



Osakidetza

ARABAKO
ERAKUNDE SANITARIO INTEGRATUA
ORGANIZACIÓN SANITARIA
ARABA

3^a

Jornada
de Actualización
**EN CÁNCER
GINECOLÓGICO**



Bilbao

**12-13
junio
2025**

Mesa 3: Cáncer de cérvix
Tratamiento de la enfermedad recurrente y metastásica

Yolanda García
Oncología Médica
Hospital Universitario de Álava
Vitoria-Gasteiz



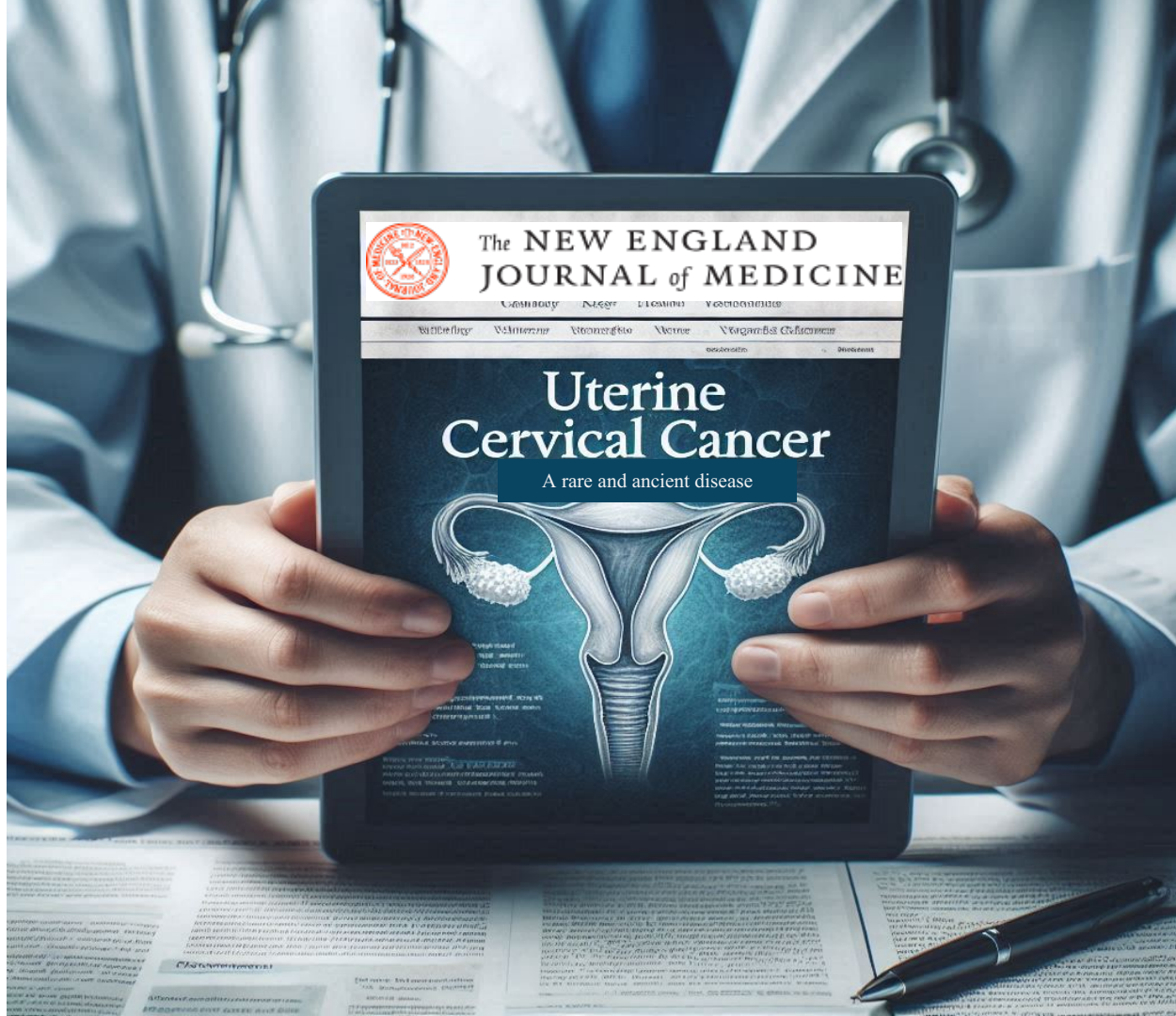
**EUSKO JAURLARITZA
GOBIERNO VASCO**

OSASUN SAILA
DEPARTAMENTO DE SALUD



Receipt of honoraria or consultation fees: GSK, MSD, AZ, Lilly, Roche, Pharmamar, Clovis, Abbvie

Participation in a company-sponsored speaker's bureau: GSK, MSD, AZ, Lilly, Roche, Novartis, Clovis, Tesaro



Cáncer de cérvix es una enfermedad prevenible
relacionada con infección por HPV

Vacunación

Prevención primaria

Programas de
cribado

Prevención secundaria



Toda paciente con cáncer de cérvix debería recibir combinación de QT/IT +/- bev en 1L *

Toda paciente con cáncer de cérvix metastásico debería recibir IT *

En pacientes pre-tratadas con IT los ADC's (TV con el desarrollo más Avanzado) es el futuro cercano *

La vacunación y el cribado son las armas que han de impedir tener que aplicar lo anterior



Cáncer de cérvix recurrente

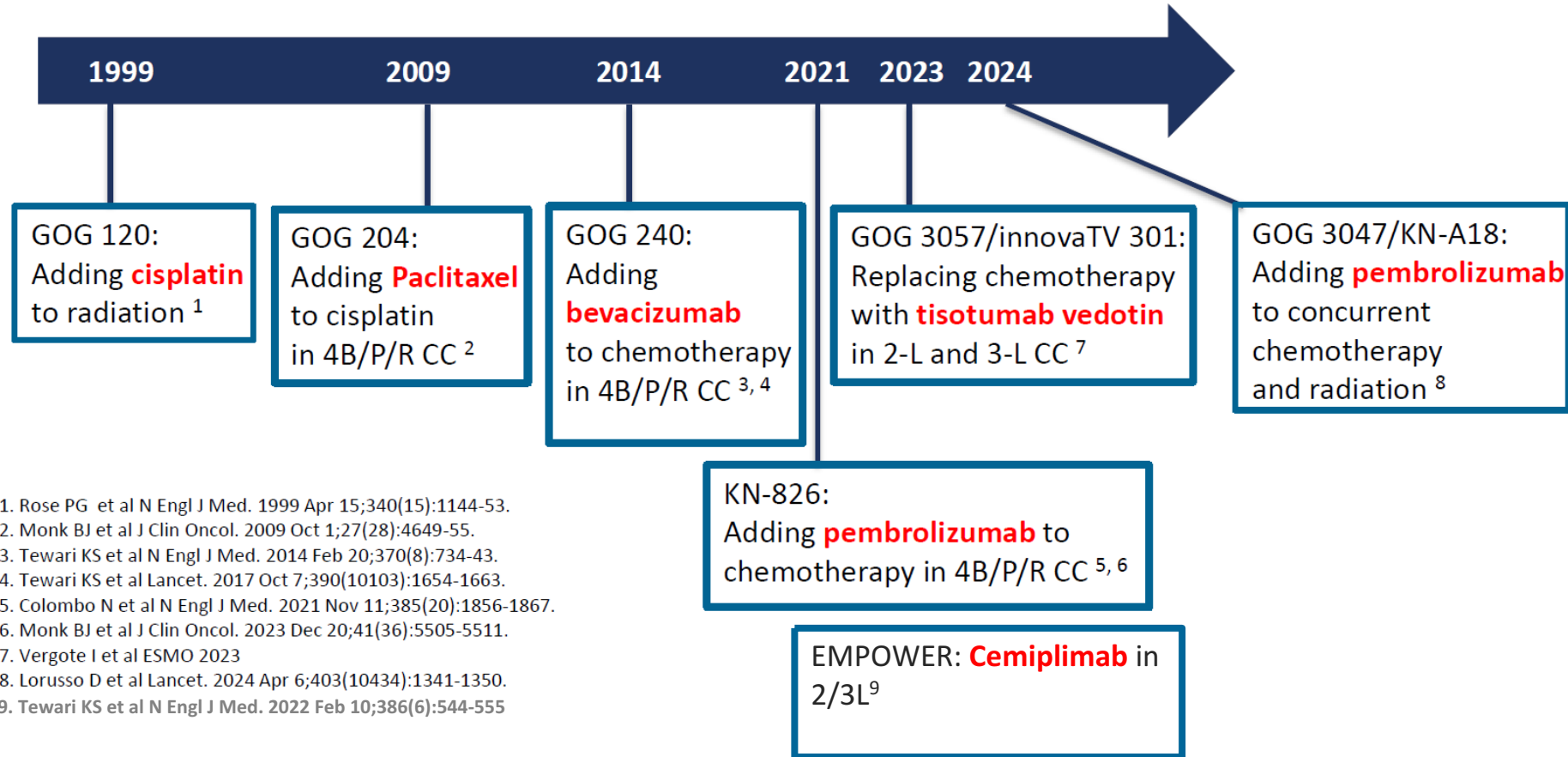
Posibilidad de tratamiento radical

* Radioterapia concurrente a tratamiento sistémico

RTE + BQT + (cis)platino
semanal + (pembrolizumab)

* Cirugía

- **Exanteración** en diferentes modalidades
 - Conceptualmente tratamiento paliativo
 - Tener en consideración calidad de vida y morbi-mortalidad quirúrgica
 - Selección adecuada de pacientes



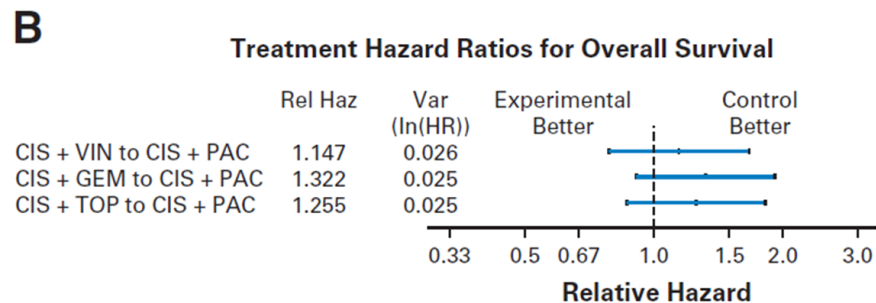
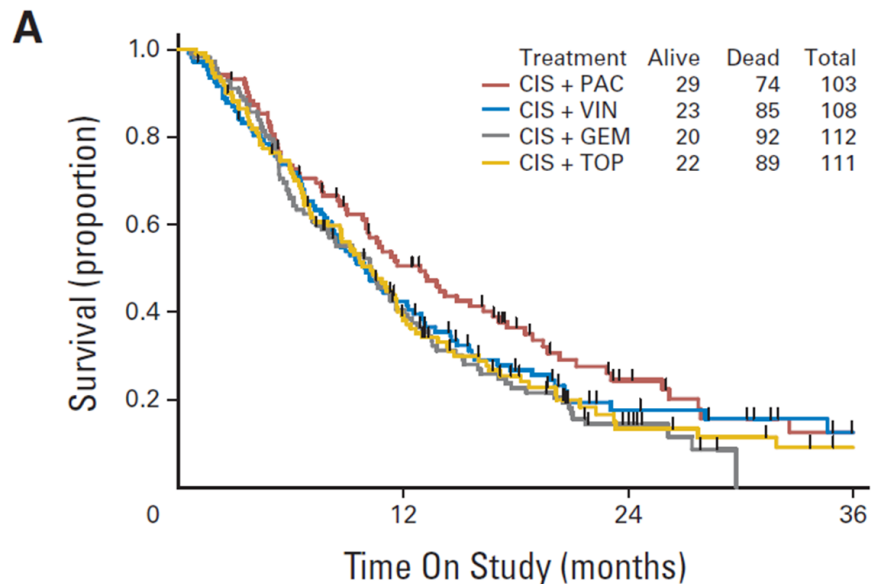


Phase III Trial of Four Cisplatin-Containing Doublet Combinations in Stage IVB, Recurrent, or Persistent Cervical Carcinoma: A Gynecologic Oncology Group Study

Bradley J. Monk, Michael W. Sill, D. Scott McMeekin, David E. Cohn, Lois M. Ramondetta, Cecelia H. Boardman, Jo Benda, and David Cella

Dobletes platino 1L

ORR: 28.9%



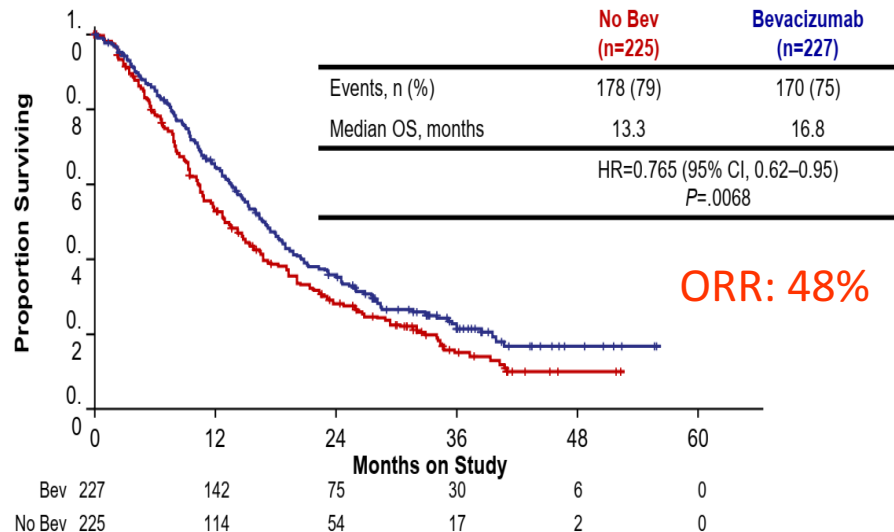
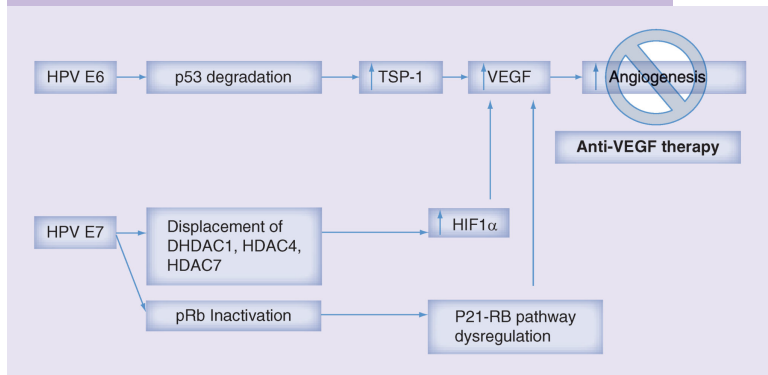
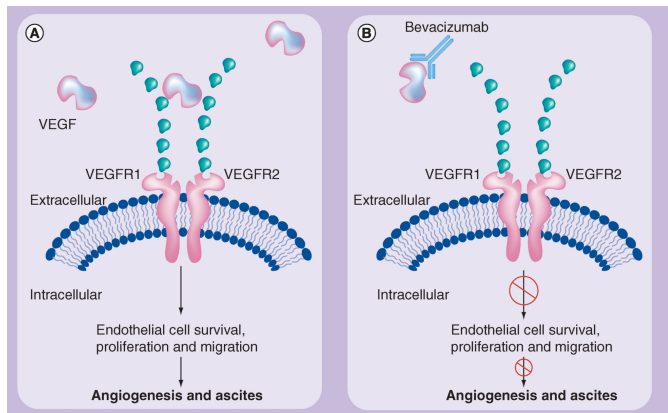
Bevacizumab 1L: GOG 240 (Tewari NEJM 2014)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Improved Survival with Bevacizumab in Advanced Cervical Cancer

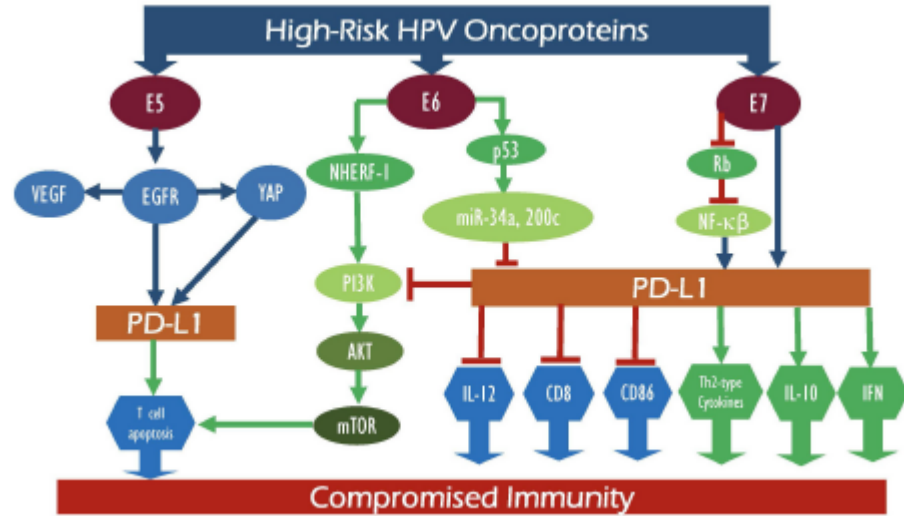
Krishnansu S. Tewari, M.D., Michael W. Sill, Ph.D., Harry J. Long III, M.D.,
Richard T. Penson, M.D., Helen Huang, M.S., Lois M. Ramondetta, M.D.,
Lisa M. Landrum, M.D., Ana Oaknin, M.D., Thomas J. Reid, M.D.,
Mario M. Leitao, M.D., Helen E. Michael, M.D., and Bradley J. Monk, M.D.



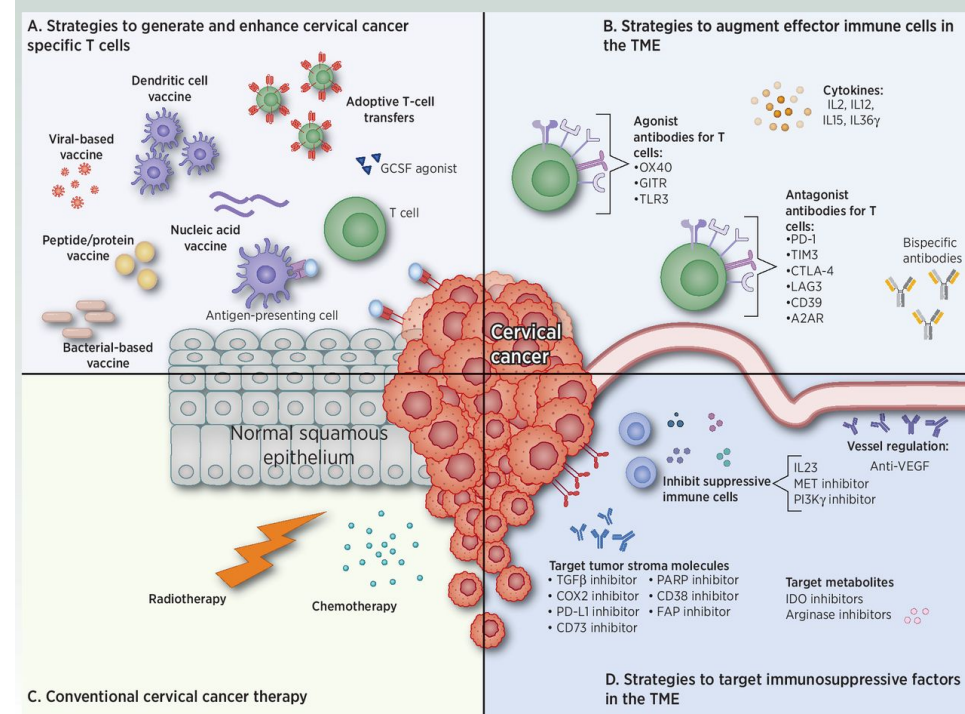
mOS=13,3 vs 16,8 m

HR: 0,765 (0,62-0,95)

Bases inmunoterapia en cáncer de cérvix



Alouch S et al Frontiers Oncol 2020



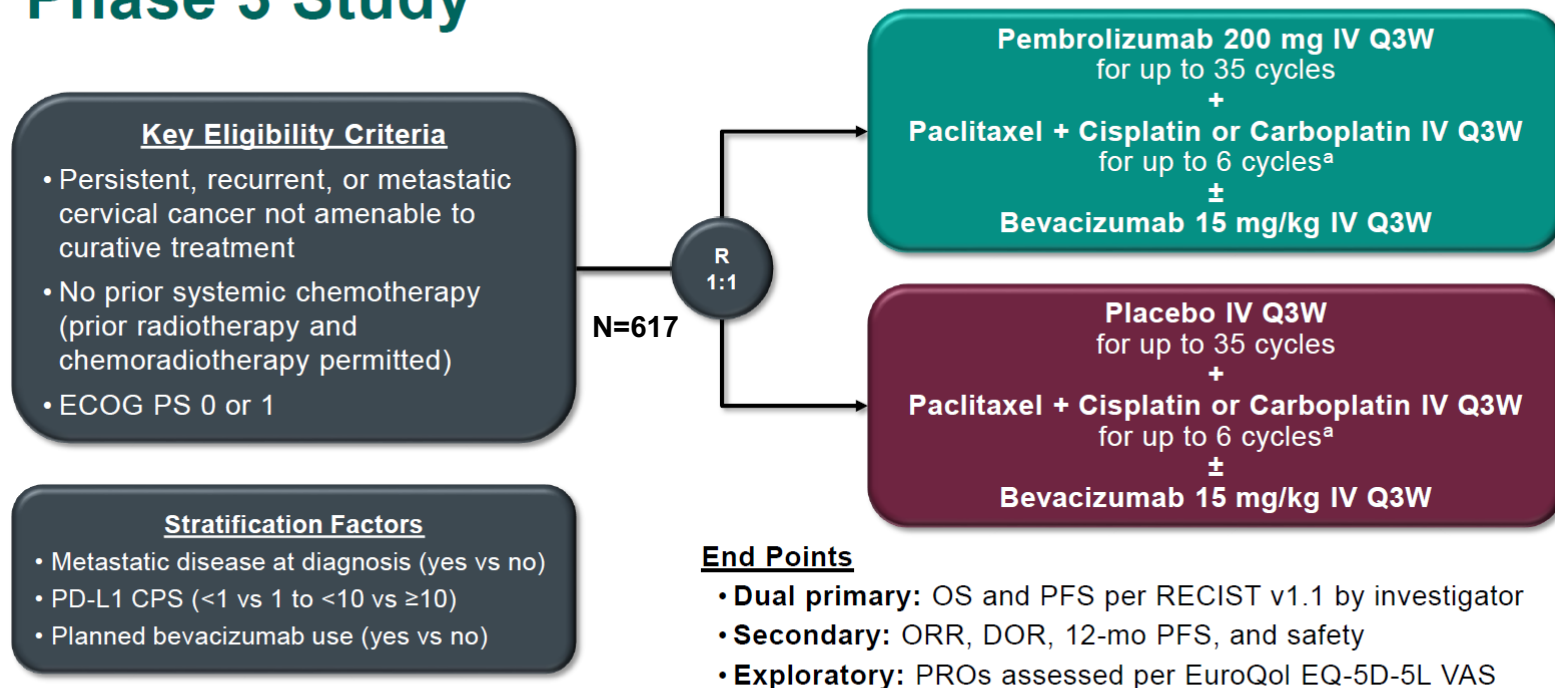
Ferrall L et al Clin Cancer Res. 2021

ORIGINAL ARTICLE

Pembrolizumab for Persistent, Recurrent, or Metastatic Cervical Cancer

N. Colombo, C. Dubot, D. Lorusso, M.V. Caceres, K. Hasegawa,
R. Shapira-Frommer, K.S. Tewari, P. Salman, E. Hoyos Usta, E. Yañez, M. Gümüş,
M. Olivera Hurtado de Mendoza, V. Samouëlian, V. Castonguay, A. Arkhipov,
S. Toker, K. Li, S.M. Keefe, and B.J. Monk, for the KEYNOTE-826 Investigators*

KEYNOTE-826: Randomized, Double-Blind, Phase 3 Study



^aPaclitaxel: 175 mg/m². Cisplatin: cisplatin 50 mg/m². Carboplatin: AUC 5 mg/mL/min. The 6-cycle limit was introduced with protocol amendment 2, although participants with ongoing clinical benefit who were tolerating chemotherapy could continue beyond 6 cycles after sponsor consultation.

CPS, combined positive score (number of PD-L1–staining cells [tumor cells, lymphocytes, macrophages] divided by the total number of viable tumor cells, multiplied by 100); PROs, patient-reported outcomes; VAS, visual analog scale. KEYNOTE-826 ClinicalTrials.gov identifier, NCT03635567.

Baseline Characteristics, All-Comer Population

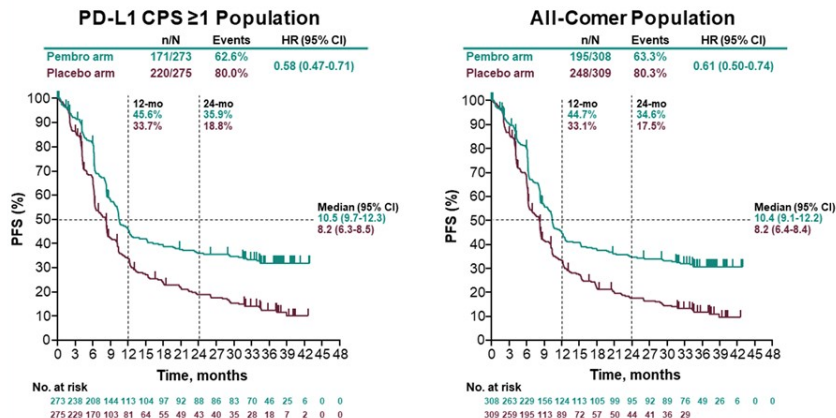
	Pembro Arm ^a (N = 308)	Placebo Arm ^a (N = 309)
Age, median (range)	51 y (25-82)	50 y (22-79)
ECOG PS 1	128 (41.6%)	139 (45.0%)
Squamous cell carcinoma	235 (76.3%)	211 (68.3%)
PD-L1 CPS		
<1	35 (11.4%)	34 (11.0%)
1 to <10	115 (37.3%)	116 (37.5%)
≥10	158 (51.3%)	159 (51.5%)
Prior therapy		
Chemoradiation or radiation with surgery	71 (23.1%)	79 (25.6%)
Chemoradiation or radiation only	156 (50.6%)	142 (46.0%)
Surgery only	23 (7.5%)	24 (7.8%)
None	58 (18.8%)	64 (20.7%)

	Pembro Arm ^a (N = 308)	Placebo Arm ^a (N = 309)
Stage at initial diagnosis (FIGO 2009/NCCN 2017 criteria)		
I	67 (21.8%)	58 (18.8%)
II	85 (27.6%)	93 (30.1%)
III	5 (1.6%)	8 (2.6%)
IIIA	4 (1.3%)	8 (2.6%)
IIIB	46 (14.9%)	42 (13.6%)
IVA	7 (2.3%)	4 (1.3%)
IVB	94 (30.5%)	96 (31.1%)
Disease status at study entry		
Metastatic ^b	58 (18.8%)	64 (20.7%)
Persistent or recurrent with distant metastases	199 (64.6%)	179 (57.9%)
Persistent or recurrent without distant metastases	51 (16.6%)	66 (21.4%)
Bevacizumab use during the study	196 (63.6%)	193 (62.5%)

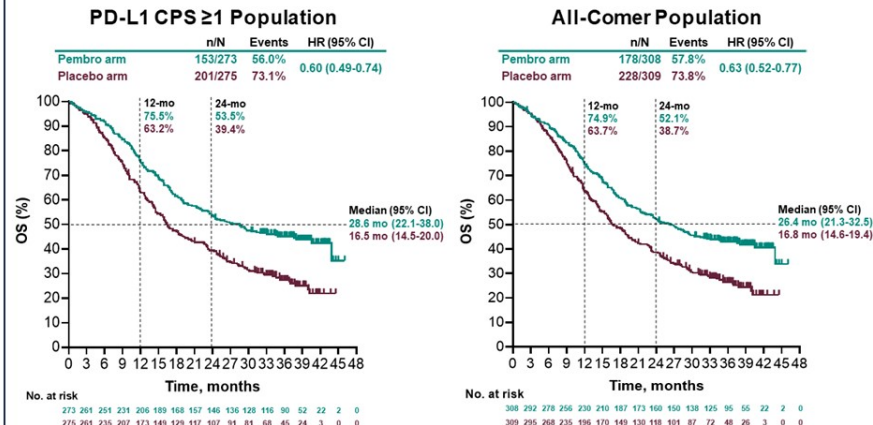
^aThe treatment regimen in both arms included chemo ± bev.

^bIncludes participants with para-aortic lymph node involvement. These participants were diagnosed with stage IVB disease and entered the study with no prior treatment for cervical cancer. Data cutoff date: May 3, 2021.

PFS



OS



Final OS results (median follow up: 39.1 mo):

+CPS ≥ 1 : 28.6 vs 16.5 mo

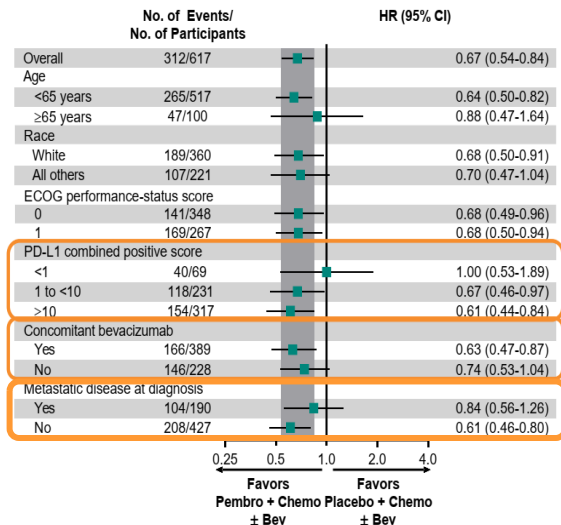
HR: 0.60 (0.49-0.74)

+All-comers: 26.4 vs 16.8 mo

HR: 0.63 (0.52-0.77)

ORR: 69%

OS: Protocol-Specified Subgroups, All-Comer Population



Data cutoff date: May 3, 2021.

Approvals

October 2021



FDA approves pembrolizumab combination for the first-line treatment of cervical cancer

On October 13, 2021, the Food and Drug Administration approved pembrolizumab (Keytruda, Merck) in combination with chemotherapy, with or without bevacizumab, for patients with persistent, recurrent or metastatic cervical cancer whose tumors express PD-L1 (CPS≥1), as determined by an FDA-approved test.

April 2022



European Commission Approves Pembrolizumab/Chemotherapy With or Without Bevacizumab for PD-L1+ Metastatic Cervical Cancer

Atezolizumab plus bevacizumab and chemotherapy for metastatic, persistent, or recurrent cervical cancer (BEATcc): a randomised, open-label, phase 3 trial

*Ana Oaknin, Laurence Gladieff, Jerónimo Martínez-García, Guillermo Villacampa, Munetaka Takekuma, Ugo De Giorgi, Kristina Lindemann, Linn Woelber, Nicoletta Colombo, Linda Duska, Alexandra Leary, Ana Godoy-Ortiz, Shin Nishio, Antoine Angelergues, Maria Jesús Rubio, Lorena Fariñas-Madrid, Satoshi Yamaguchi, Domenica Lorusso, Isabelle Ray-Coquard, Luis Manso, Florence Joly, Jesús Alarcón, Philippe Follana, Ignacio Romero, Coriolan Lebreton, J Alejandro Pérez-Fidalgo, Mayu Yunokawa, Hanna Dahlstrand, Véronique D'Hondt, Leslie M Randall for the ENGOT-Cx10-GEICO 68-C-JGOG1084-GOG-3030 Investigators**

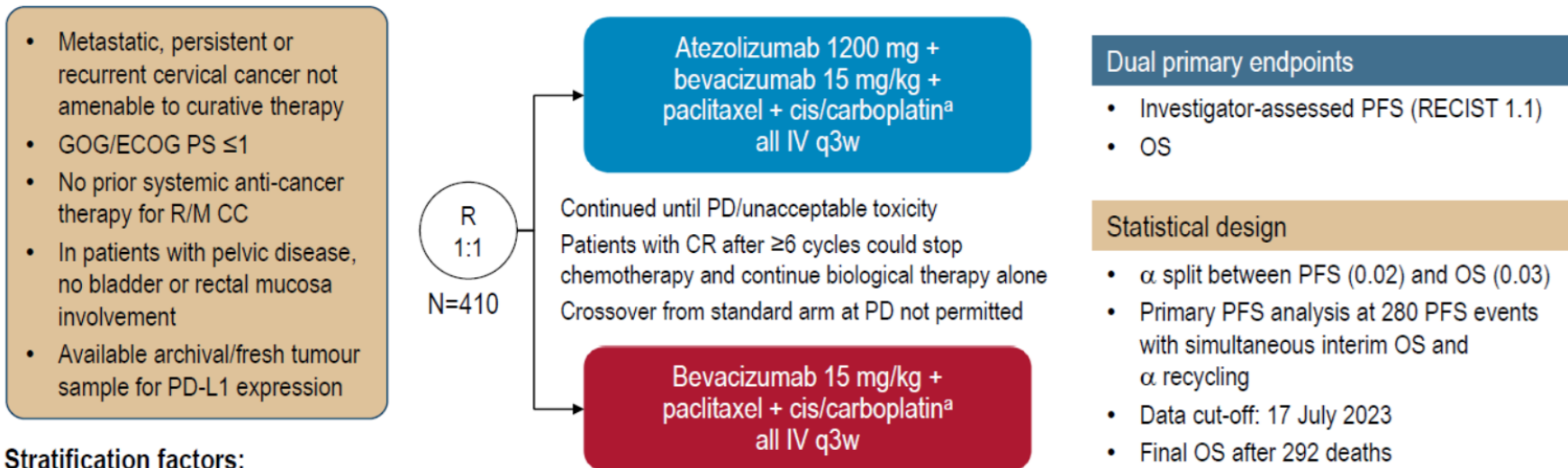
Lancet 2024; 403: 31–43

Published **Online** December 1, 2023

[https://doi.org/10.1016/S0140-6736\(23\)02405-4](https://doi.org/10.1016/S0140-6736(23)02405-4)

BEATcc (NCT03556839)

Open-label randomised phase 3 trial evaluating dual blockade of PD-L1 and VEGF



Stratification factors:

- Prior concurrent chemoradiation (yes vs no)
- Histology (squamous cell carcinoma vs adenocarcinoma^b including adenosquamous carcinoma)
- Chemotherapy (cisplatin vs carboplatin)

^aPaclitaxel 175 mg/m² day 1 + platinum (cisplatin 50 mg/m² or carboplatin AUC5) day 1; ^bCapped at 20% of the overall population

CR = complete response; OS = overall survival; PD = disease progression; PD-L1 = programmed death ligand 1; PFS = progression-free survival; R/M CC = metastatic, persistent or recurrent cervical cancer; VEGF = vascular endothelial growth factor PS = performance status; q3w = every 3 weeks

Baseline characteristics

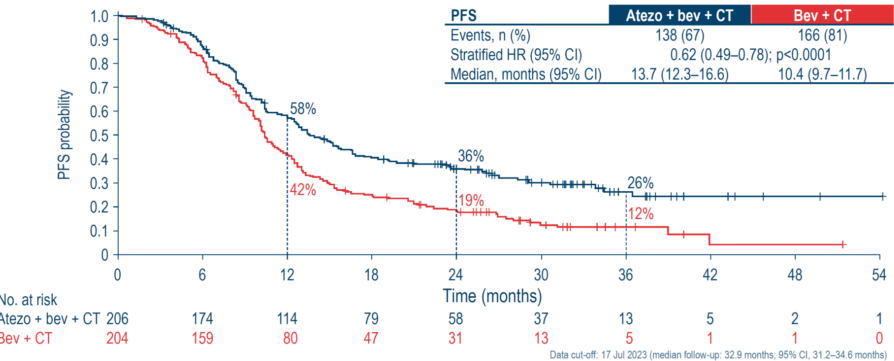


Characteristic, n (%)		Atezo + bev + CT (n=206)	Bev + CT (n=204)
Median (range) age, years		51.0 (24–90)	52.5 (21–79)
Age, n (%)	<65 years	171 (83)	168 (82)
GOG/ECOG PS, n (%) ^a	0	138 (67)	128 (63)
	1	68 (33)	73 (36)
Race, n (%)	White	111 (54)	113 (55)
	Other ^b	45 (22)	42 (21)
	Not available ^c	50 (24)	49 (24)
Histology, n (%)	Squamous cell carcinoma	164 (80)	157 (77)
	Adenocarcinoma/adenosquamous carcinoma	42 (20)	47 (23)
Disease status at screening, n (%)	Metastatic (stage IVB)	43 (21)	47 (23)
	Recurrent	150 (73)	151 (74)
	Persistent	13 (6)	6 (3)
Disease location at screening, n (%)	Pelvic and distant	102 (50)	90 (44)
	Distant only	71 (34)	74 (36)
	Pelvic only	33 (16)	40 (20)
Primary therapy	Concurrent chemoradiotherapy	70 (34)	85 (42)
	Surgery followed by chemoradiotherapy	64 (31)	44 (22)
	Surgery and/or radiotherapy	16 (8)	28 (14)
	None	56 (27)	47 (23)

^aMissing in three patients. ^bAsian (n=58), Latin (n=18), Arab (n=5), Black (n=5), Gypsy (n=1). ^cPer local legislation

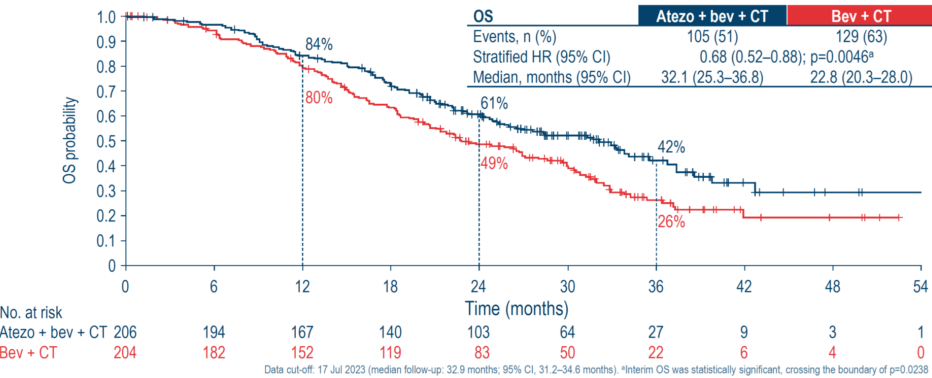
Dual primary endpoint: PFS

Statistically significant 38% reduction in risk of progression or death

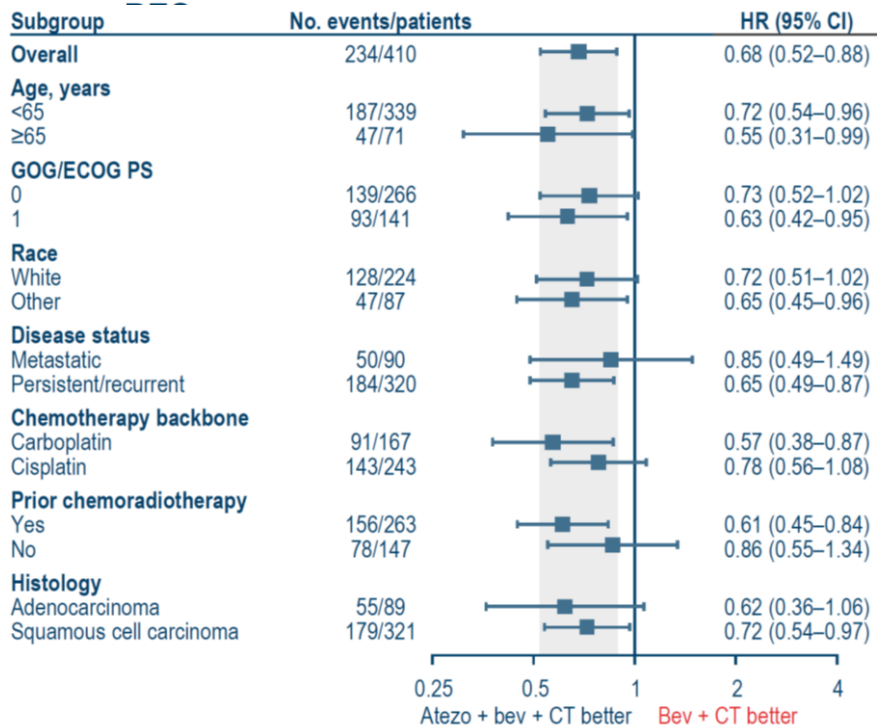


Dual primary endpoint: OS (interim analysis)

Statistically significant 32% reduction in risk of death



OS in protocol-specified subgroups



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

Incluido en guías NCCN



To bev or not to bev...



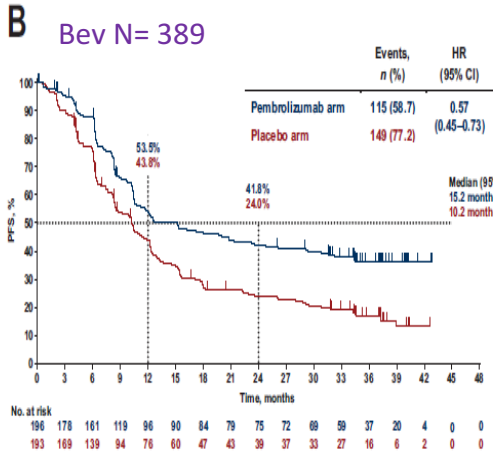
ORIGINAL ARTICLE

Pembrolizumab plus chemotherapy for advanced and recurrent cervical cancer: final analysis according to bevacizumab use in the randomized KEYNOTE-826 study[☆]

D. Lorusso^{1,†}, N. Colombo^{2,3}, C. Dubot⁴, M. V. Cáceres⁵, K. Hasegawa⁶, R. Shapira-Frommer⁷, P. Salman⁸, E. Yañez⁹, M. Gümüş¹⁰, M. Olivera¹¹, V. Samouëlian¹², V. Castonguay¹³, A. Arkhipov¹⁴, K. Li¹⁵, S. Toker¹⁵, C. Tekin¹⁵, K. S. Tewari¹⁶ & B. J. Monk¹⁷

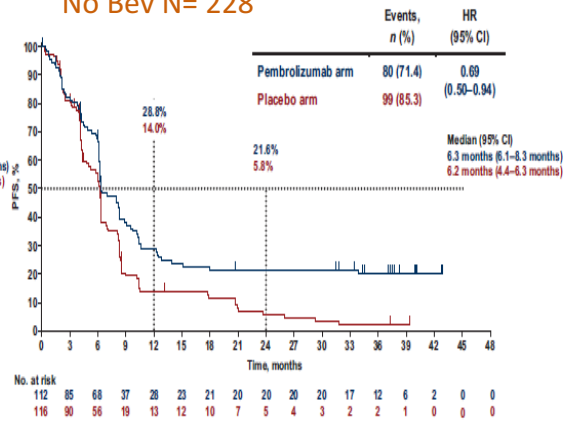
This subgroup analysis was exploratory and not controlled for multiplicity. Treatment outcomes were assessed in

To bev or not to bev...



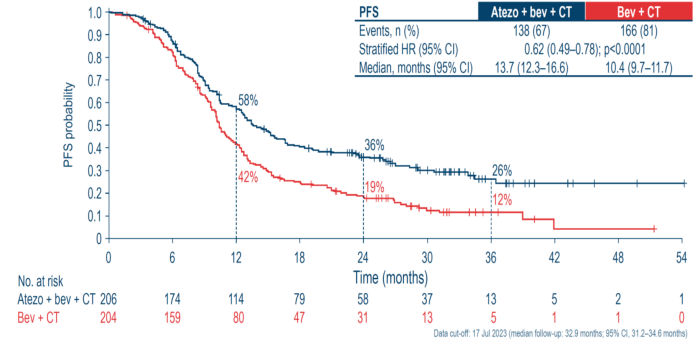
Lorusso D, et al. Ann Oncol. 2025;36(1):65-75.

No Bev N= 228



Dual primary endpoint: PFS

Statistically significant 38% reduction in risk of progression or death



Oaknin A, et al. Lancet 2024; (203) 41-43

In the absence of formal contraindication to bev use—> Do bev!

Fistulae (8-18%), short interval RT (<10 mo), kidney disease, pelvic disease ...

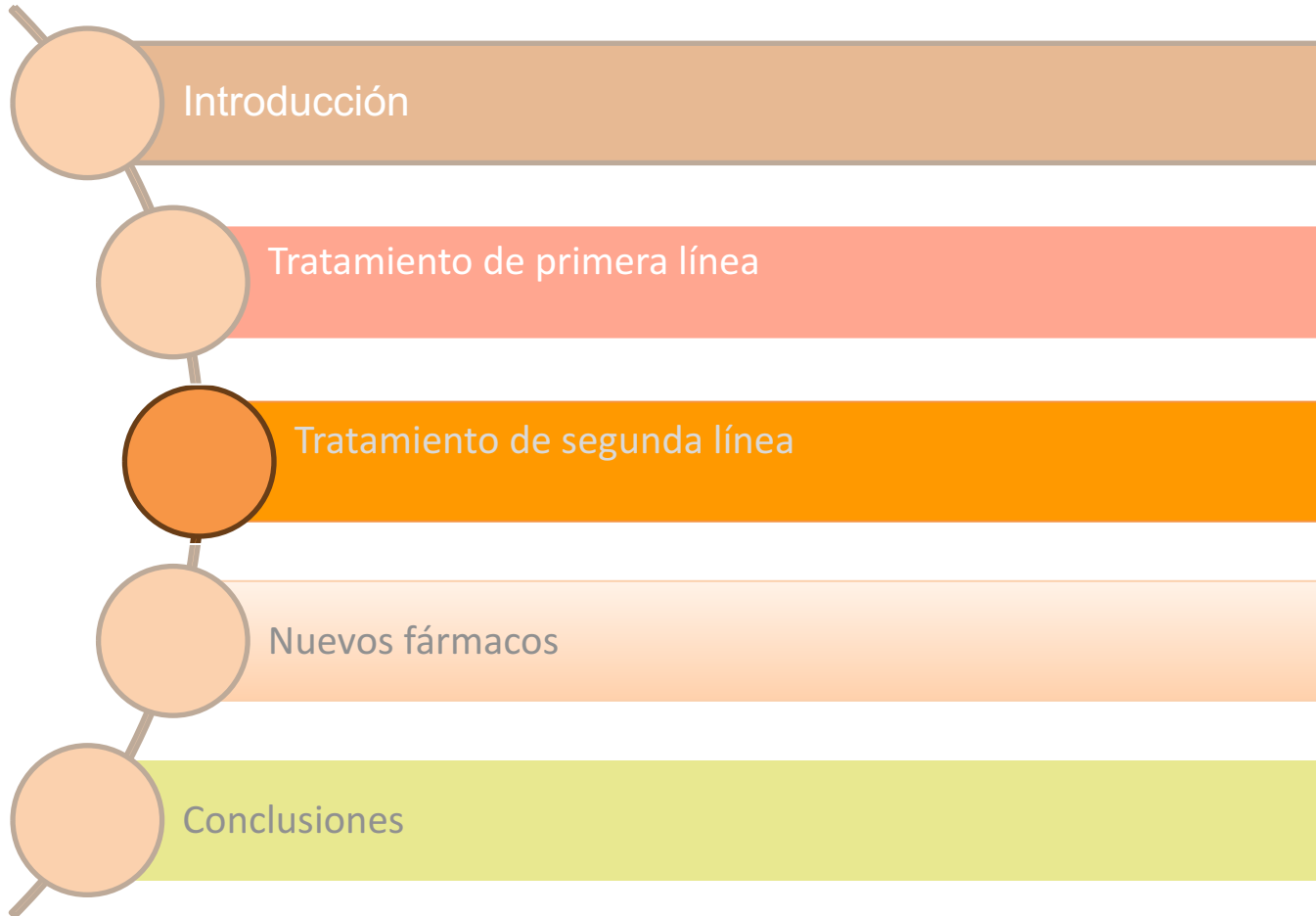


Table 4. Second-line therapy for metastatic cervical cancer

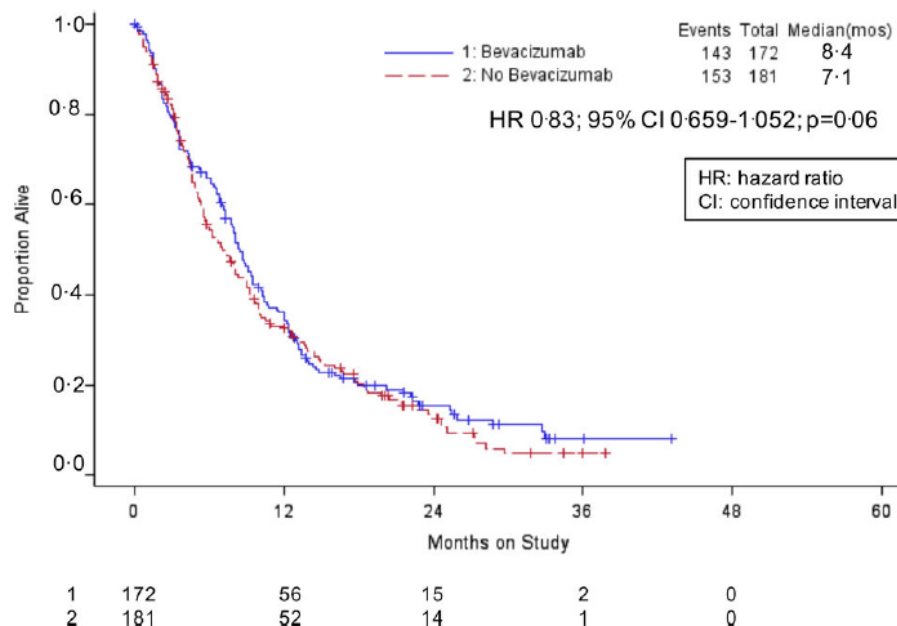
Agent	N	CR+PR (%)	PFS (months)	OS (months)
Bevacizumab [48]	46	11	3.4	7.3
Topotecan [62, 63]	94	13-19	2.1-2.4	6.4-6.6
Vinorelbine [64]	44	14	-	-
Gemcitabine [65]	22	5	2.1	6.5
Albumin-bound paclitaxel [66]	35	29	5.0	9.4
Docetaxel [67]	23	9	3.8	7.0
Pemetrexed [68, 69]	72	14-15	2.5-3.1	7.4-8.8
Irinotecan [70]	42	21	4.5	6.4
Sunitinib [71]	19	0	3.5	-
Erlotinib [72]	28	0	1.9	5.0
Lapatinib [73]	78	5	4.2	9.7
Pazopanib [73]	74	9	4.5	12.7
Pegylated liposomal doxorubicin [74]	27	11	3.2	8.9

CR, complete response; OS, overall survival; PFS, progression-free survival; PR, partial response.

Marth C, ESMO guidelines CC Ann Oncol 2017

ORR ≤ 15% PFS ≤ 3.8 m OS ≤ 8 m

GOG 240: MATURE POST PROGRESSION OS



Tewari KS, Lancet 2007

Anti PD1 monotherapy

Author (year)	Trial name/ID	P	Treatment arms (dose)	Endpoints	Number of evaluable cases	Disease status	PD-L1 positive (CPS ≥ 1) (%)
Chung et al. (2019) [16]	KEYNOTE-158/ NCT02628067	II	Pembrolizumab 200 mg Q3W	ORR	98	Previously treated advanced cervical cancer	83.7
Santin et al. (2020) [17]	NRG-GY002/ NCT02257528	II	Nivolumab 3 mg/kg Q2W	Objective tumor response	25	Persistent/recurrent cervical cancer, failure of prior systemic therapy	72.7
O'Malley et al. (2021) [21]	NCT02257528	II	Balstilimab (AGEN2034, anti-PD-1)	ORR	161	Previously treated advanced cervical cancer	61.5

Approvals



June 2018

FDA approves pembrolizumab for advanced cervical cancer with disease progression during or after chemotherapy

On June 12, 2018, the Food and Drug Administration approved pembrolizumab for patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.



**NCCN Guidelines Version 4.2025
Cervical Cancer**

Second-line or Subsequent Therapy^{h,k}

Preferred Regimens

- Pembrolizumab for TMB-H tumors^{f,l} or PD-L1-positiveⁱ or MSI-H/dMMR tumors^{f,17}
- Tisotumab vedotin-tftv (category 1)^{18,19}

ESMO VIRTUAL PLenary



GOG FOUNDATION®
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ENGOT
European Network of
Gynaecological Oncological Trial groups

EMPOWER-CERVICAL 1/GOG-3016/ENGOT-CX9: RESULTS OF PHASE 3 TRIAL OF CEMIPIMAB VS INVESTIGATOR'S CHOICE (IC) CHEMOTHERAPY (CHEMO) IN RECURRENT/METASTATIC (R/M) CERVICAL CARCINOMA

Krishnansu S Tewari,* Bradley J Monk,* Ignace Vergote, Austin Miller, Andreia Cristina de Melo, Hee Seung Kim, Yong Man Kim, Alla Lisianskaya, Vanessa Samouëlian, Domenica Lorusso, Fernanda Damian, Chih-Long Chang, Evgeniy A Gotovkin, Shunji Takahashi, Daniella Ramone, Joanna Pikiel, Beata Maćkowiak-Matejczyk, Eva Maria Guerra, Nicoletta Colombo, Yulia Makarova, Jingjin Li, Shaheda Jamil, Vladimir Jankovic, Chieh-I Chen, Frank Seebach, David M Weinreich, George D Yancopoulos, Israel Lowy, Melissa Mathias, Matthew G Fury, and Ana Oaknin

12 May 2021

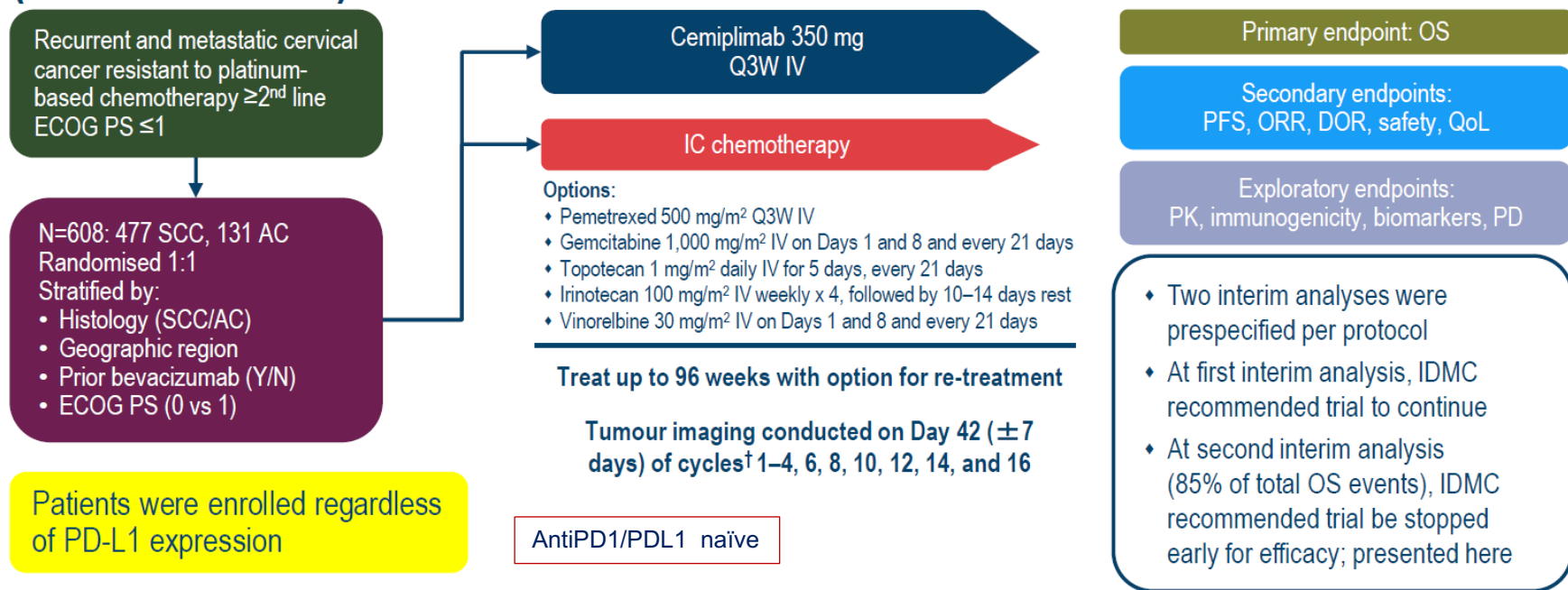


*Contributed equally to this presentation.

This study (NCT03257267) was sponsored by Regeneron Pharmaceuticals, Inc. and Sanofi.



EMPOWER-CERVICAL 1/GOG-3016/ENGOT-CX9 STUDY DESIGN* (NCT03257267)



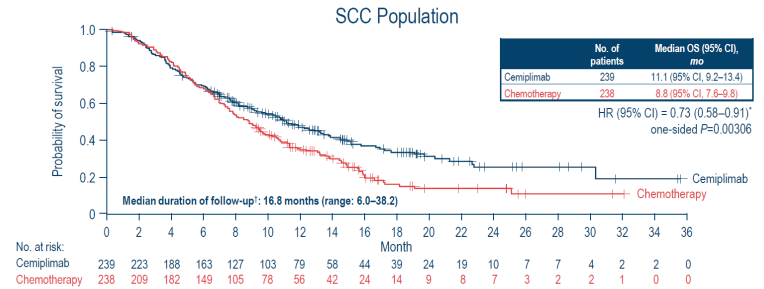
*Performed according to ENGOT Model C.^{1†}To account for differences in drug administration schedules, one cycle is defined as 6 weeks.

AC, adenocarcinoma or adenosquamous carcinoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, investigator's choice; IDMC, Independent Data Monitoring Committee; IV, intravenously; ORR, objective response rate; OS, overall survival; PD, pharmacodynamics; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; QoL, quality of life; SCC, squamous cell carcinoma.

1. Vergote I et al. *Int J Gynecol Cancer*. 2019;0:1–4.

OVERALL SURVIVAL

At second interim analysis (85% of total OS events), IDMC recommended trial be stopped early for efficacy

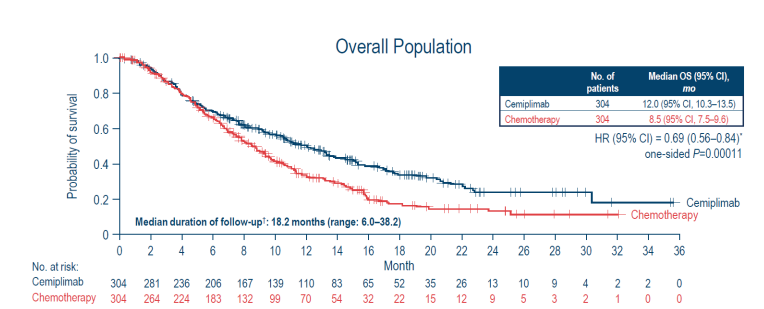


*Stratified by geographic region (North America vs Asia vs ROW) according to interactive web response system. †From randomisation to data cutoff date.
CI, confidence interval; HR, hazard ratio; IDMC, Independent Data Monitoring Committee; mo, month; OS, overall survival; ROW, rest of world; SCC, squamous cell carcinoma.

ESMO VIRTUAL PLenary

Data cutoff date: 4 Jan 2021

OVERALL SURVIVAL

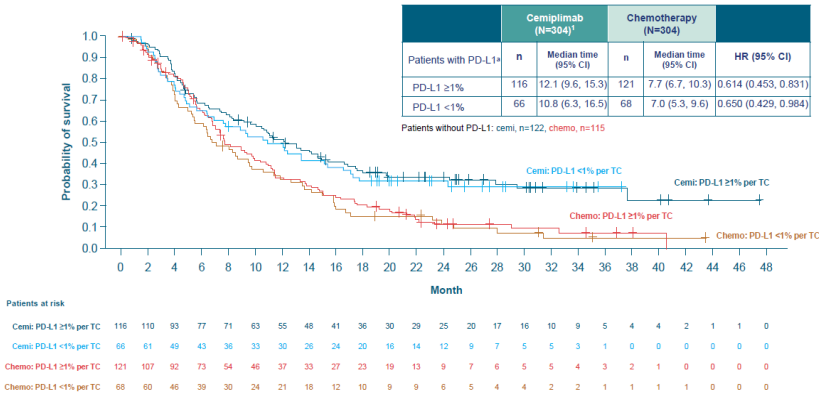


*Stratified by geographic region (North America vs Asia vs ROW) and Histology (SCC vs AC) according to interactive web response system. †From randomisation to data cutoff date.
AC, adenocarcinoma or adenocarcinoma; CI, confidence interval; HR, hazard ratio; mo, month; OS, overall survival; ROW, rest of world; SCC, squamous cell carcinoma.

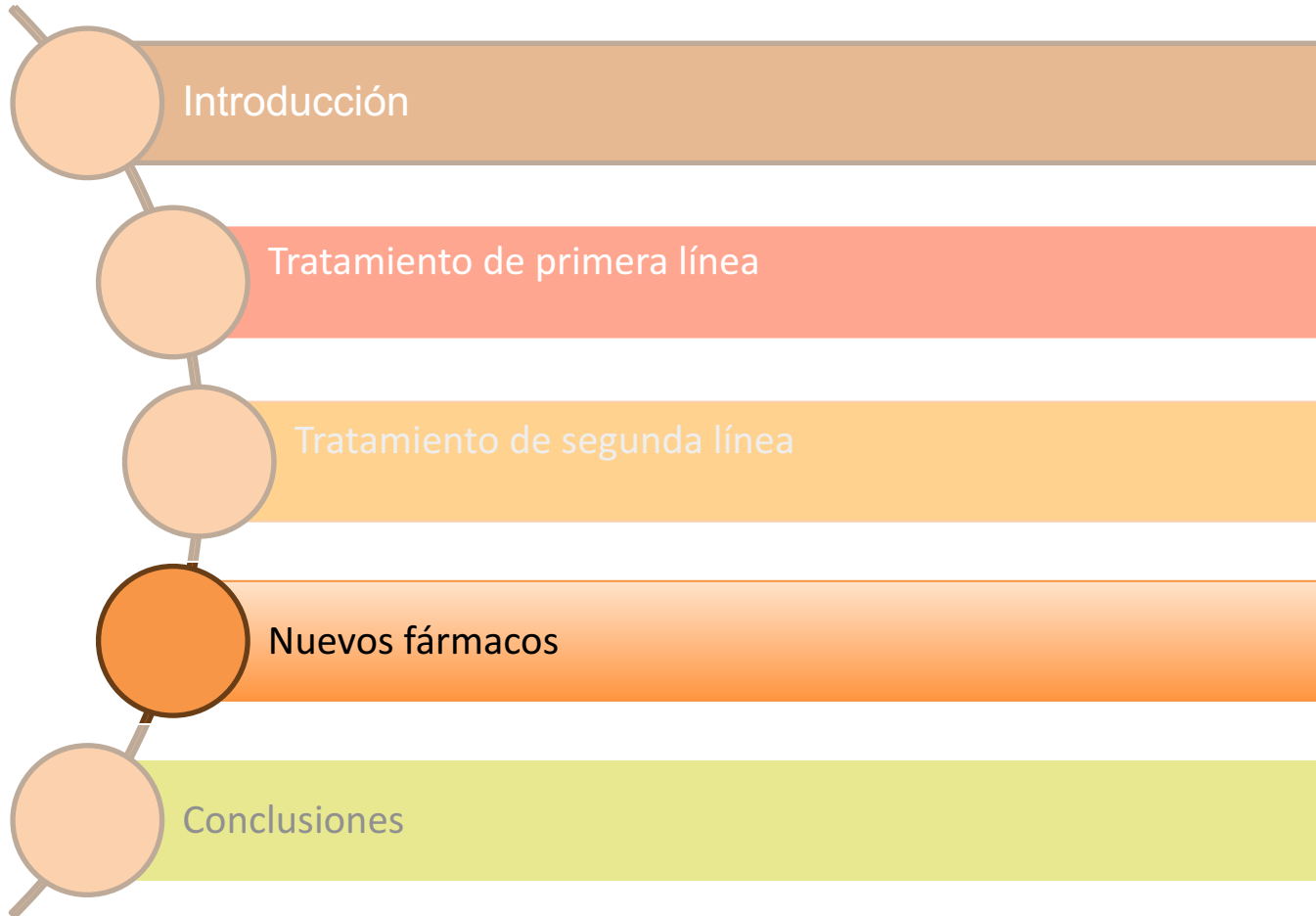
ESMO VIRTUAL PLenary

Data cutoff date: 4 Jan 2021

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9: Overall Survival
Regardless of PD-L1 Status



Tewari KS et al; ESMO virtual plenary 2021; Tewari KS et al N Engl J Med 2022;386:544-55; Oaknin et al, ESMO Congress 2022

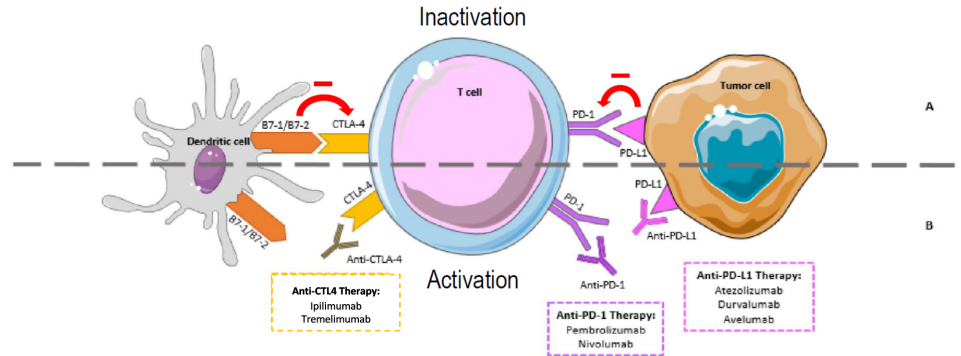
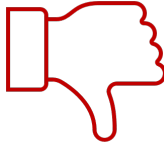


- PD-1 & CTLA-4

- Nivolumab + Ipilimumab
- Balstilimab + Zalifrelimab
- Cadonilimab

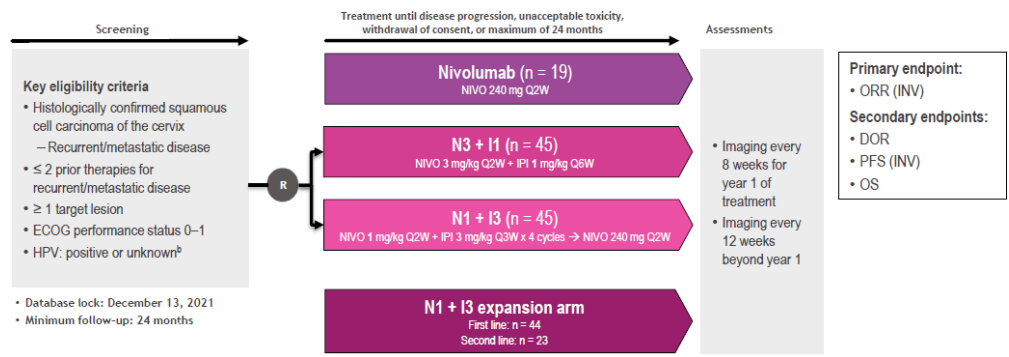
- PD-(L)1 & TIGIT

- Atezolizumab + Tiragolumab
- Tislelizumab + Ociperlimab
- Pembrolizumab + Vibostolimab



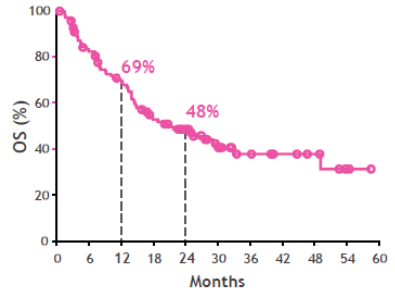
CheckMate 358: Nivolumab +/- Ipilimumab

Design: phase 1/2



CheckMate 358: Nivolumab +/- Ipilimumab

mOS and mPFS



	N1 + I3 pooled (n = 112)
mOS, m (95% CI)	20.9 (14.4–32.8)
mPFS, m (95% CI)	5.8 (3.8–9.3)

Seems impressive but...

62% 1st line
38% 2nd line

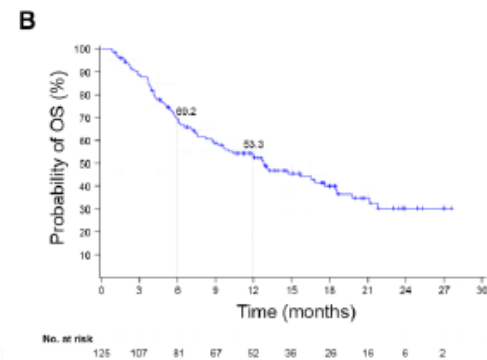
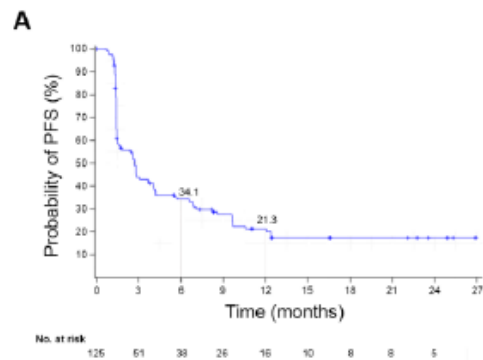
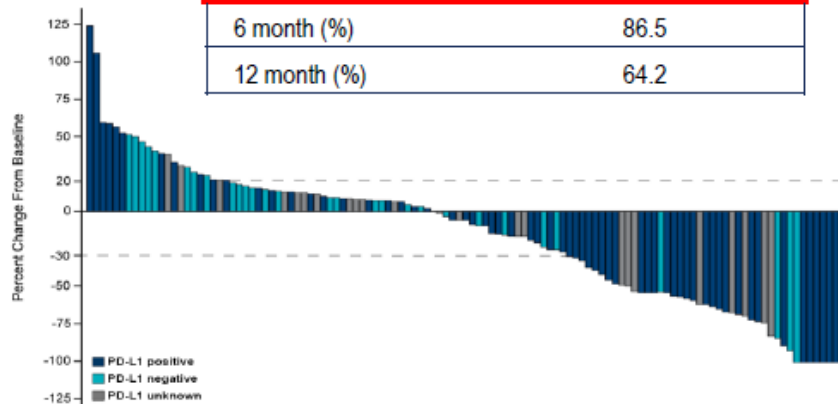
For comparison:

	KN826 (all comers) (1 st line)	Single agent chemo (≥ 2 nd line)
mOS	26.4	≤ 8
mPFS	10.4	≤ 3.8

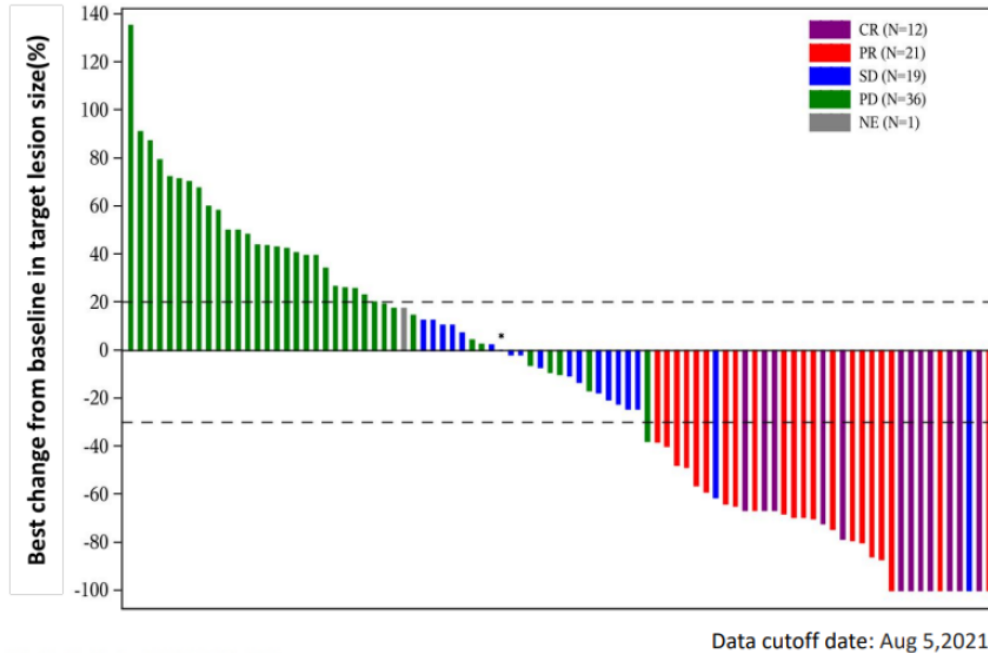
Balstilimab and Zalifrelimab phase II

ORR, N (%)	32 (25.6)
CR	10 (8.0)
PR	22 (17.6)
PD-L1 ⁺ (n = 67)	22 (32.8)
PD-L1 ⁻ (n = 33)	3 (9.1)
DOR, months [range]	NR [9.3, NR]
6 month (%)	86.5
12 month (%)	64.2

mPFS, months	2.7
(95%CI)	(1.5-3.7)
mOS, months	12.8
(95%CI)	(8.8-17.6)



AK104-201-AV- Cadonilimab phase II (China)

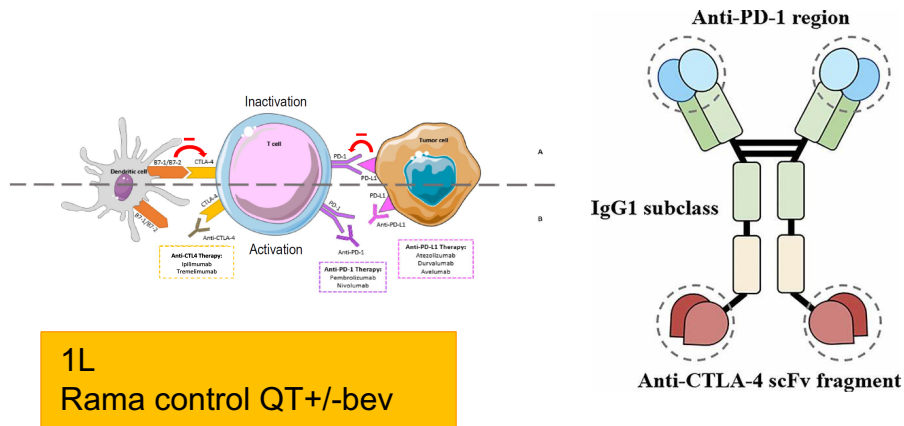


IRCC evaluated patients N=100	
ORR, n(%) (95%CI)	33 (33) (23.9 – 43.1)
CR	12 (12)
PR	21 (21)
SD	19 (19)
DCR, n(%)	52 (52)
mDoR (95%CI)	NR (0.95 – 16.43)
mPFS (range)	3.75 (0.03+ – 18.46+)
mOS (range)	17.51 (0.62 – 19.78+)

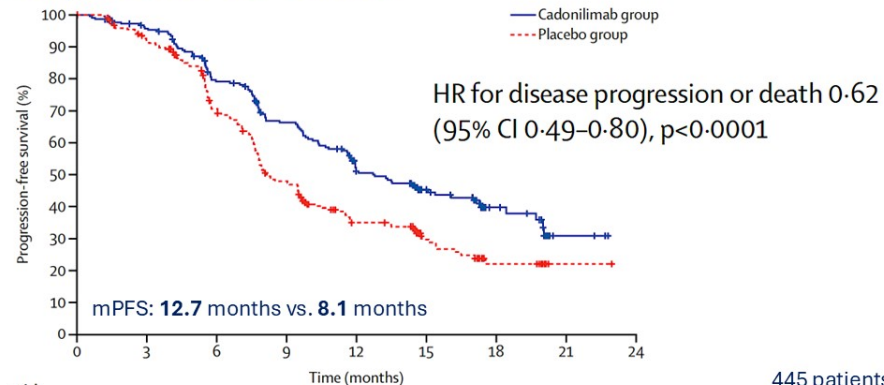
Cadonilimab plus platinum-based chemotherapy ± bevacizumab for persistent, recurrent, or metastatic cervical cancer: subgroup analyses of COMPASSION-16

Xiaohua Wu¹, Yang Sun², Hongying Yang³, Hanmei Lou⁴, Jing Wang⁵, , Dan Li⁶, Tao Wu⁷, Hui Zhang⁸, Ke Wang⁹, Yuzhi Li¹⁰, Chunyan Wang¹¹, Guiling Li¹², Yifeng Wang¹³, Dapeng Li¹⁴, Hongyi Cai¹⁵, Mei Pan¹⁶, Ying Tang¹⁷, Ting Liu¹⁸, Yu Xia¹⁸

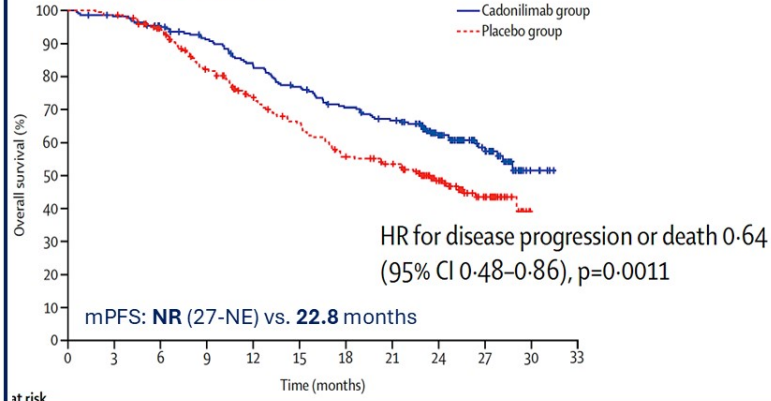
¹Fudan University Shanghai Cancer Center, Shanghai, China; ²Clinical Oncology School of Fujian Medical University, Fujian Cancer Hospital, Fuzhou, China; ³Yunnan Cancer Hospital, Kunming, China; ⁴Zhejiang Cancer Hospital, Hangzhou, China; ⁵Shunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya 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



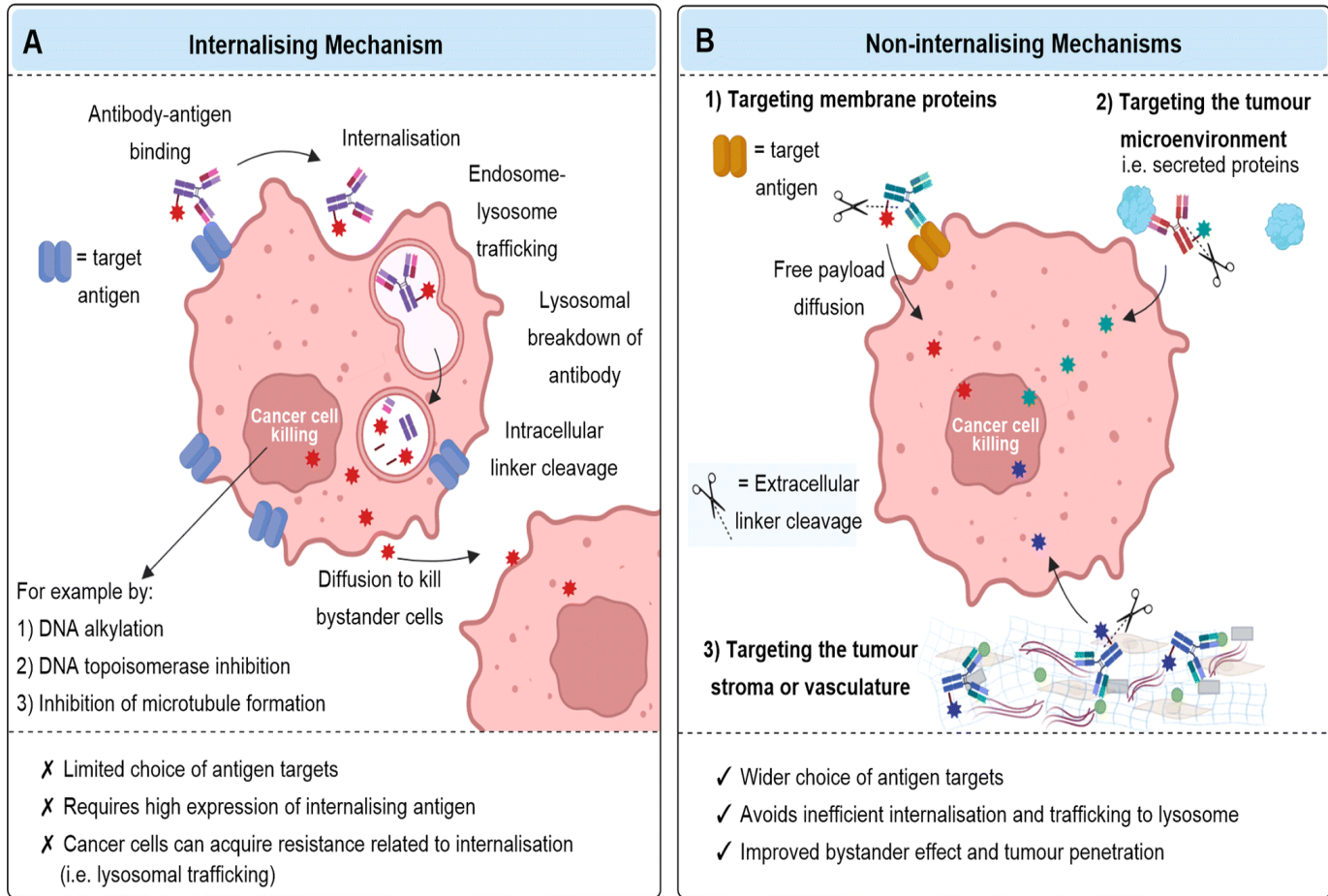
Progression-Free Survival



Overall Survival



Antibody Drug Conjugates



ADC's in cervical cancer

TF	Tisotumab vedotin
HER2	Trastuzumab deruxtecan Disitamab vedotin
TROP2	Sacituzumab govitecan Sacituzumab tirumotecan
B7H3	DB-1311/BNT324
Nectin-4	SYS6002 (CRB-701) 9MW282

ORIGINAL ARTICLE

Tisotumab Vedotin as Second- or Third-Line Therapy for Recurrent Cervical Cancer

I. Vergote, A. González-Martín, K. Fujiwara, E. Kalbacher, A. Bagaméri, S. Ghamande, J.-Y. Lee, S. Banerjee, F.C. Maluf, D. Lorusso, K. Yonemori, E. Van Nieuwenhuysen, L. Manso, L. Woelber, A. Westermann, A. Covens, K. Hasegawa, B.-G. Kim, M. Raimondo, M. Bjurberg, F.M. Cruz, A. Angeleagues, D. Cibula, L. Barraclough, A. Oaknin, C. Gennigens, L. Nicacio, M.S.L. Teng, E. Whalley, I. Soumaoro, and B.M. Slomovitz, for the innovaTV 301/ENGOT-α12/GOG-3057 Collaborators*

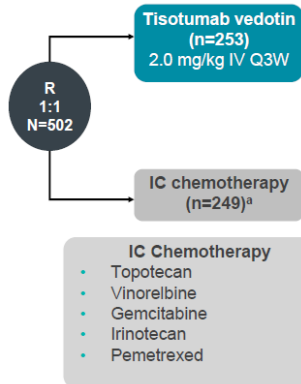
Key Eligibility Criteria²

- 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)

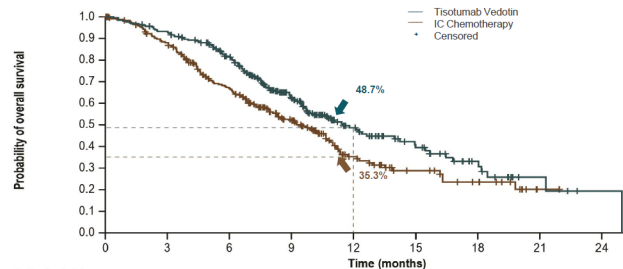
Previous anti-PD-1 or anti-PD-L1 therapy was permitted



Primary endpoint: OS^b

Secondary endpoints:
PFS^c, ORR^c, Safety

Overall Survival (Primary endpoint)



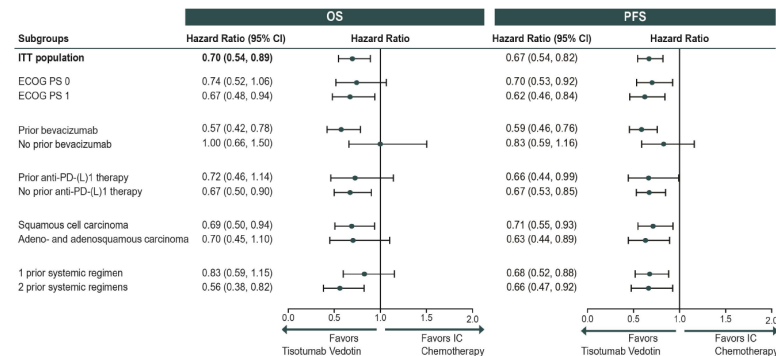
Treatment	Events/Total	Median (95% CI)
Tisotumab Vedotin	123/253	11.5 (9.8, 14.9)
IC Chemotherapy	140/249	9.5 (7.9, 10.7)

Stratified log-rank P value^a: 0.0038

HR (95% CI): 0.70 (0.54, 0.89)

OS: 9 vs 11 m

InnovaTV 301 (ENGOT cx-12/GOG 3057): Key Subgroups – OS and PFS



DESTINY-PanTumor02: Study Design

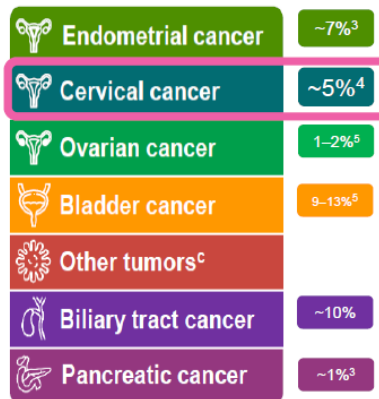
A phase 2, multicenter, open-label study to evaluate the efficacy and safety of trastuzumab deruxtecan for the treatment of selected HER2 expressing tumors^{1,2}

Key Eligibility Criteria

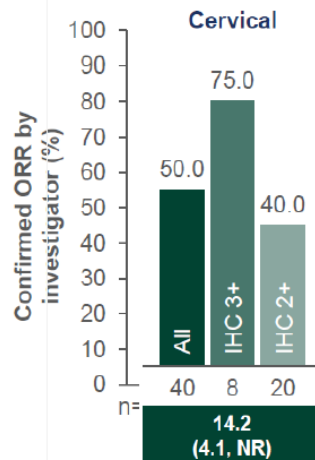
- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
- Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer scoring)
- Prior HER-targeting therapy allowed
- ECOG/WHO PS ≤1

T-DXd
5.4 mg/kg Q3W
40 per cohort^b

Frequency of HER2 mutations across tumor types



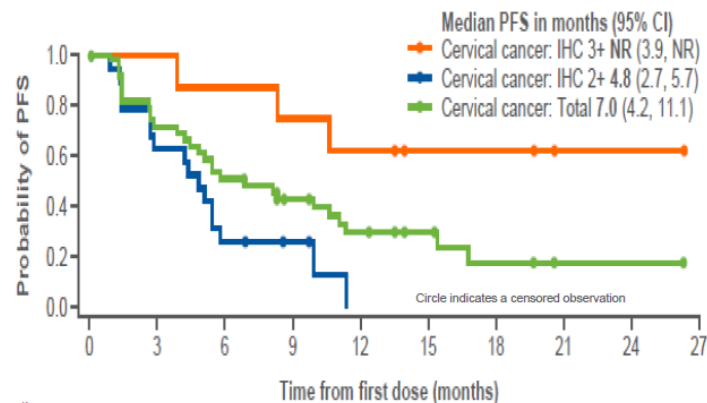
ORR by HER2 status in Cervical Cancer



All patients were HER2-positive per local determination

DESTINY-PanTumor02:

PFS by HER2 status in Cervical Cancer



Number at risk, month

Cervical cancer: IHC 3+	8	8	7	6	5	3	3	1	1	0
Cervical cancer: IHC 2+	20	12	5	3	0					
Cervical cancer: Total	40	28	20	14	9	6	3	1	1	0

TEAEs	All patients (N=267); n (%)
Any drug-related TEAEs	226 (84.6)
Drug-related TEAEs Grade ≥3	109 (40.8)
Serious drug-related TEAEs	36 (13.5)
Drug-related TEAEs associated with dose discontinuations	23 (8.6)
Drug-related TEAEs associated with dose interruptions	54 (20.2)
Drug-related TEAEs associated with dose reductions	54 (20.2)
Drug-related TEAEs associated with deaths	4 (1.5) ^a

Most common TEAEs	Any Grade	Grade ≥3
Nausea	55.1	3.7
Fatigue	40.1	7.1
Neutropenia	32.6	19.1
Anemia	27.7	10.9
Diarrhea	25.8	3.7
Vomiting	24.7	1.5
Decreased appetite	17.6	1.5
Thrombocytopenia	17.2	5.6
Alopecia	16.9	
Increased transaminases	10.1	0.4
Leukopenia	10.1	2.6

OS: 7 (NR in Her2 3+)

ILD/pneumonitis adjudicated as T-DXd related, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
All patients (N=267)	7 (2.6)	17 (6.4)	1 (0.4)	0	3 (1.1)	28 (10.5)

Recurrent CC Management: Sacituzumab-Govitecan & Sacituzumab tirumotecan

Sacituzumab Govitecan (N=18)		Sacituzumab-Tirumotecan + Pembrolizumab (n=38)
Payload	SN3-Topoisomerase I	Belotecan derivative Topoisomerase I
DAR	7.6	7.4
Linker	pH sensitive hydrolysable linker	Sulfonyl pyrimidine CL2A-carbonate linker
Trial	NCT05838521	NCT05642780
Prior Bev	61%	52.6%
Prior CPI	78%	42.1%
ORR	50%	57.9% (33.4, 66.6)
DoR	9.2 months	NR (NE, NE)
mPFS	8.1 months	NR (95% CI 5.6- NE)

Protein expression n, total	TROP2, n (%) n = 501
3+	185 (37 %)
2+	157 (31 %)
1+	127 (25 %)
0	32 (7 %)
High (3+ and 2+)	342 (68 %)
Low (1+ and 0)	159 (32 %)

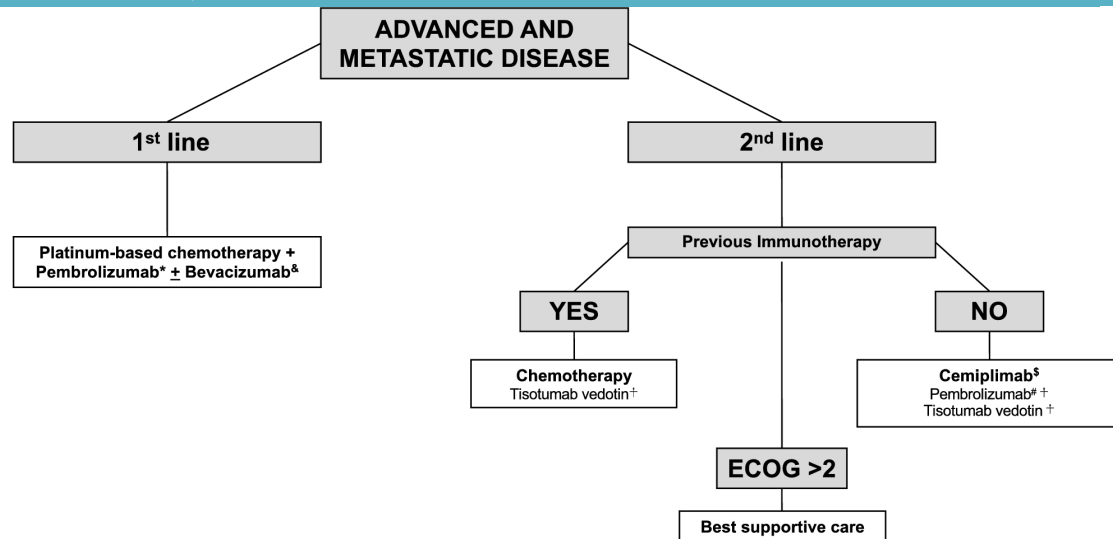
Level of high (2+, 3+) recurrent lesion expression:

· TROP2: 56%

An J et al. SGO 2024, Plana et al. Cancer Discovery 2022

Halle et al. ESMO Gyn 2024

Agent		N	ORR, %	mPFS, m	mOS	Prior IO use	Prior lines			
							0	1	2	>2
All single agent chemo			4.5 – 15	2.1 – 3.8	6.5 – 9.5	No				
PD-1 & CTLA-4	Nivolumab + Ipilimumab	43	35	5.8	20.9	No	64	28	8	-
	Balstilimab + Zalifrelimab	155	26	2.7	12.8	No	-	?	?	?
	Cadonilimab	100	33	3.8	17.5	No	-	63	37	-
PD-1 & TIGIT	Atezolizumab + Tiragolumab	171	19	2.8	11.1	No	-	72	26	-
	Tislelizumab + Ociperlimab	138	23	3.5	9.0	No	-	58	31	11
	Pembrolizumab + Vibostolimab	126	20	2.2	10.8	No	5	59	27	9
PD-L1 & TGFβ	Bintrafusp alfa	39	28	2.1	13.4	No	-	35	29	36
PD-1 + vaccination	Atezolizumab + VB10.16	47	19	4.1	16.9	No	4	50	46	
	Pembrolizumab + GX-188E	60	32	3.0	17.2	No	5	45	35	15
	Cemiplimab + ISA101b	113	17	3.0	13.3	No	-	26	46	28
ADCs	Tisotumab Vedotin	249	18	4.2	11.5	27%	-	61	38	-
	Trastuzumab Deruxtecan	40	50	7.0	13.6	?	-	15	38	48
	Sacituzumab Govitecan	18	50	8.1	NR	78%	-	33	53	13



* PD-L1 positive tumors, assessed as combined positive score (CPS) of 1 or more.
* When the risk of significant gastrointestinal/genitourinary toxicities has been carefully assessed.
* Regardless of PD-L1 tumor status.
* PD-L1-positive.
† US only.

ORR: >60%
PFS: 14-15 m
OS: 26-32 m

Clinical and Translational Oncology (2024) 26:2771–2782
<https://doi.org/10.1007/s12094-024-03604-3>

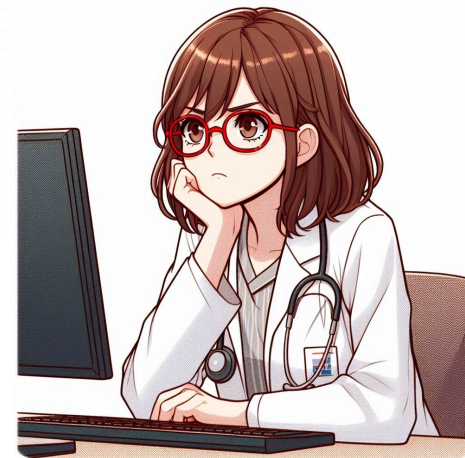
CLINICAL GUIDES IN ONCOLOGY

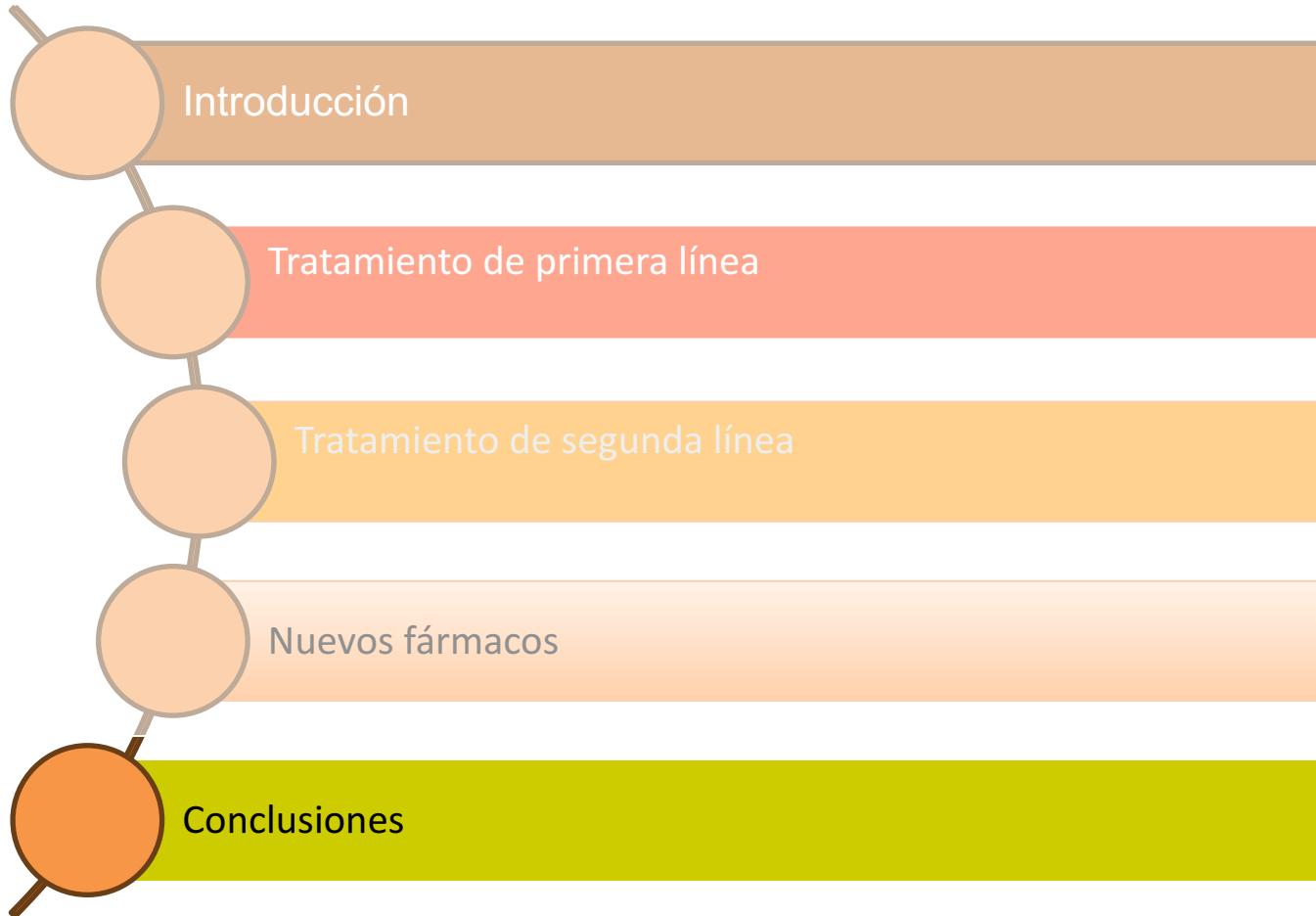


SEOM-GEICO Clinical Guidelines on cervical cancer (2023)

Luis Manso¹ · Avinash Ramchandani-Vaswani² · Ignacio Romero³ · Luisa Sánchez-Lorenzo⁴ · María José Bermejo-Pérez⁵ · Purificación Estévez-García⁶ · Lorena Fariña-Madrid⁷ · Yolanda García García⁸ · Marta Gil-Martin⁹ · María Quindós¹⁰

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Toda paciente con cáncer de cérvix debería recibir combinación de QT/IT +/- bev en 1L

Toda paciente con cáncer de cérvix metastásico debería recibir IT

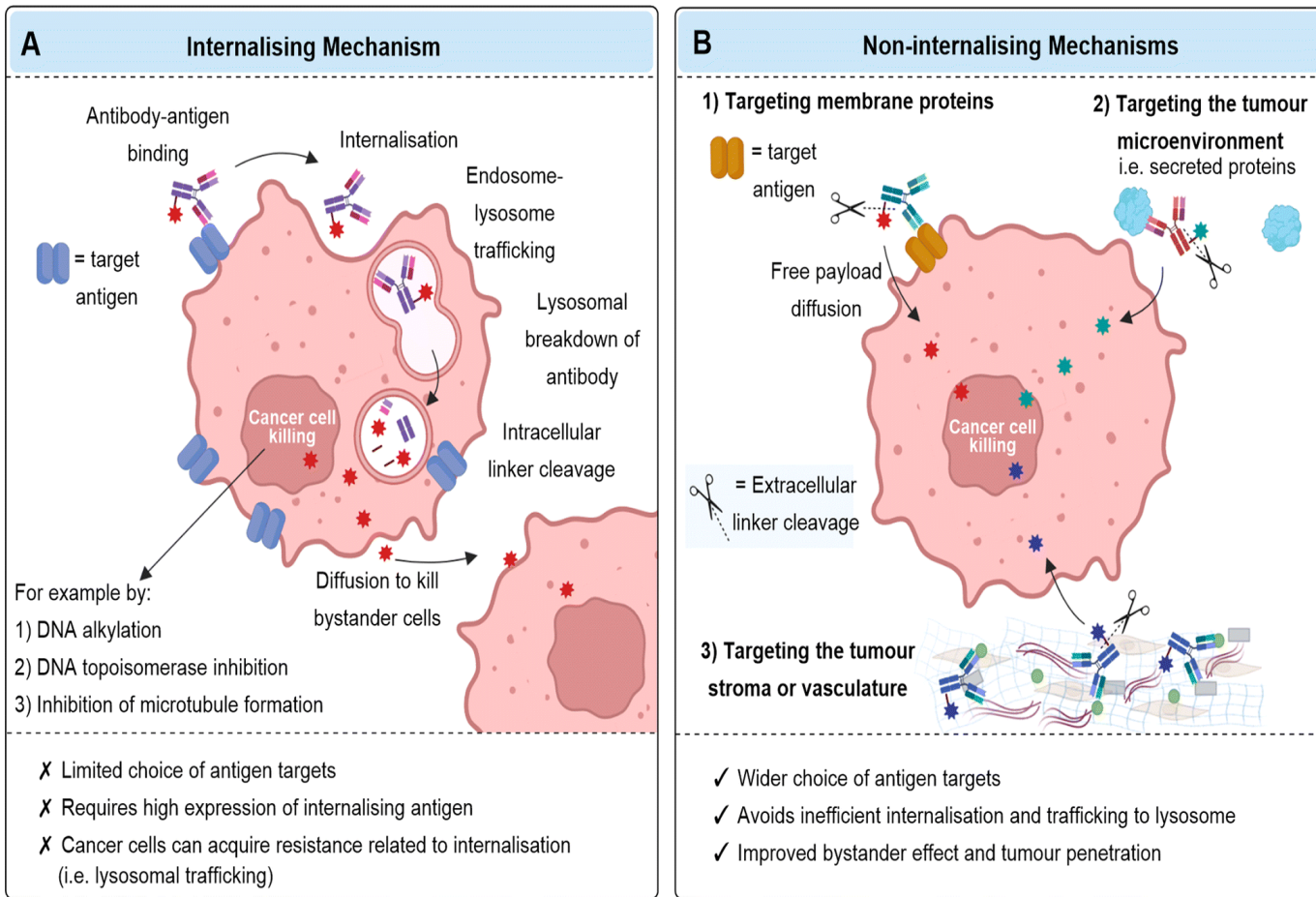
En pacientes pre-tratadas con IT los ADC's (TV con el desarrollo más Avanzado) es el futuro cercano

La vacunación y el cribado son las armas que han de impedir tener que aplicar lo anterior



yolanda.garciagarcia@osakidetza.eus

Eskerrik asko!
Moltes gràcies!
Moitas grazas!
¡Muchas gracias!



Recurrent CC Management: ICIs pretreated patients

the ADC era

TF

Tisotumab vedotin

HER2

**Trastuzumab deruxtecan
Disitamab vedotin**

TROP2

**Sacituzumab govitecan
Sacituzumab tirumotecan**

B7H3

DB-1311/BNT324

Nectin-4

**SYS6002 (CRB-701)
9MW282**

... and many more!