ESMO 2024: Updates on gynecological malignancies

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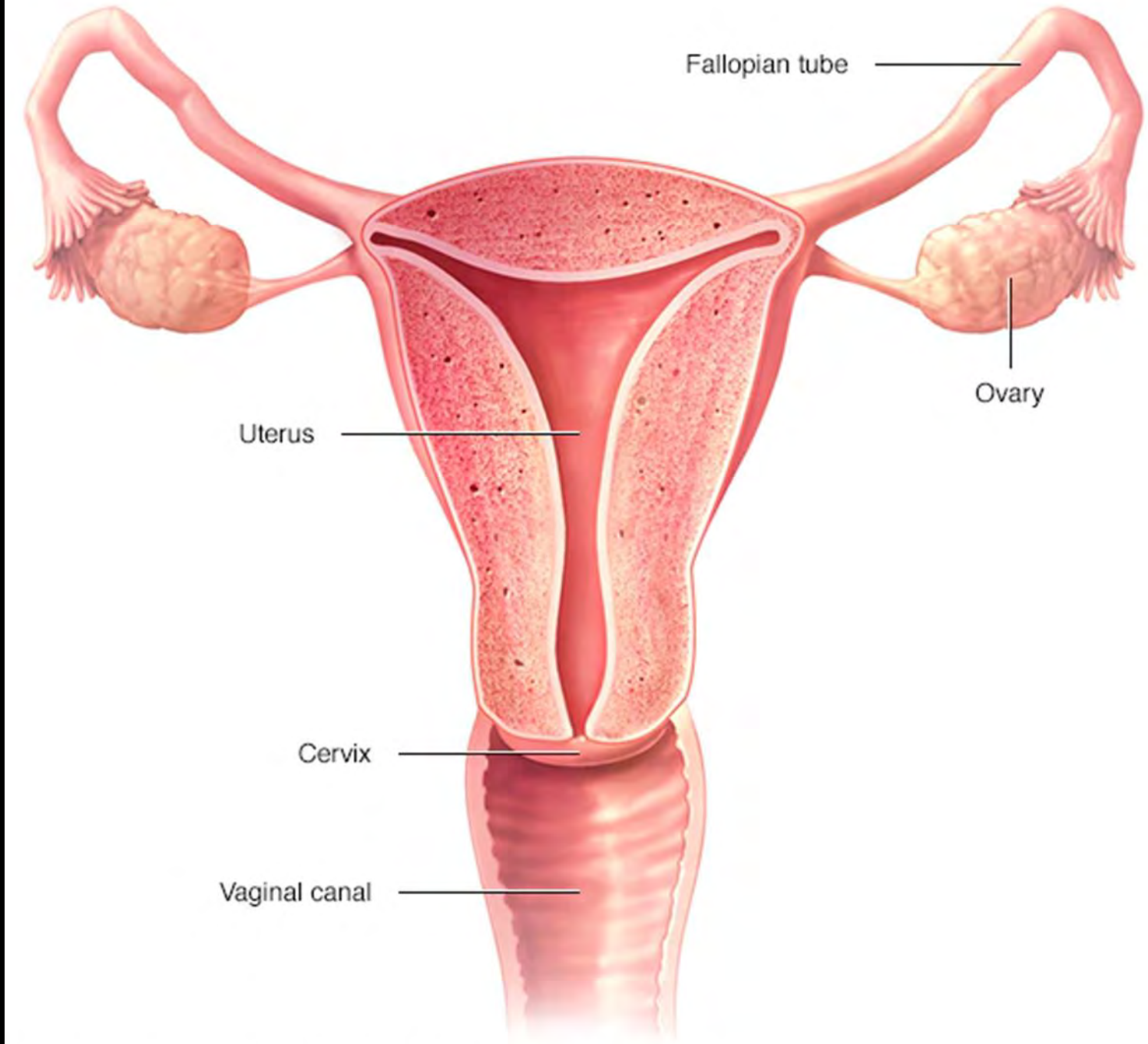
February 2025



ESMO 2024

Barcelona, Spain
September 2024

CONTENT

- ***OVARIAN***
- PRIMA (Annals of Oncology)
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- INTERLACE QOL DATA (Lancet)
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- ADC: Trastuzumab deruxtecan breast cancer (Nature Med)

OVARIAN CANCER: PRIMA

ELSEVIER

Annals of Oncology

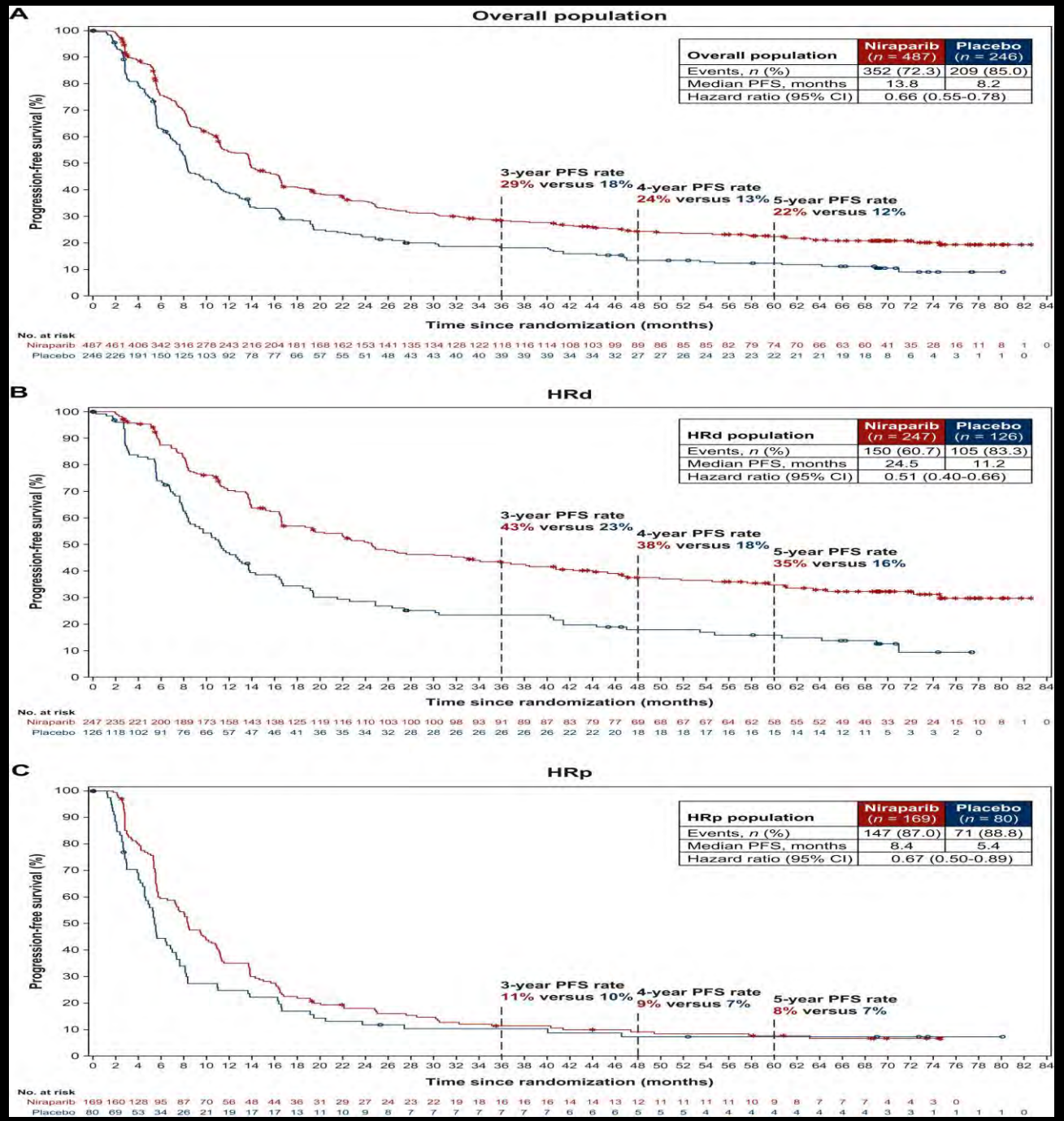
Available online 14 September 2024

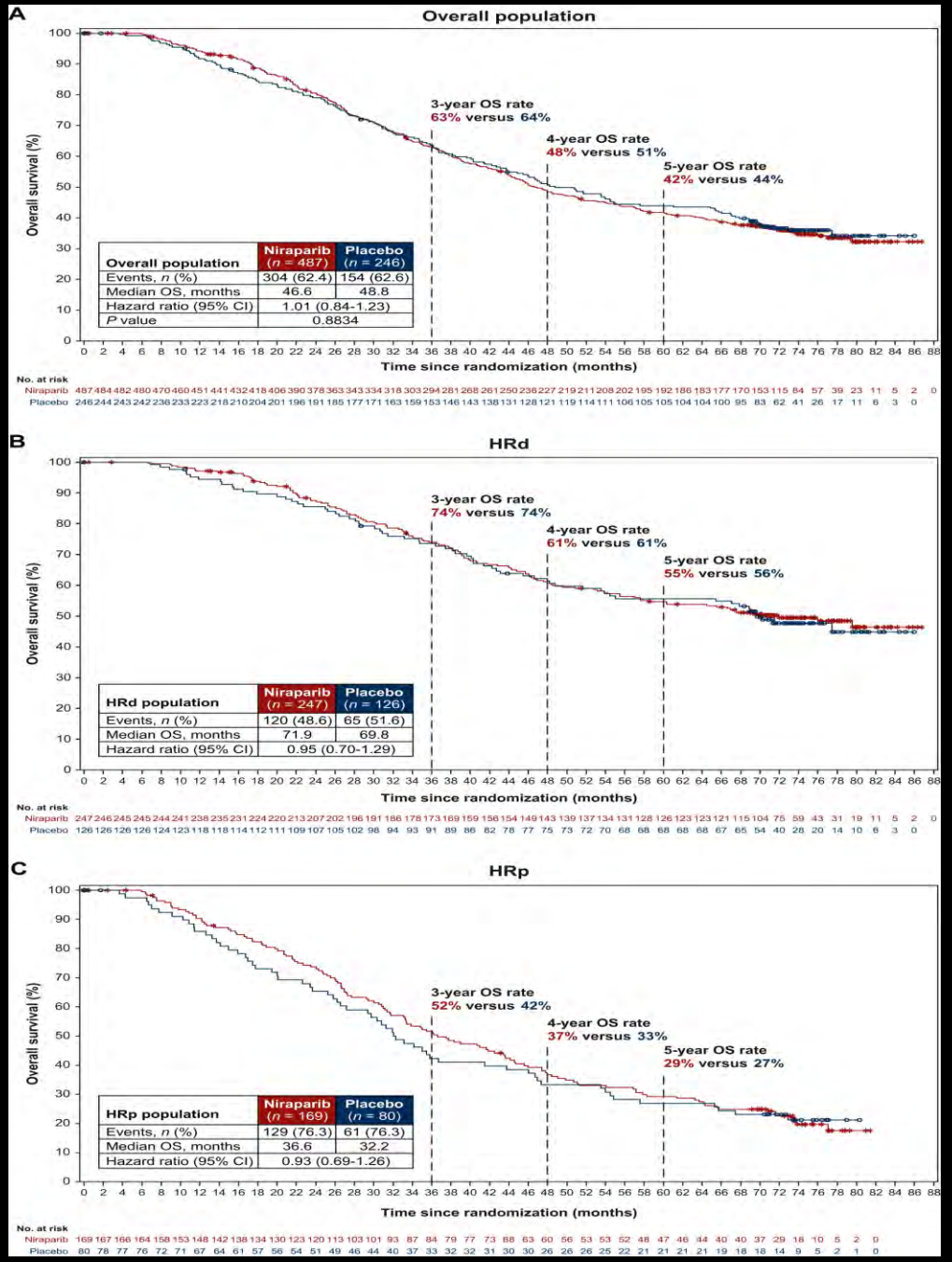
In Press, Corrected Proof ? What's this?

Original article

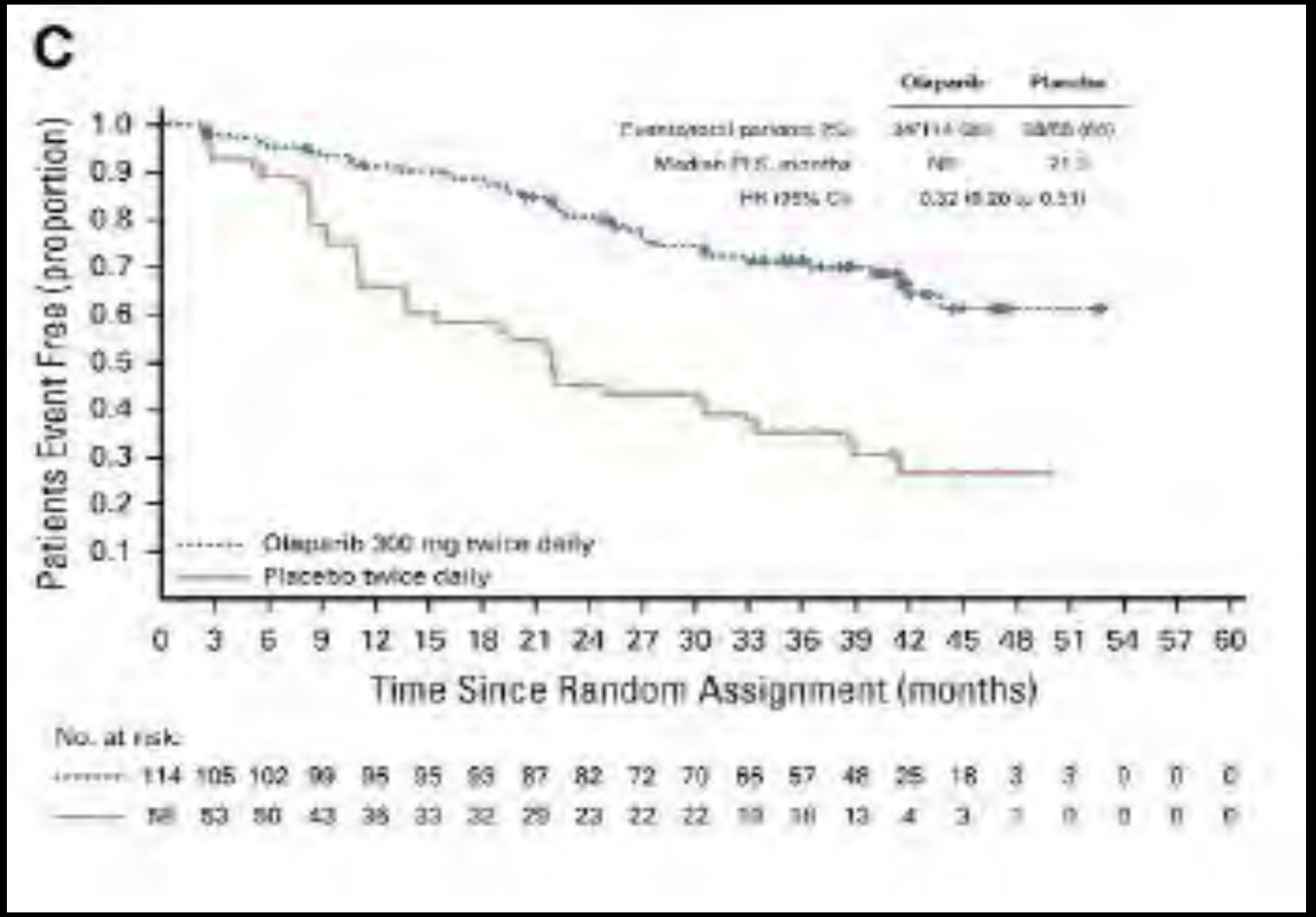
Niraparib first-line maintenance therapy in patients with newly diagnosed advanced ovarian cancer: final overall survival results from the PRIMA/ENGOT-OV26/GOG-3012 trial ☆

B.J. Monk [1 2], M.P. Barretina-Ginesta [3 4], B. Pothuri [1 5], I. Vergote [6 7], W. Graybill [8], M.R. Mirza [9 10], C.C. McCormick [11 †], D. Lorusso [12 13 ‡], R.G. Moore [14], G. Freyer [15], R.E. O'Cearbhaill [1 16 17], F. Heitz [18 19 20 §], D.M. O'Malley [21], A. Redondo [22], M.S. Shahin [23], C. Vulsteke [24 25], W.H. Bradley [26], C.A. Haslund [10 27], D.M. Chase [28], C. Pisano [13 29]... A. González-Martín [4 41]

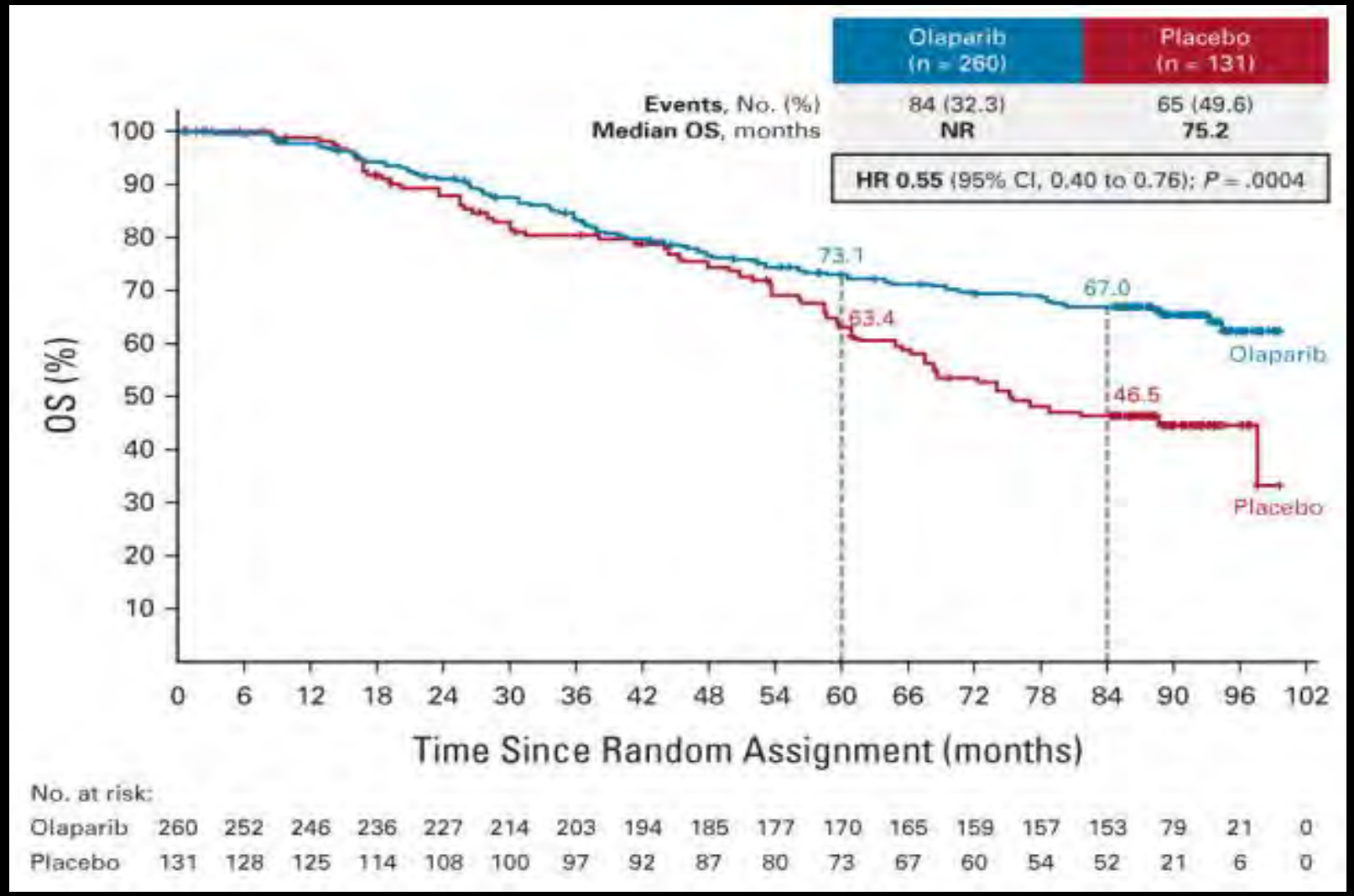




SOLO 1: PFS


C
Olaparib
Placebo
Patients Event Free (proportion)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Olaparib 300 mg twice daily
Placebo twice daily
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60
Time Since Random Assignment (months)
No. at risk
114 105 102 99 95 95 89 87 82 72 70 65 57 48 25 18 3 3 0 0 0
53 50 43 35 33 32 29 23 22 22 13 4 3

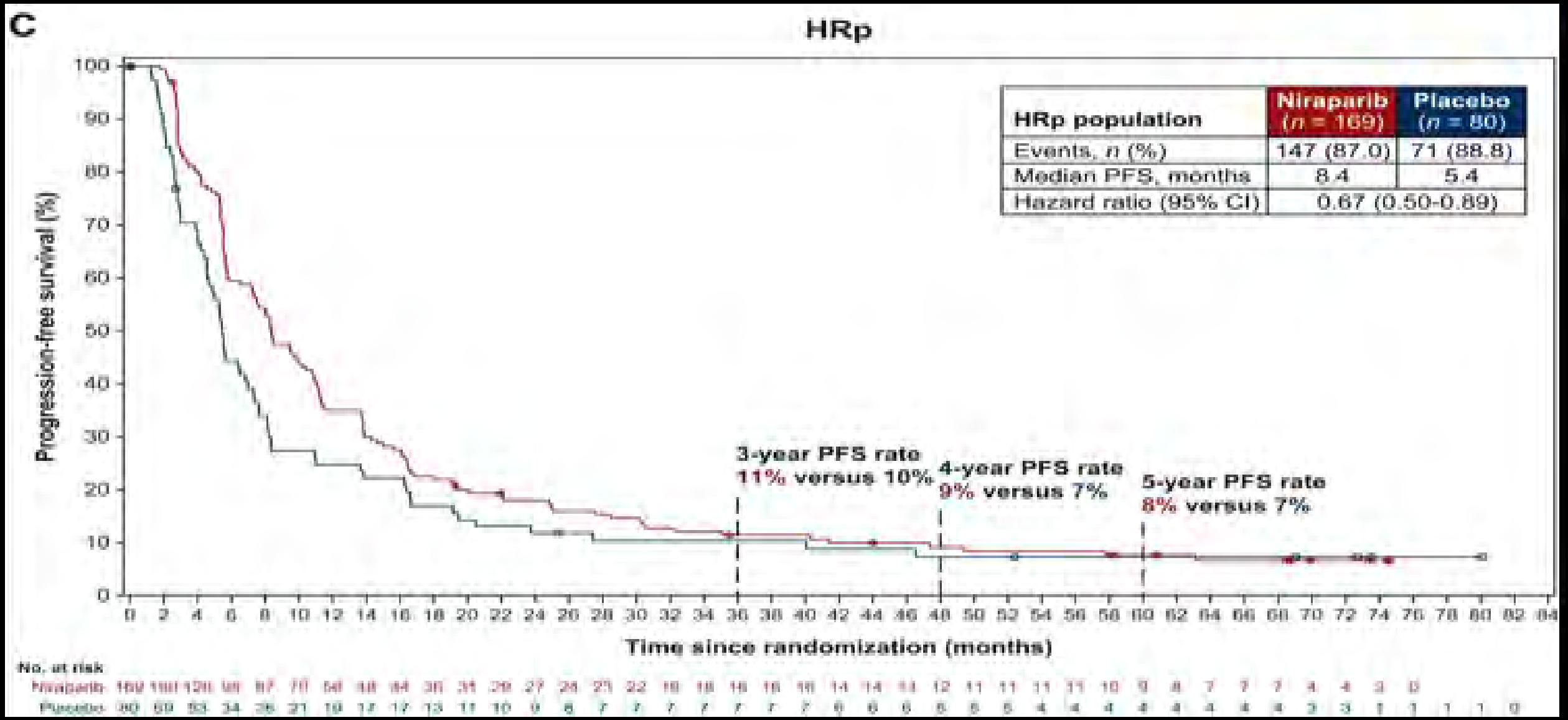
SOLO1 OS data JCO 2023



OVARIAN CANCER : PRIMA

- “Taken together, the long-term data support the benefit of niraparib first-line maintenance therapy in patients with newly diagnosed advanced OC regardless of HRD status.”

C


HRp
HRp population
Niraparib (n = 169)
Placebo (n = 80)
Events, n (%)
147 (87.0)
71 (88.8)
Median PFS, months
8.4
5.4
Hazard ratio (95% CI)
0.67 (0.50-0.89)
Progression-free survival (%)
3-year PFS rate
11% versus 10%
4-year PFS rate
9% versus 7%
5-year PFS rate
8% versus 7%
Time since randomization (months)
No. at risk
Niraparib
Placebo

Phase III Randomized Trial of 12 Versus 3 Months of Maintenance Paclitaxel in Patients With Advanced Ovarian Cancer After Complete Response to Platinum and Paclitaxel-Based Chemotherapy: A Southwest Oncology Group and Gynecologic Oncology Group Trial

By Maurie Markman, P.Y. Liu, Sharon Wilczynski, Bradley Monk, Larry J. Copeland, Ronald D. Alvarez, Caroline Jiang, and David Alberts

Purpose: To determine whether continuing paclitaxel for an extended time period in women with advanced ovarian cancer who had achieved a clinically defined complete response to a platinum/paclitaxel-based chemotherapy could prolong subsequent progression-free survival (PFS) and affect ultimate survival.

Patients and Methods: Patients were randomly assigned to either three or 12 cycles of single-agent paclitaxel administered every 28 days and were then followed up for progression-free and overall survival.

Results: As of September 6, 2001, 277 patients (262 assessable) had entered the trial, with a total of 54 PFS events having developed among 222 patients with follow-up data. With the exception of peripheral neuropathy, there were no major differences in toxicity between the regimens. The median PFS was 21 and 28 months in the three-cycle and 12-cycle paclitaxel arms, respectively. One-sided *P* values from an unadjusted log-rank test and an adjusted Cox model analysis (for stratification factors) were .0035 and .0023, respectively, both in favor of the 12-cycle arm. The Cox model-adjusted three-cycle versus the 12-cycle progression hazard ratio was estimated to be 2.31 (99% confidence interval, 1.08 to 4.94). With a protocol-specified early termination boundary of $P = .005$, these findings led the Southwest Oncology Group Data Safety Monitoring Committee to discontinue the trial. As of the date of study closure, there was no difference in overall survival between the treatment arms.

Conclusion: Twelve cycles of single-agent paclitaxel administered to women with advanced ovarian cancer who attain a clinically defined complete response to initial platinum/paclitaxel-based chemotherapy significantly prolongs the duration of PFS.

J Clin Oncol 21:2460-2465. © *2003 by American Society of Clinical Oncology.*

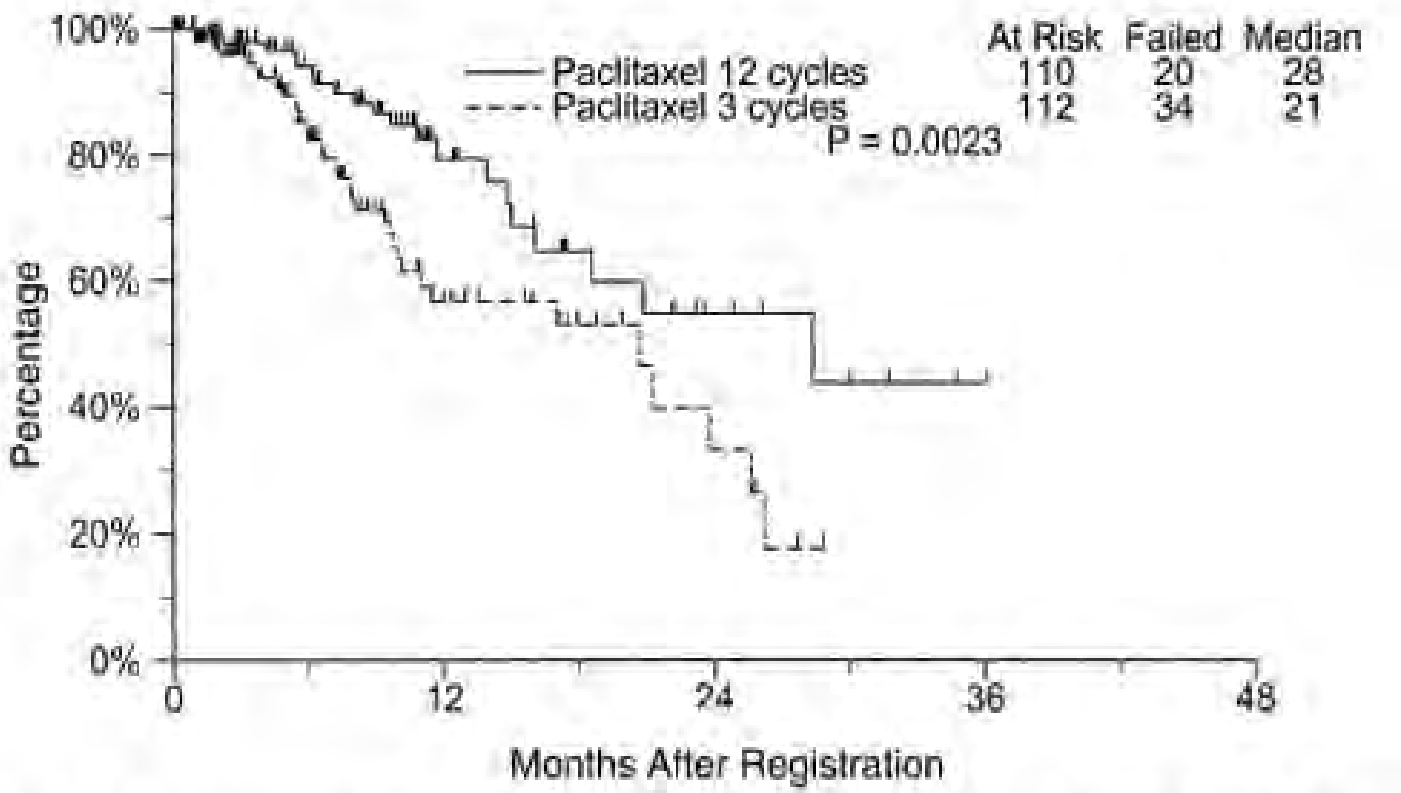


Fig 1. Progression-free survival of 222 assessable patients treated with either three monthly cycles or 12 monthly cycles of single-agent paclitaxel as consolidation therapy of stages III/IV advanced ovarian cancer after the attainment of a clinically defined complete response.

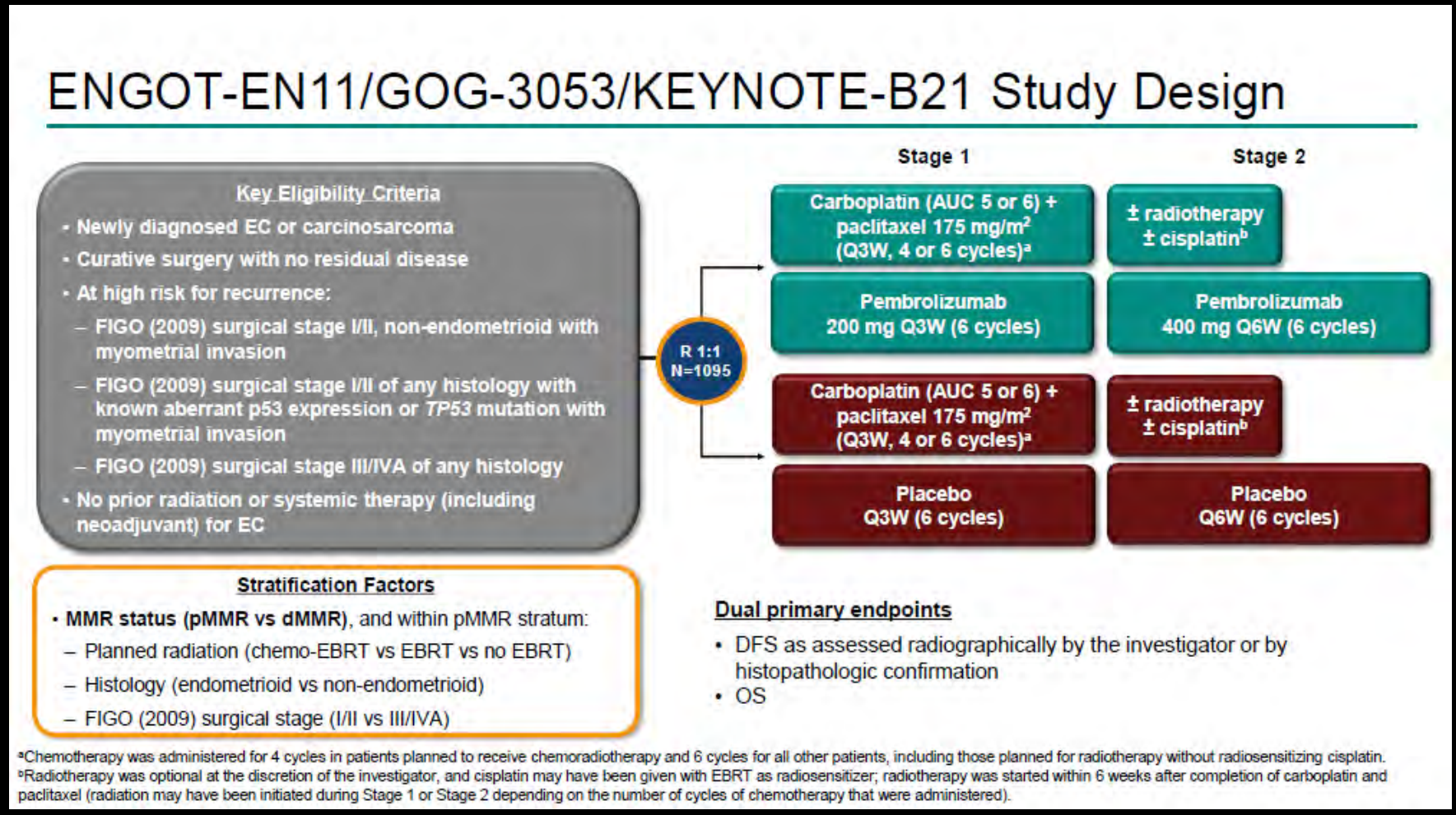
ENDOMETRIAL: PEMBROLIZUMAB ADJUVANTLY: KEYNOTE B21

ENGOT-EN11/GOG-3053/KEYNOTE-B21: A Phase 3 Study of Pembrolizumab or Placebo in Combination With Adjuvant Chemotherapy With or Without Radiotherapy in Patients With Newly Diagnosed, High-Risk Endometrial Cancer

Toon Van Gorp,[1] Lukáš Rob,[2] Weiguo Lv,[3] Floor Backes,[4] Fırat Ortaç,[5] Kosei Hasegawa,[6] Sakari Hietanen,[7] Antonella Savarese,[8] Annouschka Laenen,[9] Yong Man Kim,[10] Lubomir Bodnar,[11] Maria-Pilar Barretina-Ginesta,[12] Lucy Gilbert,[13] Bhavana Pothuri,[14] Xiaojun Chen,[15] Jasmine Lichfield,[16] Wei Wang,[17] Robert Orlowski,[18] Alain Lortholary,[19] Brian Slomovitz[20]

[1]University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium; and BGOG; [2]3rd Faculty Medicine Charles University and Faculty Hospital Kralovske Vinohrady, Prague, Czech Republic; and CEEGOG; [3]Zhejiang University, Hangzhou, Zhejiang, China; [4]Ohio State University and James Cancer Hospital, Columbus, OH, USA; and GOG; [5]Ankara University School of Medicine, Ankara, Turkey; and TRSGO; [6]Saitama Medical University, Hidaka, Saitama Prefecture, Japan; [7]Turku University Hospital and University of Turku, Turku, Finland; TYKS Cancer Centre, FICAN West, Organization of EU Cancer Institutes, Finland; and NSGO-CTU; [8]IRCCS - Istituto Nazionale Tumori

ENDOMETRIAL: PEMBROLIZUMAB ADJUVANTLY: KEYNOTE B21



ENDOMETRIAL: PEMBROLIZUMAB ADJUVANTLY: KEYNOTE B21

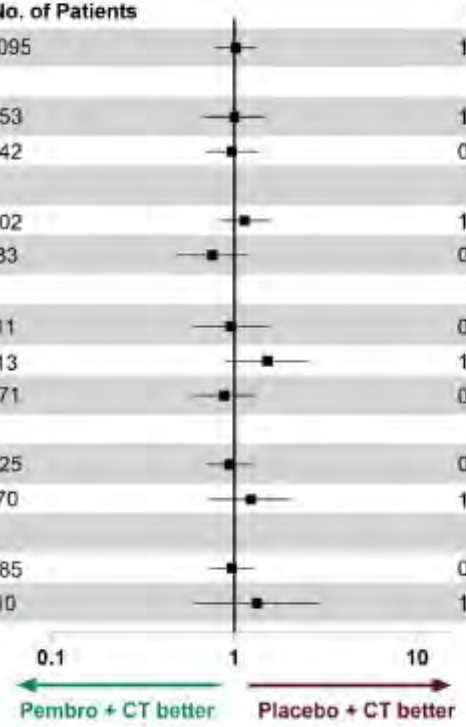
Characteristic	Pembro + Chemo (n = 545)	Placebo + Chemo (n = 550)
Age, median (range), y	62 (29–95)	62 (27–89)
ECOG PS 0	409 (75%)	416 (76%)
Race		
White	315 (58%)	362 (66%)
Asian	189 (35%)	157 (29%)
Multiple	23 (4%)	10 (2%)
Black or African American	11 (2%)	13 (2%)
American Indian or Alaska Native	2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

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

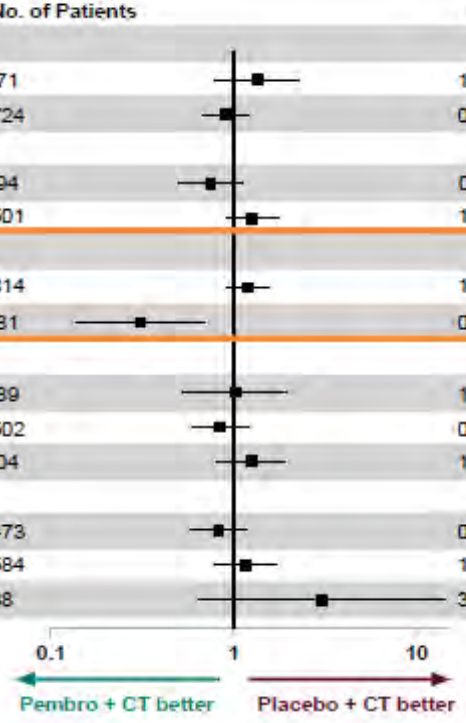
ENDOMETRIAL: PEMBROLIZUMAB ADJUVANTLY: KEYNOTE B21

DFS[a] in Protocol-Specified Subgroups: ITT Population

	No. of Events/No. of Patients	HR (95% CI)
Overall	240/1095	1.02 (0.79-1.32)
Age		
<65 y	108/653	1.00 (0.68-1.46)
≥65 y	132/442	0.97 (0.69-1.37)
Race		
White	164/702	1.14 (0.84-1.55)
Non white	75/383	0.76 (0.48-1.19)
Region		
Western Europe	70/311	0.96 (0.60-1.54)
North America	56/213	1.52 (0.90-2.57)
Rest of World	114/571	0.88 (0.61-1.27)
ECOG PS		
0	181/825	0.94 (0.70-1.25)
1	59/270	1.23 (0.73-2.05)
Lymph node dissection		
Yes	214/985	0.97 (0.74-1.27)
No	26/110	1.33 (0.60-2.93)



	No. of Events/No. of Patients	HR (95% CI)
FIGO (2009) stage		
I/II	58/371	1.35 (0.80-2.27)
III/IV	182/724	0.91 (0.68-1.22)
Histology		
Endometrioid	98/594	0.75 (0.50-1.11)
Non-endometrioid	142/501	1.26 (0.91-1.76)
MMR status		
pMMR	207/814	1.20 (0.91-1.57)
dMMR	33/281	0.31 (0.14-0.69)
Planned radiotherapy		
EBRT with cisplatin	36/189	1.02 (0.53-1.96)
EBRT without cisplatin	122/502	0.85 (0.60-1.22)
No EBRT	82/404	1.25 (0.81-1.92)
Lymph node involvement		
Yes	127/473	0.83 (0.58-1.18)
No	103/584	1.17 (0.80-1.73)
Not evaluable	10/38	3.05 (0.65-14.4)



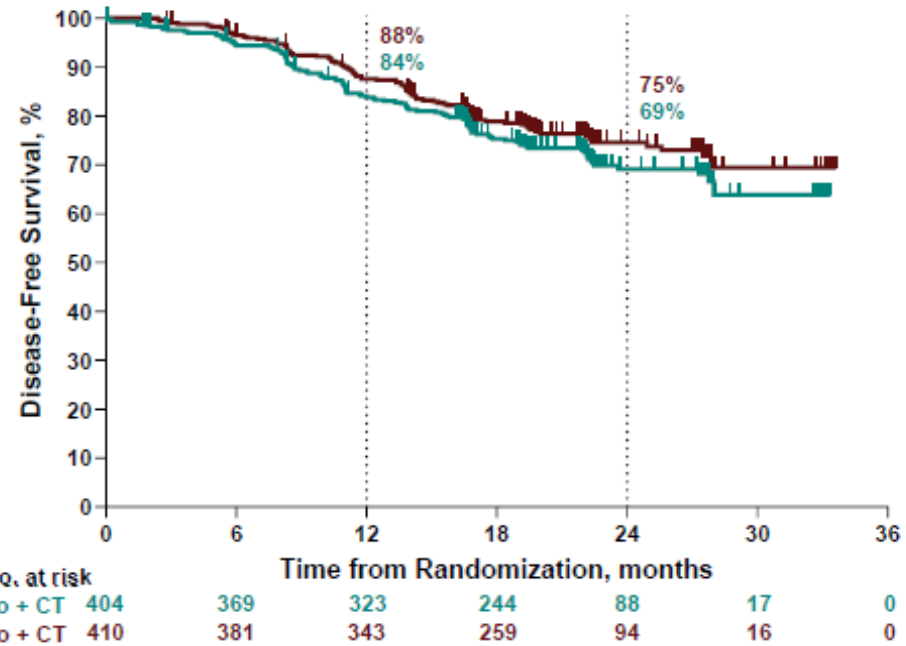
[a]DFS was defined as the time from randomization to local or distant recurrence of EC (assessed radiographically by the investigator or by histopathologic confirmation) or death from any cause.
Data cutoff date: March 4, 2024.

ENDOMETRIAL: PEMBROLIZUMAB ADJUVANTLY: KEYNOTE B-21

Pembrolizumab Plus Chemotherapy Improved DFS[a] in dMMR Subgroup

pMMR Subgroup

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

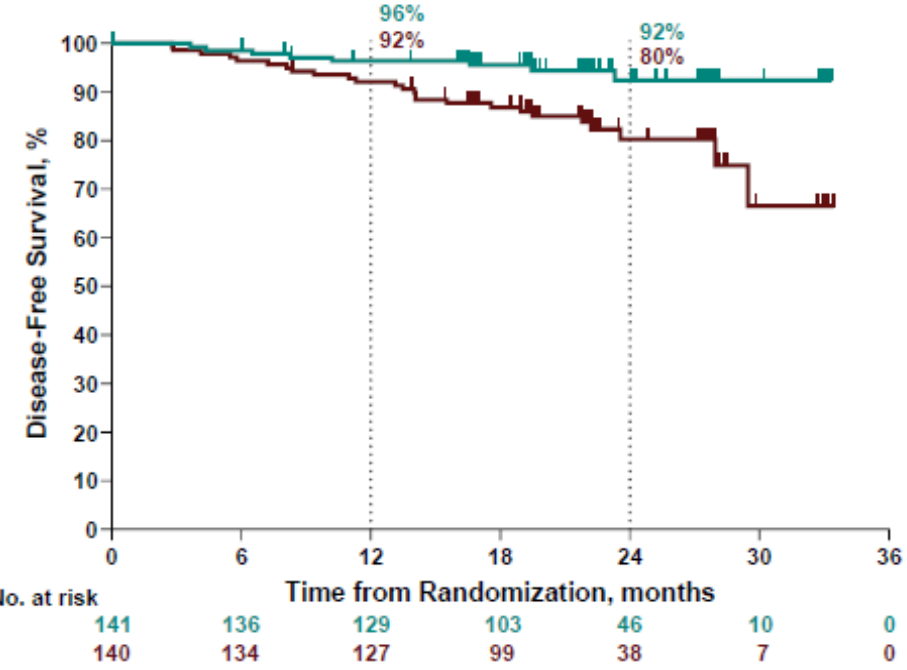


No. at risk

Pembro + CT	404	369	323	244	88	17	0
Placebo + CT	410	381	343	259	94	16	0

dMMR Subgroup

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



No. at risk

Pembro + CT	141	136	129	103	46	10	0
Placebo + CT	140	134	127	99	38	7	0

[a]DFS was defined as the time from randomization to local or distant recurrence of EC (assessed radiographically by the investigator or by histopathologic confirmation) or death from any cause.
Data cutoff date: March 4, 2024.

CERVICAL CANCER: KEYNOTE A18

Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial

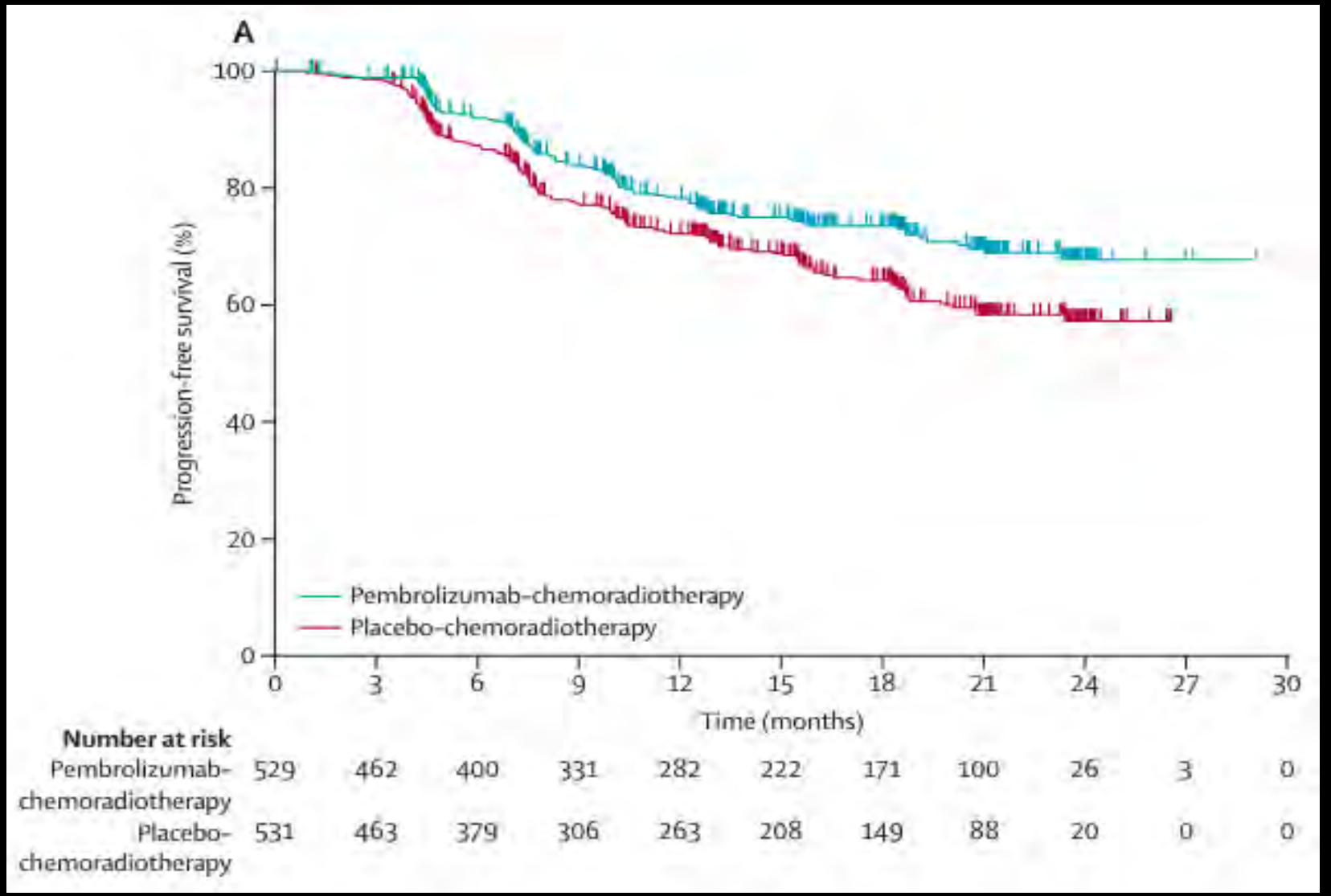
Domenica Lorusso, Yang Xiang, Kosei Hasegawa, Giovanni Scambia, Manuel Leiva, Pier Ramos-Elias, Alejandro Acevedo, Vladyslav Sukhin, Noelle Cloven, Andrea J Pereira de Santana Gomes, Fernando Contreras Mejía, Ari Reiss, Ali Ayhan, Jung-Yun Lee, Valeriya Saevets, Flora Zagouri, Lucy Gilbert, Jalid Sehouli, Ekkasit Tharavichitkul, Kristina Lindemann, Roberta Lazzari, Chih-Long Chang, Rudolf Lampé, Hong Zhu, Ana Oaknin, Melissa Christiaens, Stephan Polterauer, Tomoka Usami, Kan Li, Karin Yamada, Sarper Toker, Stephen M Keefe, Sandro Pignata, Linda R Duska*, on behalf of the ENGOT-cx11/GOG-3047/KEYNOTE-A18 investigators†*

Summary

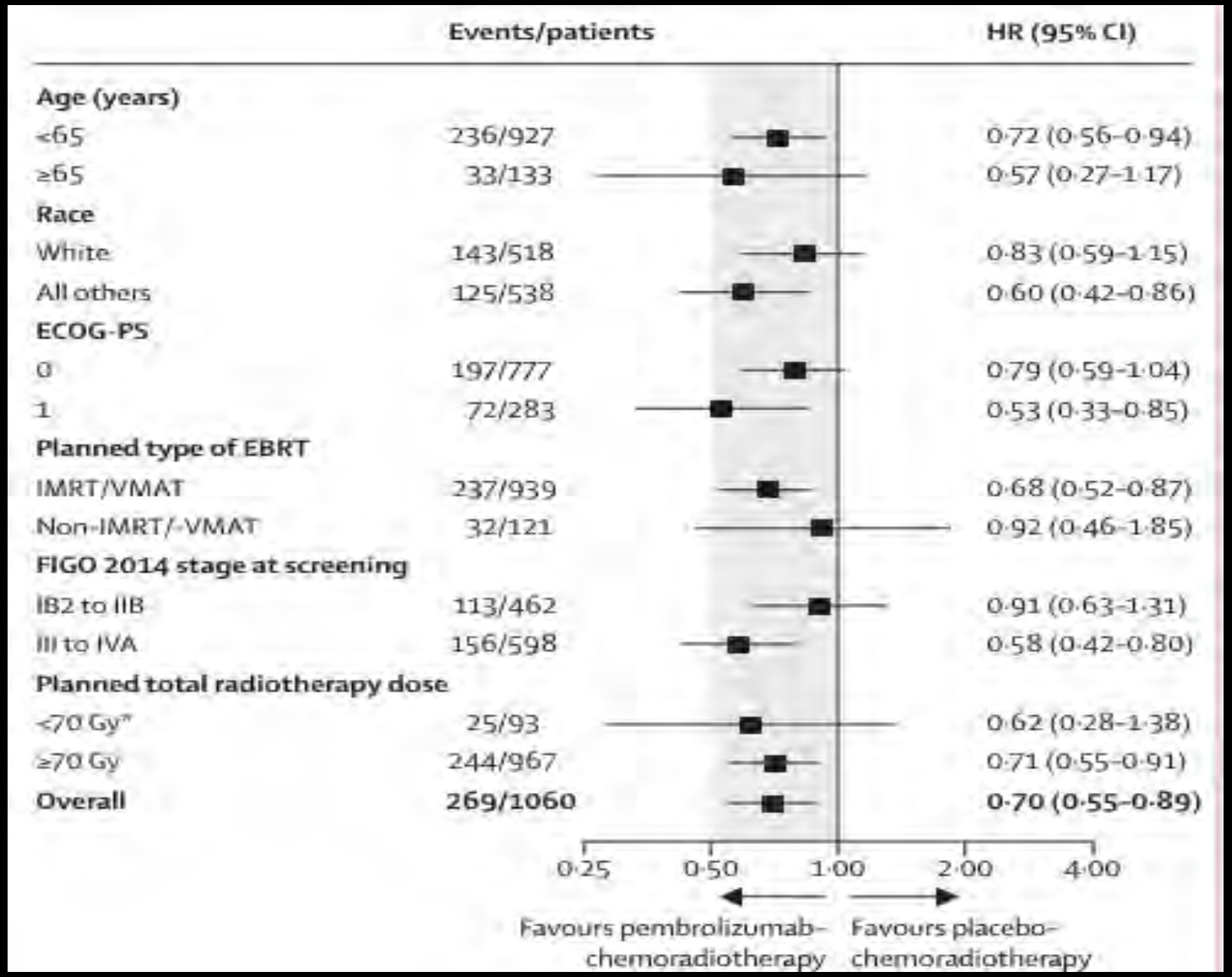
Background Pembrolizumab has shown efficacy in persistent, recurrent, or metastatic cervical cancer. The effect of

Lancet 2024; 403: 1341–50

CERVICAL CANCER: KEYNOTE A18



CERVICAL CANCER: KEYNOTE A18



CERVICAL CANCER: KEYNOTE A18

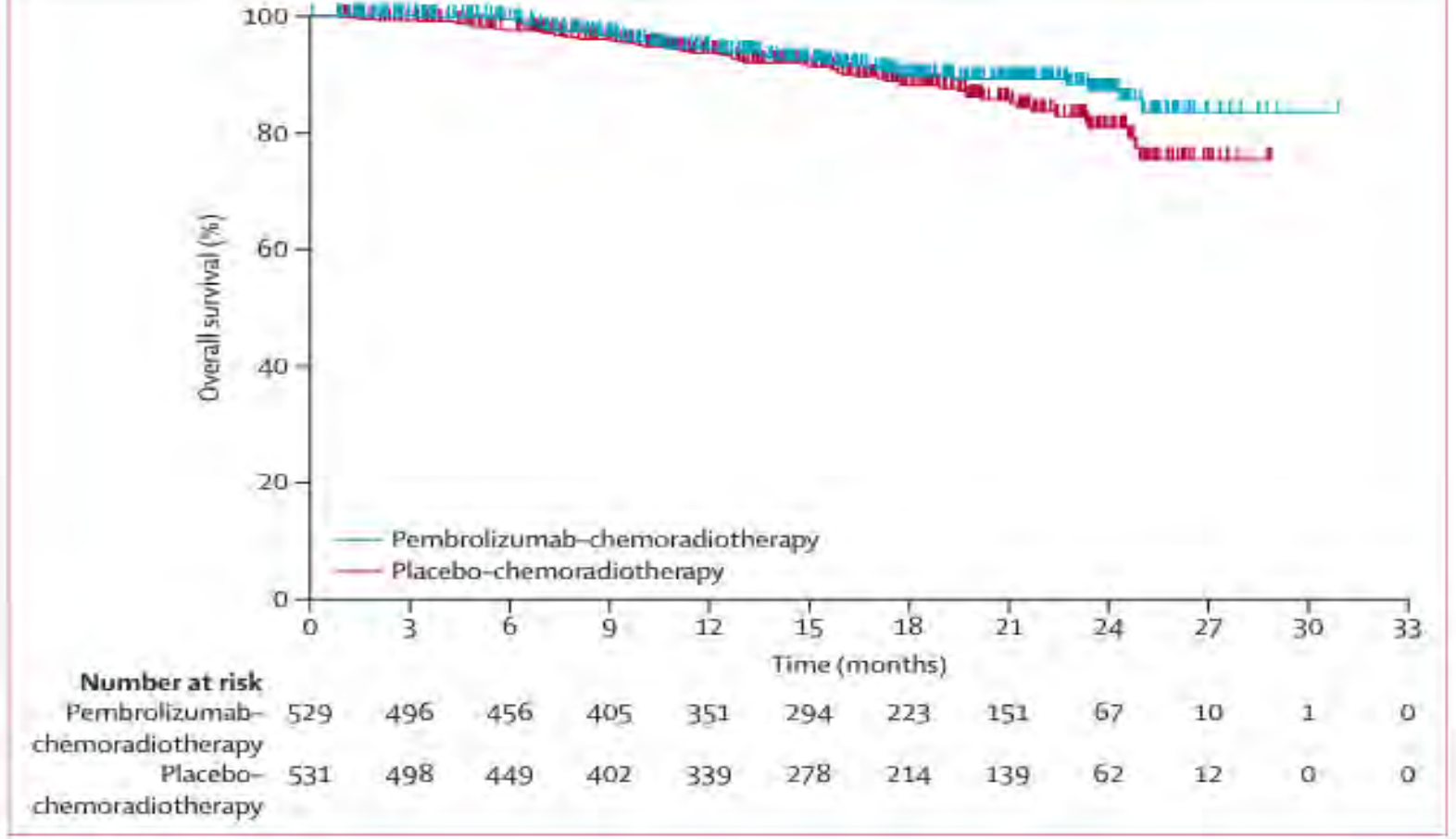


Figure 3: **Overall survival**
Kaplan–Meier estimates of overall survival in the intention-to-treat population. Tick marks indicate censoring of data.

Articles

Induction chemotherapy followed by standard chemoradiotherapy versus standard chemoradiotherapy alone in patients with locally advanced cervical cancer (GCIG INTERLACE): an international, multicentre, randomised phase 3 trial

*Mary McCormack, Gemma Eminowicz, Dolores Gallardo, Patricia Diez, Laura Farrelly, Christopher Kent, Emma Hudson, Miguel Panades, Tony Mathew, Anjana Anand, Majca Persic, Jennifer Forrest, Rajanee Bhana, Nicholas Reed, Anne Drake, Madhavi Adusumalli, Asima Mukhopadhyay, Margaret King, Karen Whitmarsh, John McGrane, Nicoletta Colombo, Choi Mak, Ranajit Mandal, Rahul Roy Chowdhury, Gabriela Alamilla-Garcia, Adriana Chávez-Blanco, Hilary Stobart, Amanda Feeney, Simran Vaja, Anne-Marie Hacker, Allan Hackshaw, Jonathan Andrew Ledermann, on behalf of the INTERLACE investigators**

INTERLACE Trial Design

Key eligibility criteria

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

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

Randomised (n=500)

Induction chemotherapy (n=250)
Carboplatin (AUC2) & paclitaxel (80mg/m²) given weekly for **6 weeks**

Week 7

Standard CRT (n=250)
Chemotherapy: cisplatin (40mg/m²) weekly for 5 weeks
Radiotherapy: EBRT (40-50.4Gy in 20-28 fractions) & BT to give a *minimum* total EQD2 dose of 78Gy to point A, 3D IGABT recommended
Overall treatment time ≤50days
All centres underwent RT QA

Follow-up
3-monthly for 2 years then 6-monthly for 5 years

Stratified by

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

Primary endpoints

- PFS
- OS

Secondary endpoints

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

MADRID 2020 ESMO congress

Mary McCormack

Demographics at Baseline

	CRT alone (n=250)	Induction Chemo + CRT (n=250)
Age, years median (range)	46 (24-78)	46 (26-78)
ECOG status	No. of patients (%)	
0	221 (88)	214 (86)
1	29 (12)	36 (14)
Country		
UK	190 (76)	190 (76)
Mexico	51 (20)	49 (20)
Italy	3 (1)	5 (2)
India	5 (2)	5 (2)
Brazil	1 (<1)	1 (<1)

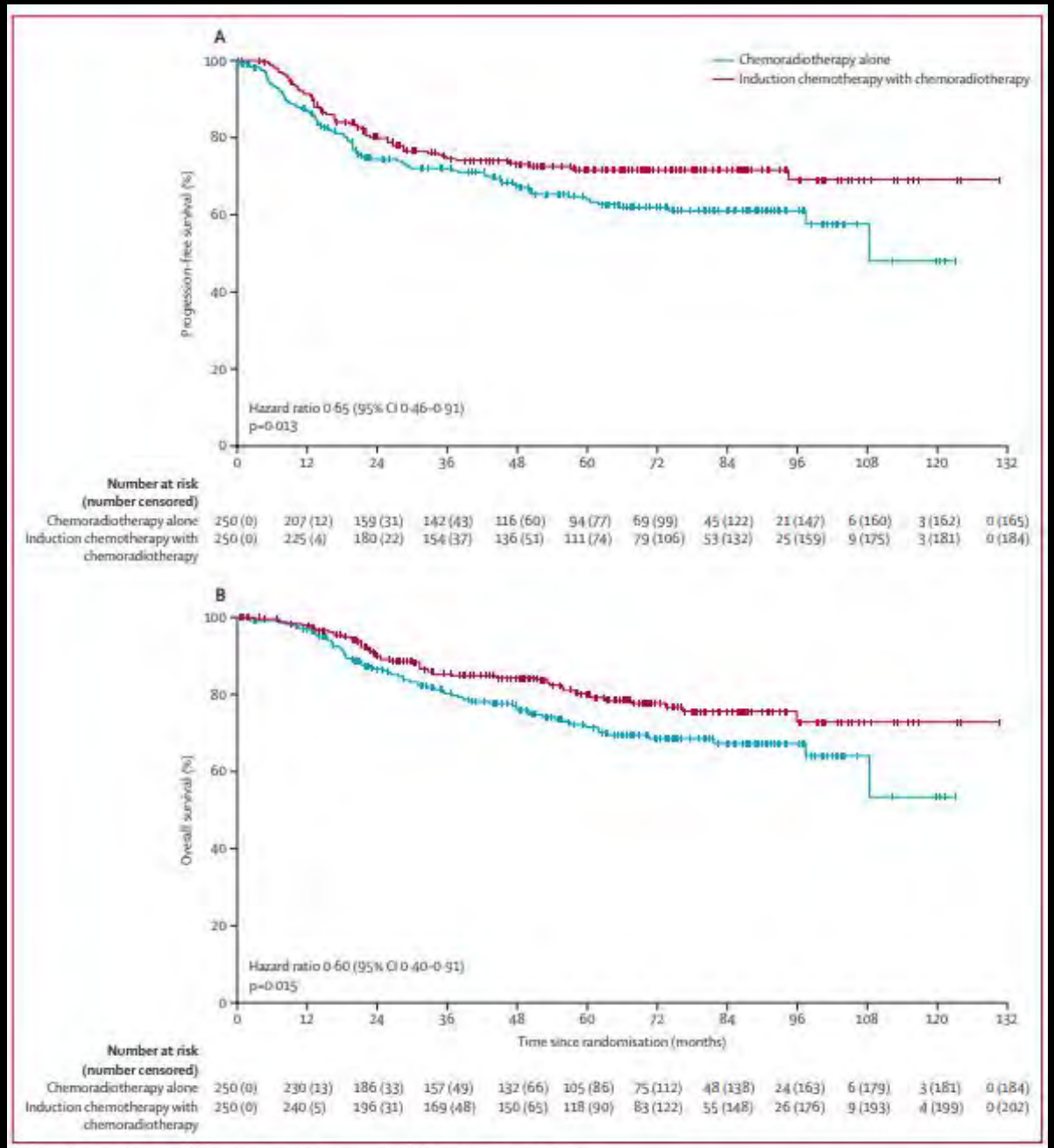
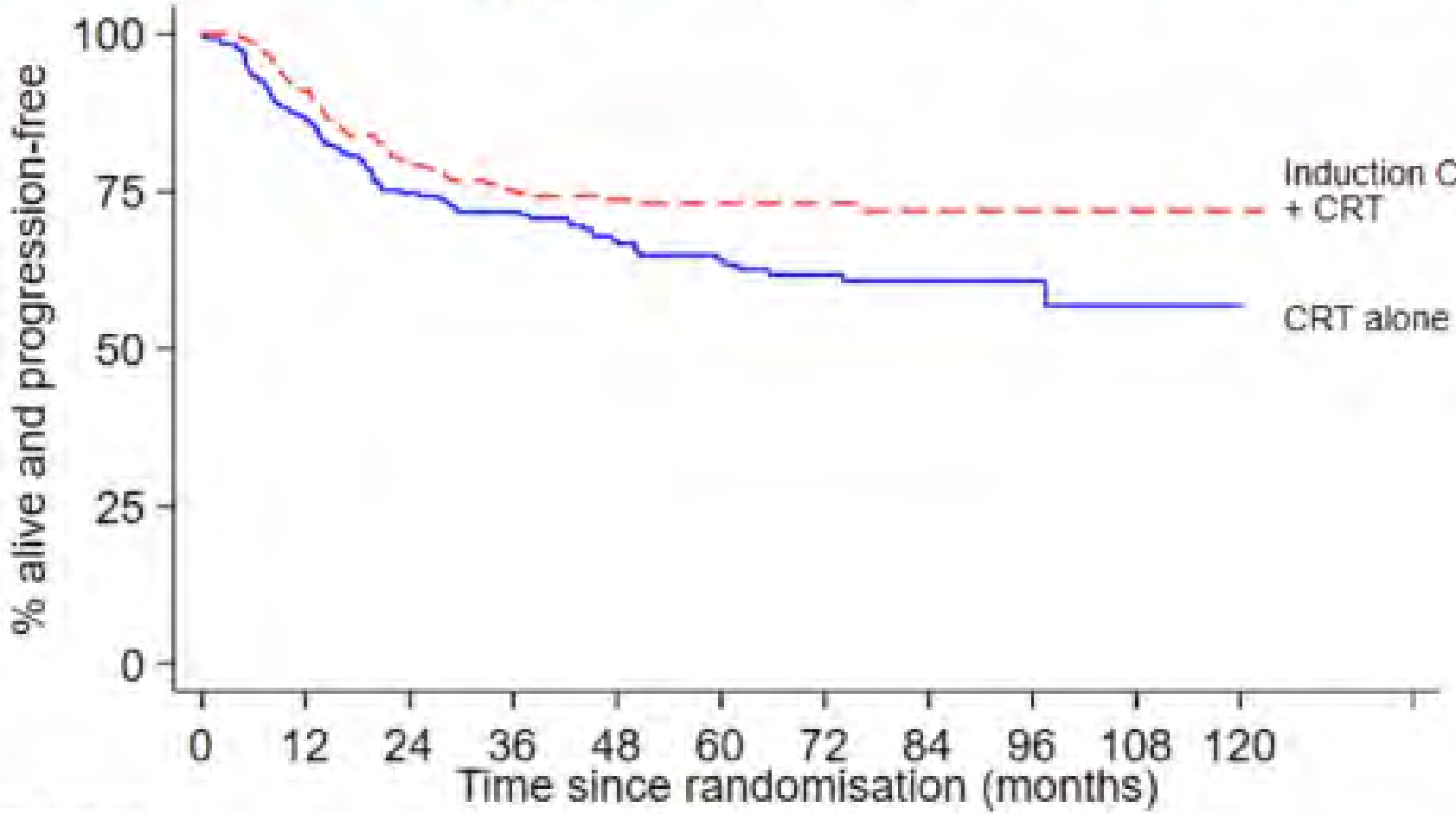


Figure 2: Kaplan-Meier estimates of progression-free survival (A) and overall survival (B)

INTERLACE Progression-Free Survival (median FU 64m)



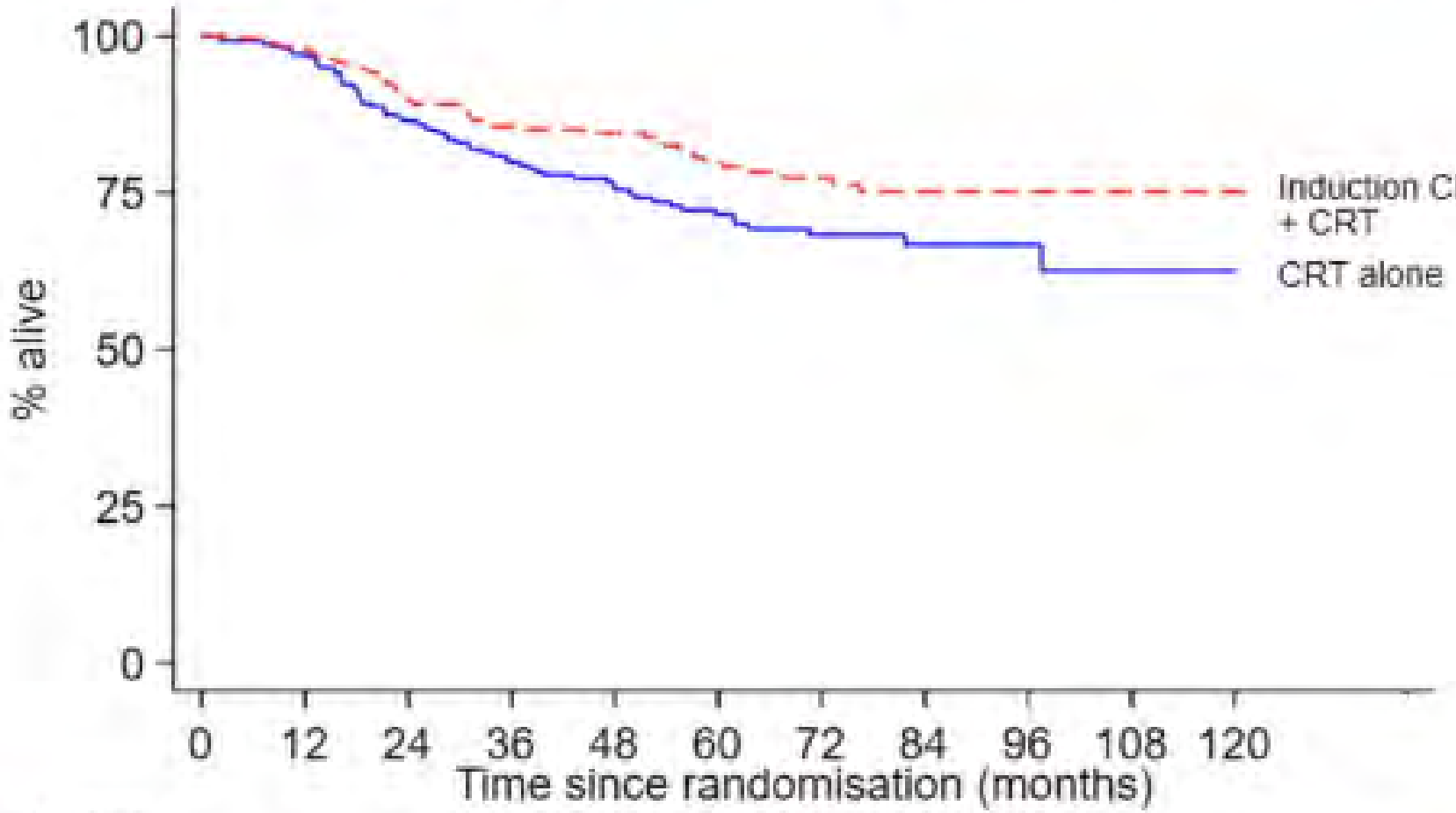
146 PFS events
HR 0.65;95% CI:0.46 -0.91
P=0.013

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

Number at risk											
CRT alone	250	204	157	140	110	88	63	36	16	5	1
Induction Chemo + CRT	250	220	178	152	132	105	72	40	19	8	1

Mary McCormack

INTERLACE Overall Survival (median FU 64m)



109 deaths
HR 0.61;95% CI: 0.40-0.91
P=0.04

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

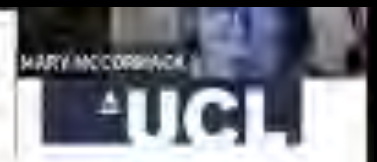
Number at risk

CRT alone	250	228	181	154	124	99	67	39	16	5	1
Induction Chemo + CRT	250	236	195	168	146	111	75	42	19	8	1

Patterns of Relapse

	CRT alone (n=250)	Induction Chemo + CRT (n=250)
	No. of patients (%)	
Local/pelvic	21 (8)	26 (10)
Local/pelvic & distant	20 (8)	14 (6)
Distant	30 (12)	16 (6)
Total local/pelvic relapses	41 (16)	40 (16)
Total distant relapses	50 (20)	30 (12)

CONCLUSIONS



- **Induction chemotherapy prior to chemoradiation led to a 9% improvement in PFS rate and an 8% improvement in OS rate at 5 years.**

  PFS : HR 0.65 (95%CI: 0.46-0.91) p=0.013

  OS : HR 0.61 (95%CI: 0.40-0.91) p=0.04 Follow up continues

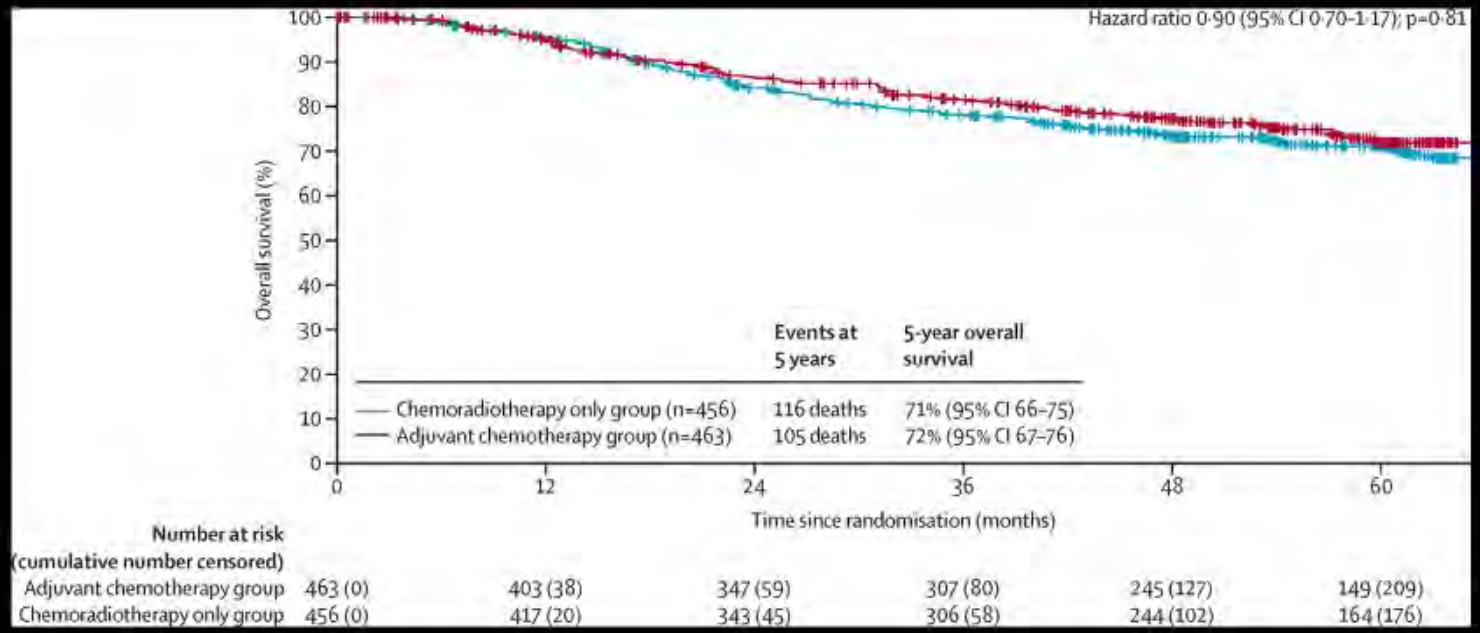
- Adherence to standard chemoradiation was high in both arms and reflected best clinical practice.

- OS in the standard CRT arm is similar to that in the recent published literature.

- As anticipated haematological toxicity was greater in the IC/CRT arm but this did not compromise the delivery of radiotherapy.

- **Induction chemotherapy with weekly paclitaxel and carboplatin before CRT should be considered the new standard in locally advanced cervical cancer and is feasible across diverse healthcare settings.**

Lancet Oncology 2023: OUTBACK Trial



N ENGL J MED 380;24 NEJM.ORG JUNE 13, 2019

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjuvant Chemotherapy plus Radiation for Locally Advanced Endometrial Cancer

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GOG 258

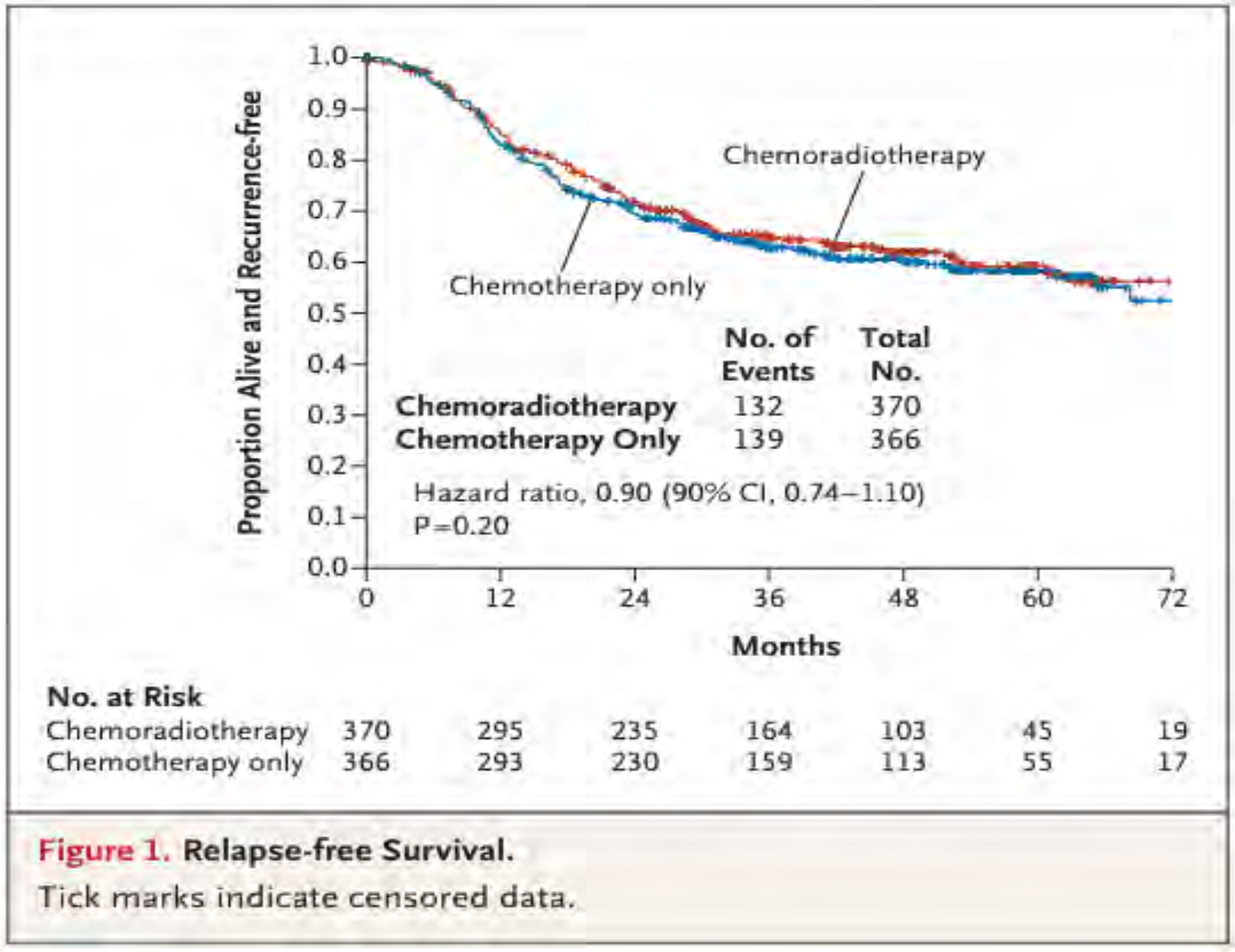
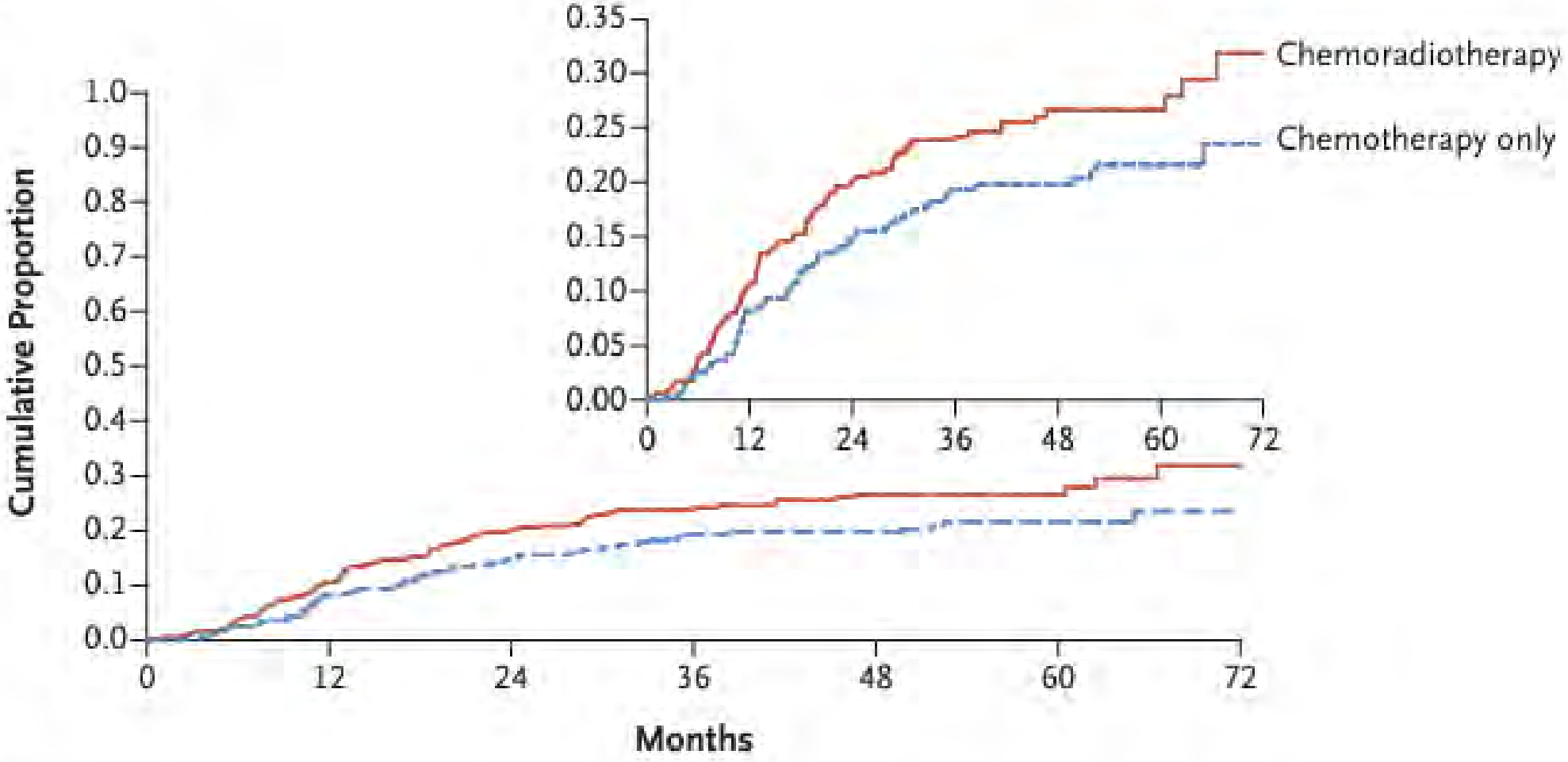


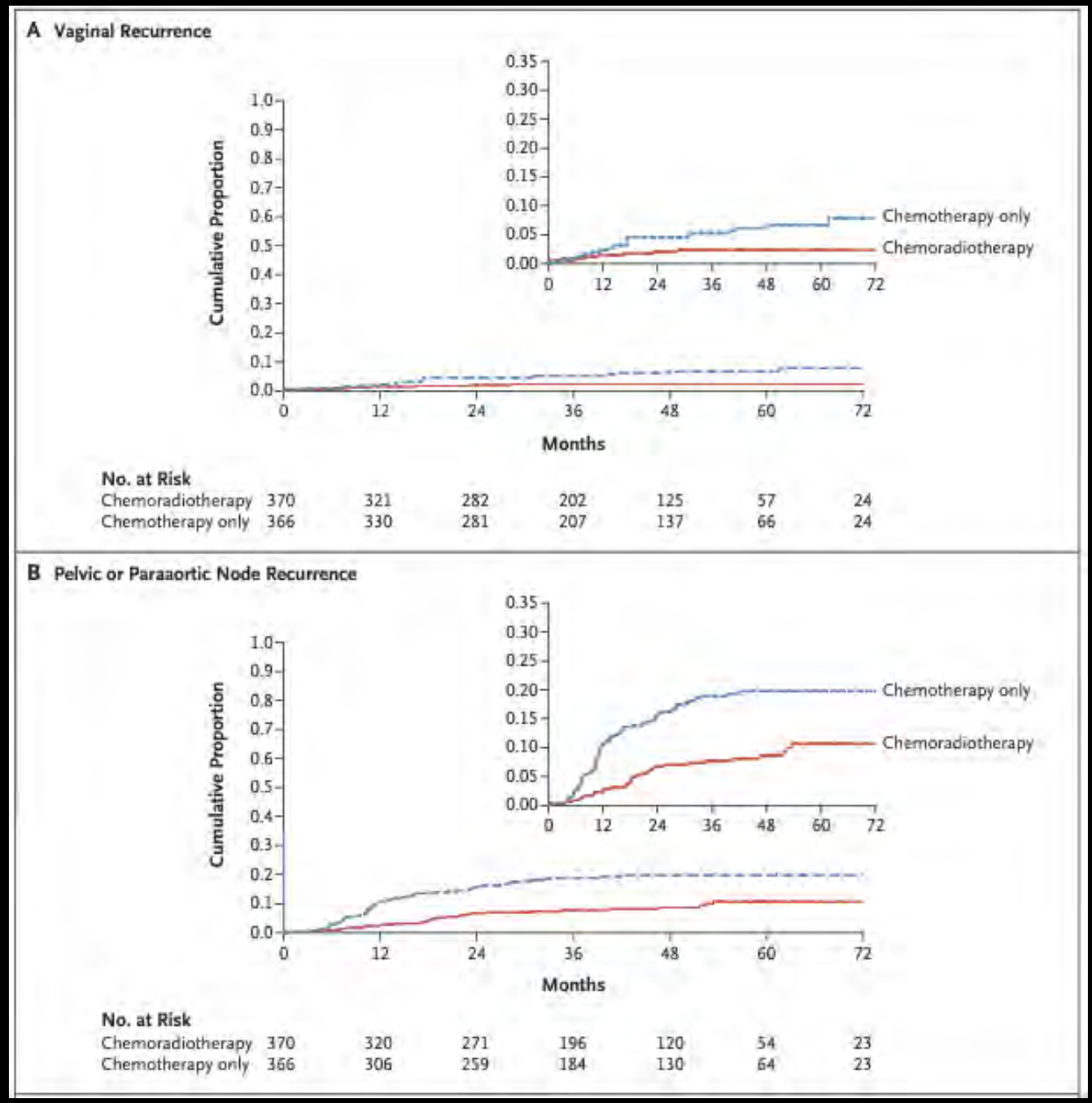
Figure 1. Relapse-free Survival.

Tick marks indicate censored data.

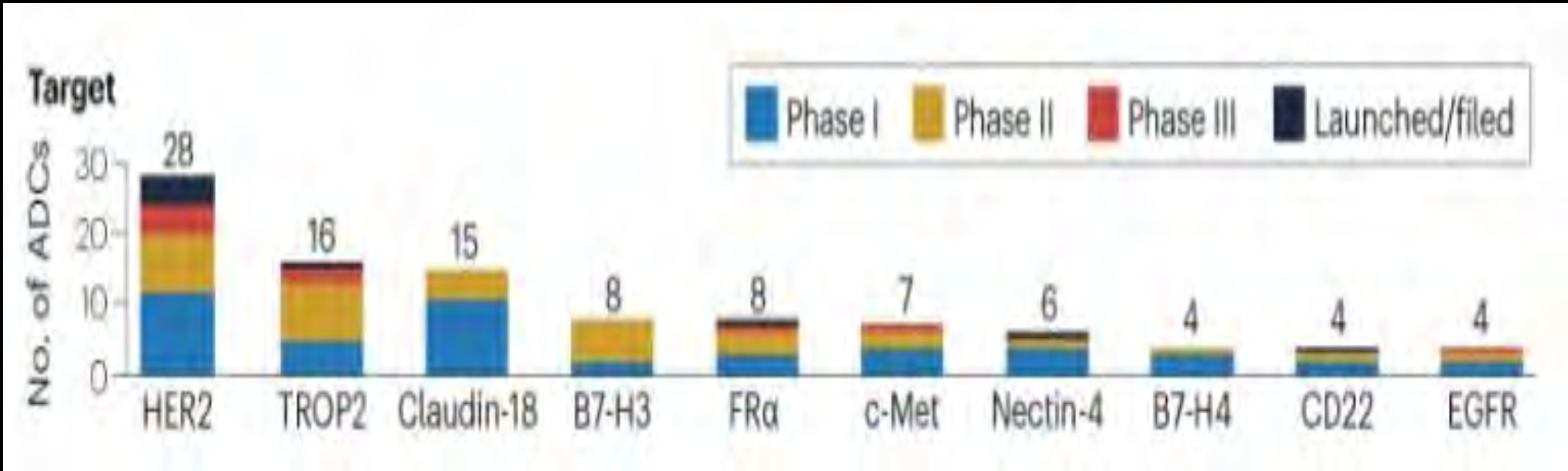
C Distant Recurrence



No. at Risk							
Chemoradiotherapy	370	302	249	175	111	51	20
Chemotherapy only	366	316	263	186	132	62	22


A Vaginal Recurrence
Cumulative Proportion
Months
Chemotherapy only
Chemoradiotherapy
No. at Risk
Chemoradiotherapy 370 321 282 202 125 57 24
Chemotherapy only 366 330 281 207 137 66 24
B Pelvic or Paraaortic Node Recurrence
Cumulative Proportion
Months
Chemotherapy only
Chemoradiotherapy
No. at Risk
Chemoradiotherapy 370 320 271 196 120 54 23
Chemotherapy only 366 306 259 184 130 64 23

ADCs in Development 2024
Flynt et al Nature Reviews Drug Discovery , April 16, 2024



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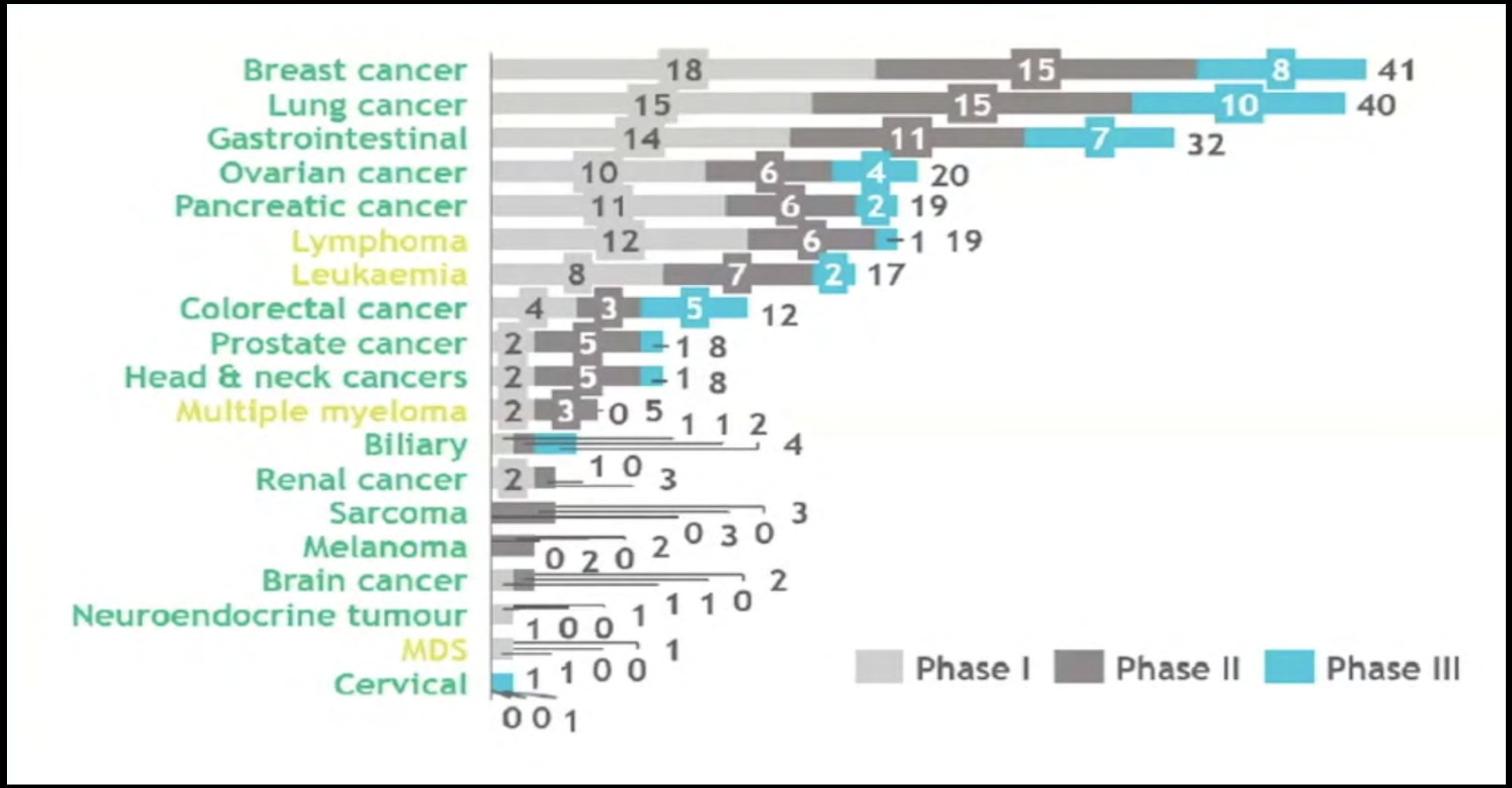

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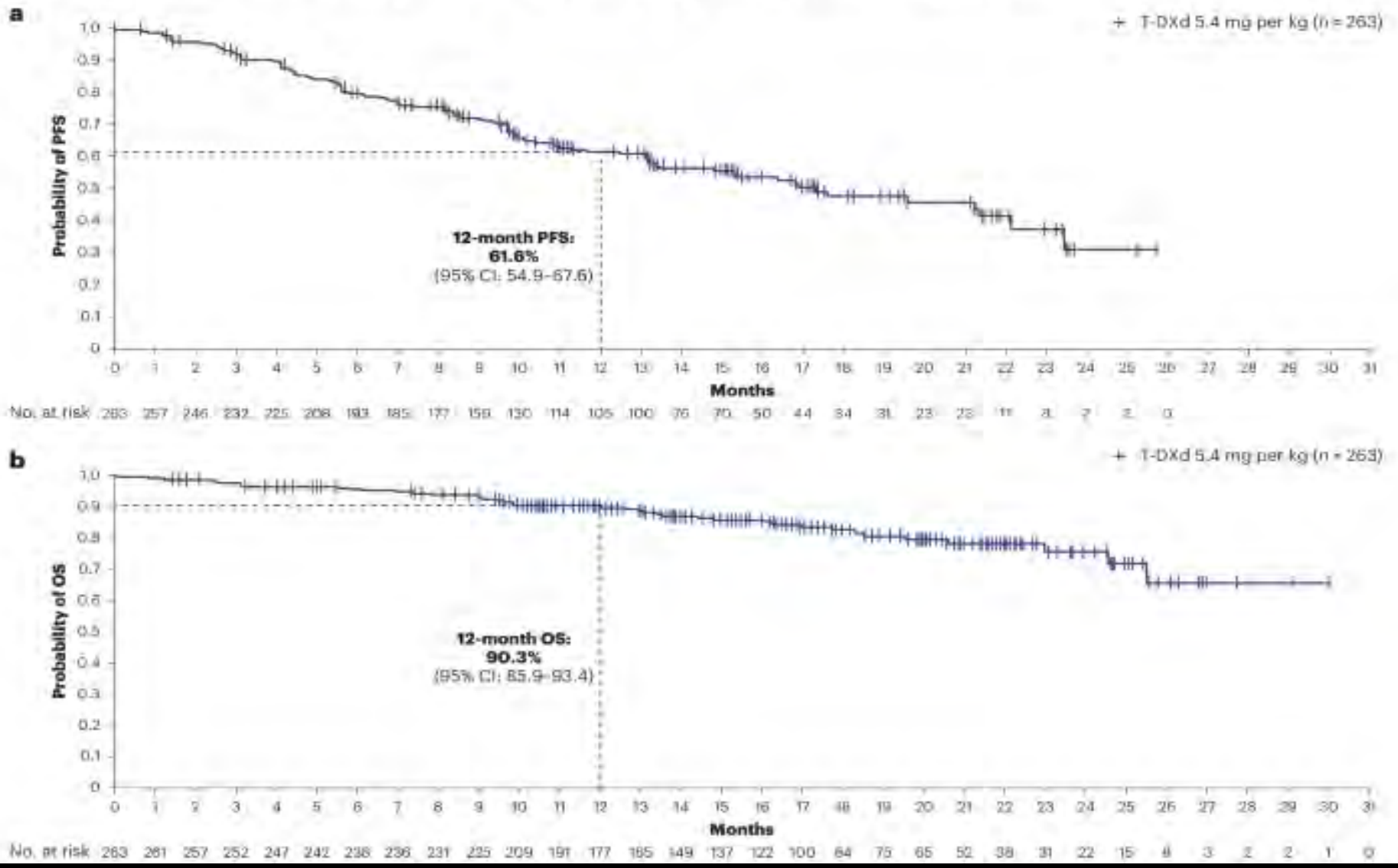
Trastuzumab deruxtecan in HER2-positive advanced breast cancer with or without brain metastases: a phase 3b/4 trial

Nadia Harbeck, Eva Ciruelos, Guy Jerusalem, Volkmar Müller, Naoki Niikura, Giuseppe Viale, Rupert Bartsch, Christian Kurzeder, Michaela J. Higgins, Roisin M. Connolly, Sally Baron-Hay, María Gión, Valentina Guarneri, Giampaolo Bianchini, Hans Wildiers, Santiago Escrivá-de-Romaní, Manoj Prahladan, Helen Bridge, Nataliya Kuptsova-Clarkson, Nana Scotto, Sunil Verma, Nancy U. Lin & the DESTINY-Breast12 study group

Nature Medicine (2024) | Cite this article

Fig. 2: Kaplan–Meier analysis of key efficacy endpoints in patients with baseline BMs.



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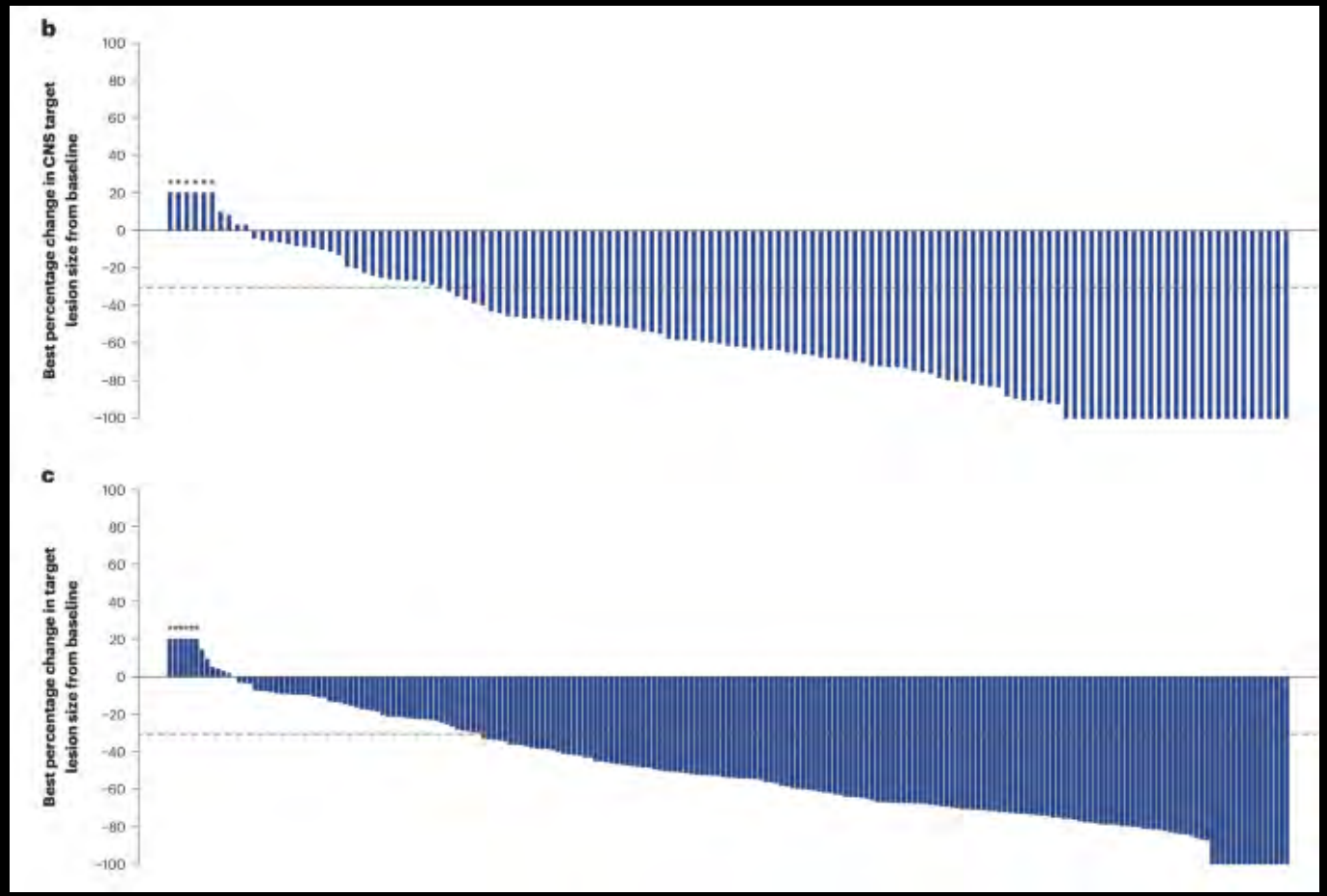
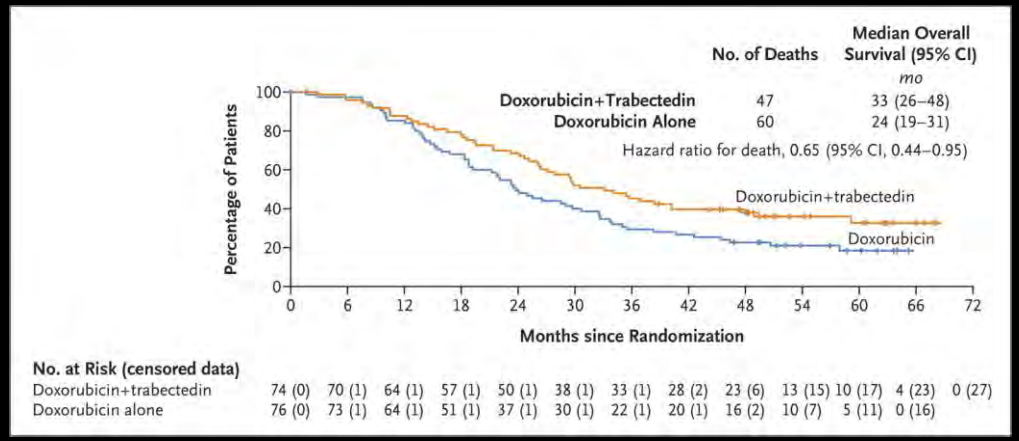


CONCLUSIONS (5)

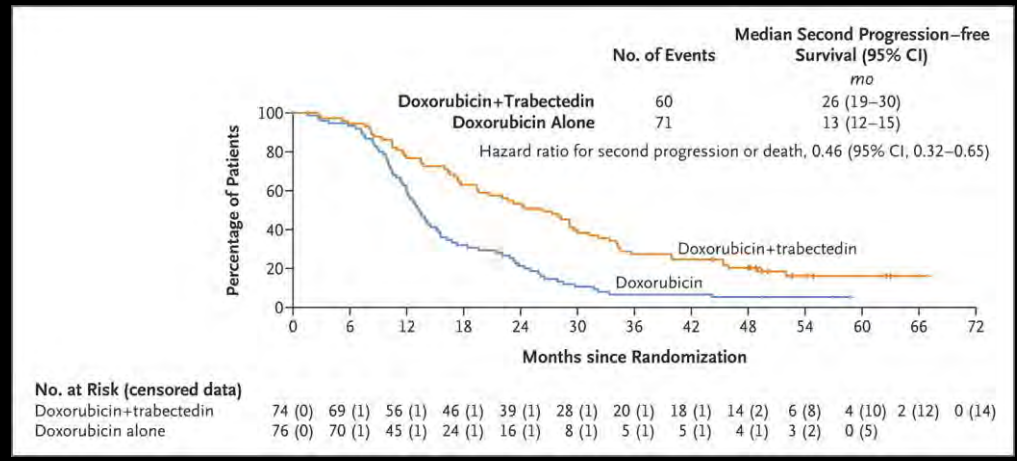
- No clinically significant benefit in 3y DFS nor OS from niraparib in HRP patients (PRIMA)
- Pembrolizumab is of benefit in adjuvant treatment of dMMR endometrial cancer (KEYNOTE B-21)
- OS benefit of pembrolizumab added to CRT in cervical cancer (KEYNOTE A-18)
- Possible benefit of upfront chemotherapy in cervical cancer prior to CRT (INTERLACE)
- Trastuzumab deruxtecan is very active in brain metastasis (breast cancer)

Pautier et al: NEJM September 2024

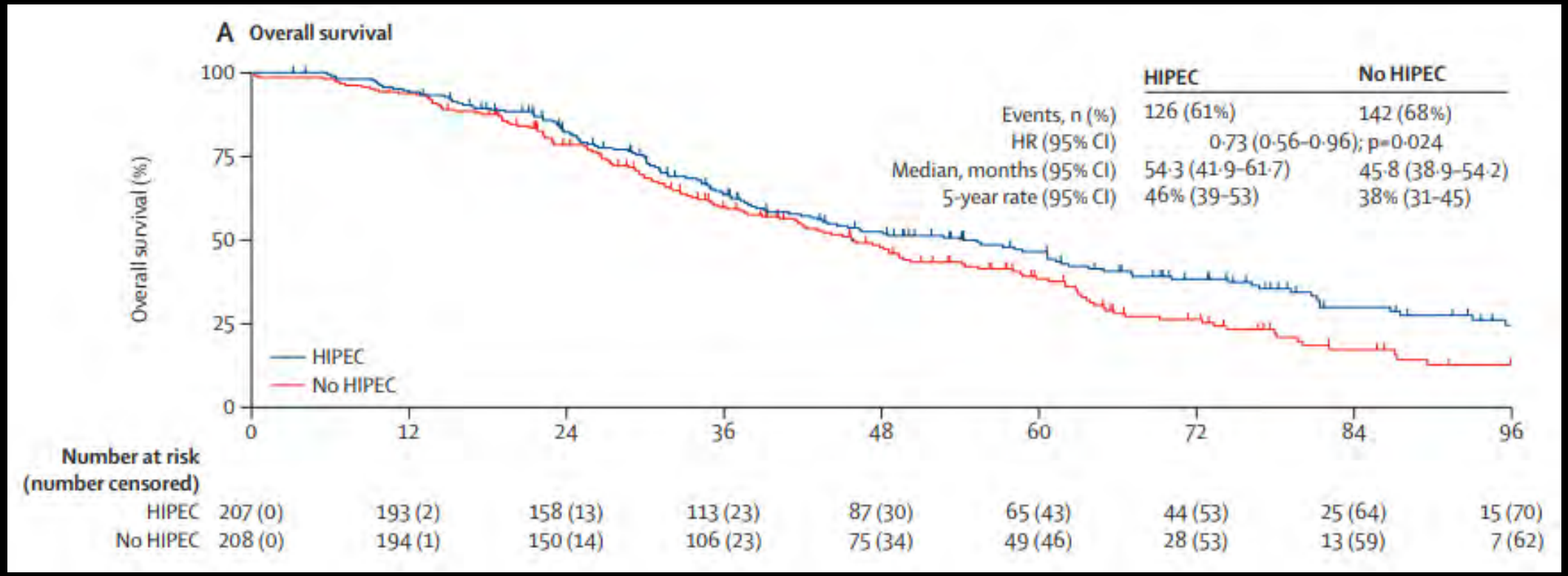
OVERALL SURVIVAL



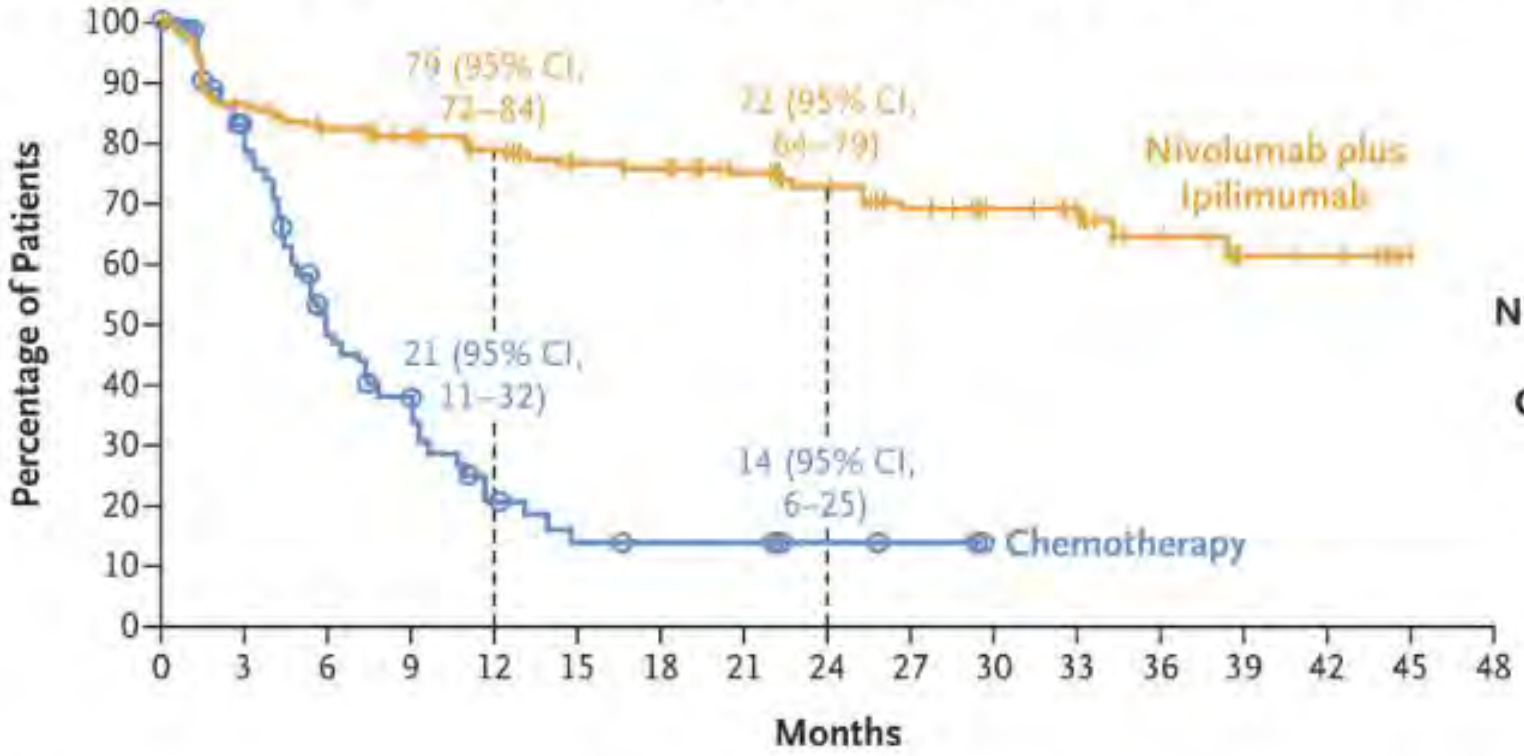
PROGRESSION FREE SURVIVAL



LANCET ONCOLOGY November 2024



A Progression-free Survival in Patients with Centrally Confirmed MSI-H or dMMR Metastatic Colorectal Cancer



	No. of Events/ No. of Patients	Median Progression-free Survival (95% CI)
		mo
Nivolumab plus Ipilimumab	48/171	NR (38.4–NE)
Chemotherapy	52/84	5.9 (4.4–7.8)

Adjusted difference in restricted mean survival time at 24 mo, 10.6 mo (95% CI, 8.4–12.9)
P<0.001 with the use of a two-sided stratified log-rank test

No. at Risk

Nivolumab plus ipilimumab	171	144	132	122	108	95	92	77	64	53	42	37	22	10	9	1	0
Chemotherapy	84	53	29	20	10	6	5	5	3	2	0	0	0	0	0	0	0

Thank You for your attention!