Latest Molecular-Driven Clinical Trial Data in Front-Line Advanced Endometrial Cancer

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Declaration of Interest

- Honoraria: AstraZeneca, Clovis, Genmab, Immunogen, Merck, Roche, Tesaro/GSK, PharmaMar
- Consulting or Advisory Role: AstraZeneca, Clovis Oncology, GSK, MSD, Immunogen, Genmab, Amgen, Seagen, PharmaMar, AstraZeneca, Merck Serono, Seagen, Genmab, Oncoinvest, Corcept, Sutro
- Speakers' Bureau: AstraZeneca, Clovis Oncology, GSK, MSD, PharmaMar
- Research Funding: Clovis (Inst), Merck (Inst), PharmaMar (Inst), Tesaro/GSK (Inst)
- Expert Testimony: Clovis
- Travel, Accommodations, Expenses: AstraZeneca, Clovis, PharmaMar, Roche, Tesaro

Study funding, medical writing, and editorial support: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

Recurrent Endometrial Cancer: Data for approved single-agent immunotherapies

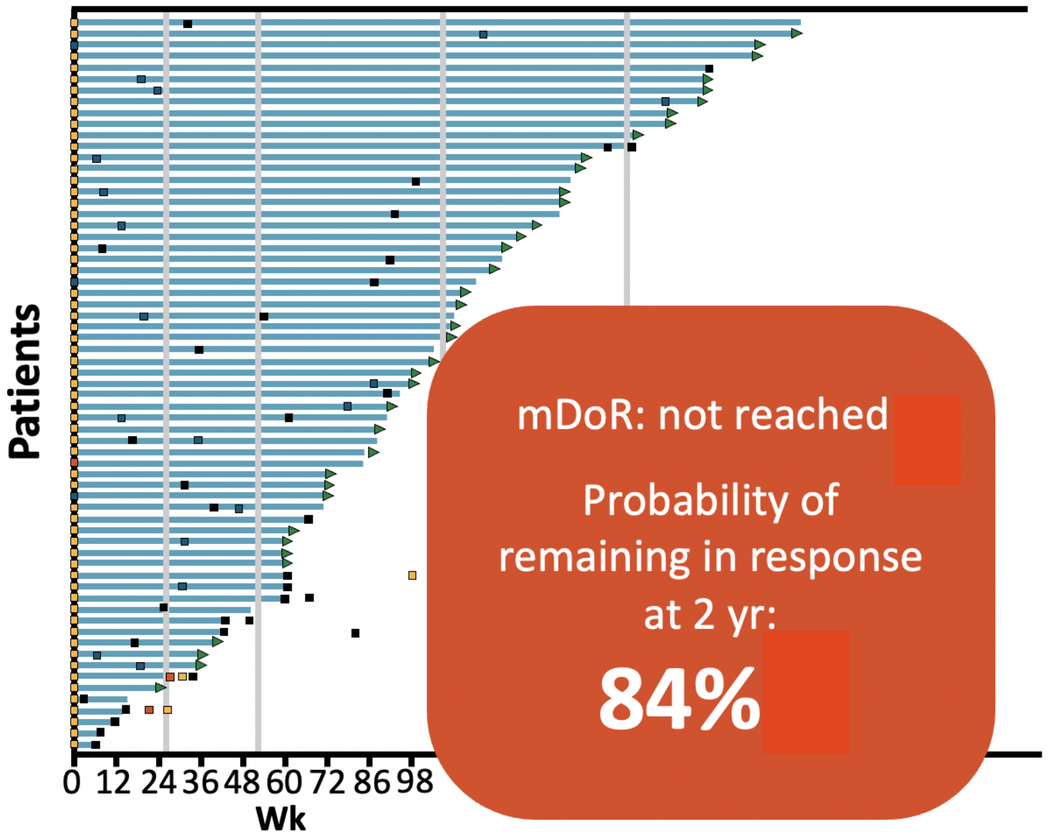
Parameter	KEYNOTE-158[1]: Pembrolizumab in MSI-H EC Cohorts D + K (n = 99)	GARNET[2]: Dostarlimab	
		Cohort A1† MMRd EC (n = 106*)	Cohort A2† pMMR EC (n = 142)[2]
ORR, % (95% CI)	**48 (37-60)**	**43.4 (33.8-53.4)**	**13.4 (8.3-20.1)**
Best overall response n (%)			
▪ CR	11 (14)	11 (10.4)	3 (2.1)
▪ PR	27 (34)	35 (33.0)	16 (11.3)
▪ SD	14 (18)	13 (12.3)	31 (21.8)
▪ PD	23 (29)	39 (36.8)	77 (54.2)
Median DoR, mo (range)	NR (2.9-49.7+)	NR	NR

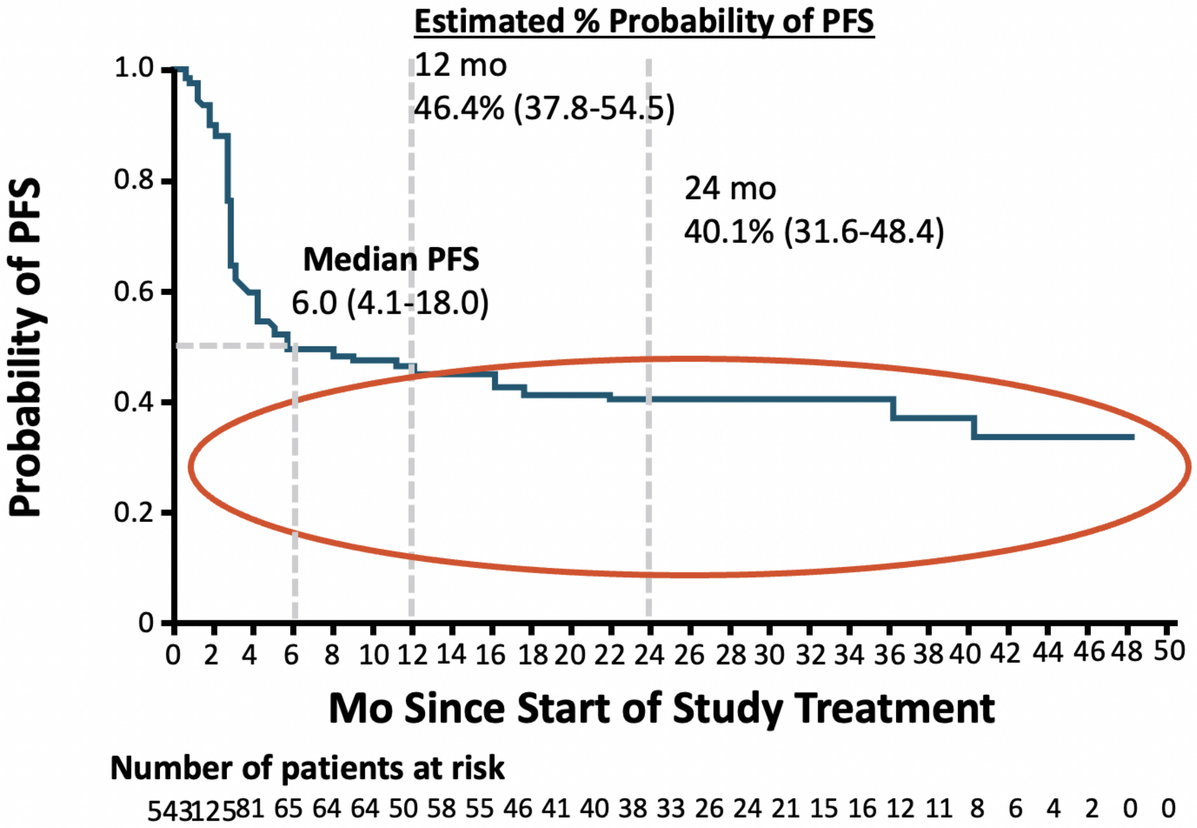
*3 patients were not evaluable for a response. †Median follow-up time for cohort A1 was 13.8 mo (9.5-22.1) and cohort A2 was 11.5 mo (11.0-25.1).

1. O'Malley. JCO. 2022;40:752. 2. Oaknin. J Immunother Cancer. 2022;10:e003777.

Immune-Checkpoint Inhibitor in Biomarker-Selected EC Following Platinum: Phase I GARNET Study

dMMR/MSI-H EC Cohort





Oaknin. ASCO 2022. Abstr 5509.

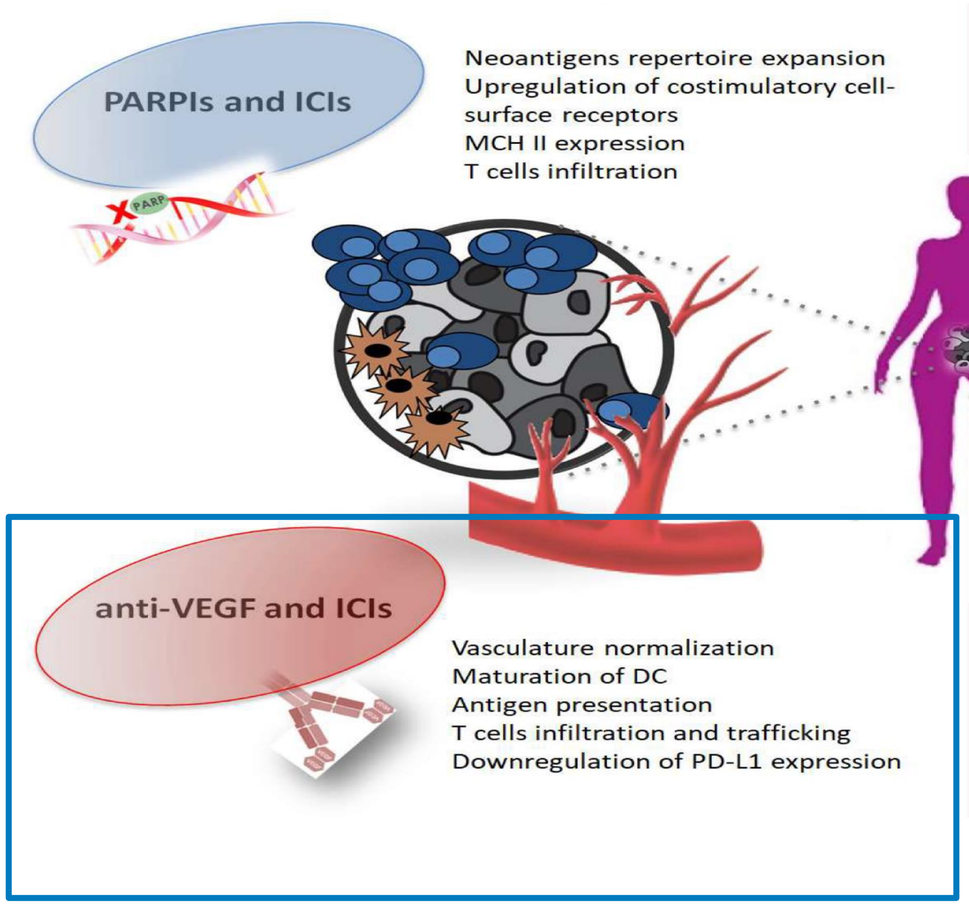
Historical Response to Anti–PD-1 Therapy pMMR/MSS Disease

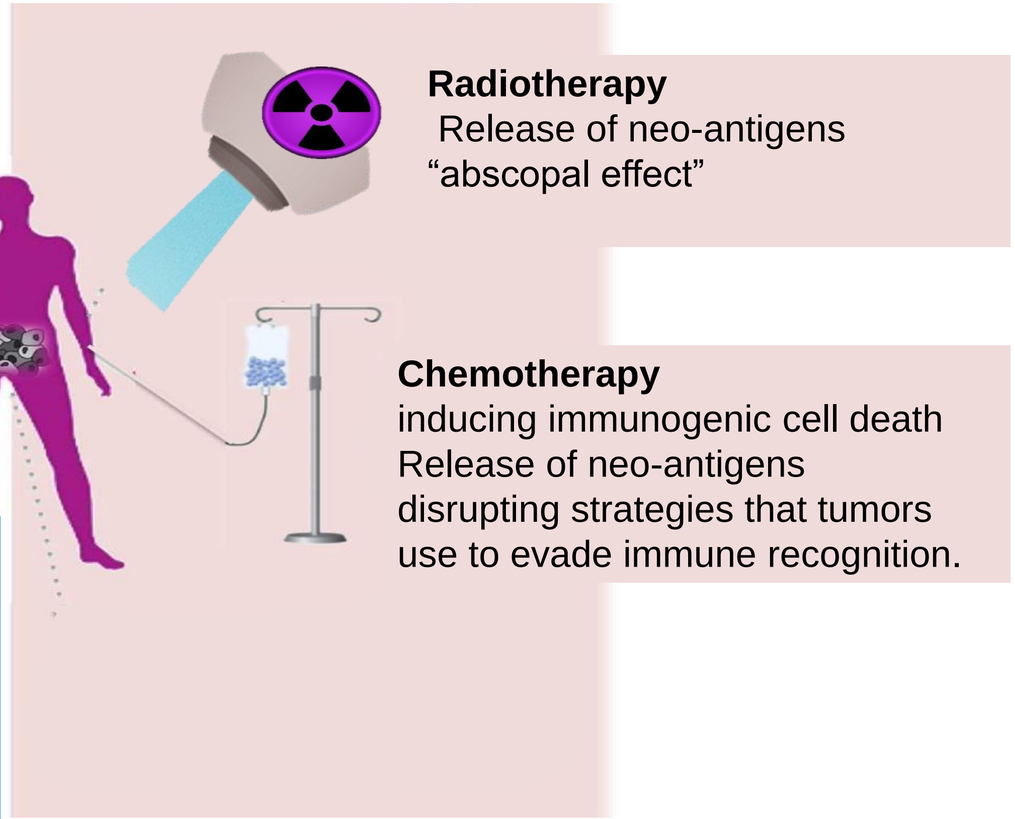
Parameter	KEYNOTE-028[1]	NCT01375842[2]	GARNET[3]	NCT02912572[4]	PHAEDRA[5]
Treatment	Pembrolizumab	Atezolizumab	Dostarlimab	Avelumab	Durvalumab
Phase	Ib	Ia	I/II	II	II
Cohort	Previously treated or metastatic PD-L1+ EC	Incurable or metastatic EC	Previously treated recurrent/ advanced pMMR EC	pMMR recurrent EC	Recurrent pMMR EC
Patients, n	23	15	142	16	35
ORR, %	13*	13†	13.4	6	3
mPFS	1.8 mo	1.4 mo	--	1.9 mo	--
mOS	NR	9.6 mo	--	6.6 mo	--

1. Olt. JCO. 2017;35:2636. 2. Fleming. ASCO 2017. Abstr 5585. 3. Oaknin. ESMO 2020. Abstr LBA36. 4. Konstantinopoulos. JCO.2019;37:2786. 5. Antill. ASCO 2019. Abstr 5501

Immunotherapy Combination

Leveraging ICI's Activity





Radiotherapy
Release of neo-antigens
"abscopal effect"

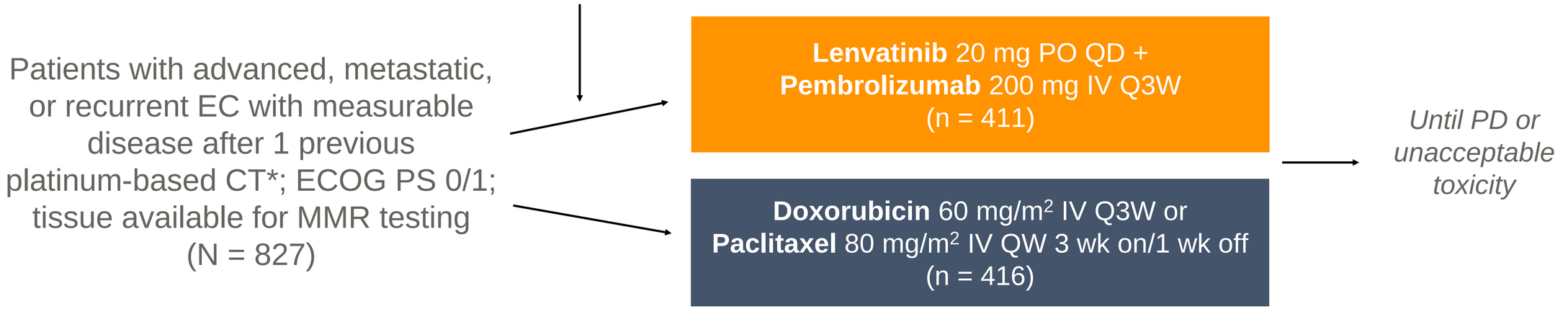
Chemotherapy
inducing immunogenic cell death
Release of neo-antigens
disrupting strategies that tumors use to evade immune recognition.

Study 309/KEYNOTE-775: Lenvatinib + Pembrolizumab After Platinum in Advanced EC

- **Confirmatory, randomized, open-label phase III study**

FDA Accelerated Approval September 2019
FDA Priority Review May 2021
For patients with endometrial cancer who are not MSI-H or dMMR

Stratified by MMR status (pMMR vs dMMR), within pMMR by region, ECOG PS 0 vs 1, prior history of pelvic radiation

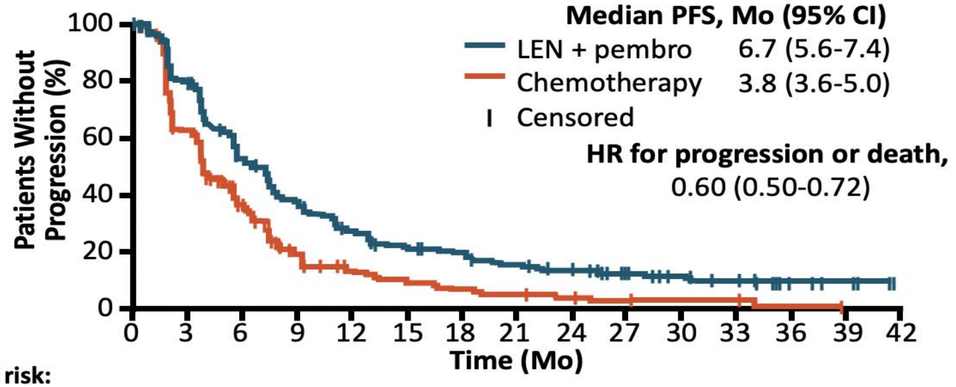


Primary endpoints: PFS by BICR, OS

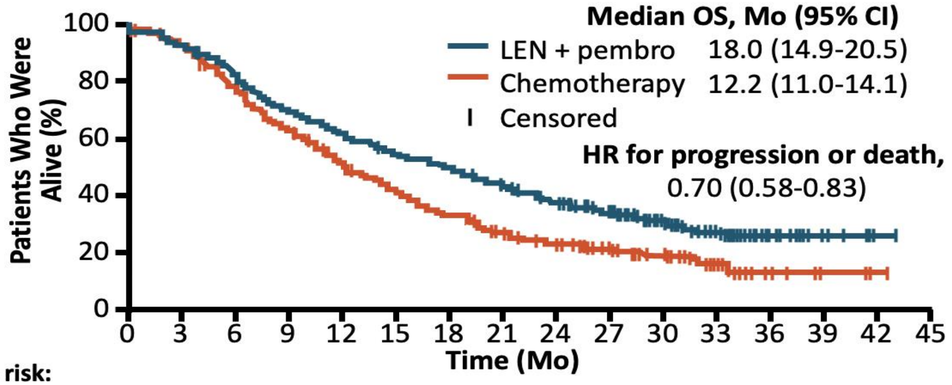
- Secondary endpoints: ORR, health-related quality of life, pharmacokinetics, safety
- Key exploratory endpoint: DoR

Study 309/KEYNOTE-775: PFS and OS Benefit

pMMR

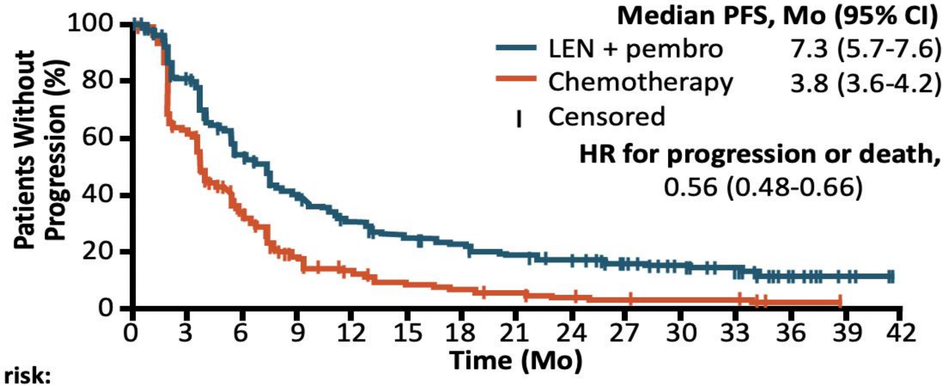


No. at risk:															
LEN + pembro	346	265	166	116	80	61	55	43	36	24	18	14	6	4	0
Chemotherapy	351	177	83	38	23	16	12	9	6	4	3	3	1	0	0

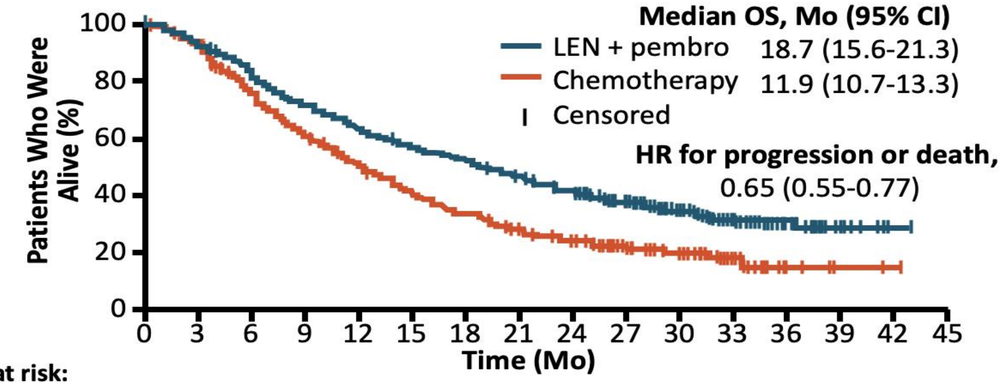


No. at risk:															
LEN + pembro	346	322	285	242	214	188	171	148	124	95	65	41	20	7	2
Chemotherapy	351	324	267	217	171	138	111	86	71	53	40	21	6	3	1

All Comers



No. at risk:															
LEN + pembro	411	317	203	148	109	87	79	65	57	45	35	23	10	4	0
Chemotherapy	416	214	95	43	27	19	15	11	8	6	5	5	1	0	0



No. at risk:															
LEN + pembro	411	383	337	292	258	229	211	186	160	125	91	58	30	10	2
Chemotherapy	416	378	305	246	196	158	129	104	84	64	49	28	6	3	1

Makker. NEJM. 2022;386:437. Makker. JCO. 2023;[Epub].

Treatment Exposure, Safety, and Discontinuation in All Comers

	LEN + PEMBRO (n = 406)	TPC (n = 388)
Median duration of treatment, days (range)	231 (1-817)	104.5 (1-785)
Patients with any TEAEs (%)	99.8	99.5
Grade ≥ 3	88.9	72.7
Patients with any TEAEs leading to dose reductions (%)[a]	66.5	12.9
Patients with any grade TEAEs leading to discontinuation (%)[b]	33.0	8.0
LEN[c]	30.8	--
Pembro[c]	18.7	--
LEN + pembro	14.0	--
Patients with any grade TEAEs leading to interruption (%)[b]	69.2	27.1
LEN[c]	58.6	--
Pembro[c]	50.0	--
LEN + pembro	30.8	--

[a]Includes LEN only or Treatment of Physician's Choice (TPC). [b]Includes LEN or pembro or LEN + pembro or TPC. [c]Regardless of action taken with the other drug in the combination arm.

Study 309/KEYNOTE-775: TEAEs

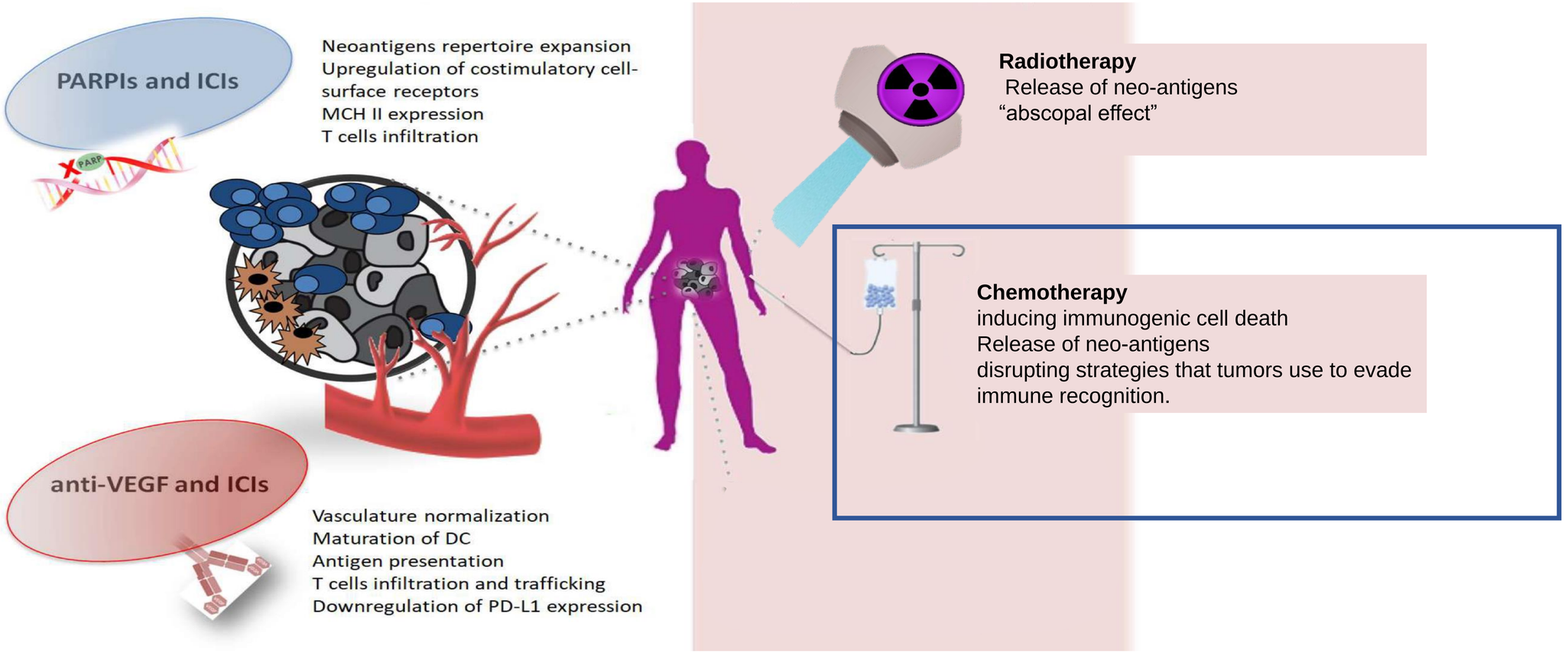
TEAE, %	Lenvatinib + Pembrolizumab (n = 406)		Doxorubicin or Paclitaxel (n = 388)	
	Any Grade	Grade ≥3*	Any Grade	Grade ≥3*
Hypertension	65.0	39.2	5.2	2.6
Hypothyroidism	58.9	1.5	0.8	0
Diarrhea	55.7	8.1	20.4	2.1
Nausea	51.7	3.4	46.4	1.3
Decreased appetite	46.6	7.6	21.4	0.5
Vomiting	37.7	3.0	21.1	2.6
Weight decrease	35.5	10.8	5.9	0.3
Fatigue	34.0	5.4	27.6	3.1
Arthralgia	32.3	1.7	8.0	0

TEAE, %	Lenvatinib + Pembrolizumab (n = 406)		Doxorubicin or Paclitaxel (n = 388)	
	Any Grade	Grade ≥3*	Any Grade	Grade ≥3*
Proteinuria	30.5	5.2	3.4	0.3
Constipation	28.3	0.7	24.5	0.5
Anemia	28.1	6.9	48.7	15.5
UTI	27.6	4.2	10.3	1.0
Headache	26.4	0.5	9.0	0.3
Neutropenia	9.1	2.0	34.0	26.0
Alopecia	5.9	0	30.9	0.3

*In the lenvatinib and pembrolizumab arm, 6.4% of patients suffered grade 5 AEs, and 5.2% of patients in the TPC arm suffered grade 5 AEs.

Makker. NEJM. 2022;386:437. Makker. JCO. 2023;[Epub].

ICIs in unselected EC population
Combination approaches to enhance ICIs efficacy



Clinically Significant Data

ENGOT European Network of Gynaecological Oncological Trial groups | NSGO-CTU Nordic Society of Gynaecological Oncology - Clinical Trial Unit | GOG FOUNDATION

Dostarlimab in Combination with Chemotherapy for the Treatment of Primary Advanced or Recurrent Endometrial Cancer: a Placebo-Controlled Randomized Phase 3 Trial (ENGOT-EN6-NSGO/GOG-3031/RUBY)

Mansoor R. Mirza,[1] Dana Chase,[2] Brian Slomovitz,[3] René DePont Christensen,[4] Zoltán Novák,[5] Destin Black,[6] Lucy Gilbert,[7] Sudarshan Sharma,[8] Giorgio Valabrega,[9] Lisa M. Landrum,[10] Lars C. Hanker,[11] Ashley Stuckey,[12] Ingrid Boere,[13] Michael A. Gold,[14] Sarah E. Gill,[15] Bradley J. Monk,[16] Zangdong He,[17] Shadi Stevens,[18] Robert L. Coleman,[19] Matthew A. Powell[20]

[1]Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, and Nordic Society of Gynaecologic Oncology-Clinical Trial Unit, Copenhagen Denmark; [2]*David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [3]Department of Gynecologic Oncology, Mount Sinai Medical Center, and Department of Obstetrics and Gynecology, Florida International University, Miami Beach, FL, USA; [4]Research Unit for General Practice, University of Southern Denmark, Institute of Public Health, Odense, Denmark; [5]Department of Gynecology, Hungarian National Institute of Oncology, Budapest, Hungary; [6]Department of Obstetrics and Gynecology, LSU Health Shreveport, and Willis-Knighton Physician Network, Shreveport, LA, USA; [7]Division of Gynecologic Oncology, McGill University Health Centre, Montreal, Quebec, Canada; [8]Department of Obstetrics/Gynecology, AMITA Adventist Hinsdale Hospital, Hinsdale, IL, USA; [9]University of Torino, AO Ordine Mauriziano, Torino, Italy; [10]Indiana University Health and Simon Cancer Center, Indianapolis, IN, USA; [11]Department of Gynecology and Obstetrics, University Hospital Schleswig-Holstein, Campus Lübeck, Lübeck, Germany; [12]Women and Infants Hospital, Providence, RI, USA; [13]Department of Medical Oncology, Erasmus MC Cancer Centre, Rotterdam, The Netherlands; [14]Oklahoma Cancer Specialists and Research Institute, Tulsa, OK, USA; [15]Division of Gynecologic Oncology, Nancy N. and J.C Lewis Cancer and Research Pavilion, Savannah, GA, USA; [16]HonorHealth Research Institute, University of Arizona College of Medicine, Phoenix, and Creighton University School of Medicine, Phoenix, AZ, USA; [17]GSK, Collegeville, PA, USA; [18]GSK, London, UK; [19]US Oncology Research, The Woodlands, TX, USA; [20]National Cancer Institute sponsored NRG Oncology, Washington University School of Medicine, St Louis, MO, USA;

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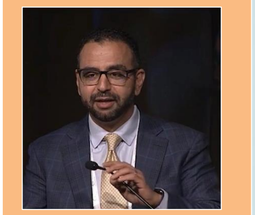
Scan for slides



Pembrolizumab Versus Placebo in Addition to Carboplatin and Paclitaxel for Measurable Stage III or IVA, Stage IVB, or Recurrent Endometrial Cancer: The Phase 3, NRG GY018 Study

Ramez N. Eskander, MD, Michael W. Sill, PhD, Lindsey Beffa, MD, Richard G. Moore, MD, Joanie Mayer Hope, MD, Fernanda B. Musa, MD, Robert Mannel, MD, Mark S. Shahin, MD, Guilherme H. Cantuaria, MD, Eugenia Girda, MD, Cara Mathews, MD, Juraj Kavecansky, MD, Charles A. Leath, III, MD, MSPH, Lilian T. Gien, MD, Emily M. Hinchcliff, MD, MPH, Shashikant B. Lele, MD, Lisa M. Landrum, MD, Floor Backes, MD, Roisin E. O'Cearbhaill, MD, Tareq Al Baghdadi, MD, Emily K. Hill, MD, Premal H. Thaker, MD, MS, Veena Susan John, MD, Stephen Welch, MD, Amanda N Fader, MD, Matthew A. Powell, MD, Carol Aghajanian, MD

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Dr. Mirza presents RUBY Part 1 data[1]

Dr. Eskander presents GY018 data[2]

July 31, 2023: Dostarlimab + chemotherapy approved as 1L treatment for dMMR/MSI-H EC (US)[1]

Eskander RN, Pembrolizumab plus Chemotherapy in Advanced Endometrial Cancer; N Engl J Med 2023; 388:2159-2170;

Mirza MR, Dostarlimab for Primary Advanced or Recurrent Endometrial Cance;; N Engl J Med 2023; 388:2145-2158

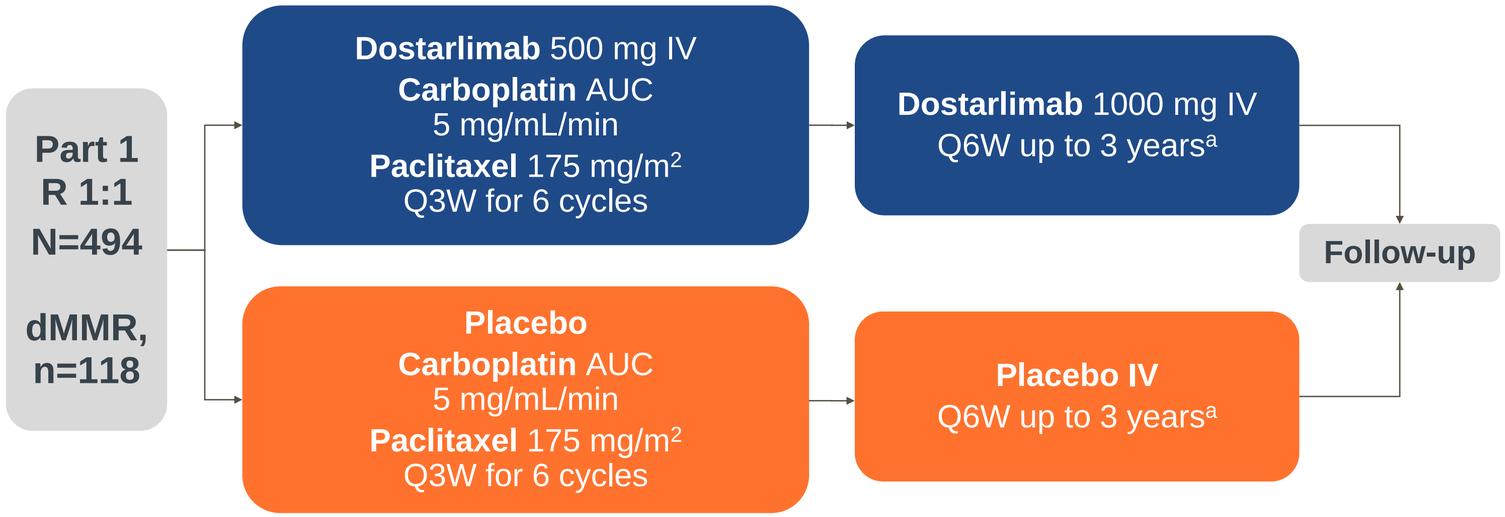
RUBY Part 1 | ENGOT-en6 | GOG-3031[1]

Eligible patients

- Histologically or cytologically proven EC with recurrent or advanced disease
- Stage III or IV disease or first recurrence of EC with low potential for cure by use of radiation therapy or surgery alone or in combination
  - Carcinosarcoma, clear cell, serous, or mixed histology
- Naive to systemic therapy or systemic anticancer therapy and recurrence or PD ≥6 months after completing treatment
- ECOG PS 0 or 1
- Adequate organ function

Stratification

- MMR/MSI status
- Prior radiotherapy
- Disease status



Primary end points: PFS (IA), OS

Secondary end points: PFS (BICR), PFS2, ORR/DOR/DCR, QOL, PK and immunogenicity, safety

. 1..Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.
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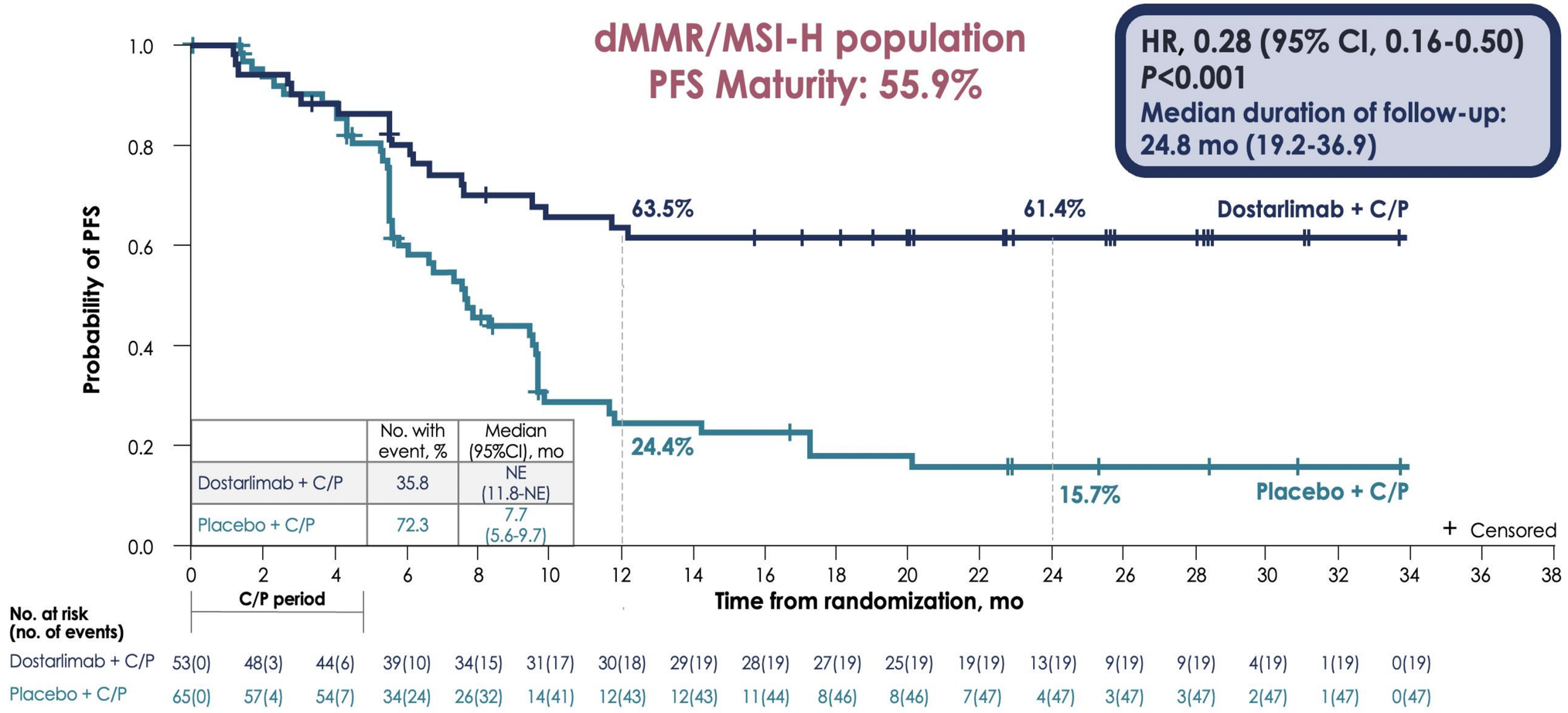
RUBY Part 1 | ENGOT-en6 | GOG-3031[1]



. 1..Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.
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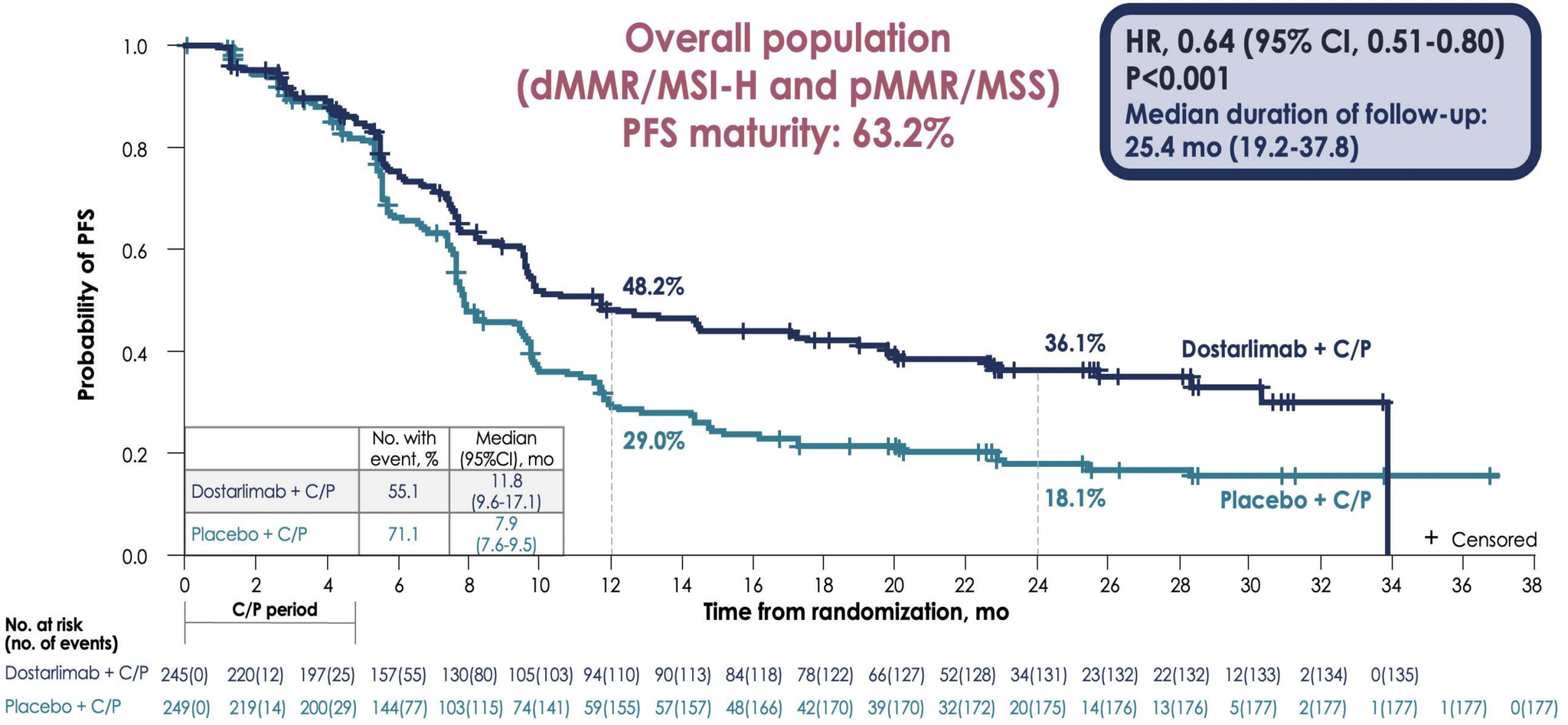
RUBY Part 1 | ENGOT-en6 | GOG-3031[1]



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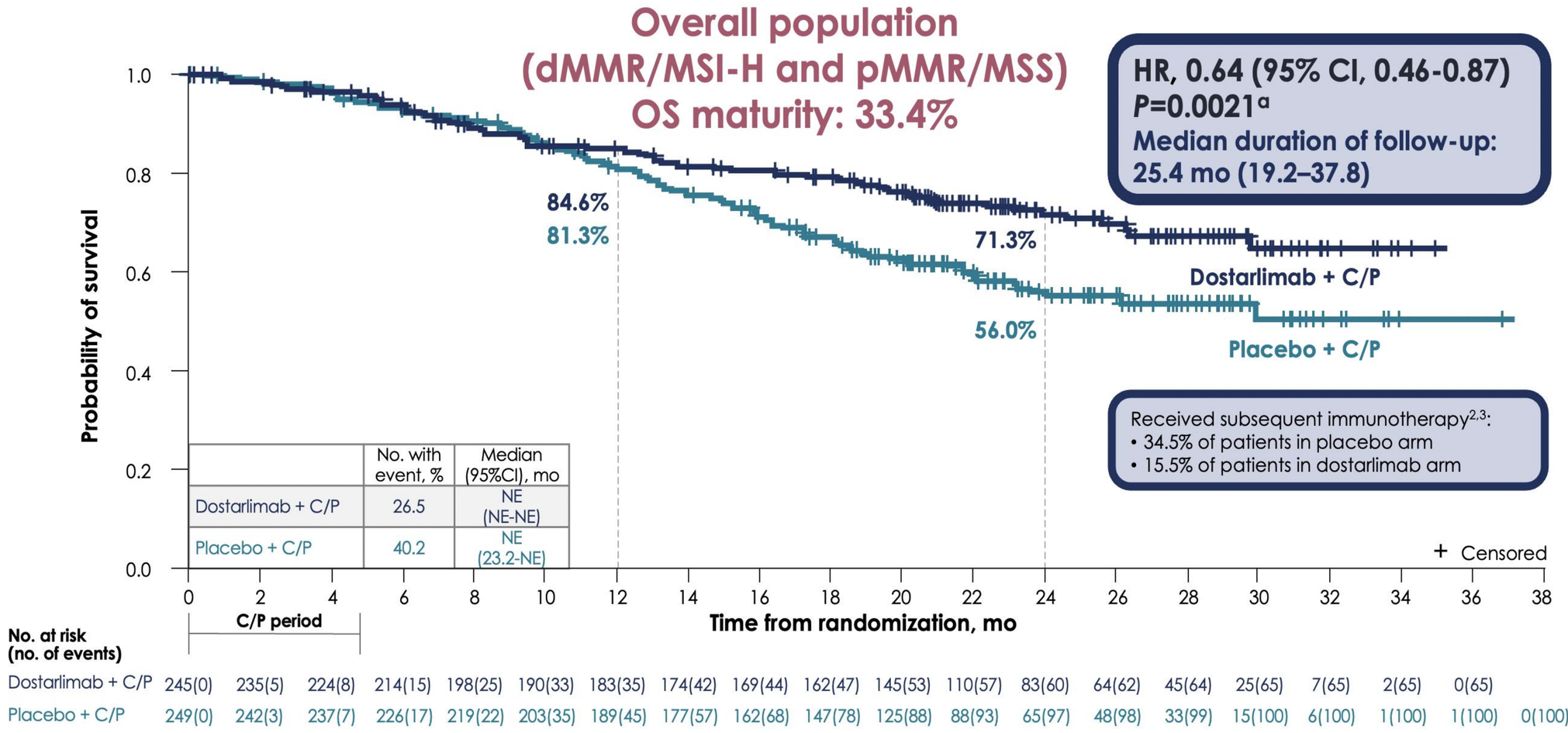
RUBY Part 1 | ENGOT-en6 | GOG-3031[1]



. 1..Mirza MR, et al. *N Engl J Med*. 2023;388:2145-2158.
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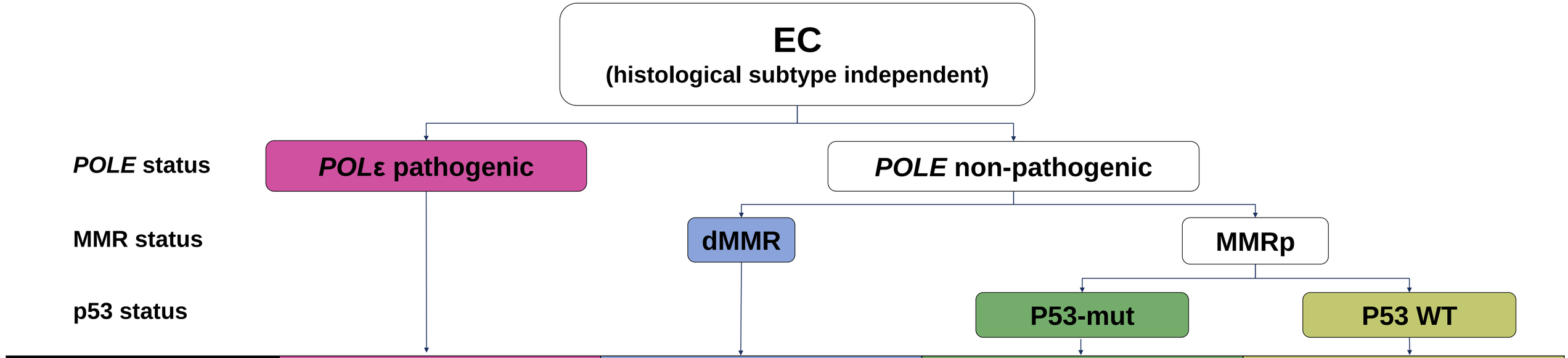
RUBY Molecular Classification Algorithm

- In RUBY Part 1, molecular classification was performed for all participants with WES results – 400 of 494 patients

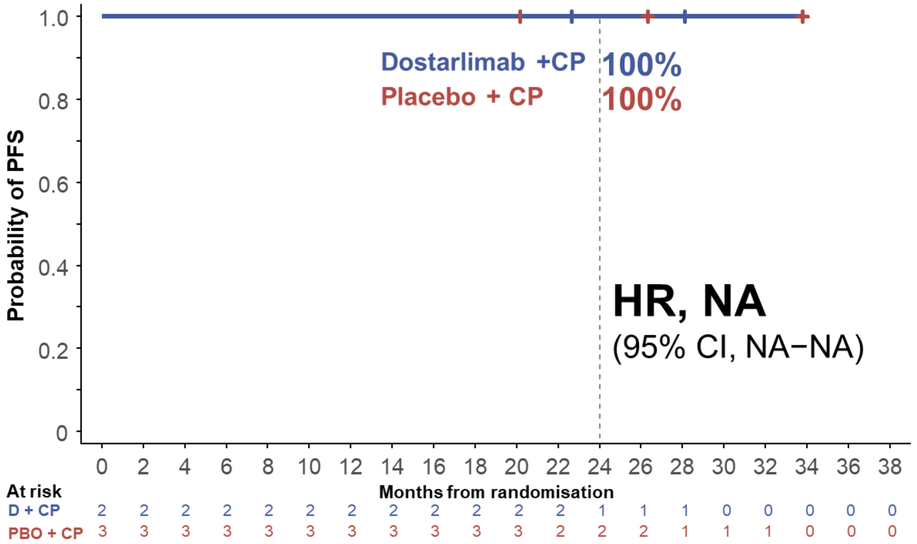


Integrated diagnosis	POLεmut (EDM)	dMMR (or MSI-H)	TP53 aberrant	NSMP
Prevalence in RUBY (n/N)	**1.25%** (5/400)	**22.75%** (91/400)	**22%** (88/400)	**54%** (216/400)
Diagnostic test	WES	Results of local (IHC, NGS, PCR) or central test (IHC) provided for RUBY at randomization	WES	

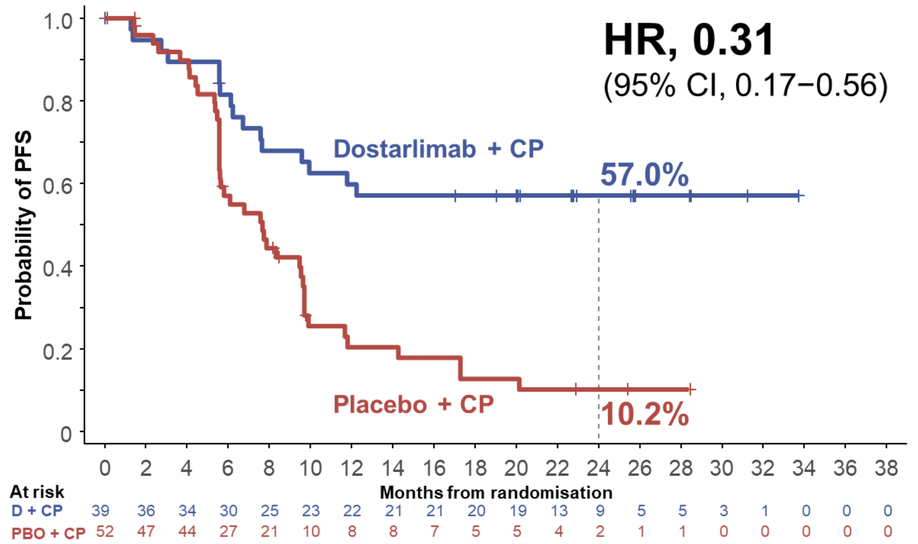
Efficacy per molecular classification was an exploratory analysis.
dMMR, mismatch repair deficient; IHC, immunohistochemistry; MMRp, mismatch repair proficient; MSI-H, microsatellite instability-high; mut, mutated; NGS, next generation sequencing; NSMP, no specific molecular profile; PCR, polymerase chain reaction; POLε , polymerase epsilon; SCNA, somatic copy number alterations; TIL, tumor-infiltrating lymphocytes; TLS, tertiary lymphoid structures; TP53, tumor protein 53; WES, whole exome DNA sequencing; WT, wild type.

PFS According to Molecular Subgroup

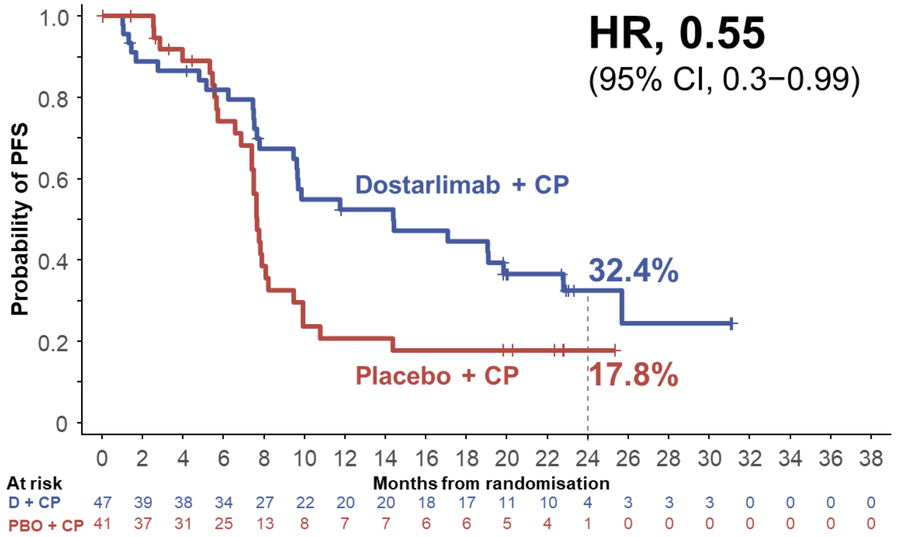
POLε mut



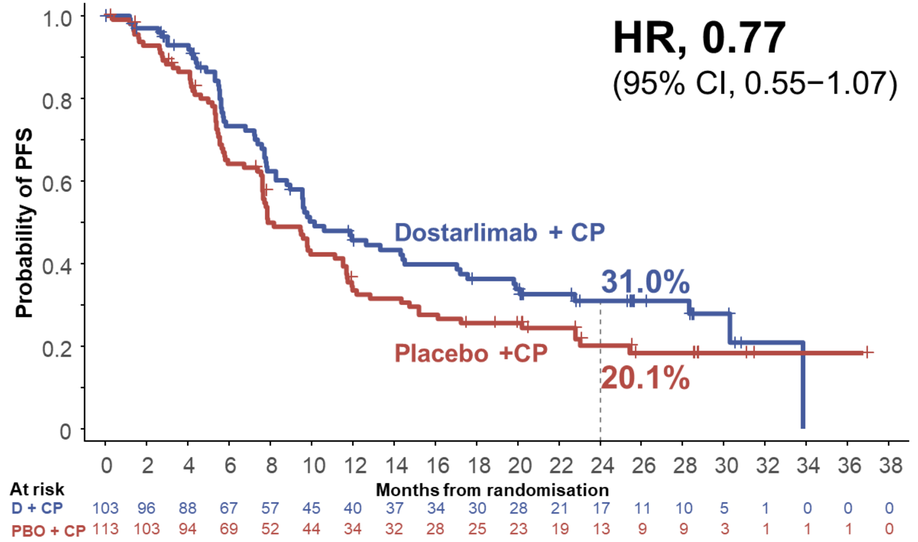
dMMR/MSI-H



TP53 mut



NSMP



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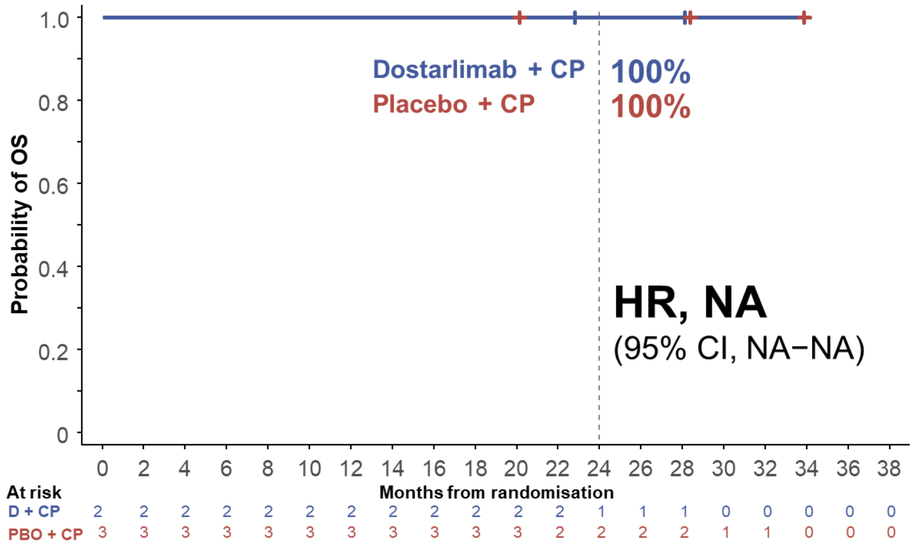
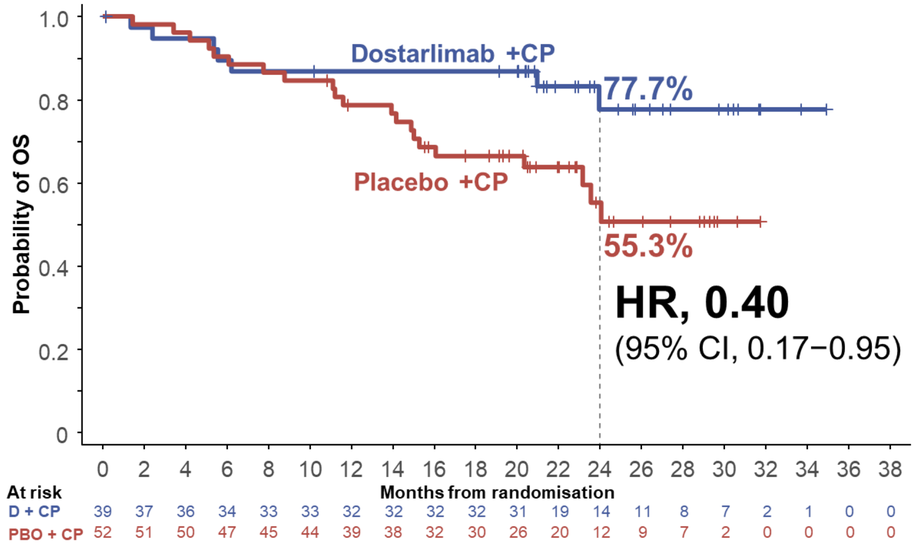
Data based on exploratory analysis based on 400 patients from the RUBY trial with known molecular classification with whole exome sequencing.
CP, carboplatin-paclitaxel; D, dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability–high; mut, mutated; NR, not reached; NSMP, no specific molecular profile; OS, overall survival; PBO, placebo; POLε , polymerase epsilon; TP53, tumor protein 53.

OS According to Molecular Subgroup

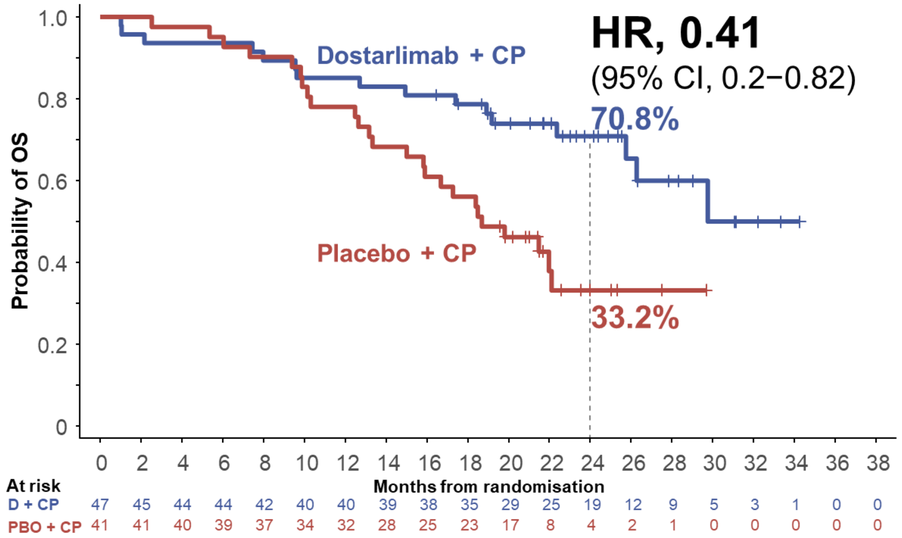
POLε mut



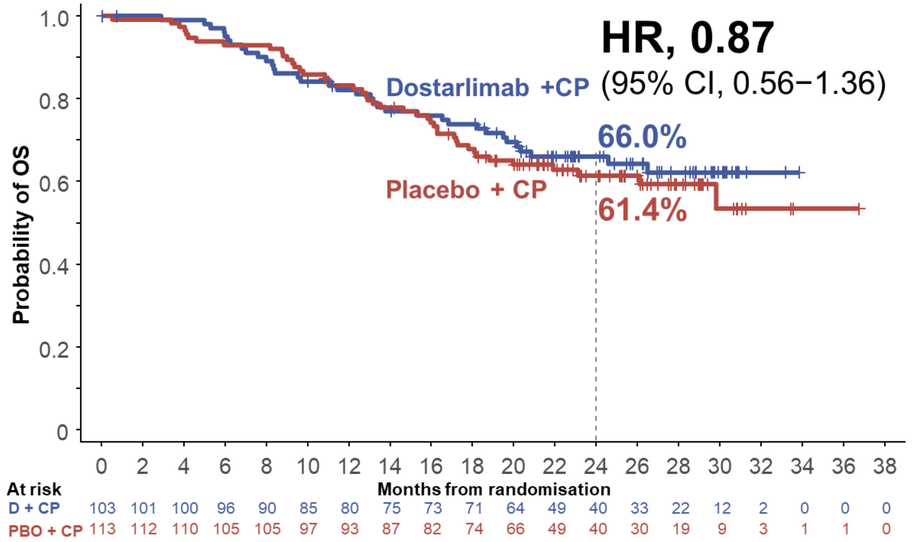
dMMR/MSI-H



TP53 mut



NSMP



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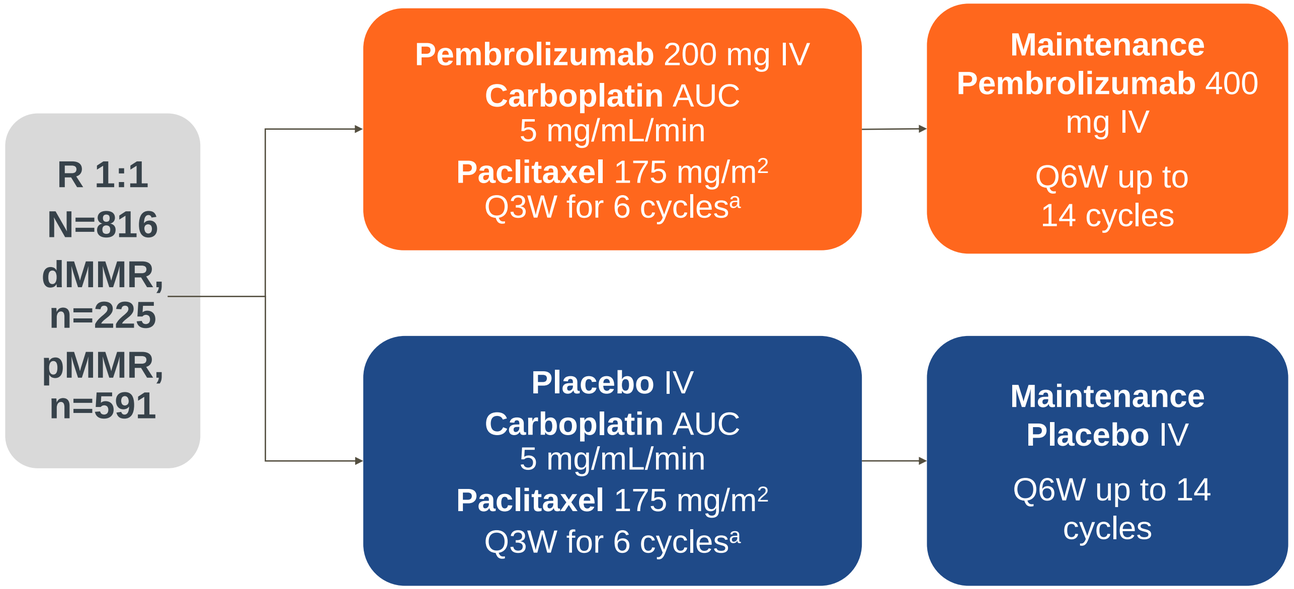
GY018 | KEYNOTE-868[1]

Eligible patients

- Histologically confirmed recurrent or advanced (stage III, IVA, or IVB) EC
- ECOG PS of 0-2
- Results of institutional MMR IHC testing
- Submission of tumor specimens for centralized MMR IHC testing
- No prior chemotherapy treatment for EC
- Prior adjuvant chemotherapy allowed if completed ≥12 months before enrollment

Stratification

- MMR status
- ECOG PS (0, 1 or 2)
- Prior chemotherapy (yes/no)

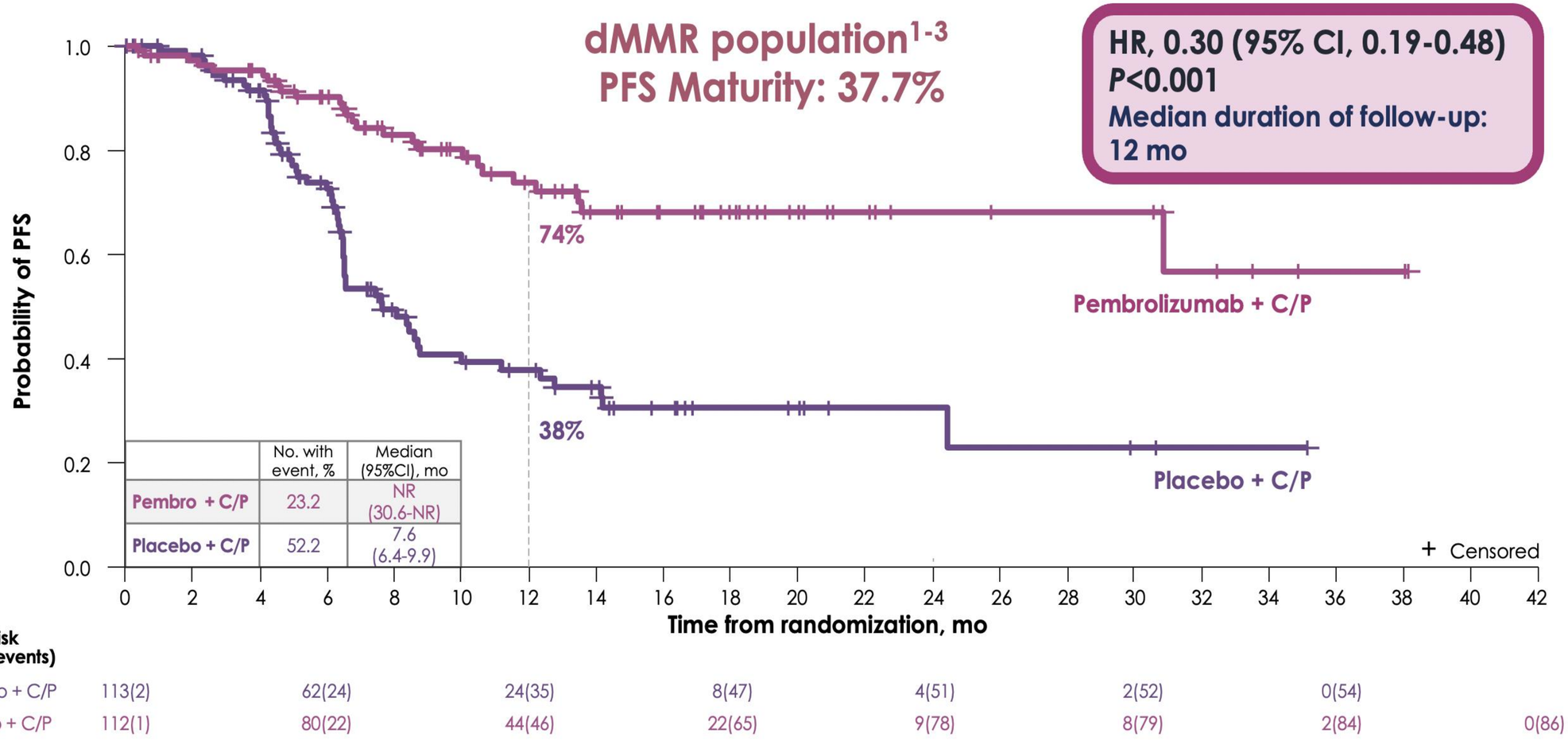


Primary end point: PFS (IA)

Secondary end points: AEs, ORR, DOR, OS, QOL, concordance between institutional MMR IHC and centralized MMR IHC

1. Eskander RN, et al. *N Engl J Med*. 2023;388:2159-2170.

GY018 | KEYNOTE-868[1]

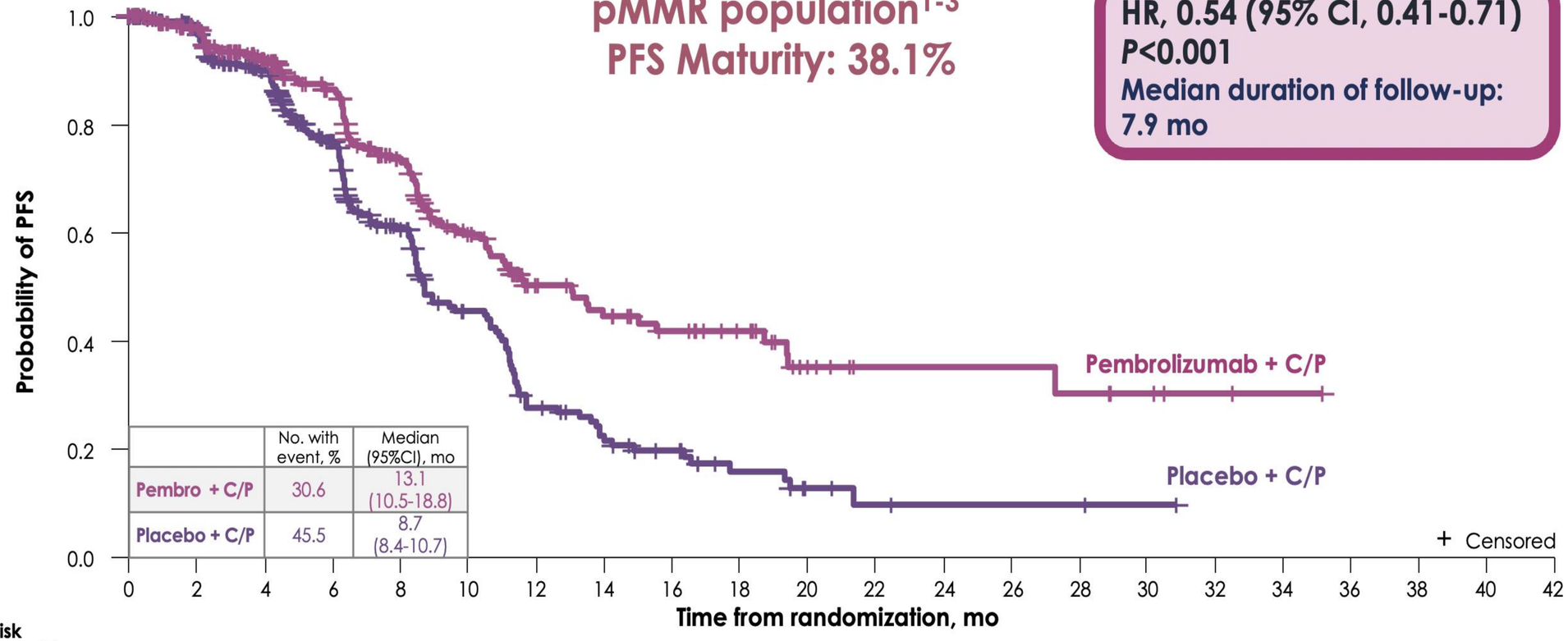


1. Eskander RN, et al. *N Engl J Med*. 2023;388:2159-2170.

GY018 | KEYNOTE-868[1]

pMMR population[1-3]
PFS Maturity: 38.1%

HR, 0.54 (95% CI, 0.41-0.71)
***P*<0.001**
Median duration of follow-up: 7.9 mo



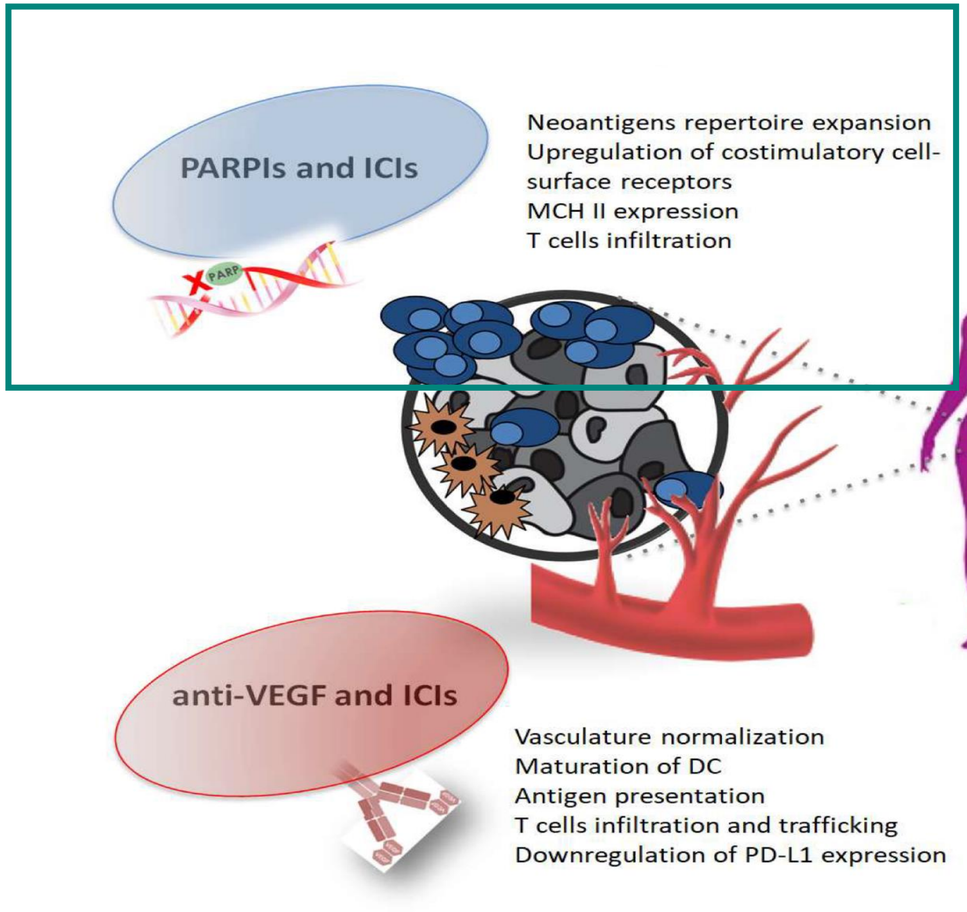
	No. with event, %	Median (95%CI), mo
Pembro + C/P	30.6	13.1 (10.5-18.8)
Placebo + C/P	45.5	8.7 (8.4-10.7)

No. at risk (no. of events)

Placebo + C/P	292(14)	129(115)	33(141)	10(152)	2(157)	1 (158)	0(159)
Pembro + C/P	290(15)	150(112)	45(167)	20(185)	7(195)	3(198)	0(201)

1. Eskander RN, et al. *N Engl J Med*. 2023;388:2159-2170.

ICIs in unselected EC population
Combination approaches to enhance ICIs efficacy

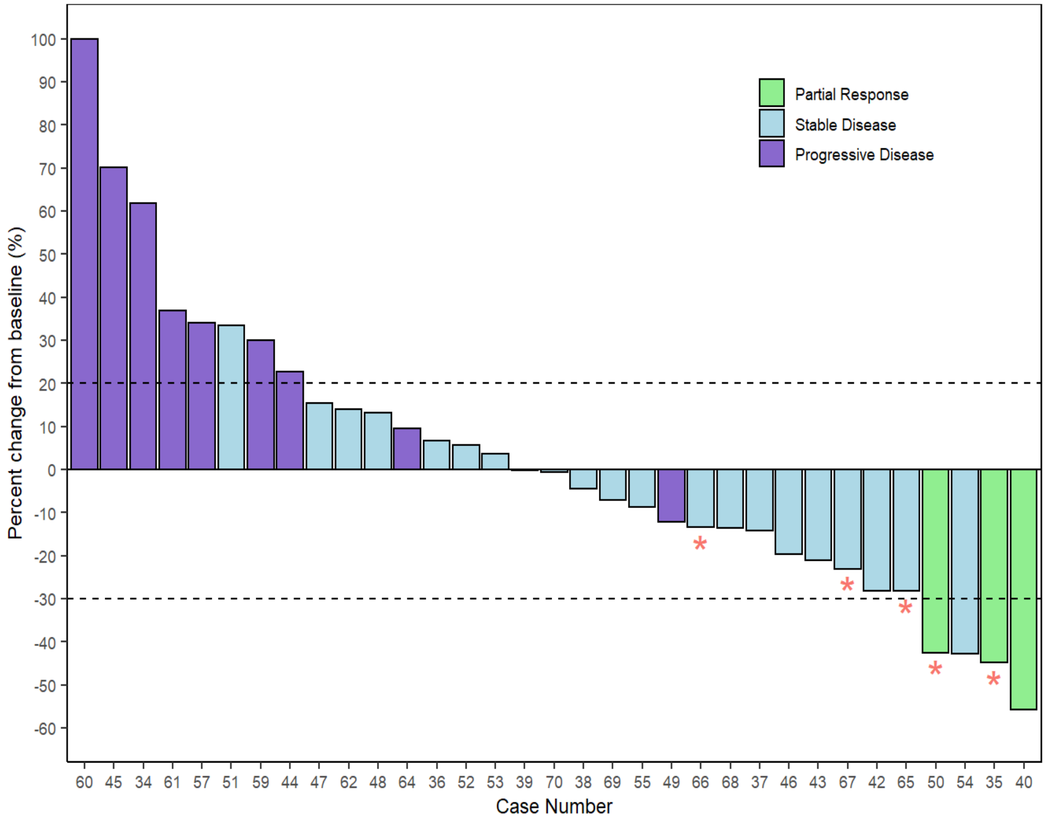


Radiotherapy
Release of neo-antigens
"abscopal effect"

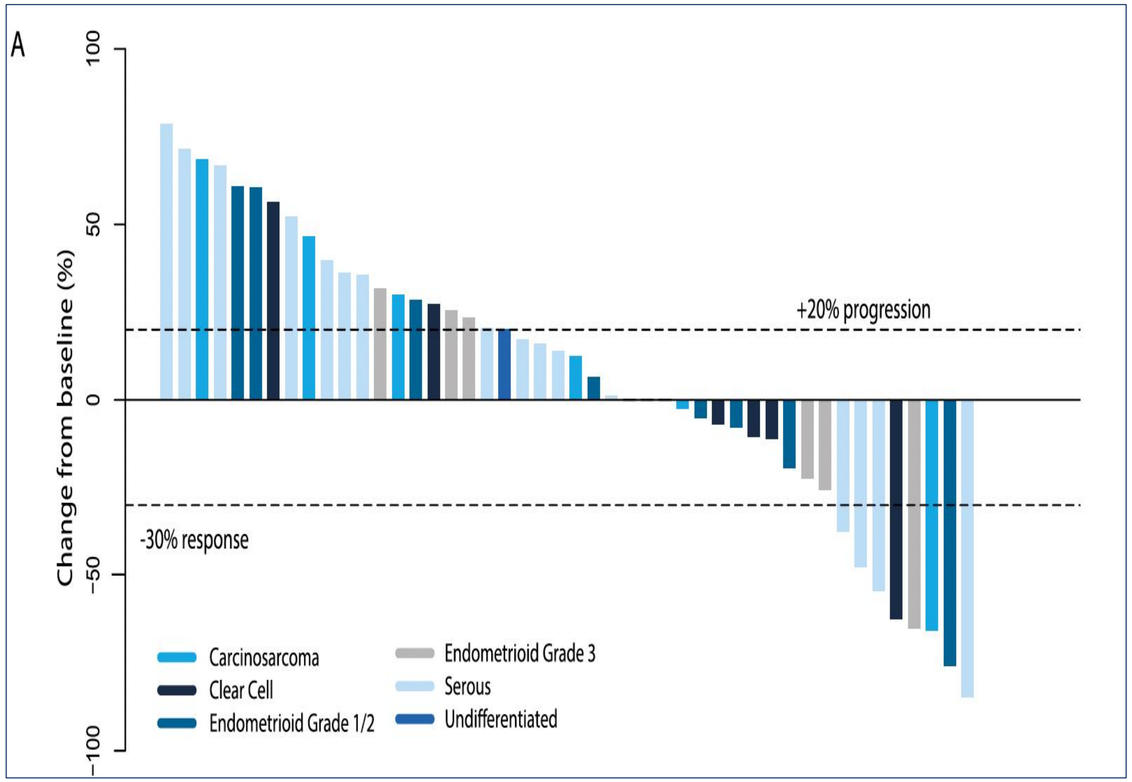
Chemotherapy
inducing immunogenic cell death
Release of neo-antigens
disrupting strategies that tumors use to evade immune recognition.

ICI's Activity and PARP inhibitors: Combination Approaches

- **Phase 2:Talazoparib** 1mg PO daily and **Avelumab** 10 mg/kg IV every 2 weeks **in N= 35 previously pretreated recurrent MSS EC patients.**



- **Phase 2 DOMEC trial: Durvalumab** 1500 mg i.v. every 4weeks **and Olaparib** 300mg/12h **in N=50 previously pretreated recurrent (20%dMMR) EC patients.**

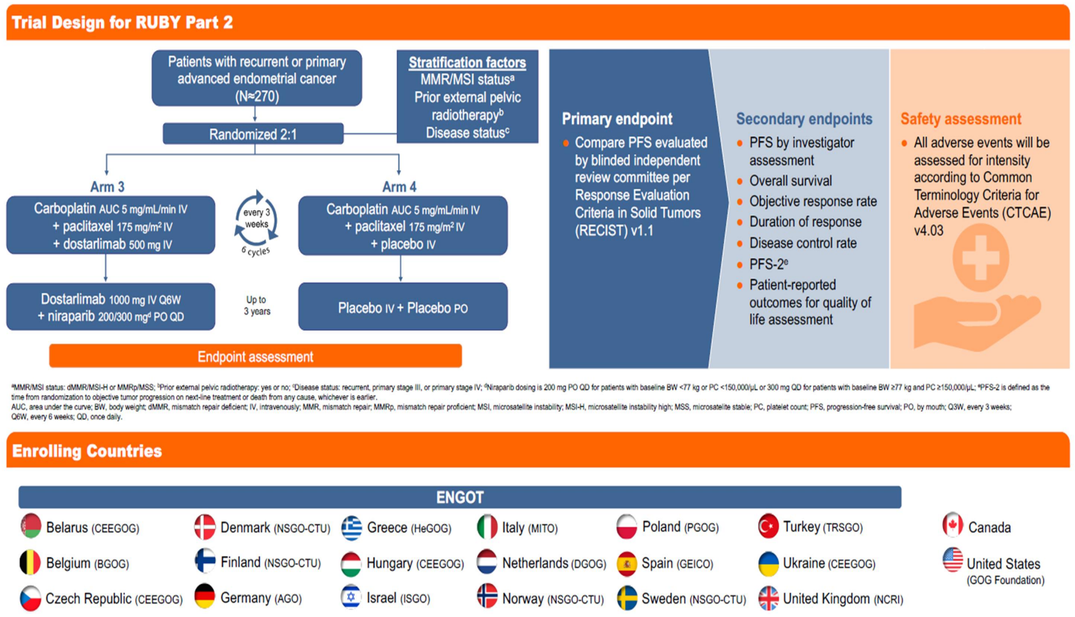


SEOUL IGCS 2023

PARPis plus ICIs in advanced Endometrial Cancer
Ongoing phase III randomized trials

RUBY trial: Study design

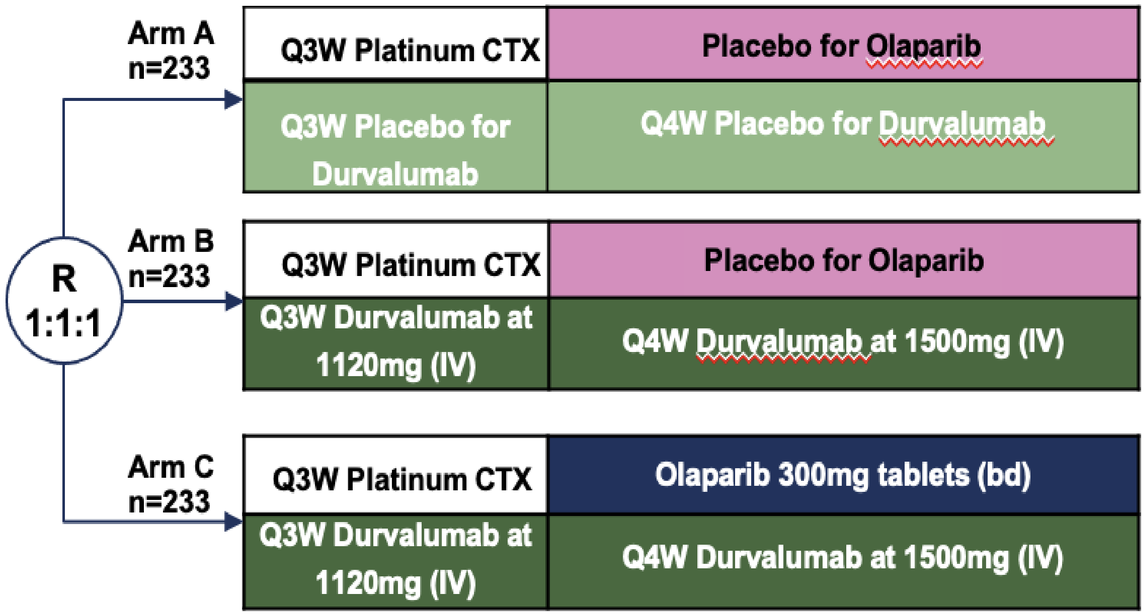
Multicenter Phase 3 study that will evaluate the efficacy and safety of DOSTARLIMAB + carboplatin-paclitaxel followed by DOSTARLIMAB + NIRAPARIB



clinicaltrials.gov:01244789;

DUO-E trial: Study design

Multicenter Phase 3 study that will evaluate the efficacy and safety of DURVALUMAB + carboplatin-paclitaxel followed by DURVALUMAB + OLAPARIB or DURVALUMAB or OLAPARIB

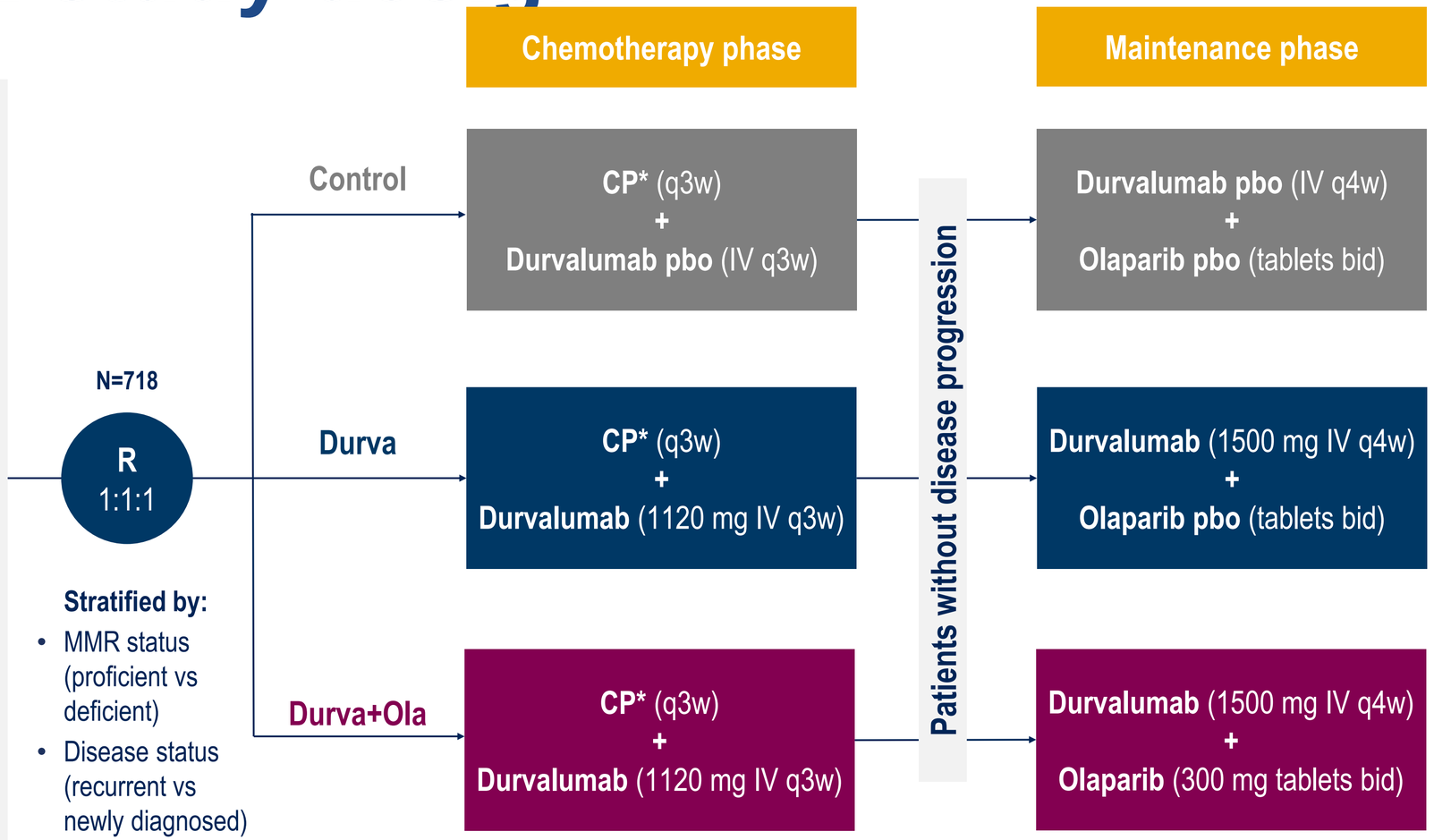


clinicaltrials.gov:05173987

DUO-E study design

Patients

- Newly diagnosed FIGO 2009 Stage III/IV or recurrent endometrial cancer
- Known MMR status
- Naïve to first-line systemic anticancer treatment for advanced disease
- Naïve to PARP inhibitors and immune-mediated therapy
- Adjuvant chemotherapy allowed if ≥12 months from last treatment to relapse
- All histologies except sarcomas



Stratified by:

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

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

Endpoints

Primary

- PFS (RECIST per investigator) in:
  - Durva vs Control
  - Durva+Ola vs Control

Key secondary

- OS (analytical)
- Safety

Exploratory

- PFS in Durva+Ola vs Durva
- Subgroup analyses of PFS
  - Including MMR, PD-L1, HRRm

*Six cycles of carboplatin at an area under the concentration–time curve of 5 or 6 mg per mL/min and paclitaxel 175 mg/m^2.

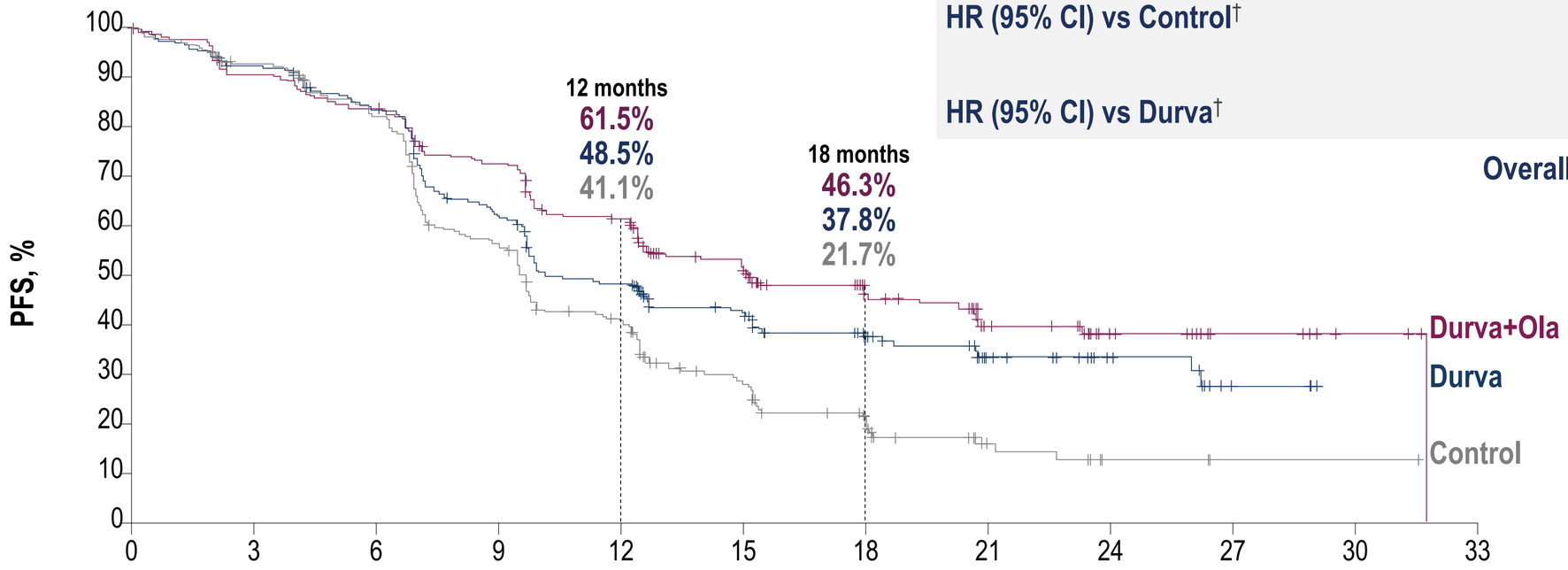
bid, twice daily; CP, carboplatin/paclitaxel; durva, durvalumab; FIGO, International Federation of Gynaecology and Obstetrics; IV, HRRm, homologous recombination repair mutation; intravenously; ola, olaparib; pbo, placebo; q3(4)w, every 3(4) weeks; R, randomisation; RECIST, Response Evaluation Criteria for Solid Tumours.

PFS: ITT population

Primary endpoint

	Control (N=241)	Durva (N=238)	Durva+Ola (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
HR (95% CI) vs Durva†			0.78 (0.61–0.99)

Overall data maturity 61.0%



No. at risk

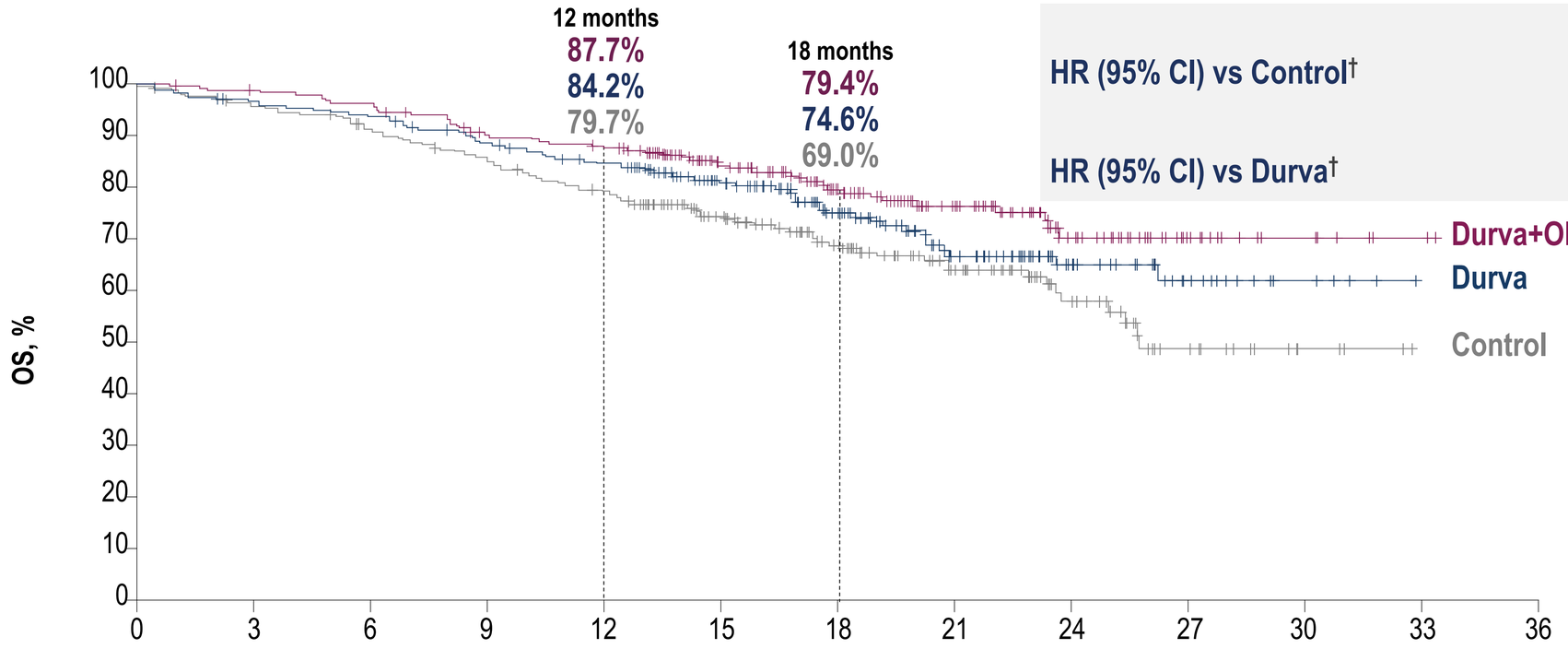
Durva+Ola	239	214	198	169	139	95	51	30	16	7	3	0
Durva	238	211	188	138	105	69	45	26	13	5	0	0
Control	241	213	184	125	86	45	26	10	3	1	1	0

The median (range) duration of follow-up for PFS was 12.6 (0.0–31.6), 15.4 (0.0–29.1), and 15.4 (0.0–31.7) months in censored patients for the Control, Durva, and Durva+Ola arms, respectively. PFS rates were estimated by the KM method. *CI for median PFS is derived based on the Brookmeyer–Crowley method; †The primary PFS analysis for each comparison was performed separately. The HR and CI were estimated from a Cox proportional hazards model stratified by MMR and disease status. The CI was calculated using a profile likelihood approach. The *P* value was calculated using a log-rank test stratified by MMR and disease status. HR, hazard; ITT, intent-to-treat; KM, Kaplan–Meier.

OS: ITT population

Secondary endpoint; interim analysis

	Control (N=241)	Durva (N=238)	Durva+Ola (N=239)
Events, n (%)	82 (34.0)	65 (27.3)	52 (21.8)
Median OS (95% CI),* months	25.9 (23.9–NR)	NR (NR–NR)	NR (NR–NR)
HR (95% CI) vs Control†		**0.77** (0.56–1.07); *P*=0.120	**0.59** (0.42–0.83); *P*=0.003
HR (95% CI) vs Durva†			**0.77** (0.53–1.10)



No. at risk

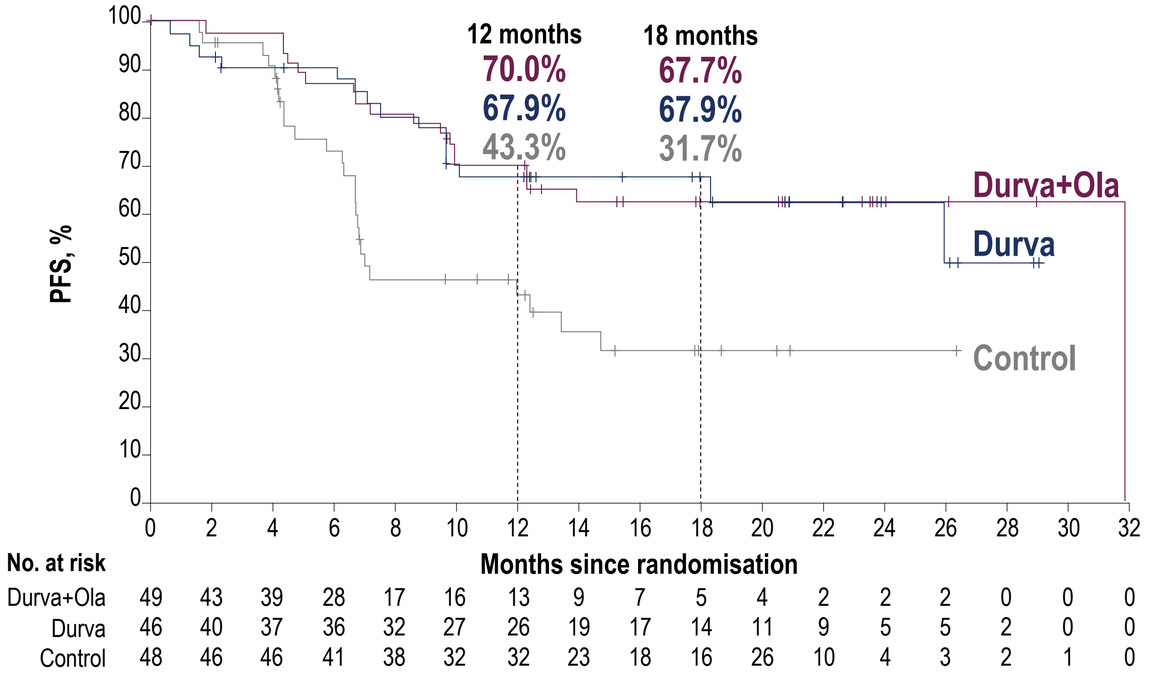
Durva+Ola	239	233	227	208	202	152	109	77	38	18	8	2	0
Durva	238	227	221	205	192	147	105	64	34	17	6	0	0
Control	241	229	215	201	185	136	104	69	35	15	4	0	0

The median (range) duration of follow-up for OS was 18.6 (0.5–32.9), 18.4 (2.1–33.0), and 18.7 (1.1–33.4) months in censored patients for the Control, Durva, and Durva+Ola arms, respectively. OS rates were estimated by the KM method. *CI for median OS is derived based on the Brookmeyer–Crowley method; †The HRs were estimated from an unstratified Cox proportional hazards model. The CI was calculated using a profile likelihood approach. *P* values were calculated using an unstratified log-rank test. *P* values failed to reach statistical significance.
NR, not reached.

Subgroup analysis of PFS by MMR status

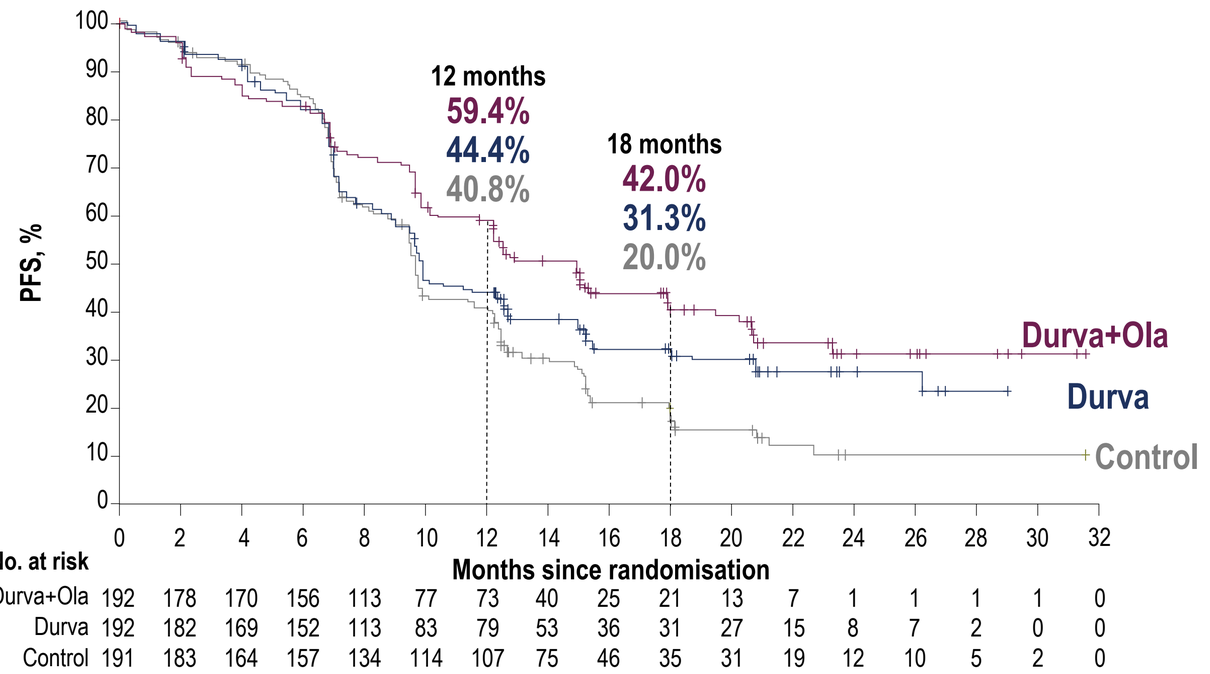
Prespecified exploratory analysis

dMMR (20% of population)



	Control (N=49)	Durva (N=46)	Durva+Ola (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)**
HR (95% CI) vs Durva†			**0.97 (0.49–1.98)**

pMMR (80% of population)



	Control (N=192)	Durva (N=192)	Durva+Ola (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)**
HR (95% CI) vs Durva†			**0.76 (0.59–0.99)**

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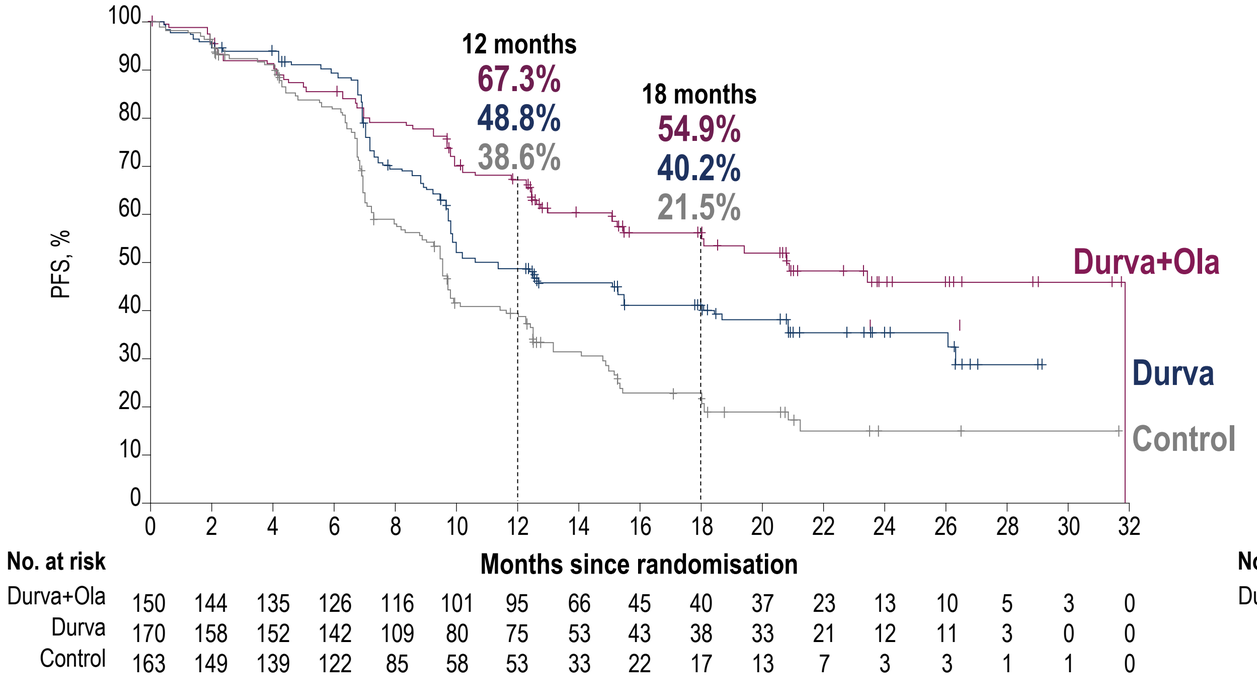
Exploratory subgroup analysis. MMR status evaluated using the Ventana immunohistochemistry MMR panel. Rates were estimated by the KM method.
*CI for median PFS was derived based on the Brookmeyer–Crowley method; †The HR and CI were estimated from an unstratified Cox proportional hazards model.

Subgroup analysis of PFS by PD-L1 status

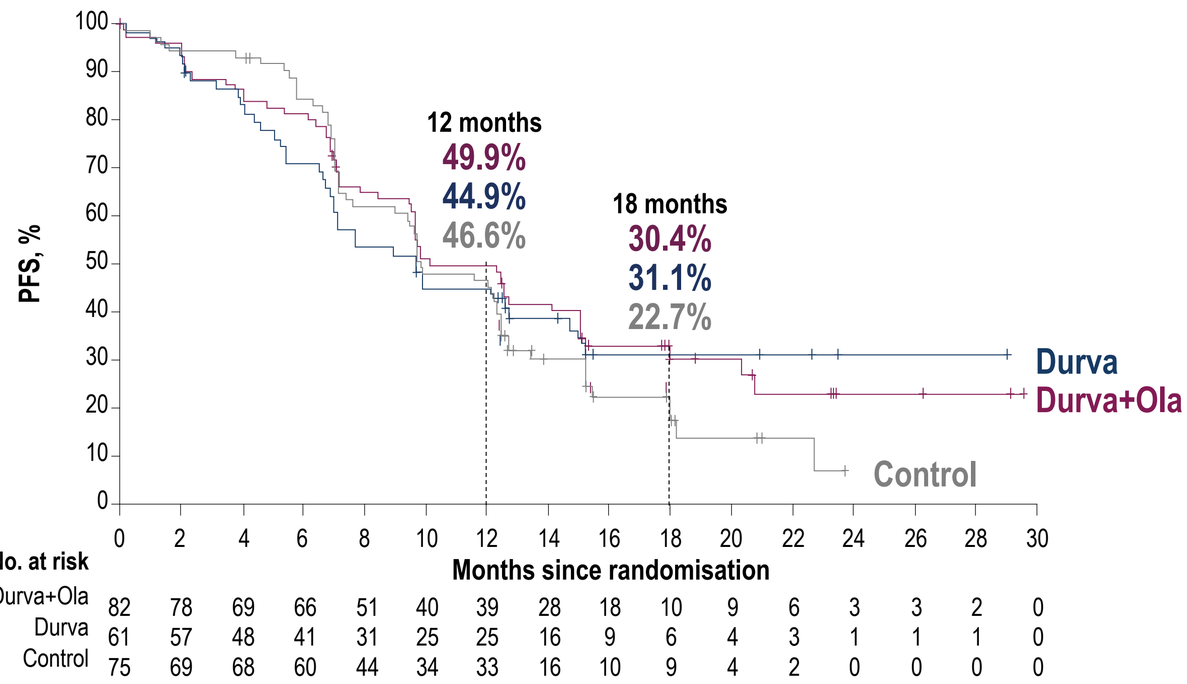
Prespecified exploratory analysis

PD-L1 positive (TAP≥1%; 69% of population)



	Control (N=163)	Durva (N=170)	Durva+Ola (N=150)
Events, n (%)	114 (69.9)	97 (57.1)	68 (45.3)
Median PFS (95% CI),* months	9.5	11.3	20.8
HR (95% CI) vs Control†		**0.63 (0.48–0.83)**	**0.42 (0.31–0.57)**
HR (95% CI) vs Durva†			**0.67 (0.49–0.91)**

PD-L1 negative (TAP<1%; 31% of population)



	Control (N=75)	Durva (N=61)	Durva+Ola (N=82)
Events, n (%)	57 (76.0)	38 (62.3)	55 (67.1)
Median PFS (95% CI),* months	9.9	9.7	10.1
HR (95% CI) vs Control†		**0.89 (0.59–1.34)**	**0.80 (0.55–1.16)**
HR (95% CI) vs Durva†			**0.93 (0.61–1.41)**

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Exploratory subgroup analysis. PD-L1 expression evaluated using Ventana SP263. Prevalence shown is based on patients with known PD-L1 status.
*CI for median PFS was derived based on the Brookmeyer–Crowley method; †The HR and CI were estimated from an unstratified Cox proportional hazards model.