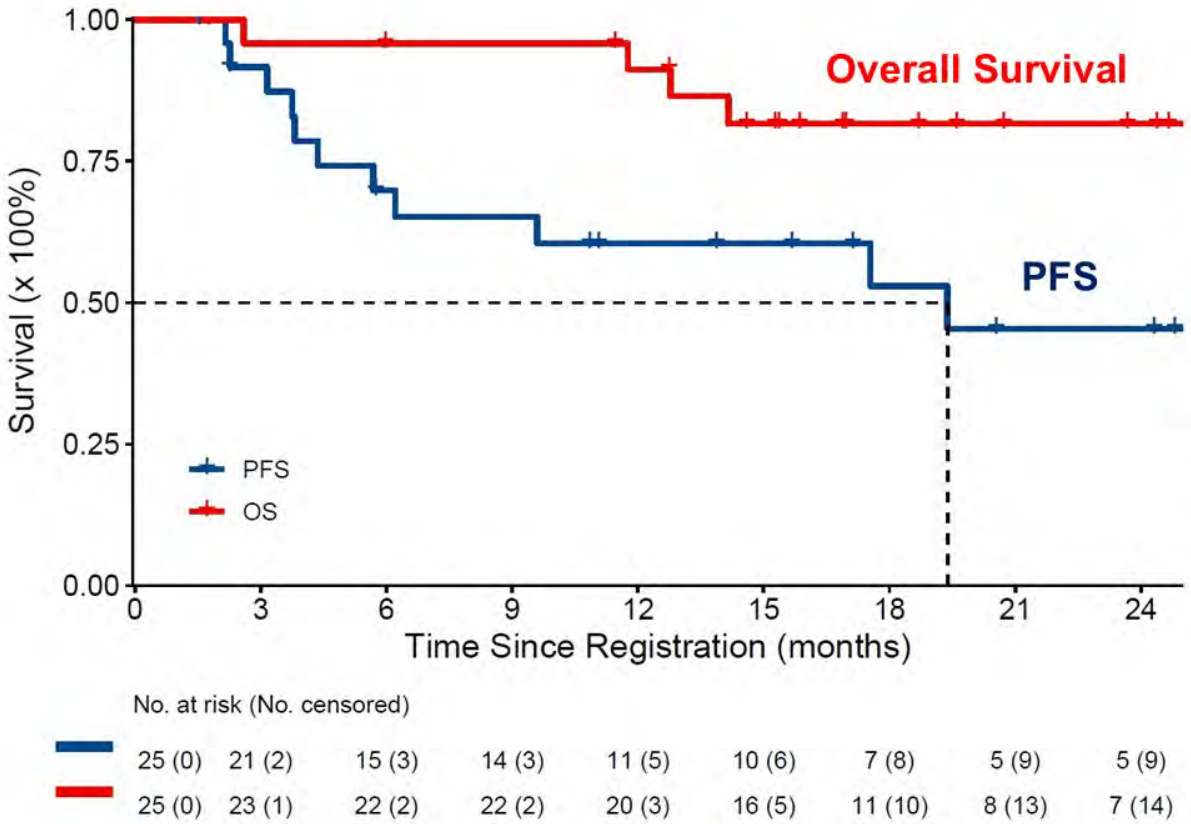
PATIENT CHARACTERISTICS (n=25)	
AGE	
Median	64.2 (49.7 – 84.2) years
RACE	
Black or African American	2 (8%)
Other	3 (12%)
White	20 (80%)
GRADE	
1	13 (52%)
2	8 (32%)
3	4 (16%)
PRIOR HORMONAL THERAPY	
Yes	18 (72%)
No	7 (28%)
PRIOR SYSTEMIC THERAPIES	
Median	2 (0 – 8)

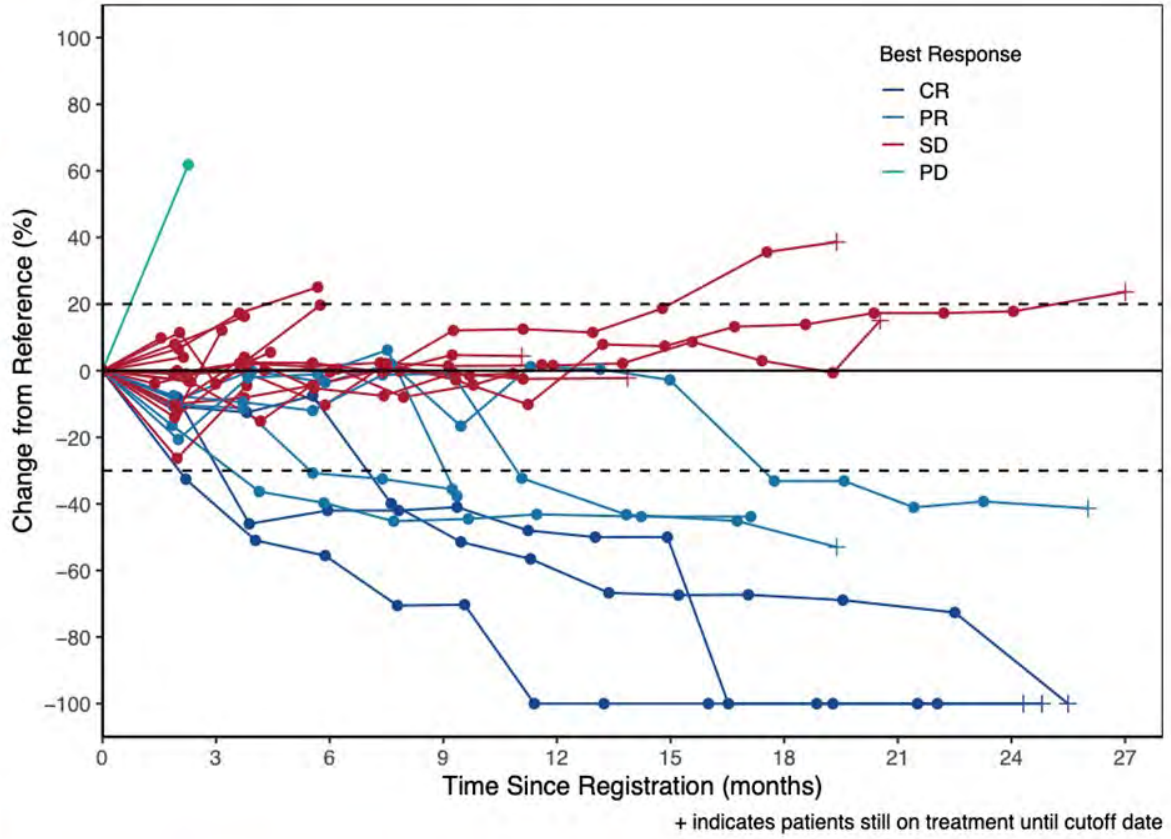
Objective Response Rate (ORR)

RESPONSE	Overall (N=25) n (%)
Complete Response (CR)	3 (12%) (1 unconfirmed CR but confirmed PR)
Partial Response (PR)	5 (20%) (1 unconfirmed)
Stable Disease (SD) ≥ 6 months	7 (28%)
SD < 6 months	9 (36%)
Progressive Disease	1 (4%)
ORR	**8 (32%)**



Progression Free Survival (PFS)





Median PFS 19.4 months (median follow-up time 18.7 months)
Kaplan Meier estimate of PFS6: 69.8% (95% CI: 46.9% to 84.3%)

Treatment Related Adverse Events (top 10 ranked by # G3+)

N=25 patients	Grade 1	Grade 2	Grade 3
Decreased neutrophil count	3(12%)	7(28%)	**6(24%)**
Fatigue	7(28%)	7(28%)	**4(16%)**
Anemia	6(24%)	10(40%)	**2(8%)**
Increased aspartate aminotransferase	4(16%)	0(0%)	**2(8%)**
Decreased platelet count	10(40%)	1(4%)	1(4%)
Increased alanine aminotransferase	3(12%)	0(0%)	1(4%)
Hepatic infection	0(0%)	0(0%)	1(4%)
Hypermagnesemia	0(0%)	0(0%)	1(4%)
Hypertension	0(0%)	0(0%)	1(4%)
Diarrhea	**13(52%)**	**3(12%)**	0(0%)

Treatment Related Adverse Events (top 10 ranked by # G3+)

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Inc			**2(8%)**
			1(4%)
			1(4%)
Hepatic infection	0(0%)	0(0%)	1(4%)
Hypermagnesemia	0(0%)	0(0%)	1(4%)
Hypertension	0(0%)	0(0%)	1(4%)
Diarrhea	**13(52%)**	**3(12%)**	0(0%)

No patients discontinued protocol therapy for toxicity

Molecular Profiling

- **4 *TP53* mutated** and **21 NSMP tumors,** (no MMRD, no *POLE* mutated)
- Of the **21 NSMP tumors**, **5 had *RB1* or *CCNE1* alterations**; such alterations have been previously associated with *de novo* or acquired resistance to CDK4/6 inhibition **as they facilitate G1->S phase transition without dependence on CDK4/6**

	NSMP without *CCNE1* and *RB* alterations (N=16)	NSMP with *CCNE1* or *RB* alterations (N=5)	*TP53*-mutated (N=4)
Complete Response	3 (18.8%)	0 (0%)	0 (0%)
Partial Response	5 (31.3%)	0 (0%)	0 (0%)
Stable Disease >= 6 months	6 (37.5%)	0 (0%)	1 (25.0%)
Stable Disease < 6 months	2 (12.5%)	5 (100%)	2 (50.0%)
Progressive Disease	0 (0%)	0 (0%)	1 (25.0%)
Objective Response	**8 (50%)**	**0 (0%)**	**0 (0%)**

Significant correlations with ORR and clinical benefit rate

	Objective Response			Clinical Benefit*		
	Yes	No	p value**	Yes	No	p value**
Molecular Subtype			**0.056**			**0.002**
NSMP without *RB1/CCNE1* alterations	8 (50.0%)	8 (50.0%)		14 (87.5%)	2 (12.5%)	
NSMP with *RB1/CCNE1* alterations	0 (0.0%)	5 (100.0%)		0 (0.0%)	5 (100.0%)	
TP53 mutated	0 (0.0%)	4 (100.0%)		1 (25.0%)	3 (75.0%)	
***CTNNB1* mutations**			0.194			**0.018**
Present (n=10)	5 (50.0%)	5 (50.0%)		9 (90.0%)	1 (10.0%)	
Absent (n=15)	3 (20.0%)	12 (80.0%)		6 (40.0%)	9 (60.0%)	

** Objective response or being progression free ≥6 months after initiation of therapy*

*** Two-sided Fisher Exact test*

PRESENTED BY: Panagiotis A. Konstantinopoulos

Conclusions / Key Takeaways

- Addition of metformin to letrozole/abemaciclib is **feasible and tolerable** and appears to **induce deeper and more prolonged responses (including complete responses)** than letrozole/abemaciclib alone
- Tumor profiling revealed several mechanistically relevant candidate predictors of response (***CTNNB1*** mutations) or absence of response (***TP53/RB1/CCNE1*** alterations) which require independent validation
- Responses were observed **regardless of PrgR expression** or **prior receipt of hormonal therapy**
- PK analyses suggest that the **500mg metformin once daily dose** is **sufficient to facilitate PI3K pathway inhibition** based on previous metformin window of opportunity studies in endometrial cancer

Thank you