Domenica Lorusso

3°Edizione

I tumori femminili

Dal gene profiling alla terapia personalizzata

22-23 Novembre 2023

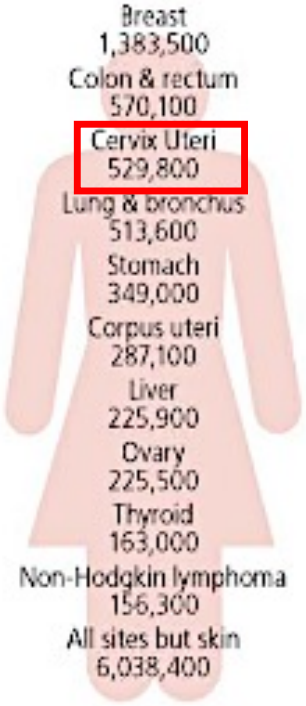
Casale Monferrato, AL

Hotel Candiani

Carcinoma della cervice

Terapia Medica: la rivoluzione dell'immunoterapia

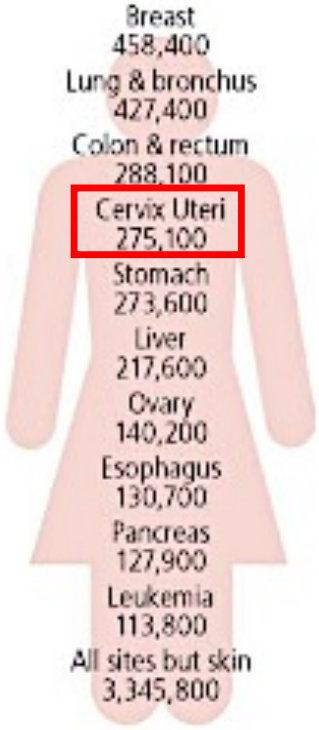
The global burden of cancer on women worldwide



9% of all new cancer cases
>58,000 new cases every year

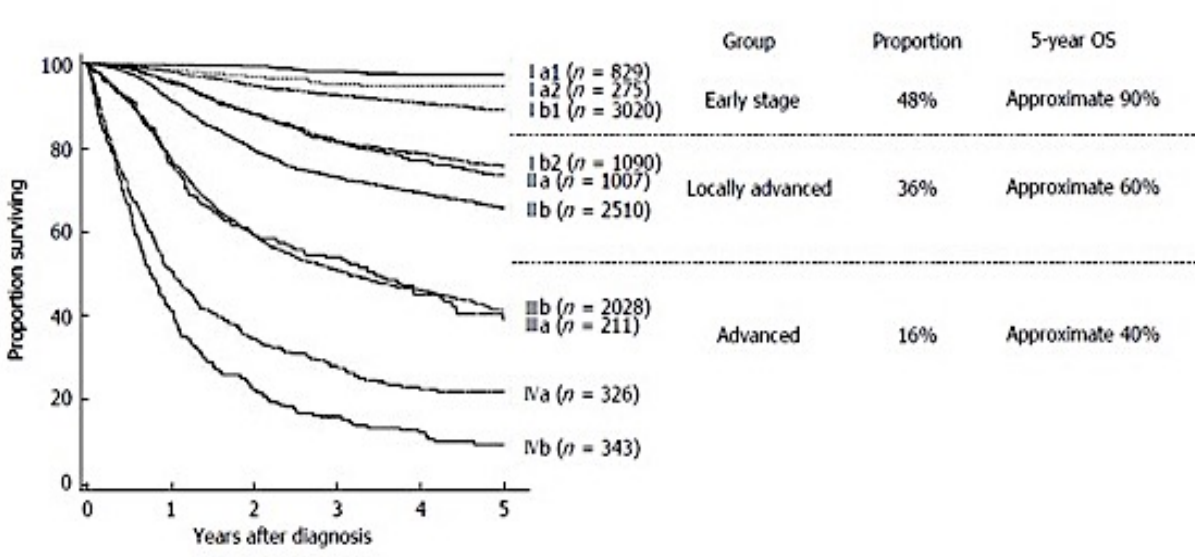
8% of total cancer deaths
>24,000 deaths every year

85% of new cases
87% of deaths occur in developing countries



Jemal A et al. *CA Cancer J Clin* 2011;61:69–90.

Cervical cancer: 5-year survival according to stage



- Early stage CC may be cured by radical surgery with tailored adjuvant therapy
- Patients diagnosed with locally advanced disease (FIGO IB2-IVA) despite radical chemoradiation experience 5-year DFS and OS of 47–80%
- The management of women with advanced (FIGO stage IVB) and recurrent disease has represented an unmet clinical need for decades.

OS, overall survival; PFS, progression-free survival.
Cancer Stat Facts: Cervical Cancer. https://seer.cancer.gov/statfacts/html/cervix.html. Accessed 21 March 2022.

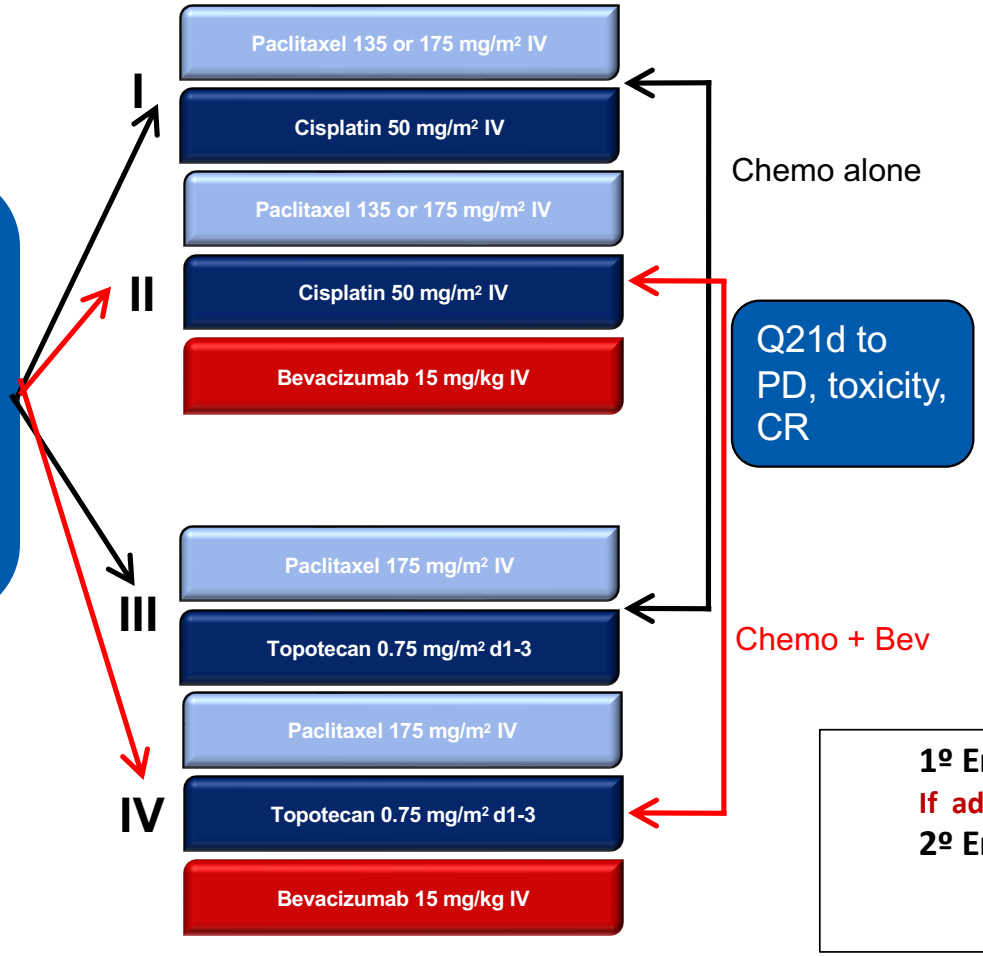
GOG #240: Incorporation of Bevacizumab in the treatment of Recurrent and Metastatic Cervical Cancer: Schema

Activated: 4/6/09
Closed to accrual: 1/3/12

Carcinoma of the cervix
- Primary stage IVB
- Recurrent/persistent
- Measureable disease
- GOG PS 0–1
- No prior chemotherapy for recurrence

(N=452)

Stratification factors:
- Stage IVB vs recurrent/persistent disease
- Performance status
- Prior cisplatin Rx as radiation-sensitizer



1º End-Points:

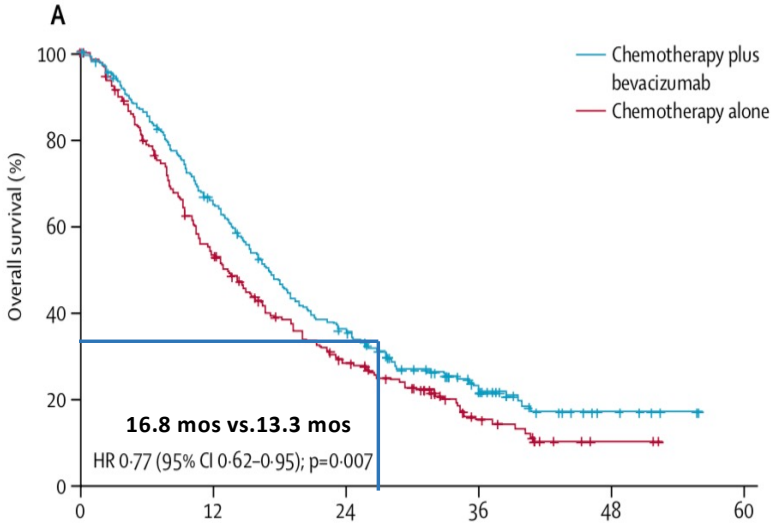
If adding BEV to Chemo improves OS

2º End-Points:
- **PFS**
- **ORR**

Tewari KS, et al. *N Engl J Med* 2014;370:734-43

GOG #240: Bevacizumab in the treatment of Recurrent and Metastatic Cervical Cancer

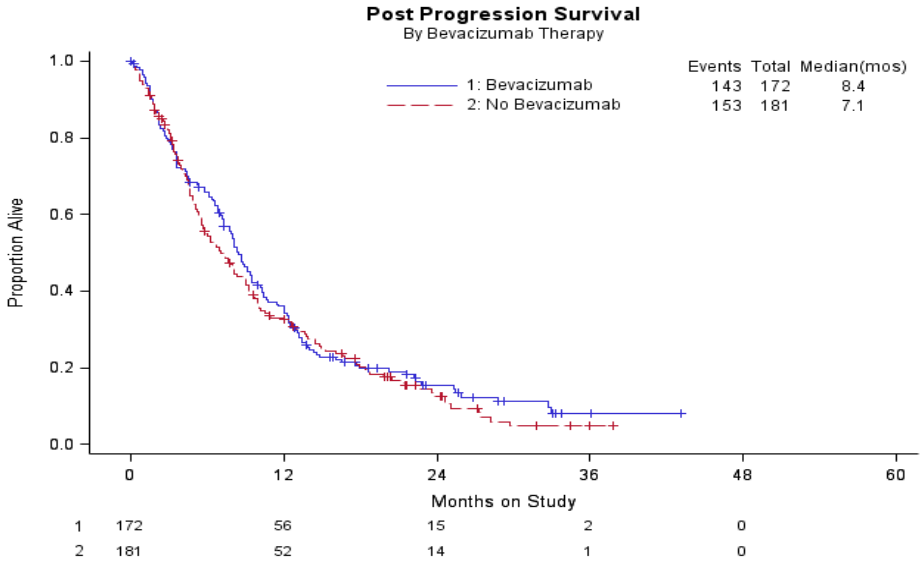
Mature Overall Survival



Number at risk (number censored)						
Chemotherapy plus bevacizumab	227 (0)	142 (9)	75 (12)	30 (31)	6 (51)	0 (57)
Chemotherapy alone	225 (0)	114 (9)	54 (18)	17 (35)	2 (45)	0 (47)

Tewari KS, et al. *Lancet*. 2017;390(10103):1654-1663

Mature Post-Progression Overall Survival



Regimen for 2L+ Metastatic Cervical Cancer

Design	N	ORR (%)	PFS (months)	OS (months)
Topotecan	45	12.5	2.1	6.6
Vinorelbine	44	13.7	NS	NS
Pemetrexed	29	15	3.1	7.4
Pemetrexed	43	13.9	2.3	8.05
Docetaxel	27	8.7	3.8	7.0
Gemcitabine	22	4.5	2.1	6.5
Bevacizumab	46	10.9	3.4	7.29

Yu et al. *Am J Hematol Oncol.* 2015;11:27-31.

What is the Rationale to Pursue ICI in Cervical Cancer?

1.Cervical Cancer is a Virally Driven Cancer:

- Almost all cases are driven by **HPV infection.** The virus has evolved many ways of evading the immune system

2. Immune-Privilege State: PD-L1 expression and Tumour Infiltrating Lymphocytes(TILs)

- **PD-L1 is** not expressed in normal cervical tissue, but is **overexpressed in SCC(19% to 88%) and Adenocarcinoma(14%)**
- The tumour microenvironment(the composition of) has an impact on survival rates:
  - Patients w negative LN have higher numbers of intraepithelial CD8+ cells than positive LN patients

3. Cervical Cancers Have an Increased Tumor Mutational Burden(TMB) Rate

- The rate of **TMB in cervical cancers is about 5-6 mutations per megabase**(behind melanoma, lung, bladder, oesophageal and colorectal cancers)
- Increased TMB lead to the presence of more neoantigens that then stimulate the immune system.

Smola, S, et al. *Ther Adv Vaccines.* 2017;5(3):69-82.Dyer et al JNCCN; Volume 17 Number 1 January 2019
S.J. Otter et al. / Clinical Oncology 31 (2019) 834e843; J. Otter et al. / Clinical Oncology 31 (2019) 834e843; Piersma SJ et al; Cancer Res 2007; 67: (1). January 1, 2007Alexandrov LB et al Nature 2013;500:415e421; S.J. Otter et al. Clinical Oncology 31 (2019) 834e843

Summary of ICI's Activity following Failure to Platinum

Early Development: Phase I/II Clinical Trials

	Keynote-158	Checkmate 358	Balstilimab
Population	Advanced cervical cancer with progression on or intolerance to ≥1 line of prior therapy. **Regardless of PD-L1 Status**	Recurrent or metastatic cervical cancer HPV+ **Regardless of PD-L1 Status**	Recurrent/Metastatic Cervical Cancer. **Regardless of PD-L1 status**
N. patients	98	19	140
Histology	Squamous cell carcinoma (93.9%) **Adenocarcinoma (5.1%)** Adenosquamous (1.0%)	Squamous cell (100%)	Squamous cell carcinoma (60%) **Adeno/AdenoSq. (40%)**
N. of prior lines	No. of previous lines of therapy • Adjuvant and/or neoadjuvant (4.1%) • 1 line (30.6%) • 2 lines (34.7%) • 3+ lines (30.6)	Prior lines of systemic therapy • 1 line (42.1%) • 2 lines (42.1%) • 3+ lines (15.8%)	Prior systemic therapy (PST) in the R/M setting • 1 (99%) • >1 (1%)
Biomarkers	CPS ≥ 1% (83.7%)	PD-L1 ≥ 1%	CPS ≥ 1 (61%)
Type of treatment	**Pembrolizumab**	**Nivolumab**	**Bastilimab**
ORR	Overall: 14.3% **CPS ≥ 1% 17%** **CPS< 1%:0%**	Overall: 26.3% ***PD-L1 positive: 20%** **PD-L1 negative: 16.7%**	Overall:15% **CPS ≥ 1% 20%** **CPS< 1%:7.9%**
mDOR	NR	NR	15.4
mPFS / 6-m PFS	Overall: 2.1m / 25% PD-L1 positive: 21.m / 25%	5.1m	NA
mOS / 6-m OS	Overall: 9.4m / 75.2% PD-L1 positive: 11m / 80.2%	21.9m	NA
Safety: % Grade 3-4 TRAE / % discontinuation due to TRAE	12.2% / 4.1%	15.8% / 5.3%	11.8%/4.3%

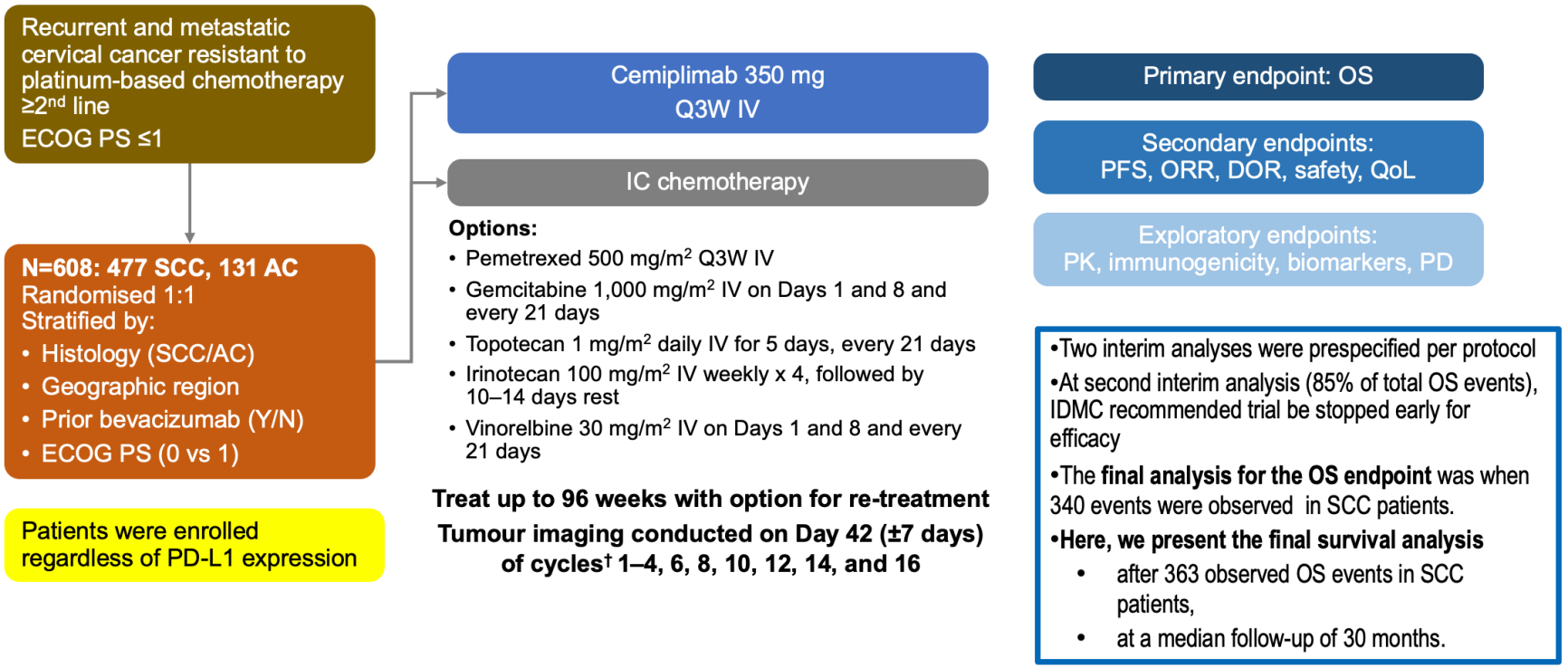
Pembrolizumab FDA approval (June 2018): patients with recurrent or metastatic cervical cancer who had **progressed on or after platinum-based** chemotherapy and whose tumours **express CPS ≥1** as determined by an FDA-approved test

*Tumor cell PD-L1 expression was defined as the percentage of tumor cells exhibiting membrane staining at any intensity

Chung HC et al; J Clin Oncol 2019 Jun 10;37(17); Naumann RW et al J Clin Oncol. 2019 Sep 5;O'Malley et al; Presented ar ESMO Virtual Meeting 2020

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9

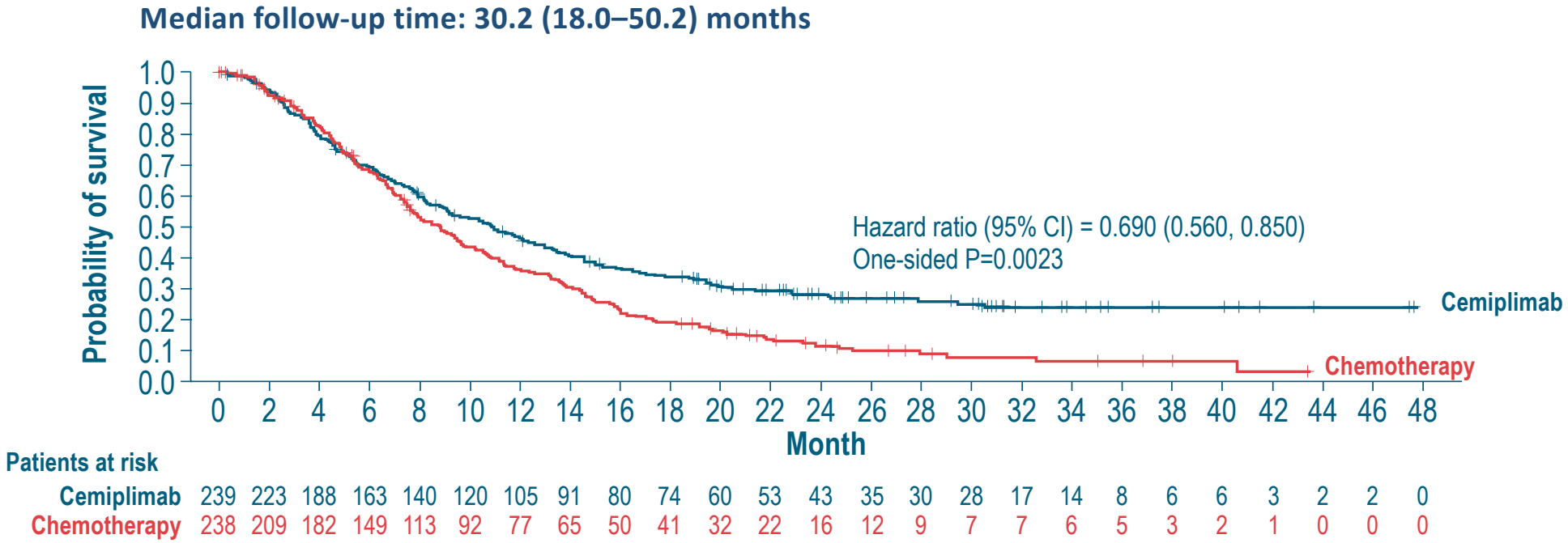
Study Design



Tewari K et al. N Engl J Med 2022;386:544-55; Oaknin A et al. Presented at ESMO Congress 2022

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9

Cemiplimab monotherapy significantly improved OS vs chemotherapy in patients with squamous cell histology

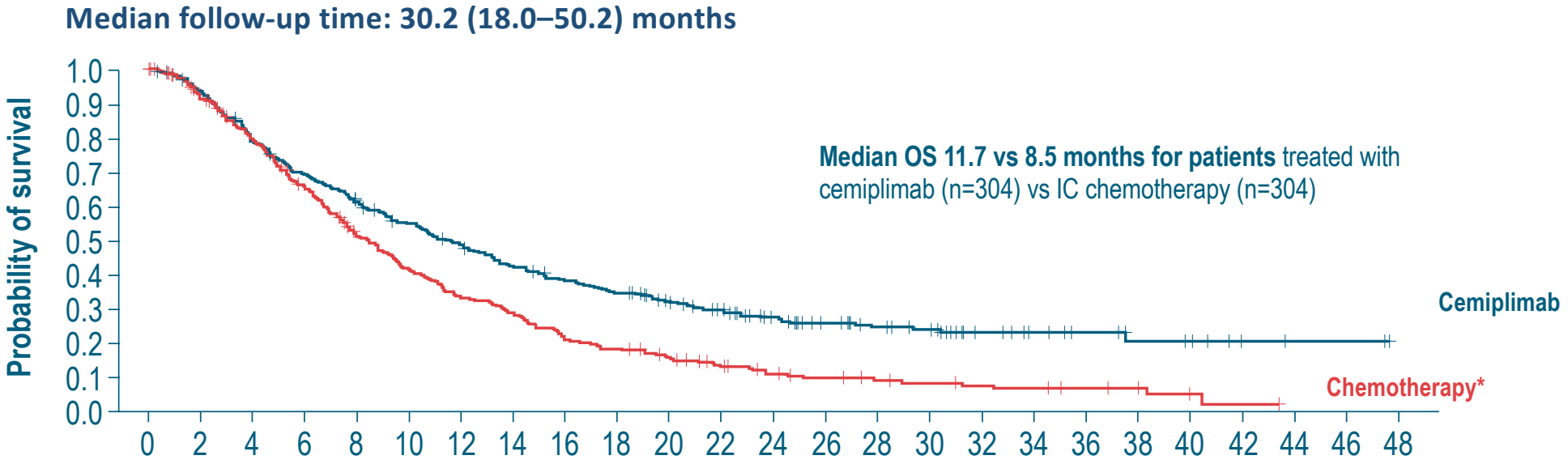


Kaplan–Meier curves of overall survival in the full analysis set.
CI, confidence interval; IC, investigator's choice; OS, overall survival. **Data cutoff date: 4 Jan 2022**

Oaknin A et al. Presented at ESMO Congress 2022

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9

Cemiplimab monotherapy significantly improved OS vs chemotherapy in the overall population



Patients at risk

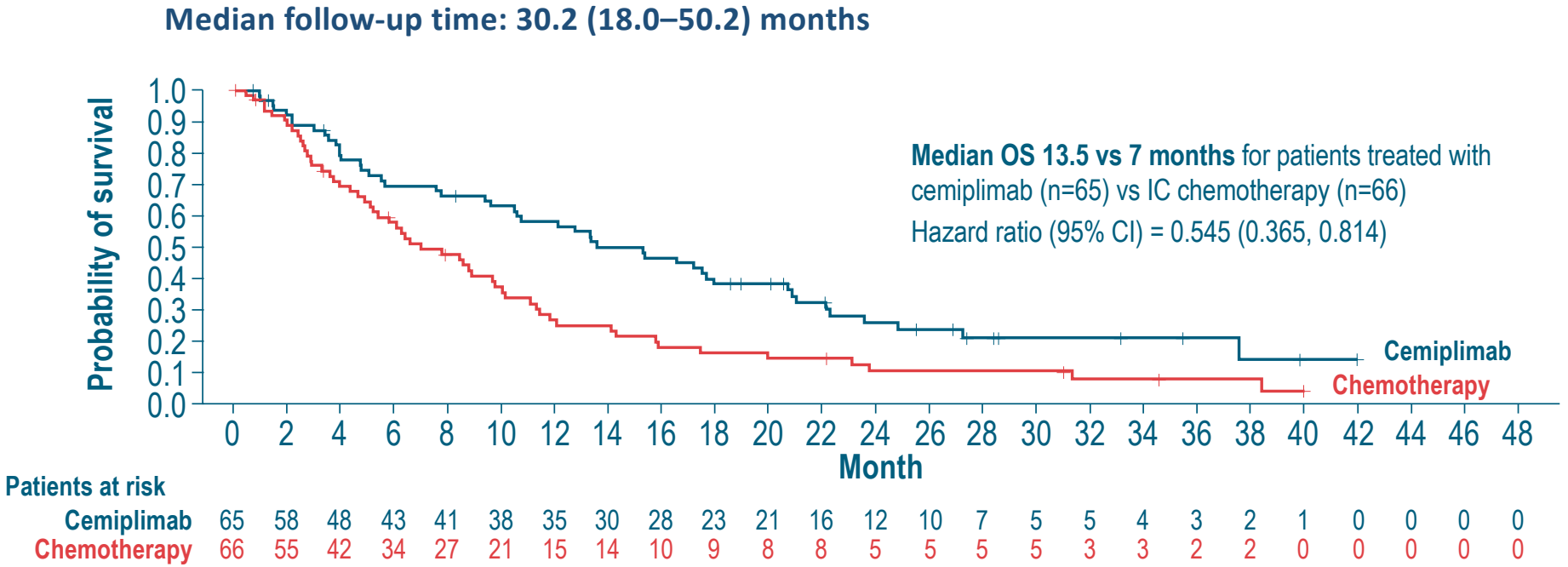
Cemiplimab	304	281	236	206	181	158	140	121	108	97	81	69	55	45	37	33	22	18	11	8	7	3	2	2	0
Chemotherapy	304	264	224	183	140	113	92	79	60	50	40	30	21	17	14	12	10	9	7	5	2	1	0	0	0

Oaknin A et al. Presented at ESMO Congress 2022

Kaplan–Meier curves of overall survival in the full analysis set.
CI, confidence interval; IC, investigator's choice; OS, overall survival. **Data cutoff date: 4 Jan 2022**

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9

Cemiplimab monotherapy significantly improved OS vs chemotherapy in patients with adenocarcinoma or adenosquamous carcinoma histology



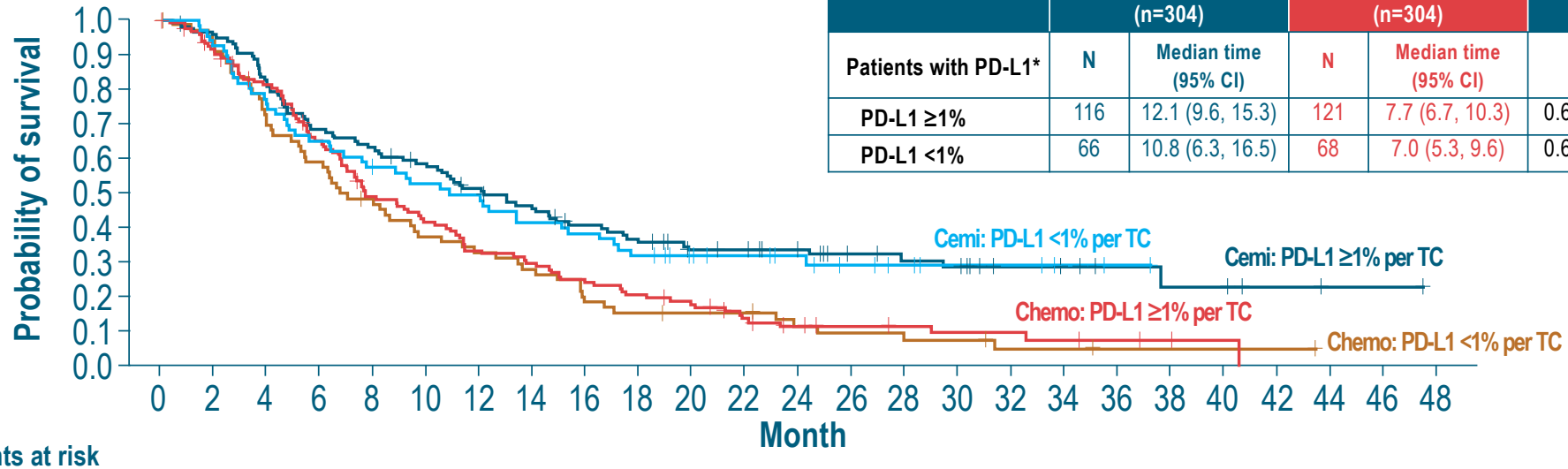
Oaknin A et al. Presented at ESMO Congress 2022

CI, confidence interval; IC, investigator's choice; OS, overall survival. **Data cutoff date: 4 Jan 2022**

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9

Cemiplimab monotherapy significantly improved OS vs chemotherapy regardless of PD-L1 status

	Cemiplimab (n=304)		Chemotherapy (n=304)		
Patients with PD-L1*	N	Median time (95% CI)	N	Median time (95% CI)	HR (95% CI)
PD-L1 ≥1%	116	12.1 (9.6, 15.3)	121	7.7 (6.7, 10.3)	0.614 (0.453, 0.831)
PD-L1 <1%	66	10.8 (6.3, 16.5)	68	7.0 (5.3, 9.6)	0.650 (0.429, 0.984)



Patients at risk

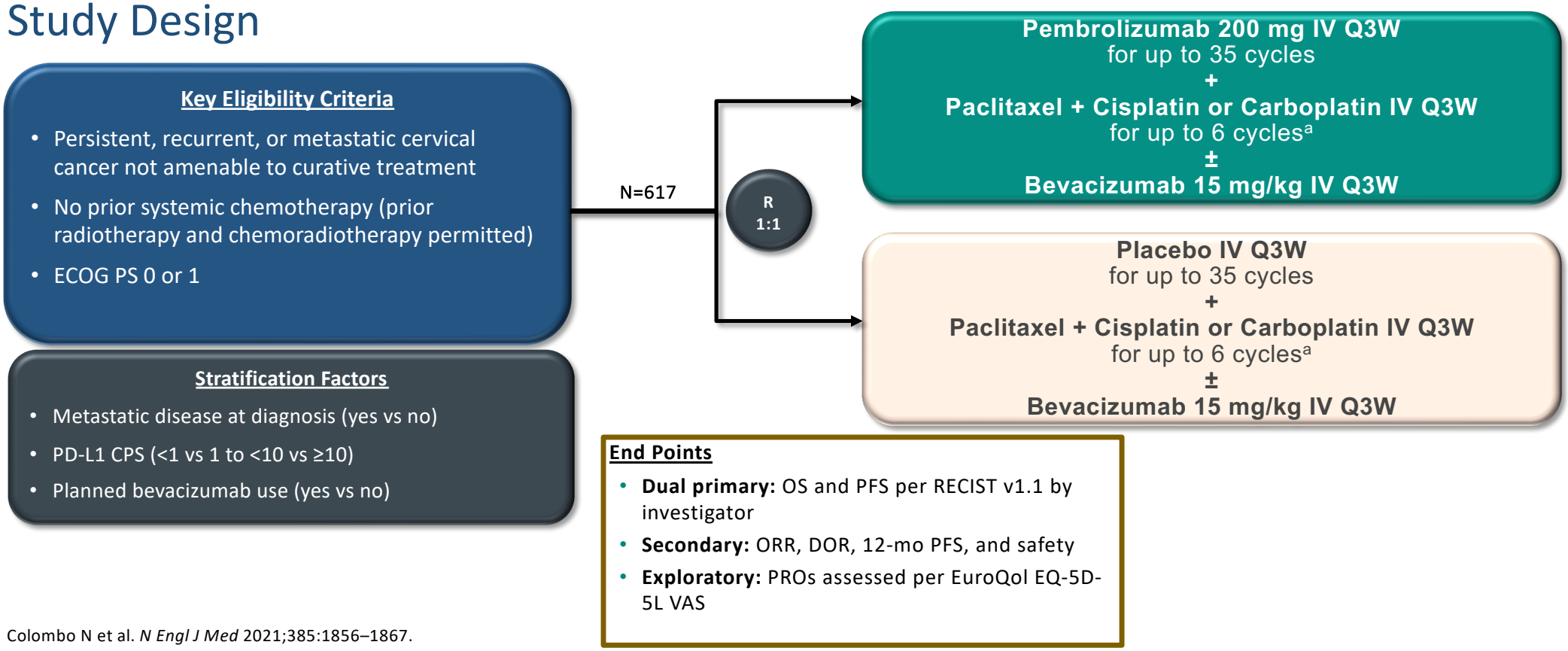
Cemi: PD-L1 ≥1% per TC	116	110	93	77	71	63	55	48	41	36	30	29	25	20	17	16	10	9	5	4	4	2	1	1	0
Cemi: PD-L1 <1% per TC	66	61	49	43	36	33	30	26	24	20	16	14	12	9	7	5	5	3	1	0	0	0	0	0	0
Chemo: PD-L1 ≥1% per TC	121	107	92	73	54	46	37	33	27	23	19	13	9	7	6	5	5	4	3	2	1	0	0	0	0
Chemo: PD-L1 <1% per TC	68	60	46	39	30	24	21	18	12	10	9	9	6	5	4	4	2	2	1	1	1	1	0	0	0

Kaplan–Meier curves of overall survival in the full analysis set.
Data cutoff date: 4 Jan 2022

Oaknin A et al. Presented at ESMO Congress 2022

controlled trial of pembrolizumab + chemotherapy vs chemotherapy + placebo for the first-line treatment of persistent, recurrent, or metastatic cervical cancer

Study Design

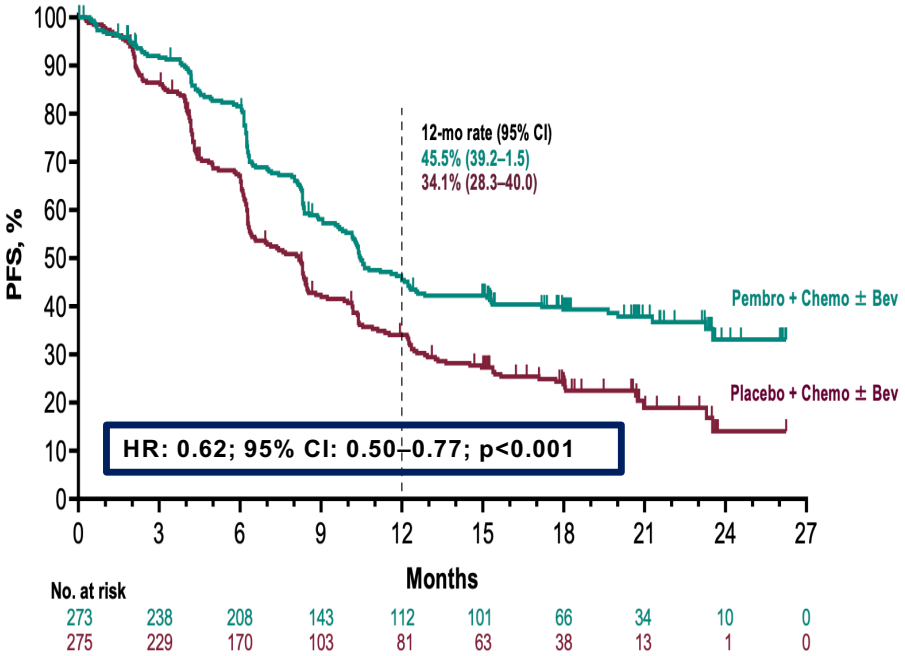


Colombo N et al. *N Engl J Med* 2021;385:1856–1867.

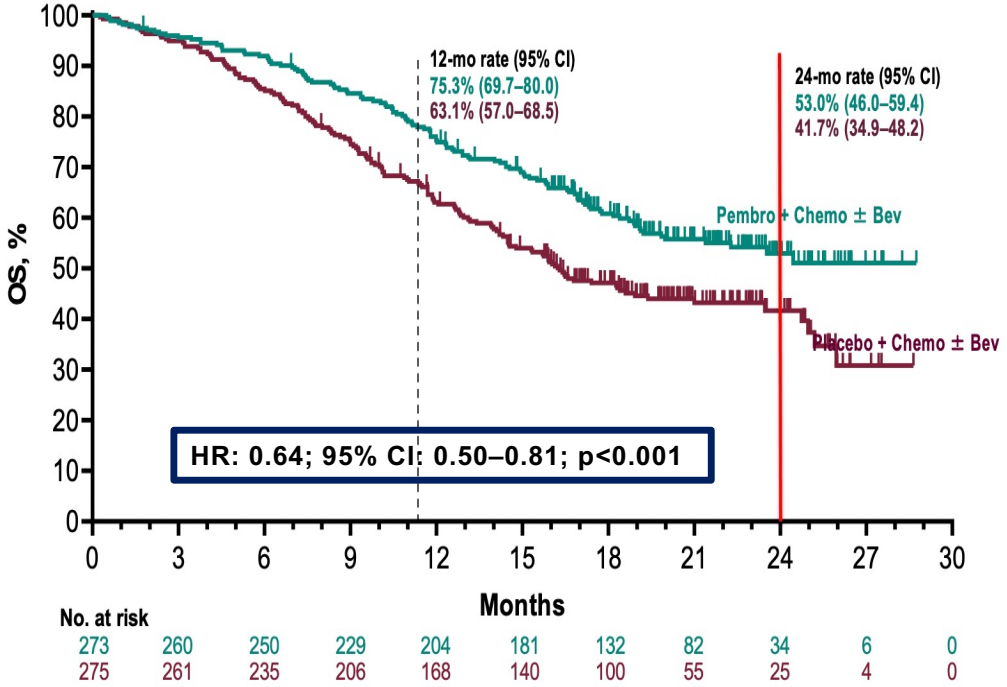
KEYNOTE-826: Dual Primary Endpoints

PD-L1 CPS ≥1 population

PFS	Pts w/Event	Median, mo (95% CI)
Pembro + Chemo ± Bev	57.5%	10.4 (9.7-12.3)
Pbo + Chemo ± Bev	72%	8.2 (6.3-8.5)



OS	Pts w/Event	Median, mo (95% CI)
Pembro + Chemo ± Bev	43.2%	NR (19.8-NR))
Pbo + Chemo ± Bev	56.0%	16.3 (14.5-19.4)



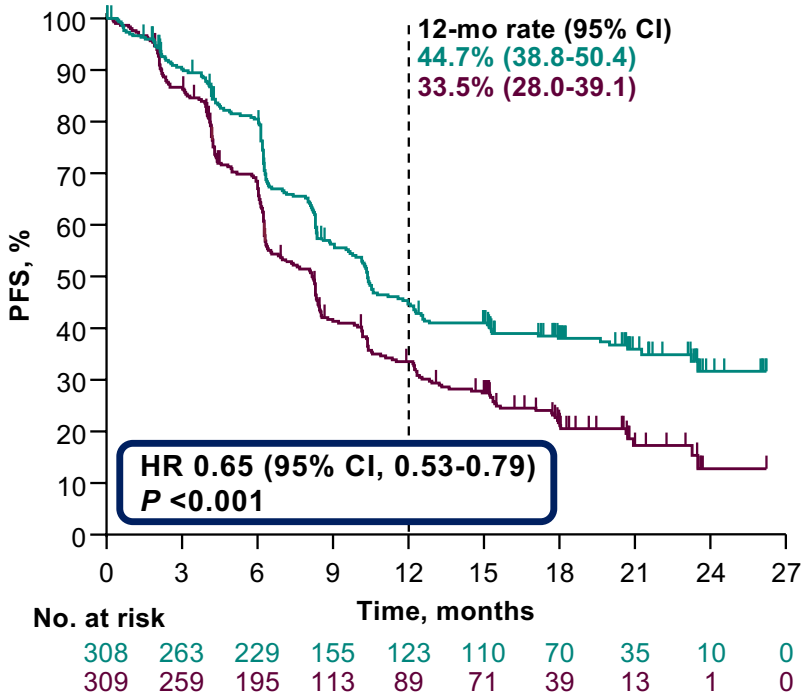
Colombo N et al. *N Engl J Med* 2021;385:1856–1867.

KEYNOTE-826: Dual Primary Endpoints

All comers population

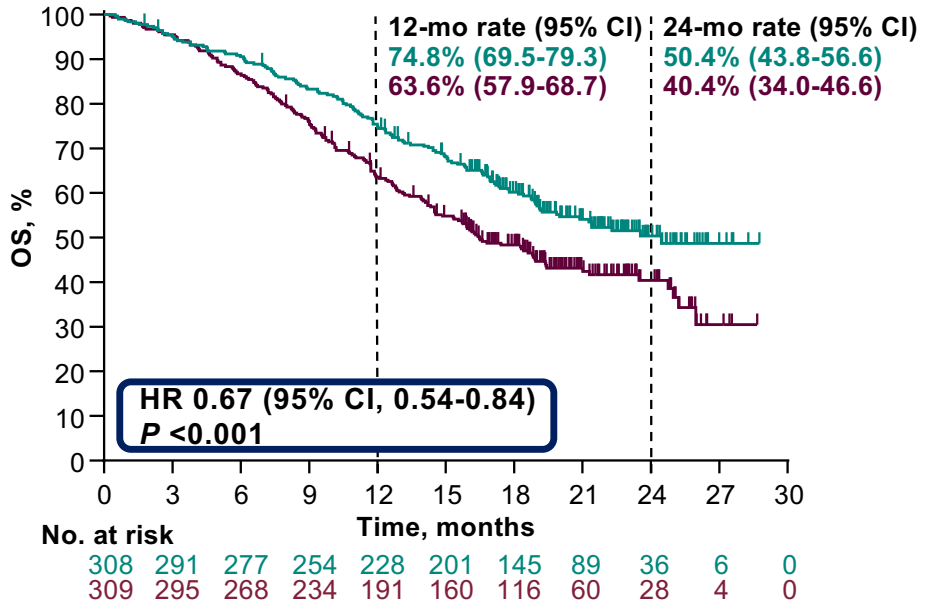
PFS

	Pts w/Event	Median, mo (95% CI)
Pembro + Chemo ± Bev	58.4%	10.4 (9.1-12.1)
Pbo + Chemo ± Bev	73.1%	8.2 (6.4-8.4)



OS

	Pts w/Event	Median, mo (95% CI)
Pembro + Chemo ± Bev	44.8%	24.4 (19.2-NR))
Pbo + Chemo ± Bev	56.3%	16.5 (14.5-19.4)

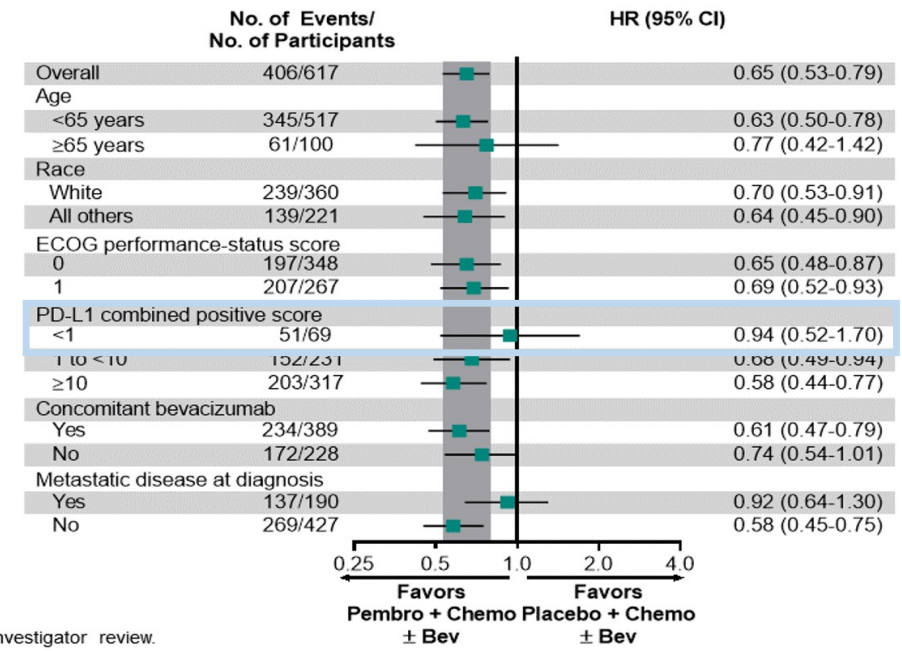


Colombo N et al. *N Engl J Med* 2021;385:1856–1867.

KEYNOTE-826: Protocol-Specified Subgroups

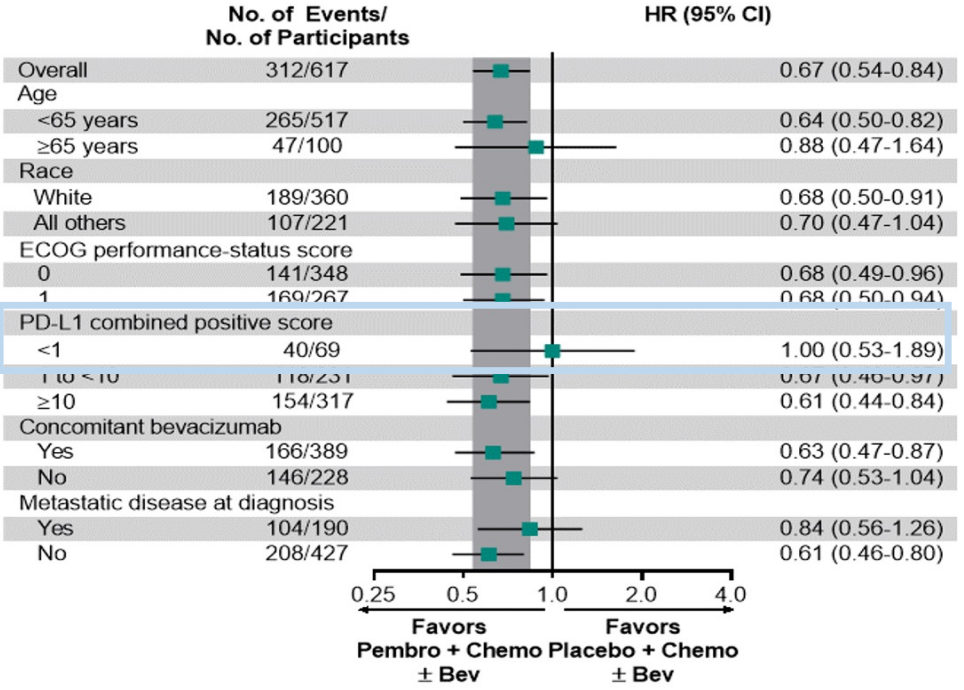
All comer population

PFS



/ investigator review.

OS

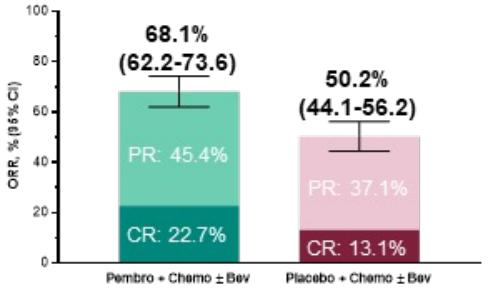


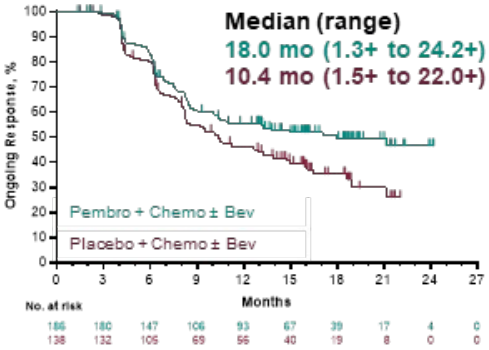
Colombo N et al. *N Engl J Med* 2021;385:1856–1867.

KEYNOTE-826: ORR and DOR

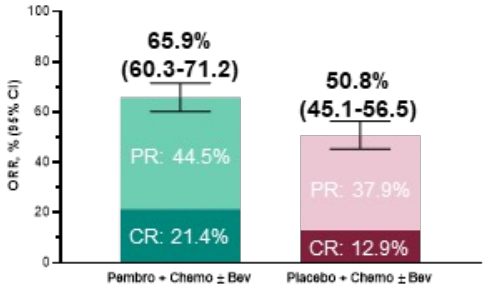
All of the analysis populations

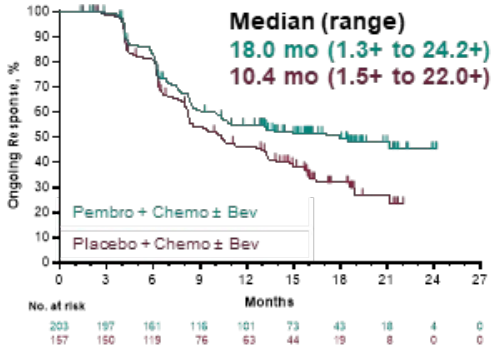
PD-L1 CPS ≥1 population



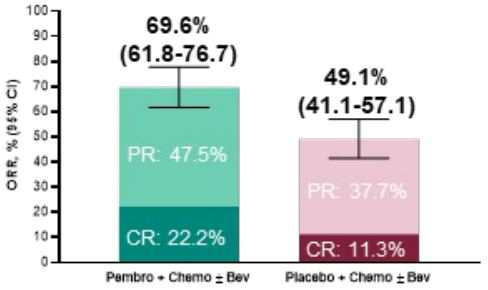


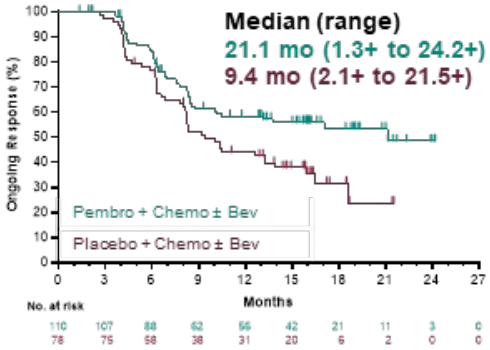
All-Comer population





PD-L1 CPS ≥10 population





Data cutoff date: 3 May 2021. Response assessed per RECIST v1.1 by investigator review. Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; CR, complete response; CPS, combined positive score; DOR, duration of response; HR, hazard ratio; mo, months; ORR, objective response rate; PD-L1, programmed death ligand-1; Pembro, pembrolizumab; PFS, progression- free survival; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (supplementary data).

KEYNOTE-826: AEs and exposure

	All-cause AEs, n (%)		Treatment-related AEs[a], n (%)		Immune-mediated AEs[b], n (%)	
	Pembrolizumab[c] (n=307)	Placebo[c] (n=309)	Pembrolizumab[c] (n=307)	Placebo[c] (n=309)	Pembrolizumab[c] (n=307)	Placebo[c] (n=309)
Any grade	305 (99.3)	307 (99.4)	298 (97.1)	300 (97.1)	104 (33.9)	47 (15.2)
Grade 3–5	251 (81.8)	232 (75.1)	210 (68.4)	198 (64.1)	35 (11.4)	9 (2.9)
Serious	153 (49.8)	131 (42.4)	93 (30.3)	71 (23.0)	22 (7.2)	7 (2.3)
Led to death	14 (4.6)	14 (4.5)	2 (0.7)[d]	4 (1.3)[e]	1 (0.3)[d]	0
Led to discontinuation						
Any treatment	115 (37.5)	82 (26.5)	96 (31.1)	69 (22.3)	16 (5.2)	1 (0.3)
All treatment	18 (5.9)	15 (4.9)	10 (3.3)	6 (1.9)	3 (1.0%)	0

Median no. of cycles (pembrolizumab vs placebo)
- Any treatment: 14 vs 11
- Pembrolizumab or placebo: 13 vs 11
- Chemotherapy: 6 vs 6
- Bevacizumab: 13 vs 11

Treatment duration, months (pembrolizumab vs placebo)
- Median: 10.0 vs 7.7
- Mean: 11.8 vs 9.4

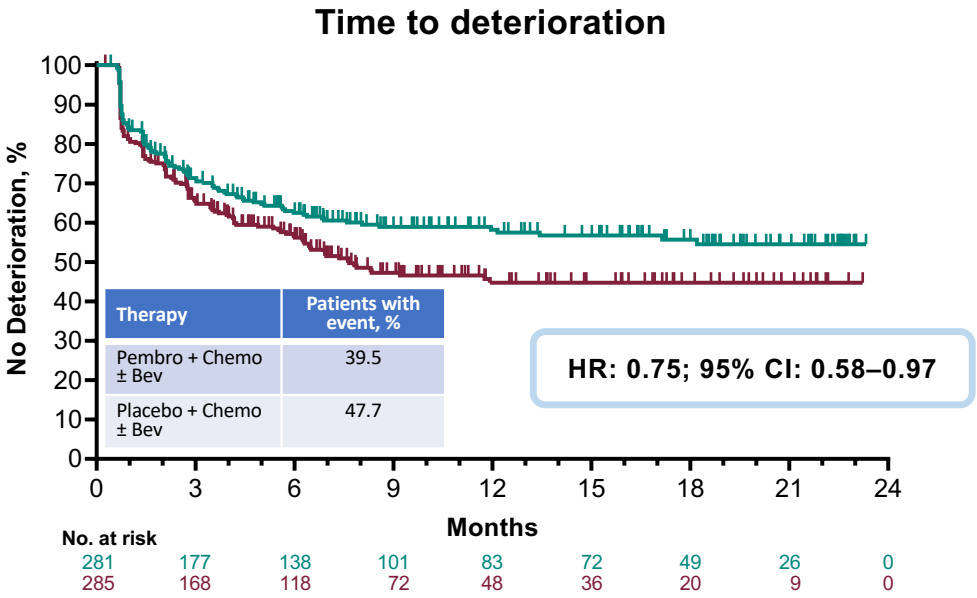
Data cutoff date: 3 May 2021. [a]Per investigator assessment; [b]Events were considered regardless of attribution to treatment by the investigator; [c]The treatment regimen in each arm included chemotherapy ± bevacizumab; [d]Encephalitis autoimmune (also immune-mediated) and intestinal perforation; [e]Embolism, female genital tract fistula, large intestine perforation, and pulmonary sepsis.
AE, adverse event.

Colombo N et al. *N Engl J Med* 2021;385:1856–1867 (supplementary data).

KEYNOTE-826: Euroqol EQ-5D-5L VAS

All comers population

- Administered before study treatment at Cycles 1–14 and every other cycle thereafter
  - Compliance between baseline and Week 30[a]: ≥94.0% with pembrolizumab + chemotherapy ± bevacizumab, ≥88.9% with placebo + chemotherapy ± bevacizumab
- Analysis population: all treated participants with ≥1 available PRO assessment
- Time to deterioration: time from first EQ-5D-5L VAS assessment to first onset of a ≥10-point decrease in score from baseline with confirmation under the right censoring rule or death, whichever occurred first



Data cutoff date: 3 May 2021.

[a]Compliance was defined as the proportion of participants who completed the patient-reported outcome questionnaire among those who were expected to complete the questionnaire at the time point, excluding those missing by design; missing by design includes adverse event, death, discontinuation, translations not available, and no visit scheduled.

Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; Pembro, pembrolizumab; PRO, patient-reported outcome; VAS, visual analog scale.

BEATcc trial design (NCT03556839)

Open-label, multicentre, randomised, phase 3 trial in an all-comer population

- Metastatic, persistent or recurrent cervical cancer not amenable to curative therapy
- GOG/ECOG PS ≤1
- No prior systemic anti-cancer therapy for metastatic/persistent/recurrent disease
- In patients with pelvic disease, no bladder or rectal mucosa involvement
- Available archival or fresh tumour sample for PD-L1 expression

Stratification factors:
- Prior concurrent chemoradiation (yes vs no)
- Histology (squamous cell carcinoma vs adenocarcinoma[b] including adenosquamous)
- Chemotherapy backbone (cisplatin vs carboplatin)

R
1:1
N=410

Atezolizumab 1200 mg + bevacizumab 15 mg/kg + paclitaxel + cis/carboplatin[a] all IV q3w

Bevacizumab 15 mg/kg + paclitaxel + cis/carboplatin[a] all IV q3w

- Continued until disease progression/unacceptable toxicity
- Patients with CR after ≥6 cycles could stop chemotherapy and continue biological therapy alone
- Crossover from standard arm at progression not permitted

Dual primary endpoints
- Investigator-assessed PFS (RECIST 1.1)
- Overall survival

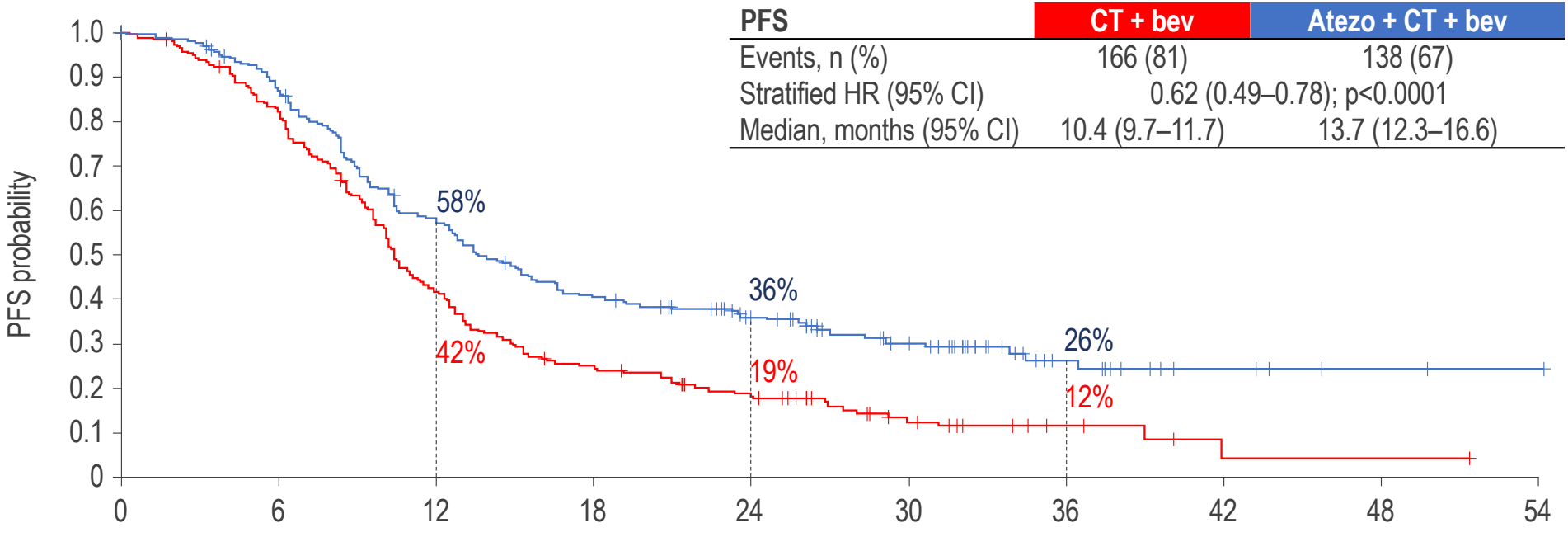
Key secondary endpoints
- ORR (RECIST v1.1)
- DoR (RECIST v1.1)
- TFST
- PFS2
- Safety

[a]Paclitaxel 175 mg/m^2 day 1 + platinum (cisplatin 50 mg/m^2 or carboplatin AUC5) day 1
[b]Capped at 20% of the overall population
CR = complete response; GOG/ECOG = Gynecologic Oncology Group/Eastern Cooperative Oncology Group performance status; PFS2: time from randomisation to second progression or death; TFST = time from randomisation to first subsequent therapy or death

Dual primary endpoint: PFS

Statistically significant 38% reduction in risk of progression or death

PFS	CT + bev	Atezo + CT + bev
Events, n (%)	166 (81)	138 (67)
Stratified HR (95% CI)	0.62 (0.49–0.78); p<0.0001	
Median, months (95% CI)	10.4 (9.7–11.7)	13.7 (12.3–16.6)

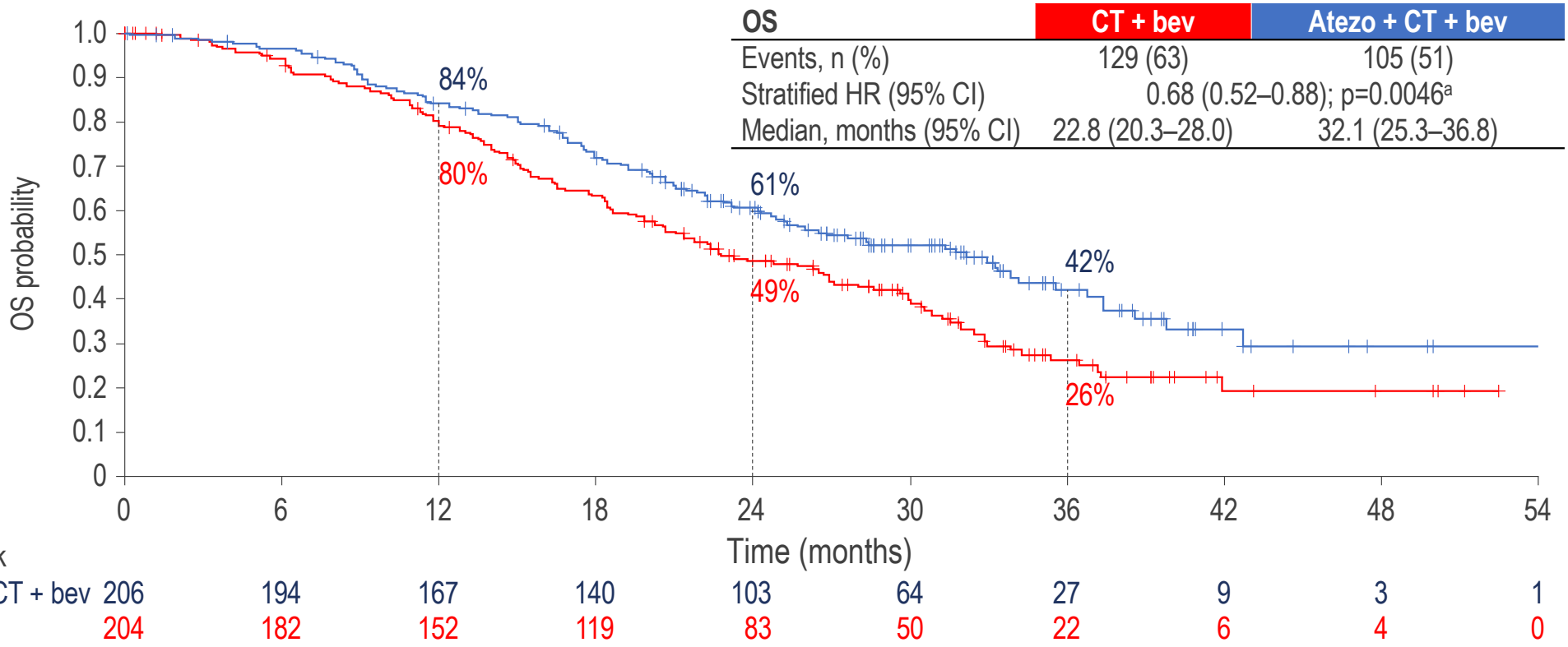


No. at risk										
Atezo + CT + bev	206	174	114	79	58	37	13	5	2	1
CT + bev	204	159	80	47	31	13	5	1	1	0

Data cut-off: 17 Jul 2023 (median follow-up: 32.9 months; 95% CI, 31.2–34.6 months)
HR = hazard ratio

Dual primary endpoint: OS (interim analysis)

Statistically significant 32% reduction in risk of death



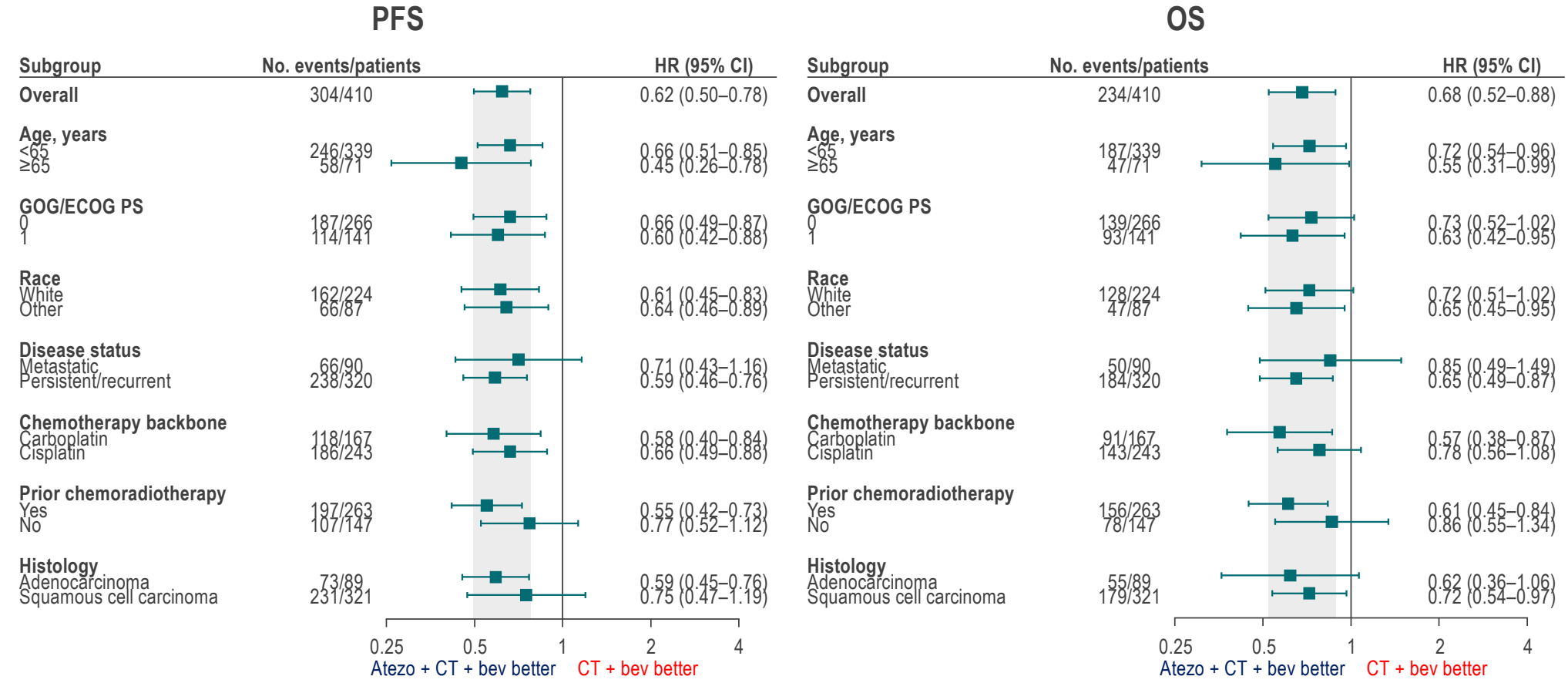
OS	CT + bev	Atezo + CT + bev
Events, n (%)	129 (63)	105 (51)
Stratified HR (95% CI)	0.68 (0.52–0.88); p=0.0046[a]	
Median, months (95% CI)	22.8 (20.3–28.0)	32.1 (25.3–36.8)

No. at risk										
Atezo + CT + bev	206	194	167	140	103	64	27	9	3	1
CT + bev	204	182	152	119	83	50	22	6	4	0

Data cut-off: 17 Jul 2023 (median follow-up: 32.9 months; 95% CI, 31.2–34.6 months)

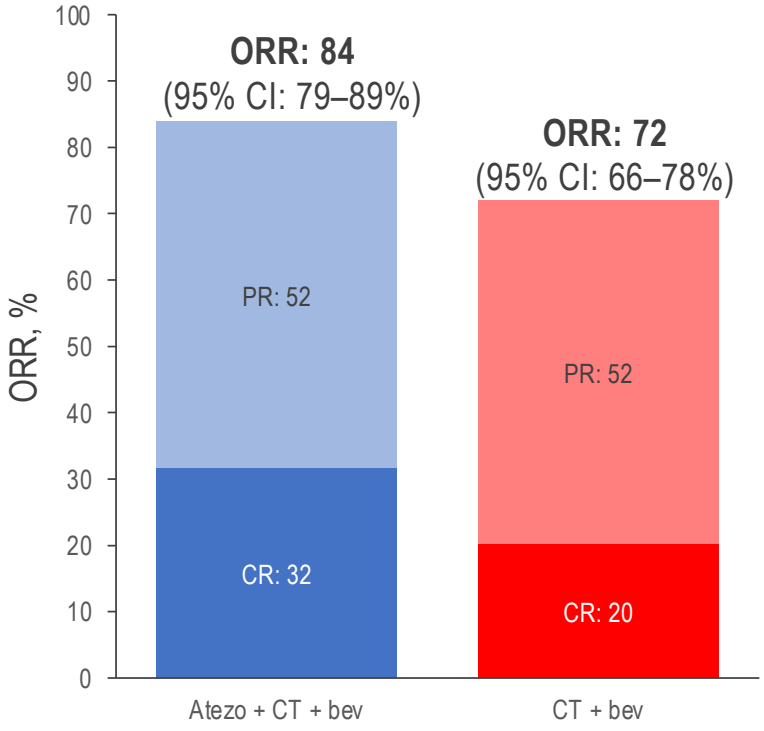
[a]Boundary for statistical significance at the interim OS analysis: p=0.0238

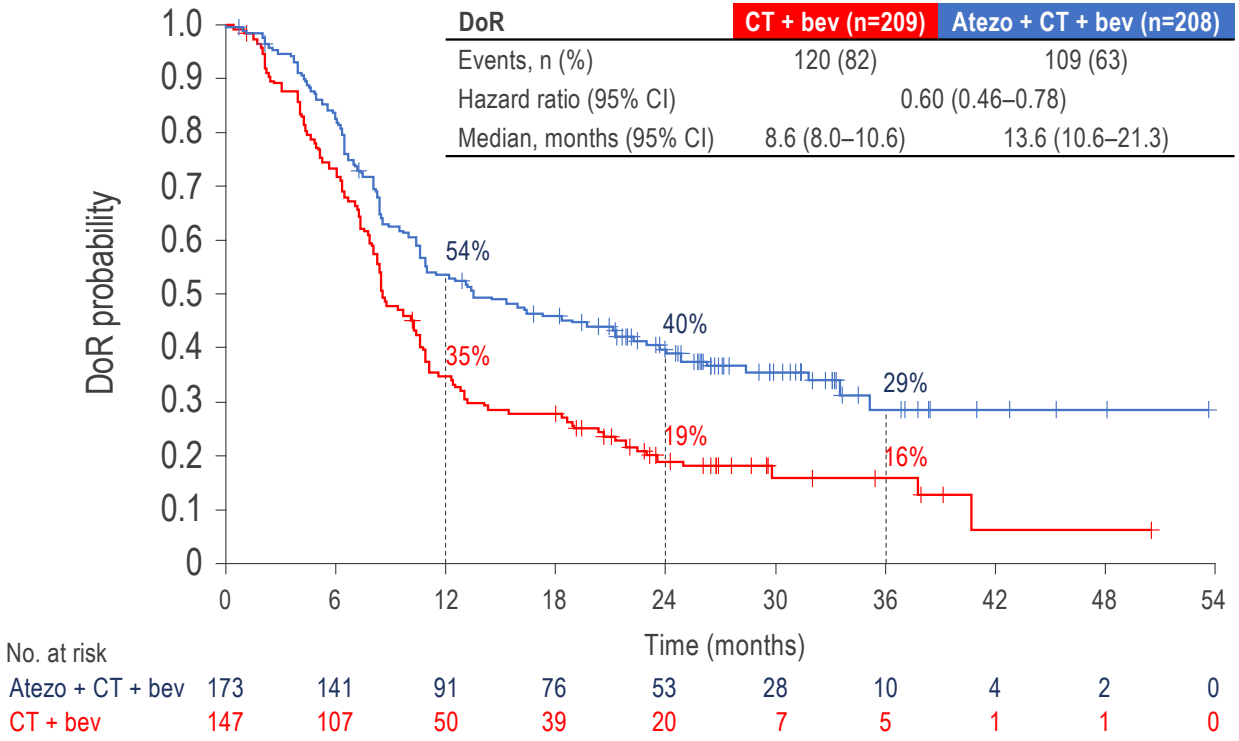
PFS and OS in protocol-specified subgroups



Data cut-off: 17 Jul 2023 (median follow-up: 32.9 months; 95% CI, 31.2–34.6 months)

Secondary endpoints: ORR and DoR





DoR	CT + bev (n=209)	Atezo + CT + bev (n=208)
Events, n (%)	120 (82)	109 (63)
Hazard ratio (95% CI)	0.60 (0.46–0.78)	
Median, months (95% CI)	8.6 (8.0–10.6)	13.6 (10.6–21.3)

No. at risk										
Atezo + CT + bev	173	141	91	76	53	28	10	4	2	0
CT + bev	147	107	50	39	20	7	5	1	1	0

Data cut-off: 17 Jul 2023 (median follow-up: 32.9 months; 95% CI, 31.2–34.6 months)
CR = complete response; PR = partial response

Summary of safety

AE, n (%)	Atezo + CT + bev (n=206)	CT + bev (n=204)
Any AE	202 (99)	197 (99)
Grade ≥3	161 (79)	149 (75)
Grade 5	7 (3)[a]	6 (3)[b]
AESI for bevacizumab	105 (51)	100 (50)
Grade ≥3	42 (21)	40 (20)
AESI for atezolizumab	43 (21)	NA
Grade ≥3	11 (5)	NA
AE leading to any treatment discontinuation	31 (15)	31 (16)
Chemotherapy	42 (21)	40 (20)
Carboplatin	4 (2)	5 (3)
Cisplatin	12 (6)	10 (5)
Paclitaxel	14 (7)	14 (7)
Bevacizumab	18 (9)	19 (10)
Atezolizumab	13 (6)	NA

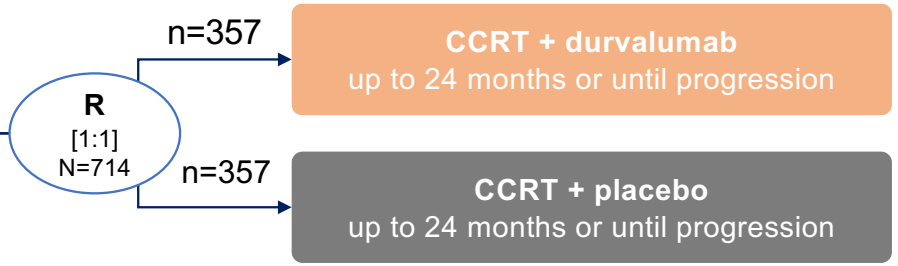
[a]One case each of vaginal haemorrhage, obstructive jaundice and ileal perforation (all considered treatment-related); one case each of intestinal occlusion, biliary bronchospiration, nausea/vomiting and septic shock (considered unrelated to treatment). [b]One case each of respiratory failure, intestinal perforation, cardiopulmonary arrest, respiratory infection, COVID infection and intestinal occlusion (considered unrelated to treatment)

CALLA Trial: Durvalumab added to SOC CCRT

Study Design

A Phase 3, randomized, multicenter, double-blind, global study to determine the efficacy and safety of durvalumab in combination with and following CRT compared with CRT alone for treatment in women with LACC

Key eligibility criteria
- Primary locally advanced carcinoma of the cervix (IB2–IIB node-positive or IIIA–IVA any nodal status)
- Measurable disease by RECIST v1.1
- ECOG PS 0 or 1



Stratification factors
- Stage <3 and node positive, Stage ≥3 and node negative, Stage ≥3 and node positive
- Geographical region

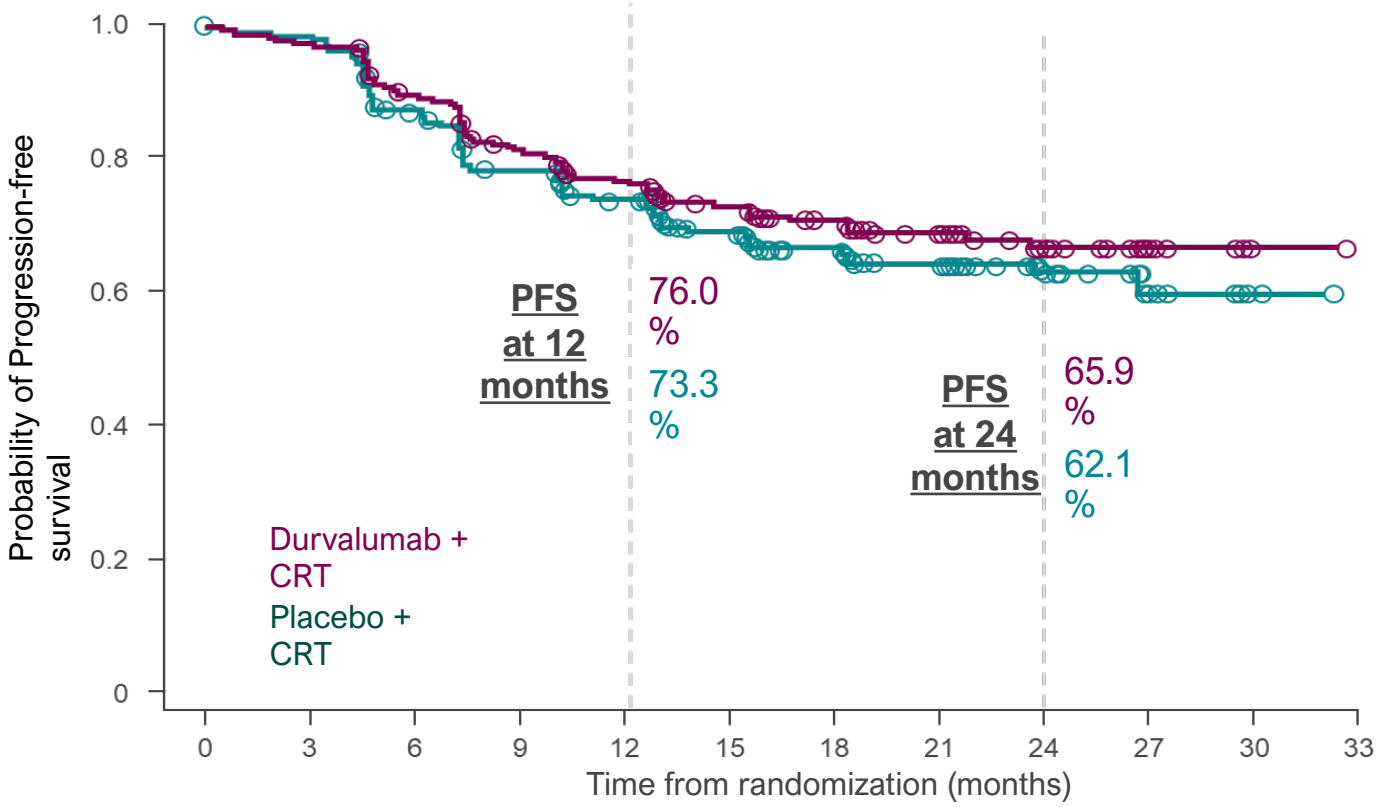
Endpoints
- **Primary:** PFS
- **Secondary:** OS, ORR, DOR, safety, HRQoL

24 March 2022
The CALLA Phase III trial for durvalumab given concurrently with chemoradiotherapy (CRT) **did not achieve statistical significance for the primary endpoint of improving progression-free survival (PFS)** versus CRT alone in the treatment of patients with locally advanced cervical cancer.

NCT03830866.;Mayadev J et al. *Int J Gynecol Cancer* 2020;30:1065–1070.

CALLA Trial: Primary Endpoint

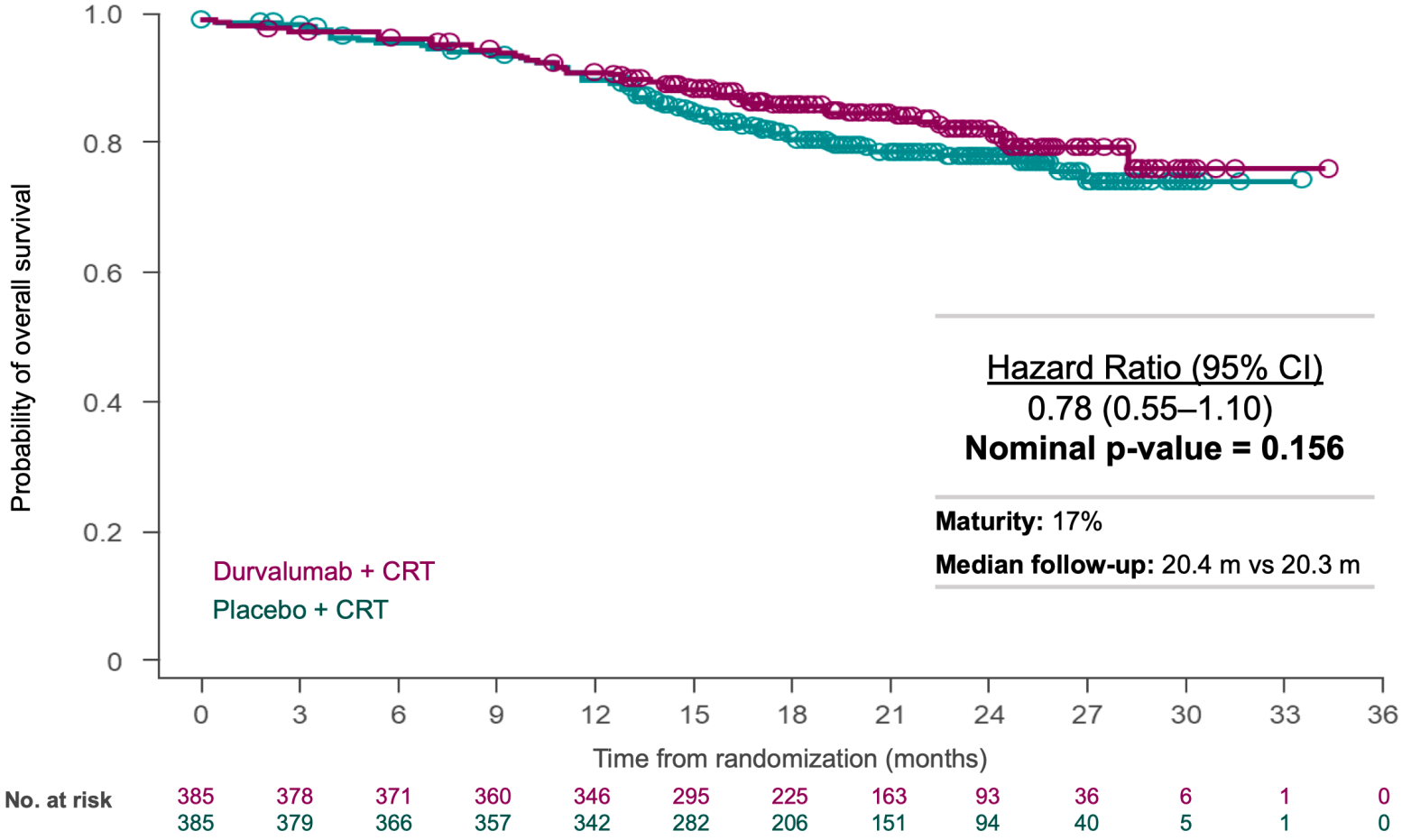
Progression-Free Survival



Hazard Ratio (95% CI)
0.84 (0.65–1.08)
p-value = 0.174
Maturity: 31%
Median follow-up: 18.5 m vs 18.4 m

NCT03830866.;Mayadev J et al. *Int J Gynecol Cancer* 2020;30:1065–1070.

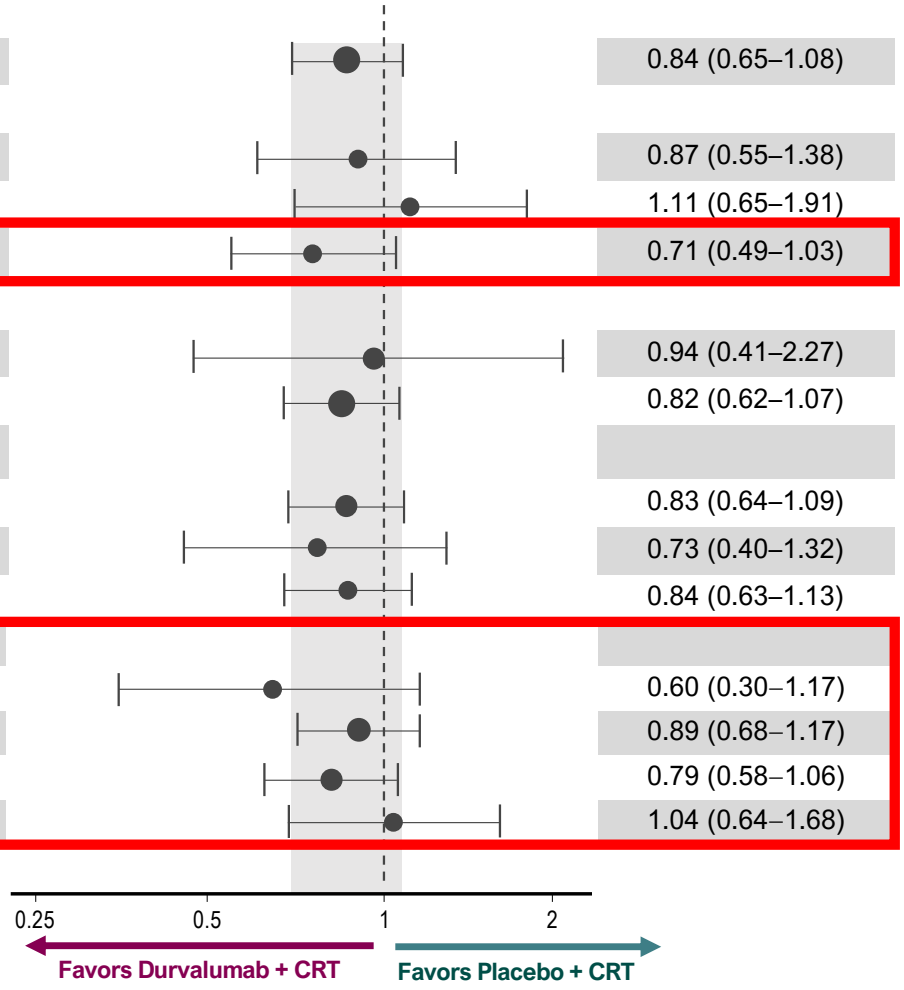
Overall Survival



PFS Subgroup Analysis

Are there some patients that seem to benefit more? Hypothesis generating

	Durvalumab + CRT (Events/Total)	Placebo + CRT (Events/Total)	Hazard Ratio (95% CI)
All patients	112/385	128/385	0.84 (0.65–1.08)
Disease stage (FIGO 2009)			
Stage IB2-IIB, node positive	35/134	39/133	0.87 (0.55–1.38)
Stage ≥III, LN-	28/108	26/107	1.11 (0.65–1.91)
Stage ≥III, LN+	49/143	63/145	0.71 (0.49–1.03)
Chemotherapy received			
Carboplatin	14/26	9/20	0.94 (0.41–2.27)
Cisplatin	98/359	118/363	0.82 (0.62–1.07)
PD-L1 expression status			
≥1%	102/356	117/352	0.83 (0.64–1.09)
<5%	19/60	25/64	0.73 (0.40–1.32)
≥5%	85/311	95/300	0.84 (0.63–1.13)
Lymph nodes			
Para-aortic lymph node	15/47	20/38	0.60 (0.30–1.17)
No para-aortic lymph node	97/338	108/347	0.89 (0.68–1.17)
Pelvic lymph node	75/246	97/268	0.79 (0.58–1.06)
No pelvic lymph node	37/139	31/117	1.04 (0.64–1.68)



MADRID 2023 ESMO congress

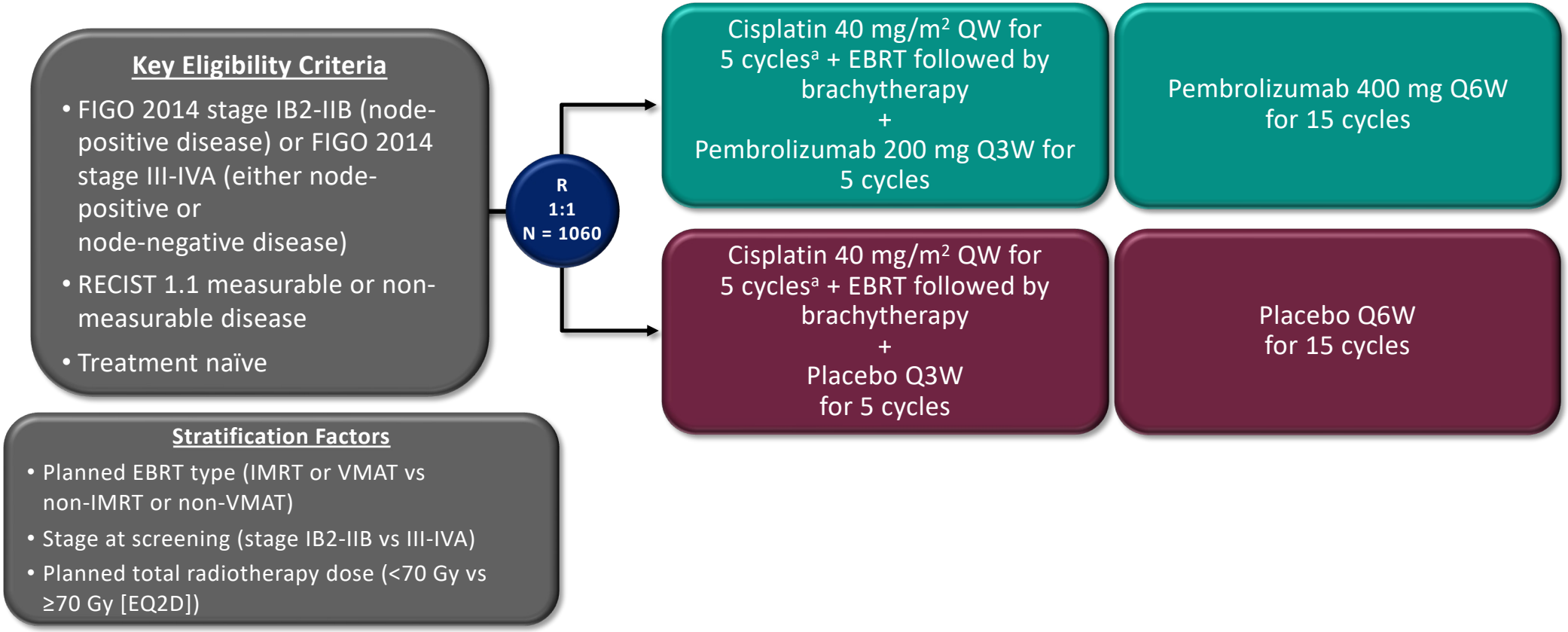
Pembrolizumab Plus Chemoradiotherapy for High-Risk Locally Advanced Cervical Cancer: The Randomized, Double-Blind, Phase 3 ENGOT-cx11/GOG-3047/KEYNOTE-A18 Study

Domenica Lorusso,[1] Yang Xiang,[2] Kosei Hasegawa,[3] Giovanni Scambia,[4] Manuel Leiva,[5] Pier Ramos-Elias,[6] Alejandro Acevedo,[7] Julia Vizkeleti,[8] Andrea Gomes,[9] Fernando Contreras Mejía,[10] Ari Reiss,[11] Ali Ayhan,[12] Jung-Yun Lee,[13] Valeriya Saevets,[14] Flora Zagouri,[15] Kan Li,[16] Karin Yamada,[16] Sarper Toker,[16] Sandro Pignata,[17*] Linda R. Duska[18*] on behalf of the ENGOT-cx11/GOG-3047/KEYNOTE-A18 investigators

[1]Gynaecology Oncology Unit, Fondazione Policlinico Universitario A Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; [2]Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, National Clinical Research Center for Obstetric & Gynecologic Diseases, Beijing, China; [3]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [4]Scientific Directorate, Fondazione Policlinico Universitario Agostino Gemelli IRCCS and Catholic University of the Sacred Heart, Rome, Italy; [5]Instituto de Oncologia y Radioterapia Clinica Ricardo Palma, Lima, Peru; [6]Integra Cancer Institute, Edificio Integra Medical Center, Guatemala City, Guatemala; [7]Oncocentro, Valparaiso, Chile; [8]National Institute of Oncology, Centre of Radiotherapy, Budapest, Hungary; [9]Liga Norte Riograndense Contra o Cancer Rio Grande do Norte, Brazil; [10]Instituto Nacional de Cancerologia, Bogota, Colombia; [11]Rambam Medical Center, Gyneco-oncology Unit, Haifa, Israel; [12]Turkish Society of Gynecologic Oncology (TRSGO), Başkent University, Ankara, Turkiye; [13]Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; [14]Chelyabinsk Regional Clinical Center Oncology and Nuclear Medicine, Chelyabinsk, Russia; [15]Alexandra Hospital, Athens, Greece; [16]Merck & Co., Inc., Rahway, NJ, USA; [17]Department of Urology and Gynecology, Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli, Italy; [18]University of Virginia School of Medicine, Charlottesville, VA, USA

*Drs. Pignata and Duska contributed equally to this presentation.

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



[a]A 6th cycle was allowed per investigator discretion. EBRT, external beam radiotherapy; FIGO, International Federation of Gynecology and Obstetrics; Gy, grays; IMRT, intensity-modulated radiotherapy; Q3W, every 3 weeks; Q6W, every 6 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; VMAT, volumetric-modulated arc therapy. ENGOT-cx11/GOG-3047/KEYNOTE-A18 ClinicalTrials.gov identifier, NCT04221945.

Baseline Characteristics

	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Age, median (range)	49 y (22-87)	50 y (22-78)
Race[a]		
White	254 (48.0%)	264 (49.7%)
Asian	155 (29.3%)	148 (27.9%)
Multiple	78 (14.7%)	86 (16.2%)
American Indian or Alaska Native	24 (4.5%)	22 (4.1%)
Black or African American	14 (2.6%)	8 (1.5%)
Native Hawaiian or Other Pacific Islander	2 (0.4%)	1 (0.2%)
PD-L1 CPS		
<1	22 (4.2%)	28 (5.3%)
≥1	502 (94.9%)	498 (93.8%)
Missing	5 (0.9%)	5 (0.9%)
ECOG PS 1	149 (28.2%)	134 (25.2%)
Squamous cell carcinoma	433 (81.9%)	451 (84.9%)

	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Stage at screening (FIGO 2014 criteria)		
IB2-IIB	235 (44.4%)	227 (42.7%)
III-IVA	294 (55.6%)	304 (57.3%)
Lymph node involvement[b]		
Positive pelvic only	326 (61.6%)	324 (61.0%)
Positive para-aortic only	14 (2.6%)	10 (1.9%)
Positive pelvic and para-aortic	105 (19.8%)	104 (19.6%)
No positive pelvic or para-aortic	84 (15.9%)	93 (17.5%)
Planned type of EBRT		
IMRT or VMAT	469 (88.7%)	470 (88.5%)
Non-IMRT and non-VMAT	60 (11.3%)	61 (11.5%)
Planned total radiotherapy dose (EQD2)		
<70 Gy	47 (8.9)	46 (8.7)
≥70 Gy	482 (91.1)	485 (91.3)

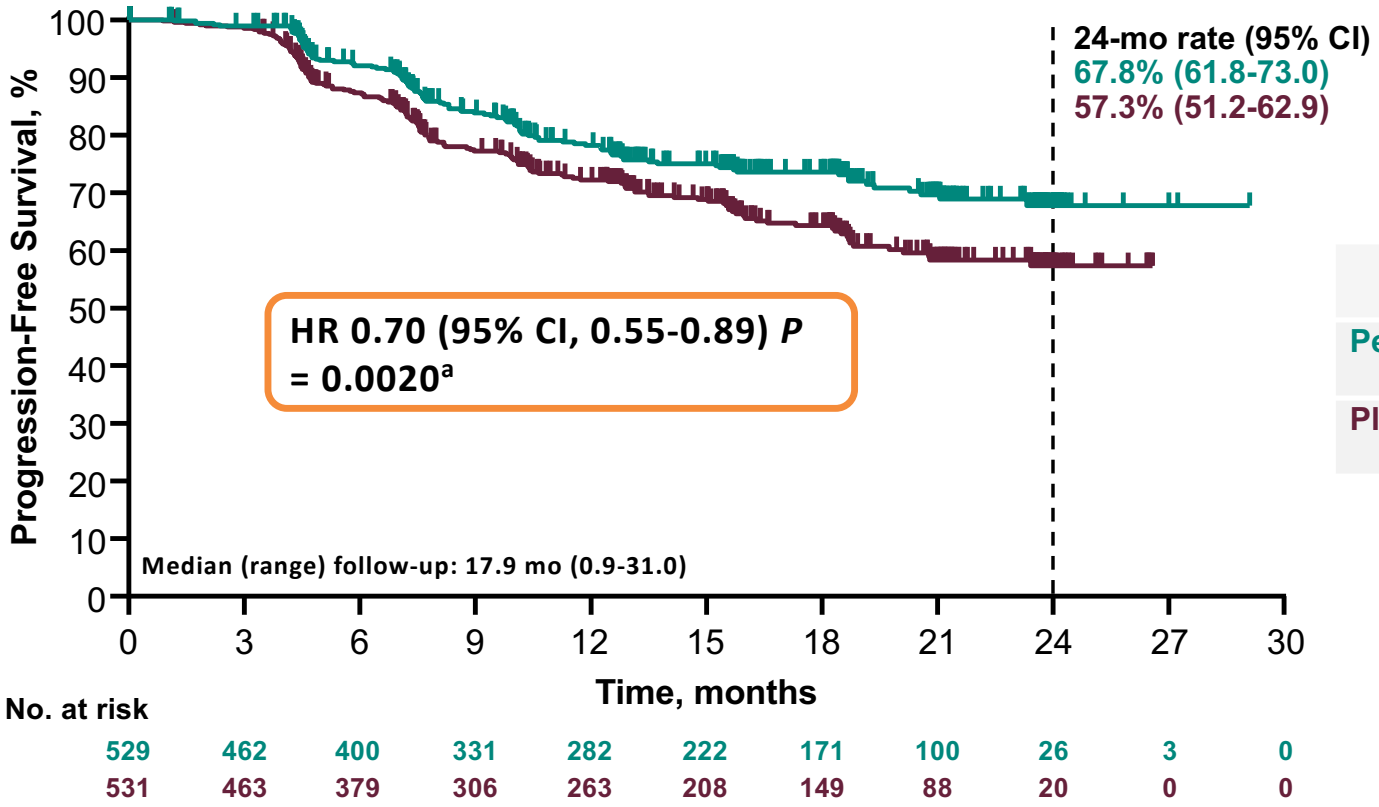
[a]In each treatment arm, 2 patients (0.4%) had missing information for race. [b]Per protocol, a positive lymph node is defined as ≥1.5 cm shortest dimension by MRI or CT. Data cutoff date: January 9, 2023.

Summary of Treatment Exposure

	Pembro Arm (N = 528)	Placebo Arm (N = 530)
Total number of cycles, median (range)		
Pembro or placebo	11 (1-20)	11 (1-20)
Cisplatin[a]	5 (1-7)	5 (1-7)
Radiation therapy, median (range)[a]		
Overall treatment time (days)	52 (12-139)	52 (2-166)
Within 50 days[b], n (%)	184 (35.5%)	194 (37.2%)
Within 56 days, n (%)	386 (74.5%)	390 (74.7%)
Cervix total dose (Gy), median (range)[a]		
Total cervix physical dose	76 (14-94)	76 (3-125)
Total cervix EQD2 dose	87 (14-118)	87 (3-207)

[a]Includes participants who completed concurrent chemoradiotherapy at this interim analysis and had final data review by the vendor (pembro arm N=518; placebo arm N=522). [b]Total radiation therapy (EBRT and brachytherapy) should not exceed 50 days, with extension to a maximum of 56 days for unforeseen delays, as per the study protocol. Data cutoff date: January 9, 2023.

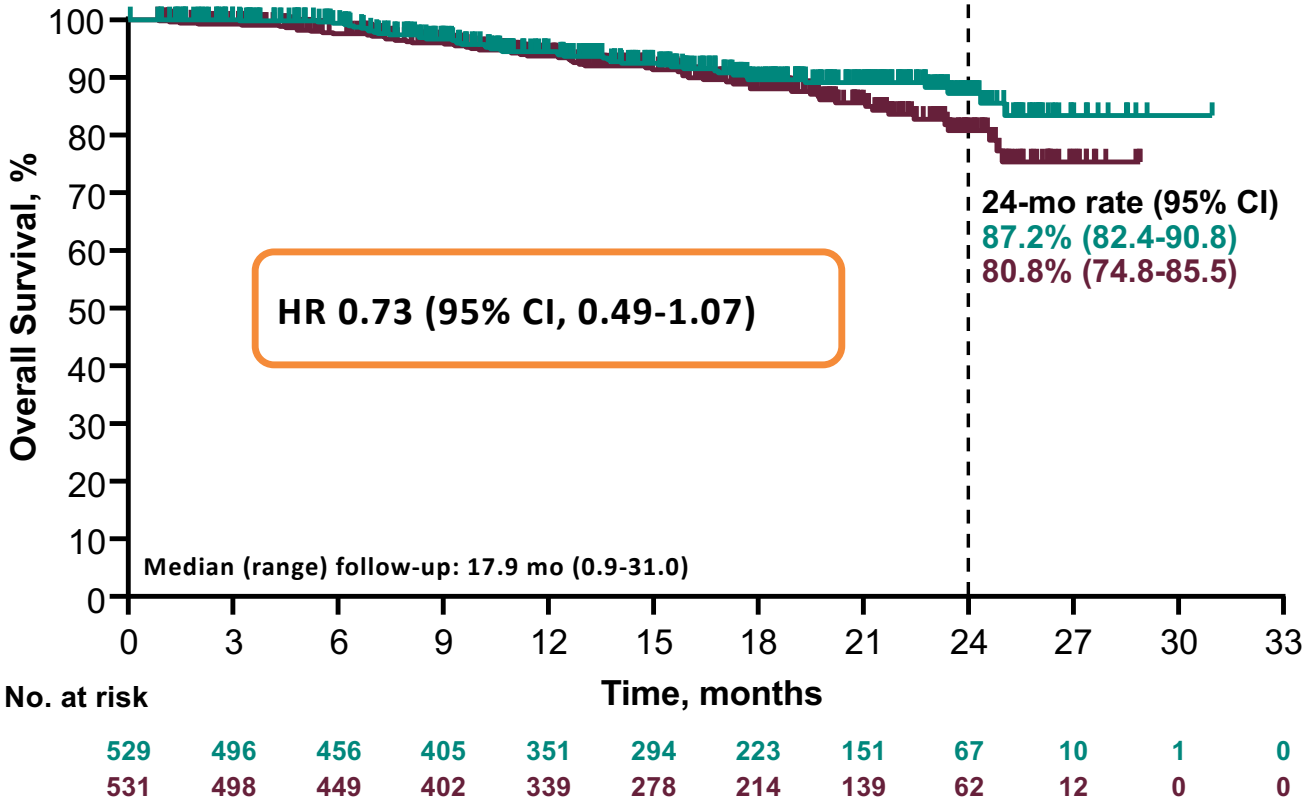
Primary Endpoint: Progression-Free Survival



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	21.7%	NR (NR-NR)
Placebo Arm	29.0%	NR (NR-NR)

Response assessed per RECIST v1.1 by investigator review or histopathologic confirmation. [a]With 269 events (88.5% information fraction), the observed *P* = 0.0020 (1-sided) crossed the prespecified nominal boundary of 0.0172 (1-sided) at this planned first interim analysis. The success criterion of the PFS hypothesis was met, and thus no formal testing of PFS will be performed at a later analysis. Data cutoff date: January 9, 2023.

Primary Endpoint: Overall Survival



	Pts w/ Event*	Median, mo (95% CI)
Pembro Arm	8.3%	NR (NR-NR)
Placebo Arm	11.1%	NR (NR-NR)

*42.9% information fraction[a]

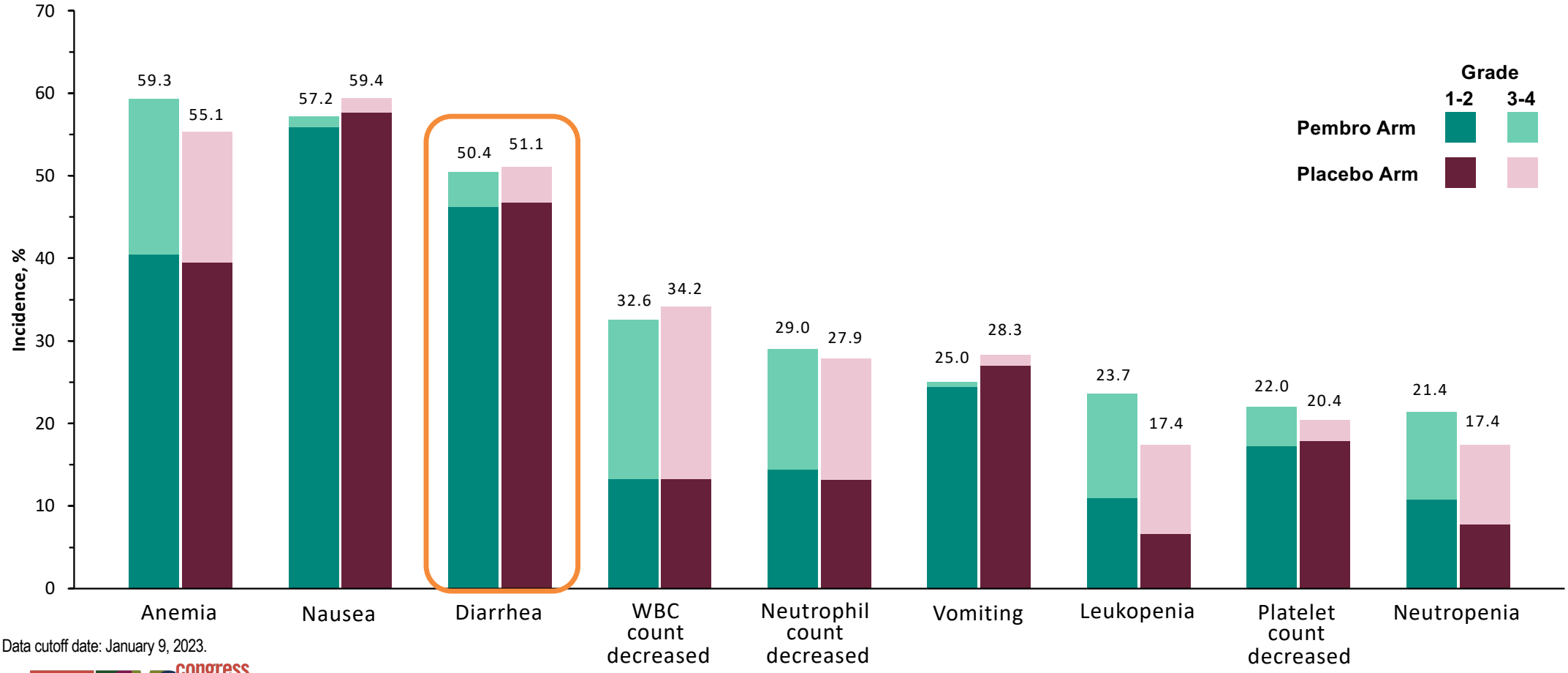
[a]At this analysis, 103 of the 240 deaths expected at the final analysis had occurred.
Data cutoff date: January 9, 2023.

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	525 (99.4%)	526 (99.2%)	507 (96.0%)	509 (96.0%)	172 (32.6%)	62 (11.7%)
Grade ≥3	394 (74.6%)	364 (68.7%)	354 (67.0%)	321 (60.6%)	22 (4.2%)	6 (1.1%)
Serious	150 (28.4%)	131 (24.7%)	91 (17.2%)	65 (12.3%)	15 (2.8%)	6 (1.1%)
Led to death	5 (0.9%)	6 (1.1%)	2 (0.4%)[c]	2 (0.4%)[d]	0	0
Led to discontinuation						
Any treatment	92 (17.4%)	75 (14.2%)	81 (15.3%)	67 (12.6%)	12 (2.3%)	2 (0.4%)
All treatment	1 (0.2%)	2 (0.4%)	0	1 (0.2%)	0	0

[a]Per investigator assessment. [b]Events were considered regardless of attribution to treatment by the investigator. [c]Immune-mediated gastritis and large intestine perforation. [d]Bone marrow failure and neutropenic colitis.
Data cutoff date: January 9, 2023.

Treatment-Related AEs, Incidence ≥20% in Either Arm



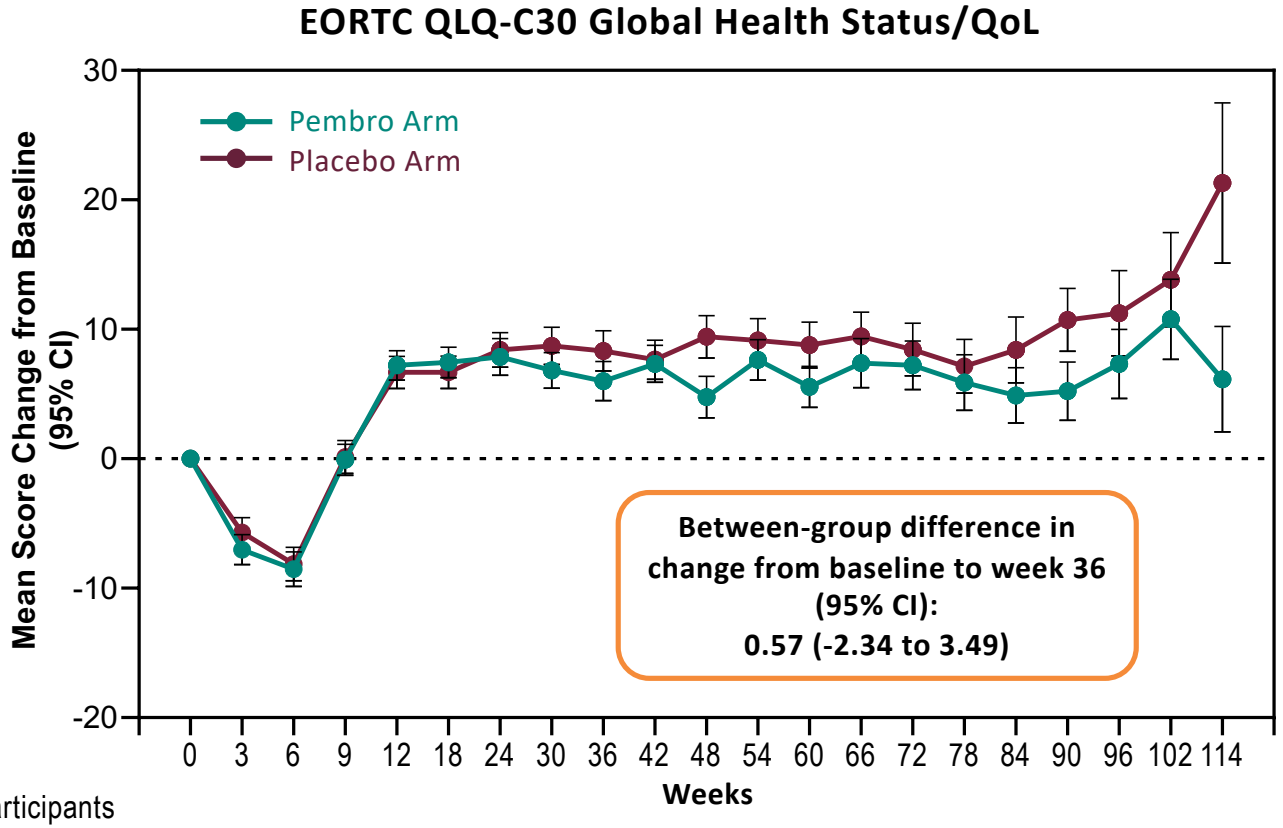
Data cutoff date: January 9, 2023.

MADRID 2023 ESMO congress

Presented by: Domenica Lorusso

EORTC Quality-of-Life Core 30 (QLQ-C30)

- Administered at each treatment cycle
- Compliance[a] at week 36:
  - 96.0% for both pembrolizumab and placebo arms
- Analysis population: all treated participants with ≥1 available PRO assessment
- No clinically meaningful between-group differences in changes in score from baseline to week 36 were observed for QLQ-C30 global health status/QoL or QLQ-C30 physical functioning scores



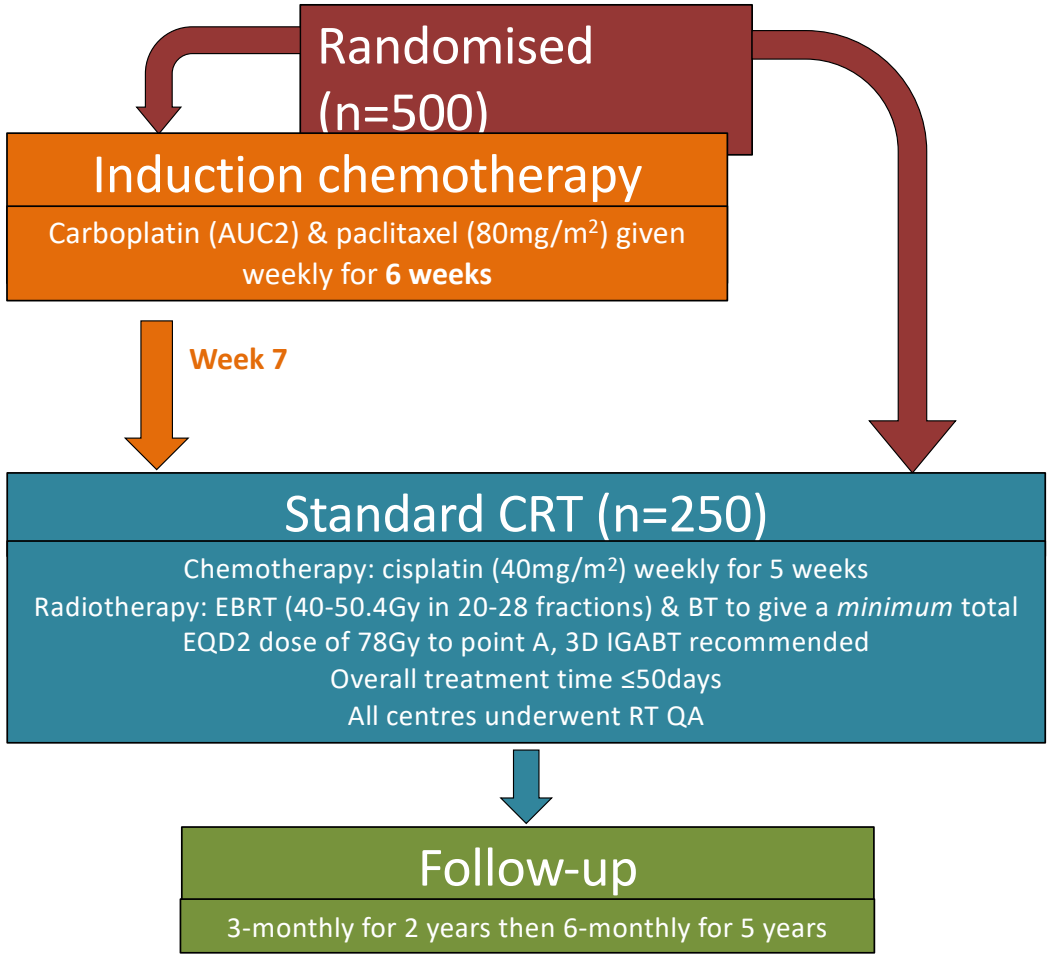
[a]Compliance was defined as the proportion of participants who completed the questionnaire among those who were expected to complete the questionnaire at the time point, excluding those missing by design such as death, discontinuation, or translation not available. Data cutoff date: January 9, 2023.

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



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

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)

Disease Characteristics at Baseline

	CRT alone (N=250)	Induction Chemo + CRT (N=250)
FIGO stage (2008)	**No. of patients (%)**	
IB1	2 (<1)	2 (<1)
IB2	23 (9)	19 (8)
IIA	14 (6)	17 (7)
IIB	176 (70)	178 (71)
IIIB	30 (12)	26 (10)
IVA	5 (2)	8 (3)
Cell type		
Non-squamous	45 (18)	44 (18)
Squamous	205 (82)	206 (82)
Nodal status		
Negative	142 (57)	146 (58)
Positive	108 (43)	104 (42)
Longest tumour diameter, cm median (range)	4.9 (1.8-12.8)	4.8 (1.3-13.5)

Adherence to Induction Chemotherapy

Paclitaxel/Carboplatin (n=250)	No. of patients (%)
Completed 6 weekly cycles	211 (84)
Completed at least 5 cycles	230 (92)
Main reasons for <6 cycles:	
Adverse events:	29 (11)
Haematological	9
Non-haematological	17
Both	3
Withdrawal/other	10 (4)
Median Interval from IC to RT days (range)	7 (5-53)

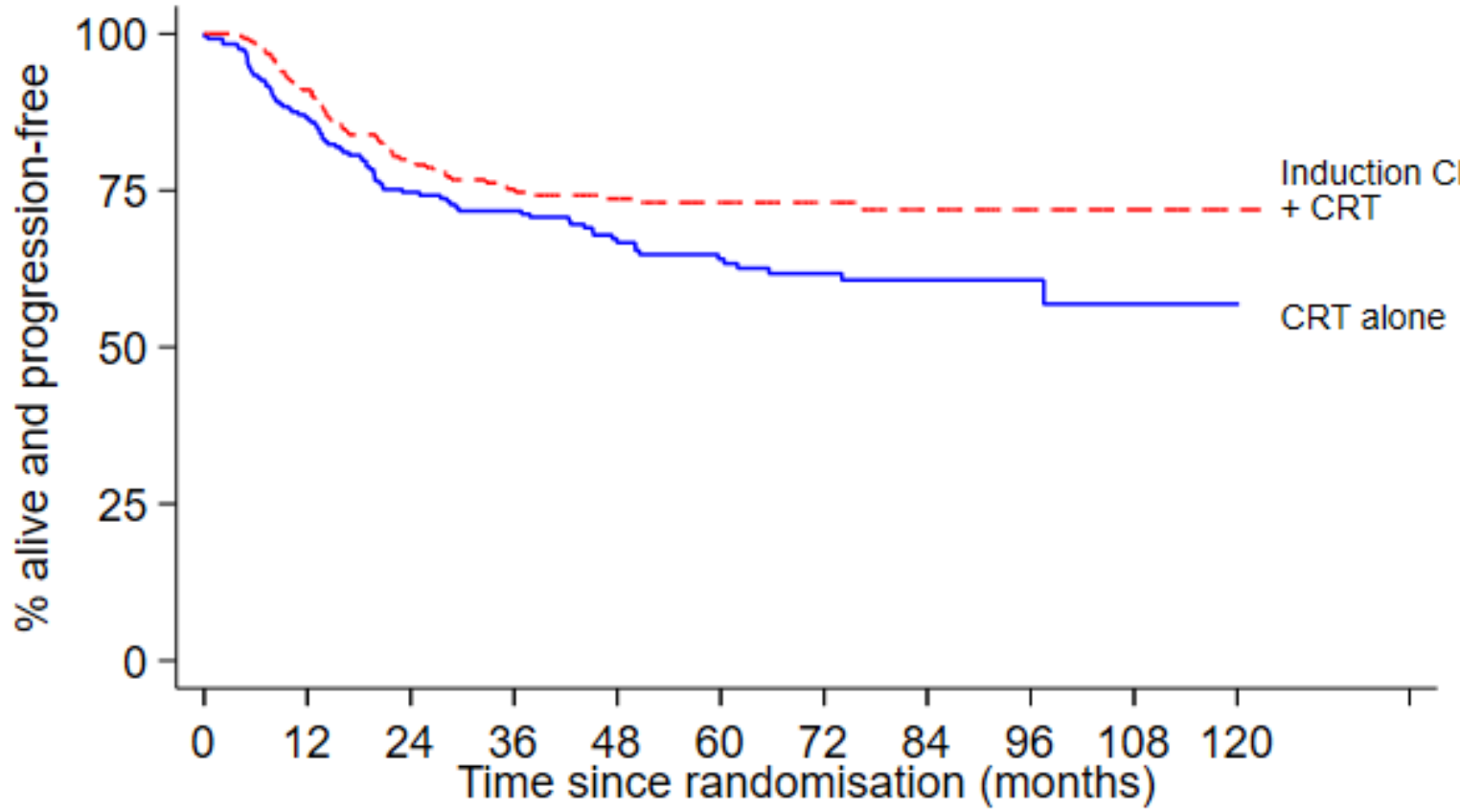
Adherence to Cisplatin

	CRT alone (n=250)	IC+ CRT (n=250)
	No. of patients (%)	
Completed 5 weekly cycles	197 (79)	169 (68)
Completed at least 4 cycles	224 (90)	212 (85)
Main reasons for <5 cycles:		
Adverse events leading to discontinuation:	33 (13)	68 (27)
Haematological	4	34
Non-haematological	25	20
Both	4	14
Other	20 (8)	13 (5)

Adherence to Radiation

	CRT alone (n=250)	Induction Chemo + CRT (n=250)
	No. of patients (%)	
Received external beam radiotherapy	**231 (92)**	**242 (97)**
IMRT	93 (40)	102 (42)
3D conformal	138 (60)	140 (58)
Received brachytherapy	**223 (97)**	**238 (98)**
2D point A	49(22)	46 (19)
3D point A	106 (48)	120 (51)
3D HRCTV D90	68 (30)	72 (30)
Median overall treatment time days(range)	**45 (37-88)**	**45 (36-70)**

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%

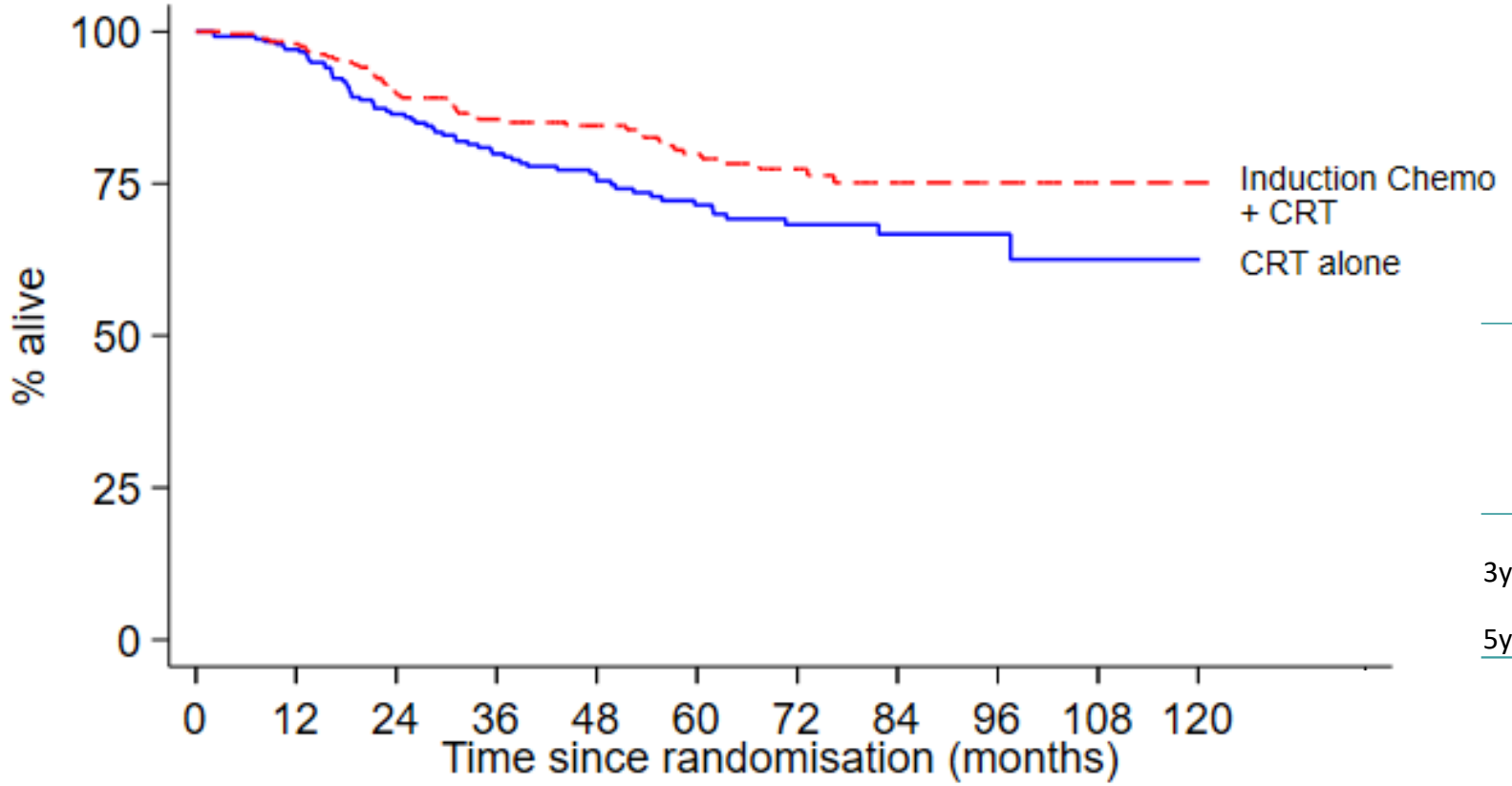
Number at risk

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

PARIS 2022 ESMO congress

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%

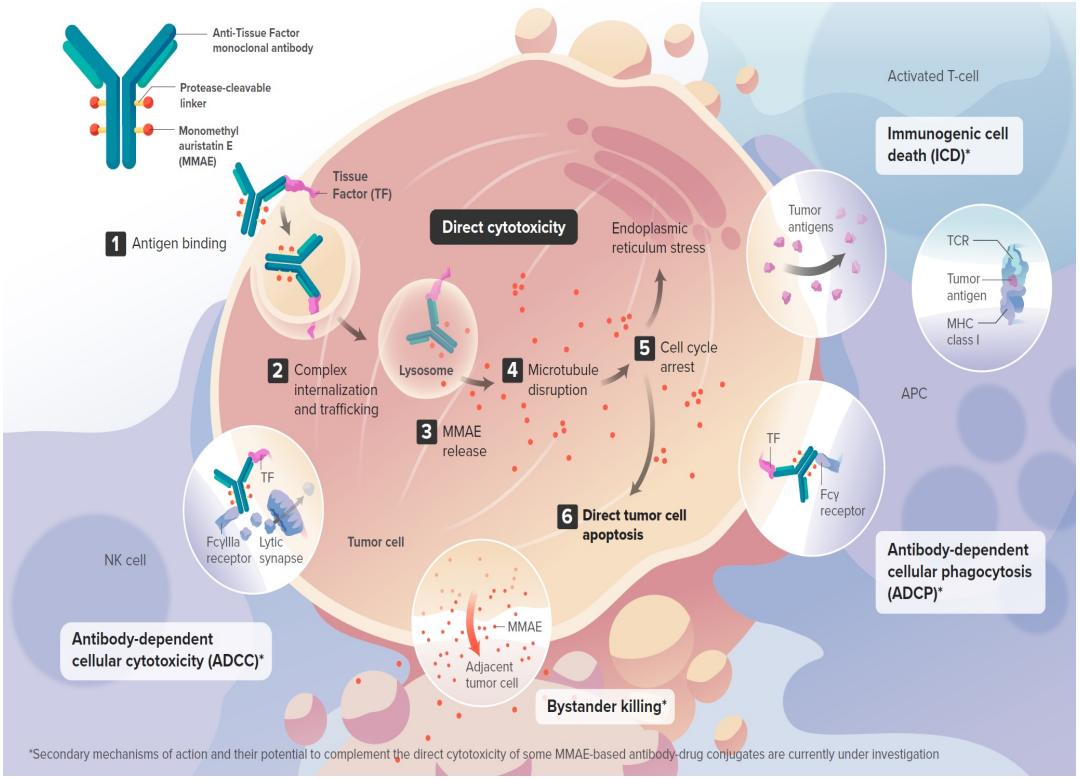
Number at risk

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

PARIS 2022 ESMO congress

Antibody-drug conjugates: Tisotumab Vedotin

- ***Tisotumab vedotin*** *is an investigational antibody-drug conjugate* ***directed to tissue factor (TF)*** *and covalently linked to the microtubule-disrupting agent MMAE via a protease-cleavable linker*[1,2]
- *TF is highly prevalent in cervical cancer and other solid tumors and is associated with cancer pathophysiology and poor prognosis*[3-5]
  - TF is co-opted by tumor cells to promote tumor growth, angiogenesis, and metastasis[6]
  - In normal physiology, TF's primary role is to initiate the coagulation cascade after vascular injury[6]
- *Tisotumab vedotin has multiple anti-tumor effects*[1,2,7]



Tisotumab vedotin is an investigational agent, and its safety and efficacy have not been established.

1. Breij EC et al. *Cancer Res*. 2014;74(4):1214-1226. 2. De Goeij BE et al. *Mol Cancer Ther*. 2015;14(5):1130-1140. 3. Pan L et al. *Mol Med Rep*. 2019;19:2077-2086. 4. Cocco E et al. *BMC Cancer*. 2011;11:263. 5. Zhao X et al. *Exp Ther Med*. 2018;16:4075-4081. 6. Forster Y et al. *Clin Chim Acta*. 2006;364:12-21 7. Alley SC et al. American Association for Cancer Research Annual Meeting; March 29 – April 3, 2019; Atlanta, GA, USA; Abstract #221.
ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; MMAE, monomethyl auristatin E; MOA, mechanism of action; TF, tissue factor.

InnovaTV 204: Study Design

innovaTV 204 (NCT03438396) is a pivotal phase 2 single-arm, multicenter (United States and Europe) study evaluating tisotumab vedotin in patients with previously treated recurrent and/or metastatic cervical cancer

Key Eligibility Criteria

- Recurrent or extrapelvic metastatic cervical cancer
- **Progressed during or after doublet chemotherapy[a] with bevacizumab (if eligible)**
- Received ≤2 prior systemic regimens[b]
- ECOG PS 0-1

Enrolled: 102[c]
Treated: 101*

Tisotumab vedotin
2.0 mg/kg IV Q3W

Until PD or unacceptable toxicity

Tumor responses assessed using CT or MRI at baseline, every 6 weeks for the first 30 weeks, and every 12 weeks thereafter

*Study sample size calculated assuming a confirmed ORR of 21% to 25% with tisotumab vedotin and to provide ≥80% power to exclude an ORR of ≤11%[e]

Primary Endpoint
- ORR[d] per RECIST v1.1, by independent imaging review committee (IRC)

Secondary Endpoints
- ORR[d] per RECIST v1.1, by investigator
- DOR, TTR, and PFS by IRC and investigator
- OS
- Safety

Exploratory Endpoints
- Biomarkers
- HRQoL

[a]Paclitaxel plus platinum (cisplatin or carboplatin) or paclitaxel plus topotecan. [b]Adjuvant or neoadjuvant chemotherapy or if administered with radiation therapy, was not counted as a prior systemic regimen. [c]June 2018 to April 2019. [d]Responses were confirmed by subsequent repeat imaging performed ≥4 weeks after initial response assessment. [e]Using one-sided exact binomial test at 0.025 significance level.
CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IRC, independent review committee; IV, intravenous; MRI, magnetic resonance imaging; OS, overall survival; PD, progressive disease; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; TTR, time to response.

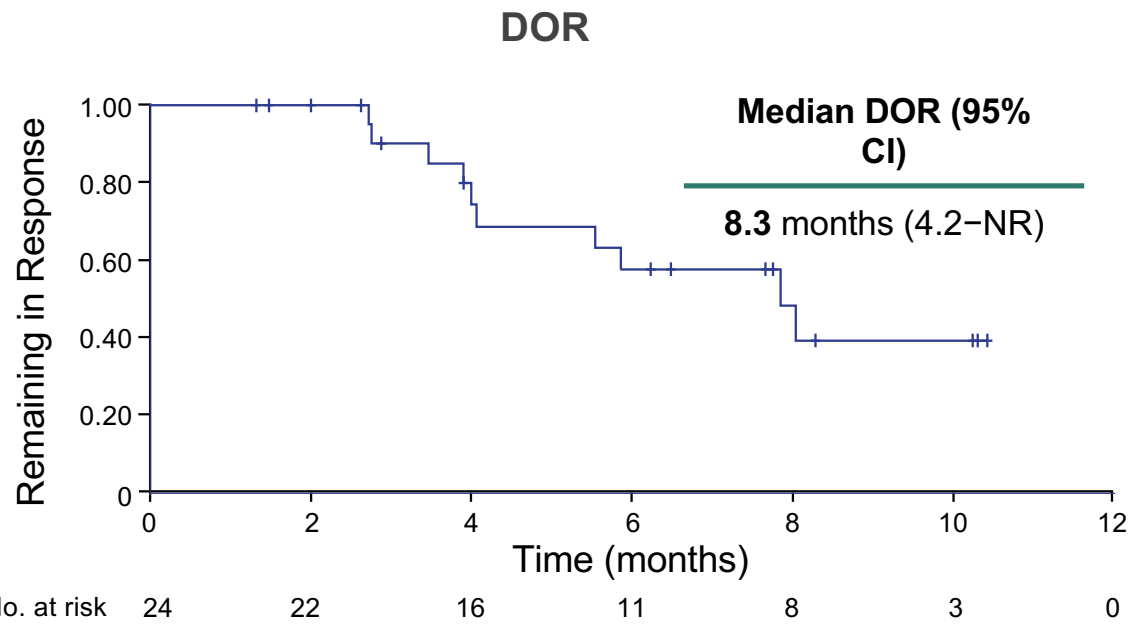
Coleman R. et al. Presented at ESMO Meeting 2020

Clinical Efficacy

IRC-Assessed

	N=101
Confirmed ORR (95% CI)[a], %	**24 (16–33)**
CR, n (%)	7 (7)
PR, n (%)	17 (17)
SD, n (%)	49 (49)
PD, n (%)	24 (24)
Not evaluable, n (%)	4 (4)
DCR (95% CI)[b], %	72 (63–81)

- 62% (95% CI, 37–80) of patients had an ongoing confirmed response ≥6 months



Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months.
[a]Exact 95% CI based on the Clopper-Pearson method. [b]Disease control rate is the proportion of patients with best overall response of confirmed CR, PR, and SD.
CI, confidence interval; CR, complete response; DOR: duration of response; IRC, independent review committee; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.
Table 2 and Figure S2, Coleman RL et al. *Lancet Oncol.* Published online April 9, 2021.

InnovaTV 301 (ENGOT cx-12/GOG 3057): Study Design

A randomized, open-label, phase 3 confirmatory trial of tisotumab vedotin vs investigator's choice chemotherapy in 2L/3L recurrent or metastatic cervical cancer[1]

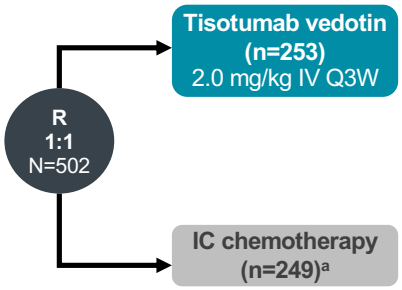
Key Eligibility Criteria[2]

- Recurrent or metastatic cervical cancer
- Disease progression on or after chemotherapy doublet ± bevacizumab and an anti-PD-(L)1 agent, if eligible and available
- ≤2 prior lines
- Measurable disease per RECIST v1.1
- ECOG PS 0-1

Stratification Factors

- ECOG PS (0 vs 1)
- Prior bevacizumab (yes vs no)
- Prior anti-PD-(L)1 therapy (yes vs no)
- Geographic region (US, Europe, Other)

Previous anti–PD-1 or anti–PD-L1 therapy was permitted



IC Chemotherapy

- Topotecan
- Vinorelbine
- Gemcitabine
- Irinotecan
- Pemetrexed

Primary endpoint: OS[b]

Secondary endpoints: PFS[c], ORR[c], Safety

Baseline Patient and Disease Characteristics

	Tisotumab Vedotin (N=253)	IC Chemotherapy (N=249)
Number of prior r/m systemic regimens, n(%)		
1	159 (62.8)	149 (59.8)
2	93 (36.8)	100 (40.2)
Unknown	1 (0.4)	0
Prior bevacizumab, n (%)	164 (64.8)	157 (63.1)
Prior anti-PD-(L)1 therapy, n (%)	**71 (28.1)**	**67 (26.9)**
Prior radiation therapy for cervical cancer, n (%)	205 (81.0)	203 (81.5)

Baseline patient demographics were balanced across both arms

Data presented herein are a planned interim analysis

End of treatment visit occurred 30 days after the last dose of treatment. Survival follow-up occurred every 60 days after the last dose of treatment.

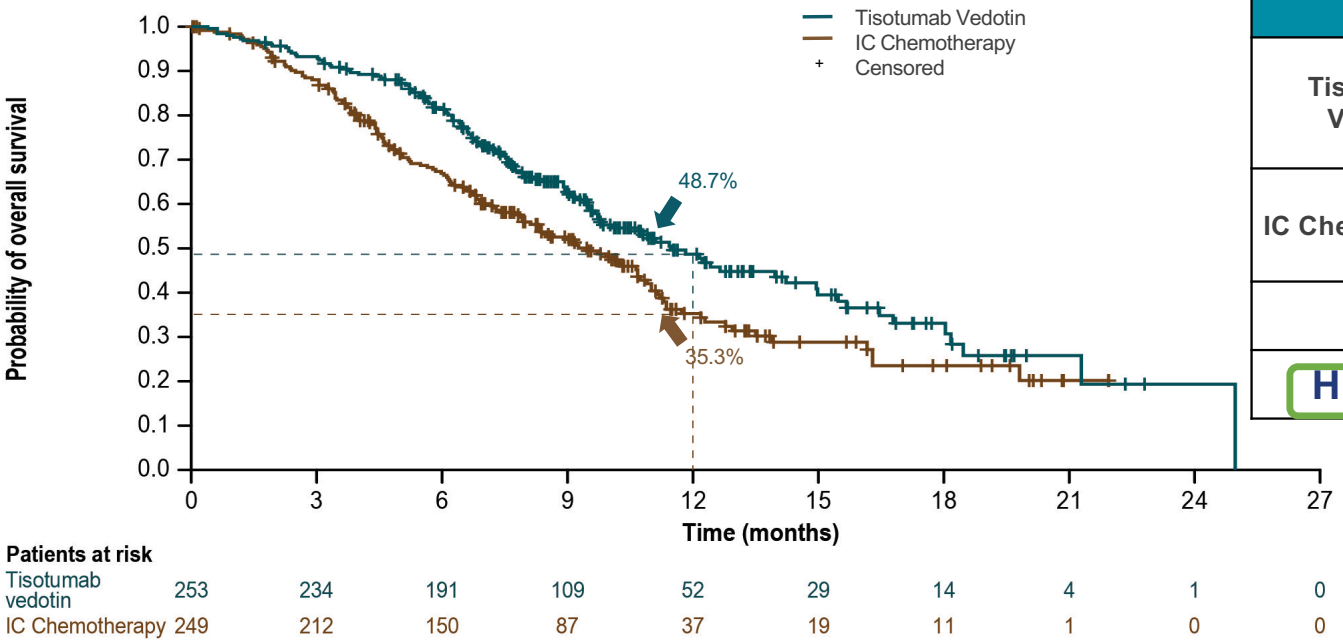
[a]Chemotherapy regimens were given at the following doses: topotecan 1 or 1.25 mg/m^2 IV on Days 1 to 5 of a 21-day cycle; vinorelbine 30 mg/m^2 IV on Days 1 and 8 of a 21-day cycle; gemcitabine 1000 mg/m^2 IV on Days 1 and 8 of a 21-day cycle; irinotecan 100 or 125 mg/m^2 IV weekly for 28 days every 42 days; pemetrexed 500 mg/m^2 on Day 1 of a 21-day cycle; [b]OS was defined as the time from the date of randomization to the date of death due to any cause; [c]Assessed by investigator.

ECOG PS, eastern cooperative oncology group performance status; IC, investigator's choice; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, response evaluation criteria in solid tumors; 2L, second-line; 3L, third-line.

Vergote I. Presented at ESMO 2023: Presidential Symposium (Oral Presentation) LBA9.

InnovaTV 301 (ENGOT cx-12/GOG 3057): Overall Survival

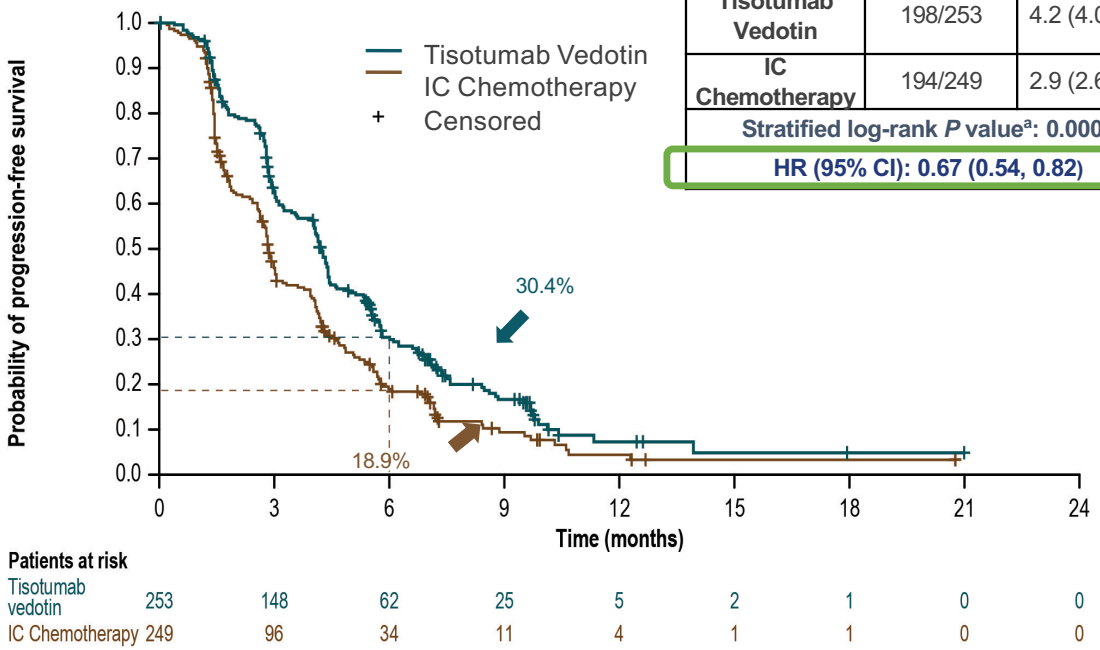
Overall Survival (Primary endpoint)



Treatment	Events/Total	Median (95% CI)
Tisotumab Vedotin	123/253	11.5 (9.8, 14.9)
IC Chemotherapy	140/249	9.5 (7.9, 10.7)
Stratified log-rank *P* value[a]: 0.0038		
HR (95% CI): 0.70 (0.54, 0.89)		

[a]The threshold for statistical significance is 0.0226 (2-sided), based on the actual number of OS events at interim analysis.
IC, investigator choice; PD-L1, Programmed death-ligand 1;
Vergote I. Presented at ESMO 2023: Presidential Symposium (Oral Presentation) LBA9.

InnovaTV 301 (ENGOT cx-12/GOG 3057): PFS Per Investigator

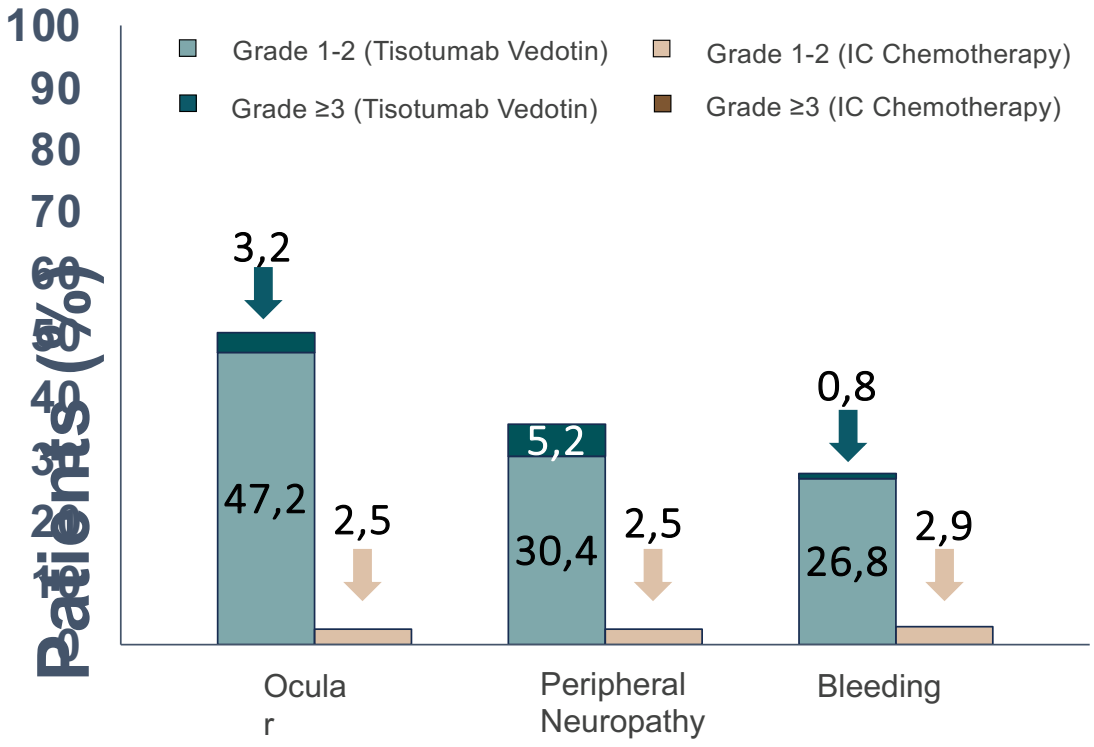


Treatment	Events/Total	Median (95% CI)
Tisotumab Vedotin	198/253	4.2 (4.0, 4.4)
IC Chemotherapy	194/249	2.9 (2.6, 3.1)
Stratified log-rank *P* value[a]: 0.0001		
HR (95% CI): 0.67 (0.54, 0.82)		

	Tisotumab Vedotin (N=253)	IC Chemotherapy
ORR, % (95% CI)	**17.8 (13.3 - 23.1)**	**5.2 (2.8-8.8)**
Odds ratio (95% CI) *P* value	4.0 (2.1-7.6) *P*<0.0001	
Best Overall Response, n (%)		
CR	6 (2.4)	0
PR	39 (15.4)	13 (5.2)
SD	147 (58.1)	132 (53.0)
PD	46 (18.2)	74 (29.7)
Not evaluable/Not available	15 (5.9)	30 (12.0)
DCR[b], % (95% CI)	75.9 (70.1-81.0)	58.2 (51.8-64.4)
Median DOR (95% CI)	5.3 (4.2-8.3)	5.7 (2.8-NR)

[a]The threshold for statistical significance is 0.0453 (2-sided), based on the actual number of PFS events at interim analysis. [b]DCR is defined as CR+PR+SD; CR and PR were confirmed responses. The minimum criteria for SD duration was ≥5 weeks after the date of randomization.
CI, confidence interval; CR, complete response; DCR, disease control rate; HR, hazard ratio; IC, investigator choice; ORR, overall response rate; PD, progressive disease; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; SD, stable disease.
Vergote I. Presented at ESMO 2023: Presidential Symposium (Oral Presentation) LBA9.

Adverse Events of Special Interest for Tisotumab Vedotin[a]



Three most common preferred terms for each AESI	
Ocular	Conjunctivitis (30.4%), keratitis (15.6%), dry eye (13.2%)
Peripheral neuropathy	Peripheral sensory neuropathy (26.8%), paresthesia (2.8%), muscular weakness (2.4%), peripheral sensorimotor neuropathy (2.4%)
Bleeding	Epistaxis (22.8%), hematuria (3.2%), vaginal hemorrhage (3.2%)

- There were no grade 4 or 5 AESIs
- Dose discontinuation due to ocular and peripheral neuropathy events occurred in 5.6% of patients for each

[a]Treatment-related AESIs
AESI, adverse events of special interest; IC, investigator's choice;
Vergote I. Presented at ESMO 2023: Presidential Symposium (Oral Presentation) LBA9.

MEDICAL TREATMENTS IN CERVCAL CANCER: CONCLUSION

- Immunotherapy is changing the face of Cervical Cancer Treatment
- ICIs in first line and relapsed settings have demonstrated improvements in OS and PFS with respect to standard of care.
- ICIs in combination with chemoradiotherapy has reported increase in pfs with respect to CHT-RT in locally advanced disease
- TV increases OS with respect to CHT in 2nd line treatment
- Despite encouraging data, there are still several open questions:
  - Is there any rationale for using Anti-PD1 agents after Anti-PD1?
  - Could Anti-PD1/Anti-CTL4 combinations be a choice for those patients immunotherapy pre-treated?