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ASCO 2025 CERVICAL CANCER UPDATES

- DANA M. CHASE, MD
- PROFESSOR
- JONSSON COMPREHENSIVE CANCER CENTER
- DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA

WAGO 2025 Annual Meeting
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Western Association of Gynecologic Oncology

DISCLOSURES

ABSTRACTS

- Phenix Trial: sentinel LND vs pelvic LND
- PROs from OUTBACK Trial
- ctDNA from CALLA Trial
- Keynote A18 Overall Survival
- Cadonilimab +/- Bev + C/T in Met/Recurrent/Advanced
- Nimotuzimab + C/T in Met/Recurrent/Advanced
- CisRT + Bev in Vulvar CA

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SURGERY IN EARLY CERVICAL CANCER

- Less is More

Radical Hyst → Simple Hyst

Radical trachelectomy → CKC

Full Pelvic Lympadenectomy → Sentinel LND

2025 ASCO ANNUAL MEETING

Sentinel Lymph Node Biopsy versus Pelvic Lymphadenectomy in Early-stage Cervical Cancer: a Multicentre Randomized Phase III trial (the PHENIX Trial)

Jihong Liu, Hua Tu, He Huang, Yanfang Li, Xiaojun Chen, Chunyan Wang, Min Zheng, Yanna Zhang, Weidong Zhao, Yanling Feng, Ting Wan, Yongwen Huang, Aijun Yu, Weiguo Lu, Jing Xiao, Weiwei Shan, Ping Zhang, Changkun Zhu, Danbo Wang, Hu Zhou, Jibin Li, Beihua Kong, Weiwei Feng, Xipeng Wang, Rongzhen Luo, and Shuzhong Yao, for the PHENIX investigators

Speaker: Jihong Liu

Key Takeaway Points

- Sentinel lymph node biopsy (SLNB) demonstrated **noninferiority** to lymphadenectomy in disease-free survival for cervical cancer

- SLNB alone without lymphadenectomy may reduce the risk of retroperitoneal nodal recurrence and cancer-specific death

?

PHENIX-I Schema

Eligibility Criteria

- ✓ Age between 18 and 65 yrs
- ✓ squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma
- ✓ FIGO 2009 stage IA1 (LVSI+), IA2, IB1 and IIA1
- ✓ The diameter of tumor ≤ 3 cm
- ✓ No suspected LN on imaging examination
- ✓ No distant metastasis
- ✓ No desire to preserve fertility

SLNB * and frozen section examination

SLN negative N = 838

R 1:1

Intraoperative randomization

Arm 1

Radical hysterectomy (no PL)**

Arm 2

Radical hysterectomy + PL

Adjuvant Treatment

- CCRT
- Radiotherapy
- Chemotherapy

Depended on **Pathological Factors**

- Positive margin
- Positive LNs
- LVSI+
- Deep stromal invasio
- G3 and >2 cm

* No restriction for tracer type or surgical approach

Side-specific PL were performed in cases of **unilateral SLN detection

Primary Endpoint: **Disease-free survival**

Secondary Endpoints: **Rate of retroperitoneal LN recurrence, Cancer-specific survival**, Surgical outcomes and morbidity

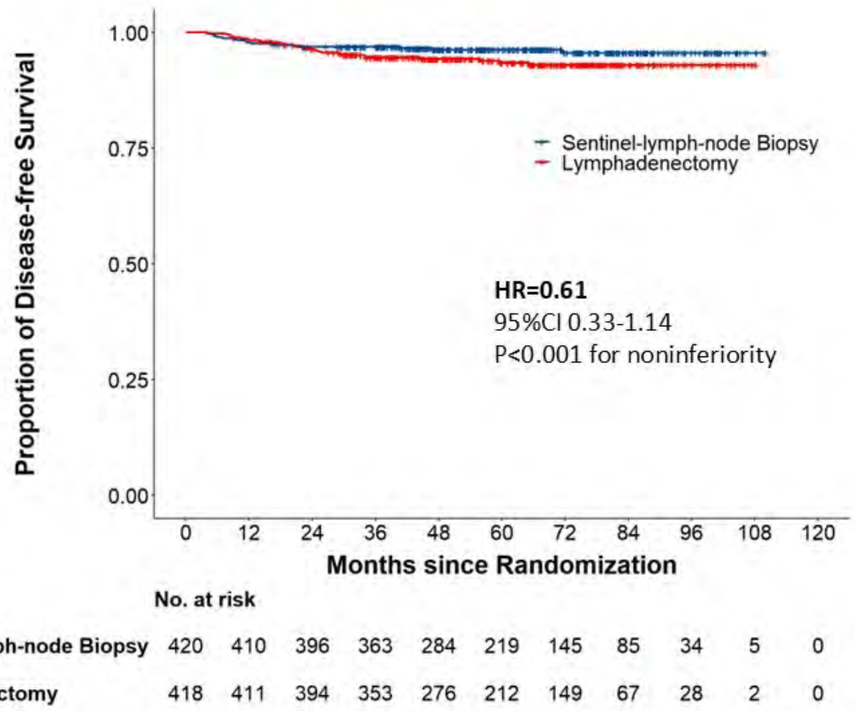
FIGO, International Federation of Gynecology and Obstetrics; **PL**, pelvic lymphadenectomy; **SLNB**, sentinel lymph node biopsy; **SLN**, sentinel lymph node; **LN**, lymph node; **CCRT**, concurrent radiochemotherapy; **LVSI**, lymphovascular space involvement; **QoL**, quality of life; **G**, histological grade.

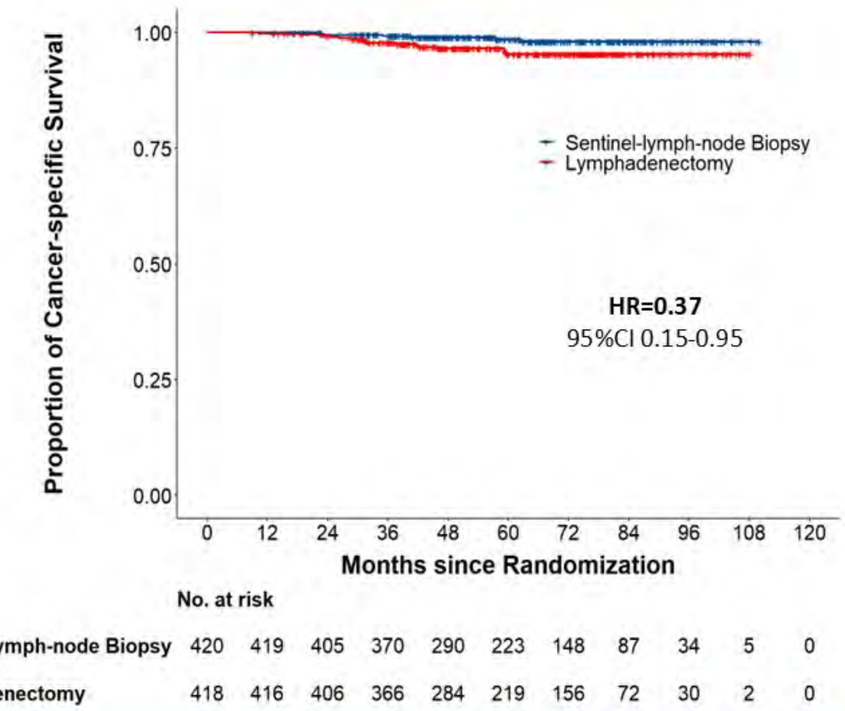
Recurrence and Death

The median follow-up time was 62.8 months

	PHENIX-I cohort (SLN-negative)		PHENIX-II cohort (SLN-positive)	
	Sentinel Node Biopsy (N = 420)	Lymphadenectomy (N = 418)	Sentinel Node Biopsy (N = 35)	Lymphadenectomy (N = 35)
Total case with recurrences	16 (3.8)	26 (6.2)	6 (17.1)	9 (25.7)
Location of recurrences				
Vaginal stump	7 (1.7)	4 (1.0)	.9)	2 (5.7)
Retroperitoneal nodes	0	9 (2.2)	.7)	3 (8.6)
Pelvic	0	3 (0.7)	(2.9)	1 (2.9)
Para-aortic	0	1 (0.2)	1 (2.9)	1 (2.9)
Both	0	5 (1.2)	0	1 (2.9)
Pelvis (non-vaginal stump)	0	10 (2.4)	0	5 (14.3)
Abdomen	0	3 (0.7)	0	3 (8.6)
Distant	9 (2.1)	17 (4.1)	4 (11.4)	3 (8.6)
Multiple	0	10 (2.4)	1 (2.9)	4 (11.4)
Undefined	0	1 (0.2)	0	1 (2.9)
Died from cervical cancer	6 (1.4)	16 (3.8)	2 (5.7)	9 (25.7)
Died from other causes	3 (0.7)	1 (0.2)	0	0

PHENIX-I: Survivals for ITT population

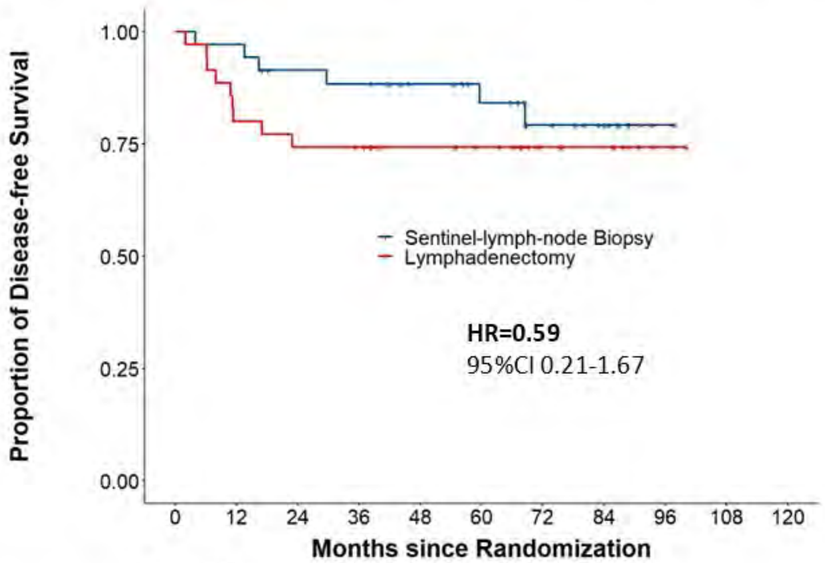




	DFS Events	3-year DFS rate	HR and P-value
Arm1	16	96.9%	HR=0.61 95%CI 0.33-1.14
Arm2	26	94.6%	P<0.001 for noninferiority

	CSS Events	3-year CSS rate	HR
Arm1	6	99.2%	HR=0.37 95%CI 0.15-0.95
Arm2	16	97.8%	

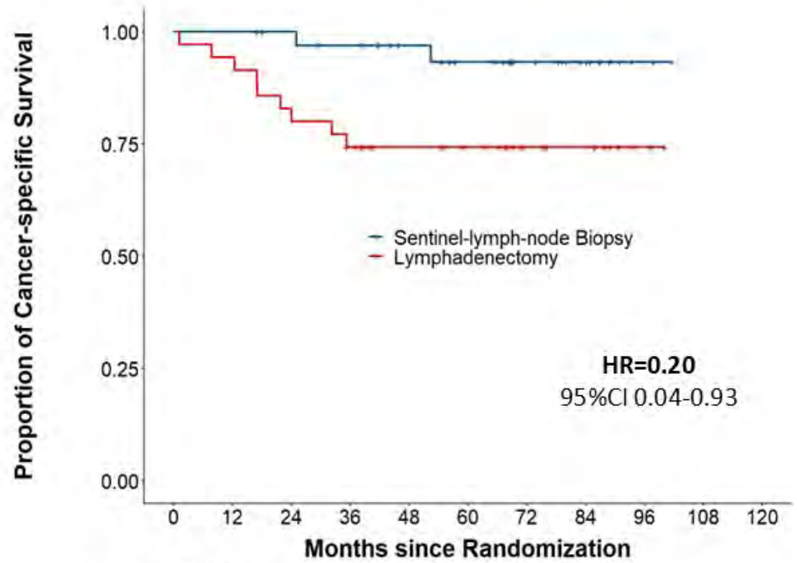
PHENIX-II: Survivals for ITT population



No. at risk

Sentinel-lymph-node Biopsy	35	34	30	29	24	20	14	9	1	0	0
Lymphadenectomy	35	28	26	25	20	17	10	8	2	0	0

	DFS Events	3-year DFS rate	HR
Arm1	6	88.4%	HR=0.59
Arm2	9	74.3%	95%CI 0.21-1.67



No. at risk

Sentinel-lymph-node Biopsy	35	35	33	31	26	22	16	10	2	0	0
Lymphadenectomy	35	33	29	25	20	17	10	8	2	0	0

	CSS Events	3-year CSS rate	HR
Arm1	2	97.0%	HR=0.20
Arm2	9	74.3%	95%CI 0.04-0.93

Due to the premature termination, the **PHENIX-II** part lacked sufficient statistical power
Nevertheless, preliminary analysis appeared to indicate trends consistent with those observed in PHENIX-I

Conclusions

- SLNB demonstrates noninferior disease-free survival to lymphadenectomy in cervical cancer patients, with superior surgical outcomes
- SLNB alone without lymphadenectomy may reduce retroperitoneal nodal recurrence and cancer-specific death
- Omitting lymphadenectomy after SLNB appears to improve disease-free survival in patients undergoing minimally invasive surgery

LOCALLY ADVANCED CERVICAL CANCER

- How do we improve survival?
  - Better monitoring?
  - New therapeutic agents?
  - Quality of life? (remember QOL associated with OS in cervical cancer)

2025 ASCO ANNUAL MEETING

Patient-reported outcomes (PROs) in locally advanced cervical cancer (LACC): insights from the OUTBACK trial

Rebecca Mercieca-Bebber, Elizabeth Barnes, Kathleen Moore, Yeh Chen Lee, Kailash Narayan, Pearly Khaw, Martin Buck, Anthony Fyles, Susan Brooks, Jayanthi Lea, Ashley Stuckey, Thomas Lad, Christine Holschneider, Nick Spiritos, Leslie Boyd, William Small Jr., Bradley J. Monk, Martin Stockler, Madeleine King, Linda Mileshkin

Professor Linda Mileshkin

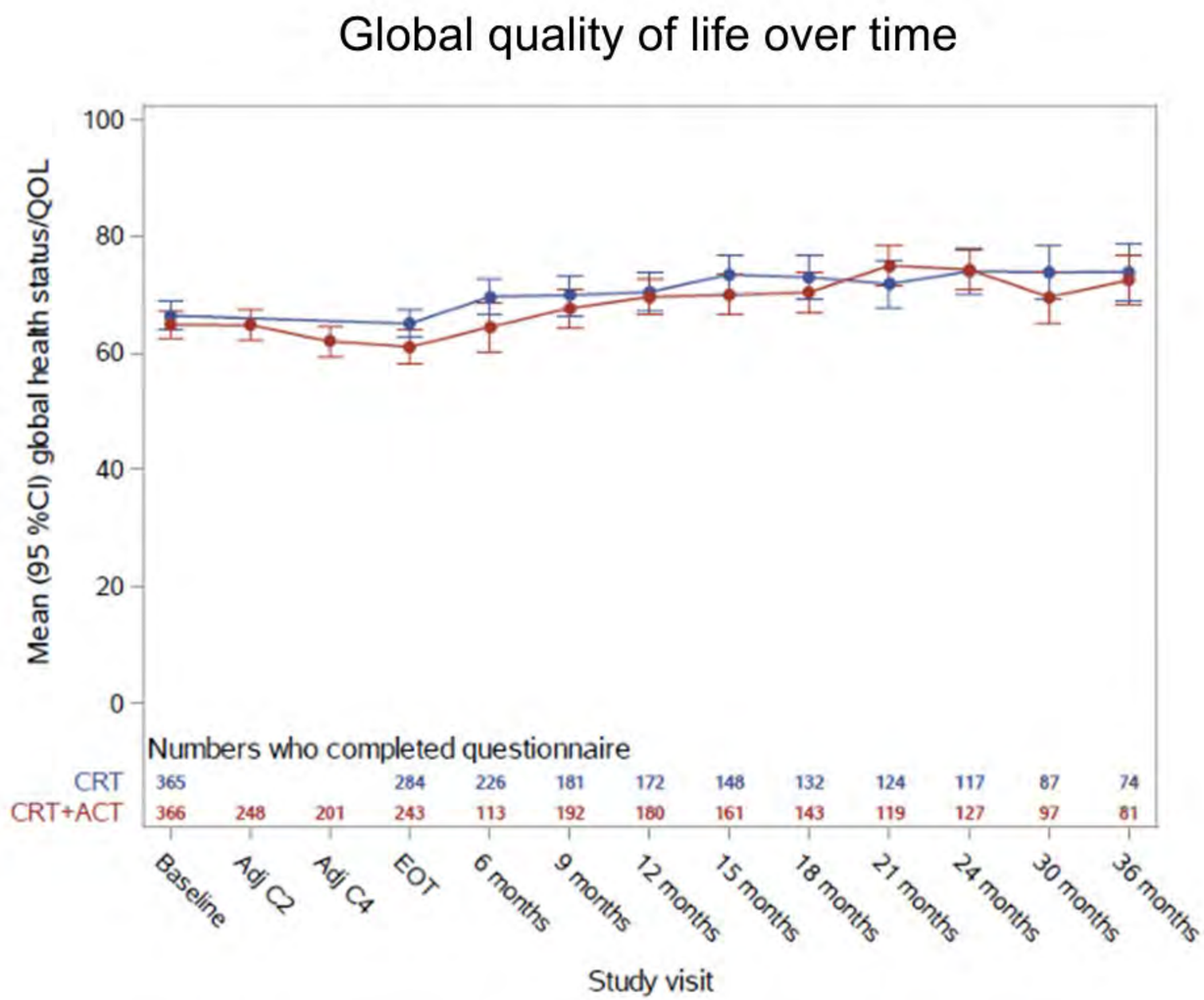
Key Takeaway Points/Conclusions

Long-term symptom/sexual function concerns are common and persistent following chemoradiation +/- adjuvant chemo for locally advanced cervical cancer and need dedicated survivorship care.

- The 3 most common issues after 1 year were:
  - worry about future health (44%)
  - hot flushes/ sweats (37%)
  - frequent urination (35%).
- All were persistent in Years 2-3.
- Concerns at Years 1, 2 or 3 with sexual activity (affecting 92%) and enjoyment (68%), likely driven by vaginal tightness and dryness.

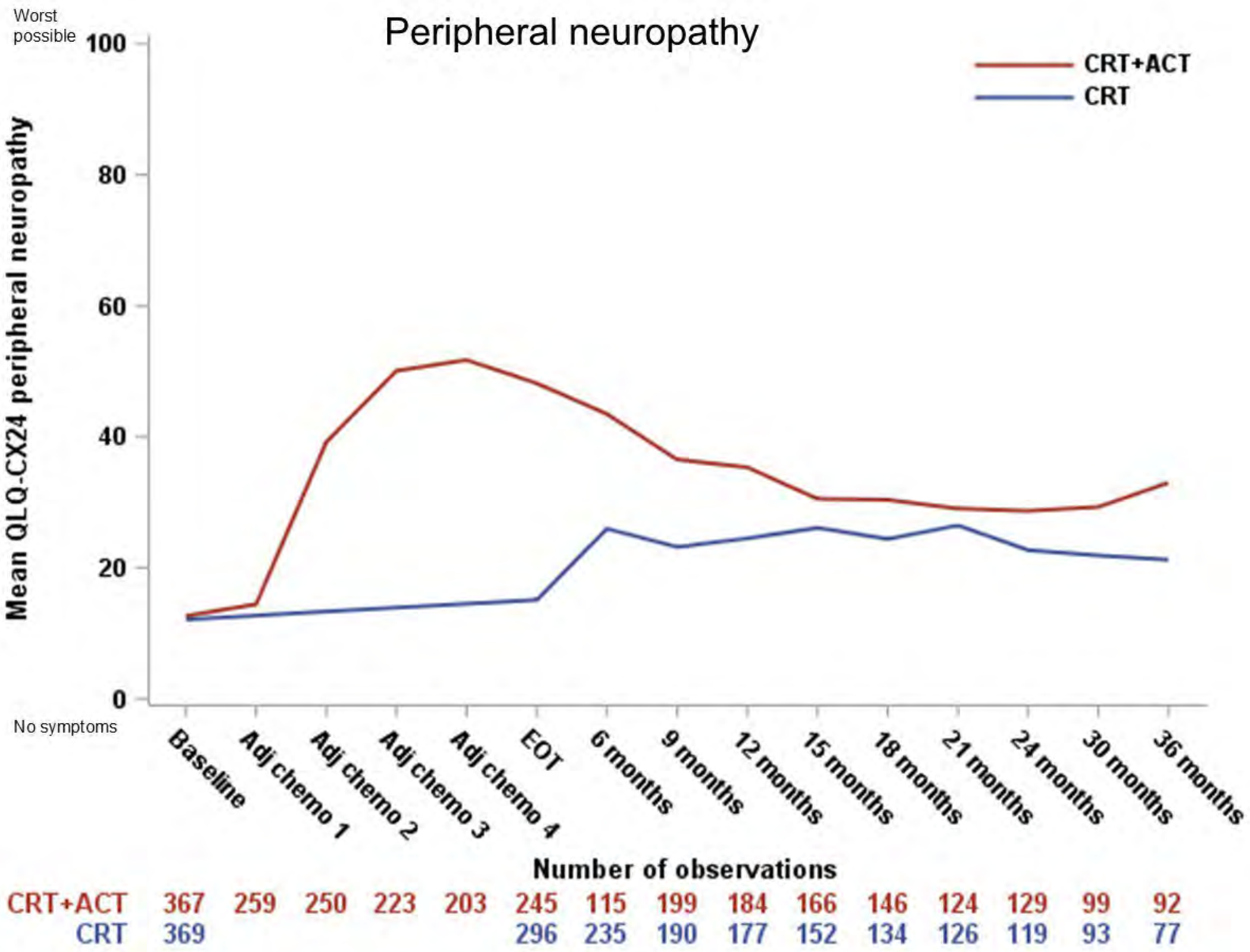
Background

- OUTBACK Phase 3 RCT (n=919)
- Locally-advanced cervical cancer
- Chemoradiotherapy + adjuvant chemotherapy (CRT+ACT), as compared with chemoradiotherapy alone (CRT-alone):
  - Did not improve 5-year OS or PFS;
  - Increased incidence of adverse events;
  - Decreased overall QOL (QLQ-C30) at end of treatment and at 6 months



Mileshkin L, Lancet Oncol, 2023

Peripheral neuropathy



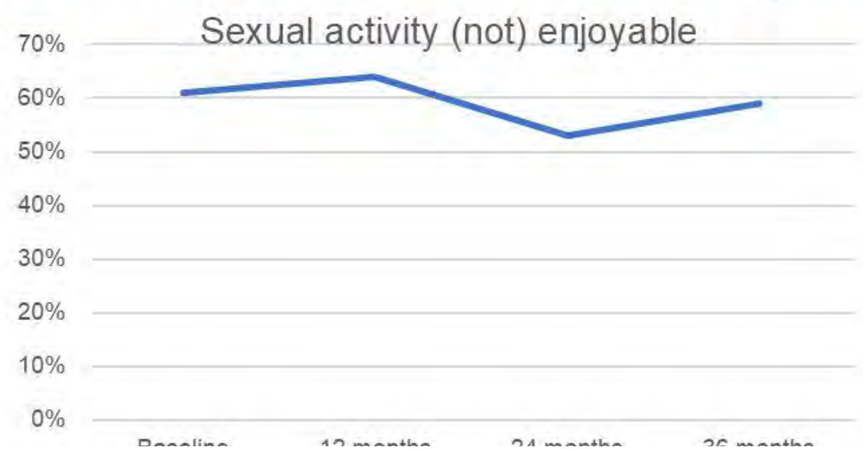
Number of observations

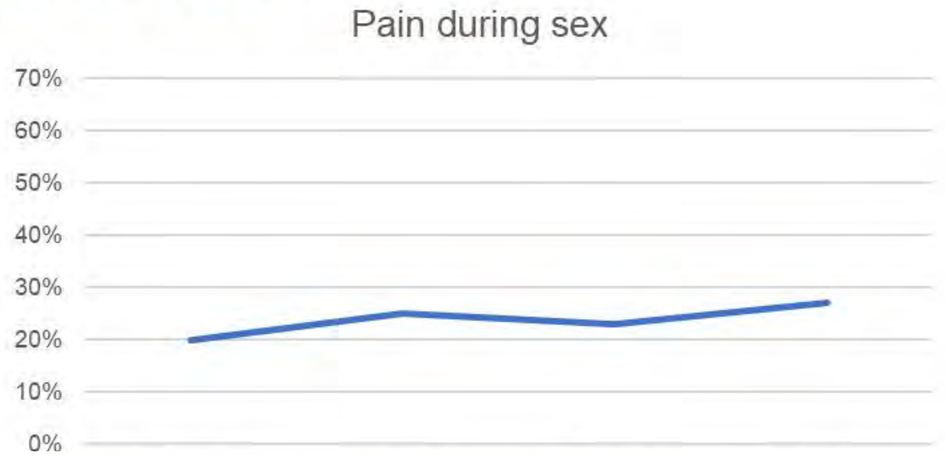
CRT+ACT	367	259	250	223	203	245	115	199	184	166	146	124	129	99	92
CRT	369					296	235	190	177	152	134	126	119	93	77

Results – rate experiencing moderate to severe PROs

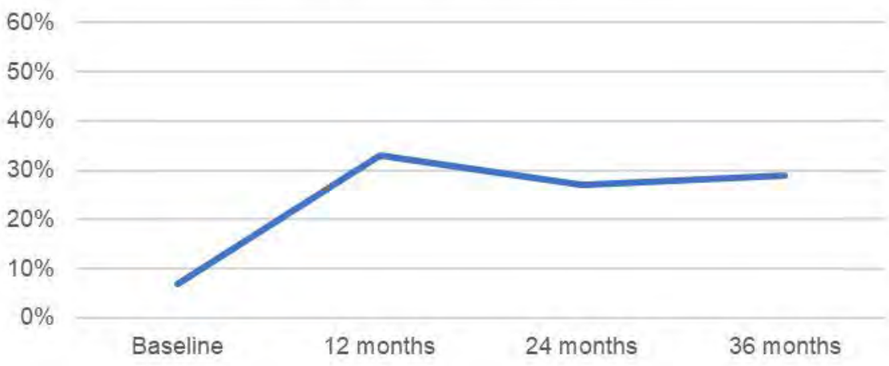
Top 10 moderate-severe issues	**CRT-alone, n (%)**	**CRT + ACT, n (%)**	**All participants n (%)**		
	Year 1	Year 1	Year 1	**Resolved** by Year 2 or 3	**Persistent** at Year 2 or 3
Worried future health	76 (50)	59 (38)	135 (44)	14 (10)	49 (36)
Hot flushes/ sweats	68 (39)	64 (35)	132 (37)	24 (18)	49 (37)
Frequent urination	67 (38)	59 (32)	126 (35)	24 (19)	45 (36)
Sexual activity (not) enjoyable	59 (63)	66 (65)	125 (64)	11 (9)	43 (34)
Trouble sleeping	62 (35)	55 (30)	117 (32)	19 (16)	37 (32)
Tired	53 (30)	51 (28)	104 (29)	22 (21)	33 (32)
Changed bowel habit	56 (32)	46 (25)	102 (28)	22 (22)	41 (40)
Financial difficulties	50 (28)	51 (27)	101 (28)	17 (17)	32 (32)
Pain	42 (24)	54 (29)	96 (27)	21 (22)	23 (24)
Dissatisfied with body	47 (27)	48 (26)	95 (26)	21 (22)	27 (28)

Moderate-severe symptoms over time





- Overall, 77% reported **no** sexual activity in past 4 weeks at baseline, 48% at Year 1.
- 92% of pts reported **low** sexual activity at years 1, 2 or 3;



Conclusions / Key Takeaways

Long-term symptoms and sexual health concerns following CRT +/-ACT for locally advanced cervical cancer:

- Are common and persistent across multiple domains;
- Were similar regardless of whether ACT was given (excl. peripheral neuropathy);
- Need more attention, research and dedicated survivorship care.

- OUTBACK PRO results support the recommendation:
  - Adjuvant chemotherapy should not be used following chemoradiotherapy to treat locally advanced cervical cancer, as no additional benefit is offered.

2025 ASCO ANNUAL MEETING

Ultrasensitive detection and tracking of circulating tumor DNA (ctDNA) and association with relapse and survival in locally advanced cervical cancer (LACC): phase 3 CALLA trial analyses

Jyoti Mayadev,[1] Juan Carlos Vázquez Limón,[2] Francisco J. Ramírez Godinez,[3] Manuel Leiva,[4] Lucely del Carmen Cetina-Pérez,[5] Szilvia Varga,[6] Alejandro Molina Alavez,[7] Ashley E. Alarcon Rozas,[8] Natalia Valdiviezo,[9] Xiaohua Wu,[10] Masaki Mandai,[11] Ronnie Shapira-Frommer,[12] Maria del Pilar Estevez-Diz,[13] Sewanti Limaye,[14] Wenjing Xin,[15] Hannah Dry,[16] Maria A.S. Broggi,[17] Daniel Y. Yuan,[17] Ross Stewart,[18] Bradley J. Monk[19]

[1]University of California San Diego Medical Center, San Diego, CA; [2]Antiguo Hospital Civil de Guadalajara "Fray Antonio Alcalde" University of Guadalajara, Guadalajara, Mexico; [3]Hospital Civil de Guadalajara, Guadalajara, Mexico; [4]Instituto de Oncologia y Radioterapia de la Clinica Ricardo Palma, San Isidro, Peru; [5]Clinical Research Department, Instituto Nacional de Cancerologia, Ciudad de México, México; [6]National Institute of Oncology, Budapest, Hungary; [7]Centro de Atención e Investigación Clinica en Oncologia, Mérida, Mexico; [8]Clinica Santa Beatriz, Lima, Peru; [9]Nacional de Enfermedades Neoplásicas, Lima, Peru; [10]Fudan University Shanghai Cancer Center, Shanghai, China; [11]Kyoto University Graduate School of Medicine, Kyoto, Japan; [12]Chaim Sheba Medical Center, Ramat Gan, Israel; [13]Instituto do Câncer do Estado de São Paulo and Universidade de São Paulo, São Paulo, Brazil; [14]Sir H N Reliance Foundation Hospital, Mumbai, India; [15]AstraZeneca, Gothenburg, Sweden; [16]AstraZeneca, Waltham, MA; [17]AstraZeneca, Gaithersburg, MD; [18]AstraZeneca, Cambridge, UK; [19]Florida Cancer Specialists and Research Institute, West Palm Beach, FL

Key Takeaway Points

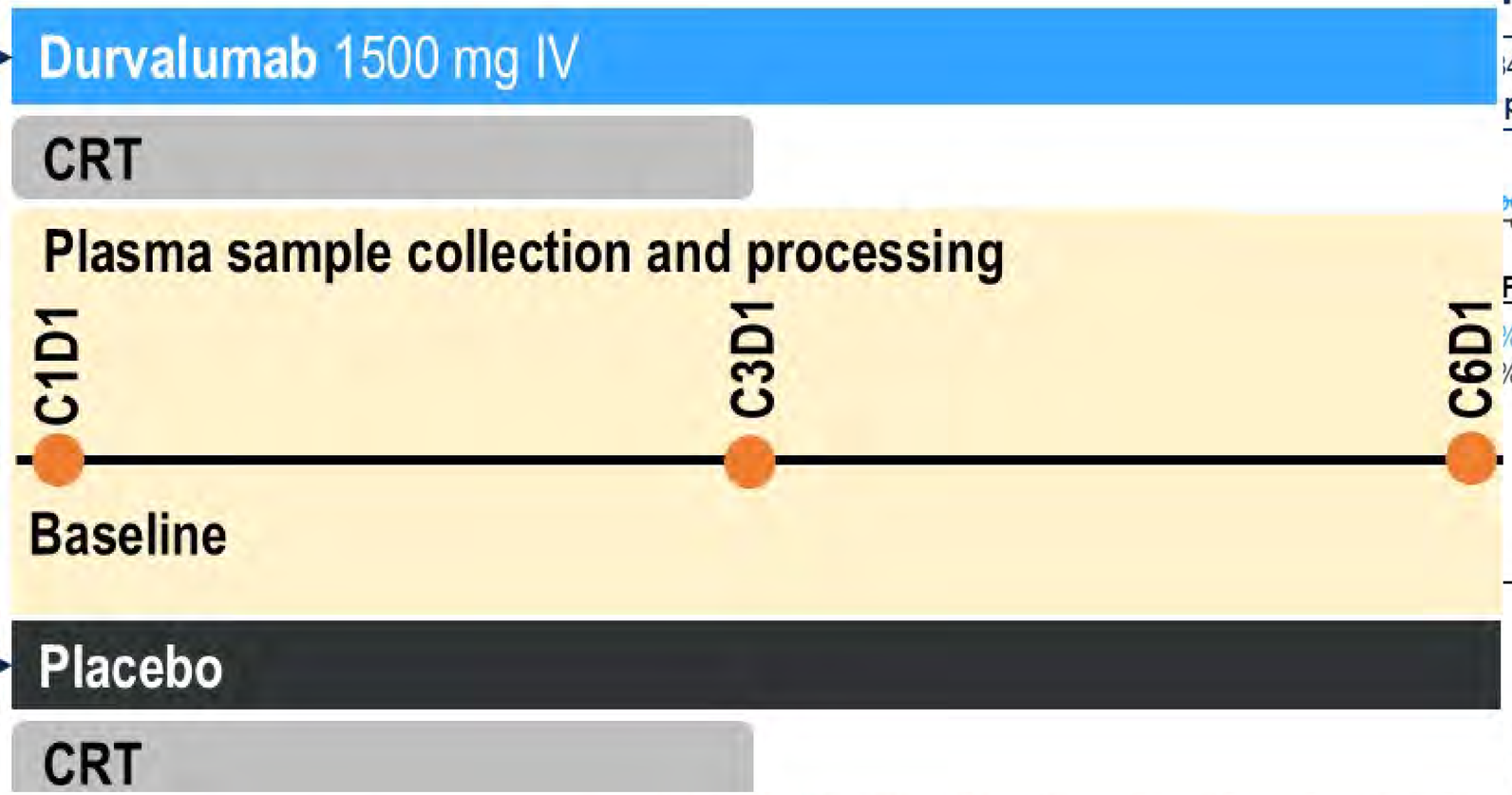
High baseline ctDNA levels were associated with <u>increased</u> risk of progression and death

Undetectable ctDNA after treatment correlated with <u>reduced</u> risk of progression and death

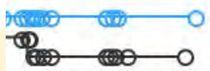
ctDNA, circulating tumor DNA.

CALLA Study Background

- CALLA did not s… statistically significant… Primary endpoint: PFS in ITT… improvement in … CRT alone in a … population[1]
  - *Post hoc* an… with durvalu… with PD-L1…
- 30–50% of patie… disease within 5… CRT[1]
  - ctDNA has … marker of re…



…4 (0.65–1.08)
p: 18.5 m vs 18.4 m



FS rate
…%
…%

27 30 33

11 1 0
14 2 0

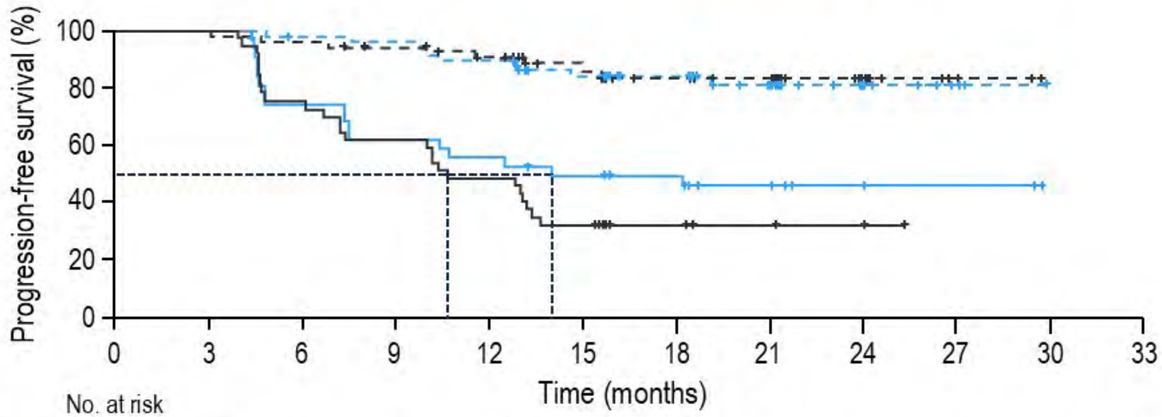
CALLA NCT03830866. Monk BJ, et al. *Lancet Oncol*. 2023;24:1334-1348. CI, confidence interval; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; HR, hazard ratio; ITT, intent to treat; LACC, locally advanced cervical cancer; m, months; PD-L1, programmed death ligand-1; PFS, progression-free survival; TAP, tumor area positivity.

1. Monk BJ, et al. *Lancet Oncol*. 2023;24:1334-1348; 2. Han K, et al. *J Clin Oncol*. 2024;42:431-440; 3. Jeannot E, et al. *Clin Cancer Res*. 2021;27:5869-5877; 4. Li L, et al. *Cancer Cell Int*. 2023;23:329; 5. Williams JR, et al. *J Clin Oncol*. 2022;40(Suppl 16).

CALLA Post-CRT: ctDNA+ Was a Negative Prognostic Factor for PFS and OS

Risk was independent of treatment arm

PFS by ctDNA+ or ctDNA- at C3D1

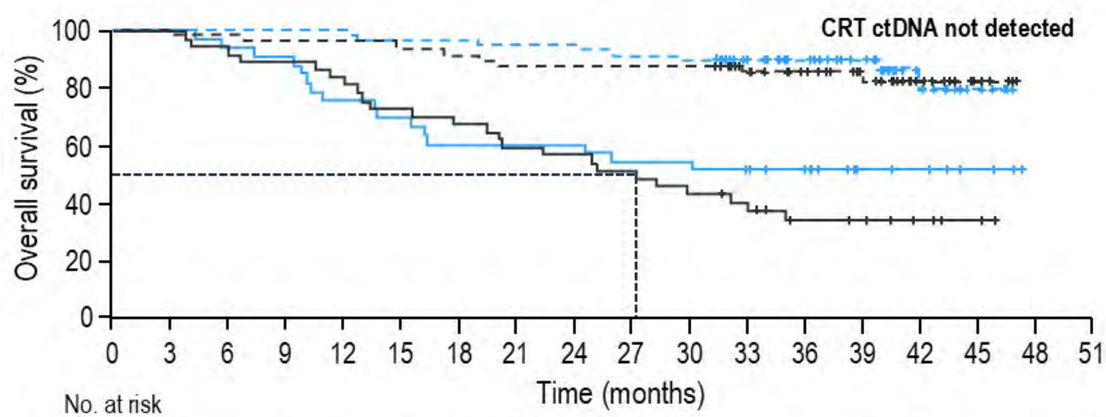


No. at risk

CRT detected	37	37	28	23	18	12	6	4	2	0	0	0
D+CRT detected	33	33	24	20	18	15	13	7	4	2	0	0
CRT not detected	56	56	54	51	46	35	28	24	11	3	0	0
D+CRT not detected	60	60	58	57	53	42	32	22	9	3	0	0

HR (95% CI)	D+CRT n/N=33/93	CRT n/N=37/93
Detected vs not detected	0.23 (0.11–0.50)	0.15 (0.07–0.33)

OS by ctDNA+ or ctDNA- at C3D1



No. at risk

CRT detected	37	37	35	33	31	27	25	22	21	19	17	14	8	7	4	2	0	0
D+CRT detected	33	33	31	30	25	23	20	20	20	18	18	16	14	7	6	3	0	0
CRT not detected	56	56	55	54	54	53	51	49	49	49	49	40	34	27	13	5	0	0
D+CRT not detected	60	60	60	60	60	58	58	57	57	55	54	45	37	29	14	5	0	0

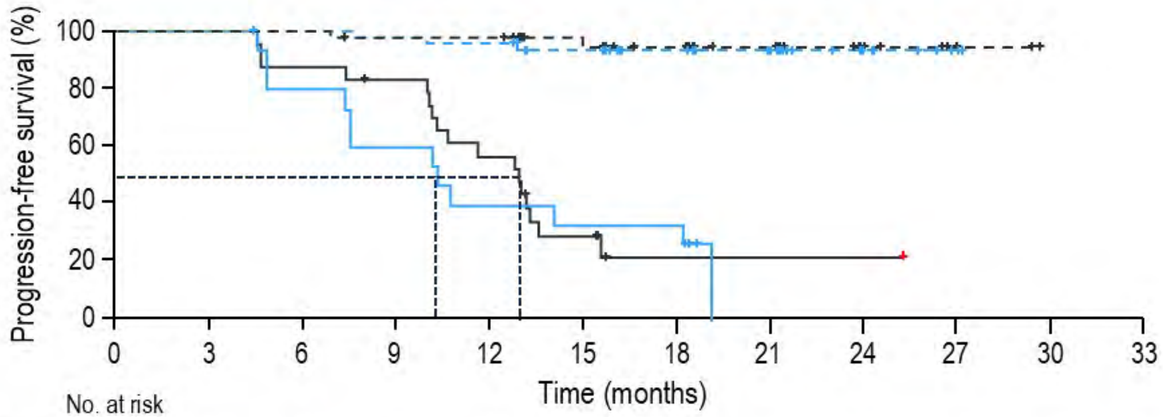
HR (95% CI)	D+CRT n/N=33/93	CRT n/N=37/93
Detected vs not detected	0.20 (0.09–0.47)	0.18 (0.08–0.38)

PFS data cutoff January 20, 2022. OS data cutoff July 3, 2023.
C, cycle; CI, confidence interval; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; D, day; D+CRT, durvalumab + chemoradiotherapy; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

CALLA 3 Months Post-CRT: ctDNA+ Was Associated With Higher Risk of Progression and Death

A lower proportion of patients were ctDNA+ in D+CRT vs CRT arm at C6D1

PFS by ctDNA+ or ctDNA- at C6D1

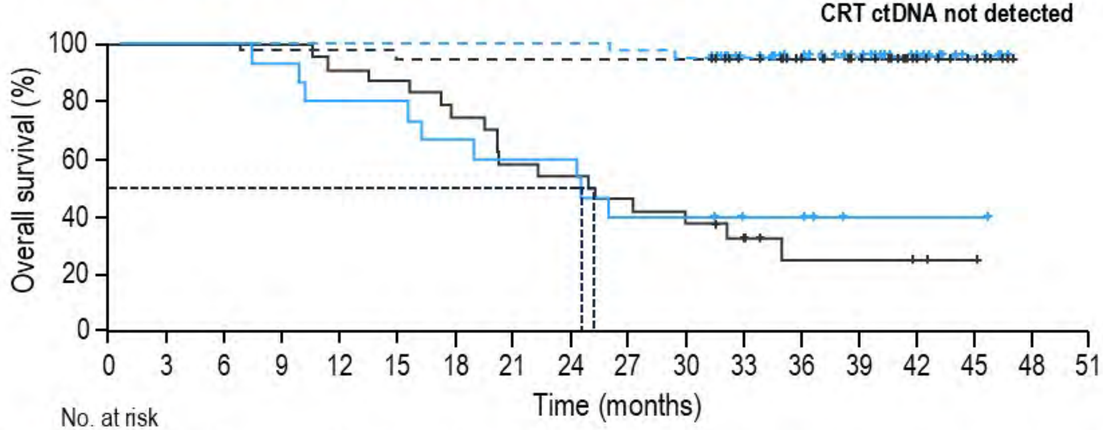


No. at risk

CRT detected	24	24	21	19	13	6	1	1	1	0	0	0
D+CRT detected	15	15	12	9	6	5	5	0	0	0	0	0
CRT not detected	42	42	42	40	40	33	26	21	10	3	0	0
D+CRT not detected	49	49	48	47	46	37	27	21	9	2	0	0

HR (95% CI)	D+CRT n/N=15/64	CRT n/N=24/66
Detected vs not detected	0.04 (0.01–0.16)	0.04 (0.01–0.17)

OS by ctDNA+ or ctDNA- at C6D1



No. at risk

CRT detected	24	24	24	24	22	21	18	14	13	11	10	7	3	3	2	1	0	0
D+CRT detected	15	15	15	14	12	12	10	9	9	6	6	5	4	1	1	1	0	0
CRT not detected	42	42	42	41	41	41	40	40	40	40	40	34	28	23	12	6	0	0
D+CRT not detected	49	49	49	49	49	49	49	49	49	48	47	38	31	24	13	4	0	0

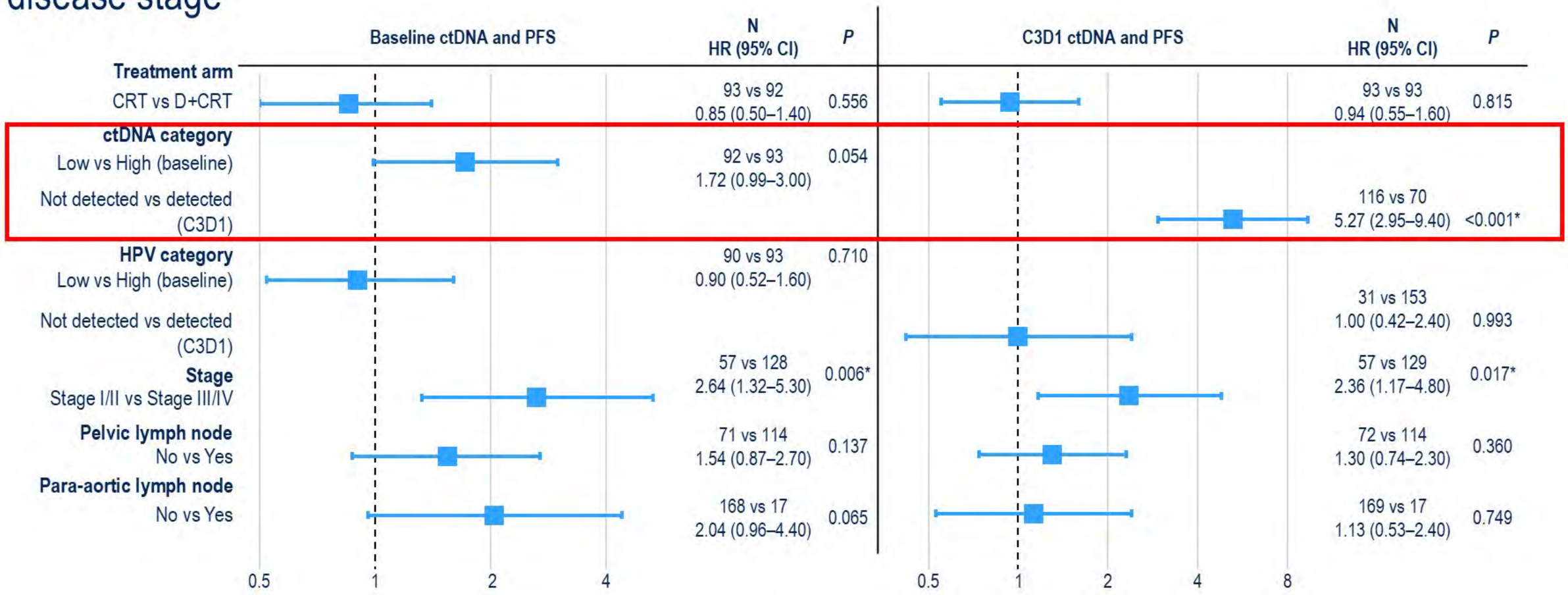
HR (95% CI)	D+CRT n/N=15/64	CRT n/N=24/66
Detected vs not detected	0.04 (0.01–0.20)	0.04 (0.01–0.19)

PFS data cutoff January 20, 2022. OS data cutoff July 3, 2023.

C, cycle; CI, confidence interval; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; D, day; D+CRT, durvalumab + chemoradiotherapy; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

CALLA Multivariate Analysis: C3D1 ctDNA+ Was The Most Significant Prognostic Factor for Progression and Independent of Disease Stage

Baseline ctDNA high was the second most significant prognostic factor for progression after disease stage



The prognostic impact of ctDNA levels, adjusting for other clinical covariates, was assessed via multivariate Cox proportional hazard models with Efron approximation tie handling. All comparisons are text vs reference. *Indicates significance. C, cycle; CI, confidence interval; ctDNA, circulating tumor DNA; CRT, chemoradiotherapy; D+CRT, durvalumab + chemoradiotherapy; OS, overall survival; PFS, progression-free survival.

Conclusions

- Slide presentation
- Plain language summary

- This preplanned exploratory ctDNA analysis of a large, global LACC population from CALLA demonstrates the high sensitivity of a personalized assay for ctDNA detection
- **Risk of progression and death were reduced by at least 95% in both treatment arms for patients with no ctDNA detected at C6D1**
  - Baseline high ctDNA level (≥ median) was associated with higher risk of progression and death
  - Continued detection of ctDNA following CRT was independently prognostic of outcome
  - Post-CRT ctDNA+ was associated with subsequent progression and was detected up to 497 days earlier than by scan
- Post-CRT, the difference in ctDNA detection between the durvalumab + CRT and CRT arms was greatest in the PD-L1 TAP ≥20% subgroup

This analysis supports the potential utility of ultrasensitive tumor-informed ctDNA analysis to help guide treatment decisions in LACC in the future

C, cycle; CRT, chemoradiotherapy; ctDNA, circulating tumor DNA; D, day; LACC, locally advanced cervical cancer; PD-L1, programmed death ligand-1; TAP, tumor area positivity.

2025 ASCO ANNUAL MEETING

Pembrolizumab with Concurrent Chemoradiotherapy in Participants with High-Risk Locally Advanced Cervical Cancer: A Descriptive Analysis of Final Survival from the Phase 3, Randomized, Double-Blind ENGOT-cx11/GOG-3047/KEYNOTE-A18 Study

Linda R. Duska,[1] Yang Xiang,[2] Kosei Hasegawa,[3] Pier Ramos-Elias,[4] Paolo Rodolfo Valdez Barreto,[5] Alejandro Acevedo,[6] Felipe José Silva Melo Cruz,[7] Valeriya Saevets,[8] Rudolf Lampé,[9] Limor Helpman,[10] Jalid Sehouli,[11] Flora Zagouri,[12] Yong Man Kim,[13] Peng Liu,[14] Karin Yamada,[14] Sarper Toker,[14] Sandro Pignata,[15] Domenica Lorusso,[16] on behalf of the ENGOT-cx11/GOG-3047/KEYNOTE-A18 investigators

[1]University of Virginia School of Medicine, Charlottesville, VA, USA; [2]Department of Obstetrics and Gynecology, National Clinical Research Center for Obstetric & Gynecologic Diseases, Peking Union Medical College Hospital, Beijing, China; [3]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [4]Integra Cancer Institute, Edificio Integra Medical Center, Guatemala City, Guatemala; [5]Hospital de Alta Complejidad de La Libertad Virgen de La Puerta, Trujillo, Peru; [6]Oncocentro, Valparaiso, Chile; [7]Instituto Brasileiro de Controle do Câncer, São Paulo, Brazil; [8]Chelyabinsk Regional Clinical Center of Oncology and Nuclear Medicine, Chelyabinsk, Russia; [9]University of Debrecen, Faculty of Medicine, Department of Obstetrics and Gynecology, Debrecen, Hungary; [10]Sheba Medical Center, Tel Aviv University Faculty of Medical and Health Sciences, Ramat Gan, Israel; [11]Charite Universitaetsmedizin, Berlin, Germany and North-Eastern German Society of Gynecological Oncology (NOGGO); [12]Alexandra Hospital, Athens, Greece; [13]Asan Medical Center, University of Ulsan, Seoul, South Korea; [14]Merck & Co., Inc., Rahway, NJ, USA; [15]Department of Urology and Gynecology, Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli, Italy; [16]Gynaecology Oncology Unit, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome and Humanitas San Pio X, Milan, Italy

Key Takeaways

Pembrolizumab plus chemoradiotherapy followed by pembrolizumab maintenance improves overall survival and progression-free survival versus chemoradiotherapy alone in participants with high-risk locally advanced cervical cancer.

The combination has a manageable safety profile.

Longer follow-up confirms the results of prior interim analyses.

ENGOT-cx11/GOG-3047/KEYNOTE-A18: Randomized, Double-Blind, Phase 3 Study

Key Eligibility Criteria

- FIGO 2014 stage IB2-IIB (node-positive disease) or FIGO 2014 stage III-IVA (either node-positive or node-negative disease)
- RECIST 1.1 measurable or non-measurable disease
- Treatment naïve

Stratification Factors

- Planned EBRT type (IMRT or VMAT vs non-IMRT or non-VMAT)

R
1:1
N = 1060

Cisplatin 40 mg/m^2 QW for 5 cycles[a] + EBRT followed by brachytherapy
+
Pembrolizumab 200 mg Q3W for 5 cycles

Pembrolizumab 400 mg Q6W for 15 cycles

Cisplatin 40 mg/m^2 QW for 5 cycles[a] + EBRT followed by brachytherapy
+
Placebo Q3W for 5 cycles

Placebo Q6W for 15 cycles

- We present the final analysis results from the ENGOT-cx11/GOG-3047/KEYNOTE-A18 study

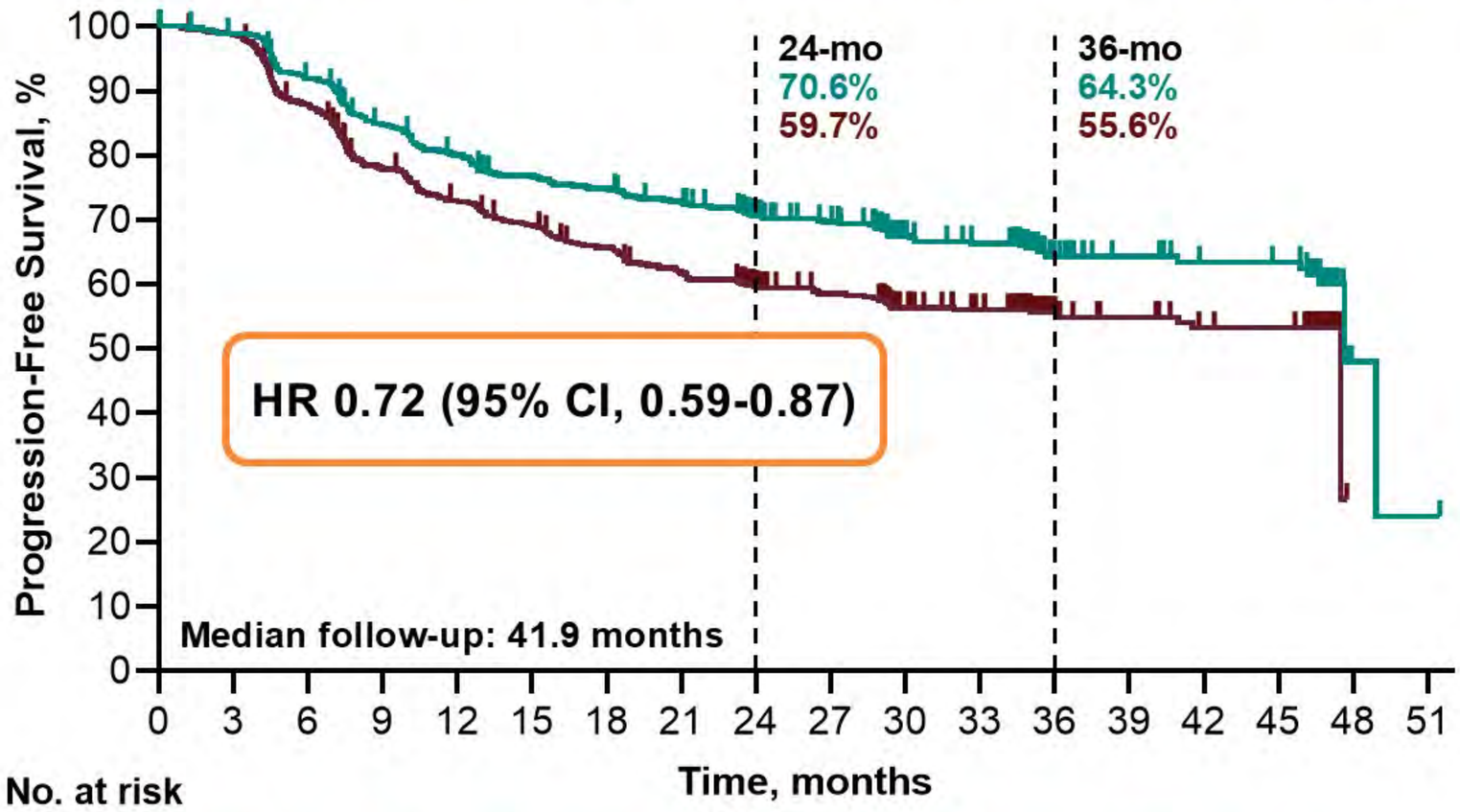
[a]A 6th cycle was allowed per investigator discretion. ENGOT-cx11/GOG-3047/KEYNOTE-A18 ClinicalTrials.gov identifier, NCT04221945.

Summary of Treatment Exposure

	Pembro Arm (N = 527)	Placebo Arm (N = 530)
Total number of cycles, median (range)		
Pembro or placebo	20 (1-20)	20 (1-20)
Cisplatin	5 (1-7)	5 (1-7)
Radiation therapy		
Overall treatment time, median (range), days	52 (12-529)	52 (2-166)
Within 50 days[a], n (%)	187 (35.5%)	195 (36.8%)
Within 56 days, n (%)	391 (74.2%)	396 (74.7%)
Duration of EBRT, median (range), days	37 (12-139)	37 (2-143)
Duration of brachytherapy, median (range),[b] days	12 (1-74)	12 (1-59)

N is the number of participants who completed CCRT at this interim analysis and had final data review by the vendor. [a]Total radiation therapy (EBRT and brachytherapy) should not exceed 50 days, with extension to a maximum of 56 days for unforeseen delays, per the study protocol. [b]Includes participants who started brachytherapy and completed CCRT at this interim analysis and had final data review by the vendor (pembro arm, n = 513; placebo arm, n = 504). Data cutoff date: January 7, 2025.

Descriptive Progression-Free Survival at Final Analysis

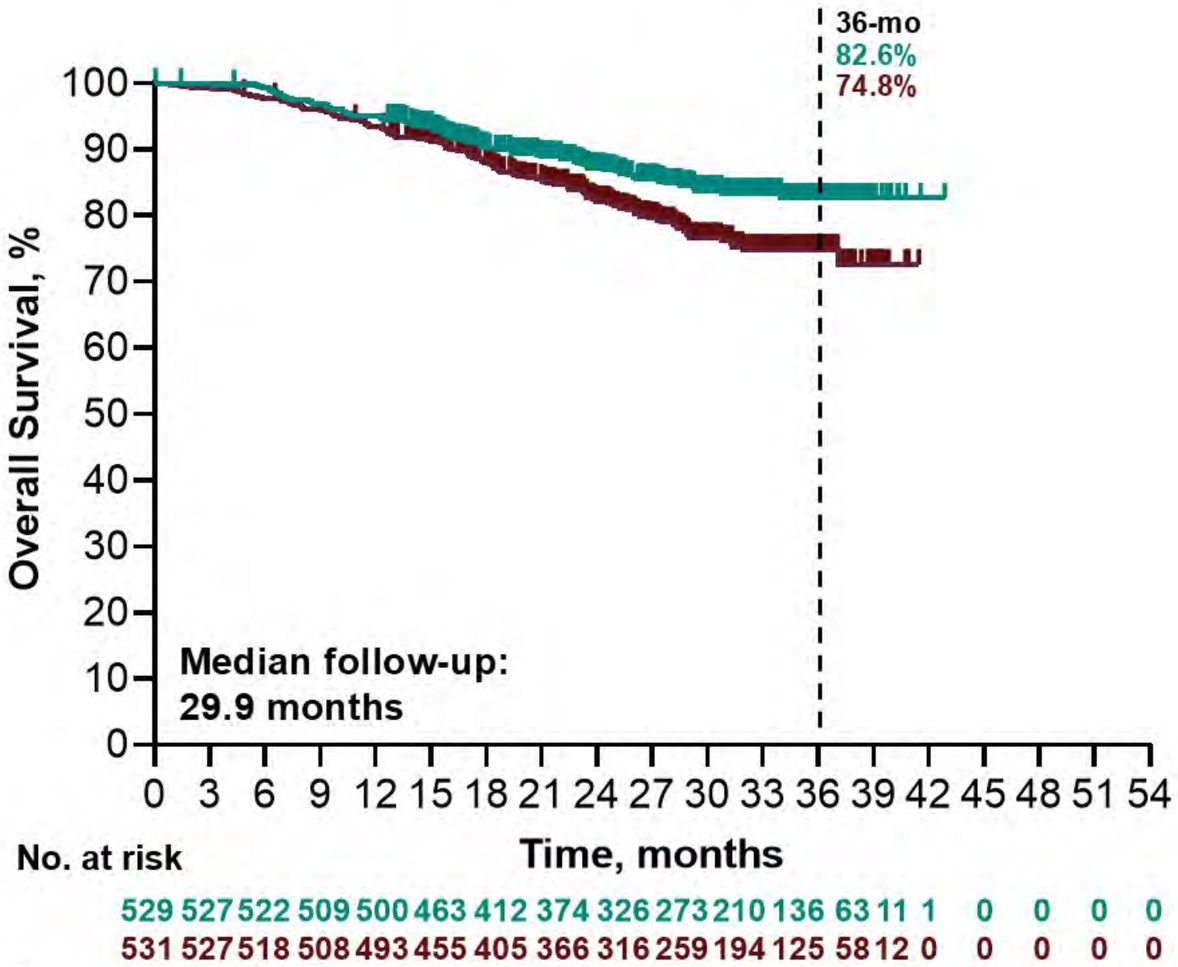


	Pts w/ Event	Pts Censored
Pembro Arm	33.5%	66.5%
Placebo Arm	42.4%	57.6%

Response assessed per RECIST v1.1 by investigator review or histopathologic confirmation. Data cutoff date: January 7, 2025.

Overall Survival at Interim Analysis 2 and Final Analysis

Interim Analysis 2

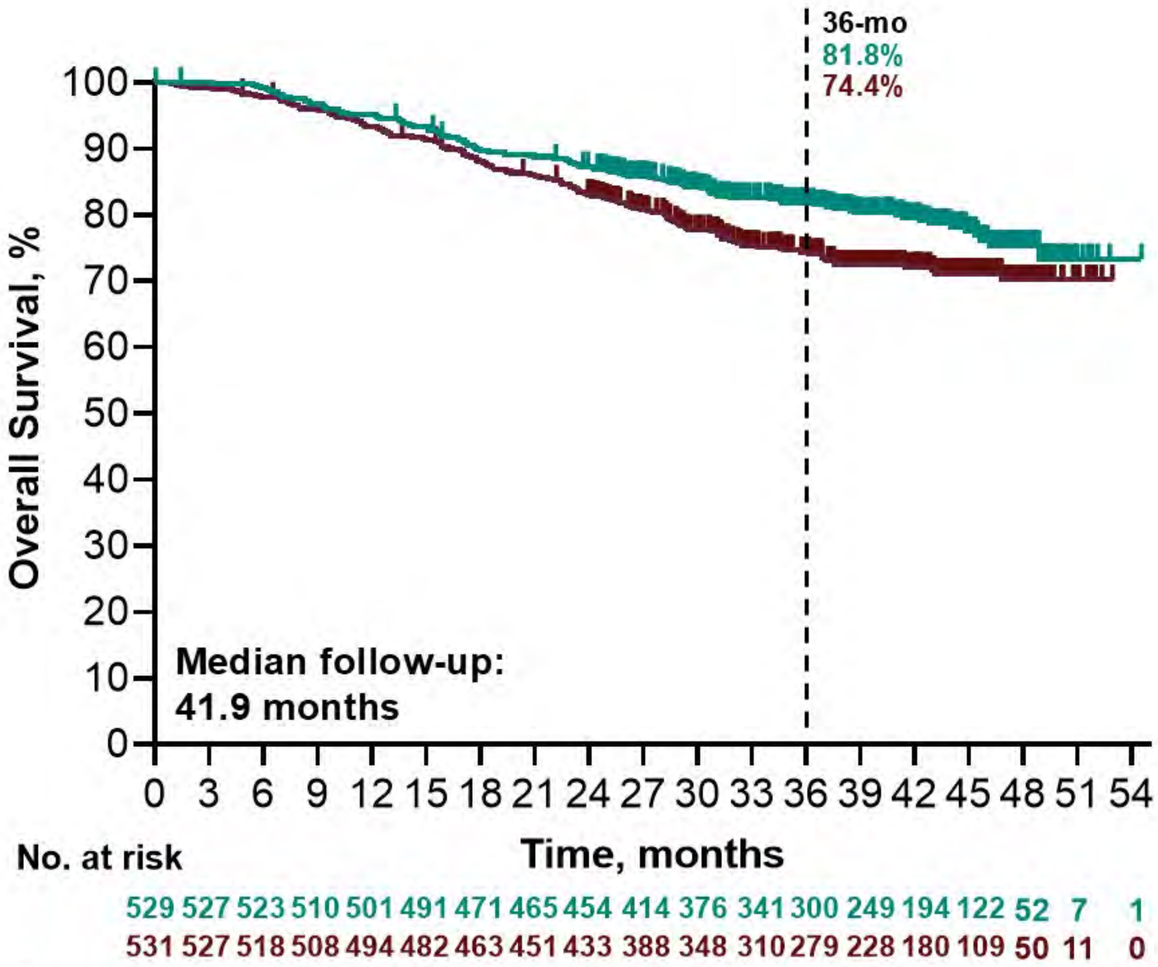


No. at risk

	529	527	522	509	500	463	412	374	326	273	210	136	63	11	1	0	0	0	0
	531	527	518	508	493	455	405	366	316	259	194	125	58	12	0	0	0	0	0

Data cutoff date: January 8, 2024.

Final Analysis



No. at risk

	529	527	523	510	501	491	471	465	454	414	376	341	300	249	194	122	52	7	1
	531	527	518	508	494	482	463	451	433	388	348	310	279	228	180	109	50	11	0

Data cutoff date: January 7, 2025.

Summary of Post-Progression Therapy at Interim Analysis 2 and Final Analysis

Interim Analysis 2

Post-Progression Therapy[a]	Pembro Arm (N = 138)	Placebo Arm (N = 193)
Immunotherapy, n (%)	15 (10.9%)	51 (26.4%)
Pembrolizumab, n (%)	10 (7.2%)	41 (21.2%)
Antibody-drug conjugates[b]	3 (2.2%)	1 (0.5%)

Data cutoff date: January 8, 2024.

Final Analysis

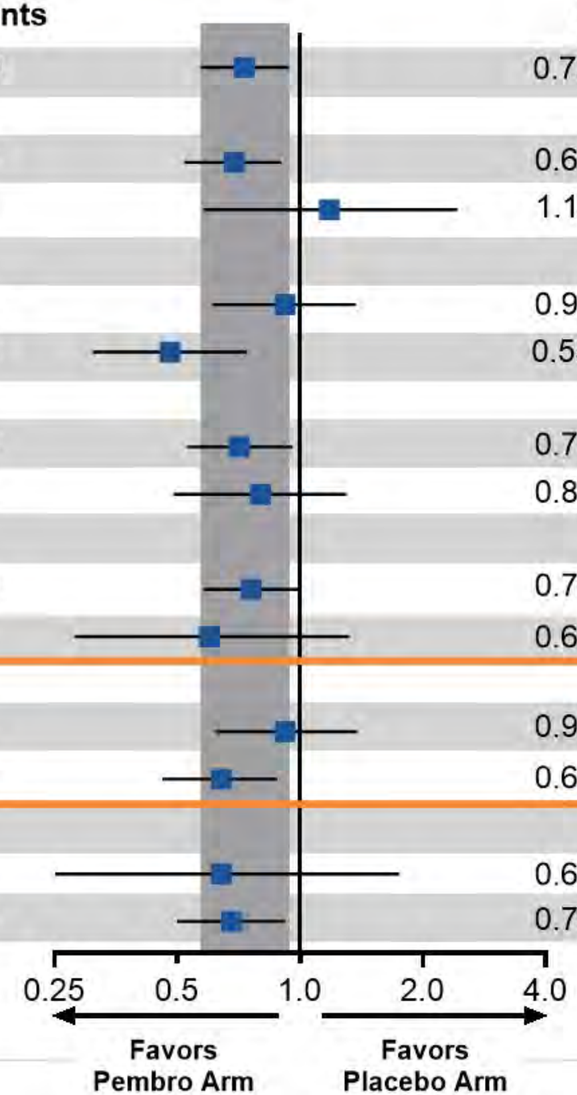
Post-Progression Therapy[a]	Pembro Arm (N = 154)	Placebo Arm (N = 204)
Immunotherapy, n (%)	18 (11.7%)	68 (33.3%)
Pembrolizumab, n (%)	12 (7.8%)	52 (25.5%)
Antibody-drug conjugates[b]	4 (2.6%)	5 (2.4%)

Data cutoff date: January 7, 2025.

[a]All lines of post-progression therapy. [b]Includes other monoclonal antibodies and antibody-drug conjugates and tisotumab vedotin.

Overall Survival in Protocol-Specified Subgroups at Final Analysis

Subgroup	No. of Events/ No. of Patients	HR (95% CI)
Overall	247/1060	0.73 (0.57-0.94)
Age		
<65 years	217/927	0.69 (0.52-0.90)
≥65 years	30/133	1.18 (0.58-2.43)
Race		
White	132/518	0.96 (0.68-1.36)
All others	114/539	0.55 (0.38-0.80)
ECOG PS score		
0	183/778	0.71 (0.53-0.96)
1	64/282	0.80 (0.49-1.30)
Planned EBRT		
IMRT/VMAT	220/939	0.76 (0.58-0.99)
non-IMRT/-VMAT	27/121	0.60 (0.28-1.32)
FIGO 2014 stage		
IB2 to IIB	95/459	0.92 (0.62-1.38)
III to IVA	152/601	0.64 (0.46-0.88)
Planned total RT dose		
<70 Gy	19/93	0.60 (0.24-1.52)
≥70 Gy	228/967	0.75 (0.58-0.97)



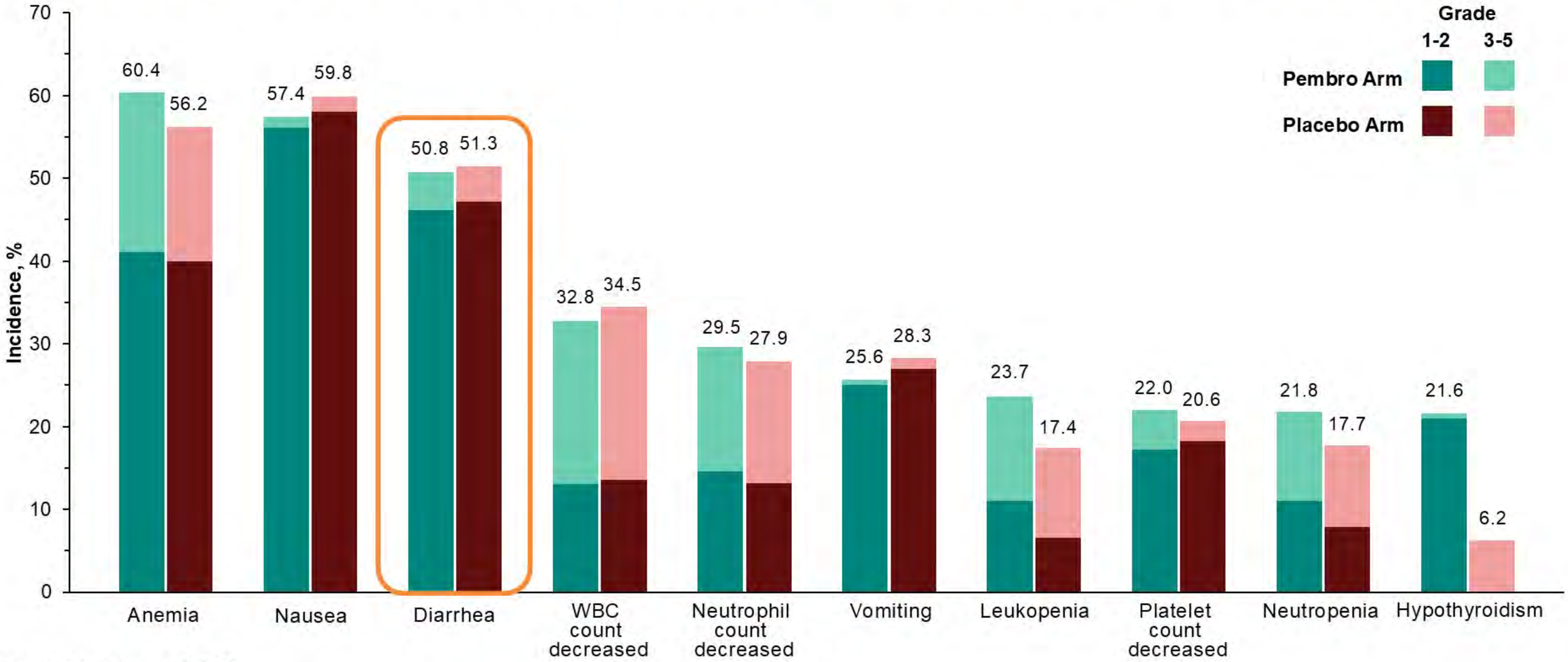
Data cutoff date: January 7, 2025.

Summary of Adverse Events

	All-Cause AEs		Treatment-Related AEs[a]		Immune-Mediated AEs[b]	
	Pembro Arm (N = 528)	Placebo Arm (N = 530)	Pembro Arm (N = 528)	Placebo Arm (N = 530)	Pembro Arm (N = 528)	Placebo Arm (N = 530)
Any grade	528 (100.0%)	526 (99.2%)	512 (97.0%)	513 (96.8%)	210 (39.8%)	93 (17.5%)
Grade ≥3	418 (79.2%)	373 (70.4%)	367 (69.5%)	326 (61.5%)	27 (5.1%)	7 (1.3%)
Serious	175 (33.1%)	153 (28.9%)	104 (19.7%)	72 (13.6%)	21 (4.0%)	6 (1.1%)
Led to death	6 (1.1%)	7 (1.3%)	2 (0.4%)[c]	2 (0.4%)[d]	1 (0.2%)[e]	0
Led to discontinuation						
Any treatment	112 (21.2%)	79 (14.9%)	100 (18.9%)	69 (13.0%)	16 (3.0%)	4 (0.8%)
All treatment	1 (0.2%)	2 (0.4%)	0	1 (0.2%)	0	0

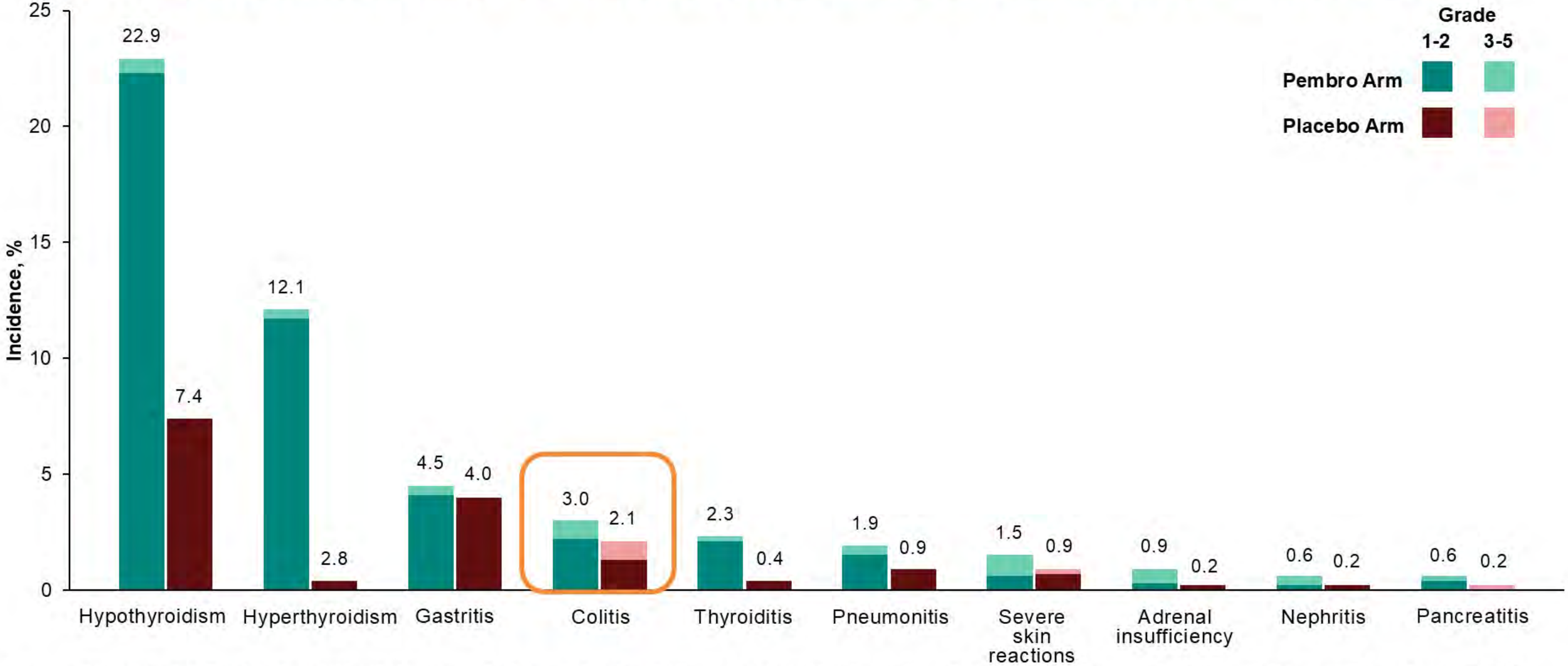
[a]Per investigator assessment. [b]Events were based on a list of preferred terms intended to capture the known risks of pembrolizumab and considered regardless of attribution to treatment by the investigator. [c]Immune-mediated gastritis and large intestine perforation. [d]Bone marrow failure and neutropenic colitis. [e]Immune-mediated gastritis. Data cutoff date: January 7, 2025.

Treatment-Related Adverse Events, Incidence ≥20% in Either Arm



Data cutoff date: January 7, 2025.

Immune-Mediated Adverse Events, Incidence ≥3 Participants in Either Arm



Events were based on a list of preferred terms intended to capture the known risks of pembrolizumab and considered regardless of attribution to treatment by the investigator. Data cutoff date: January 7, 2025.

Summary and Conclusions

- After an additional 12 months of median follow-up, pembrolizumab combined with modern, high-quality CCRT and then continued after CCRT continued to show clinically meaningful improvements in OS and PFS vs CCRT alone in participants with newly diagnosed, previously untreated, high-risk (FIGO 2014 stage IB2-IIB with node-positive disease or stage III-IVA regardless of nodal status) LACC
- The safety profile of pembrolizumab plus CCRT was manageable and consistent with the known profiles of the individual therapies, with no new safety signals after longer follow-up
- **These data are consistent with the prior interim analyses results and provide further support for pembrolizumab plus CCRT as the new standard of care for this population**

METASTATIC/ADVANCED OR RECURRENT CERVICAL CANCER

- Improvements post-826?
  - Bispecifics?
  - ADCs?
  - Novel EGF targeting agents?

2025 ASCO ANNUAL MEETING

Cadonilimab plus platinum-based chemotherapy ± bevacizumab for persistent, recurrent, or metastatic cervical cancer: subgroup analyses of COMPASSION-16

Xiaohua Wu [1], Yang Sun[2], Hongying Yang[3], Hanmei Lou[4], Jing Wang[5], , Dan Li[6], Tao Wu[7], Hui Zhang[8], Ke Wang[9], Yuzhi Li[10], Chunyan Wang[11], Guiling Li[12], Yifeng Wang[13], Dapeng Li[14], Hongyi Cai[15], Mei Pan[16], Ying Tang[17], Ting Liu[18], Yu Xia[18]

1Fudan University Shanghai Cancer Center, Shanghai, China;2Clinical Oncology School of Fujian Medical University, Fujian Cancer Hospital, Fuzhou, China; 3Yunnan Cancer Hospital, Kunming, China; 4Zhejiang Cancer Hospital, Hangzhou, China;5Hunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China;6The Affiliated Hospital of Southwest Medical University, Luzhou, China;7Changde Hospital, Xiangya School of Medicine, Central South University, Changde, China;8The Fourth Hospital of Hebei Medical University, Shijiazhuang, China;9Tianjin Medical University Cancer Institute and Hospital, Tianjin, China;10The First Affiliated Hospital of Bengbu Medical College, Bengbu, China ;11Liaoning Cancer Hospital & Institute, Shenyang, China 12Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China;13Zhujiang Hospital of Southern Medical University, Guangzhou, China;14Cancer Hospital of Shandong First Medical University, Jinan, China ;15Gansu Provincial Hospital, Lanzhou, China;16Jiangxi Maternal and Child Health Hospital, Nanchang, China;17Chongqing University Cancer Hospital, Chongqing, China;18Akeso Biopharma, Inc., Zhongshan, China

Background

- Cadonilimab is the first-in-class bispecific antibody that simultaneously binds to PD-1 and CTLA-4.
- The interim analyses of PFS and OS in the COMPASSION-16 study both showed statistically significant benefits.(*The Lancet* ,IGCS 2024)[1]
  - PFS: 13.3 vs. 8.2 months, HR 0.62,p<0.0001
  - OS: NA vs. 22.8 months, HR 0.64, p=0.0011
- This time, we will present the pre-specified subgroup analyses, including prior CCRT history, bevacizumab use, age, etc. (DCO for this presentation was April 30, 2024.)

1. Wu X, Sun Y, Yang H, et al. Cadonilimab plus platinum-based chemotherapy with or without bevacizumab as first-line treatment for persistent, recurrent, or metastatic cervical cancer (COMPASSION-16): a randomised, double-blind, placebo-controlled phase 3 trial in China. The Lancet. 2024;404(10463):1668-1676. doi:10.1016/s0140-6736(24)02135-4

Study Design

- **Randomized, placebo-controlled, multicenter, double-blind, phase III trial**

Key eligibility Criteria

- Persistent, recurrent, or metastatic cervical cancer
- Histologically types include squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma.
- No prior systemic therapy.
- ECOG PS 0-1.

R 1:1

Cadonilimab Group(n=222)
Cadonilimab 10mg/kg+Paclitaxel 175mg/m²+Cisplatin 50mg/m² or Carboplatin AUC4-5 ± Bevacizumab 15mg/kg, q3w × 6

Maintenance therapy
Cadonilimab 10mg/kg ± Bevacizumab 15mg/kg, q3w

Placebo Group(n=223)
Placebo+Paclitaxel 175mg/m²+Cisplatin 50mg/m² or Carboplatin AUC4-5 ± Bevacizumab 15mg/kg, q3w × 6

Maintenance therapy
Placebo ± Bevacizumab 15mg/kg, q3w

✓ **Treatment continued until**
- disease progression
- unacceptable toxicity
- cadonilimab/placebo treatment for 2 years.

✓ Safety and survival follow-up are performed after the end of treatment.

Stratification factors:
- Prior CCRT(Yes vs No)
- Use of Bevacizumab (Yes vs No)

Primary Endpoints:
- PFS assessed by BICR according to RECIST v1.1
- OS

Second Endpoints:
PFS assessed by INV, ORR, DoR, DCR, TTR, Safety

Baseline characteristics

- **The baseline characteristics were well balanced.**

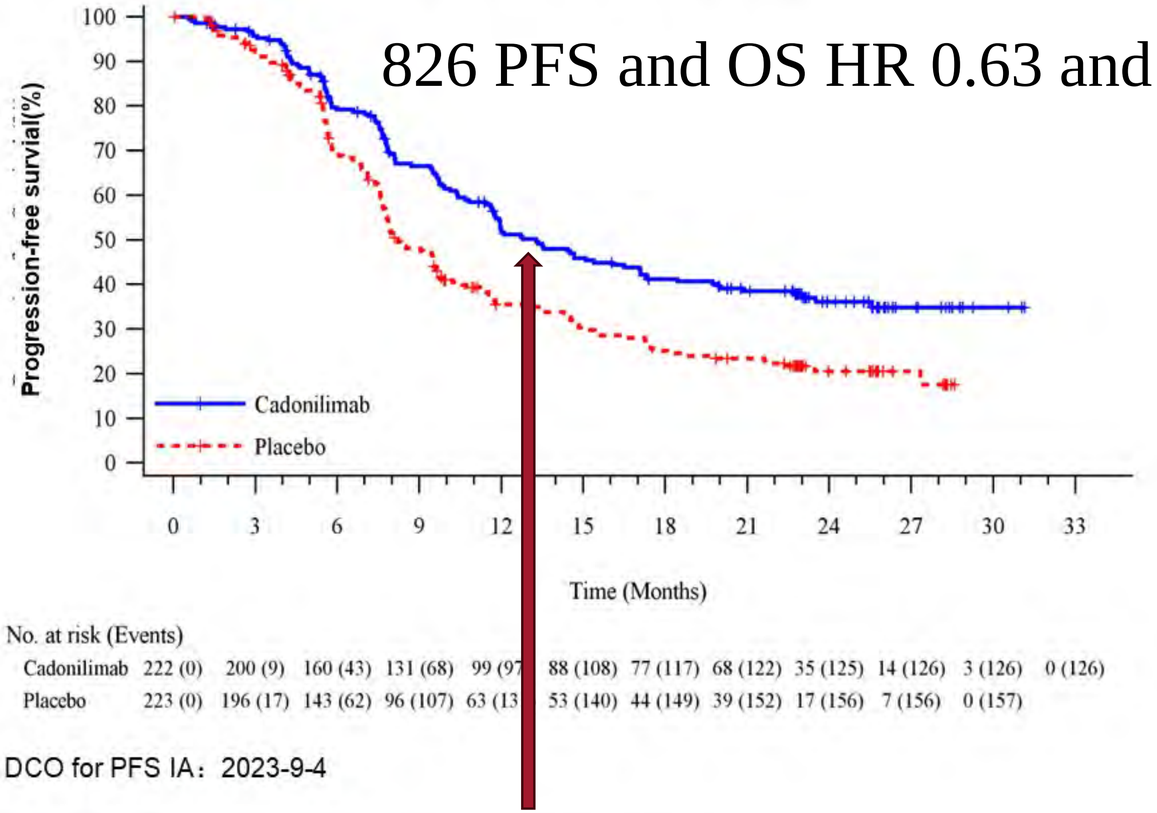
	Cadonilimab (N = 222)	Placebo (N = 223)
Age, median (range)	55.9(23,75)	55.6(23,75)
>=65y, n(%)	37 (16.7)	37 (16.6)
ECOG PS 1, n(%)	151 (68.0)	136 (61.0)
Squamous Cell Carcinoma, n(%)	182 (82.0)	188 (84.3)
FIGO Stage at initial diagnosis, n (%)		
I	47 (21.2)	40 (17.9)
II	43 (19.4)	54 (24.2)
IIIA	3 (1.4)	3 (1.3)
IIIB	17 (7.7)	17 (7.6)
IIIC	60 (27.0)	62 (27.8)
IVA	2 (0.9)	3 (1.3)
IVB	50 (22.5)	42 (18.8)
Unknown	0	2 (0.9)
Prior CCRT, n(%)	107 (48.2)	108 (48.4)
Cisplatin, n(%)	92 (41.4)	100 (44.8)
Bevacizumab Administration, n (%)	133 (59.9)	132 (59.2)

	Cadonilimab (N = 222)	Placebo (N = 223)
Metastasis Status, n (%)		
Yes	168 (75.7)	155 (69.5)
No	54 (24.3)	68 (30.5)
Common Sites of Metastasis, n (%)		
Lymph Nodes	87 (39.2)	83 (37.2)
Lung	72 (32.4)	71 (31.8)
Bone	28 (12.6)	28 (12.6)
Liver	21 (9.5)	20 (9.0)
Other	32 (14.4)	30 (13.5)
PD-L1 Expression, n (%)		
CPS<1	62 (27.9)	54 (24.2)
CPS 1 to <10	64 (28.8)	68 (30.5)
CPS>=10	91 (41.0)	89 (39.9)
Unknown	5 (2.3)	12 (5.4)

Primary Endpoints（Interim Analysis）：

- **Cadonilimab demonstrated statistically significant PFS and OS improvements.**

	Cadonilimab(n=222)	Placebo(n=223)
mPFS	13.3	8.2
	HR 0.62 (0.49,0.79) , p<0.0001	



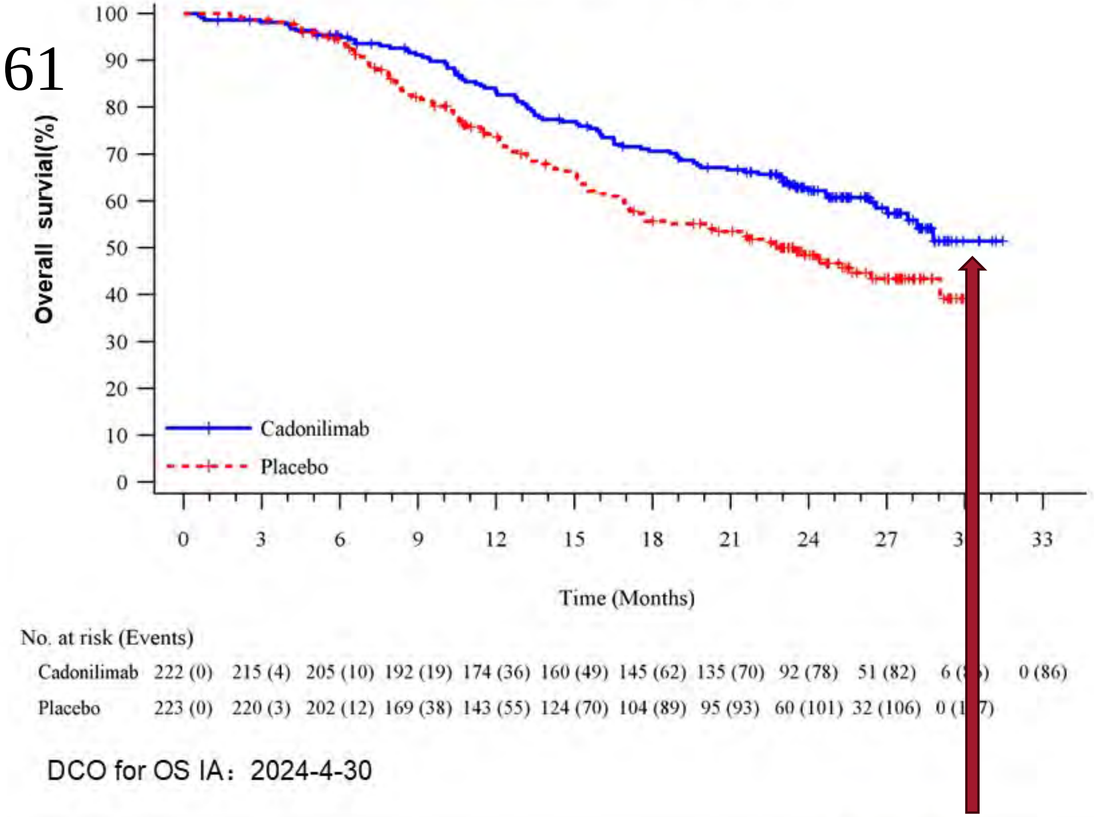
No. at risk (Events)

Cadonilimab	222 (0)	200 (9)	160 (43)	131 (68)	99 (97	88 (108)	77 (117)	68 (122)	35 (125)	14 (126)	3 (126)	0 (126)
Placebo	223 (0)	196 (17)	143 (62)	96 (107)	63 (13	53 (140)	44 (149)	39 (152)	17 (156)	7 (156)	0 (157)	

DCO for PFS IA：2023-9-4

826 PFS and OS HR 0.63 and 0.61

	Cadonilimab(n=222)	Placebo(n=223)
mOS	NA	22.8
	HR 0.64 (0.48,0.86) , p=0.0011	



No. at risk (Events)

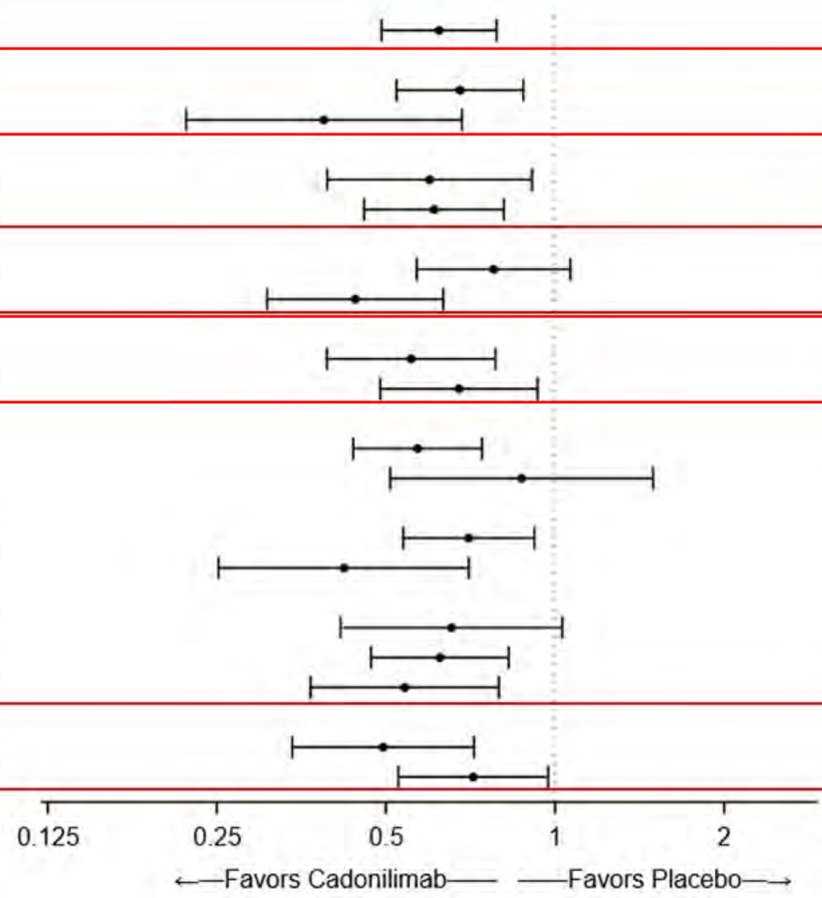
Cadonilimab	222 (0)	215 (4)	205 (10)	192 (19)	174 (36)	160 (49)	145 (62)	135 (70)	92 (78)	51 (82)	6 (	0 (86)
Placebo	223 (0)	220 (3)	202 (12)	169 (38)	143 (55)	124 (70)	104 (89)	95 (93)	60 (101)	32 (106)	0 (	

DCO for OS IA：2024-4-30

PFS：Subgroup analyses

- **All subgroups showed PFS benefits from cadonilimab.**

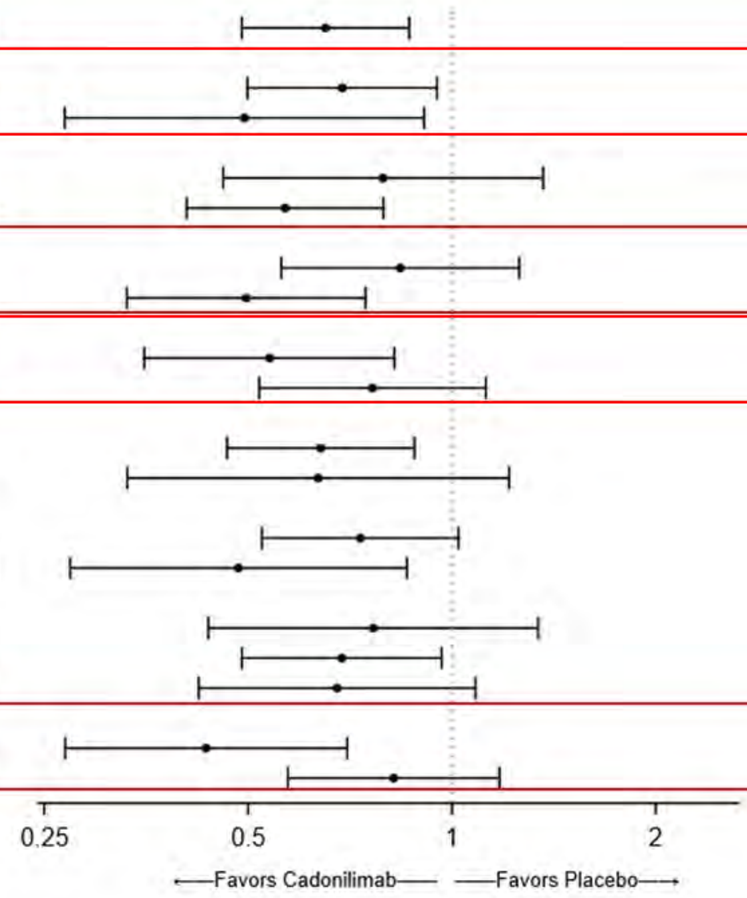
Subgroup	No. of Events/ No. of Patients: Cadonilimab	No. of Events/ No. of Patients: Placebo	Medain PFS, months (95% CI): Cadonilimab	Medain PFS, months (95% CI): Placebo	Hazard Ratio (95% CI)
Overall	126/222	157/223	13.3 (11.6, 17.1)	8.2 (7.7, 9.6)	0.62 (0.49, 0.79)
Age					
<65 years	105/185	126/186	13.5 (11.4, 17.3)	9.5 (7.8, 10.5)	0.68 (0.52, 0.88)
≥65 years	21/37	31/37	12.0 (8.1, NA)	7.4 (5.7, 8.4)	0.39 (0.22, 0.68)
ECOG performance-status					
0	36/71	57/87	17.1 (11.8, NA)	10.7 (7.9, 14.3)	0.60 (0.39, 0.91)
1	90/151	100/136	12.0 (9.7, 15.4)	7.8 (6.9, 8.5)	0.61 (0.46, 0.81)
Concomitant bevacizumab					
Yes	74/133	82/132	15.1 (11.8, 20.9)	11.5 (9.5, 15.5)	0.78 (0.57, 1.06)
No	52/89	75/91	11.7 (9.5, 14.7)	6.7 (5.6, 7.8)	0.44 (0.31, 0.63)
Prior CCRT					
Yes	58/107	76/108	16.1 (11.6, 20.9)	7.9 (7.5, 11.5)	0.55 (0.39, 0.78)
No	68/115	81/115	12.0 (9.7, 14.7)	8.5 (7.7, 9.7)	0.67 (0.49, 0.93)
Pathological Diagnosis					
Squamous cell carcinom	96/182	133/188	15.1 (11.7, 20.9)	8.1 (7.8, 9.7)	0.57 (0.44, 0.74)
Non-Squamous cell carc	30/40	24/35	11.0 (7.5, 12.7)	8.2 (5.6, 17.4)	0.87 (0.51, 1.50)
Metastatic					
Yes	104/168	110/155	12.0 (10.4, 15.1)	8.3 (7.7, 9.7)	0.70 (0.54, 0.92)
No	22/54	47/68	NA (11.9, NA)	8.0 (7.1, 11.7)	0.42 (0.25, 0.70)
PD-L1 combined positive s					
<1	37/62	39/54	12.0 (9.5, 17.1)	8.2 (7.8, 11.8)	0.65 (0.42, 1.03)
≥1	87/155	110/157	14.7 (11.4, 19.9)	8.3 (7.5, 9.7)	0.62 (0.47, 0.83)
≥10	46/91	60/89	17.1 (11.4, NA)	8.1 (6.9, 11.3)	0.54 (0.37, 0.79)
Cisplatin/Carboplatin					
Cisplatin	46/92	72/100	14.7 (11.8, NA)	8.1 (7.6, 11.7)	0.49 (0.34, 0.72)
Carboplatin	80/130	85/123	12.0 (9.6, 16.5)	8.2 (7.7, 9.7)	0.72 (0.53, 0.97)



OS： Subgroup analyses

- **All subgroups showed OS benefits from cadonilimab.**

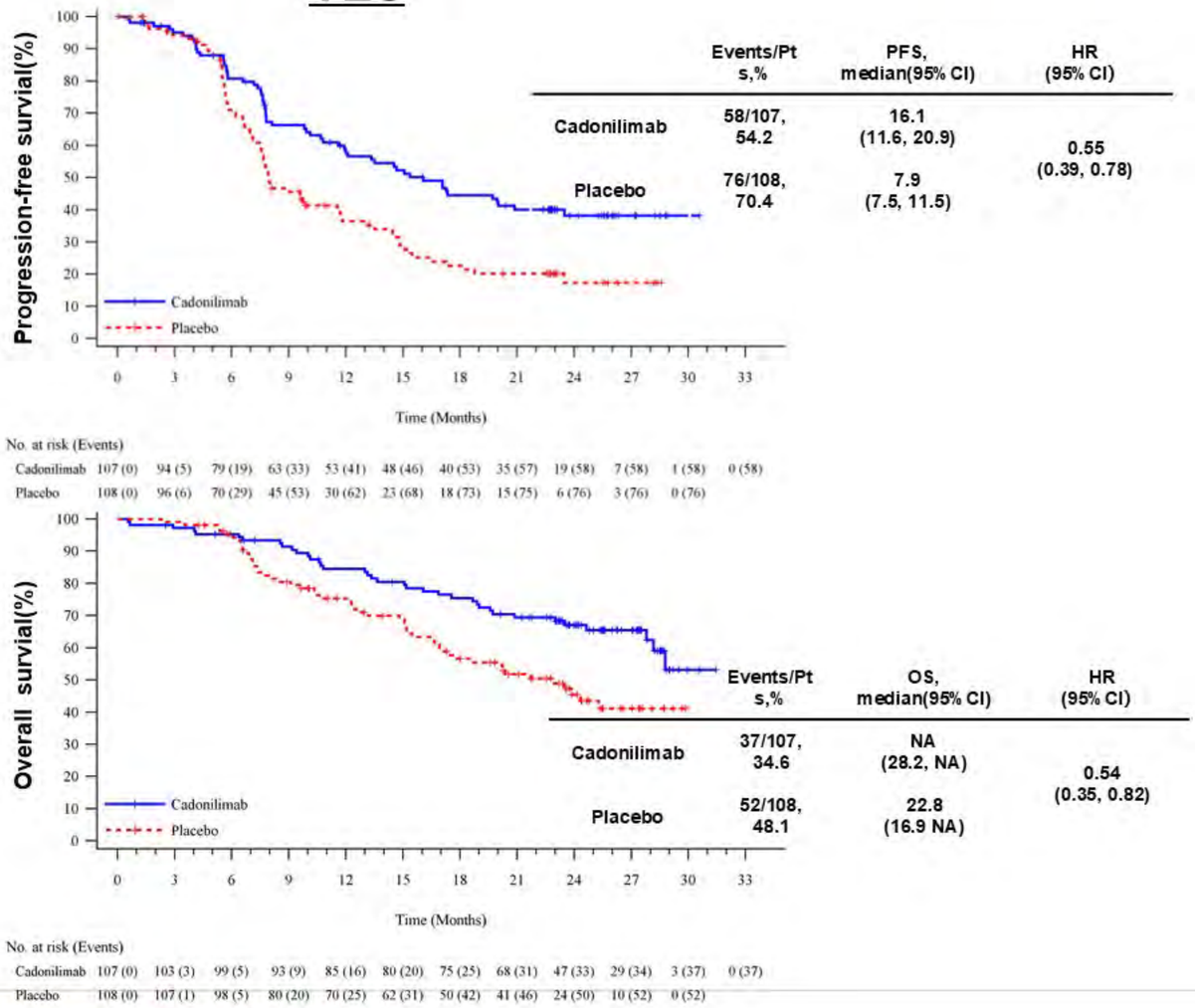
Subgroup	No. of Events/ No. of Patients: Cadonilimab	Placebo	Medain OS, months (95% CI): Cadonilimab	Placebo	Hazard Ratio (95% CI)
Overall	86/222	107/223	NA (27.0, NA)	22.8 (17.6, 29.0)	0.65 (0.49, 0.87)
Age					
<65 years	68/185	82/186	NA (27.8, NA)	25.3 (21.6, NA)	0.69 (0.50, 0.95)
≥65 years	18/37	25/37	26.6 (16.5, NA)	15.1 (9.6, 17.1)	0.49 (0.27, 0.91)
ECOG performance-status sc					
0	23/71	30/87	NA (27.0, NA)	NA (22.7, NA)	0.79 (0.46, 1.36)
1	63/151	77/136	28.8 (24.6, NA)	17.1 (15.1, 24.3)	0.57 (0.41, 0.79)
Concomitant bevacizumab					
Yes	47/133	47/132	NA (27.8, NA)	NA (25.7, NA)	0.84 (0.56, 1.26)
No	39/89	60/91	28.2 (17.5, NA)	15.1 (12.2, 17.6)	0.50 (0.33, 0.75)
Prior CCRT					
Yes	37/107	52/108	NA (28.2, NA)	22.8 (16.9, NA)	0.54 (0.35, 0.82)
No	49/115	55/115	27.0 (23.2, NA)	24.5 (15.7, NA)	0.76 (0.52, 1.12)
Pathological Diagnosis					
Squamous cell carcinoma	67/182	88/188	NA (27.0, NA)	23.5 (17.6, NA)	0.64 (0.47, 0.88)
Non-Squamous cell carcinc	19/40	19/35	27.8 (19.1, NA)	22.4 (12.6, NA)	0.63 (0.33, 1.22)
Metastatic					
Yes	68/168	70/155	28.8 (26.3, NA)	25.3 (17.7, NA)	0.73 (0.52, 1.02)
No	18/54	37/68	NA (28.2, NA)	17.6 (15.1, 26.4)	0.48 (0.27, 0.86)
PD-L1 combined positive scor					
<1	25/62	24/54	NA (23.0, NA)	25.3 (17.7, NA)	0.77 (0.44, 1.34)
≥1	61/155	74/157	NA (26.6, NA)	22.7 (15.5, NA)	0.69 (0.49, 0.97)
≥10	33/91	37/89	NA (26.6, NA)	29.0 (16.5, NA)	0.68 (0.42, 1.08)
Cisplatin/Carboplatin					
Cisplatin	26/92	48/100	NA (NA, NA)	23.9 (17.7, NA)	0.43 (0.27, 0.70)
Carboplatin	60/130	59/123	27.8 (20.9, NA)	22.8 (15.7, NA)	0.82 (0.57, 1.18)



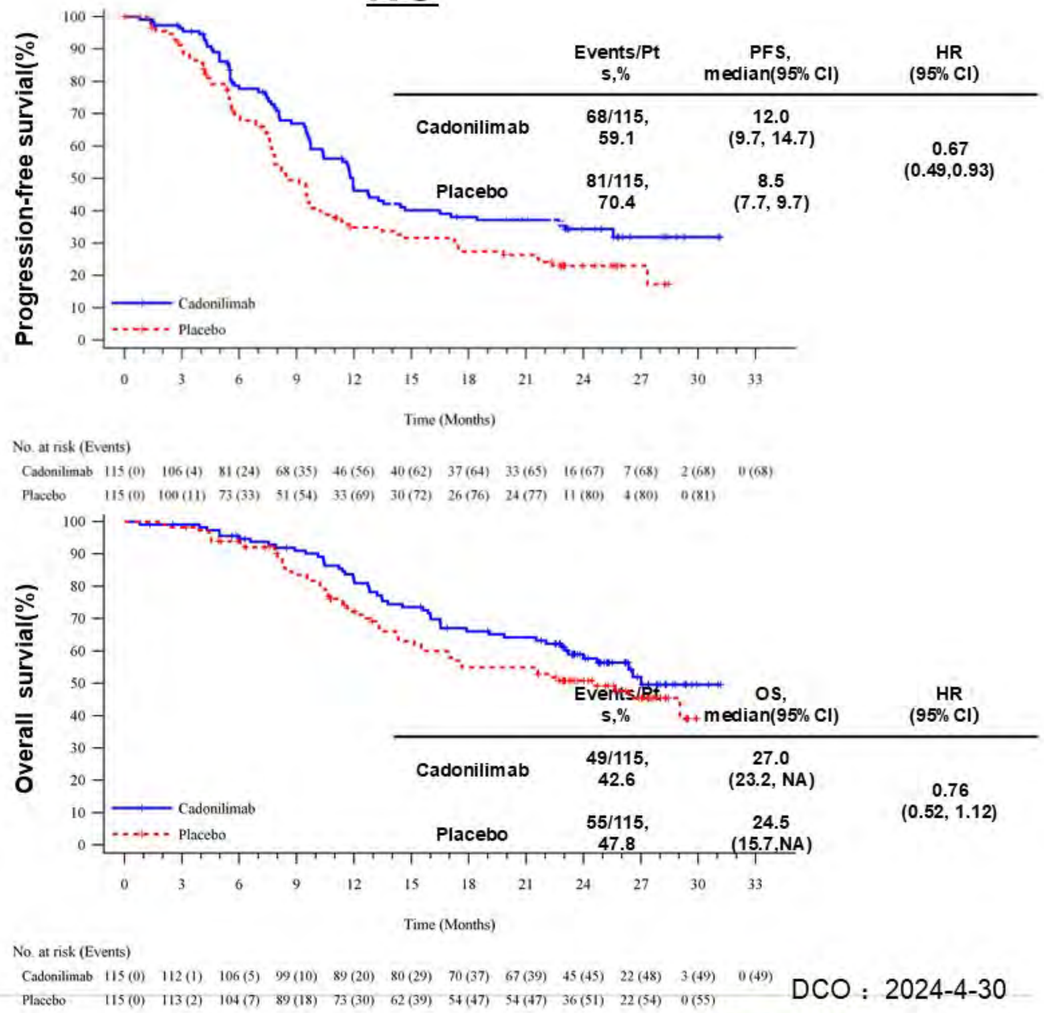
Stratification subgroups： Prior CCRT

- **Both PFS and OS showed clinically meaningful benefits, irrespective of prior CCRT.**

YES



NO



DCO： 2024-4-30

Conlusions

- Pre-specified subgroup analyses of the phase 3 COMPASSION-16 study showed that the addition of cadonilimab improved PFS and OS, consistent with results in the overall population.
  - ✓In stratification subgroups (prior CCRT and bevacizumab use), the benefit trend of cadonilimab was consistent with that in the overall population.
  - ✓Notably, cadonilimab showed greater benefit in patients with prior CCRT, no bevacizumab use, and age ≥65.
- These findings further support cadonilimab as a first-line therapeutic option for recurrent or metastatic cervical cancer.

2025 ASCO® ANNUAL MEETING

Nimotuzumab combined with chemotherapy in the first-line treatment for patients with stage IVB, recurrent or persistent cervical squamous cell carcinoma: a multi-center, randomized, double-blind, and controlled study

Jusheng An[1], Jing Wang[2], Chunyan Wang[3], Qi Zhou[4], Rutie Yin[5], Xinfeng Yang[6], Huijun Cheng[7], Hanmei Lou[8], Yunong Gao[9], Ge Lou[10], Pengpeng Qu[11], Hongying Yang[12], Cailing Ma[13], Yumei Wu[14], Qiubo Lv[15], Junjie Wang[16], Zexuan Liu[17], Lingying Wu[18]

[1]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [2]Hunan Cancer Hospital,The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; [3]Cancer Hospital of China Medical University, Liaoning Cancer Hospital and Institute, Shenyang, China; [4]Chongqing University Cancer Hospital, Chongqing, China; [5]West China Second University Hospital, Chengdu, China; [6]Jiangxi Provincial Cancer Hospital, Nanchang, China; [7]Henan Cancer Hospital/Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China; [8]Zhejiang Provincial Cancer Hospital, Hangzhou, China; [9]Beijing Cancer Hospital, Beijing, China; [10]Harbin Medical University Caner Hospital, Harbin, China; [11]Tianjin Central Obstetrics and Gynecology Hospital, Tianjin, China; [12]Peking University Cancer Hospital Yunnan, Yunnan Cancer Hospital, The Third Affiliated Hospital Kunming Medical University, Kunming, China; [13]Department of Gynecology, The First Affiliated Hospital of Xinjiang Medical University, Urumqi, China; [14]Beijing Obstetrics and Gynecolgoy Hospital, Capital Medical University, Beijing, China; [15]Beijing Hospital, Beijing, China; [16]Peking University 3rd Hospital, Beijing, China; [17]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [18]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.

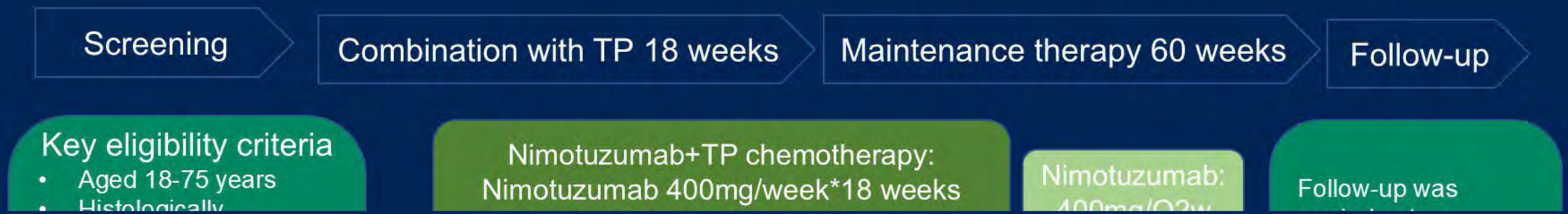
Key Takeaway Points

Incorporating nimotuzumab into first-line chemotherapy for recurrent or persistent cervical cancer demonstrate improved progression-free survival and overall survival

Nimotuzumab combined with chemotherapy should be considered as a new first-line therapy option

Study design

A multi-center, randomized, double-blind, controlled study

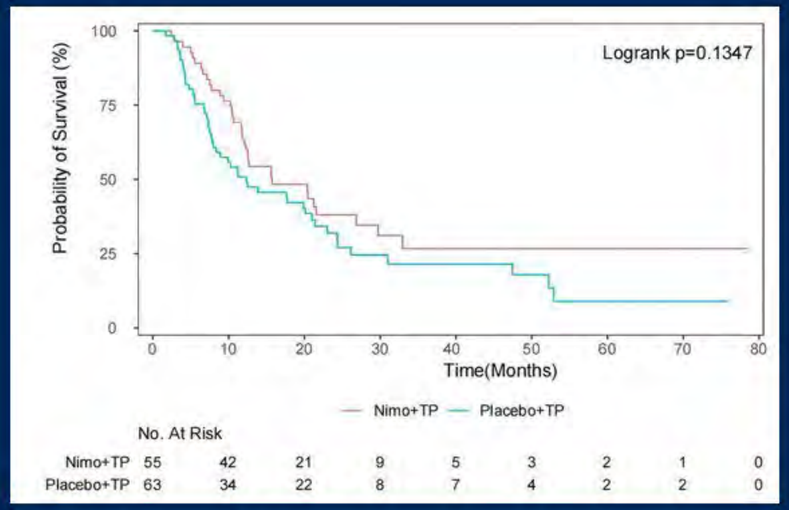


- Epidermal growth factor receptor (EGFR) overexpression is demonstrated in 80% of cervical cancers and associated with reduced survival[3-4]
- Nimotuzumab is an IgG1 humanized monoclonal antibody directed against the extracellular domain of the EGFR

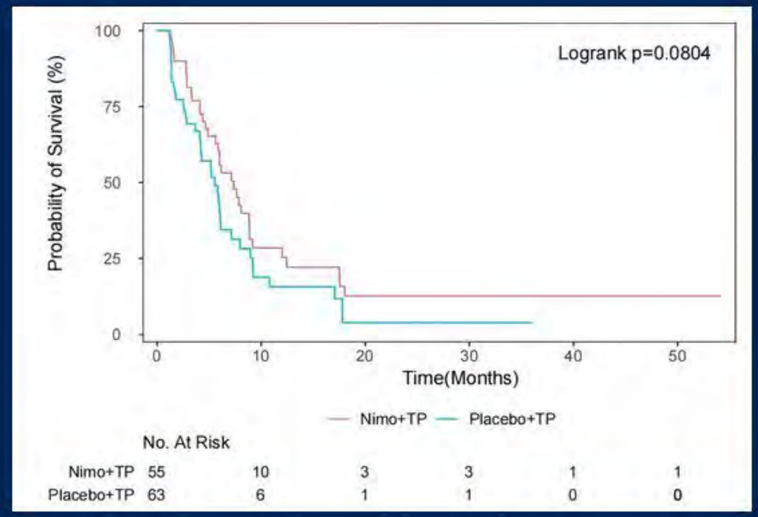
Overall survival (OS), Progression free survival (PFS), Objective response rate (ORR), Quality of life (QoL), Paclitaxel+cisplatin (TP)

Endpoints

OS



PFS



	Nimo+TP n=55 (95%CI)	Placebo+TP n=63 (95%CI)	HR (95%CI)
Median OS	15.7 (11.8, 26.9)	12.4 (7.9, 21)	0.72 (0.46, 1.11)
Median PFS	7.4 (4.9, 8.9)	5.6 (4.1, 6.1)	0.66 (0.42, 1.05)

Conclusions

- Incorporation of nimotuzumab into chemotherapy in the first-line treatment for recurrent or persistent cervical cancer could have an improvement on progression-free survival outcomes
- Combination therapy demonstrates well-tolerated toxicity

Better than bev?

- Nimotuzumab combined with chemotherapy should be considered as a new first-line therapy option in recurrent or persistent cervical cancer

+ 1 VULVAR CANCER ABSTRACT…

WAGO
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2025 ASCO ANNUAL MEETING

Primary results of a Phase 2 study of cisplatin-sensitized radiation therapy and pembrolizumab for unresectable vulvar cancer

Oladapo Yeku, Andrea Russo, Amy Bregar, Jeff Brower, Dinesh Atwal, Sara Bouberhan, Meghan Shea, Page Widick, Joanne W. Jang, Tina Colella, Jenny Filipi, Eric L. Eisenhauer, Chryssanthi S. Kournioti, Annekathryn Goodman, Richard Penson, Hang Lee, and Cesar Castro.

Oladapo Yeku, MD, PhD, FACP
Director of Translational Research, Gynecologic Oncology Program
Massachusetts General Hospital
Assistant Professor, Harvard Medical School

Key Takeaway Points

1

The study met its primary endpoint, demonstrating an objective response rate of 75%. The 6-month Recurrence Free Survival was 70% (95% CI: 48 - 85%)

2

Concurrent and maintenance pembrolizumab with cisplatin and radiation (cis-RT) for a total of 12 cycles, is safe in patients with vulvar cancer

3

This regimen is a reasonable option for patients with locally advanced or unresectable vulvar cancer

PRESENTED BY: Oladapo Yeku, MD, PhD, FACP

Study Design

Patients with **locally advanced, unresectable, metastatic, or recurrent squamous cell** carcinoma of the vulva

Day -28 to -1
Staging scans
Screening labs
Archival tissue

Cycle 1-3

Pembrolizumab (Q3 weeks)
Cisplatin (Q week)
Radiation (Daily x 2- 8 weeks)

Restaging scans

Cycle 4 - Cycle 12 (Maintenance)

Pembrolizumab (Q3 weeks)

EOT

Follow up

- **Primary Endpoint**: Overall Response Rate (ORR)
- **Secondary Endpoint**: 6-month recurrence free survival (RFS-6)
- **Exploratory Endpoints**: Increase in T-cell receptor beta clonality, changes in circulating cytotoxic T-cells, cytokine profiling, HMGB-1, PD-L1 expression, mismatch repair status, HPV status, p53 mutation.

Patient Characteristics

Characteristic	Pembrolizumab + Cisplatin/RT (N = 24)
Age	
Median (range) - yr	63 (49 – 88)
Ethnicity	
White non-Hispanic	22 (92)
Hispanic	2 (8)
FIGO stage no. (%)	
I	4 (17)
II/III	17 (71)
IV	3 (13)
HPV	
Positive no. (%)	5 (21)
Negative no. (%)	15 (63)
Unknown no. (%)	4 (17)
Mismatch repair status no. (%)	
MSS	18 (75)
MSI-H	0 (0)
Unknown	6 (24)

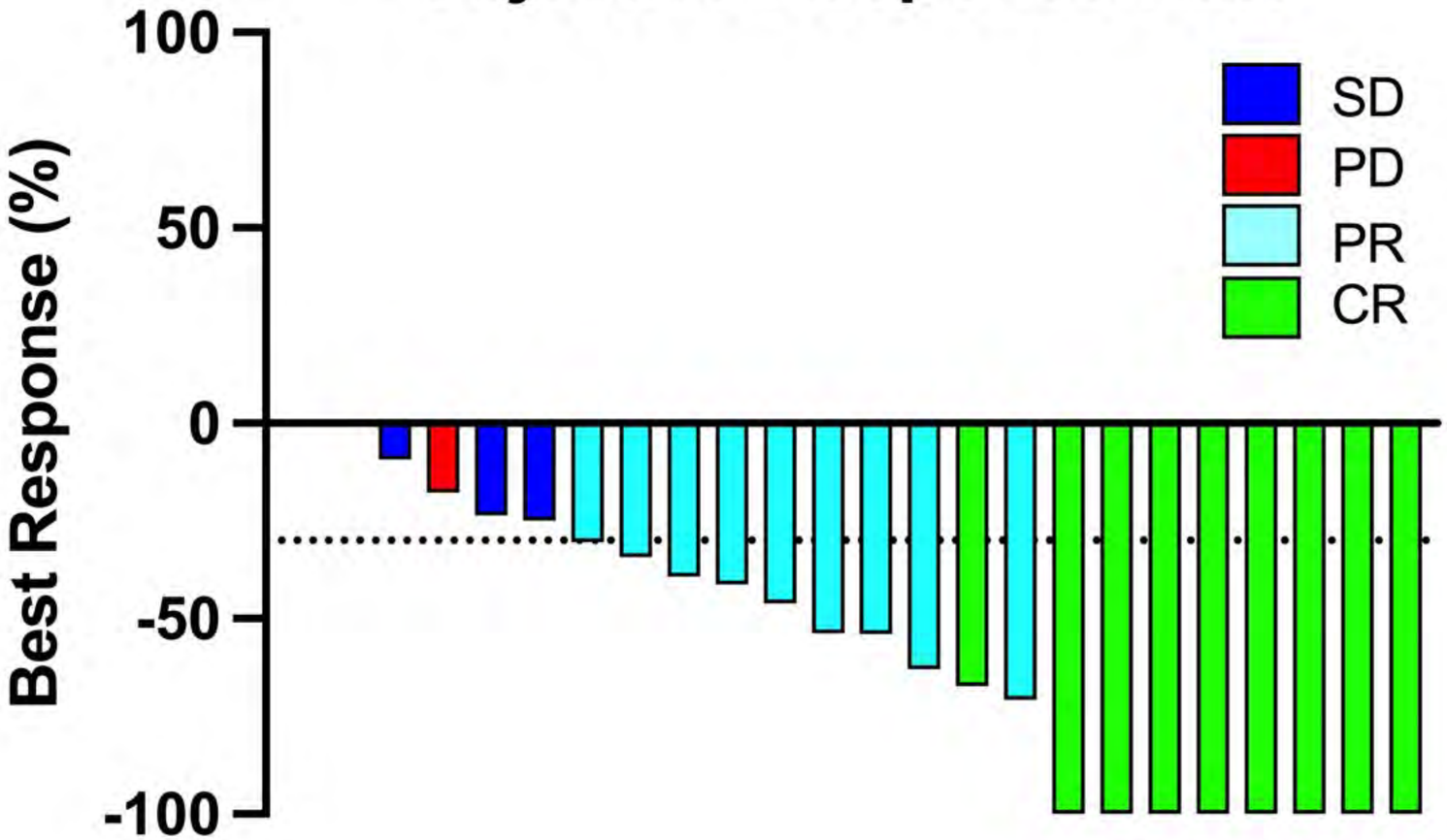
Characteristic	Pembrolizumab + Cisplatin/RT (N = 24)
p53 status no. (%)	
Wild type	6 (25)
Null/mutant	9 (38)
Unknown	9 (38)
PD-L1 CPS no. (%)	
> 10	15 (63)
1 - 10	9 (38)
< 1	0 (0)
Prior Therapy no. (%)	
None	17 (71)
Surgical resection	5 (21)
Cis-Radiation	2 (8)
Systemic chemotherapy	0 (0)
TMB no. (%)	
High	1 (4)
Low	13 (54)
Unknown	10 (42)

Radiation Treatment

- All patients were treated with definitive intent RT, with a median dose to the primary of 68.4 Gy (range, 26.2, 70.2) and 45 Gy to pelvic, inguinal, vulva CTV (range, 21.6, 50.4).

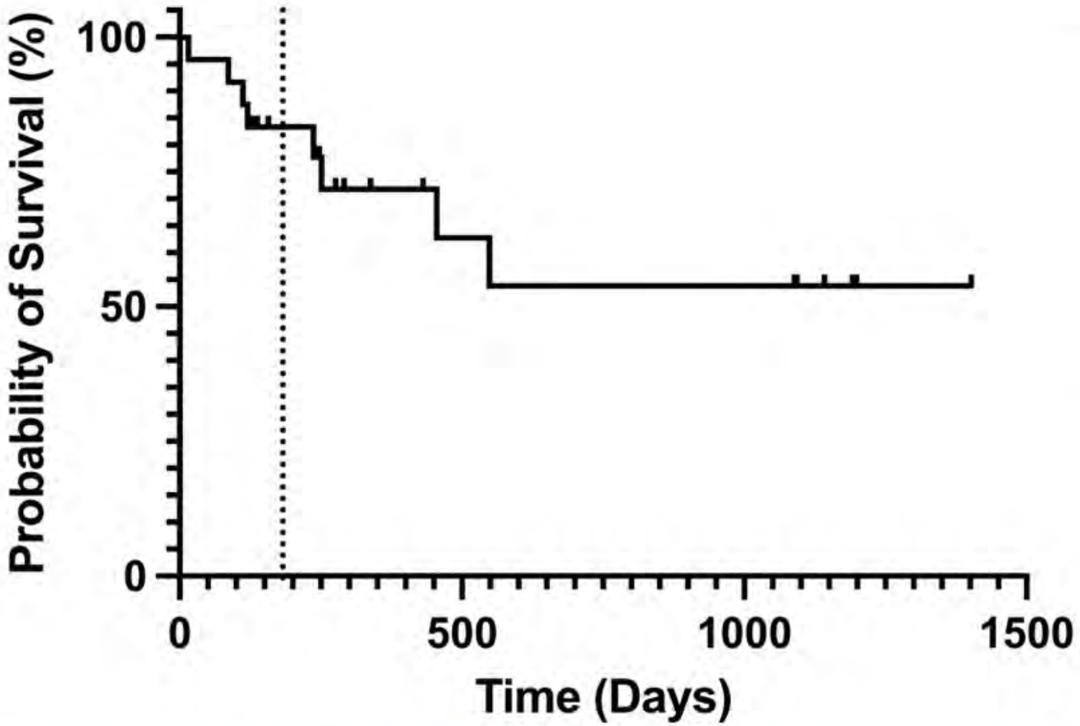
Overall Response Rate and Duration of Response

Objective Response Rate

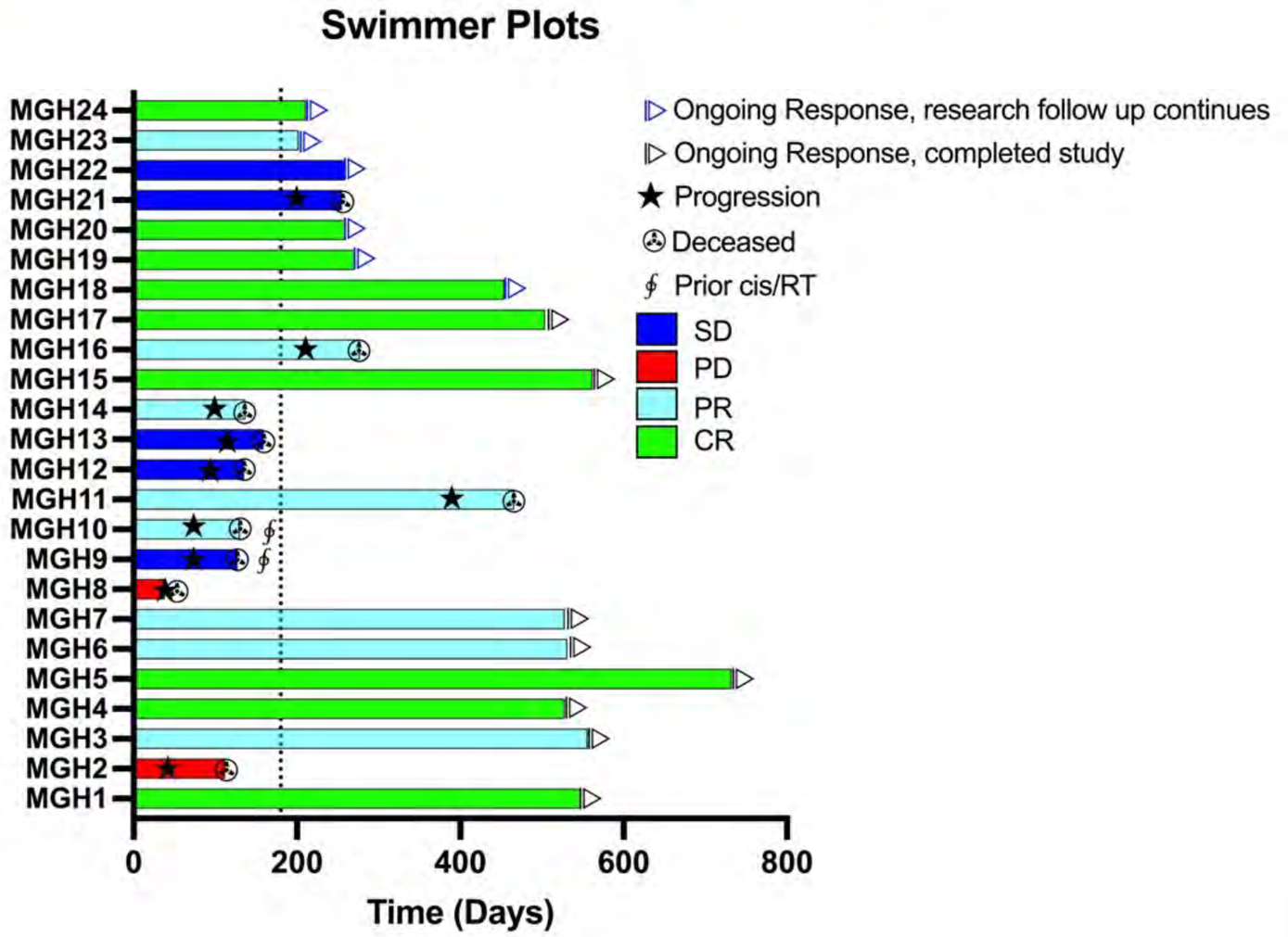


Best Response	
CR	9 (37.5%)
PR	9 (37.5%)
ORR	**18 (75%)**

Overall Response Rate and Duration of Response



Recurrence Free Survival at 6 Months	70% (95% CI: 48% - 85%)



Immune Related Adverse Events

	Grade 1 or 2	Grade 3 or 4
	Number of patients (percent)	
Immune Related Adverse Events		
Lymphocyte count decreased	1 (4)	0 (0)
Diarrhea	6 (25)	2 (8)
Constipation	1 (4)	0 (0)
Nausea	2 (8)	0 (0)
Colitis	1 (4)	0 (0)
Alanine aminotransferase increased	1 (4)	0 (0)
Pruritus	3 (13)	0 (0)
Rash maculo-papular	3 (13)	0 (0)
Dermatitis radiation	0 (0)	1 (4)
Hypothyroidism	3 (13)	0 (0)
Infusion related reaction	1 (4)	0 (0)
Acute Kidney Injury	1 (4)	0 (0)
Fatigue	8 (33)	1 (4)

Conclusions

- The study **met its primary endpoint, demonstrating an overall objective response rate of 75%.** The 6-month Recurrence Free Survival was 70% (95% CI: 48 - 85%).

- Pembrolizumab administered concurrently with cisplatin and radiation (cis-RT), and as maintenance for a total of 12 cycles is safe in patients with locally advanced, unresectable, or metastatic squamous cell carcinoma of the vulva.

- This regimen is a reasonable option for patients with advanced or unresectable vulvar cancer.

Thank you!

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