ESMO VIRTUAL JOURNAL CLUB

INTRODUCTION

Pilar Garrido

Chair

University Hospital Ramón y Cajal (IRYCIS)
Madrid

ESMO WEBINAR SERIES

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

LEARNING OBJECTIVES

- To discuss and critically evaluate notable recent publications.
- To enhance the understanding and application of the latest research in the field.
- To assess the study's robustness, its significance to oncology practice, limitations, and its place within existing research.
- To identify and highlight any unclear aspects or unmet needs.

PROGRAMME AND SPEAKERS

4 December 2024

5 min	**Welcome and introduction** Pilar Garrido
20 min	**Osimertinib after Chemoradiotherapy in Stage III EGFR-Mutated NSCLC** Mariana Brandao
20 min	**RUBY Trial in Endometrial Cancer. Overall survival in patients with endometrial cancer treated with dostarlimab plus carboplatin–paclitaxel in the randomized ENGOT-EN6/GOG-3031/RUBY trial** Domenica Lorusso
15 min	**Live Q&A and Discussion** All speakers

Pilar Garrido
Chair
University Hospital Ramón y Cajal (IRYCIS)
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Mariana Brandão
Speaker
Institut Jules Bordet
Brussels

Domenica Lorusso
Speaker
Humanitas Hospital San Pio X
Humanitas University, Rozzano
Milan

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 15, 2024 VOL. 391 NO. 7

Osimertinib after Chemoradiotherapy in Stage III *EGFR*-Mutated NSCLC

Shun Lu, M.D., Terufumi Kato, M.D., Xiaorong Dong, M.D., Ph.D., Myung-Ju Ahn, M.D., Le-Van Quang, M.D., Nopadol Soparattanapaisarn, M.D., Takako Inoue, M.D., Chih-Liang Wang, M.D., Meijuan Huang, M.D., James Chih-Hsin Yang, M.D., Ph.D., Manuel Cobo, M.D., Mustafa Özgüroğlu, M.D., Ignacio Casarini, M.D., Dang-Van Khiem, M.D., Virote Sriuranpong, M.D., Ph.D., Eduardo Cronemberger, M.D., Toshiaki Takahashi, M.D., Ph.D., Yotsawaj Runglodvatana, M.D., Ming Chen, M.D., Ph.D., Xiangning Huang, Ph.D., Ellie Grainger, M.Sc., Dana Ghiorghiu, M.D., Ph.D., Toon van der Gronde, Pharm.D., Ph.D., and Suresh S. Ramalingam, M.D., for the LAURA Trial Investigators*

Mariana Brandão
Speaker
Institut Jules Bordet
Brussels

- Phase 3, double-blind, placebo-controlled trial
- 216 patients with unresectable EGFR-mutated stage III NSCLC without progression during or after chemoradiotherapy are to receive osimertinib or placebo until disease progression
- Positive study: median PFS 39.1 months with osimertinib versus 5.6 months with placebo; HR 0.16 (0.10 to 0.24; P<0.001)

ORIGINAL ARTICLE

Overall survival in patients with endometrial cancer treated with dostarlimab plus carboplatin—paclitaxel in the randomized ENGOT-EN6/GOG-3031/RUBY trial

M. A. Powell[1], L. Bjørge[2,3], L. Willmott[4], Z. Novák[5], D. Black[6], L. Gilbert[7,8], S. Sharma[9], G. Valabrega[10], L. M. Landrum[11], M. Gropp-Meier[12,13], A. Stuckey[14], I. Boere[15], M. A. Gold[16], Y. Segev[17], S. E. Gill[18], C. Gennigens[19,20], A. Sebastianelli[21], M. S. Shahin[22], B. Pothuri[23,24], B. J. Monk[23,25], J. Buscema[26], R. L. Coleman[27], B. M. Slomovitz[28,29], K. L. Ring[30], T. J. Herzog[31], M. M. Balas[32], M. Grimshaw[33], S. Stevens[33], D. W. Lai[34], C. McCourt[35] & M. R. Mirza[36,37]*

[1]National Cancer Institute sponsored NRG Oncology, Washington University School of Medicine, St Louis, USA; [2]Haukeland University Hospital, Bergen; [3]University of Bergen, Bergen, Norway; [4]Arizona Oncology, Phoenix, USA; [5]Department of Gynecology, Hungarian National Institute of Oncology, Budapest, Hungary; [6]Willis-Knighton Cancer Center, Willis-Knighton Health System, Gynecologic Oncology Associates, Shreveport, USA; [7]Division of Gynecologic Oncology, McGill University Health Centre, Montreal; [8]Gerald Bronfman Department of Oncology, McGill University, Montreal, Canada; [9]Department of Obstetrics/Gynecology, AMITA Health Adventist Medical Center, Hinsdale, USA; [10]Ordine Mauriziano Torino and University of Torino, Torino, Italy; [11]Indiana University Health & Simon Cancer Center, Indianapolis, USA; [12]AGO Study Group, Wiesbaden; [13]Oberschwabenklinik, St. Elisabethen-Klinikum, Ravensburg, Germany; [14]Women and Infants Hospital of Rhode Island, Providence, USA; [15]Department of Medical Oncology, Erasmus MC Cancer Centre, Rotterdam, The Netherlands; [16]Oklahoma Cancer Specialists and Research Institute, Tulsa, USA; [17]Gynecology Oncology Division, Department of Obstetrics and Gynaecology, Carmel Medical Center, Haifa, Israel; [18]St. Joseph's/Candler Gynecologic Oncology & Surgical Specialists, Candler Hospital, Savannah, USA; [19]Department of Medical Oncology, CHU of Liège, Liège; [20]Belgium and Luxembourg Gynaecological Oncology Group (BGOG), Leuven, Belgium; [21]CHU de Québec-Université Laval, Quebec, Canada; [22]Hanjani Institute for Gynecologic Oncology, Abington Hospital-Jefferson Health, Asplundh Cancer Pavilion, Sidney Kimmel Medical College of Thomas Jefferson University, Willow Grove; [23]GOG Foundation, Philadelphia; [24]Departments of Obstetrics/Gynecology and Medicine, Division of Gynecologic Oncology, Laura & Isaac Perlmutter Cancer Center, NYU Langone Health, New York; [25]Florida Cancer Specialists and Research Institute, West Palm Beach; [26]Arizona Oncology, Tucson; [27]Texas Oncology, US Oncology Network, The Woodlands; [28]Department of Gynecologic Oncology, Mount Sinai Medical Center, Miami Beach; [29]Department of Obstetrics and Gynecology, Florida International University, Miami Beach; [30]University of Virginia Health System, Charlottesville; [31]Department of Obstetrics and Gynecology, University of Cincinnati Cancer Center, University of Cincinnati, Cincinnati; [32]GSK, New York, USA; [33]GSK, London, UK; [34]GSK, Los Angeles; [35]Division of Gynecologic Oncology, Washington University School of Medicine, Washington University in St Louis, St Louis, USA; [36]Rigshospitalet, Copenhagen University Hospital, Copenhagen; [37]Nordic Society of Gynaecologic Oncology-Clinical Trial Unit, Copenhagen, Denmark

Available online 10 June 2024

Domenica Lorusso
Speaker
Humanitas Hospital San Pio X
Humanitas University, Rozzano
Milan

- Phase III, global, double-blind, randomized, placebo-controlled trial.
- Part 1 enrolled 494 patients with primary advanced stage III or IV or first recurrent EC to receive either dostarlimab or placebo, plus carboplatin-paclitaxel followed by dostarlimab or placebo for up to 3 years.
- RUBY met the dual primary endpoint for OS at this second interim analysis, HR 0.69, (0.54-0.89, P . 0.0020] in patients treated with dostarlimab plus carboplatin-paclitaxel
  - dMMR/MSI-H population (HR . 0.32, 95% CI 0.17-0.63, P: 0.0002)
  - mismatch repair-proficient/microsatellite stable population (HR . 0.79, 0.60-1.04, P . 0.0493).

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OSIMERTINIB AFTER CHEMORADIOTHERAPY IN STAGE III EGFR-MUTATED NSCLC

LAURA trial

Mariana Brandão, MD/PhD

Thoracic Oncology Unit / Phase 1 Trials Unit / Meylan Lab
Institut Jules Bordet – Hôpital Universitaire de Bruxelles
Professeur Hospitalier Associée – Université Libre de Bruxelles, Belgium

4th December 2024

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DISCLOSURES

Advisory board for Janssen, Sanofi, Pierre-Fabre, Daichii, Pfizer and Amgen

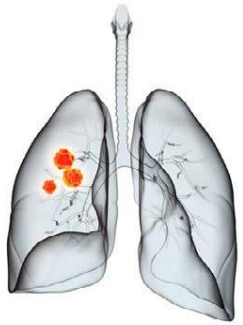
Speaker fee from AstraZeneca, BMS, Janssen, Takeda, MSD, Pfizer

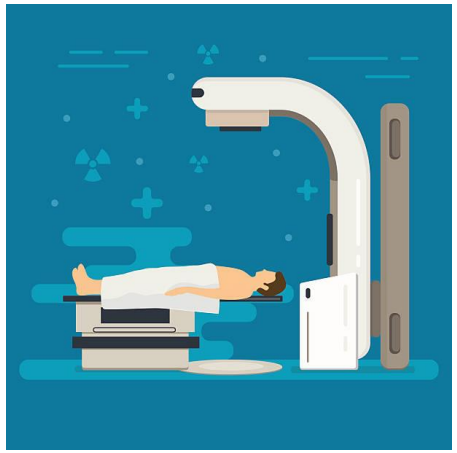
Is/was investigator for AstraZeneca, Boeringher, Merus, Merck, Roche/GNE, Sanofi, iTeos

Travel grant from Takeda, Sanofi, AstraZeneca, Roche

Consultancy for AstraZeneca

Organizations: EORTC LCG, ESMO committees





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Osimertinib after Chemoradiotherapy in Stage III *EGFR*-Mutated NSCLC

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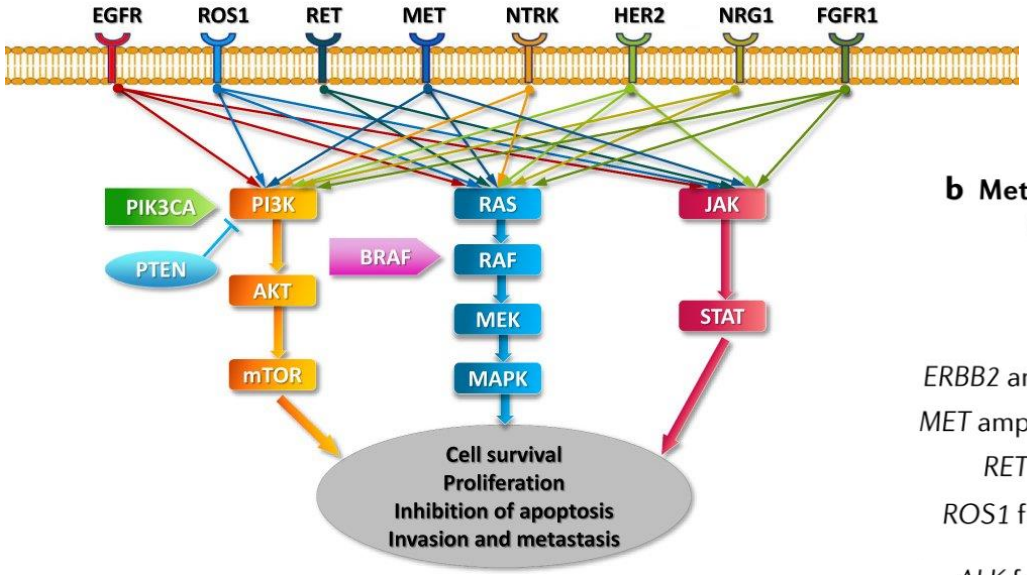
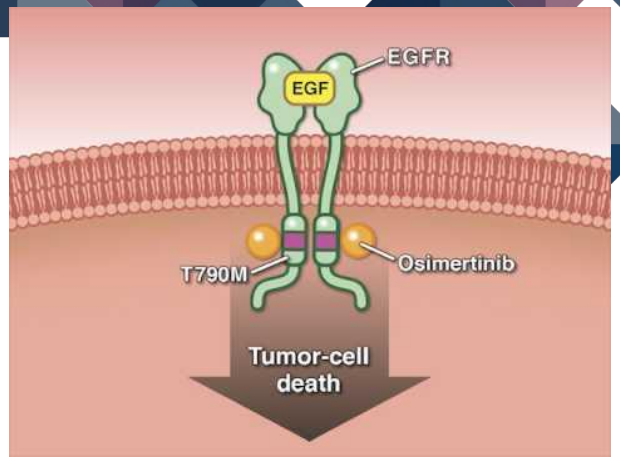
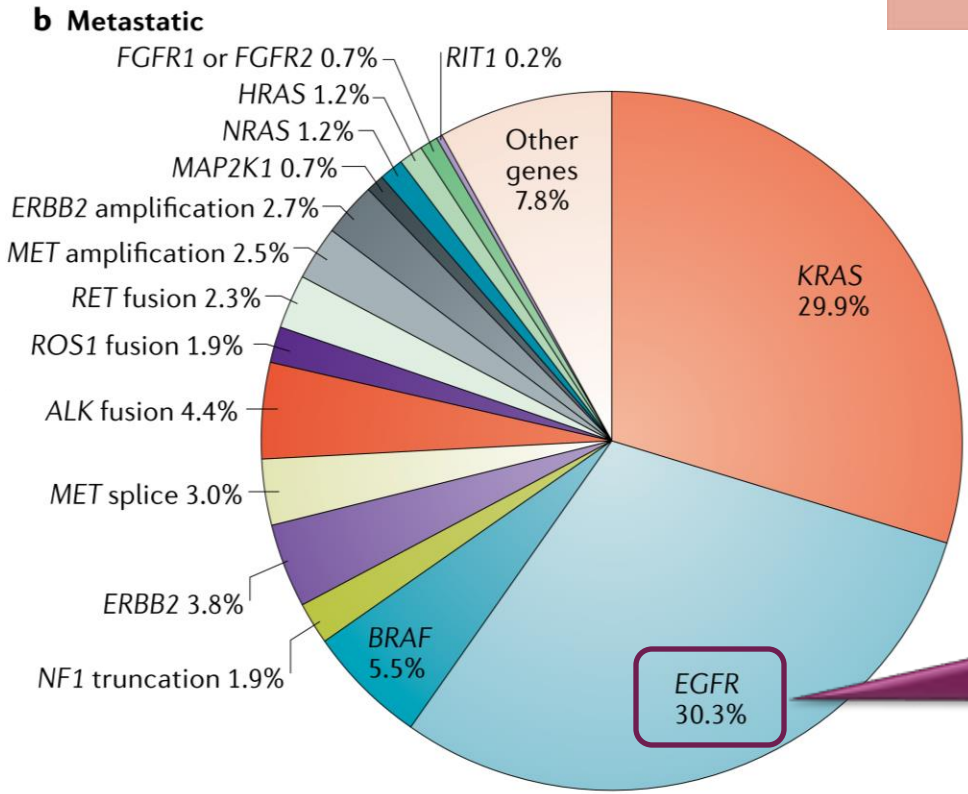
Lu et al, N Eng J Med 2024

BEFORE WE START







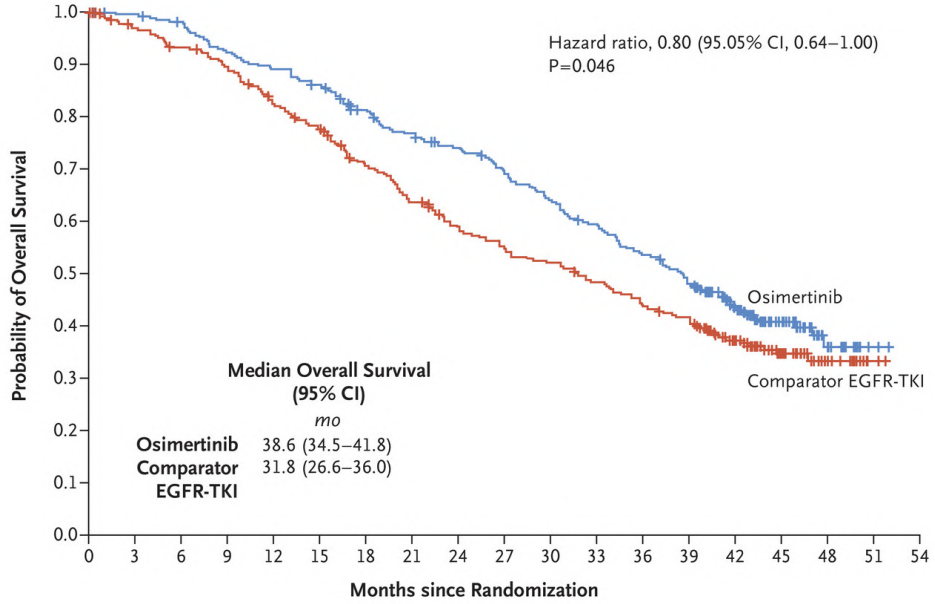
Data from MSK-IMPACT (Jordan et al.[59]) and FoundationOne (Frampton et al.[15]) panels (n = 5262)

Osimertinib
Gefinitib, Erlotinib, Afatinib (…)

Guo et al., OncoTargets and Therapy 2019;
Skoulidis et al., Nat Rev Cancer. 2019

OSIMERTINIB AS A STANDARD-OF-CARE

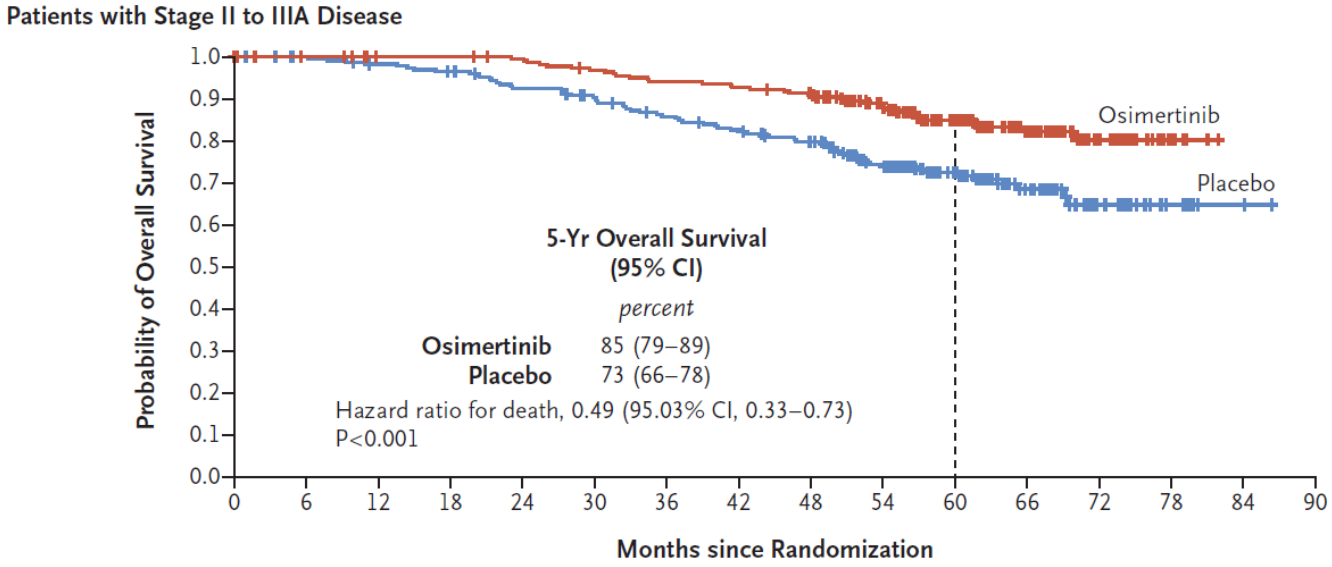
FLAURA trial: 1L Metastatic (Stage IV)



No. at Risk																			
Osimertinib	279	276	270	254	245	236	217	204	193	180	166	153	138	123	86	50	17	2	0
Comparator EGFR-TKI	277	263	252	239	219	205	182	165	148	138	131	121	110	101	72	40	17	2	0

Ramalingam et al, N Eng J Med 2019

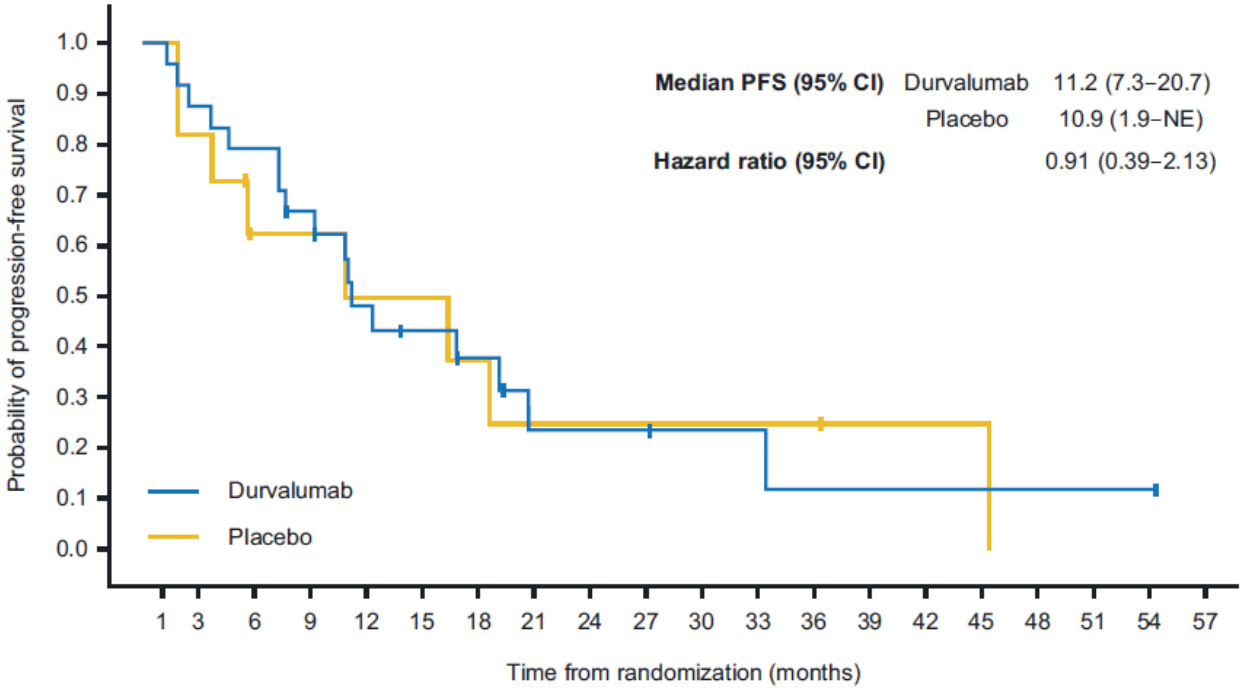
ADAURA trial: Resected Stage II-IIIA



No. at Risk															
Osimertinib	233	229	224	224	221	214	208	205	200	170	115	69	33	9	0
Placebo	237	232	226	221	210	202	190	182	171	138	94	53	25	8	2	0

Tsuboi et al, N Eng J Med 2023

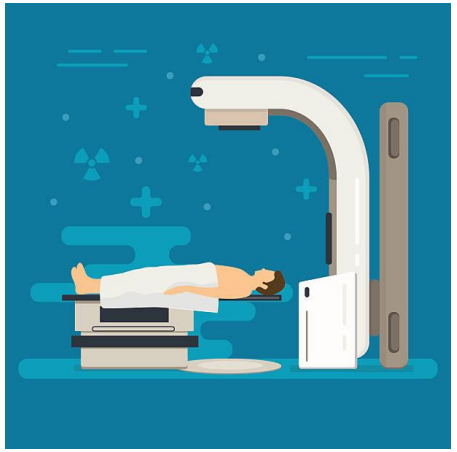
WHAT ABOUT UNRESECTABLE STAGE III EGFR+ NSCLC?



Number of patients at risk

Month	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57
Durvalumab	24	21	19	15	10	8	6	3	3	3	2	2	1	1	1	1	1	1	1	0
Placebo	11	9	5	5	4	4	3	2	2	2	2	2	2	1	1	1	0	0	0	0

mPFS ~11 months (both arms)
after chemo-radiotherapy



Naidoo et al, J Thor Onc 2023

CURRENT TREATMENT LANDSCAPE IN EGFR+ NSCLC

Stage IB-III

- Resectable
  - **Surgery** [+- neo/adj chemotherapy]
    - **Osimertinib** (3 years)
- Unresectable
  - **Chemo-radiotherapy**
    - ?

Stage IV (metastatic)

- **Osimertinib** (until progression)
  - Osimertinib + platinum-based chemotherapy
  - Lazertinib + Amivantamab
  - (…)

EGFR-directed therapy

LAURA – TRIAL DESIGN

Patients with locally advanced, unresectable stage III* EGFRm NSCLC with no progression during / following definitive CRT† treatment

Key inclusion criteria:
- ≥18 years (Japan: ≥20)
- WHO PS 0 / 1
- Confirmed locally advanced, unresectable stage III* NSCLC
- Ex19del / L858R‡
- Maximum interval between last dose of CRT and randomization: 6 weeks

≤6 w

Osimertinib 80 mg, once daily

Randomization 2:1 (N=216)

Stratification by:
Concurrent vs sequential CRT
Stage IIIA vs stage IIIB/IIIC
China vs non-China

Placebo, once daily

Treatment duration until BICR-assessed progression (per RECIST v1.1), toxicity, or other discontinuation criteria

Open-label osimertinib after BICR-confirmed progression offered to both treatment arms§

Tumor assessments:
- Chest CT / MRI and brain MRI
- At baseline, every 8 weeks to Week 48, then every 12 weeks until BICR-assessed progression

Endpoints
- **Primary endpoint:** PFS assessed by BICR per RECIST v1.1 (sensitivity analysis: PFS by investigator assessment)
- **Secondary endpoints included:** OS, CNS PFS, safety

LAURA – TRIAL DESIGN

- Planned sample size: ~200 patients randomized 2:1, osimertinib:placebo

Sequential multiple testing procedure

Primary analysis: PFS

Study designed with 90% power to detect a PFS HR of 0.53 at a 5% (2-sided) significance level (alpha); translating to improvement in median PFS from 8.0 to 15.0 months; primary analysis when approximately 120 BICR-confirmed progression events had occurred

↓ If significant, recycle alpha

OS (interim and final analyses)*

Interim OS analysis at time of primary PFS analysis; final OS analysis at 60% maturity (approximately 120 deaths)

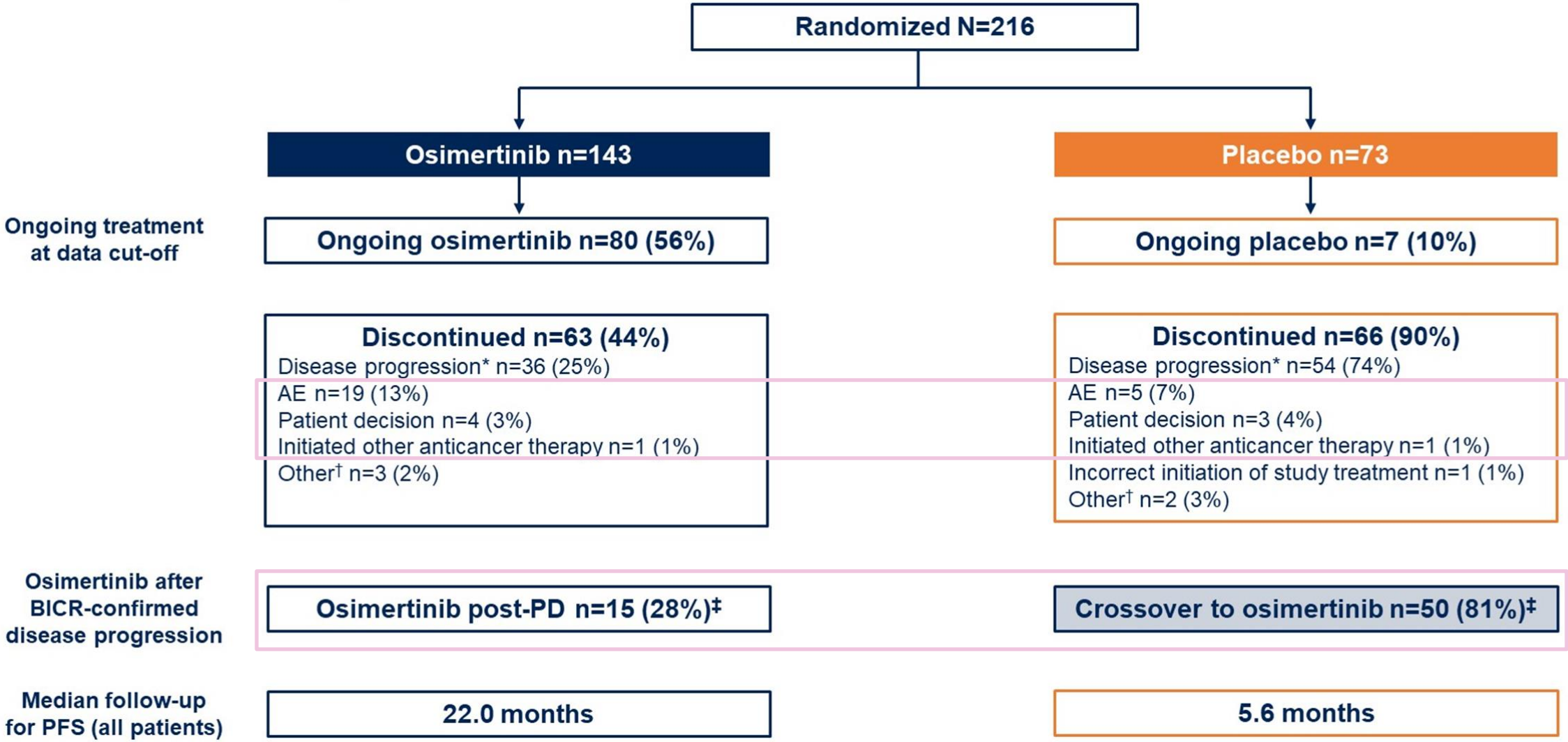
Non-statistically significant OS at interim analysis will not preclude further testing of OS

↓ If significant, recycle alpha

CNS PFS

Will be tested for significance if OS is statistically significant, either at interim or final analysis of OS

LAURA – PATIENT DISPOSITION



Ramalingam et al, ASCO 2024

LAURA – PATIENT CHARACTERISTICS

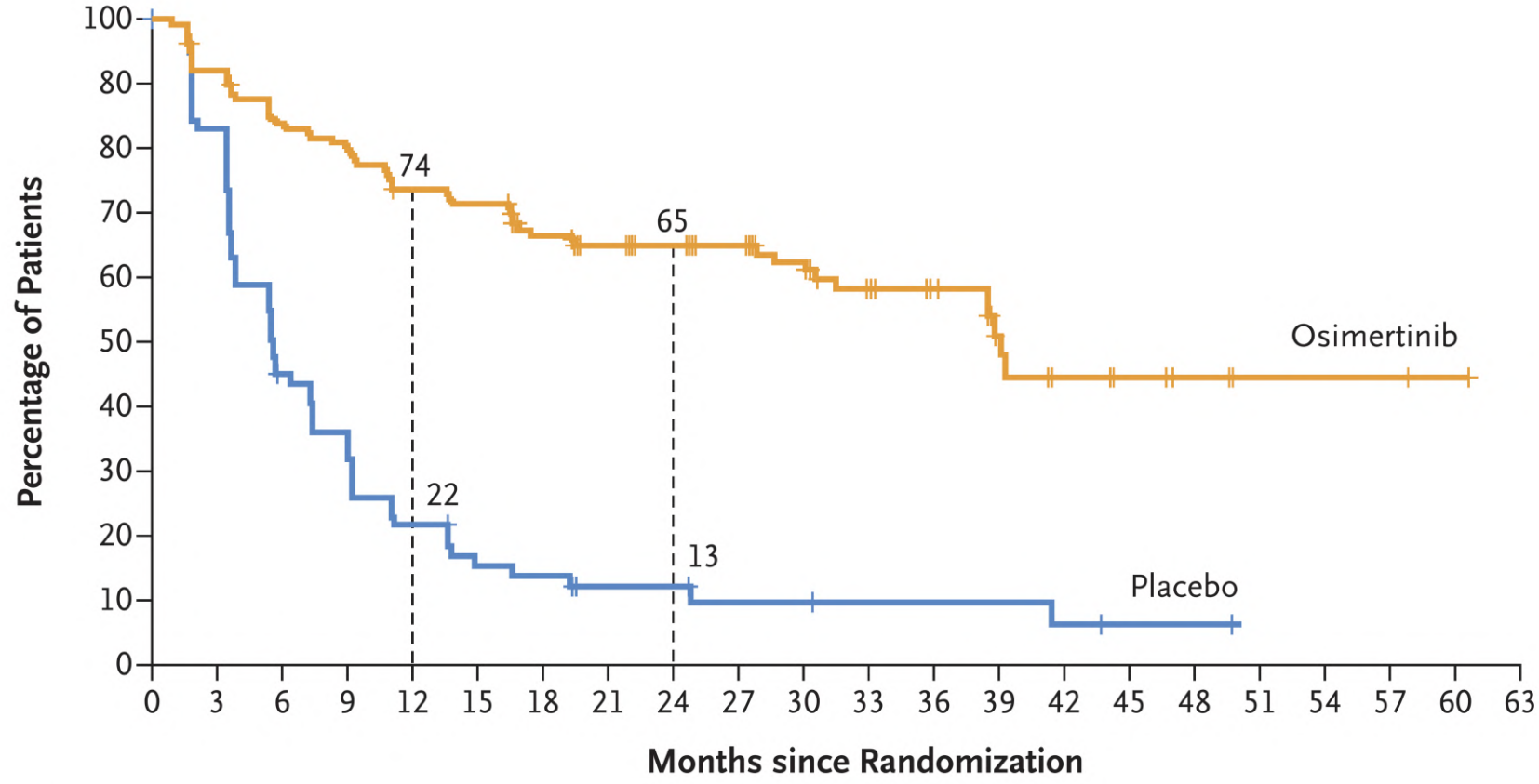
Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Osimertinib (N = 143)	Placebo (N = 73)
Sex — no. (%)		
Male	53 (37)	31 (42)
Female	90 (63)	42 (58)
Age — yr		
Median	62	64
Range	36 to 84	37 to 83
Smoking status — no. (%)		
Current	4 (3)	1 (1)
Former	37 (26)	23 (32)
Never	102 (71)	49 (67)
Race — no. (%)†		
Asian	116 (81)	62 (85)
Non-Asian	27 (19)	11 (15)
WHO performance-status score — no. (%)‡		
0	80 (56)	31 (42)
1	63 (44)	42 (58)

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Osimertinib (N = 143)	Placebo (N = 73)
AJCC–UICC disease stage — no. (%)§		
IIIA	52 (36)	24 (33)
IIIB	67 (47)	38 (52)
IIIC	24 (17)	11 (15)
Histologic type — no. (%)		
Adenocarcinoma	139 (97)	69 (95)
Squamous-cell carcinoma	3 (2)	2 (3)
Other¶	1 (1)	2 (3)
EGFR mutation type at screening — no. (%)‖		
Exon 19 deletion	74 (52)	43 (59)
L858R mutation	68 (48)	30 (41)
Type of chemoradiotherapy — no. (%)**		
Concurrent	131 (92)	62 (85)
Sequential	12 (8)	11 (15)
Best overall response to chemoradiotherapy — no. (%)††		
Complete response	4 (3)	3 (4)
Partial response	67 (47)	27 (37)
Stable disease	61 (43)	37 (51)
Not evaluable‡‡	11 (8)	6 (8)
Target-lesion size — mm§§	33±18	36±17

LAURA – PROGRESSION FREE SURVIVAL



Median Progression-free Survival (95% CI)	*mo*
Osimertinib	39.1 (31.5–NC)
Placebo	5.6 (3.7–7.4)

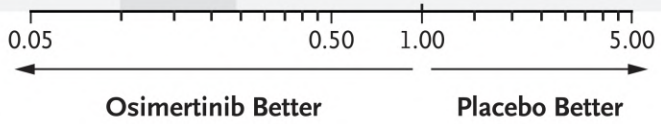
Hazard ratio for disease progression or death, 0.16 (95% CI, 0.10–0.24)
P<0.001

No. at Risk

Osimertinib	143	127	114	109	99	96	83	76	69	61	49	37	28	16	9	6	4	2	2	2	1	0
Placebo	73	59	31	25	15	10	9	6	6	4	4	3	3	3	2	1	1	0	0	0	0	0

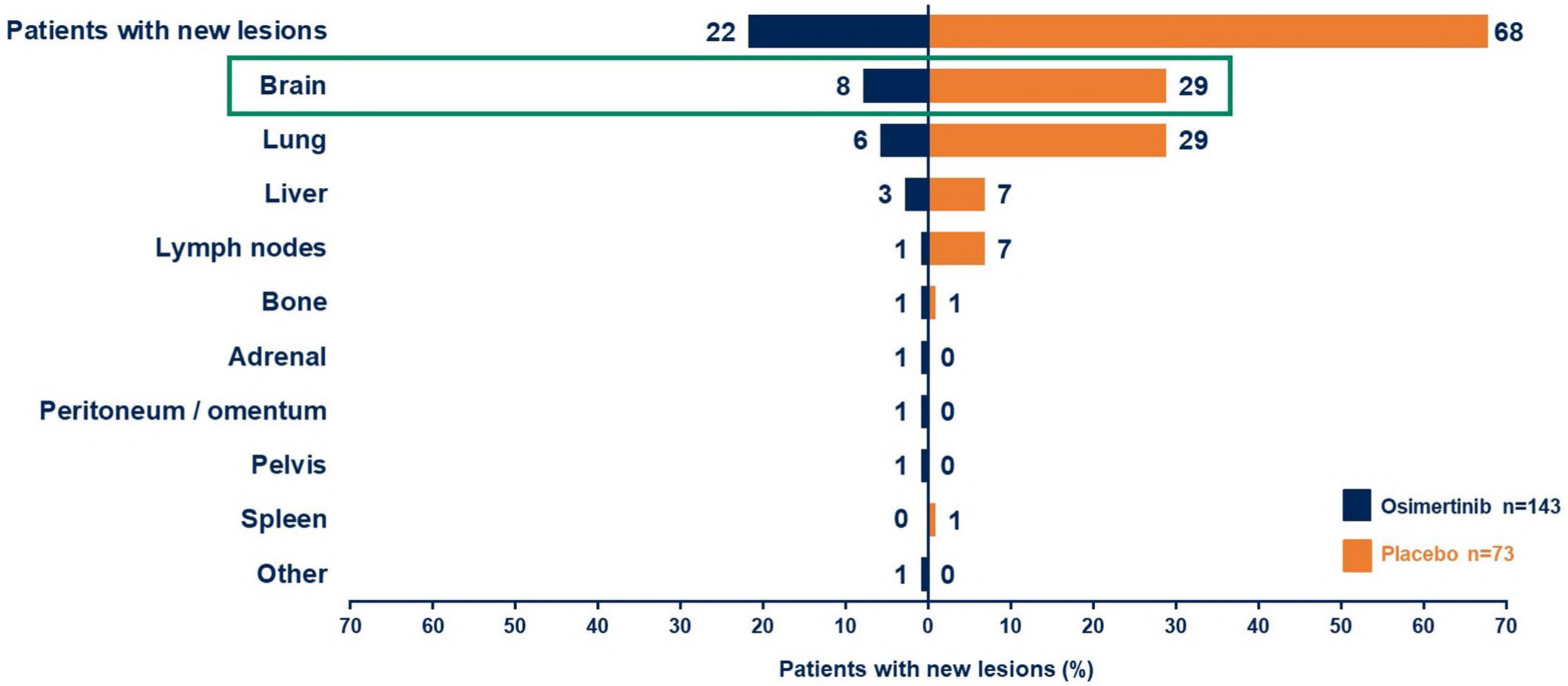
PFS

Subgroup	Osimertinib (no. of events/no. of patients)	Placebo (no. of events/no. of patients)	Hazard Ratio for Disease Progression or Death (95% CI)
Overall			
Stratified log-rank analysis	57/143	63/73	0.16 (0.10–0.24)
Unadjusted Cox proportional-hazards analysis	57/143	63/73	0.23 (0.16–0.33)
Sex			
Male	23/53	27/31	0.26 (0.15–0.46)
Female	34/90	36/42	0.21 (0.13–0.34)
Age			
<65 yr	31/81	36/39	0.16 (0.10–0.26)
≥65 yr	26/62	27/34	0.33 (0.19–0.57)
Smoking history			
Current or former	20/41	22/24	0.26 (0.14–0.48)
Never	37/102	41/49	0.22 (0.14–0.34)
Race or national group			
Chinese	7/27	11/13	NC (NC–NC)
Non-Chinese	50/116	52/60	0.26 (0.17–0.39)
Asian	43/116	55/62	0.20 (0.13–0.29)
Non-Asian	14/27	8/11	0.48 (0.20–1.19)
Stage			
IIIA	22/52	20/24	0.28 (0.15–0.52)
IIIB or IIIC	35/91	43/49	0.21 (0.13–0.33)
EGFR mutation			
Exon 19 deletion	26/74	39/43	0.17 (0.10–0.29)
L858R mutation	31/68	24/30	0.32 (0.19–0.56)
Chemoradiotherapy			
Concurrent	53/131	54/62	0.25 (0.17–0.36)
Sequential	4/12	9/11	NC (NC–NC)
Response to previous CRT			
Complete response	1/4	2/3	NC (NC–NC)
Partial response	28/67	25/27	0.20 (0.11–0.34)
Stable disease	24/61	34/37	0.18 (0.10–0.30)
Not evaluable	4/11	2/6	NC (NC–NC)



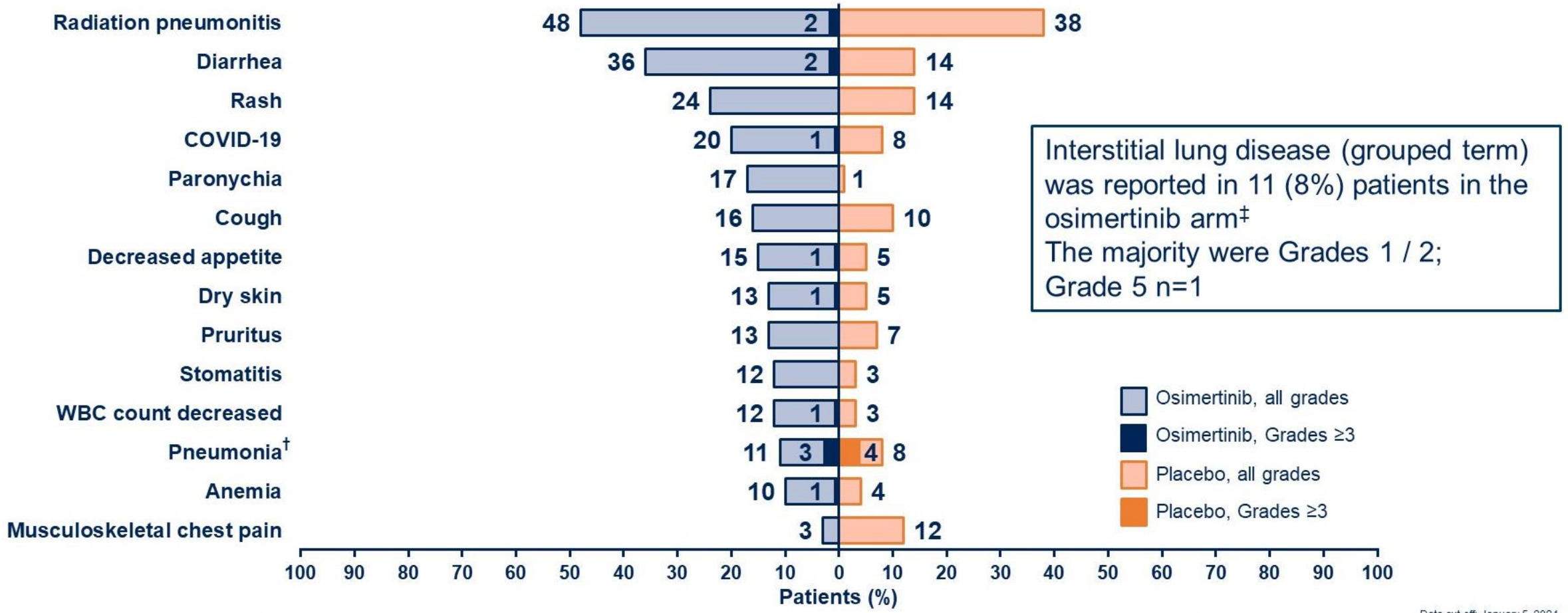
Lu et al, N Eng J Med 2024

LAURA – SITES OF NEW LESIONS



 Ramalingam et al, ASCO 2024

LAURA – TOXICITY



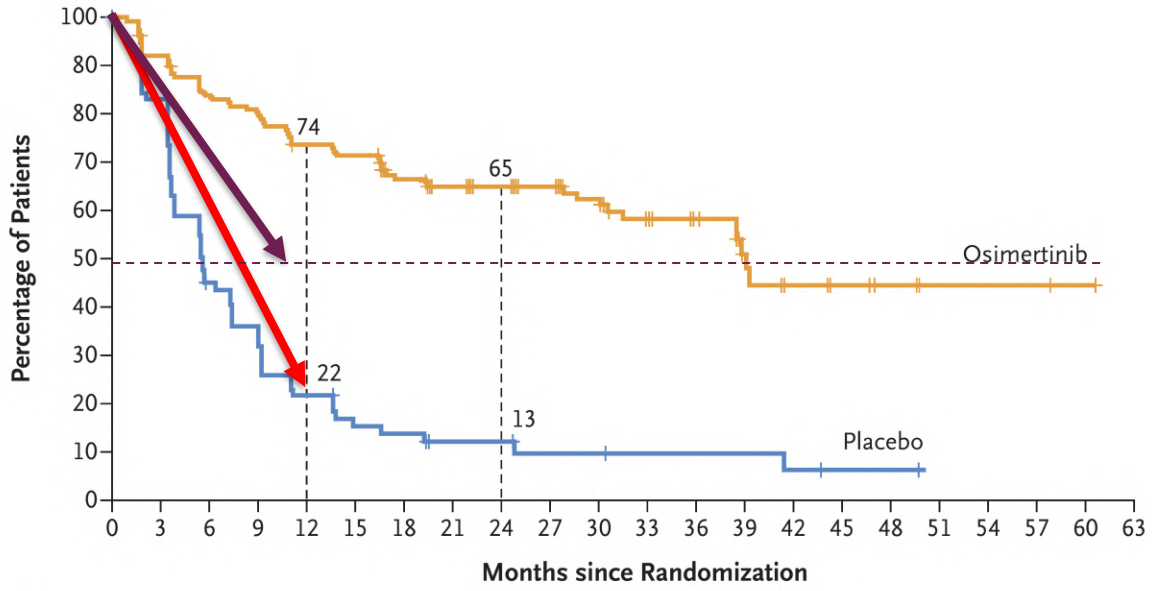
Interstitial lung disease (grouped term) was reported in 11 (8%) patients in the osimertinib arm‡
The majority were Grades 1 / 2; Grade 5 n=1

Data cut-off: January 5, 2024.

*AEs with incidence of 10% or more in either treatment arm are shown. Patients with multiple events in the same category counted only once in that category. Patients with events in more than one category are counted once in each of those categories. Includes AEs with an onset date on or after the date of first dose and up to and including 28 days following the discontinuation of study treatment and before starting subsequent cancer therapy; †One grade 5 AE of pneumonia was reported in the osimertinib arm; ‡Interstitial lung disease (grouped term) was reported in 1 patient (1%) in placebo arm; AE was pneumonitis, Grade 1.

DISCUSSION

UNDER-PERFORMANCE OF THE CONTROL ARM



No. at Risk																					
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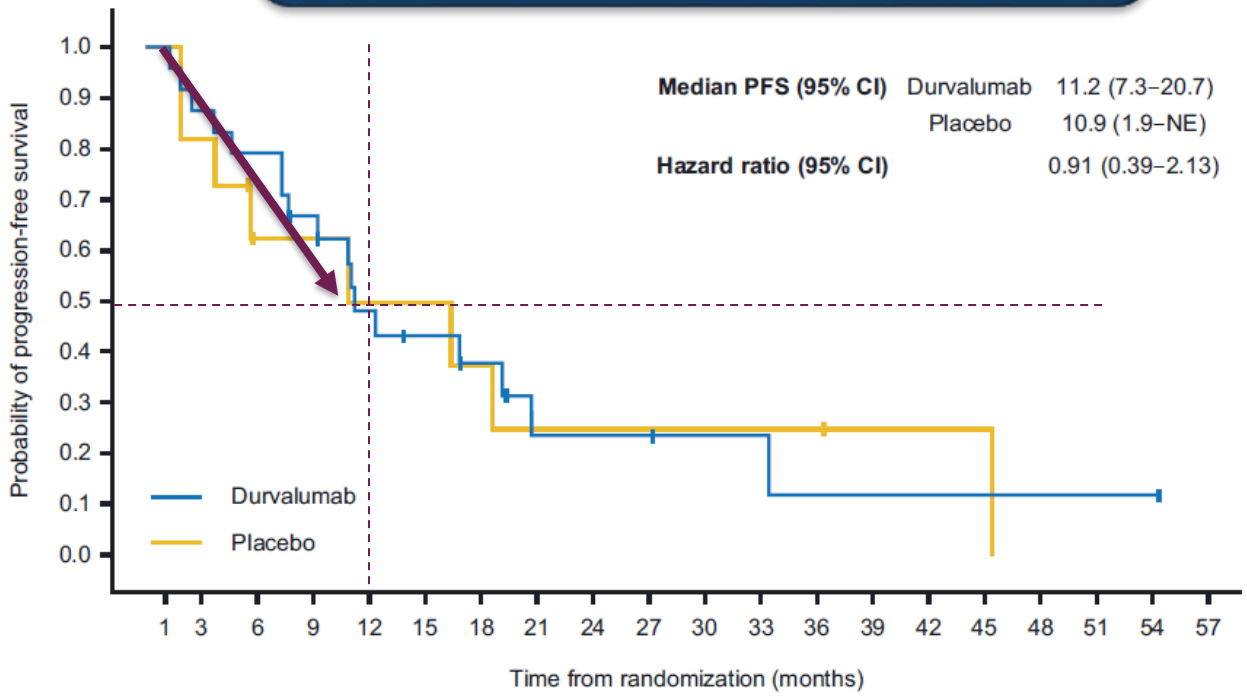
Placebo	73	59	31	25	15	10	9	6	6	4	4	3	3	3	2	1	1	0	0	0	0	0

LAURA: mPFS 5.6 months
after chemo-radiotherapy

PACIFIC: mPFS ~11 months (both arms)
after chemo-radiotherapy



Number of patients at risk

Month	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57
Durvalumab	24	21	19	15	10	8	6	3	3	3	2	2	1	1	1	1	1	1	1	0
Placebo	11	9	5	5	4	4	3	2	2	2	2	2	2	1	1	1	0	0	0	0

Lu et al, N Eng J Med 2024
Naidoo et al, J Thor Onc 2023

UNDER-PERFORMANCE OF THE CONTROL ARM: BRAIN METASTASES AT BASELINE

Table 1. Baseline demographic and clinical characteristics (all randomised patients)[24]

Characteristic	Osimertinib (n = 143)	Placebo (n = 73)
CNS metastases per investigator, n (%)	0	1 (1)
CNS metastases per neuroradiologist BICR, n (%)	14 (10)	5 (7)

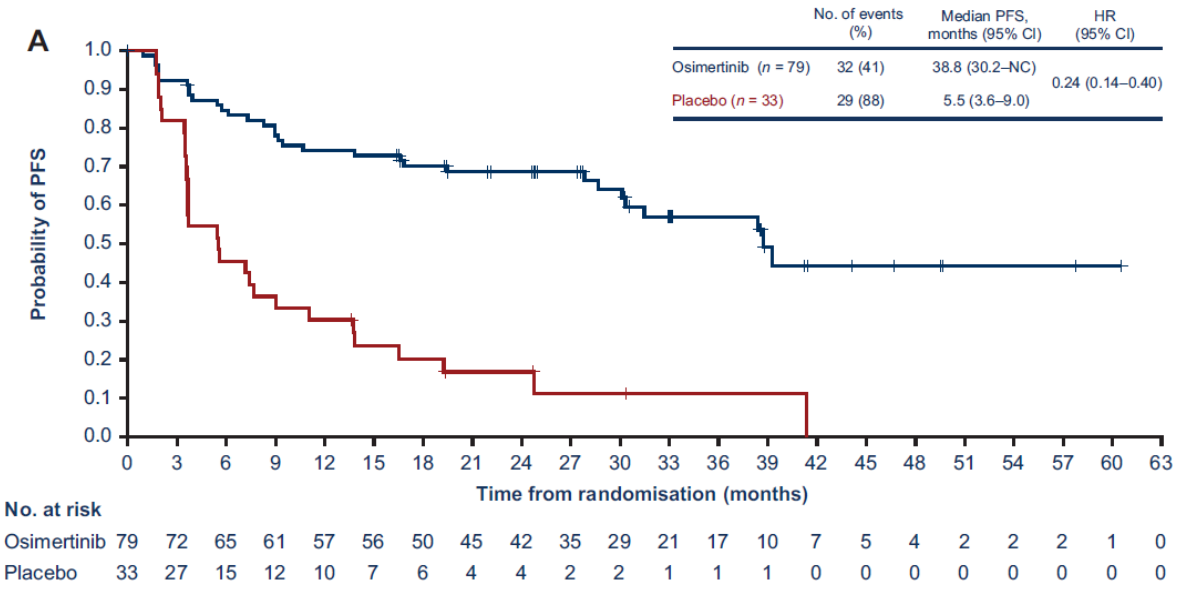
9% of the study population was **stage IV** (= ineligible) at baseline because the presence of brain metastases (*retrospectively* detected by the independent central reviewing of brain MRIs)

Lu et al, Ann Oncol 2024

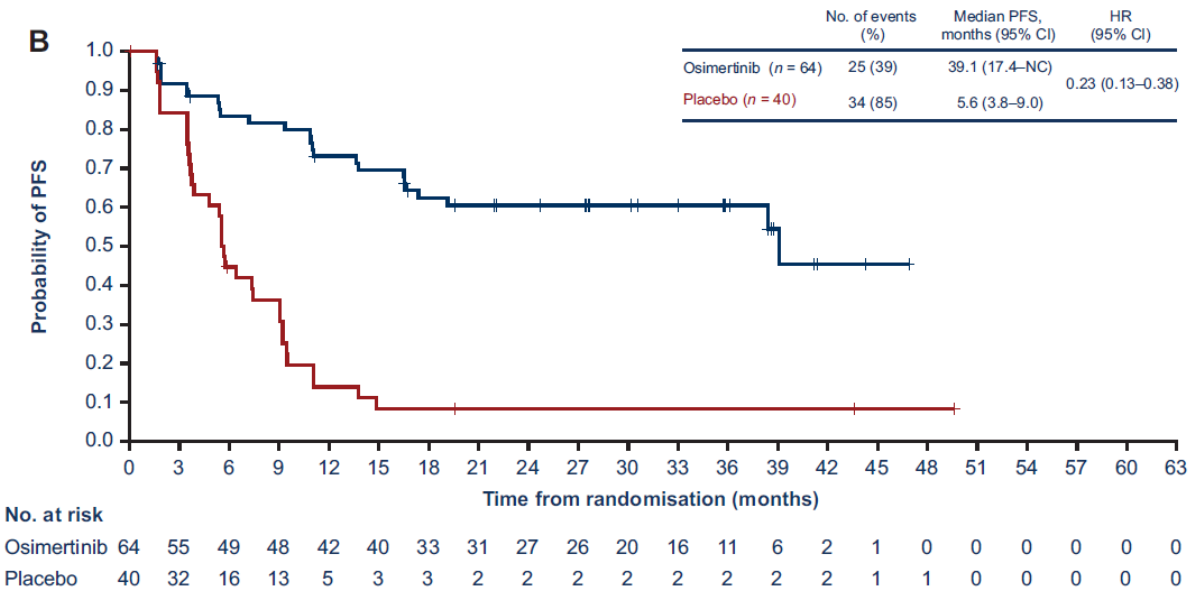
UNDER-PERFORMANCE OF THE CONTROL ARM: PET STAGING AT DIAGNOSIS

Study Protocol: "It is recommended **but not required** that except for overt cT4 disease, **nodal status N2 or N3 should have been proven by biopsy**, via endobronchial ultrasound, mediastinoscopy, or thoracoscopy ***or*** in absence of biopsy, should have been confirmed with whole body **^{18}F-fluoro-deoxyglucose PET** plus contrast-enhanced CT in addition to or in combination with PET."

With PET-CT before CT-RT



Without PET-CT before CT-RT

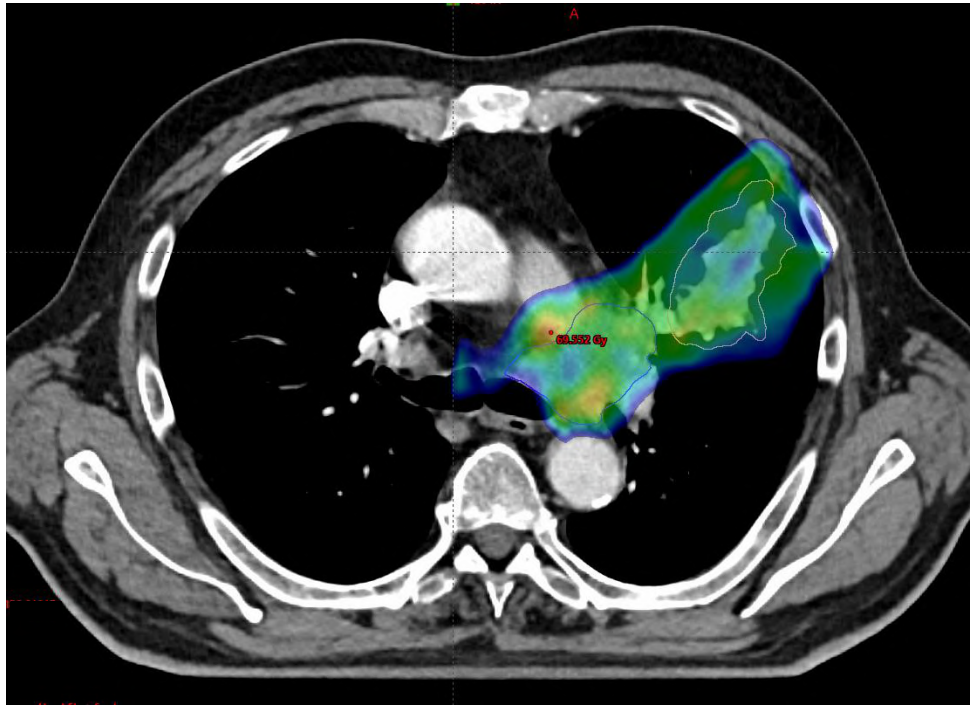


 Lu et al, Ann Oncol 2024

UNDER-PERFORMANCE OF THE CONTROL ARM: RADIOTHERAPY QUALITY

Study Protocol: "The **radiotherapy planning scans** from the definitive radiation treatment delivered prior to randomization are to be submitted to the AZ appointed imaging CRO (...) Patients **must** have received a **total dose of radiation of 60 Gy ±10% (54 to 66 Gy)** as part of the chemoradiation therapy in order to be randomized."

	Osimertinib (n=143)	Placebo (n=73)
Type of CT-RT, n (%)		
Concurrent	131 (92)	62 (85)
Sequential	12 (8)	11 (15)
RT technique, n (%)		
3D Conformal	44 (31)	18 (25)
IMRT	99 (69)	55 (75)

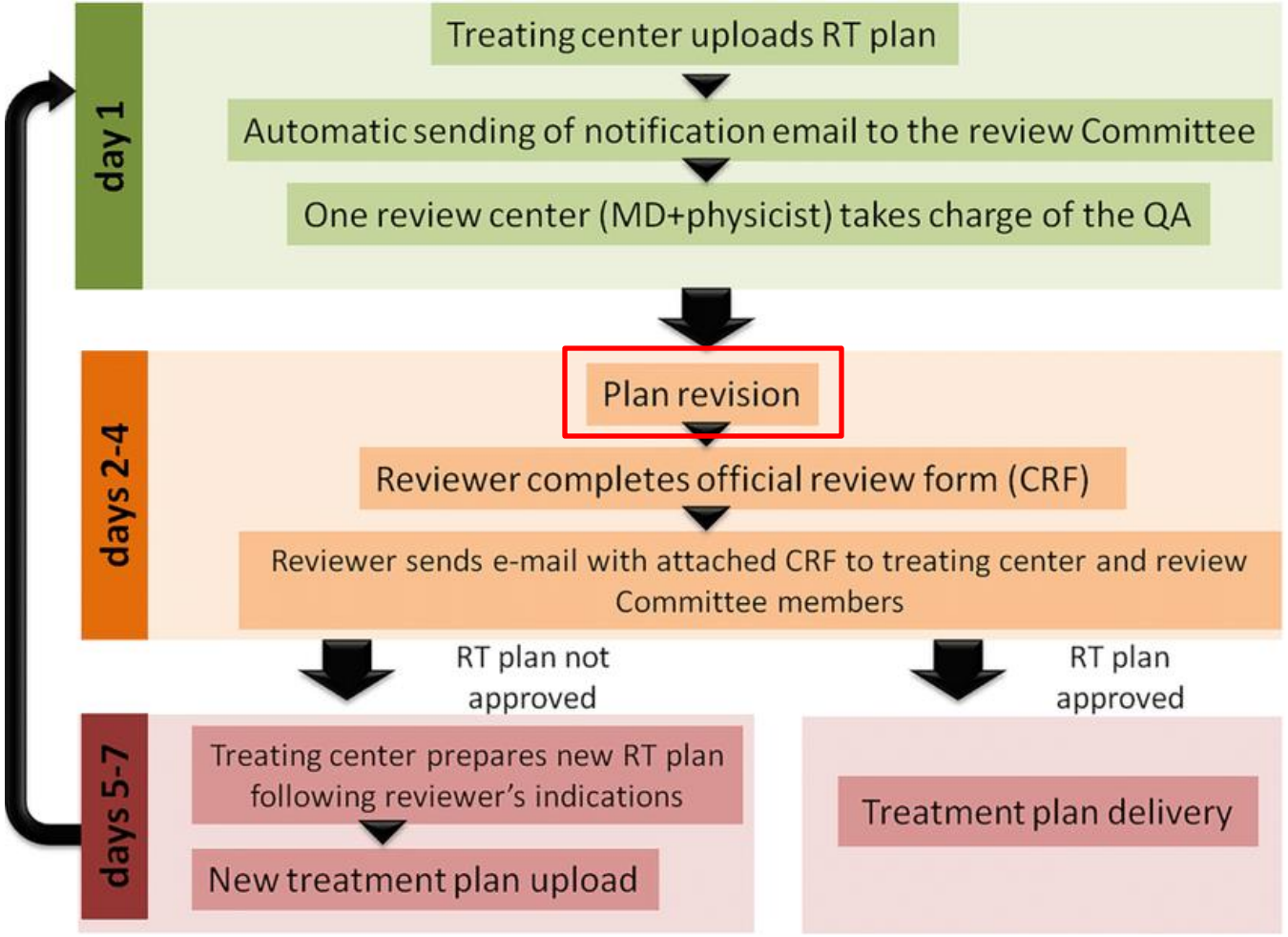


Lu et al, N Eng J Med 2024

Courtesy of Dr Alex De Caluwé

UNDER-PERFORMANCE OF THE CONTROL ARM: RADIOTHERAPY QUALITY ASSURANCE (QA)?

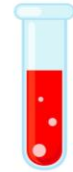
N2/N3 assessment: not mandatory at baseline



Meroni et al, Strahlentherapie und Onkologie 2019

OTHER REMAINING ISSUES

Treatment duration: until progression	How to distinguish between patients who are truly “cured” vs those with micrometastatic disease?	ctDNA assays (EGFR mutation might be “easier” to detect)
	Long-term patient adherence in the absence of visible disease? (in LAURA: 13% discontinued due to AEs, 3% to patient decision, *so far*)	Digital health: supportive treatment apps & coaching
Treatment access	Societal cost (e.g. Asia)	Generic version of Osimertinib? Other “me-too” 3rd generation TKIs?



CONCLUSIONS

CONCLUSIONS

- **Long-term Osimertinib after chemo-radiotherapy prolongs PFS in patients with stage III EGFR-mutant NSCLC** – impressive HR of 0.16 (95% CI 0.10-0.24)
  - Benefit in all subgroups & clear *brain* protection
  - More skin / GI toxicity (grade 1/2)
  - No mature data on OS

- Underperformance of the **control arm**: brain metastases at baseline in 7% of patients + questions on lymph node assessment & quality of radiotherapy

- Treatment until progression → how to select the patients? long-term adherence?
- Treatment access!

ESMO VIRTUAL JOURNAL CLUB

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RUBY TRIAL IN ENDOMETRIAL CANCER. OVERALL SURVIVAL IN PATIENTS WITH ENDOMETRIAL CANCER TREATED WITH DOSTARLIMAB PLUS CARBOPLATIN–PACLITAXEL IN THE RANDOMIZED ENGOT-EN6/GOG-3031/RUBY TRIAL

Domenica Lorusso

Humanitas University and Humanitas San Pio X Milan

ESMO WEBINAR SERIES

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RUBY Trial Background

- For over a decade, the standard of care for 1L treatment of primary advanced or recurrent EC was chemotherapy (CP); however, long-term outcomes were poor, with a median OS <3 years[1,2]

- Dostarlimab plus CP significantly improved PFS in the dMMR/MSI-H and overall populations 7with an early OS trend at the first interim analysis
  - These data led to the approval of dostarlimab plus CP in several countries for the treatment of primary advanced or recurrent dMMR/MSI-H EC[4–7]

- Here, we present updated OS, PFS2, and safety results from the second interim analysis of Part 1 of the phase 3 RUBY trial

1L, first-line; CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; EC, endometrial cancer; MSI-H, microsatellite instability high; OS, overall survival; PFS, progression-free survival.

1. Yang S, et al. *Discov Med.* 2011;12(64):205–212. 2. Fleming GF, et al. *J Clin Oncol*. 2004;22(11):2159–2166. 3. Mirza MR, et al. *N Engl J Med.* 2023;388(23):2145–2158. 4. JEMPERLI. Prescribing information. GSK; 2023. Accessed February 23, 2024. https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Jemperli/pdf/JEMPERLI-PI-MG.PDF. 5. JEMPERLI. Product characteristics. GSK; 2023. Accessed February 23, 2023. https://www.medicines.org.uk/emc/product/12669/smpc/print. 6. GSK. Accessed November 29, 2023. https://ca.gsk.com/en-ca/media/press-releases/jemperli-dostarlimab-for-injection-plus-carboplatin-and-paclitaxel-approved-in-canada-as-a-treatment-option-for-primary-advanced-or-recurrent-dmmmsi-h-endometrial-cancer/. 7. GSK. Accessed December 21, 2023. https://www.gsk.com/en-gb/media/press-releases/jemperli-plus-chemotherapy-approved-as-the-first-and-only-frontline-immuno-oncology-treatment-in-the-european-union/.

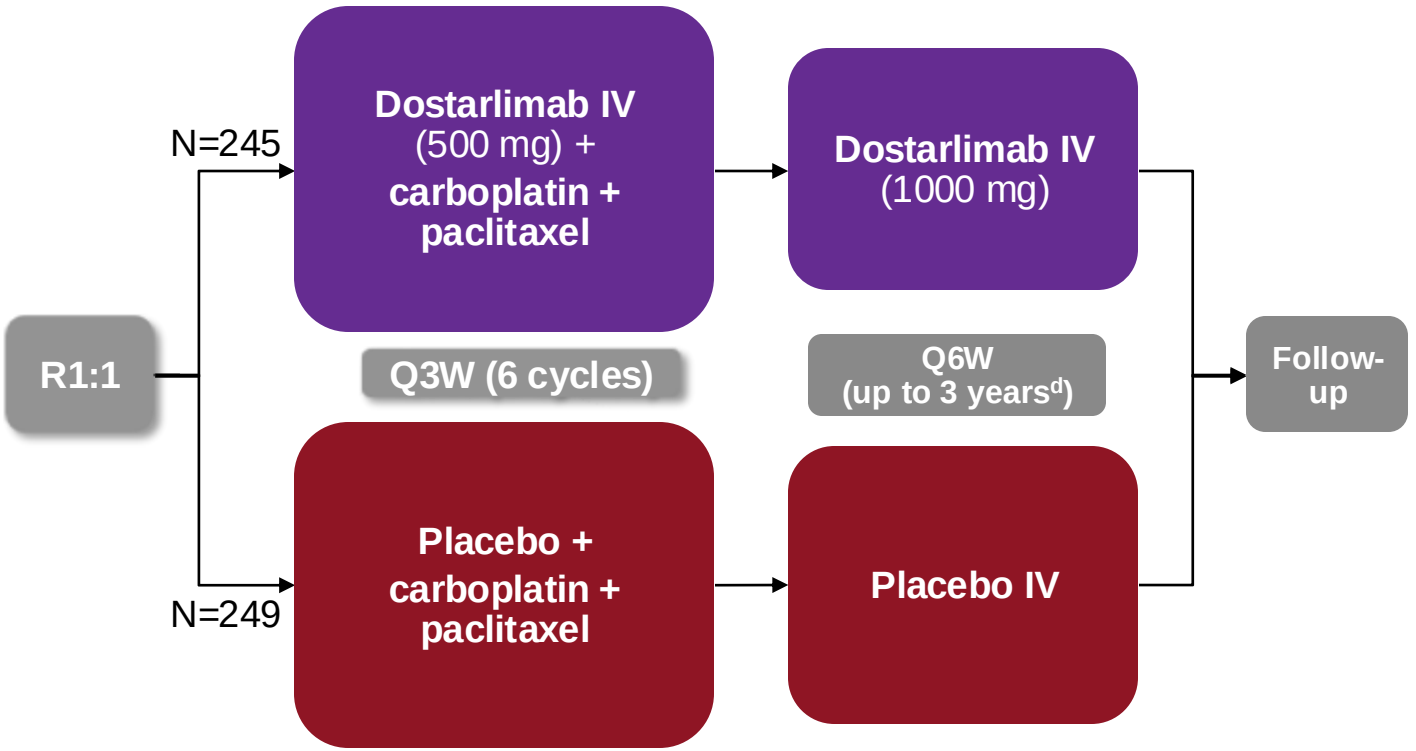
ENGOT-EN6-NSGO/GOG-3031/RUBY (NCT03981796) Part 1

Eligible patients

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

Stratification

- MMR/MSI status[c]
- Prior external pelvic radiotherapy
- Disease status



Primary endpoint

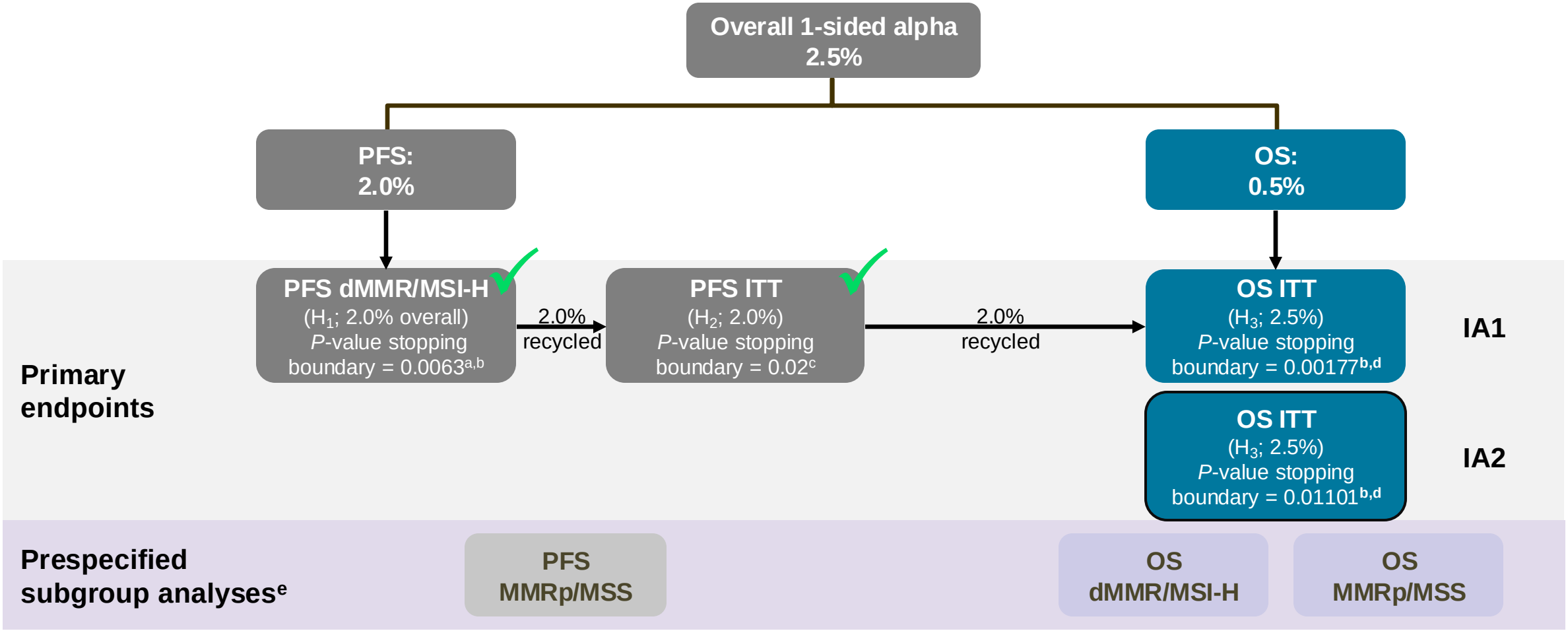
- PFS by INV[e] (IA1)
- OS (IA1 & IA2)

Secondary endpoints

- PFS by BICR (IA1)
- PFS2 (IA1 & IA2)
- ORR (IA1)
- DOR (IA1)
- DCR (IA1)
- HRQOL/PRO (IA1)
- Safety (IA1 & IA2)

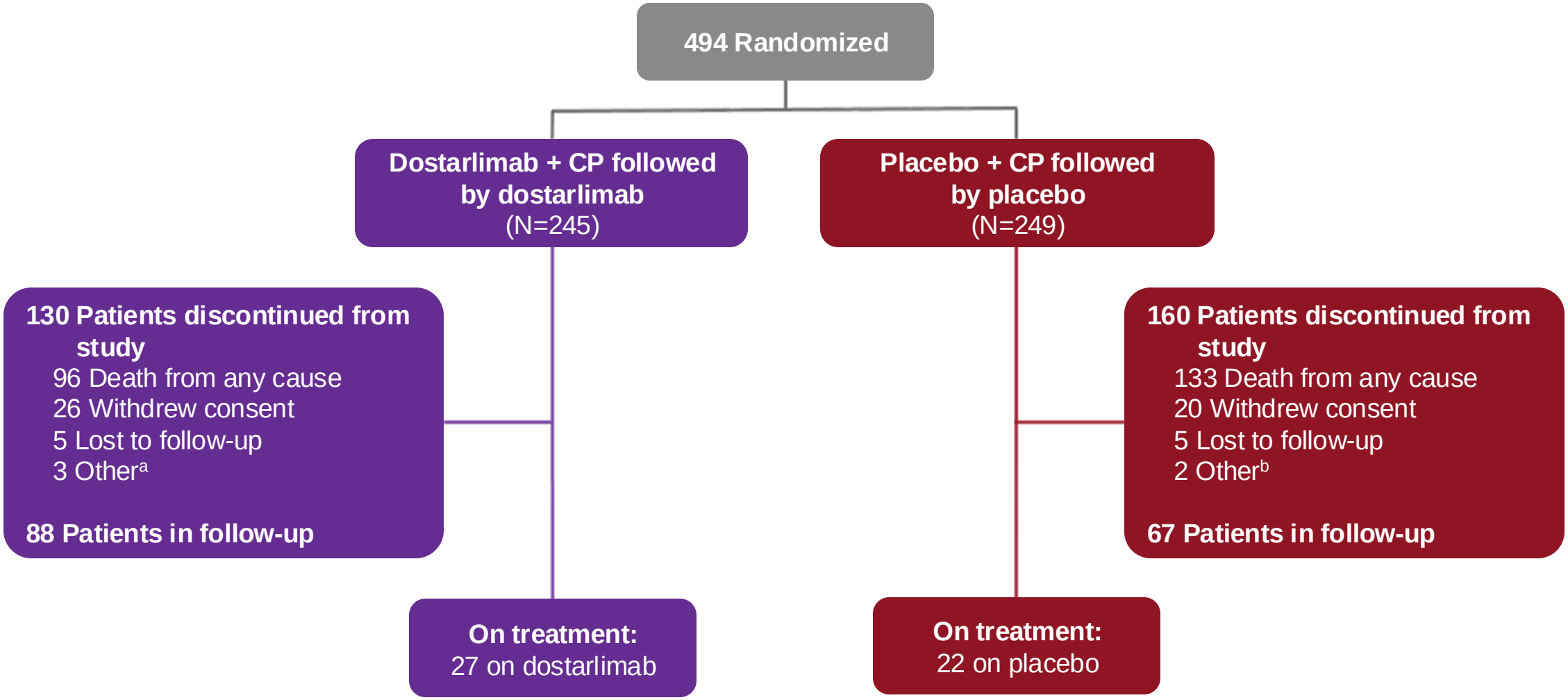
On-study imaging assessments were performed Q6W (±7 days) from the randomization date until week 25 (cycle 8), followed by Q9W (±7 days) until week 52. Subsequent tumor imaging was performed every 12 weeks (±7 days) until radiographic PD was documented by investigator assessment per RECIST v1.1 followed by one additional imaging 4–6 weeks later, or subsequent anticancer therapy was started, whichever occured first. Thereafter, scans may have been performed per standard of care.
[a]Histologically/cytologically proven advanced or recurrent EC; stage III/IV disease or first recurrent EC with low potential for cure by radiation therapy or surgery alone or in combination. [b]Carcinosarcoma, clear cell, serous, or mixed histology permitted (mixed histology containing at least 10% carcinosarcoma, clear cell, or serous histology). [c]Patients were randomized based on either local or central MMR/MSI testing results. Central testing was used with local results were not available. For local determination of MMR/MSI status, IHC, next-generation sequencing, and polymerase chain reaction assays were accepted. For central determination of MMR/MSI status, IHC per Ventana MMR RxDx panel was used. [d]Treatment ends after 3 years, PD, toxicity, withdrawal of consent, investigator's decision, or death, whichever occurs first. Continued treatment with dostarlimab or placebo beyond 3 years may be considered following discussion between the sponsor and the investigator. [e]The threshold for the primary endpoint of PFS was crossed at IA1. Therefore, IA1 was considered the final analysis for PFS.
BICR, blinded independent central review; DCR, disease control rate; DOR, duration of response; EC, endometrial cancer; HRQOL, health-related quality of life; IA, interim assessment; IHC, immunohistochemistry; INV, investigator assessment; MMR, mismatch repair; MSI, microsatellite instability; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, every 3 weeks; Q6W, every 6 weeks; Q9W, every 9 weeks; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Statistical Testing and Multiplicity Control Strategy



Multiplicity control strategy is based on the graphical method (Maurer W, et al. Stat Med. 2013;32:1739-53).
[a]Hypothesis for PFS dMMR/MSI (H_1) was tested at IA1 with 0.63% alpha spent from the overall alpha level (2.0%) initially allocated. [b]Stopping boundaries and alpha spent at each IA were adjusted based on the actual number of events/information fraction observed based on the prespecified alpha spending function at the time of analysis; *P*-value stopping boundary (IA1) = 0.0063 for PFS dMMR/MSI-H; *P*-value stopping boundary (IA1) = 0.00177 for OS ITT; *P*-value stopping boundary (IA2) = 0.01101 for OS ITT. [c]Since the null hypothesis (H_{01}) for H_1 was rejected at IA1, the 2.0% alpha for H_1 was recycled to hypothesis testing of PFS ITT (H_2). H_2 was tested at alpha level (2.0%) = 2.0% recycled + 0% initially allocated. [d]Since both null hypotheses (H_{01} and H_{02}) were rejected, 2.0% alpha for the family of hypothesis testing of PFS was recycled to testing of OS (H_3). H_3 was tested at alpha level (2.5%) = 2.0% recycled + 0.5% initially allocated. [e]Not formally tested.
dMMR, mismatch repair deficient; H, hypothesis; IA, interim analysis; ITT, intent-to-treat; MMRp, mismatch repair proficient; MSI-H, microsatellite instability high; MSS, microsatellite stable; OS, overall survival; PFS, progression-free survival.

Patient Disposition



Data cutoff date: September 22, 2023.

[a]Other includes one patient and investigator decision due to poor health, one patient randomized due to mistake and never received treatment, and one patient declined further treatment.

[b]Other includes one patient moved to hospice and one patient discharged from local practice due to move.

CP, carboplatin-paclitaxel.

Patient Population and Baseline Characteristics

Variable, n (%)	Overall	
	Dostarlimab + CP (N=245)	Placebo + CP (N=249)
MMR/MSI status		
dMMR/MSI-H	53 (21.6)	65 (26.1)
MMRp/MSS	192 (78.4)	184 (73.9)
Prior external pelvic radiation		
Yes	41 (16.7)	45 (18.1)
No	204 (83.3)	204 (81.9)
Disease status		
Primary stage III	45 (18.4)	47 (18.9)
Primary stage IV	83 (33.9)	83 (33.3)
Recurrent	117 (47.8)	119 (47.8)

Data cutoff date: September 28, 2022.
CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; MMR, mismatch repair; MMRp, mismatch repair proficient; MSI, microsatellite instability; MSI-H, microsatellite instability high; MSS, microsatellite stable.

Baseline Characteristics

Variable	Overall	
	Dostarlimab + CP (N=245)	Placebo + CP (N=249)
Age		
Median (range), y	64 (41–81)	65 (28–85)
≥65 y, n (%)	118 (48.2)	135 (54.2)
Race, n (%)		
White	189 (77.1)	191 (76.7)
Black	28 (11.4)	31 (12.4)
Asian	7 (2.9)	8 (3.2)
Other[a]	21 (8.6)	19 (7.6)
ECOG PS, n (%)[b]		
0	145 (60.2)	160 (65.0)
1	96 (39.8)	86 (35.0)
BMI		
Median (range)	30.8 (17.6–60.6)	32.8 (17.7–68.0)
Measurable disease at baseline, n (%)		
Yes	212 (86.5)	219 (88.0)
No	33 (13.5)	30 (12.0)

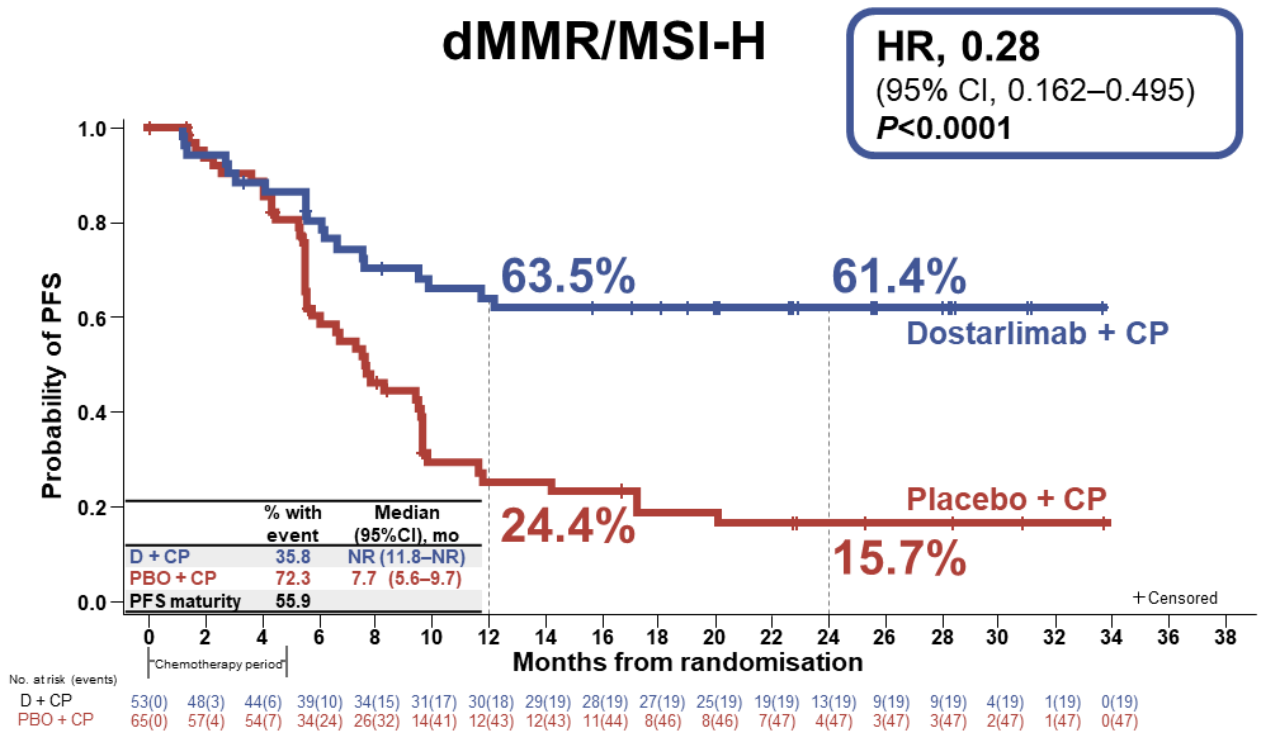
Variable	Overall	
	Dostarlimab + CP (N=245)	Placebo + CP (N=249)
Prior anticancer treatment, n (%)		
Yes	48 (19.6)	52 (20.9)
Carboplatin-paclitaxel	36 (14.7)	39 (15.7)
Histology type, n (%)		
Carcinosarcoma	25 (10.2)	19 (7.6)
Endometrioid	134 (54.7)	136 (54.6)
Mixed carcinoma[c]	10 (4.1)	9 (3.6)
Serous adenocarcinoma	50 (20.4)	52 (20.9)
Clear cell adenocarcinoma	8 (3.3)	9 (3.6)
Mucinous adenocarcinoma	0	1 (0.4)
Undifferentiated carcinoma	1 (0.4)	2 (0.8)
Other	17 (6.9)	21 (8.4)

Data cutoff date: September 28, 2022.

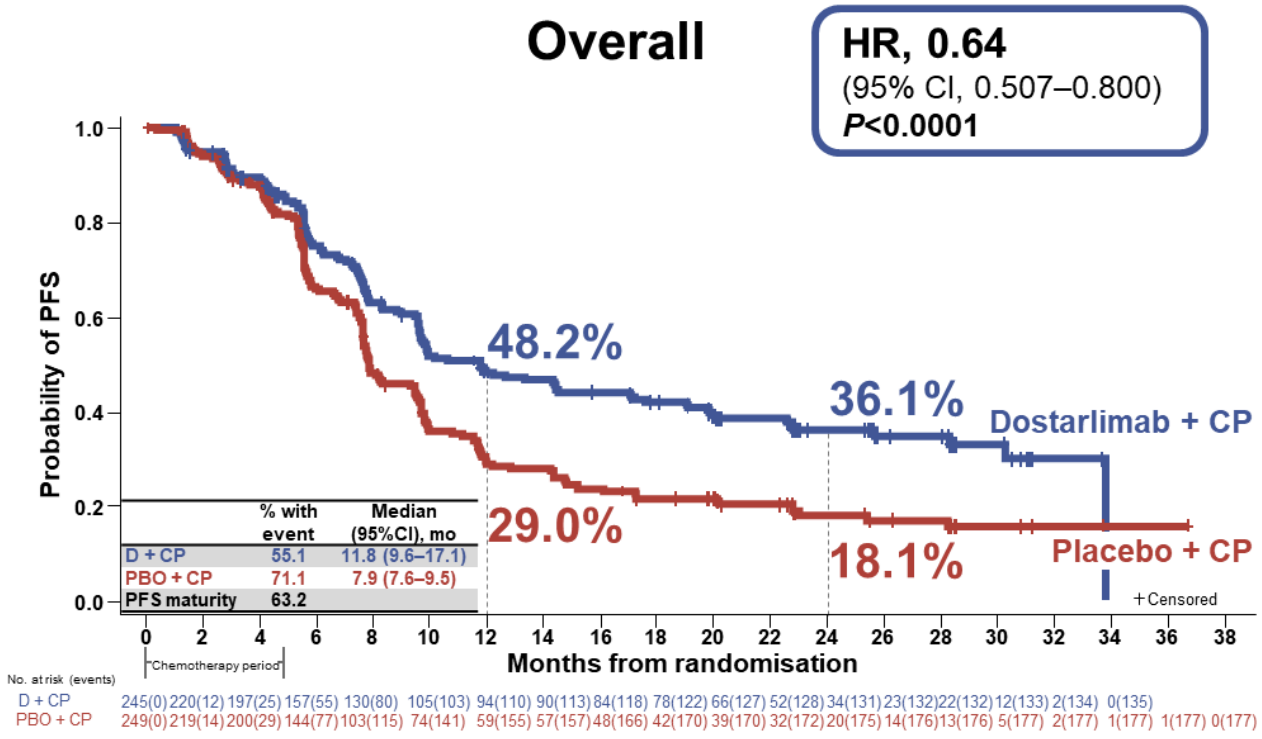
[a]Other includes patients identifying as American Indian or Alaska native, native Hawaiian or other Pacific Islander, unknown, or not reported. [b]Number of patients with ECOG PS score: 52 dostarlimab + CP dMMR/MSI-H, 65 placebo + CP dMMR/MSI-H, 241 dostarlimab + CP overall, 246 placebo + CP overall. [c]Mixed carcinoma ≥10% of carcinosarcoma, clear cell, or serous histology.

BMI, body mass index; CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; ECOG PS, Eastern Cooperative Oncology Group performance status; MSI-H, microsatellite instability high.

Statistically Significant Improvements in PFS in Patients with Primary Advanced or Recurrent EC



Median duration of follow-up: 24.8 mo



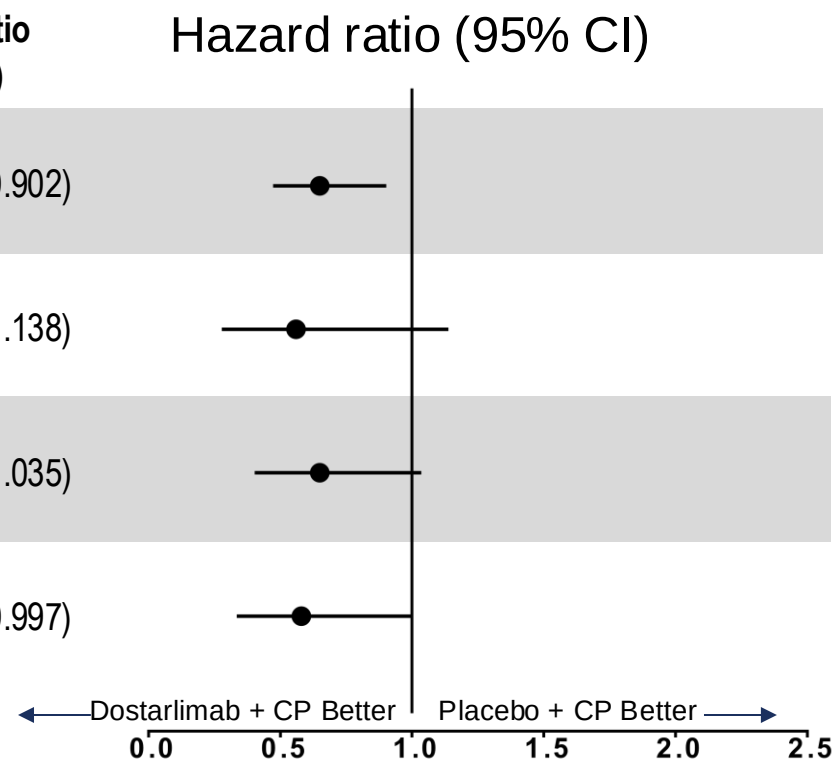
Median duration of follow-up: 25.4 mo

From *New England Journal of Medicine*, Mirza MR, Chase DM, Slomovitz MD, et al. Dostarlimab for primary advanced or recurrent endometrial cancer. DOI: 10.1056/NEJMoa2216334. Copyright © 2023 Massachusetts Medical Society.

CP, carboplatin-paclitaxel; D, dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability-high; NR, not reached, PBO, placebo; PFS, progression-free survival.

PFS According to Histological Subgroups[a]

Histology	Dostarlimab + CP (no. of events/no. of patients)	Placebo + CP (no. of events/no. of patients)	Hazard ratio (95% CI)
Endometrioid carcinoma	64/130	89/136	0.65 (0.473–0.902)
Carcinosarcoma[b]	14/24	18/22	0.56 (0.278–1.138)
Serous adenocarcinoma	36/55	35/48	0.65 (0.403–1.035)
Other	21/36	35/43	0.58 (0.335–0.997)

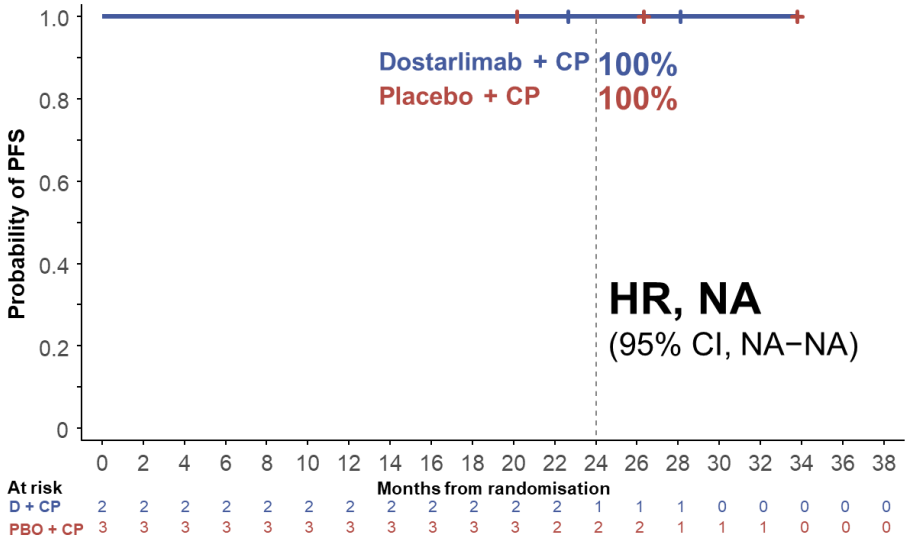


[a]Data based on exploratory analysis by histological subgroups with more than 10 patients per treatment arm (overall population).
[b]Total number of patients with carcinosarcoma was capped at approximately 10% of overall patient population.
Hazard ratios are based on unstratified Cox regression model.
CP, carboplatin-paclitaxel; HR, hazard ratio; PFS, progression-free survival.

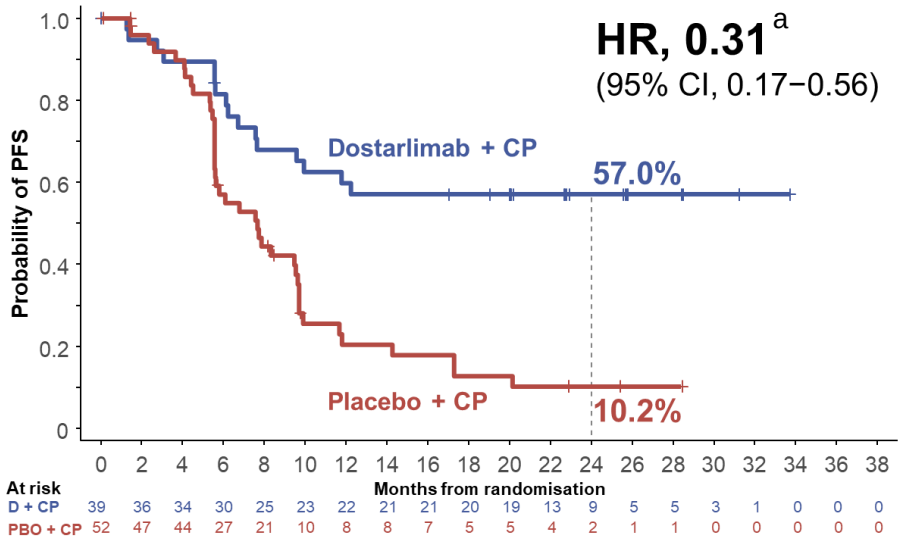
PFS According to Molecular Subgroup

Based on 400/494 patients with known molecular classification per whole exome sequencing

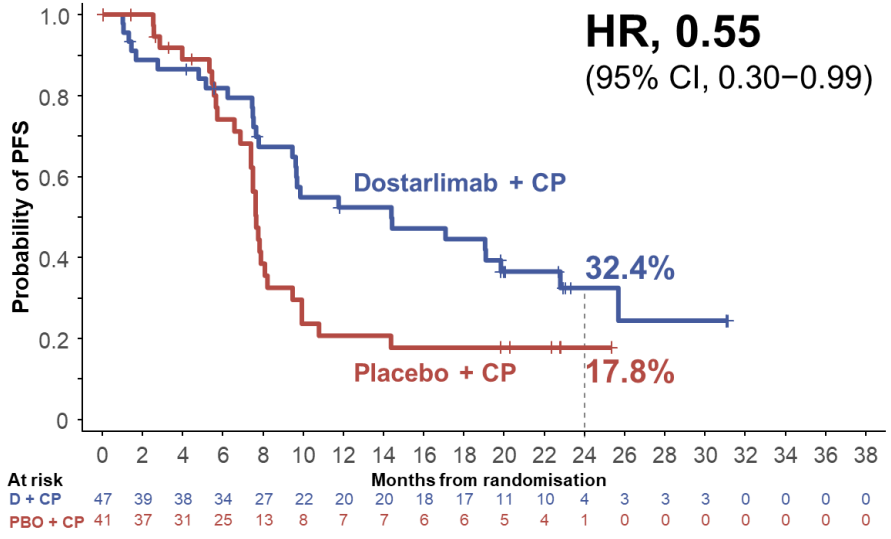
POLε mut



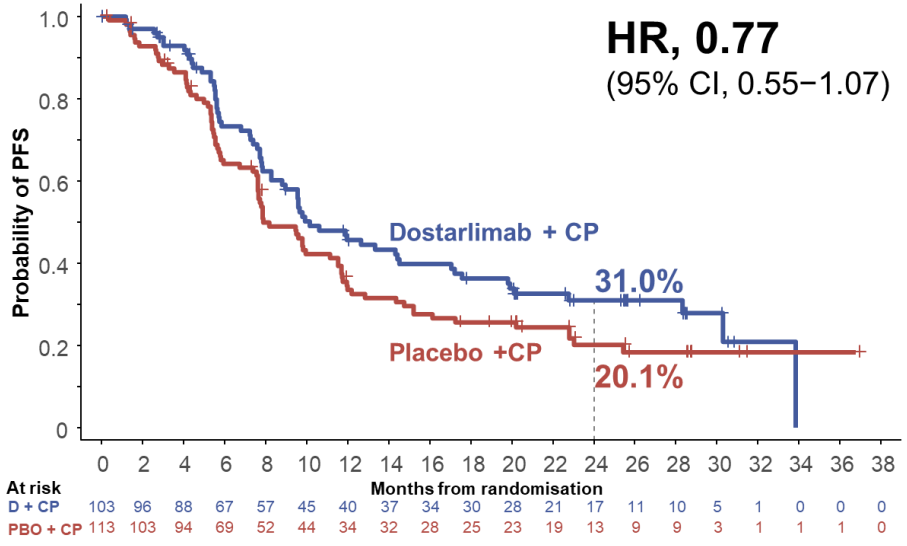
dMMR/MSI-H



TP53 mut



NSMP



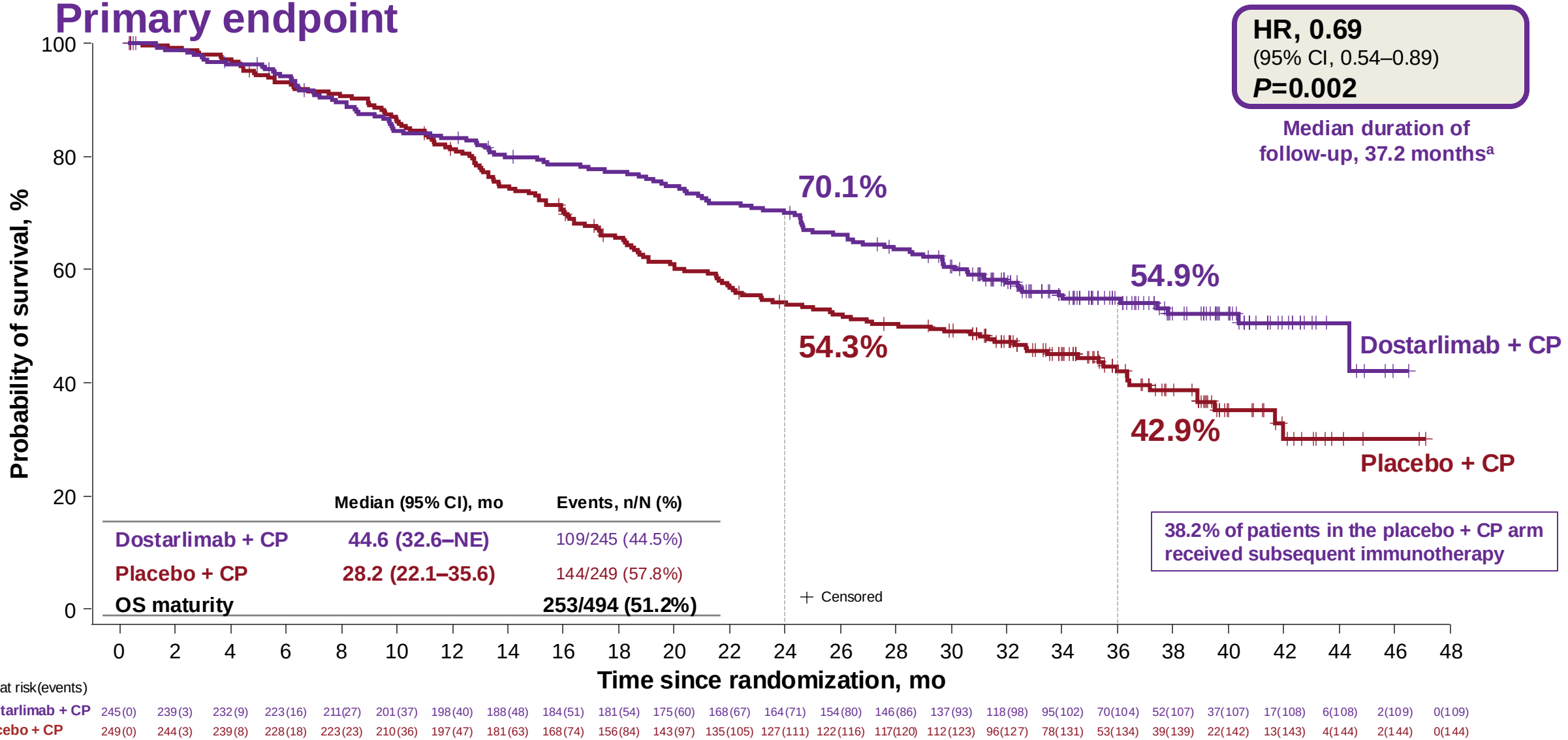
MADRID 2023 ESMO congress

[a]Primary endpoint of PFS in dMMR/MSI-H patients (n=118) showed HR, 0.28; *P*<0.0001

CP, carboplatin-paclitaxel; D, dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability–high; mut, mutated; NA, not applicable; NSMP, no specific molecular profile; PBO, placebo; PFS, progression-free survival; POLε , polymerase epsilon; TP53, tumor protein 53.

Statistically Significant OS Benefit in Overall Population

Primary endpoint

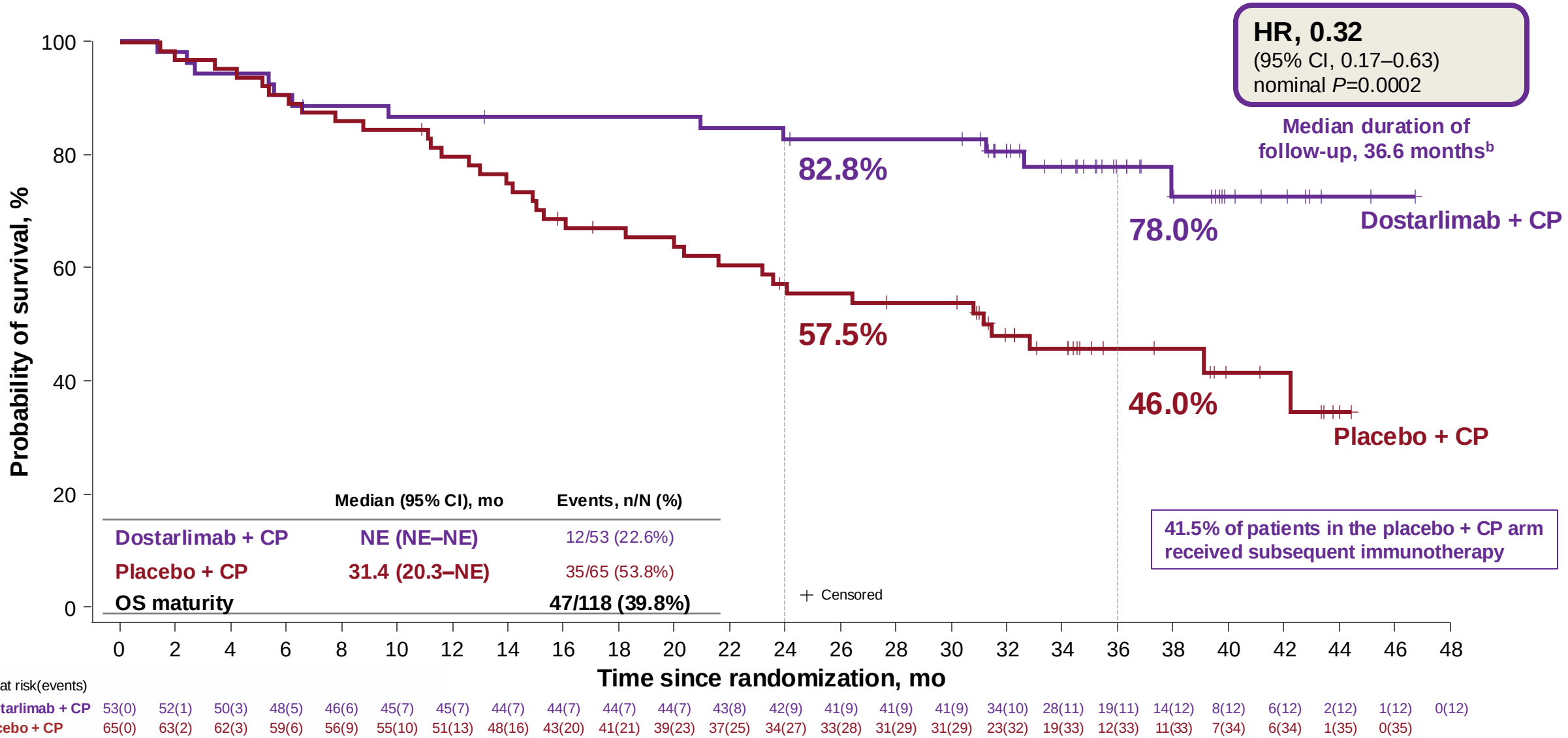


No. at risk(events)

Dostarlimab + CP	245(0)	239(3)	232(9)	223(16)	211(27)	201(37)	198(40)	188(48)	184(51)	181(54)	175(60)	168(67)	164(71)	154(80)	146(86)	137(93)	118(98)	95(102)	70(104)	52(107)	37(107)	17(108)	6(108)	2(109)	0(109)
Placebo + CP	249(0)	244(3)	239(8)	228(18)	223(23)	210(36)	197(47)	181(63)	168(74)	156(84)	143(97)	135(105)	127(111)	122(116)	117(120)	112(123)	96(127)	78(131)	53(134)	39(139)	22(142)	13(143)	4(144)	2(144)	0(144)

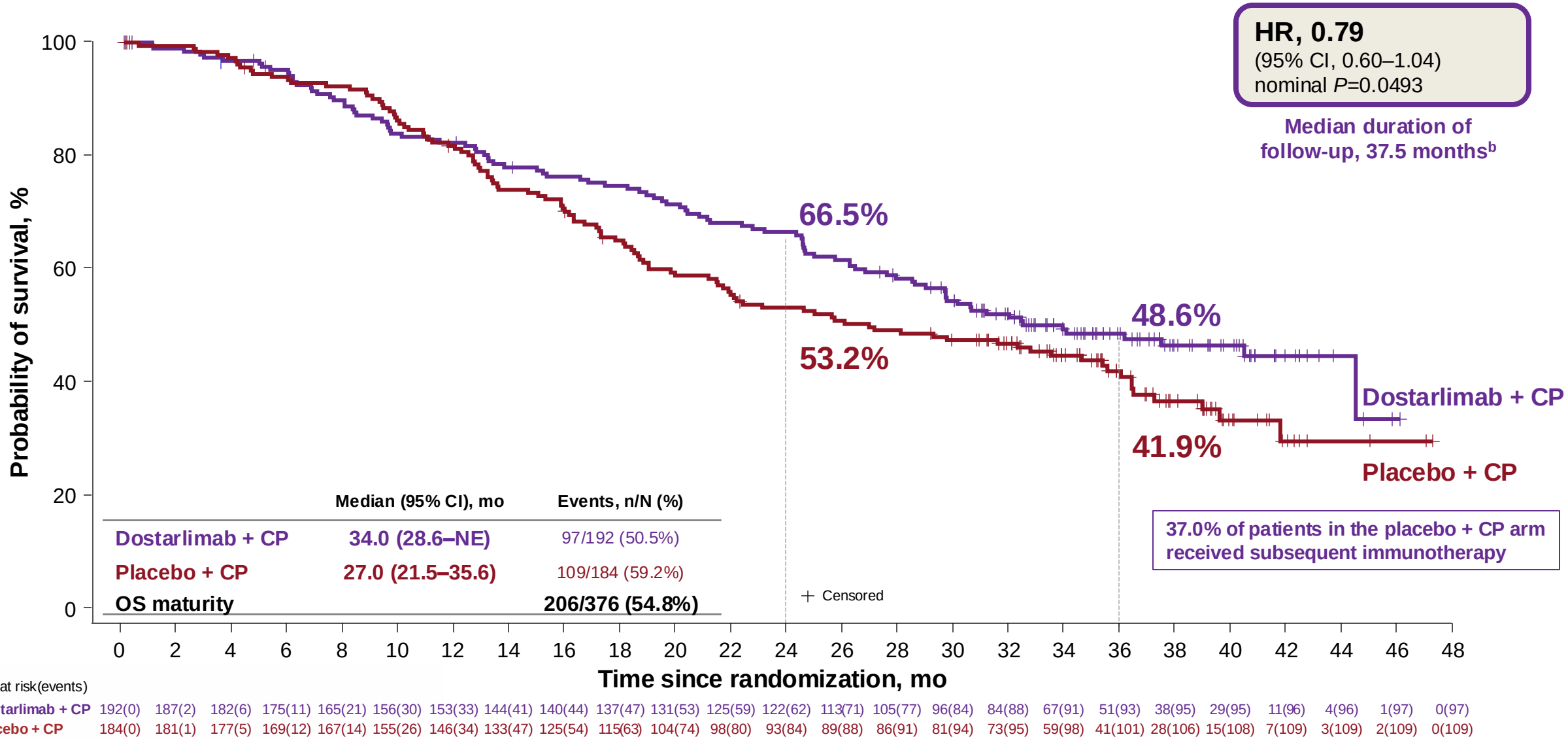
[a]Median expected duration of follow-up.
CP, carboplatin-paclitaxel; HR, hazard ratio; NE, not estimable; OS, overall survival.

Substantial OS Benefit in dMMR/MSI-H Population[a]



[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; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability high; NE, not estimable; OS, overall survival.

Clinically Meaningful OS Difference in MMRp/MSS Population[a]



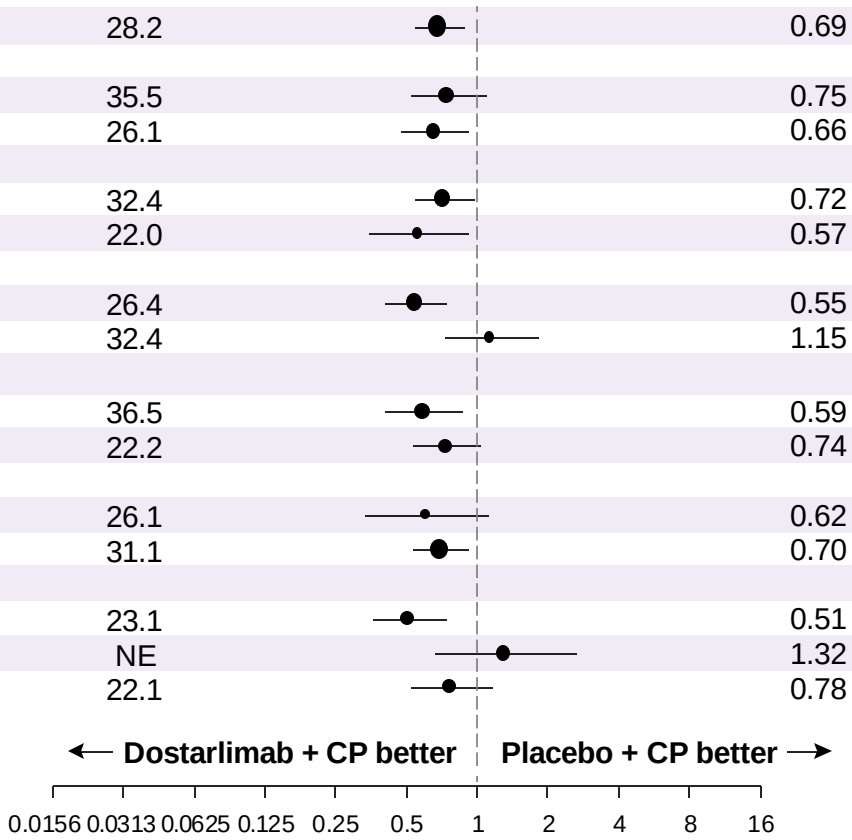
No. at risk(events)

Dostarlimab + CP	192(0)	187(2)	182(6)	175(11)	165(21)	156(30)	153(33)	144(41)	140(44)	137(47)	131(53)	125(59)	122(62)	113(71)	105(77)	96(84)	84(88)	67(91)	51(93)	38(95)	29(95)	11(96)	4(96)	1(97)	0(97)
Placebo + CP	184(0)	181(1)	177(5)	169(12)	167(14)	155(26)	146(34)	133(47)	125(54)	115(63)	104(74)	98(80)	93(84)	89(88)	86(91)	81(94)	73(95)	59(98)	41(101)	28(106)	15(108)	7(109)	3(109)	2(109)	0(109)

[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.

Consistent OS Benefit Across Most Exploratory Subgroups

Categories	Dostarlimab + CP (No. of events/No. of patients)	Placebo + CP (No. of events/No. of patients)	Dostarlimab, median OS, months	Placebo, median OS, months	HR (95% CI)
All patients	109/245	144/249	44.6	28.2	0.69 (0.54–0.89)
Age					
<65 years	54/127	57/114	44.6	35.5	0.75 (0.52–1.09)
≥65 years	55/118	87/135	37.6	26.1	0.66 (0.47–0.93)
Race					
White	82/189	104/191	44.6	32.4	0.72 (0.54–0.97)
Other	27/56	40/58	32.1	22.0	0.57 (0.35–0.93)
Region					
North America	69/171	12/187	44.6	26.4	0.55 (0.41–0.74)
Europe	40/74	32/62	28.6	32.4	1.15 (0.72–1.83)
Histology category					
Endometrioid carcinoma	44/129	70/136	44.6	36.5	0.59 (0.41–0.87)
Other	65/116	74/113	29.8	22.2	0.74 (0.53–1.04)
Prior external pelvic radiotherapy					
Yes	17/41	27/45	NE	26.1	0.62 (0.34–1.13)
No	92/204	17/204	40.6	31.1	0.70 (0.53–0.92)
Disease status					
Recurrent	48/117	77/119	44.6	23.1	0.51 (0.36–0.74)
Primary stage III	18/44	14/47	NE	NE	1.32 (0.66–2.66)
Primary stage IV	43/84	53/83	31.3	22.1	0.78 (0.52–1.17)

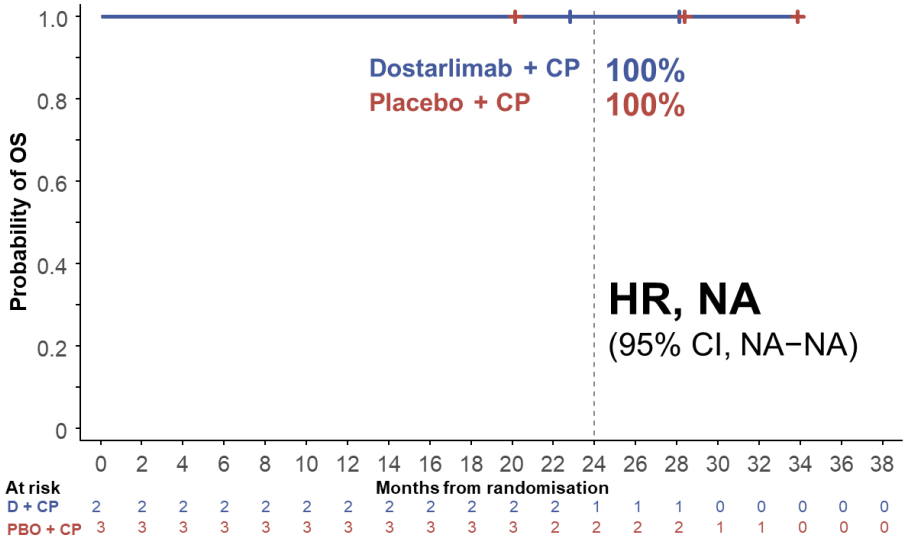


These subgroups are not powered for analyses, with low numbers and low data maturity. Therefore, results should be interpreted with caution.
CP, carboplatin-paclitaxel; HR, hazard ratio; NE, not estimable; OS, overall survival.

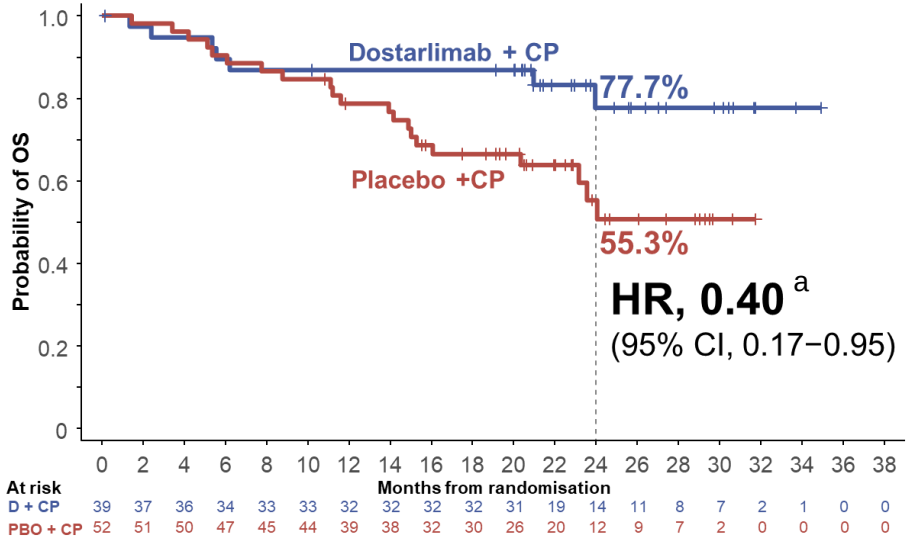
OS According to Molecular Subgroup

Based on 400/494 patients with known molecular classification per whole exome sequencing

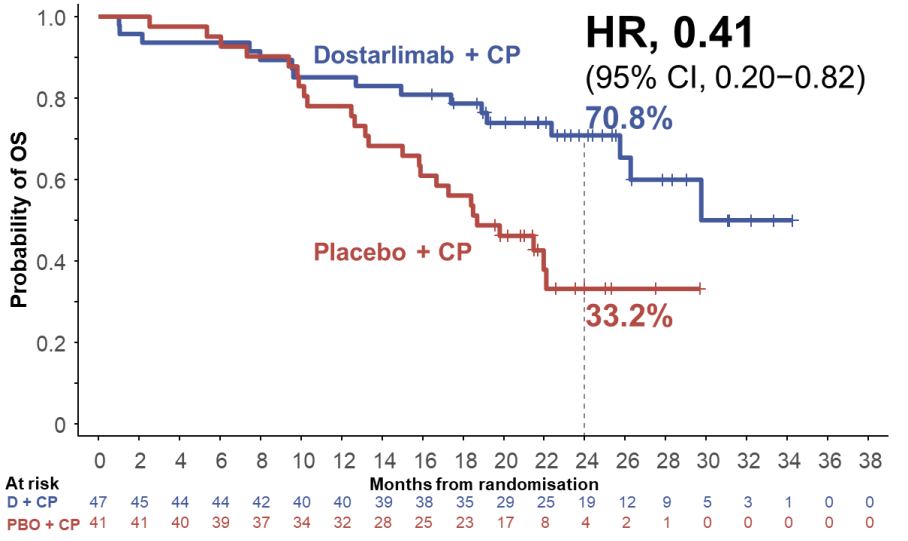
POLε mut



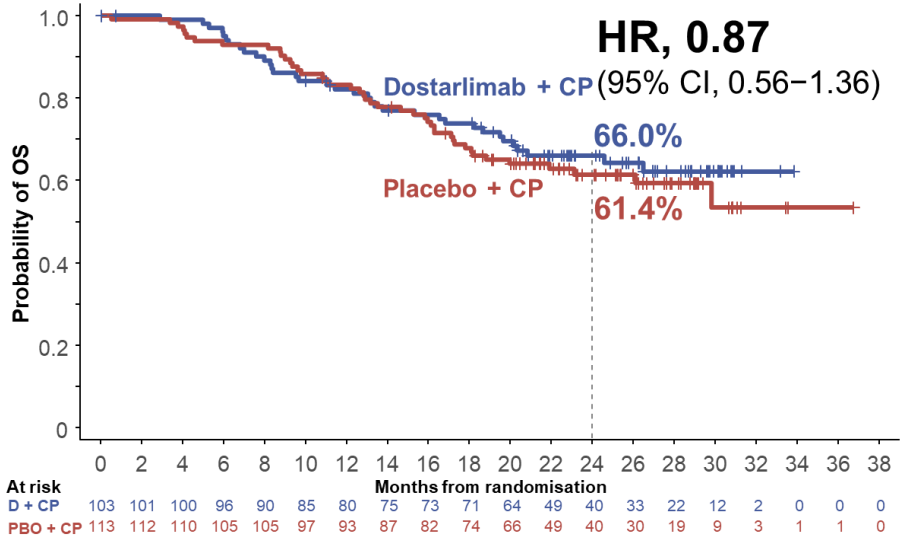
dMMR/MSI-H



TP53 mut



NSMP



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[a]Prespecified OS analysis in dMMR/MSI-H patients (n=118) showed HR, 0.30.

CP, carboplatin-paclitaxel; D, dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability–high; mut, mutated; NA, not applicable; NR, not reached; NSMP, no specific molecular profile; OS, overall survival; PBO, placebo; POLε , polymerase epsilon; TP53, tumor protein 53.

Subsequent Immunotherapy

Variable, n (%)	dMMR/MSI-H		MMRp/MSS		Overall	
	Dostarlimab + CP (N=53)	Placebo + CP (N=65)	Dostarlimab + CP (N=192)	Placebo + CP (N=184)	Dostarlimab + CP (N=245)	Placebo + CP (N=249)
Any follow-up anticancer therapy	**15 (28.3)**	**39 (60.0)**	**105 (54.7)**	**134 (72.8)**	**120 (49.0)**	**173 (69.5)**
Immunotherapy	**8 (15.1)**	**27 (41.5)**	**34 (17.7)**	**68 (37.0)**	**42 (17.1)**	**95 (38.2)**
Pembrolizumab	4 (7.5)	21 (32.3)	9 (4.7)	20 (10.9)	13 (5.3)	41 (16.5)
Pembrolizumab-lenvatinib	3 (5.7)	2 (3.1)	22 (11.5)	43 (23.4)	25 (10.2)	45 (18.1)
Dostarlimab	0	3 (4.6)	0	0	0	3 (1.2)
Other[a]	2 (3.8)	1 (1.5)	3 (1.6)	11 (6.0)	5 (2.0)	12 (4.8)

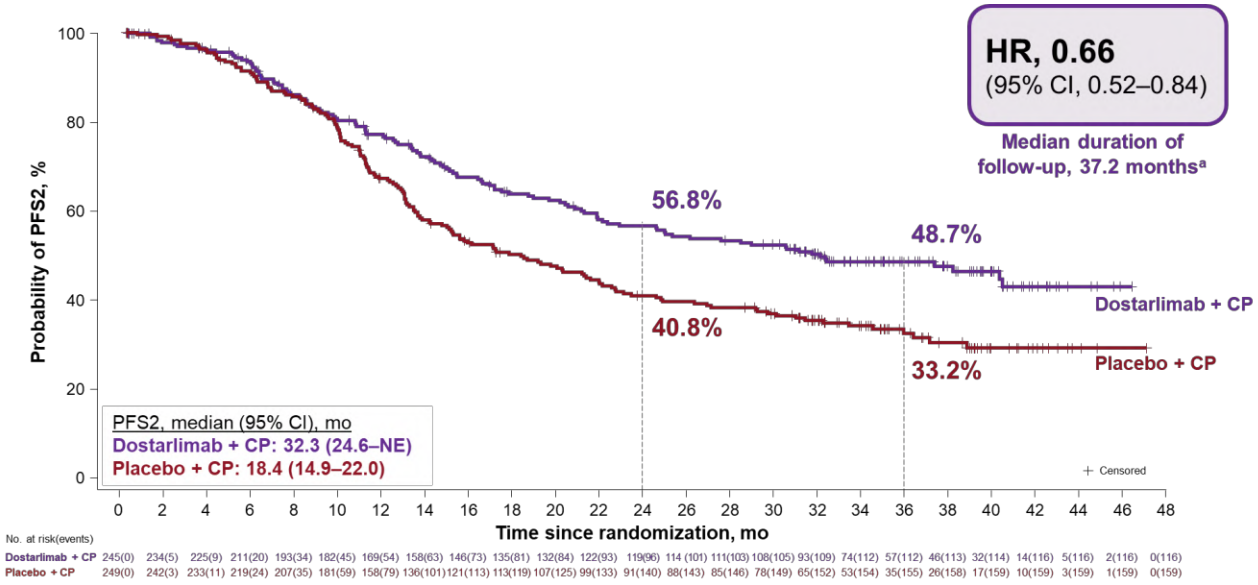
Data cutoff date: September 22, 2023.

[a]The category of other includes MK7694A, pembrolizumab-tamoxifen, retifanlimab-epacadostat, investigational product, atezolizumab-ipatasertib, avelumab-axitinib, bevacizumab-atezolizumab, durvalumab-cediranib, durvalumab-olaparib, nivolumab-BMS986207-COM701, nivolumab-lucitanib, and SGN-ALPV.

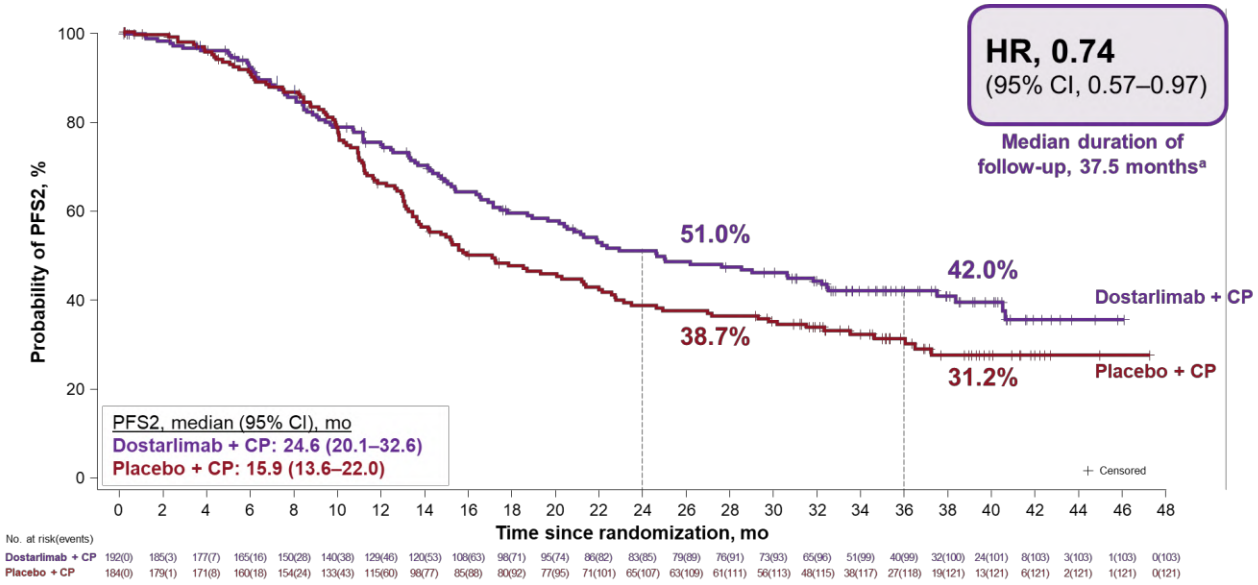
CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; MMRp, mismatch repair proficient; MSI-H, microsatellite instability high; MSS, microsatellite stable.

Clinically Meaningful Difference in PFS2 in the Overall and MMRp/MSS Populations

Overall Population

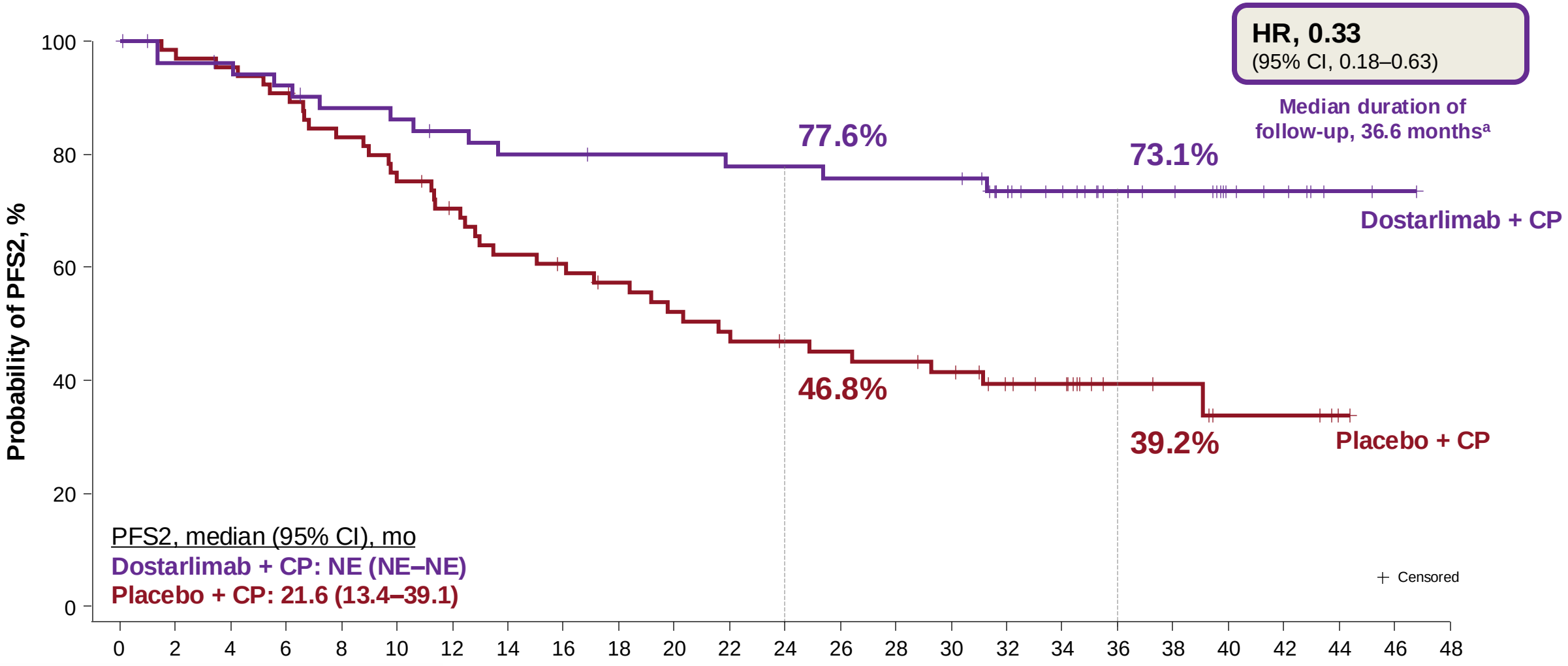


MMRp/MSS Population



PFS2 was a secondary endpoint.
[a]Median expected duration of follow-up.
CP, carboplatin-paclitaxel; HR, hazard ratio; MMRp, mismatch repair proficient; MSS, microsatellite stable; NE, not estimable; PFS2, progression-free survival 2.

Substantial PFS2 Difference in dMMR/MSI-H Population



No. at risk(events)

Dostarlimab + CP	53(0)	49(2)	48(2)	46(4)	43(6)	42(7)	40(8)	38(10)	38(10)	37(10)	37(10)	36(11)	36(11)	35(12)	35(12)	35(12)	28(13)	23(13)	17(13)	14(13)	8(13)	6(13)	2(13)	1(13)	0(13)
Placebo + CP	65(0)	63(2)	62(3)	59(6)	53(11)	48(16)	43(19)	38(24)	36(25)	33(27)	30(30)	28(32)	26(33)	25(34)	24(35)	22(36)	17(37)	15(37)	8(37)	7(37)	4(38)	4(38)	1(38)	0(38)	

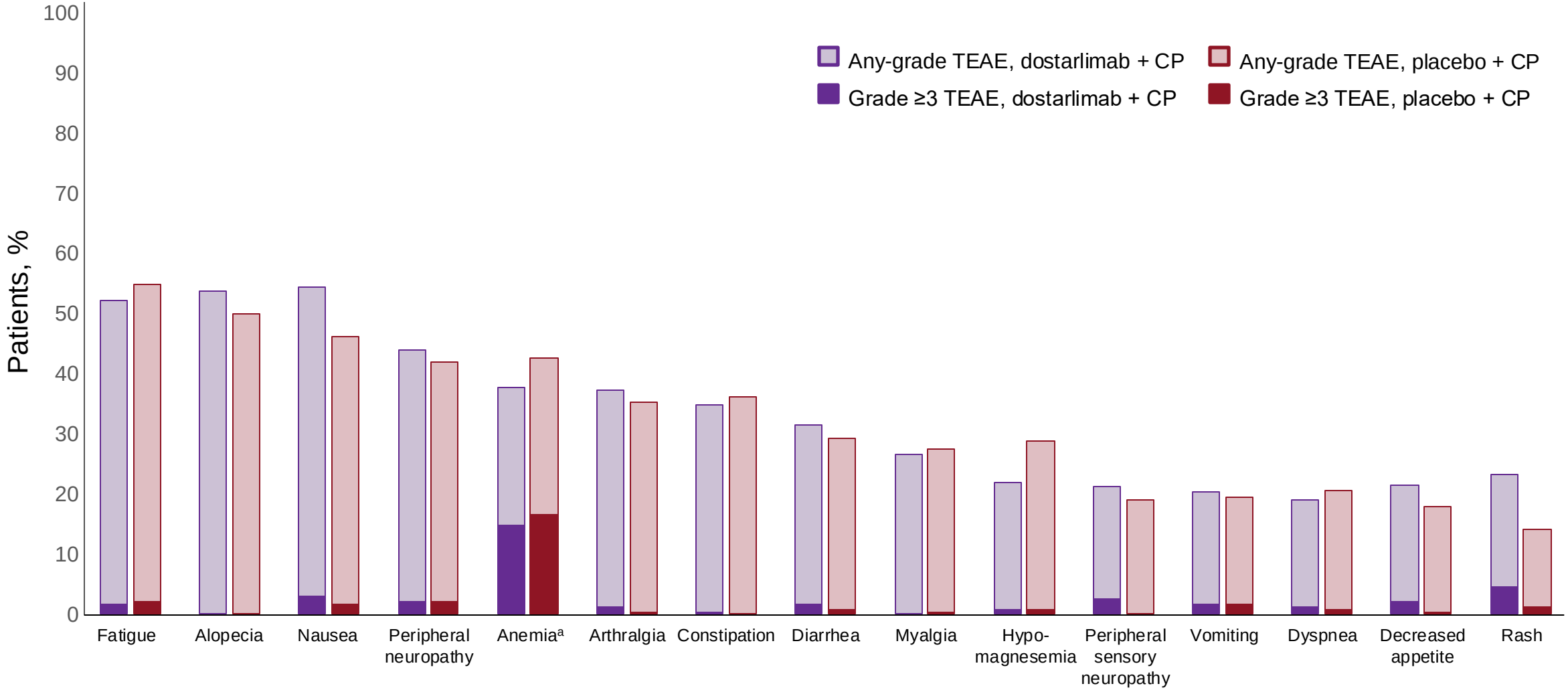
PFS2 was a secondary endpoint.
[a]Median expected duration of follow-up.
CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability high; NE, not estimable; PFS2, progression-free survival 2.

Safety Summary[a]

Parameter	Dostarlimab + CP (N=241)	Placebo + CP (N=246)
Any TEAE, n (%)	241 (100)	246 (100)
Any grade ≥3 TEAE, n (%)	174 (72.2)	148 (60.2)
Serious TEAE, n (%)	96 (39.8)	69 (28.0)
Any treatment-related irAE, n (%)	98 (40.7)	40 (16.3)
Any TEAE leading to discontinuation of dostarlimab or placebo, n (%)	46 (19.1)	20 (8.1)
Any TEAE leading to discontinuation of carboplatin, n (%)	20 (8.3)	15 (6.1)
Any TEAE leading to discontinuation of paclitaxel, n (%)	26 (10.8)	25 (10.2)
Any TEAE leading to death, n (%)	5 (2.1)[b]	0
Any TEAE related to dostarlimab leading to death, n (%)	2 (0.8)[c]	—
Duration of overall treatment, median (range), weeks	43.0 (3.0–192.6)	36.0 (2.1–193.1)

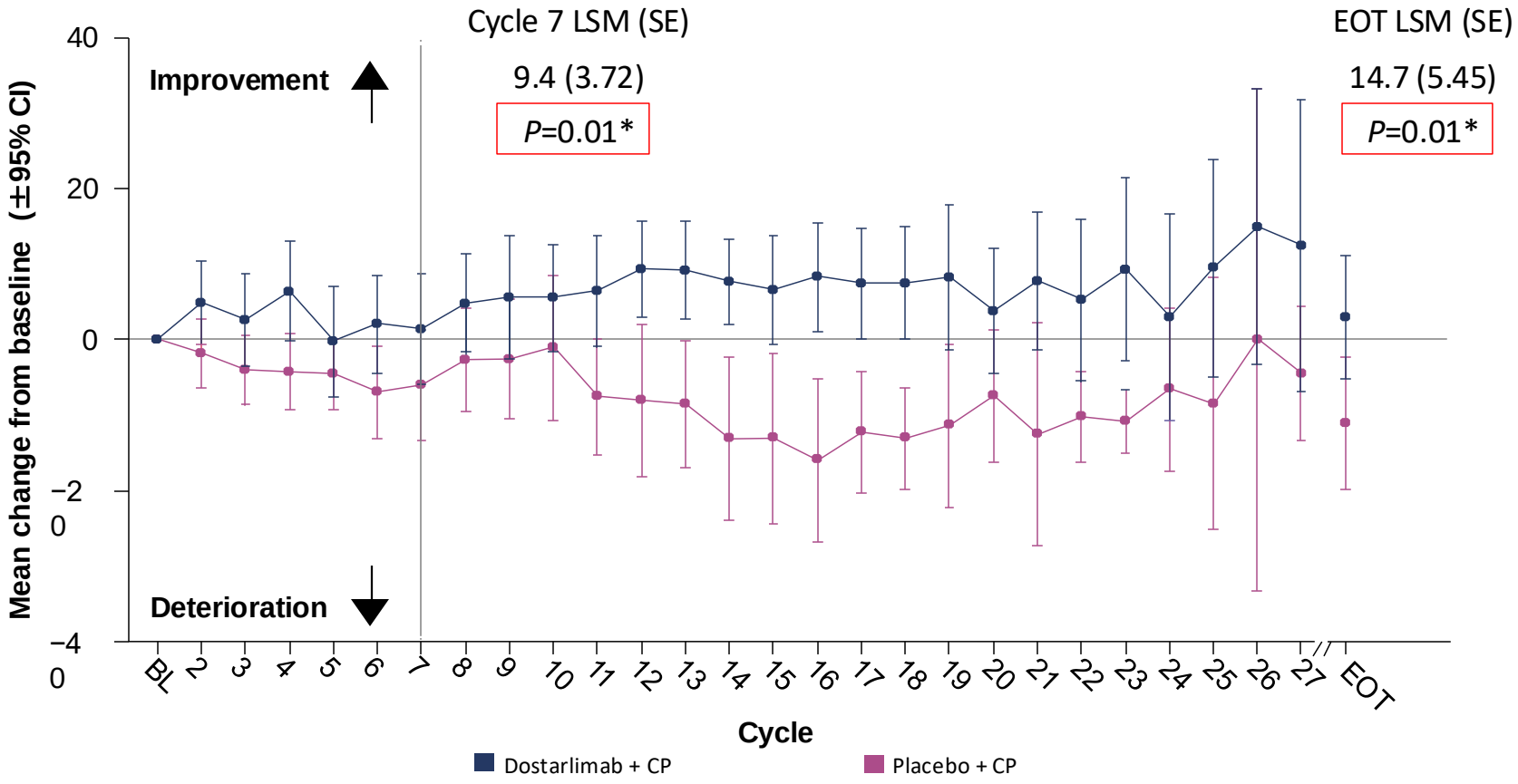
[a]Data are based on the safety analysis set, which consists of patients who received ≥1 dose of study treatment. [b]Three deaths were not related to study treatment (opiate overdose, COVID-19, and general physical health deterioration). [c]One death was considered by the investigator as related to dostarlimab, carboplatin, and paclitaxel and occurred during the first 6 cycles (myelosuppression); one death was related to dostarlimab and occurred during the 90-day safety follow-up (hypovolemic shock).
CP, carboplatin-paclitaxel; irAE, immune-related adverse event; TEAE, treatment-emergent adverse event.

Most TEAEs in ≥20% of Patients in Either Arm Were Grade 1 or 2



[a]Most cases of anemia were grade 2 or 3.
CP, carboplatin-paclitaxel; TEAE, treatment-emergent adverse event.

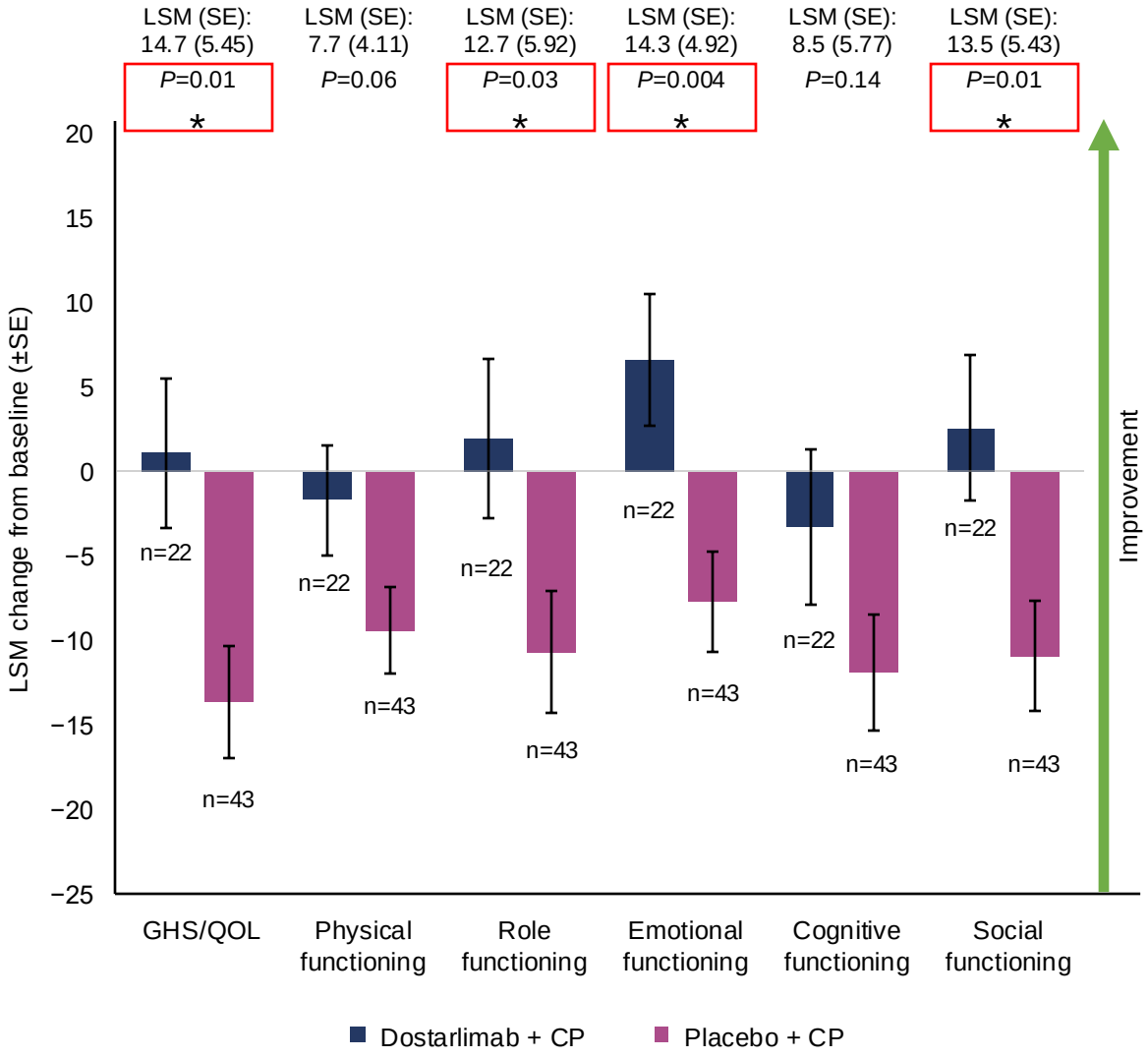
LSM change from baseline indicated a nominally significant improvement in global QOL at both Cycle 7 and EOT for patients treated with dostarlimab + CP compared with patients treated with placebo + CP



- The patient completion rates for the EORTC QLQ-C30 and QLQ-EN24 were similar between arms at baseline, Cycle 7, and EOT

*Indicates nominal significance. *P* values shown are nominal *P* values. Mixed models for repeated measures were used to generate LSMs, adjusting for within-patient correlations across time points and controlling for baseline values.
BL = baseline; CI = confidence interval; CP = carboplatin-paclitaxel; EORTC = European Organisation for Research and Treatment of Cancer; EOT = end of treatment; LSM = least square mean; QLQ-C30 = Quality of Life Questionnaire Core 30; QLQ-EN24 = Quality of Life Questionnaire Endometrial Cancer Module 24; QOL = quality of life; SE = standard error.
Valabrega G et al. Presented at European Society for Medical Oncology (ESMO) Congress. October 20-24, 2023; Madrid, Spain: Poster #749P.

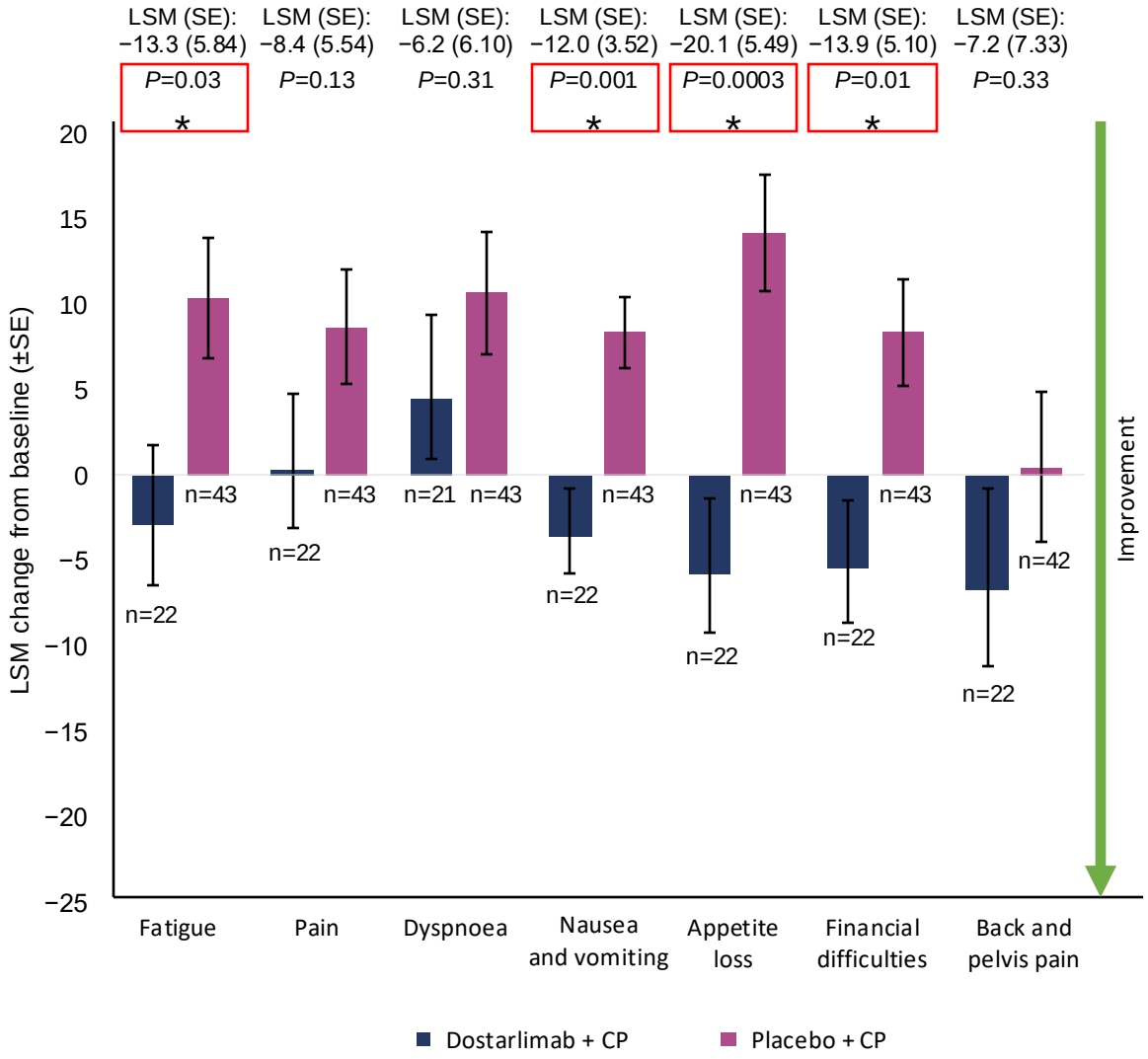
Functional scales: LSM change from baseline at EOT



- At EOT, the LSM change from baseline demonstrated nominally significant improvements in QOL (*P*=0.01), role functioning (*P*=0.03), emotional functioning (*P*=0.004), social functioning (*P*=0.01) for patients treated with dostarlimab + CP compared with those treated with placebo + CP

*Indicates nominal significance. *P* values shown are nominal *P* values. Mixed models for repeated measures were used to generate LSMs, adjusting for within-patient correlations across time points and controlling for baseline values.
CP = carboplatin-paclitaxel; EORTC = European Organisation for Research and Treatment of Cancer; EOT = end of treatment; GHS = general health score; LSM = least square mean; QLQ-C30 = Quality of Life Questionnaire Core 30; QOL = quality of life; SE = standard error.
Valabrega G et al. Presented at European Society for Medical Oncology (ESMO) Congress. October 20-24, 2023; Madrid, Spain: Poster #749P.

Symptom scales: LSM change from baseline at EOT



- At EOT, the LSM change from baseline demonstrated nominally significant improvements in the symptom scales of fatigue (*P*=0.03), nausea and vomiting (*P*=0.001), appetite loss (*P*=0.0003), and financial difficulties (*P*=0.01) for patients treated with dostarlimab + CP compared with those treated with placebo + CP
  - Only those symptom scales with nominally significant LSM results at EOT are shown

*Indicates nominal significance. *P* values shown are nominal *P* values. Mixed models for repeated measures were used to generate LSMs, adjusting for within-patient correlations across time points and controlling for baseline values.
CP = carboplatin-paclitaxel; EORTC = European Organisation for Research and Treatment of Cancer; EOT = end of treatment; LSM = least square mean; QLQ-EN24 = Quality of Life Questionnaire Endometrial Cancer Module 24; SE = standard error.
Valabrega G et al. Presented at European Society for Medical Oncology (ESMO) Congress. October 20-24, 2023; Madrid, Spain: Poster #749P.

Conclusions

- **Dostarlimab + CP demonstrated a statistically significant and clinically meaningful OS improvement in the overall population**
  - Substantial, unprecedented OS benefit in patients with dMMR/MSI-H EC[a]
  - Clinically meaningful 7-month median OS difference in patients with MMRp/MSS EC[a]
  - Consistent OS benefit across most exploratory subgroups
- PFS2 was consistent with PFS and OS
- No new safety signals were observed with additional follow-up

These data confirm dostarlimab + CP as a new standard of care for patients with primary advanced or recurrent EC, regardless of mismatch repair status

[a]OS in the dMMR/MSI-H and MMRp/MSS was a prespecified, exploratory analysis. PFS2 was a secondary endpoint.
CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MSI-H, microsatellite instability–high; MSS, microsatellite stable; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival 2.

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