# Endometrial Cancer – Molecular Driven Management: Role of Immunotherapy

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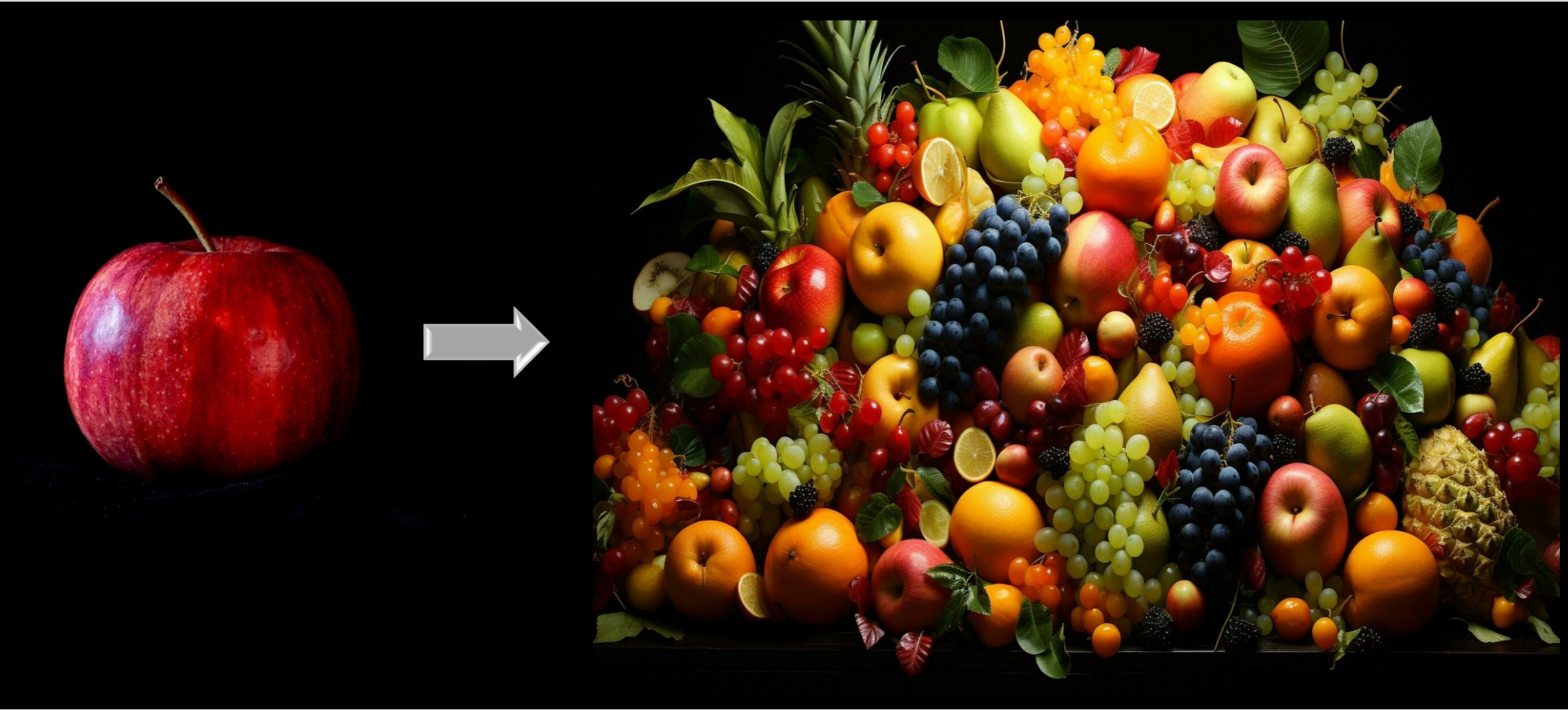
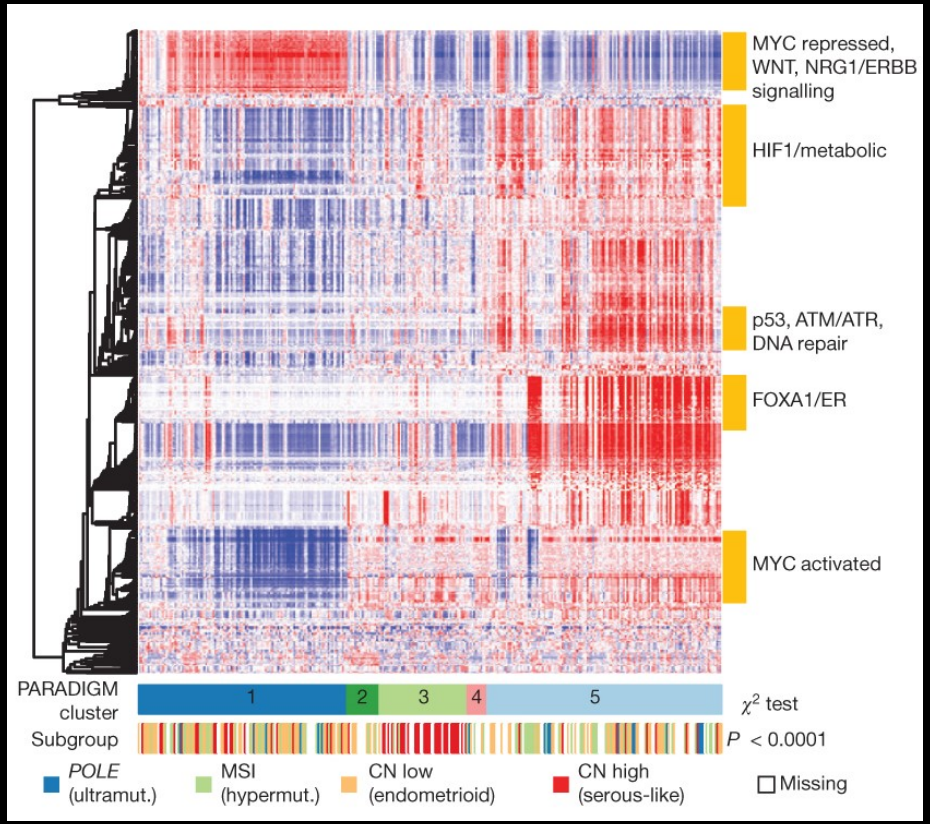
# Declaration of interests

- Funded Research: EU, FWF, Astra Zeneca, Roche
- Honoraria/Expenses: Roche, Novartis, MSD, Pharmamar, Astra Zeneca, GSK
- Consulting/Advisory Board: Roche, Novartis, MSD, Astra Zeneca, Pfizer, Pharmamar, ImmunoGen, Daiichi Sankyo, Biontech, Novocure, Eisai, GSK, Abbvie, Seagen

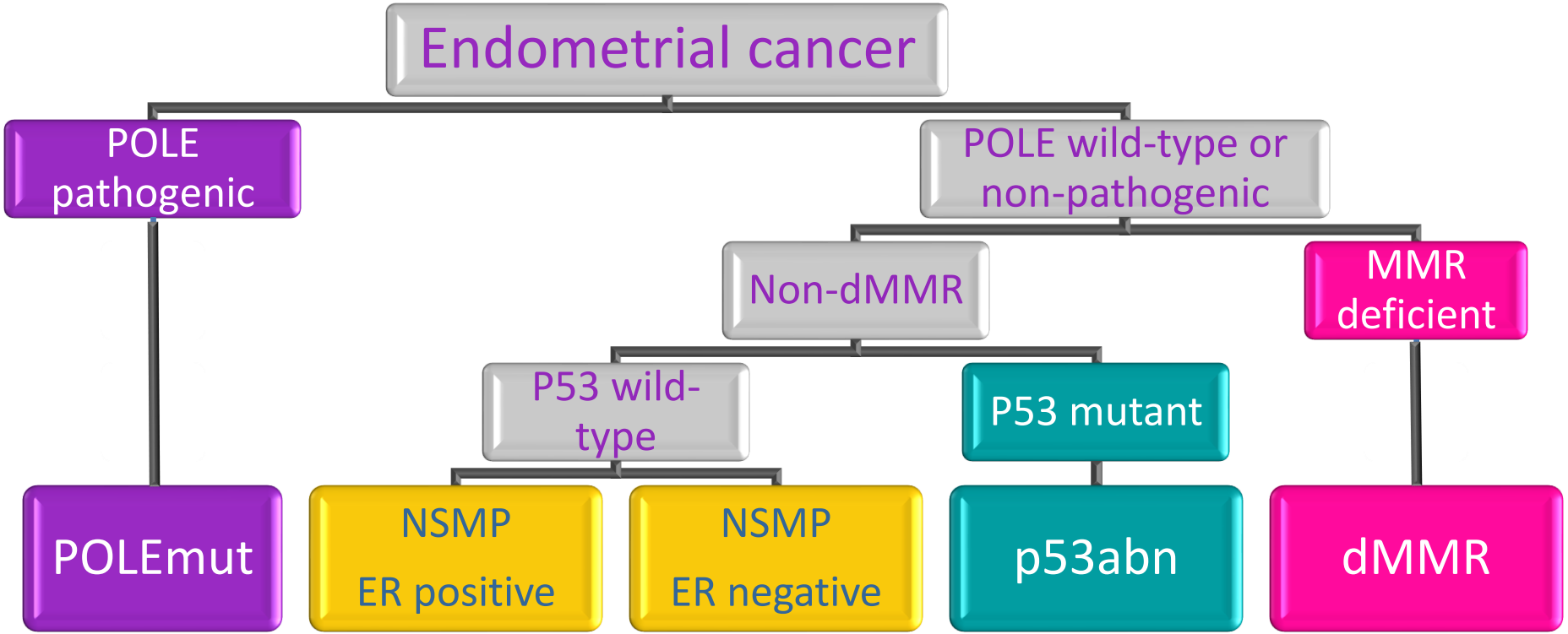
# Cancer: There isn‘t only one disease



# Cancer: There isn‘t only one disease

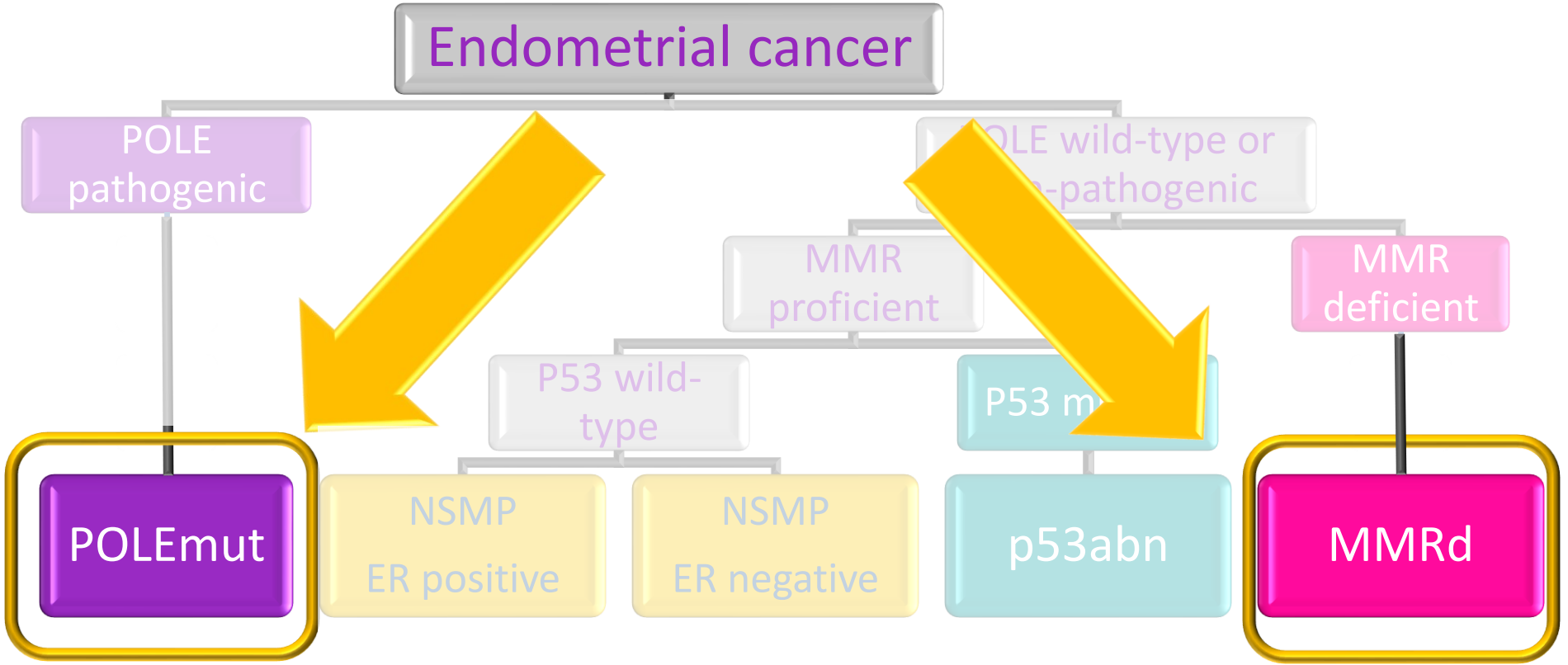


# Molecular classification of endometrial cancer



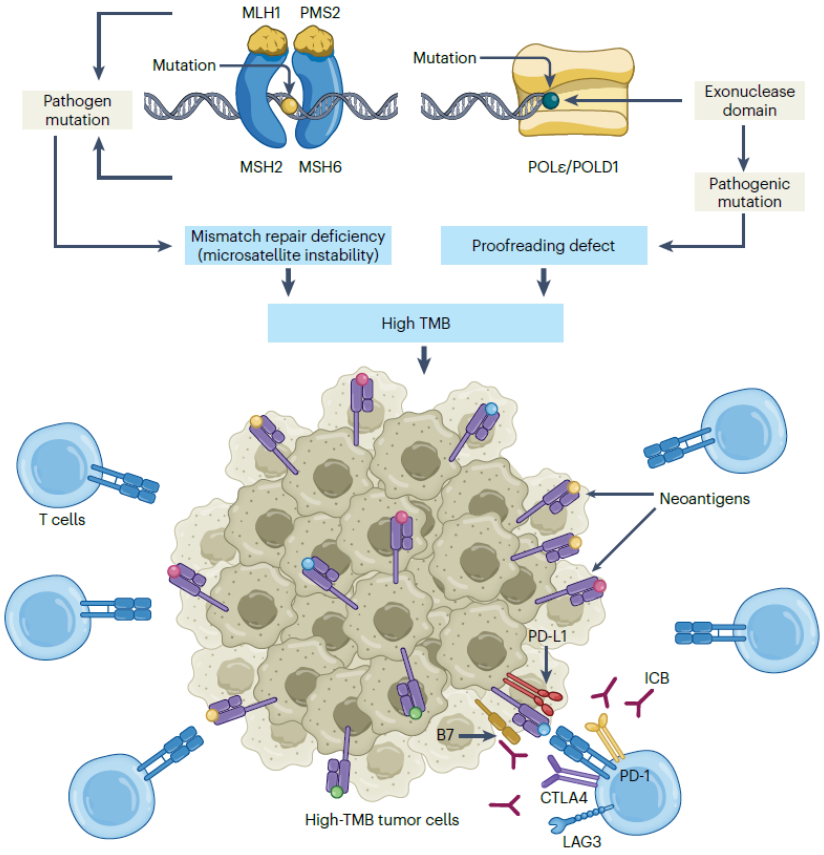

Vermij et al., British Journal of Cancer (2023) 128:1360 – 1368

# Molecular classification of endometrial cancer




Vermij et al., British Journal of Cancer (2023) 128:1360 – 1368

# MMRd and POLE-mutated tumors display high TMB and sensitivity to immunotherapy



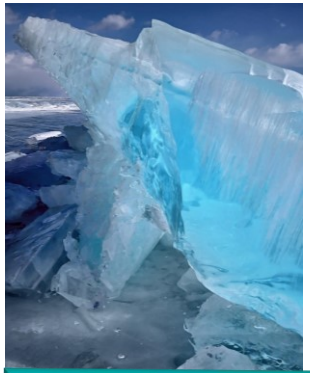

- MMRd and *POLE*-mutant tumors contain DNA repair defects responsible for the accumulation of mutations ➔ high TMB.
- As a consequence, they exhibit elevated numbers of mutation-associated neoantigens.
- Presentation of these neoantigens by MHC-I molecules can facilitate tumor recognition by CD8+ T cells and immune-mediated cancer cell killing.
- Immunotherapy can restore anti-tumor immunity and generate durable tumor responses in patients with either somatic or germinal MMRd or *POLE* mutations.

Emily Alouani, et al. Nature Cancer Dec. 2022

# Expression of IFN-gamma and PD-1 was significantly higher in "HOT" tumors

**"Hot" tumors**

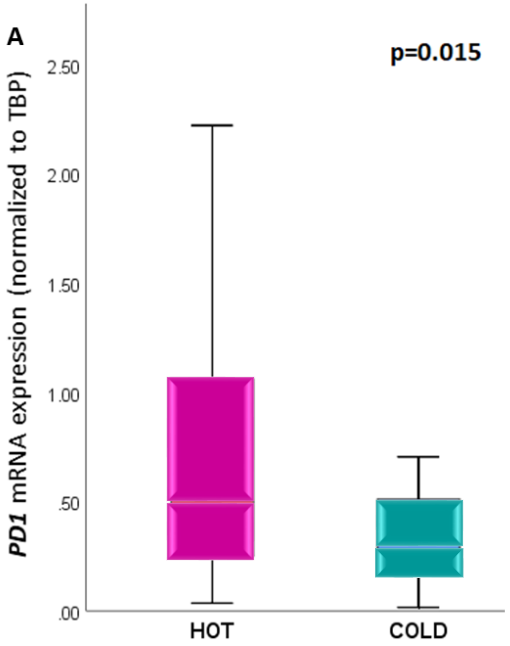
- MMRd
- POLE



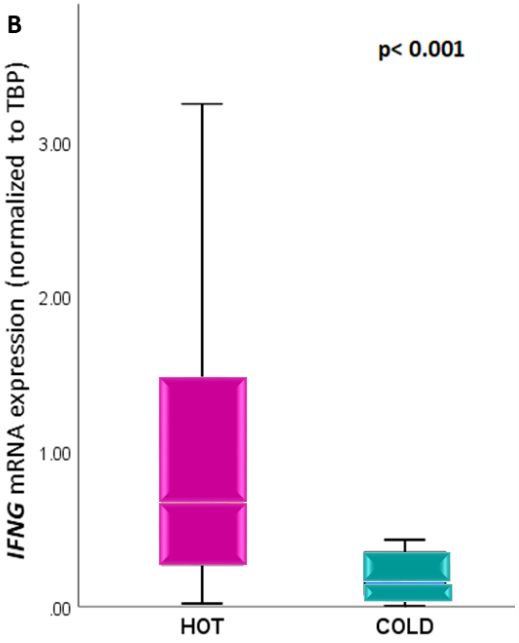
**"Cold" tumors**

- P53abn
- NSMP

PD-1




IFN-gamma




Barin Feroz,.., Christian Marth, et al. Int J Gynecol Cancer 2024 Nov 4

Innsbruck cohort:
EC n=239

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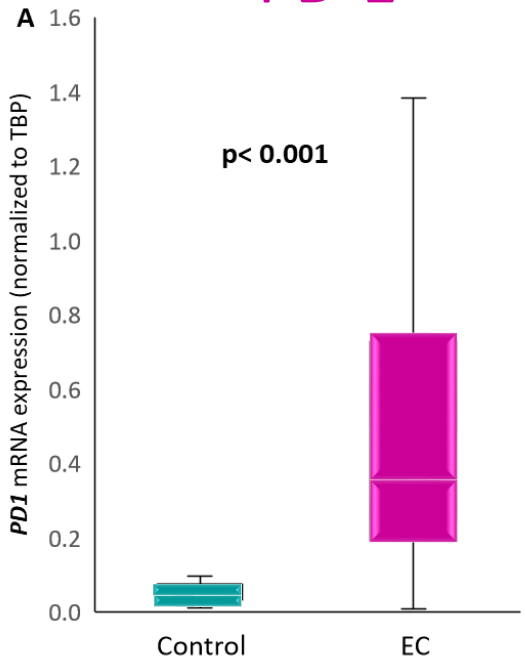
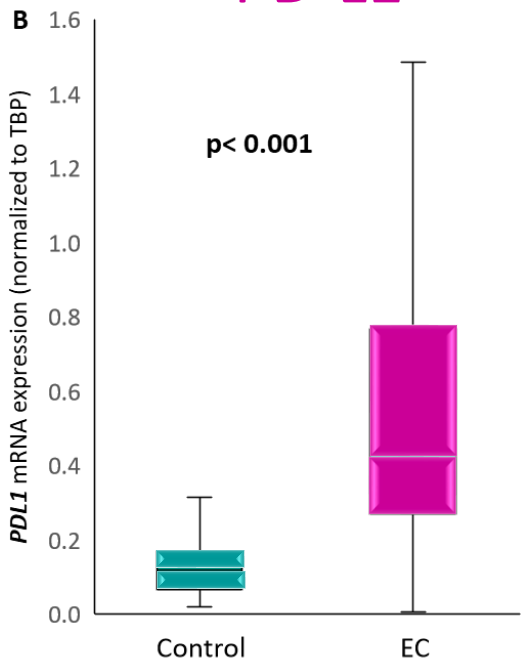
# IFN-gamma, PD-1 and PD-L1 mRNA expression are significantly increased in Endometrial carcinoma tissue compared to the control group

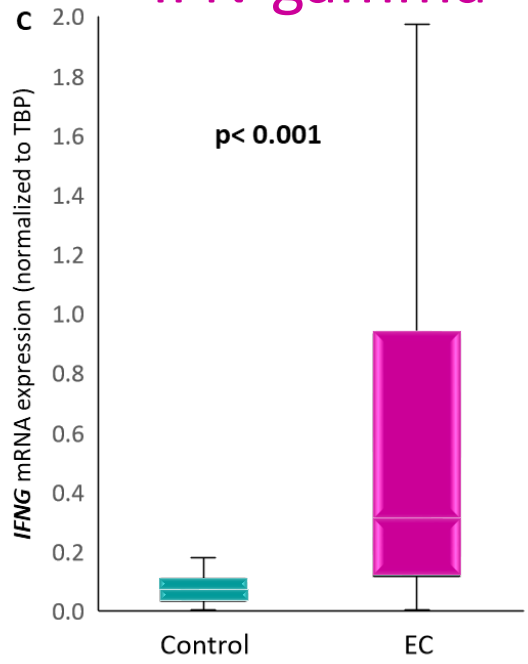
## PD-1




## PD-L1




## IFN-gamma



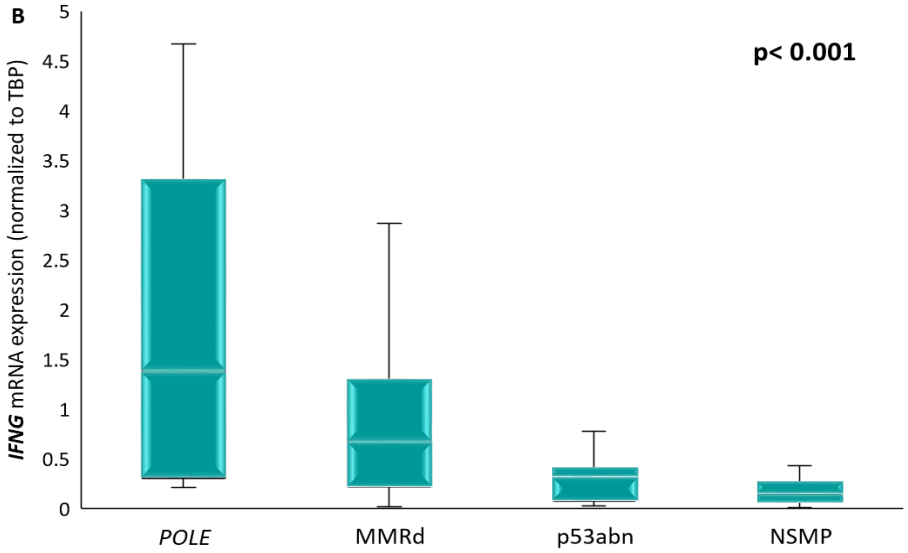

Barin Feroz,.., Christian Marth, et al. Int J Gynecol Cancer 2024 Nov 4

Innsbruck cohort:
EC n=239 and control group n=25

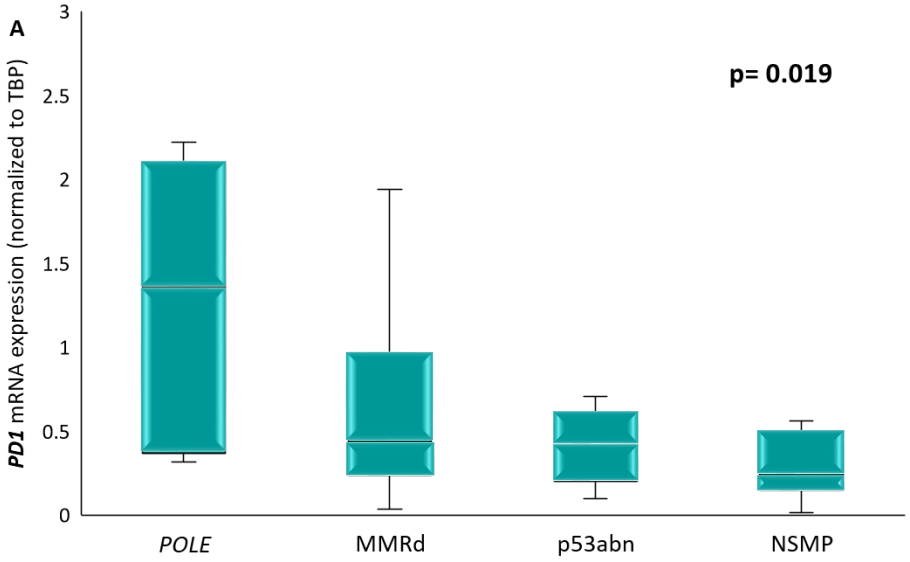
Frauenheilkunde Innsbruck

# Expression of IFN-gamma and PD-1 was highest in POLE mutated tumors

## IFN-gamma




## PD-1



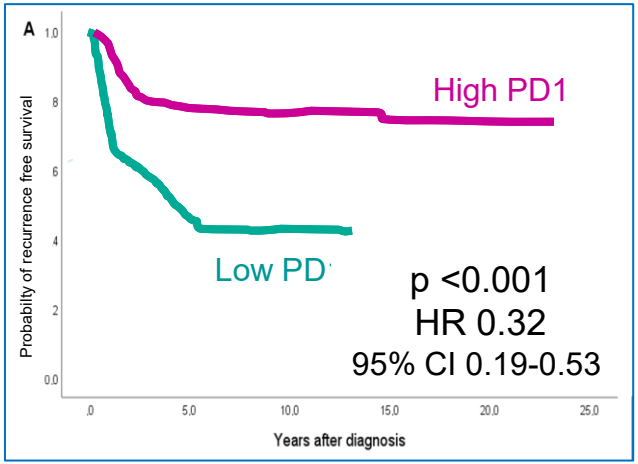

Barin Feroz,.., Christian Marth, et al. Int J Gynecol Cancer 2024 Nov 4

Innsbruck cohort:
EC n=239

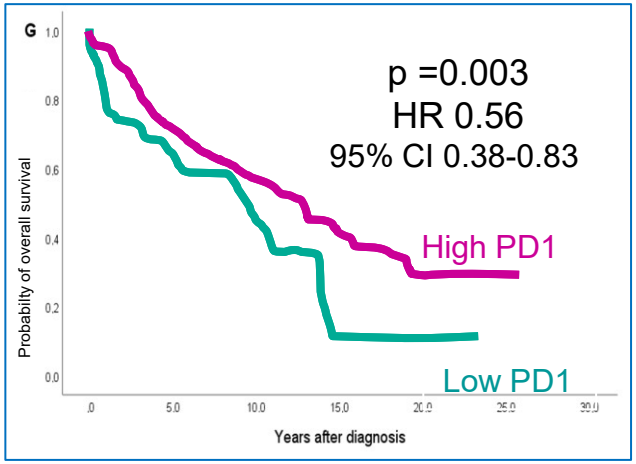
Frauenheilkunde Innsbruck

# High expression of PD-1 was associated with better outcome: RFS, OS, and DSS

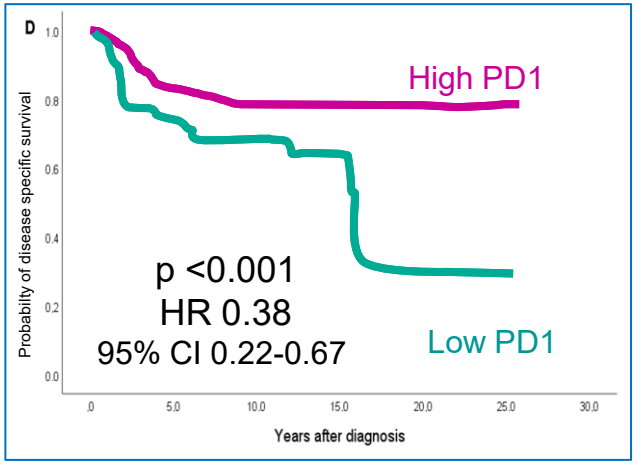
**RFS**




**OS**




**DSS**



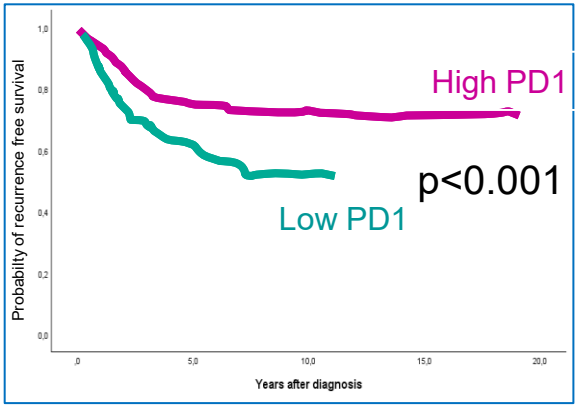

Innsbruck Cohort

Innsbruck cohort:
EC n=239

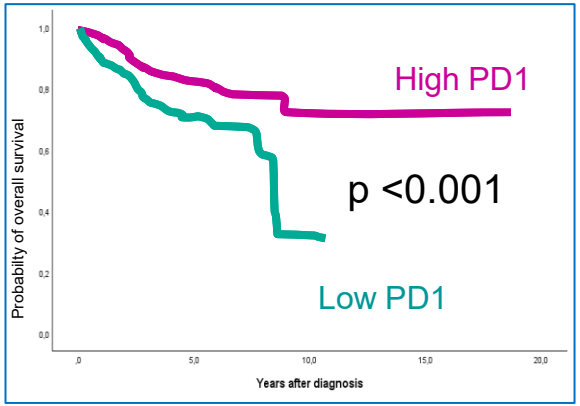
Frauenheilkunde Innsbruck

# High expression of PD-1 was associated with better outcome: RFS, OS, and DSS

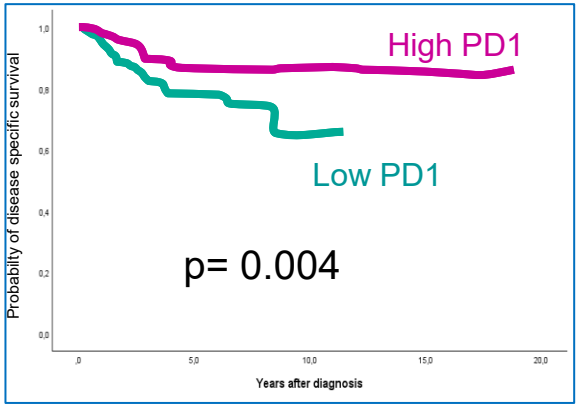
**RFS**




**OS**




**DSS**




THE CANCER GENOME ATLAS

Barin Feroz,.., Christian Marth, et al. Int J Gynecol Cancer 2024 Nov 4

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# Immune Checpoint Inhibitor Efficacy in Endometrial Cancer

| | | MMR-d | |
|---|---|---|---|
| Study | Drug | N | ORR(%) |
| KEYNOTE 158: O'Malley (2019+22) | Pembrolizumab | 79 | 48% |
| GARNET: Oaknin (2022) | Dostarlimab | 143 | 46% |
| PHAEDRA: Antill (2019) | Durvalumab | 35 | 43% |

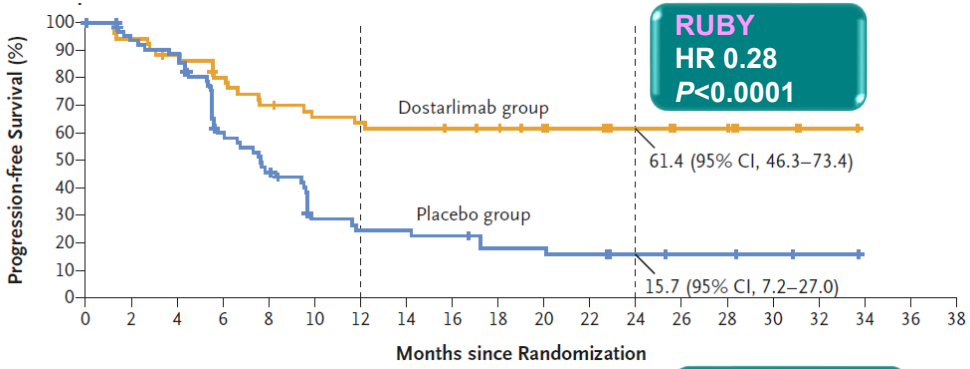
O'Malley et al. ESMO 2019. JCO2022; Oaknin, ASCO 2022; Antill ASCO 2019 ;

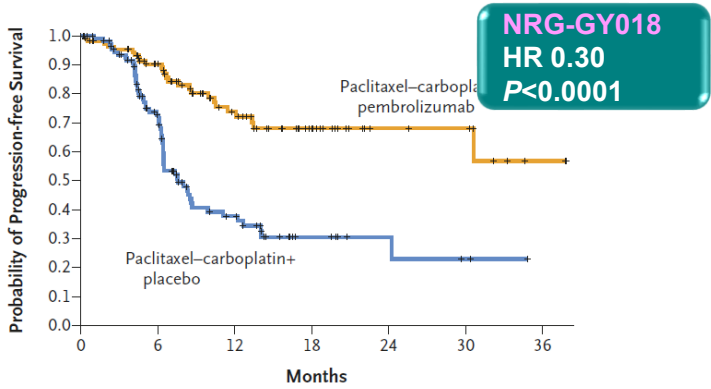
# Immune Checkpoint Inhibitor Efficacy in Endometrial Cancer

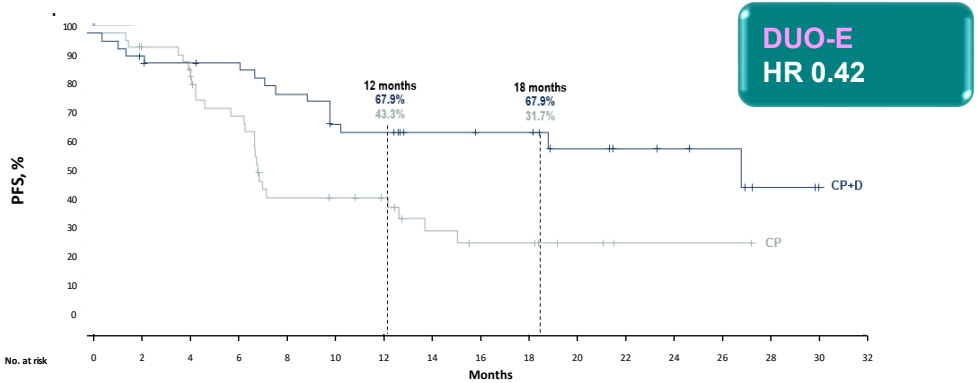
| | | MMR-d | | Non MMR-d | |
|---|---|---|---|---|---|
| Study | Drug | N | ORR(%) | N | ORR(%) |
| KEYNOTE 158: O'Malley (2019+22) | Pembrolizumab | 79 | 48% | 107 | 11% |
| GARNET: Oaknin (2022) | Dostarlimab | 143 | 46% | 156 | 15% |
| PHAEDRA: Antill (2019) | Durvalumab | 35 | 43% | 36 | 3% |

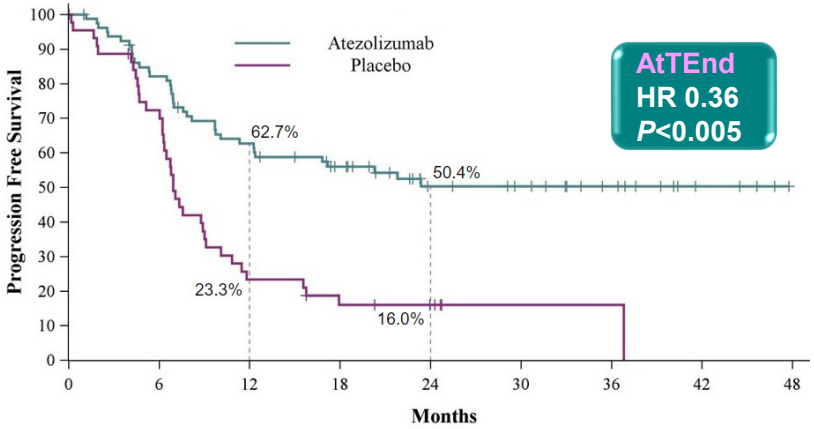
O'Malley et al. ESMO 2019. JCO2022; Oaknin, ASCO 2022; Antill ASCO 2019 ;

# Immune Checkpoint Inhibitor plus Chemotherapy in First-line Endometrial Cancer: PFS in **dMMR** Tumors



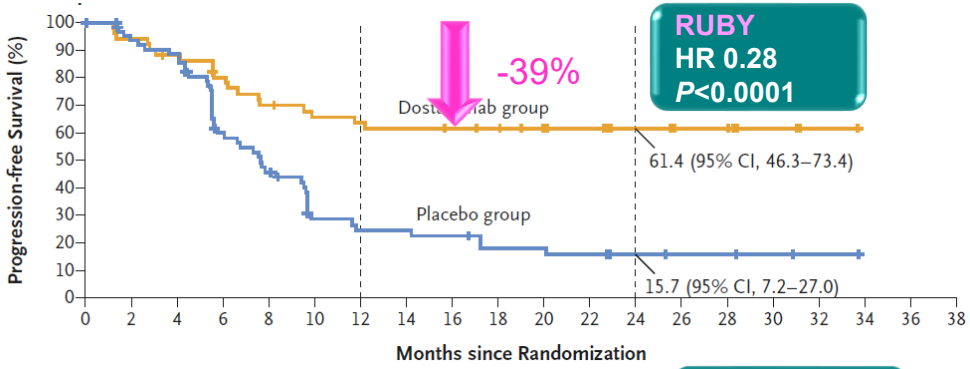



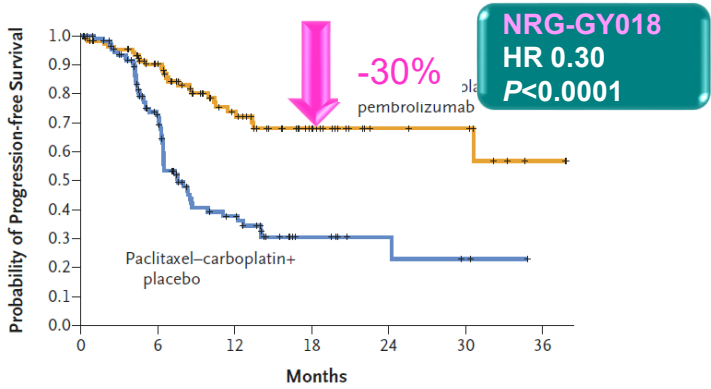



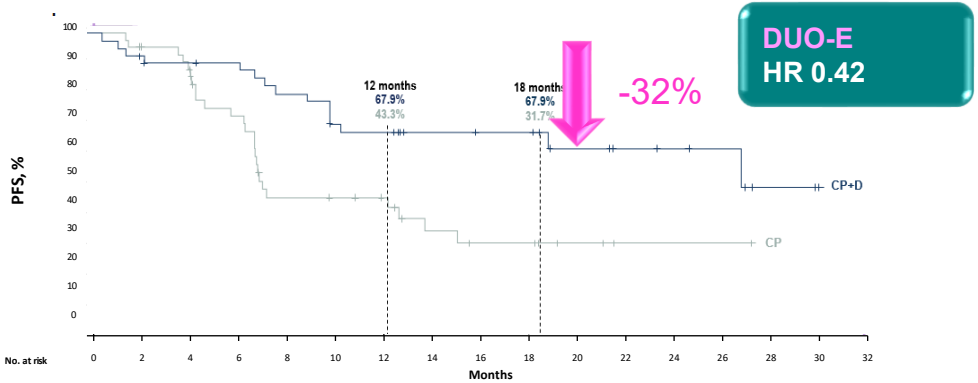



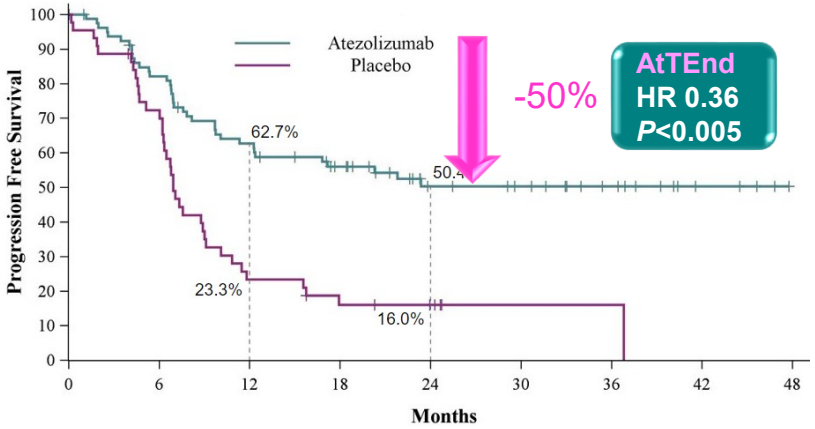

Mansoor R. Mirza et al. NEJM August 2023, Ramez N. Eskander et al. NEJM August 2023, Westin SN, et al. J Clin Oncol 2024, Nicoletta Colombo et al., Lancet Oncol 2024

# Immune Checkpoint Inhibitor plus Chemotherapy in First-line Endometrial Cancer: PFS in **dMMR** Tumors

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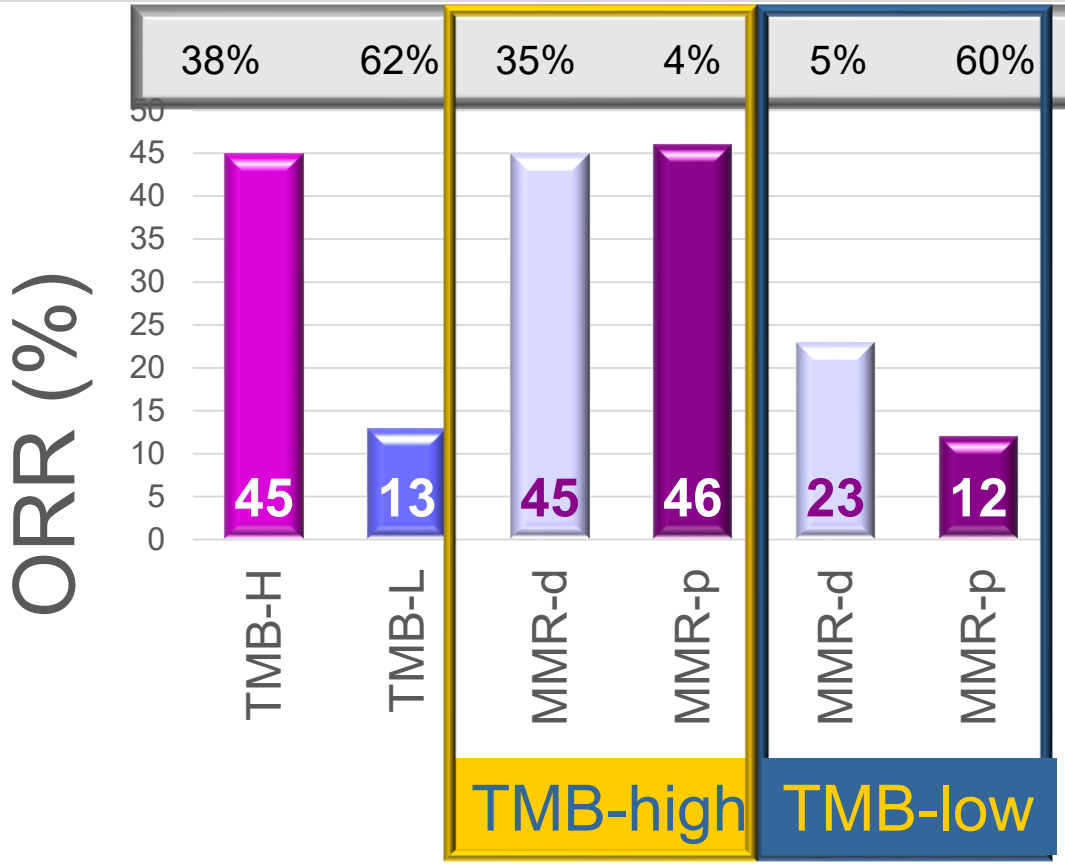
# Garnet trial and Tumor Mutational Burden (TMB)




Patients with MMR-d showed high response rates

**But**

TMB-low tumors were associated with lower responses irrespective MMRd status

Ana Oaknin et al., ESMO 2021

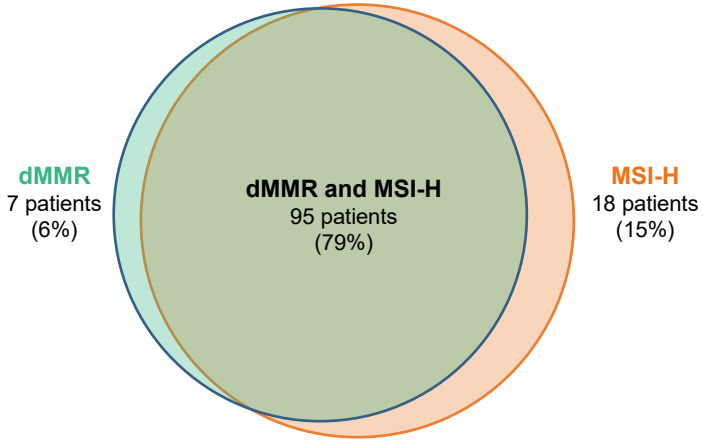
# Correlation between dMMR and MSI-H status in DUO-E

**dMMR and MSI-H concordance (N=451)**

| subpopulation, n | dMMR | pMMR | dMMR<br>MSI-H<br>MSI and MMR concordance |
|---|---|---|---|
| **MSI-H** | 95 | 18 | **113/451 patients (25%)** |
| **MSI equivocal/stable** | 7 | 331 | |
| | **102/451 patients (23%)** | | **426/451 patients (94%)** |

- 451 patients had known MSI status*
- 25% of patients with known MSI status had MSI-H tumours
- 23% of patients with known MSI status had dMMR tumours.† 20% of patients in the ITT population had dMMR tumours
- MSI-H status was highly concordant with dMMR status (94% overall percentage agreement)
- Of the patients from the combined dMMR/MSI-H subpopulation with known MSI status (N=120), 79% (n=95) had both dMMR and MSI-H tumours

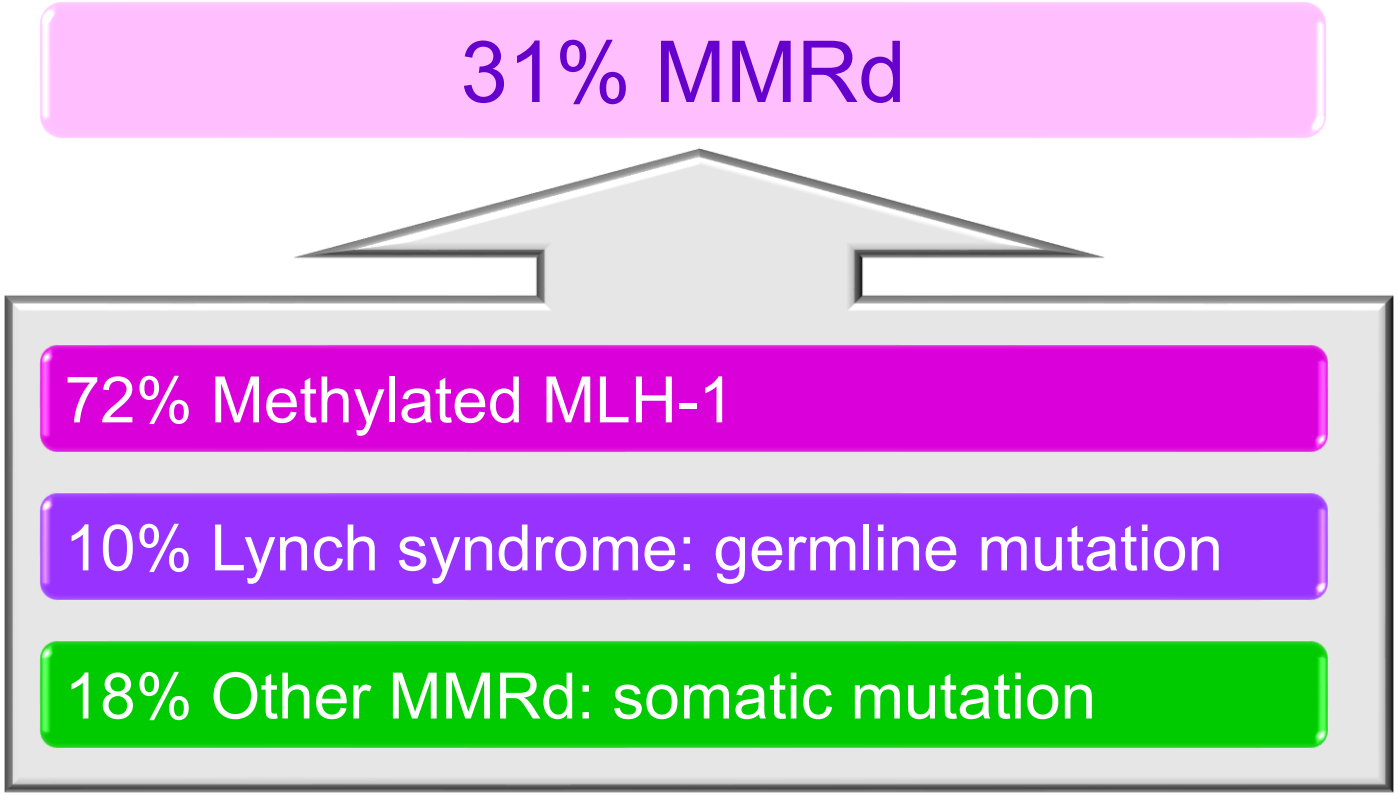
**Overlap between the dMMR and MSI-H subpopulations (N=120)**




MSI score ranges from >0.0041 to <0.0124. Overall status is defined as 'High' if ≥0.0124. *MSI status was evaluated using the tissue-based FoundationOne®CDx test (Foundation Medicine, Inc.); †MMR status was evaluated using the Ventana MMR RxDx panel (Roche Diagnostics, Rotkreuz, Switzerland).

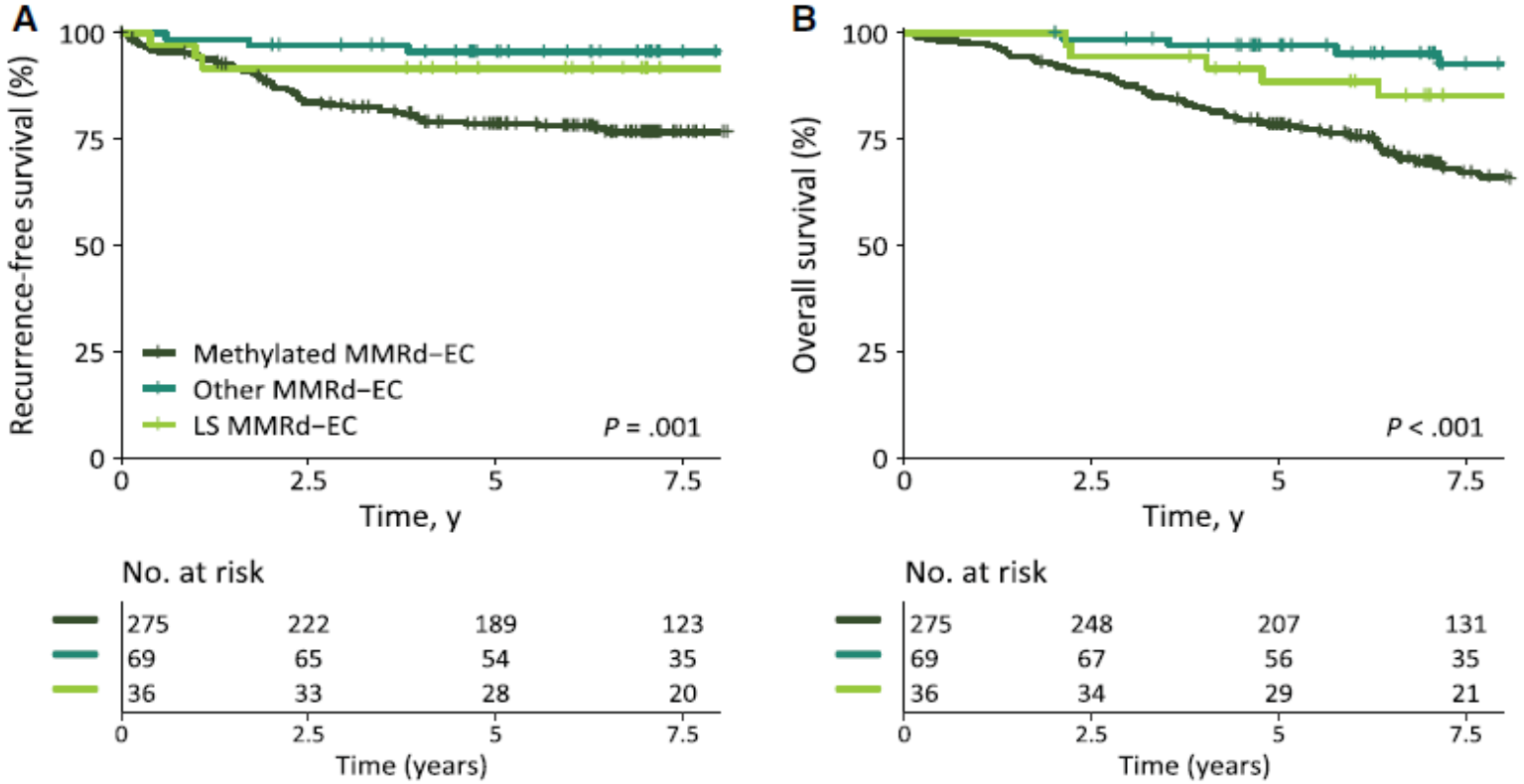
Van Nieuwenhuysen E, et al. Presented at IGCS 2024. 13-17 October. Dublin, Ireland.

# Use of DNA Mismatch-Repair Analysis in Endometrial Cancer to Guide Decisions about Treatment, Prevention, and Screening




Karen H. Lu, and Russell R. Broaddus, N Engl J Med 383;21, November 19, 2020; Cathalijne C. B. Post, et al. J Natl Cancer Inst (2021)

# Prevalence and Prognosis of Lynch Syndrome and Sporadic Mismatch Repair Deficiency in Endometrial Cancer




Note: Kaplan-Meier survival curves for recurrence-free survival (A) and overall survival (B) for patients with methylated mismatch repair deficient (MMRd), other MMRd and Lynch syndrome (LS) associated MMRd endometrial cancer (EC). All cases with MMRd phenotype are included in this analysis, including cases with a concurrent POLE variant affecting function (POLEmut-MMRd-EC). P values reflect 2-sided log-rank test.

# Post Hoc Analysis of Objective Response Rate by Mismatch Repair Protein Dimer Loss/Mutation Status in Patients with Mismatch Repair Deficient Endometrial Cancer Treated with Dostarlimab

- Most MLH1 loss was not accompanied by mutations, consistent with the estimated rate in the dMMR population[1-4]

| | Patients, N | Responders, n | ORR, % (95% exact CI) | DOR median (95% CI), mo |
|---|---|---|---|---|
| **Cohort A1 (dMMR/MSI-H EC)** | 143 | 65 | 45.5 (37.1–54.0) | NR (38.9–NR) |
| **Cohort A1 patients with available mutation data** | 101 | — | — | — |
| **MLH1 loss by IHC (any pattern)[a]** | 78 | 31 | 39.7 (28.8–51.5) | NR (38.9–NR) |
| **MLH1 loss by IHC (any pattern) and mutation in *MLH1* or *PMS2* genes** | 7 (9%) | 3 | 42.9 (9.9–81.6) | NR (NR–NR) |
| **MLH1 loss by IHC (any pattern) and no mutation in *MLH1* or *PMS2* genes** | 71 (91%) | 28 | 39.4 (28.0–51.7) | NR (38.9–NR) |

[a]Other: any other pattern of loss that is not exclusively MLH1–PMS2 or MSH2–MSH6 dimer loss. This group includes 17 patients with loss of expression of 1 MMR protein, 13 with loss of 3 proteins, 1 with loss of 2 proteins that are not a canonical dimer, and 2 with MMR unknown/MSI-H status. [b]This group includes 66 patients with loss of the MLH1–PMS2 dimer and 12 with another pattern.

dMMR, MMR deficient; EC, endometrial cancer; IHC, immunohistochemistry; MMR, mismatch repair; MSI-H, microsatellite instability–high.

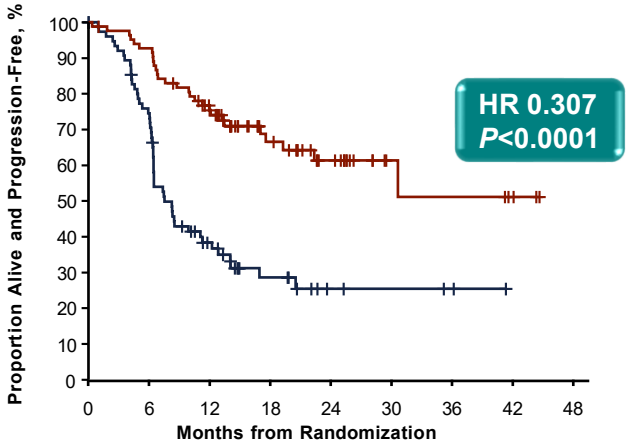
1. Pasanen, A, et al. *Mod Pathol* 2020:33;1443–1452. 2. Kurpiel B et al. *Int J Gyn Path* 2022;41:1-11. 3. Buchanan DD, et al. *J Clin Oncol* 2014;32:90-100. 4. Kahn RM et al. *Cancer* 2019;125:3172-3183.

**Tinker AV et al. Presented at the International Gynecologic Cancer Society (oral poster). September 29 - October 1, 2022; New York, USA**

# PFS by Methylation Status in dMMR Population

## Methylation
### Pembro + CP vs Placebo + CP

| | Events n/N | Median (95% CI), mo | HR (95% CI) |
|---|---|---|---|
| Placebo + CP | 51/77 | 7.5 (6.4–11.3) | 0.307 (0.19–0.49) *P* <0.0001 |
| Pembro + CP | 28/83 | NR (22.3–NR) | |

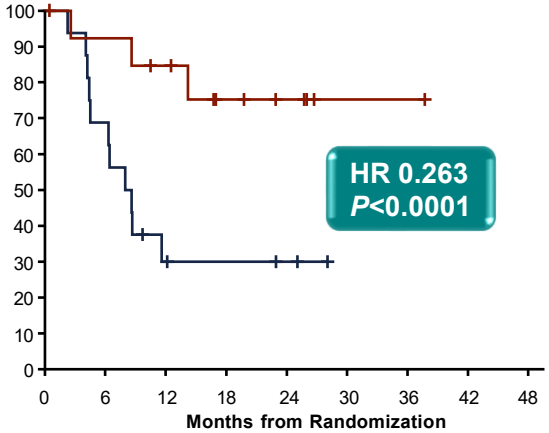



Number at risk (Cumulative number censored)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Placebo + CP | 77 (2) | 55 (3) | 23 (9) | 11 (16) | 4 (22) | 3 (23) | 2 (24) | 0 (26) |
| Pembro + CP | 83 (0) | 76 (1) | 56 (7) | 30 (28) | 18 (38) | 6 (50) | 5 (50) | 3 (52) | 0 (55) |

## No Methylation
### Pembro + CP vs Placebo + CP

| | Events n/N | Median (95% CI), mo | HR (95% CI) |
|---|---|---|---|
| Placebo + CP | 11/17 | 8.3 (4.4–NR) | 0.263 (0.07–0.99) *P* = 0.0172 |
| Pembro + CP | 3/13 | NR (14.2–NR) | |

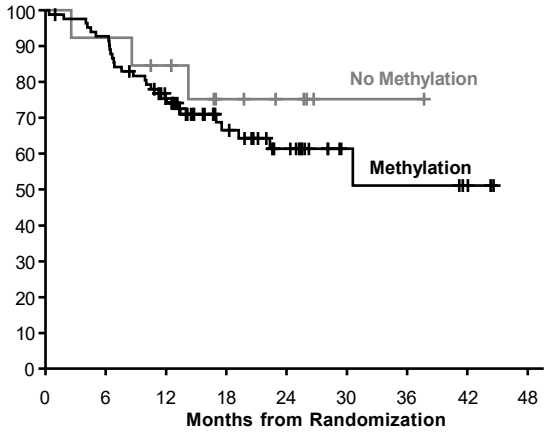



Number at risk (Cumulative number censored)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Placebo + CP | 17 (0) | 11 (1) | 4 (2) | 3 (3) | 2 (4) | 0 (6) | | |
| Pembro + CP | 13 (0) | 12 (0) | 10 (1) | 6 (4) | 4 (6) | 1 (9) | 1 (9) | 0 (10) |

## Methylation Status
### Pembro + CP Arm

| | Events n/N | Median (95% CI), mo |
|---|---|---|
| No Methylation | 3/13 | NR (14.2–NR) |
| Methylation | 28/83 | NR (22.3–NR) |




Number at risk (Cumulative number censored)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| No Methylation | 13 (0) | 12 (0) | 10 (1) | 6 (4) | 4 (6) | 1 (9) | 1 (9) | 0 (10) | |
| Methylation | 83 (0) | 76 (1) | 56 (7) | 30 (28) | 18 (38) | 6 (50) | 5 (50) | 3 (52) | 0 (55) |



Ramez N. Eskander

Data cutoff date: August 18, 2023.

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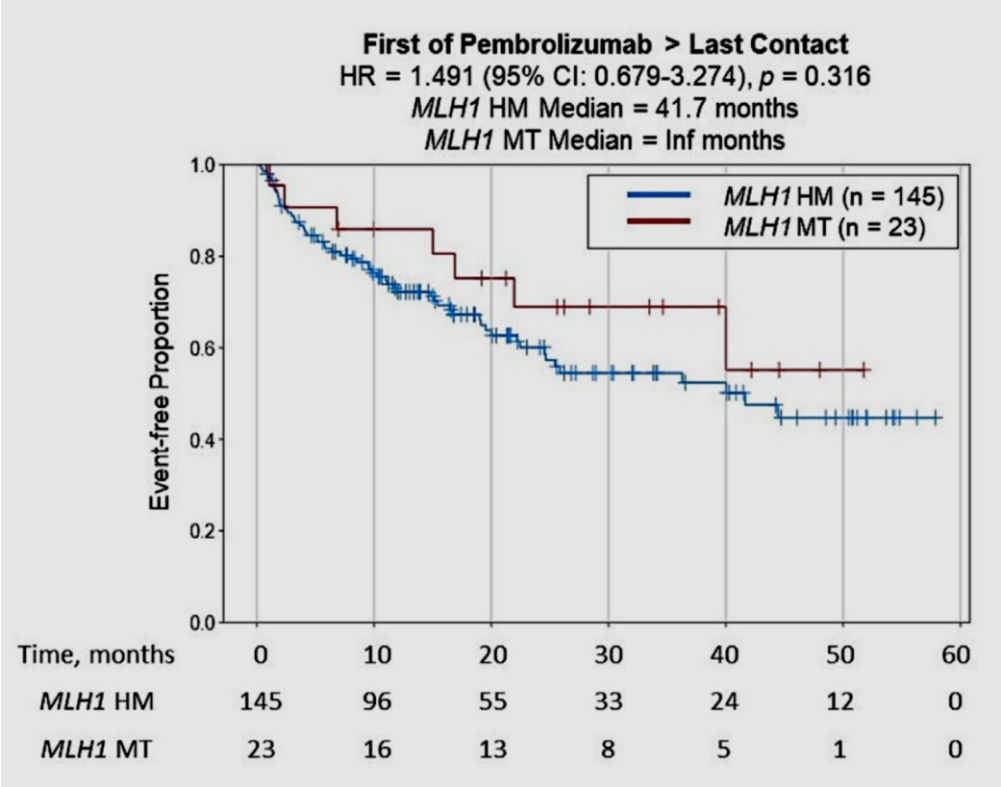
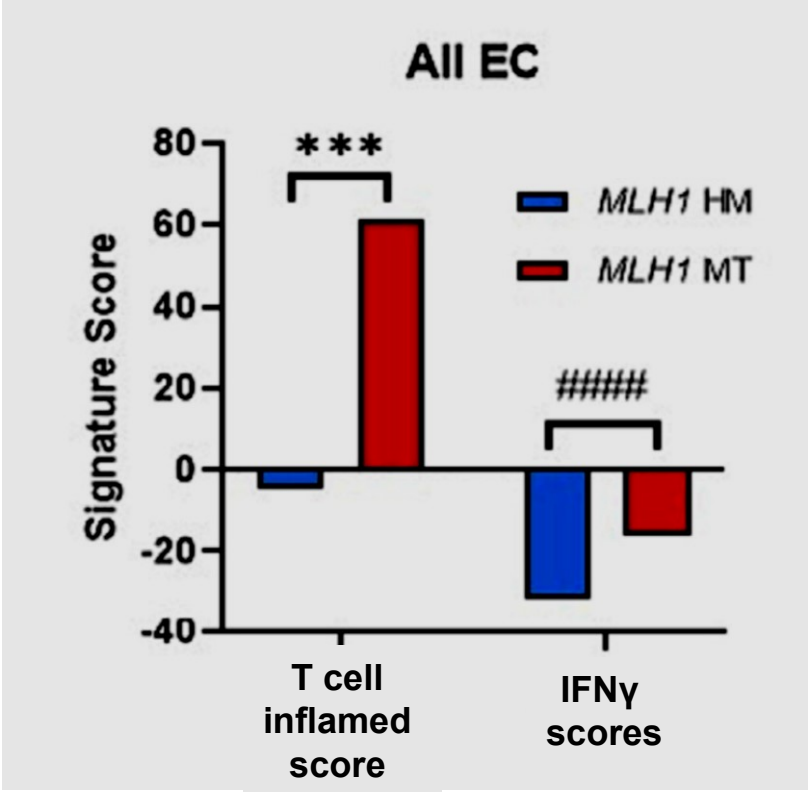
# Differential outcomes and immune checkpoint inhibitor response among endometrial cancer patients with MLH1 hypermethylation versus MLH1 "Lynch-like" mismatch repair gene mutation*




Michael D. Toboni, et al. Gynecologic Oncology 177 (2023) 132–141

*Caris Life Sciences, Phoenix, AZ

# Immune predictors of response to immune checkpoint inhibitors in mismatch repair- deficient endometrial cancer

Good immunotherapy candidate

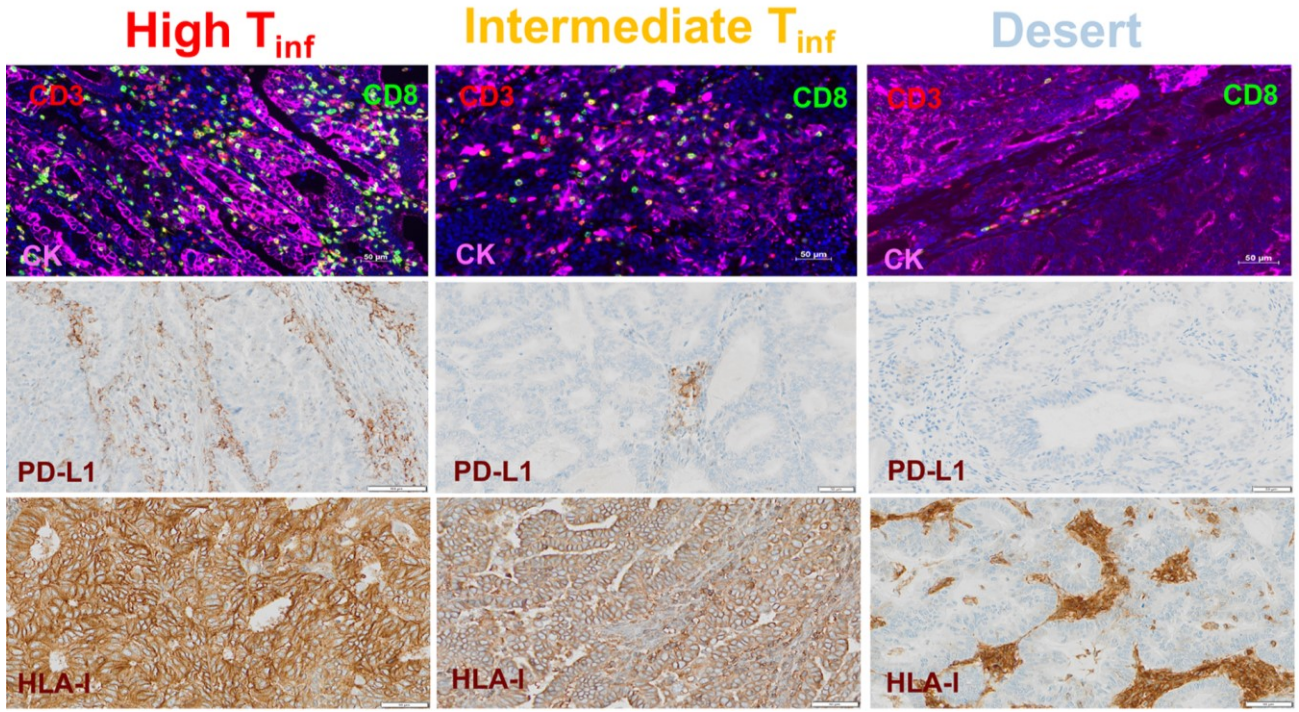
TIL$^{high}$

TIL$^{low}$

Poor immunotherapy candidate

*Considering immunotherapy*

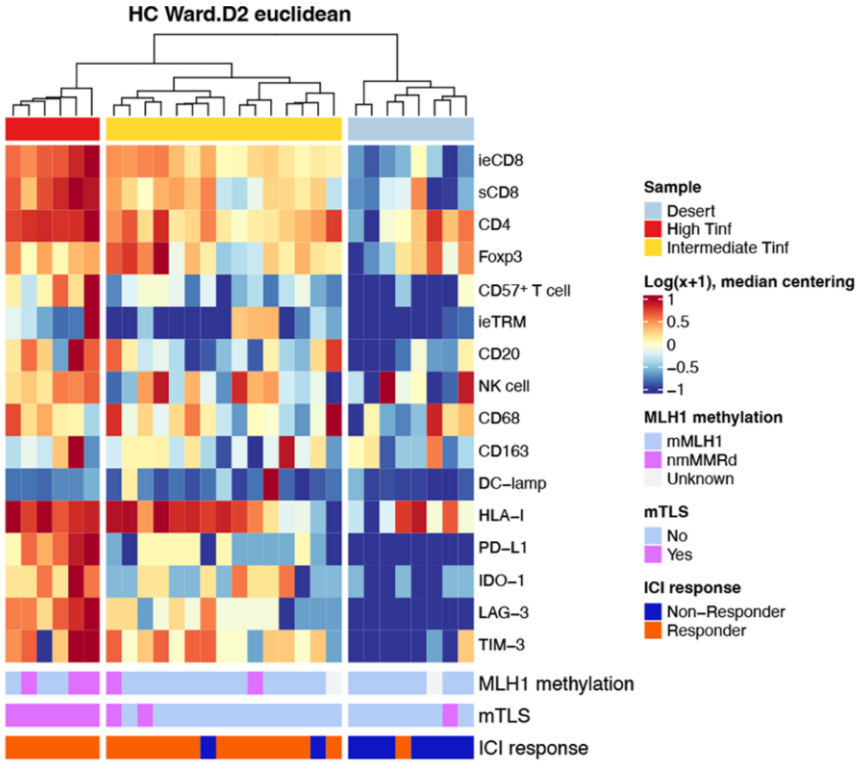
*TIL IHC* (CD3/CD8/CD79a, CD138/CD79a, PD-1/CD8/PD-L1, FoxP3/PD-1/CD3)




Grau Bejar JF, Alexandra Leary, et al. Journal for ImmunoTherapy of Cancer 2024;
Mary M. Mullen and David G. Mutch. Clin Cancer Res 2019

Frauenheilkunde Innsbruck

# Immune predictors of response to immune checkpoint inhibitors in mismatch repair- deficient endometrial cancer




## High $T_{inf}$ cluster (21%):

- highest terminally- differentiated CD57+ T cell, CD20+ cell, and NK cell infiltration.
- Preserved HLA- I and all harbored mTLS.
- Highest expression of immune co- regulators.
- 100% ICI- Responder

## Intermediate $T_{inf}$ (62%)

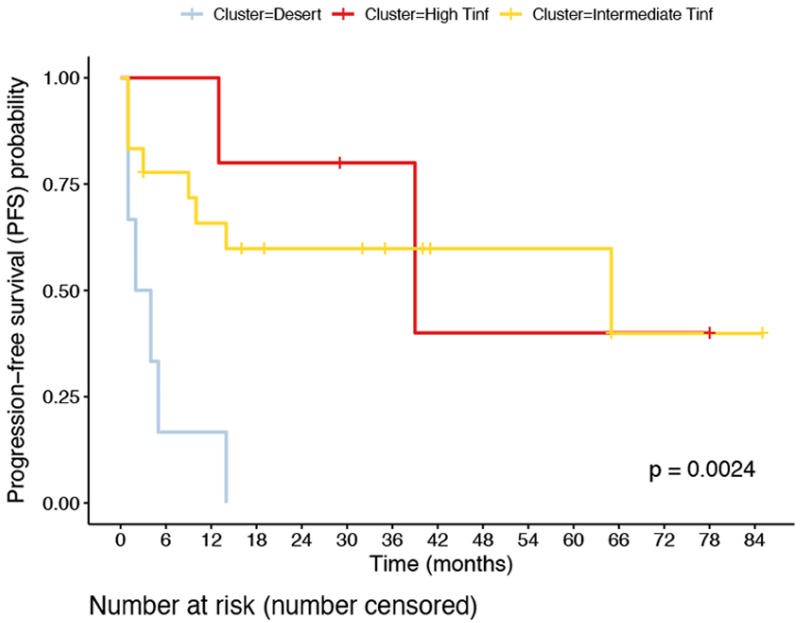
- Moderate infiltration of CD8+ cytotoxic and CD4+ helper T cells and reduced terminally differentiated CD57+ T cells, CD20+ cells, and NK cells,
- Most of the tumors had MLH1 promoter methylation
- 87% ICI- Responder

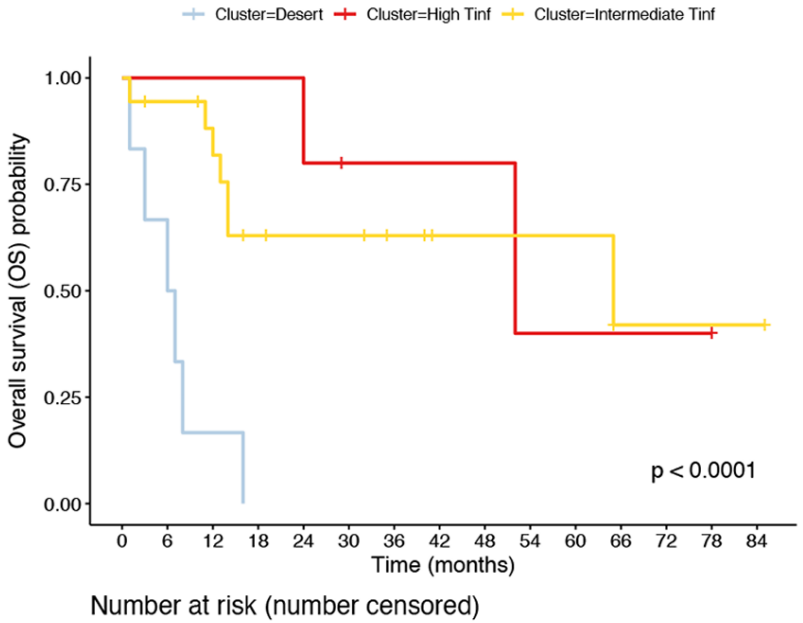
## Desert cluster (28%)

- Lowest levels of CD8+ cytotoxic, ieTRM, and terminally differentiated CD57+ T cells.
- They were uniformly PD- L1 negative.
- 13% ICI-Responder

Grau Bejar JF, Alexandra Leary, et al. Journal for ImmunoTherapy of Cancer 2024;

# Immune predictors of response to immune checkpoint inhibitors in mismatch repair- deficient endometrial cancer



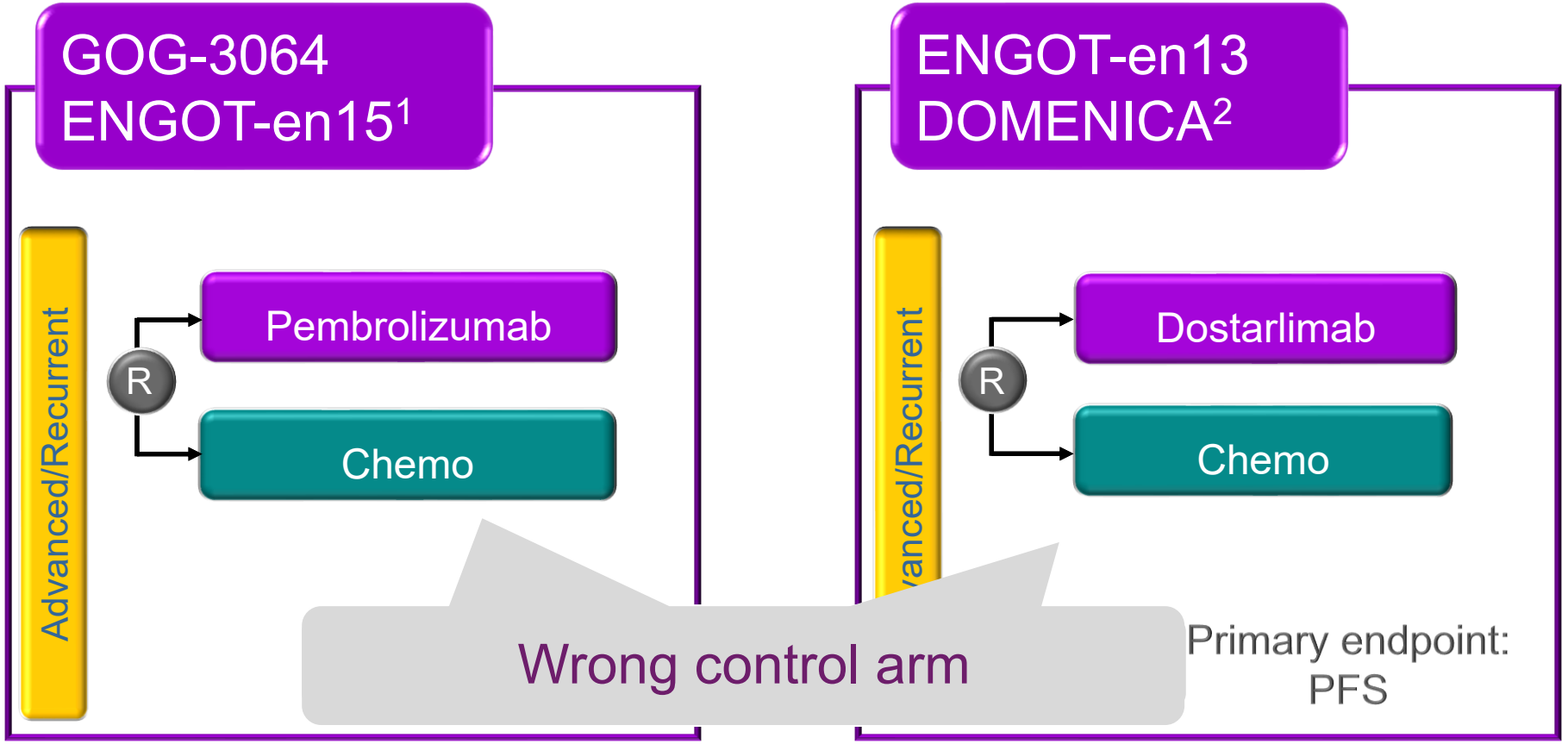




**Assessment of immune response (rather than molecular subtype) may better predict response to immunotherapy**

(0)
(3)
(10)

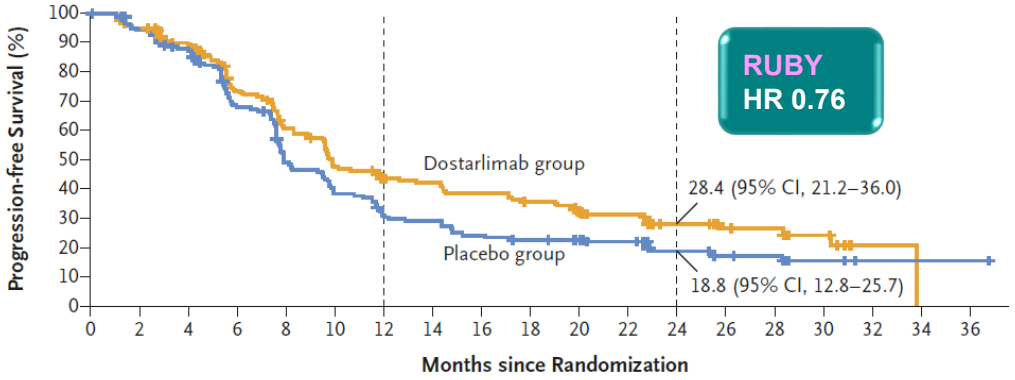
Grau Bejar JF, Alexandra Leary, et al. Journal for ImmunoTherapy of Cancer 2024

# Ongoing Phase III Trials in dMMR Endometrial Carcinoma

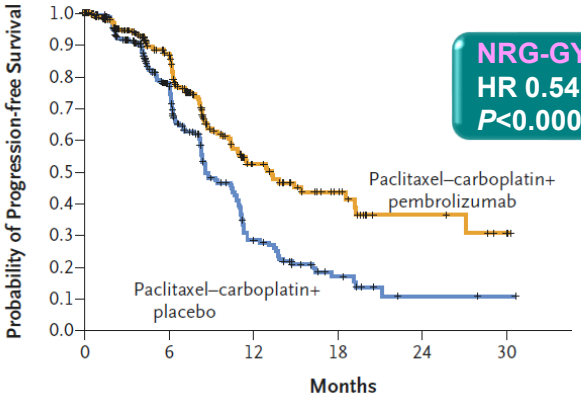



1) Slomovitz BM, et al.; J Clin Oncol. 2022 June 2; 40 (16) 2) Joly F, et al.: J Clin Oncol. 2023 May 31; 41 (16) TPS5630

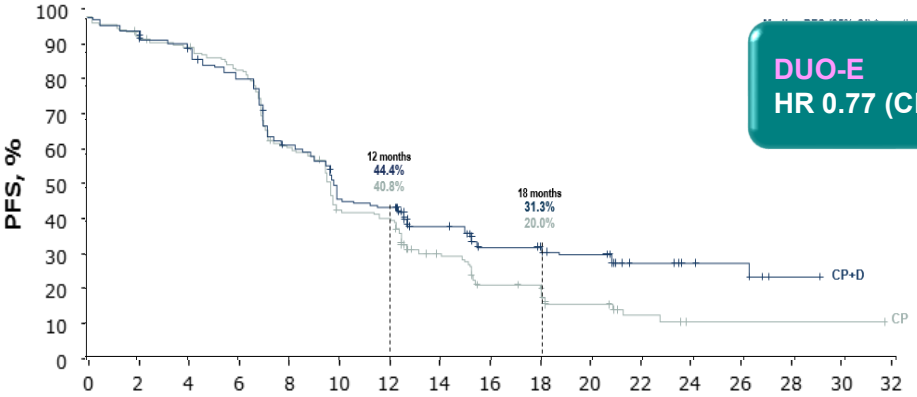
# Immune Checkpoint Inhibitor plus Chemotherapy in First-line Endometrial Cancer: PFS in **pMMR** Tumors



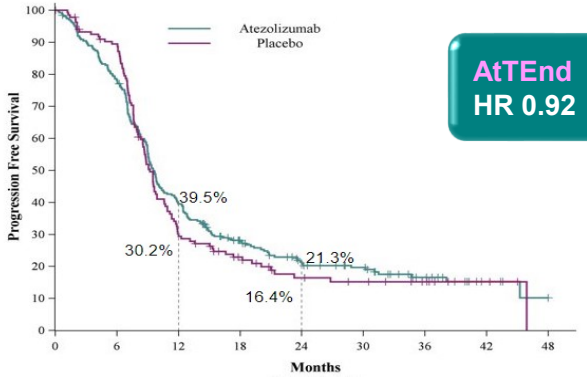

**RUBY**
**HR 0.76**




**NRG-GY018**
**HR 0.54**
***P*<0.0001**



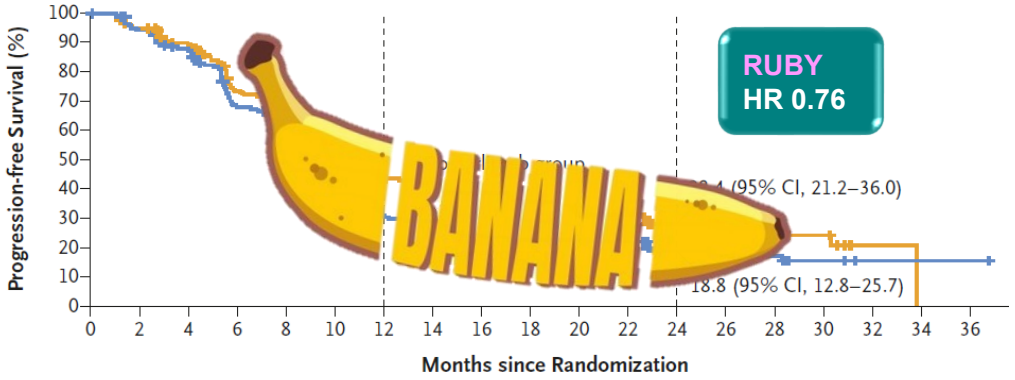

**DUO-E**
**HR 0.77 (CP↔CP+D)**




**AtTEnd**
**HR 0.92**

Mansoor R. Mirza et al. NEJM August 2023, Ramez N. Eskander et al. NEJM August 2023, Nicoletta Colombo et al., ESMO 2023, Shannon N. Westin, et al. ESGO 2023

# Immune Checkpoint Inhibitor plus Chemotherapy in First-line Endometrial Cancer: PFS in **pMMR** Tumors

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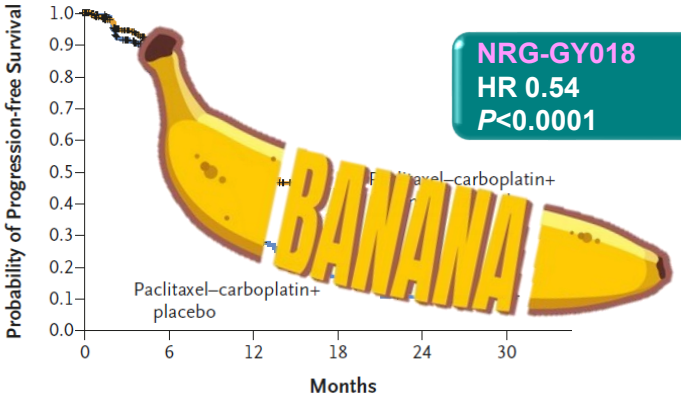
**HR 0.76**

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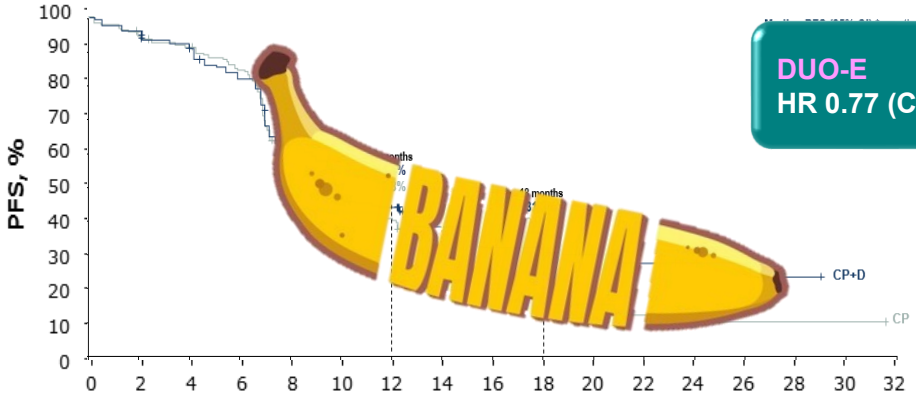
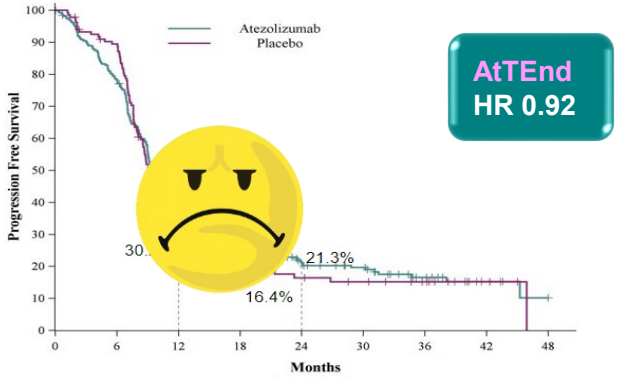


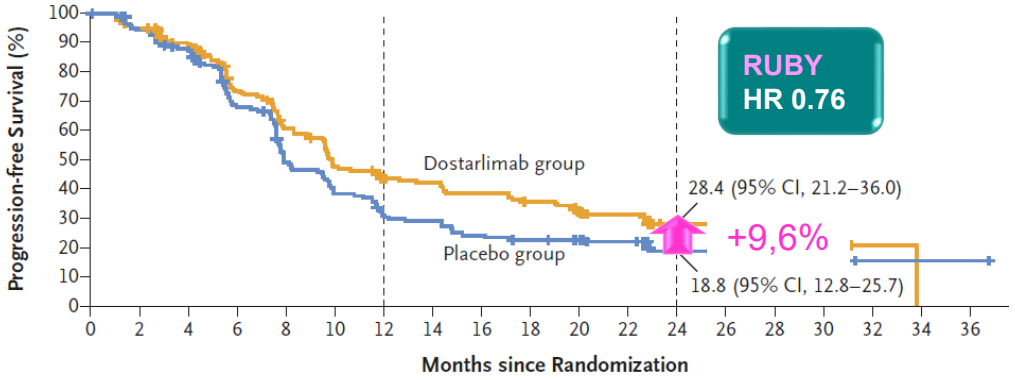

**DUO-E**
**HR 0.77 (CP↔CP+D)**



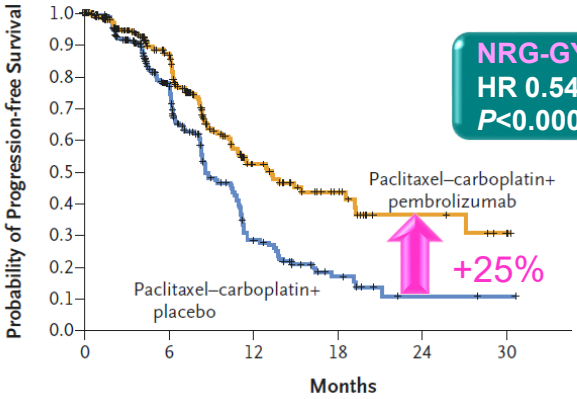

**AtTEnd**
**HR 0.92**

Mansoor R. Mirza et al. NEJM August 2023, Ramez N. Eskander et al. NEJM August 2023, S Pignata et al. The Lancet Oncology 2023, Nicoletta Colombo et al., ESMO 2023, Shannon N. Westin, et al. ESGO 2023

# Immune Checkpoint Inhibitor plus Chemotherapy in First-line Endometrial Cancer: PFS in **pMMR** Tumors




**RUBY**
**HR 0.76**

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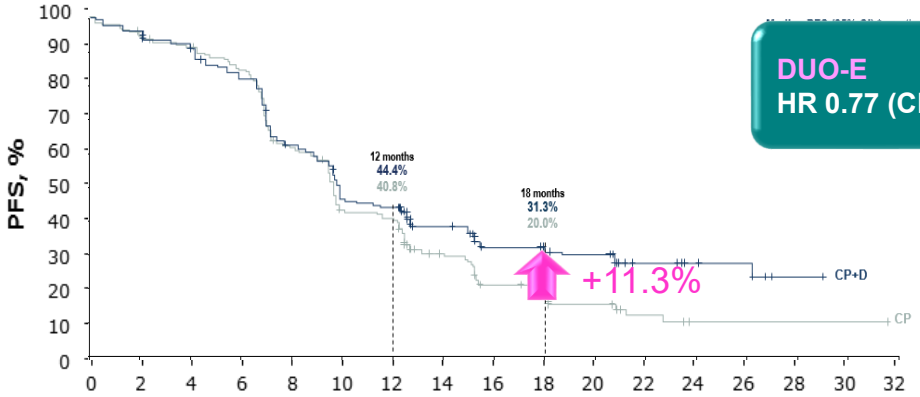


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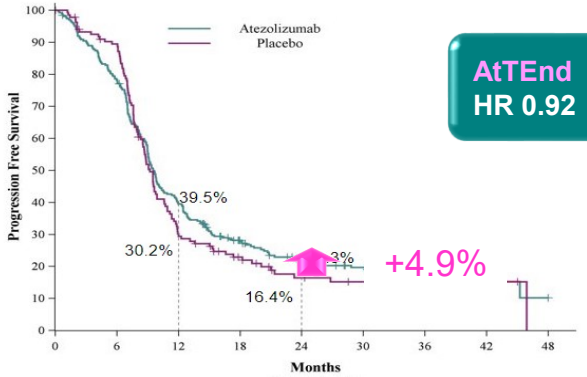
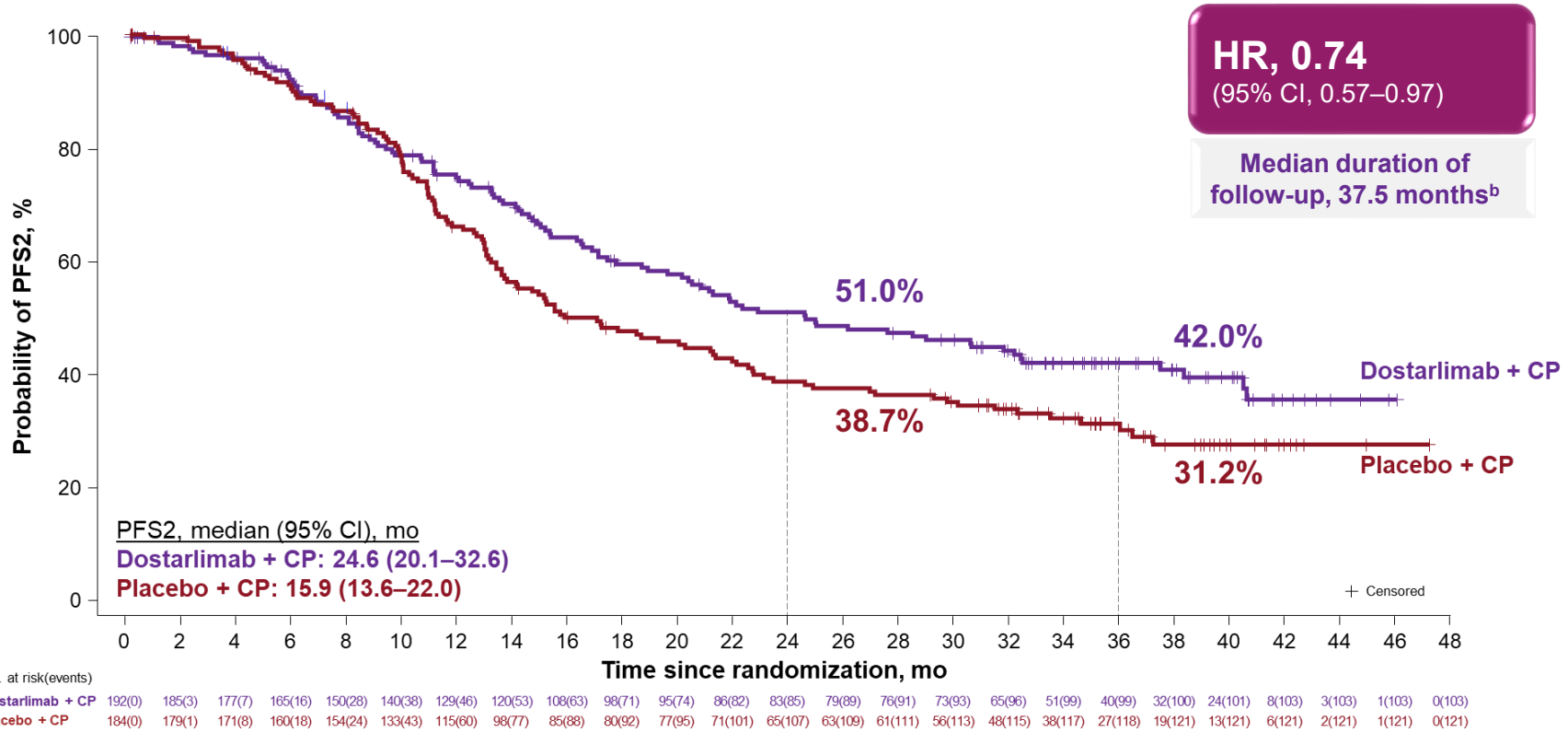



**AtTEnd**
**HR 0.92**

Mansoor R. Mirza et al. NEJM August 2023, Ramez N. Eskander et al. NEJM August 2023, Nicoletta Colombo et al., ESMO 2023, Shannon N. Westin, et al. ESGO 2023

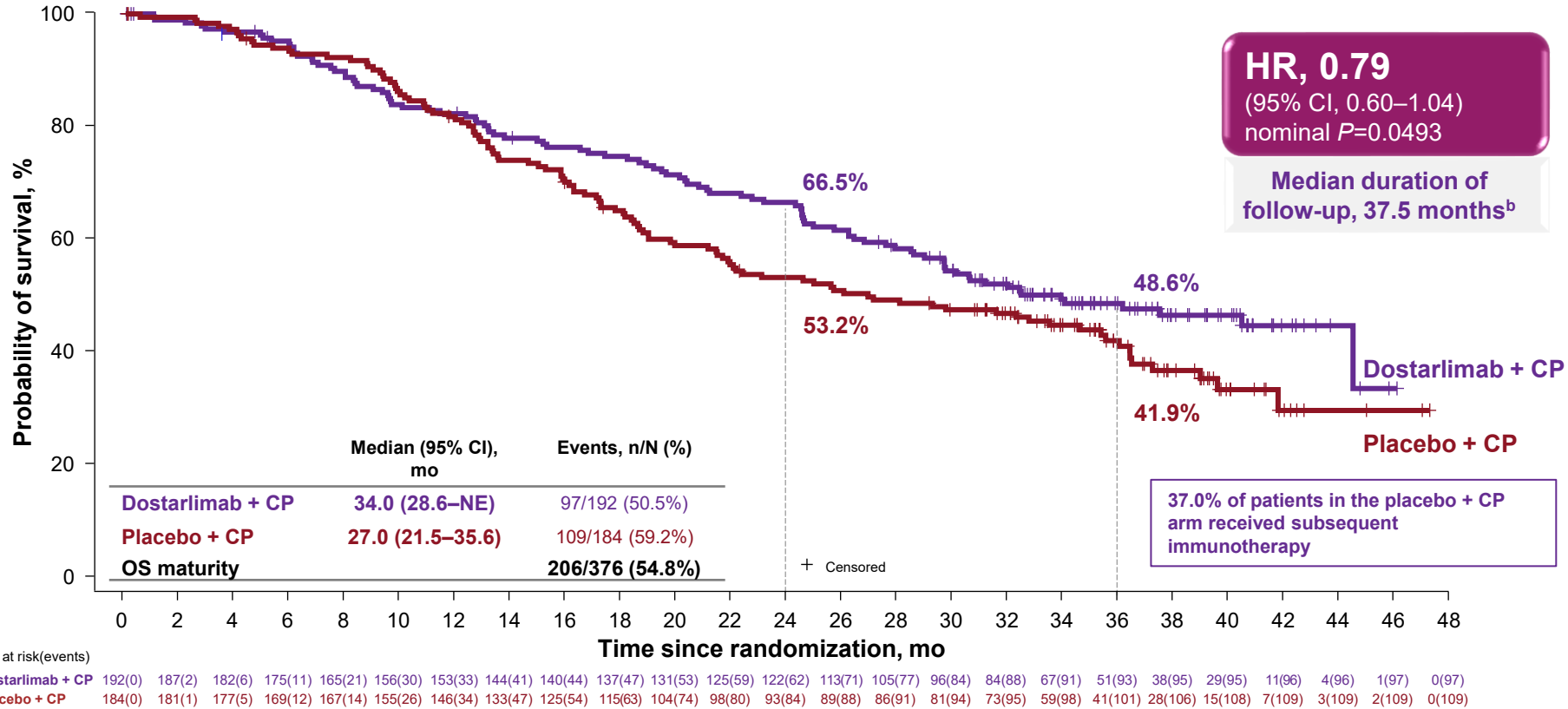
# RUBY I: Clinically Meaningful Difference in PFS2 in the MMRp/MSS Populations




M.R. Mirza et al. SGO 2024

[a]Overall survival in the dMMR/MSI-H and MMRp/MSS populations was a prespecified exploratory endpoint. [b]Median expected duration of follow-up.
CP, carboplatin-paclitaxel; HR, hazard ratio; MMRp, mismatch repair proficient; MSS, microsatellite stable; NE, not estimable; OS, overall survival.

# RUBY I: Clinically Meaningful OS Difference in MMRp/MSS [a]




M.R. Mirza et al. SGO 2024

[a]Overall survival in the dMMR/MSI-H and MMRp/MSS populations was a prespecified exploratory endpoint. [b]Median expected duration of follow-up.
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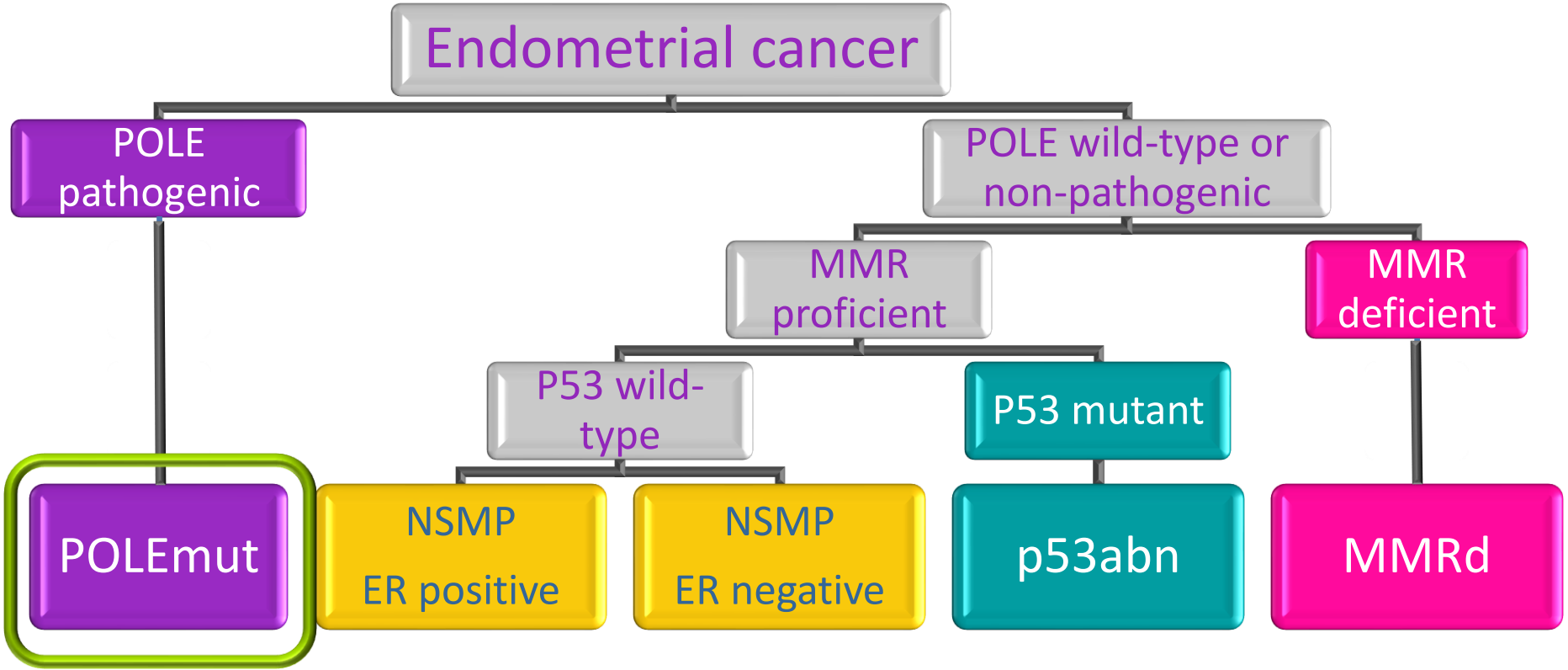
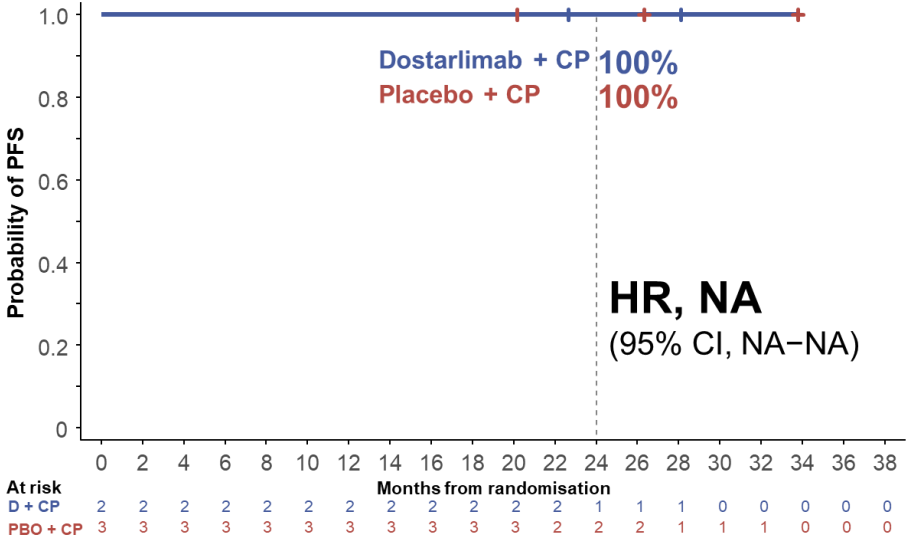
Frauenheilkunde Innsbruck

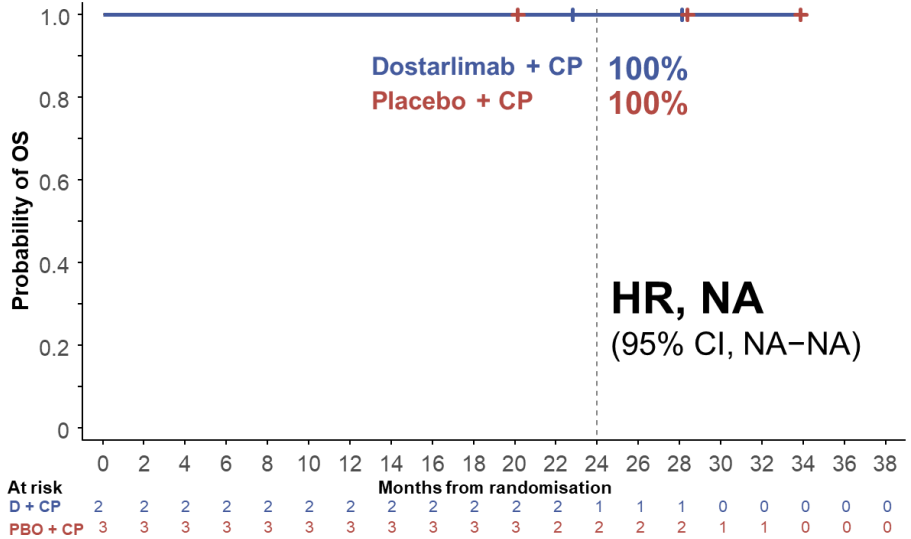
# Molecular classification of endometrial cancer




Vermij et al., British Journal of Cancer (2023) 128:1360 – 1368

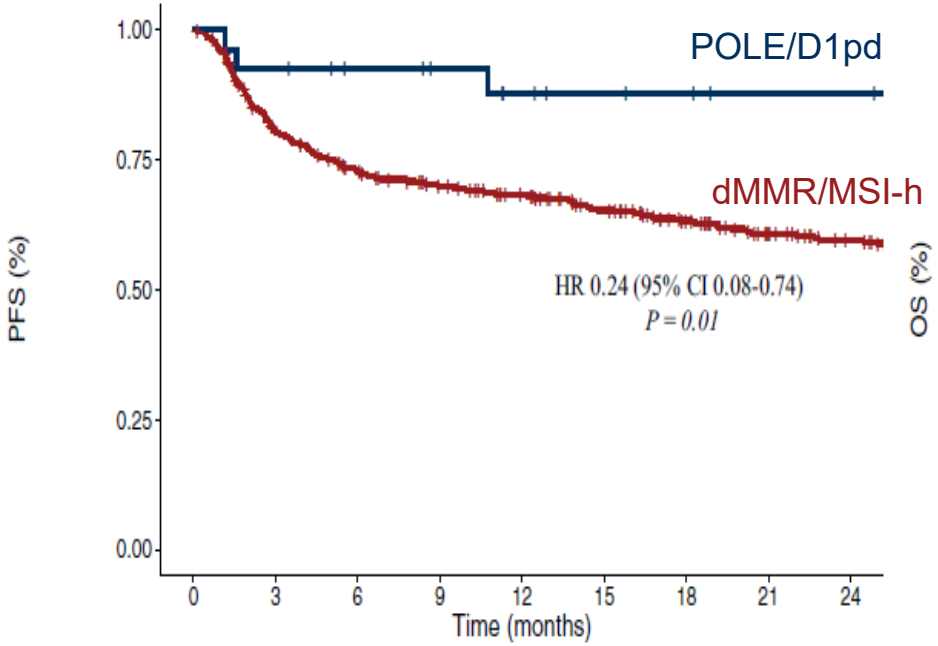
# ENGOT-EN6-NSGO/GOG-3031/RUBY: PFS and OS in POLε mut

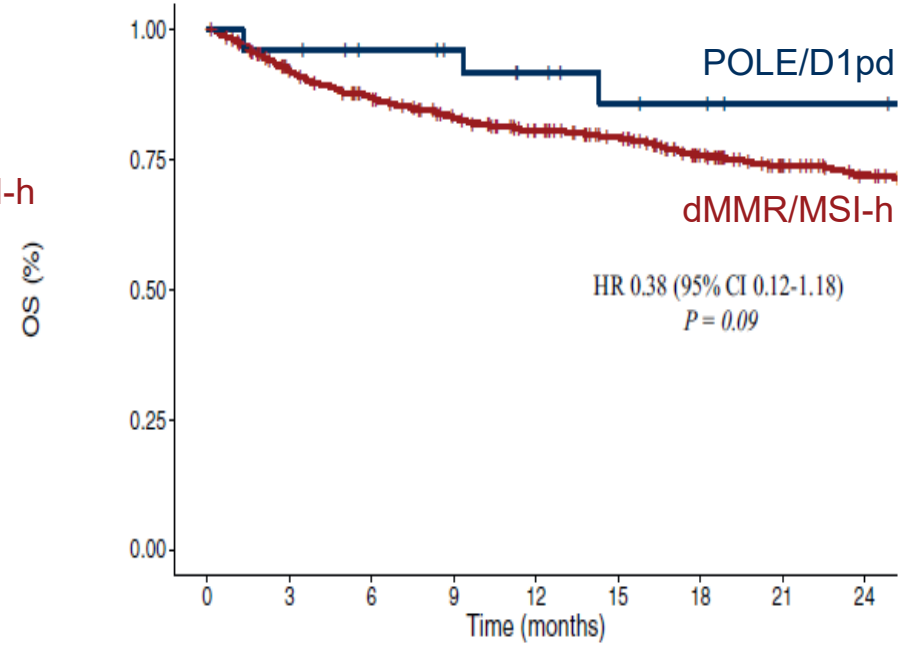



Masoor Mirza, et al. ESMO 2023

# Immune checkpoint inhibitors for POLE or POLD1 proofreading-deficient metastatic colorectal cancer

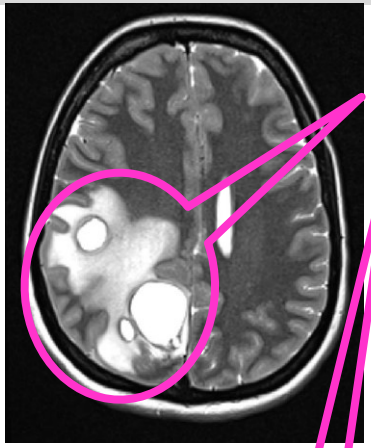


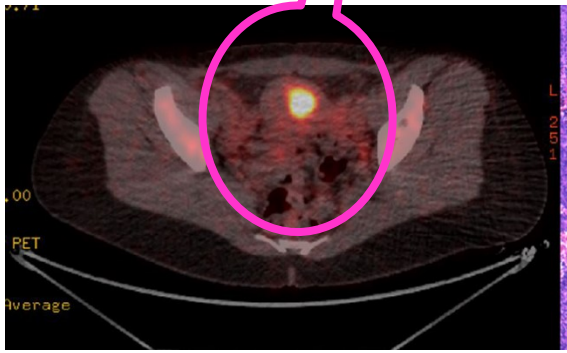

Patients with POLE and POLD1 proofreading deficiency mCRC showed more favorable outcomes compared to dMMR/MSI-H mCRC to treatment with ICIs in terms of tumor response and survival.

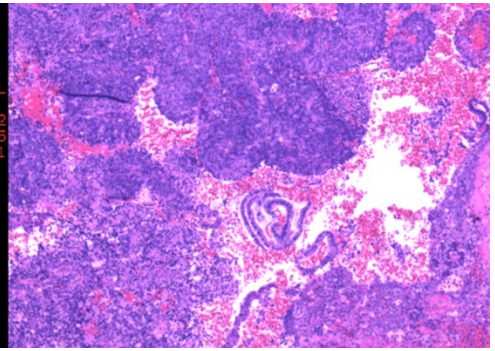
M. Ambrosini, et al. Ann Oncol 2024

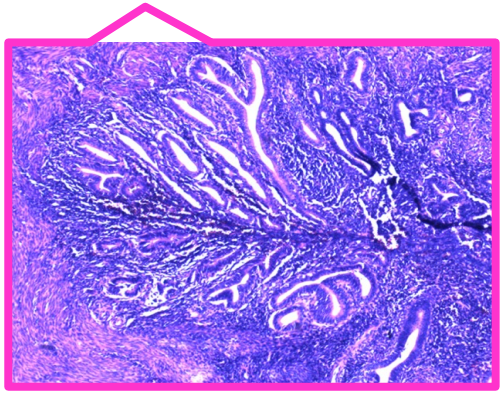
# Brain metastasis and *POLE* mutated endometrial cancer



- 31-year-old patient presented to the neurologic emergency
- Brain MRI showed a lesion
- Whole body FDG PET CT detected a hypermetabolic area in the uterus
- The brain lesion was resected
- Histologic workup showed a poorly differentiated carcinoma
- D&C confirmed the same histology
- POLEm
- 3 cycles of single agent pembrolizumab
- Hysterectomy: pCR (complex endometrial hyperplasia, but no invasive carcinoma)

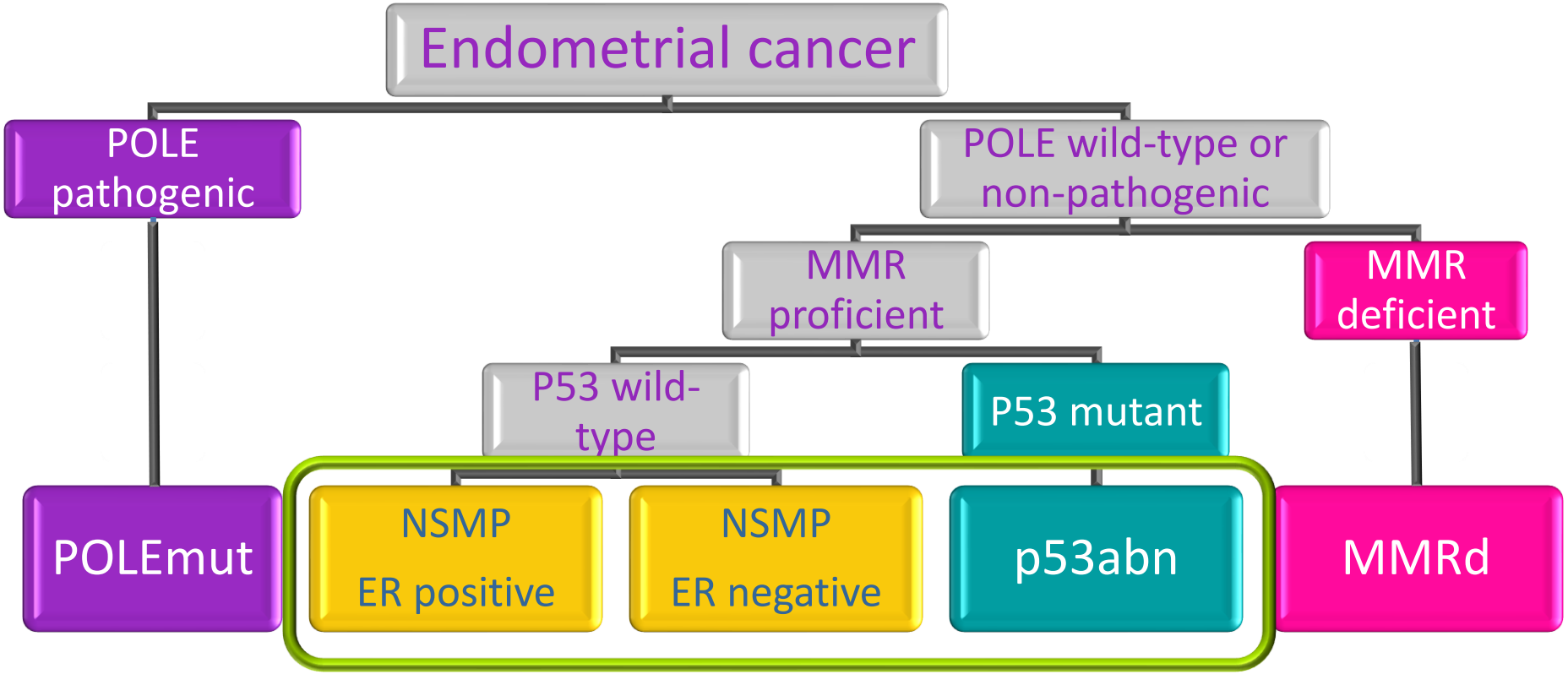




Christoph Ebner et al. submitted

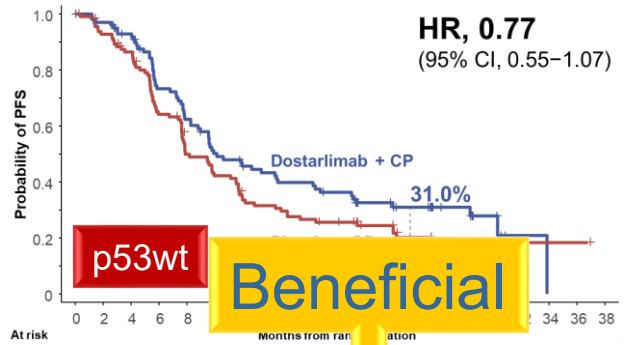
# Molecular classification of endometrial cancer




Vermij et al., British Journal of Cancer (2023) 128:1360 – 1368

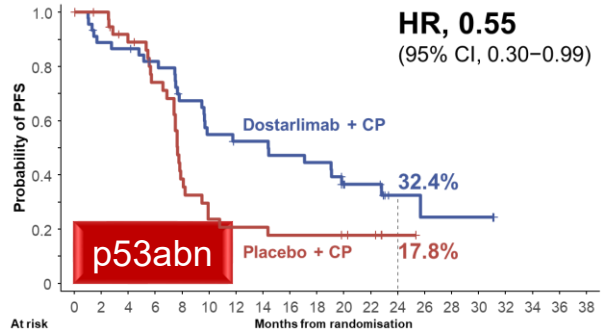
# IO and PFS in non-dMMR TP53mut and TP53wt

## ENGOT-en6/RUBY



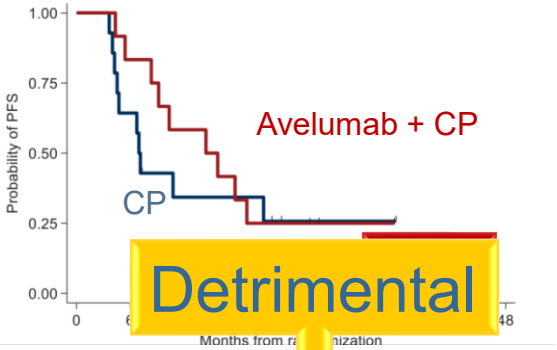

p53wt

**Beneficial**

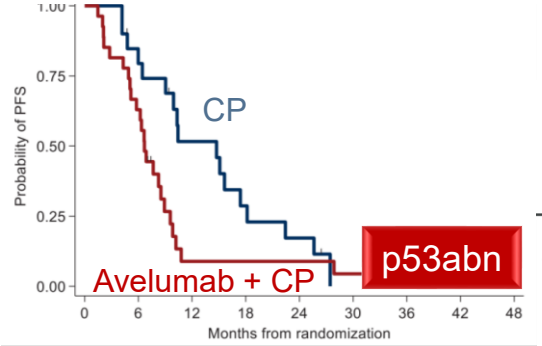



p53abn

## MITO END-3



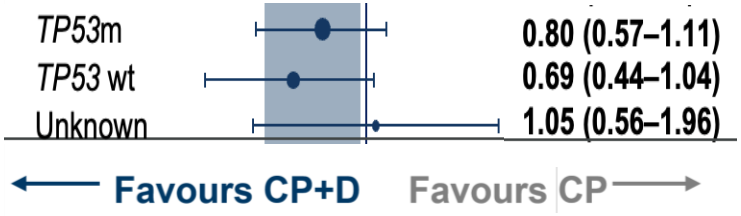

**Detrimental**




p53abn

## DUO-E

**Indifferent**




Mansoor Mirza, et al. ESMO 2023; Sandro Pignata, et al. Ann Oncol 2024, Westin et al. IGCS 2024

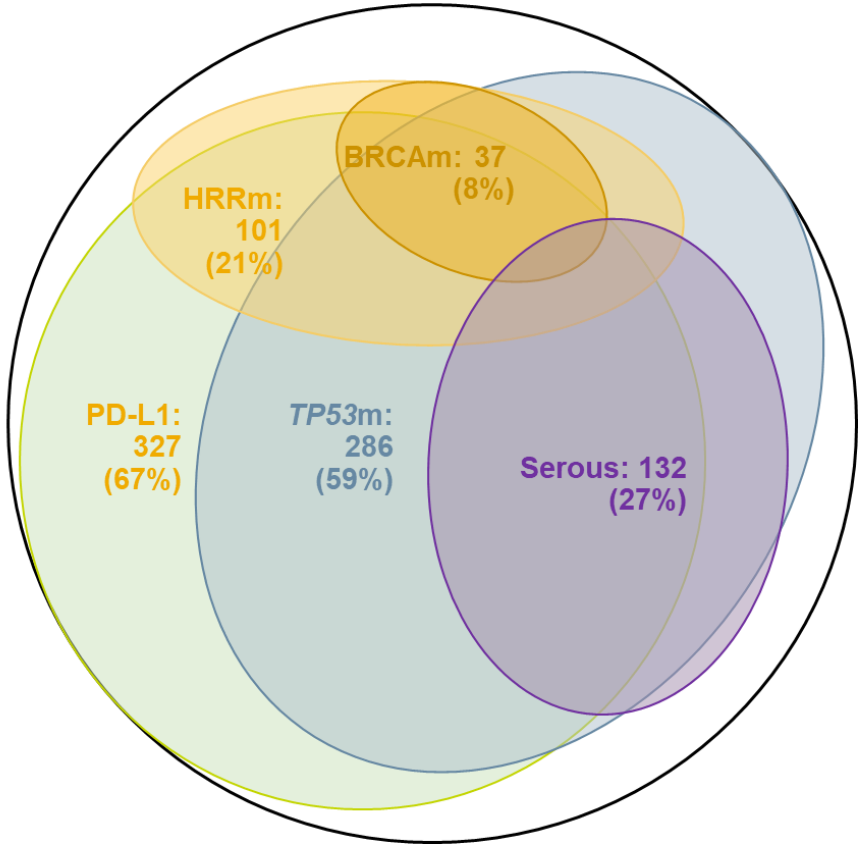

GO BACK AND
START AGAIN
ärgere
nicht
Dich

# pMMR biomarker-known subpopulation: co-prevalence of biomarkers

**The pMMR biomarker-known (n=486) subpopulation was heterogeneous, with a large overlap of biomarkers:**

- 84% of patients were positive for one or more biomarkers
- PD-L1 positive and *TP53*m were the most prevalent biomarkers

| | PD-L1 positive | *TP53*m | HRRm | BRCAm | *POLE*m | Serous |
|---|---|---|---|---|---|---|
| PD-L1 positive | 67% | 44% | 16% | 6% | 2% | 20% |
| *TP53*m | 44% | 59% | 14% | 6% | 2% | 24% |
| HRRm | 16% | 14% | 21% | 8% | 2% | 6% |
| BRCAm | 6% | 6% | 8% | 8% | 1% | 3% |
| *POLE*m | 2% | 2% | 2% | 1% | 2% | 0% |
| Serous | 20% | 24% | 6% | 3% | 0% | 27% |



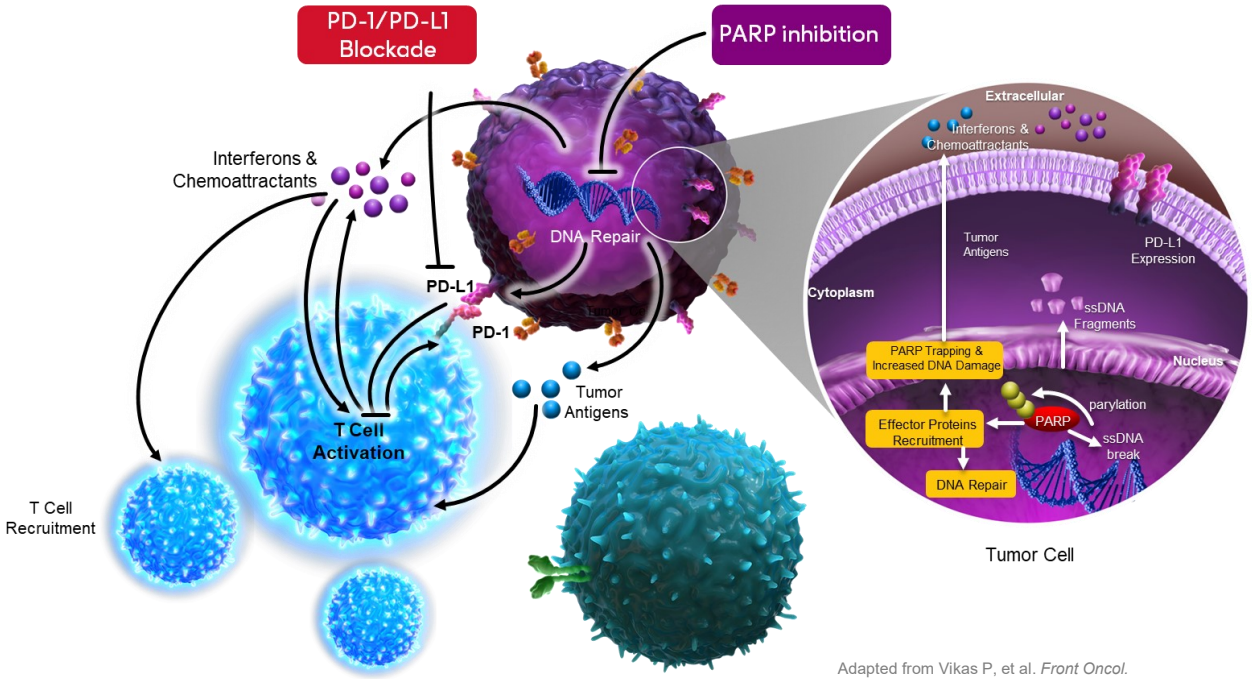
# Rationale for combining PARPi and anti–PD-(L)1[1-3]

Some ECs have HRD and high **PARP1** expression, suggesting therapeutic potential of PARP inhibitors[2]

**PARP-Inhibition** increase generation of neoantigens through the alteration of the DNA repair

**PARP-Inhibition** increased expression of PD-L1

**PARP-1 Inhibition** decreased $T_{reg}$




Adapted from Vikas P, et al. *Front Oncol.* 2020;10:570.

DNA = deoxyribonucleic acid; EC = endometrial cancer; HRD = homologous recombination deficiency; PARP poly(adenosine diphosphate-ribose) polymerase; PARPi = poly(adenosine diphosphate-ribose) polymerase inhibitor; PD-1 = programmed cell death-1; PD-L1 = programmed cell death ligand-1; ssDNA = single-stranded DNA.

1. Jiao S, et al. *Clin Cancer Res.* 2017;23:3711-3720. 2. Arciuolo DT, et al. *Int J Mol Sci.* 2022;23:11684. 3. Vikas P, et al. *Front Oncol.* 2020;10:570. 4. Mirza MR, et al. *Ann Oncol.* 2021;32:S770-S771. 5. Westin SH, et al. Presented at European Society for Medical Oncology (ESMO) Annual Meeting. October 20-24, 2023; Madrid, Spain; Presentation #LBA41.

# dMMR

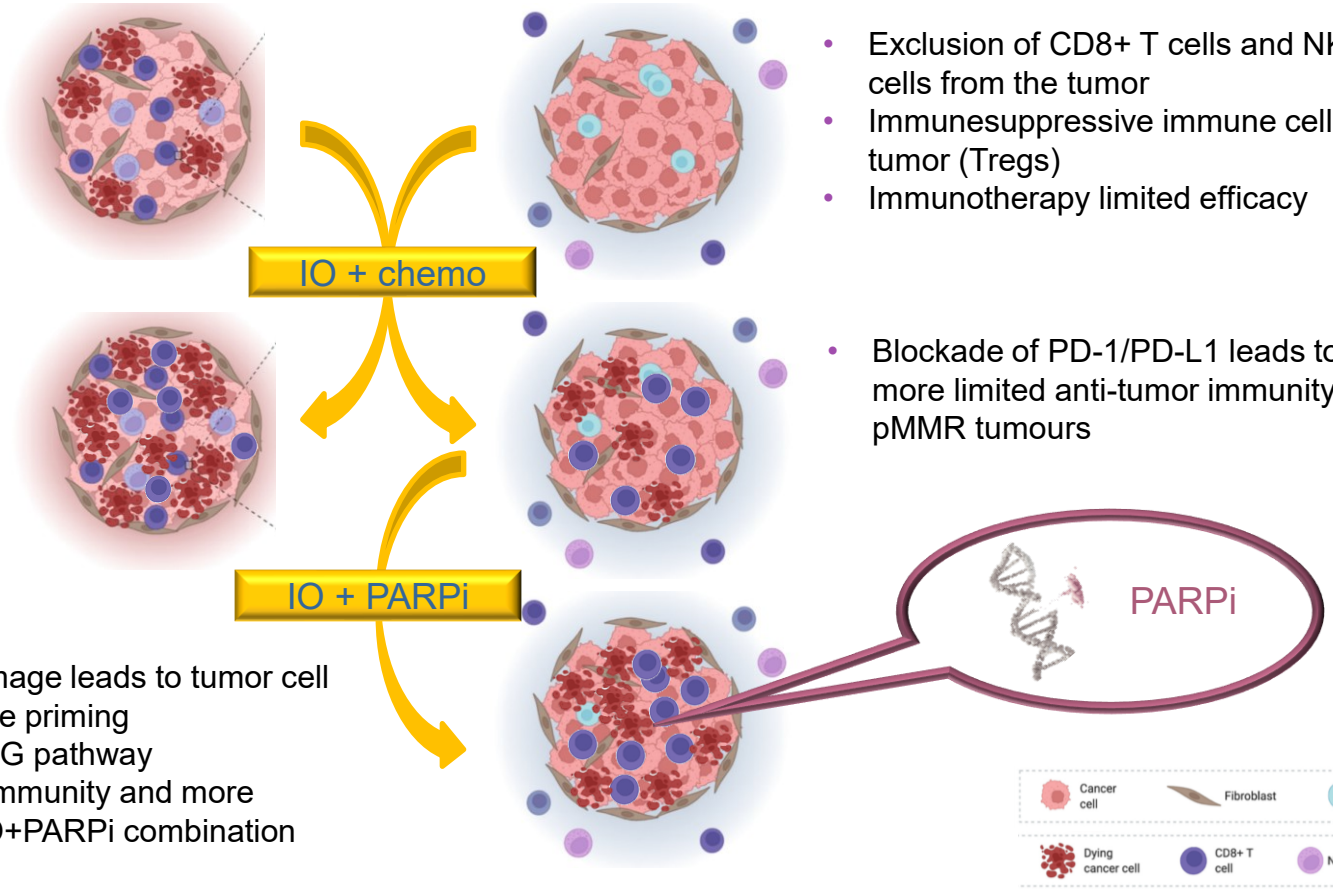
- CD8+ T cells and NK cells are present in tumor
- Suppression of immune-suppressive cell types

- Blockade of PD-1/PD-L1 with IO drives prolonged anti-tumor immunity and durable clinical activity in dMMR tumors, with limited potential for further enhancement

# pMMR

- Exclusion of CD8+ T cells and NK cells from the tumor
- Immunesuppressive immune cells in tumor (Tregs)
- Immunotherapy limited efficacy

- Blockade of PD-1/PD-L1 leads to more limited anti-tumor immunity in pMMR tumours



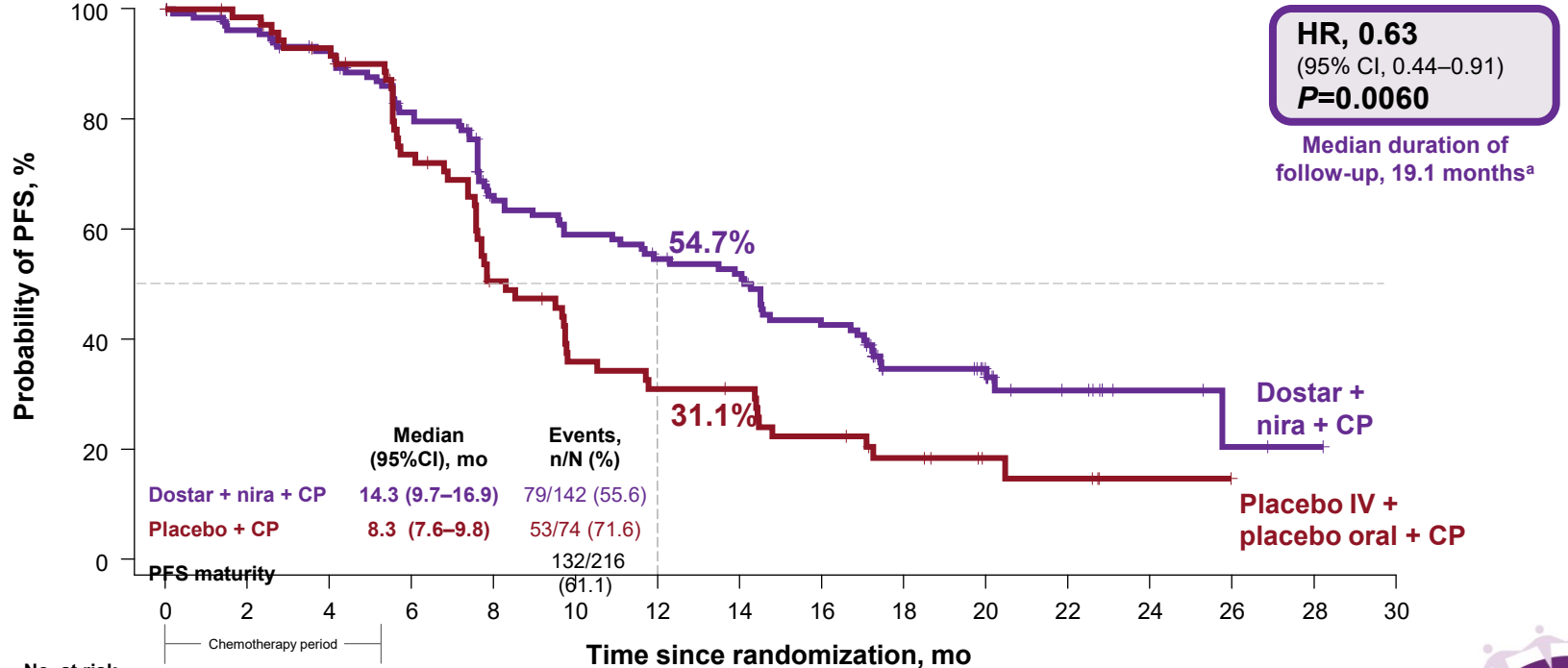

- PARPi induced DNA damage leads to tumor cell death and further immune priming
- Activation of cGAS/STING pathway
- More robust anti-tumor immunity and more durable benefit for the IO+PARPi combination

1. Stewart R, et al. *Cancer Res.* 2018;78(24):6717-6725. 2. Asaka S, et al. *Mol Pathol.* 2019;32(4):576-584. 3. Yang Y, et al. *Int J Gynecol Obstet.* 2024; 164(2):436-459. 4. Anthill Y, et al. *Cancer.* 2022;128(6):1157-1161. 5. Musacchio L et al. *Cancer Manag Res.* 2020;12:6123-6135 6. Post C.C.B., et al. *Crit Rev Oncol Hematol.* 2020;152:102973.

Scan for slides

# Statistically Significant PFS Benefit in MMRp/MSS Population

## Primary endpoint




[a]Median expected duration of follow-up.
CP, carboplatin-paclitaxel; dostar, dostarlimab; HR, hazard ratio; MMRp, mismatch repair proficient; MSS, microsatellite stable; nira, niraparib; PFS, progression-free survival.

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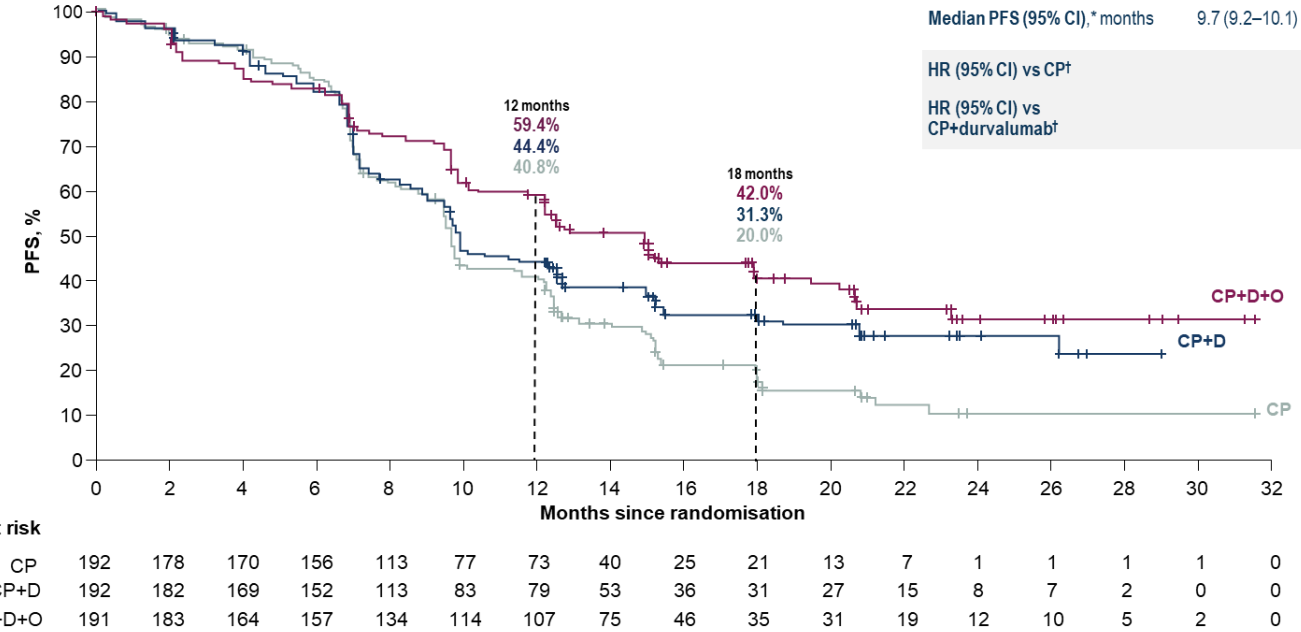
# DUO-E: pMMR PFS

## Prespecified Exploratory Subgroup Analyses

PFS: pMMR (80% of population)

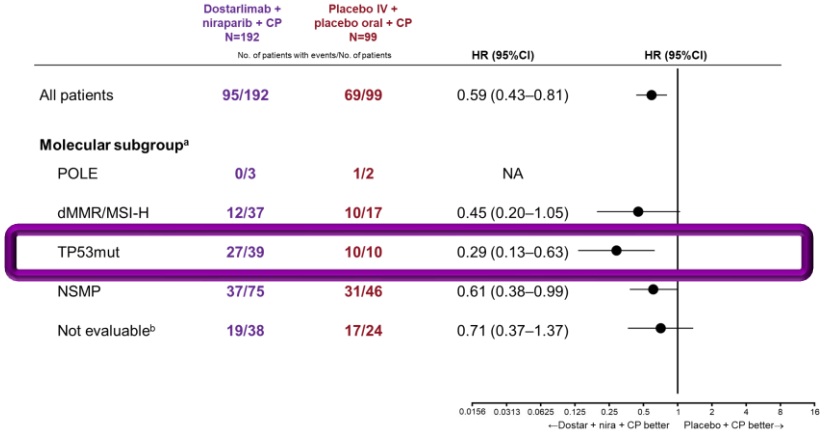
| | CP N=192 | CP+D N=192 | CP+D+O N=191 |
|---|---|---|---|
| **Events**, n (%) | 148 (77.1) | 124 (64.6) | 108 (56.5) |
| **Median PFS (95% CI)**,* months | 9.7 (9.2–10.1) | 9.9 (9.4–12.5) | 15.0 (12.4–18.0) |
| **HR (95% CI) vs CP†** | | **0.77 (0.60–0.97)** | **0.57 (0.44–0.73)** |
| **HR (95% CI) vs CP+durvalumab†** | | | **0.76 (0.59–0.99)** |




1. Westin S, et al. Presented at ESMO Congress 2023. 20-24 October. Madrid, Spain; 2. Chon HS, et al. Presented at SGO Congress 2024. 16-18 March. San Diego, CA.

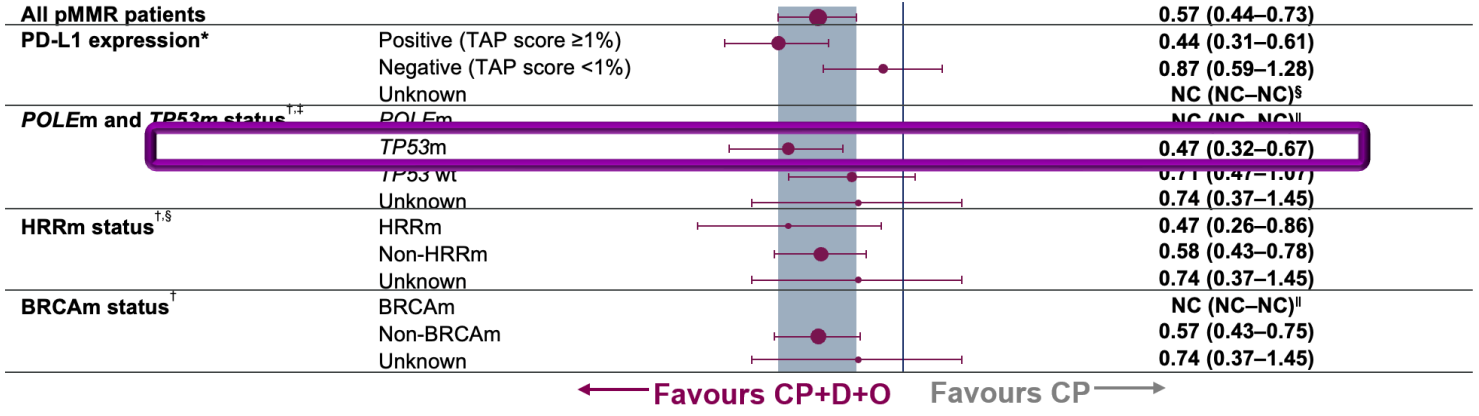
# Immune Checkpoint Inhibitor +PARPi in non-dMMR TP53mut

ENGOT-en6 /RUBY II




In the words of the economist Ronald Coarse:

**"If you torture the data enough, it will confess to anything."**




DUO-E

Mansoor Mirza, et al. ESMO 2023; Westin et al. IGCS 2024

# Endometrial Cancer – Molecular Driven Management: Role of Immunotherapy


- IO plus chemotherapy is effective in endometrial carcinoma
- ...not all patients respond
- Molecular characterisation: dMMR/POLE/NSMP/p53abn
- POLEm might respond better than dMMR to IO therapy (according mCRC)
- p53abn should not be used as selection criterion for IO therapy
- Assessment of immune response (rather than molecular subtype) may better predict response to immunotherapy


…bright future for immunotherapy
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