Antoine Lacassagne
CENTRE DE LUTTE CONTRE LE CANCER DE NICE

28 juin 2024
GYNAZUR

Prise en charge oncologique - standards actuels et perspectives :

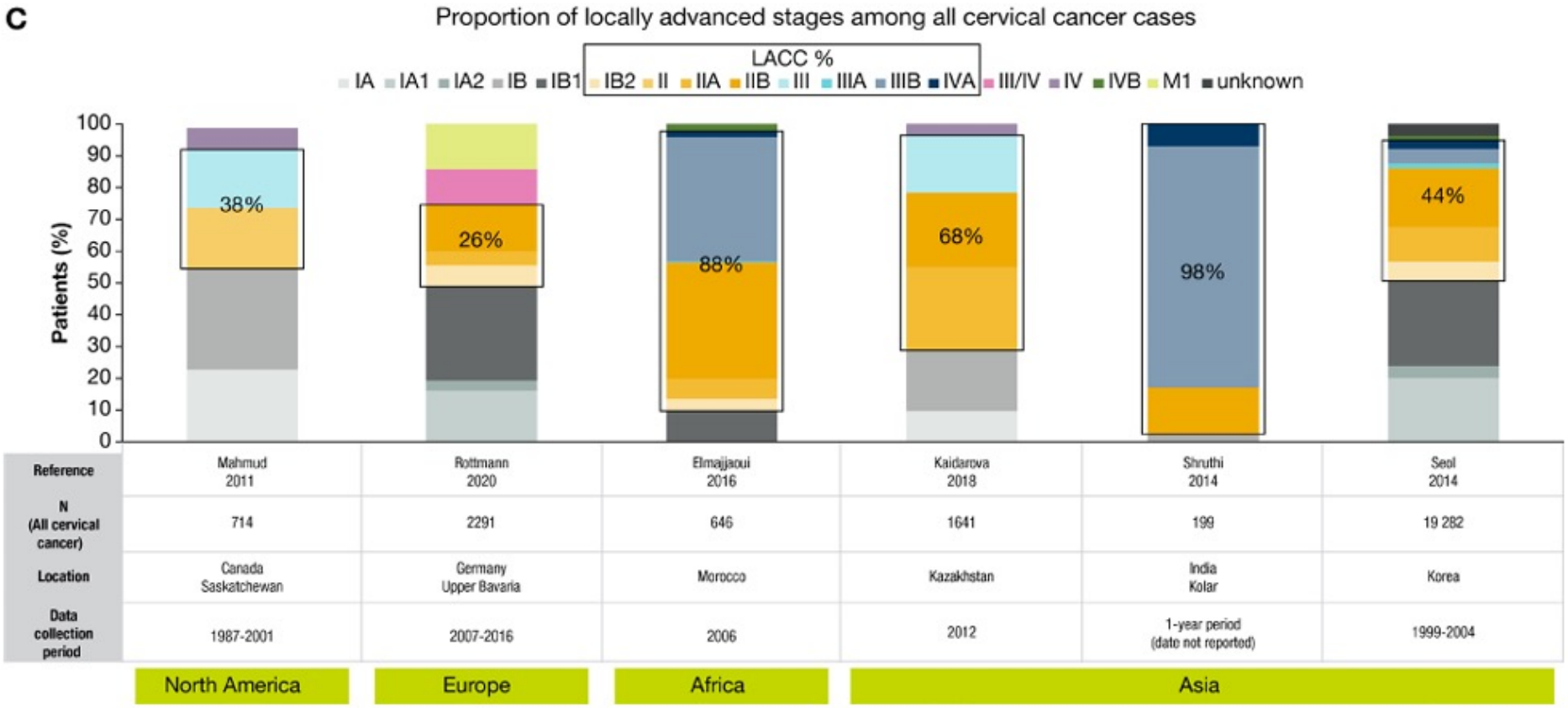
Col utérin avancé

Philippe Follana

Liens d’intérêt :

- **congrès**: AZ, Novartis, Esai, GSK
- **boards**: AZ, Novartis, GSK, Daiichi, Esai
- **honoraires**: GSK, MSD, AZ

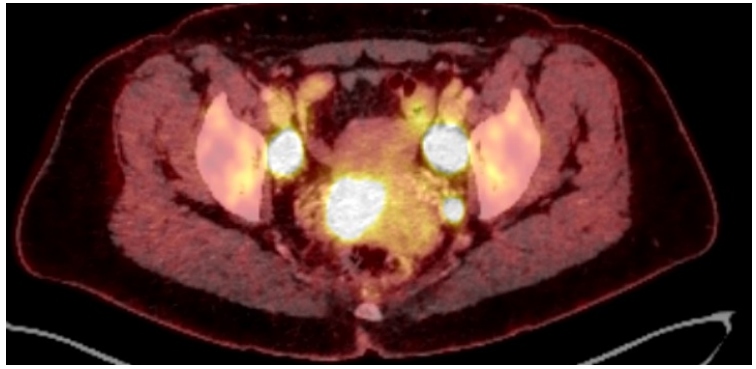
Cancers avancés ne sont pas rares

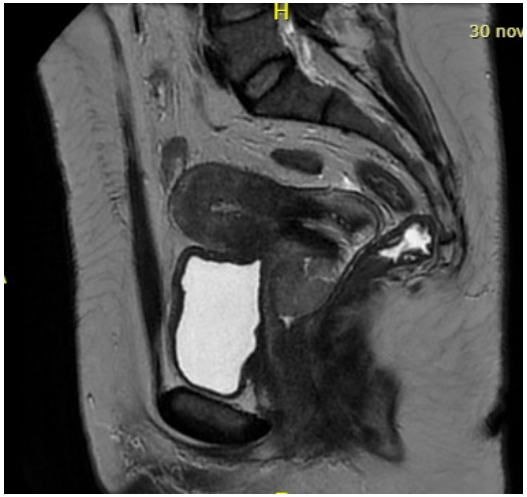


Monk bj Int J Gynecol Cancer 2022

Me MAN V âgée de 42 ans

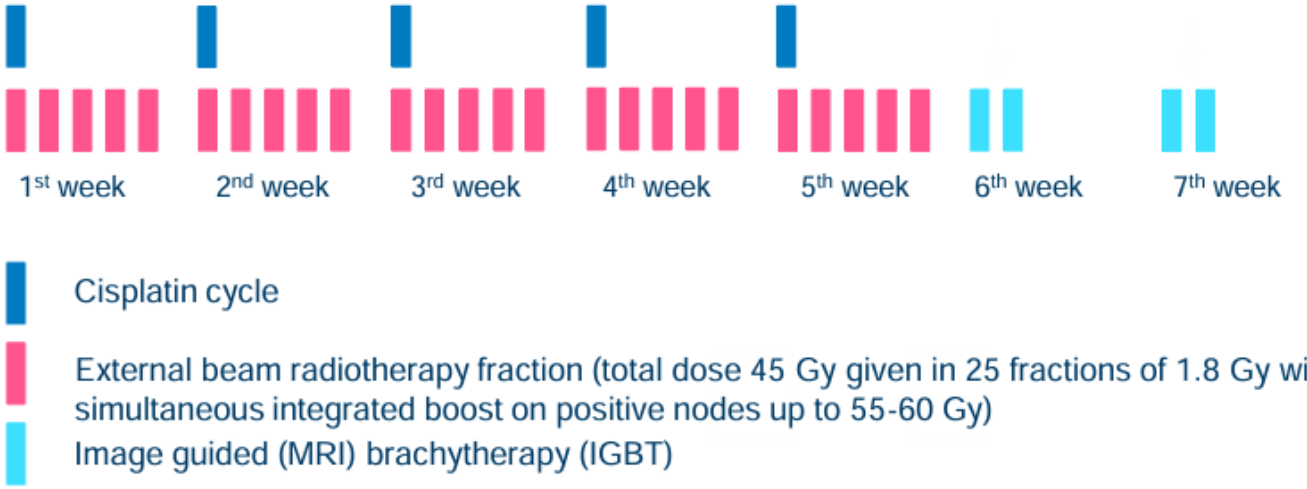
- Tabagisme 15 pquets/année, phlébite récente
- Métrorragies durant rapports depuis sept 2023
- Diagnostic dec 2023 carcinome epidermoide
- Clinique: volumineuse lésion du col avec envahissement cul de sac ant et paramètres
- Bilan PET TDM /IRM pelvienne: IIIC2





Traitement standard K col loc. avancé

Treatment schedule



Survie sans maladie à 5 ans: 58-68%

-Beaucoup de patientes non guéries !

-Survenue de métastases à distance

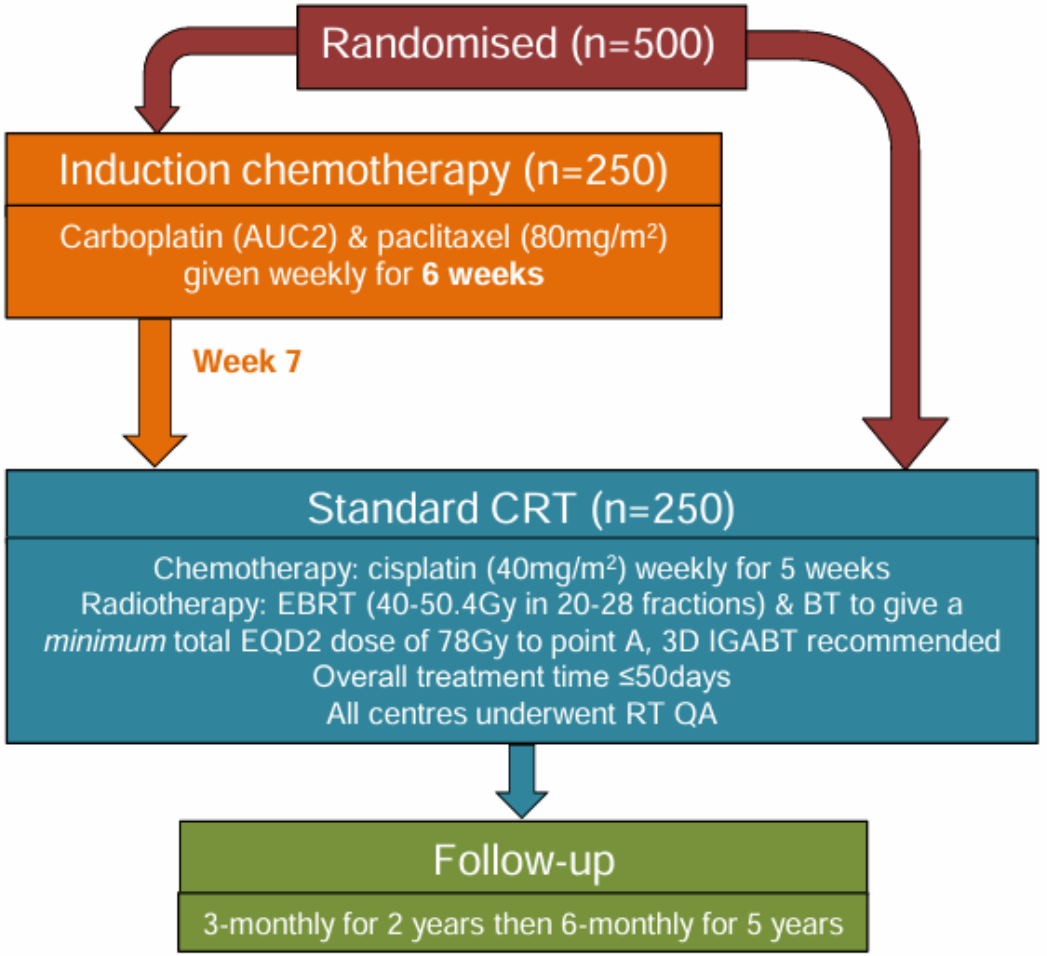
RTOG 90-01: Morris M, et al. N Engl J Med 1999;340:1137-43.
GOG 120: Rose PG, et al. N Engl J Med 1999;340:1144-53.
GOG 123: Keys HM, et al. N Engl J Med 1999;340:1154-61.
GOG 85: Whitney CW, et al. J Clin Oncol 1999;17:1339-48.
GOG 109: Peters III WA, et al. J Clin Oncol 2000;18:1606-13
Cochrane 2010

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

MADRID 2023 ESMO congress

Mary McCormack

McCormack M et al. Presented at: European Society for Medical Oncology Congress; 20–24 October 2023; Madrid, Spain. Abstract LBA8

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)

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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)

McCormack M et al. Presented at: European Society for Medical Oncology Congress; 20–24 October 2023; Madrid, Spain. Abstract LBA8

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)

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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)**

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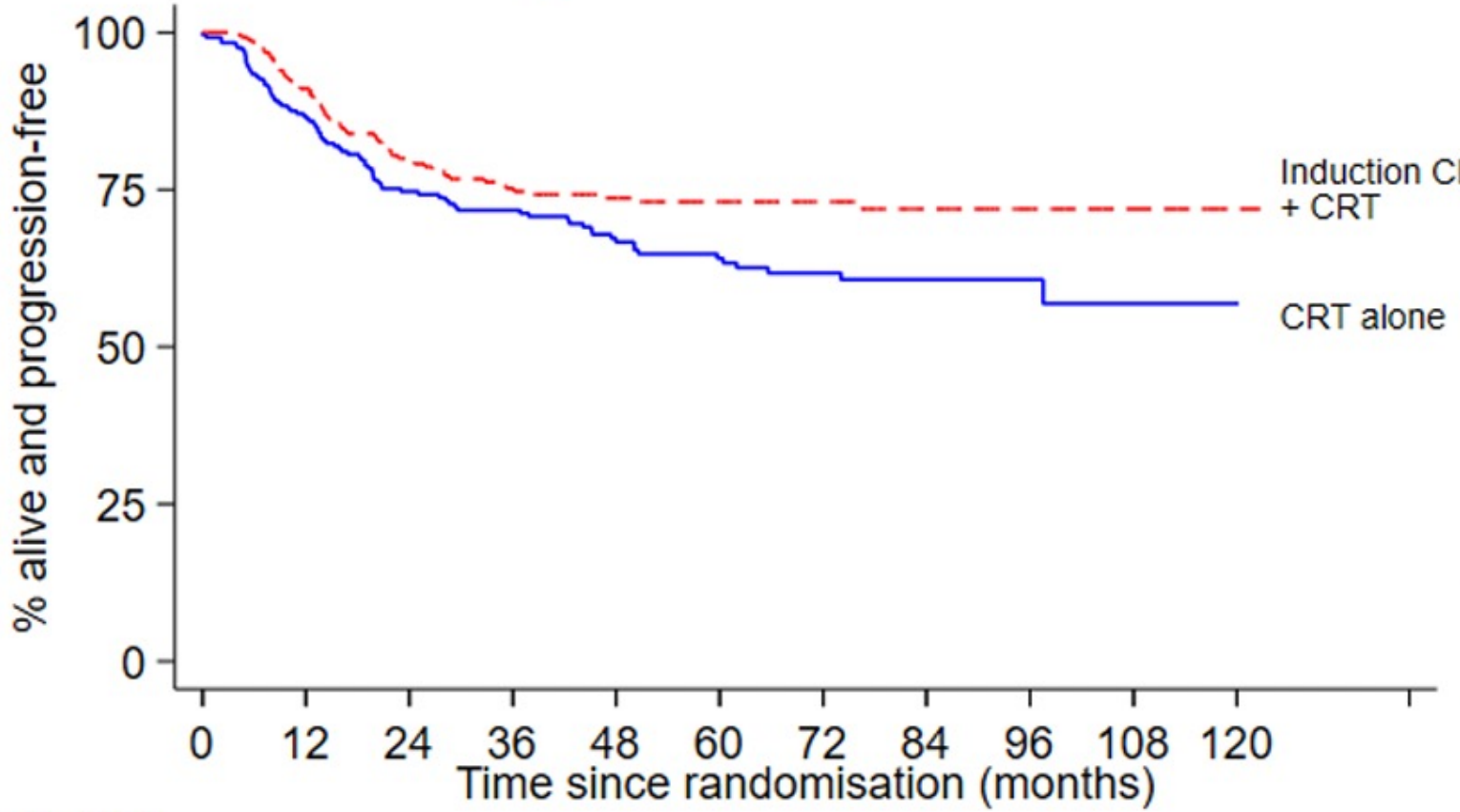
INTERLACE Progression-Free Survival (median FU 64m)



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

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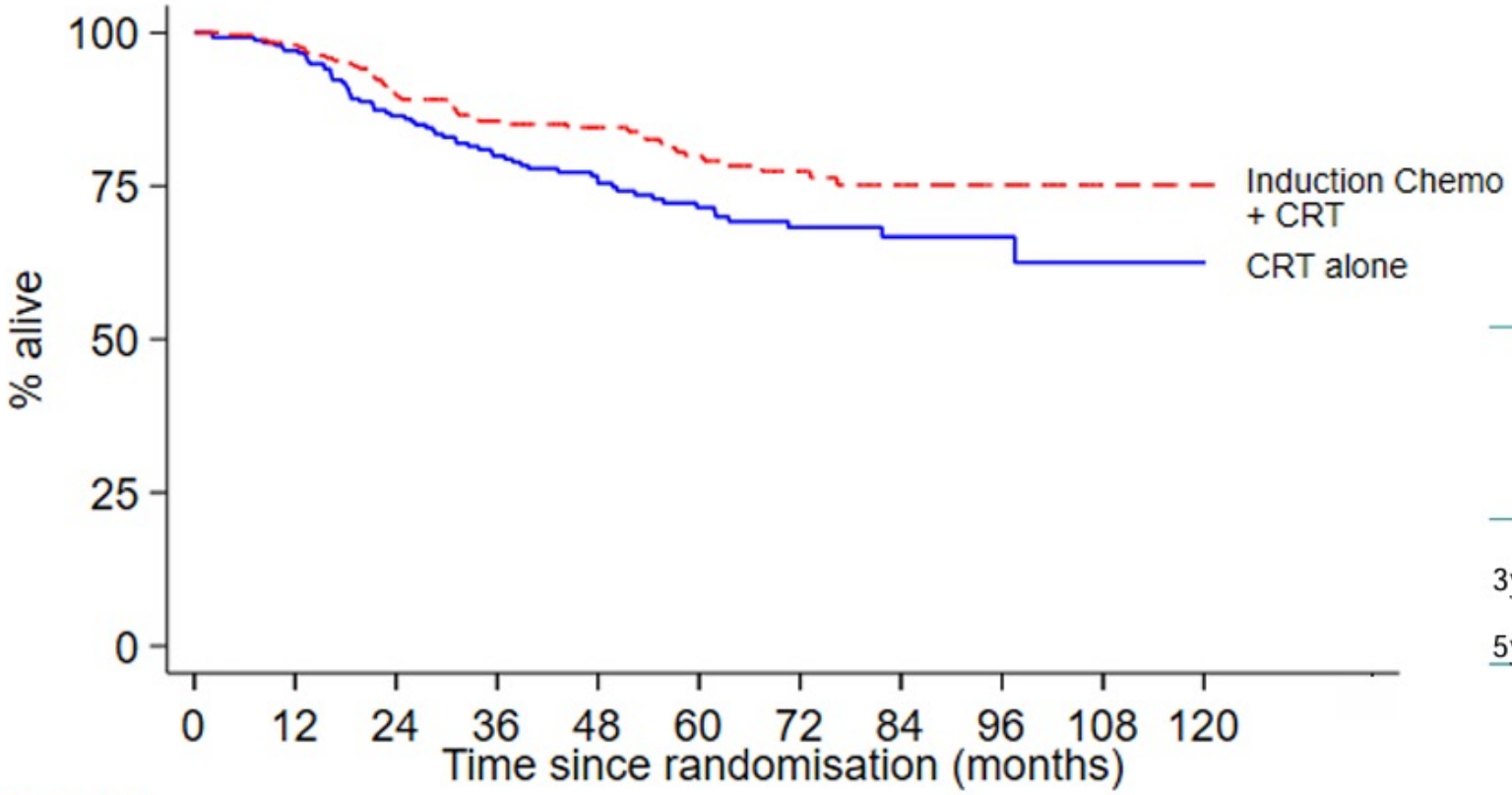
INTERLACE Overall Survival (median FU 64m)



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

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Patterns of Relapse

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

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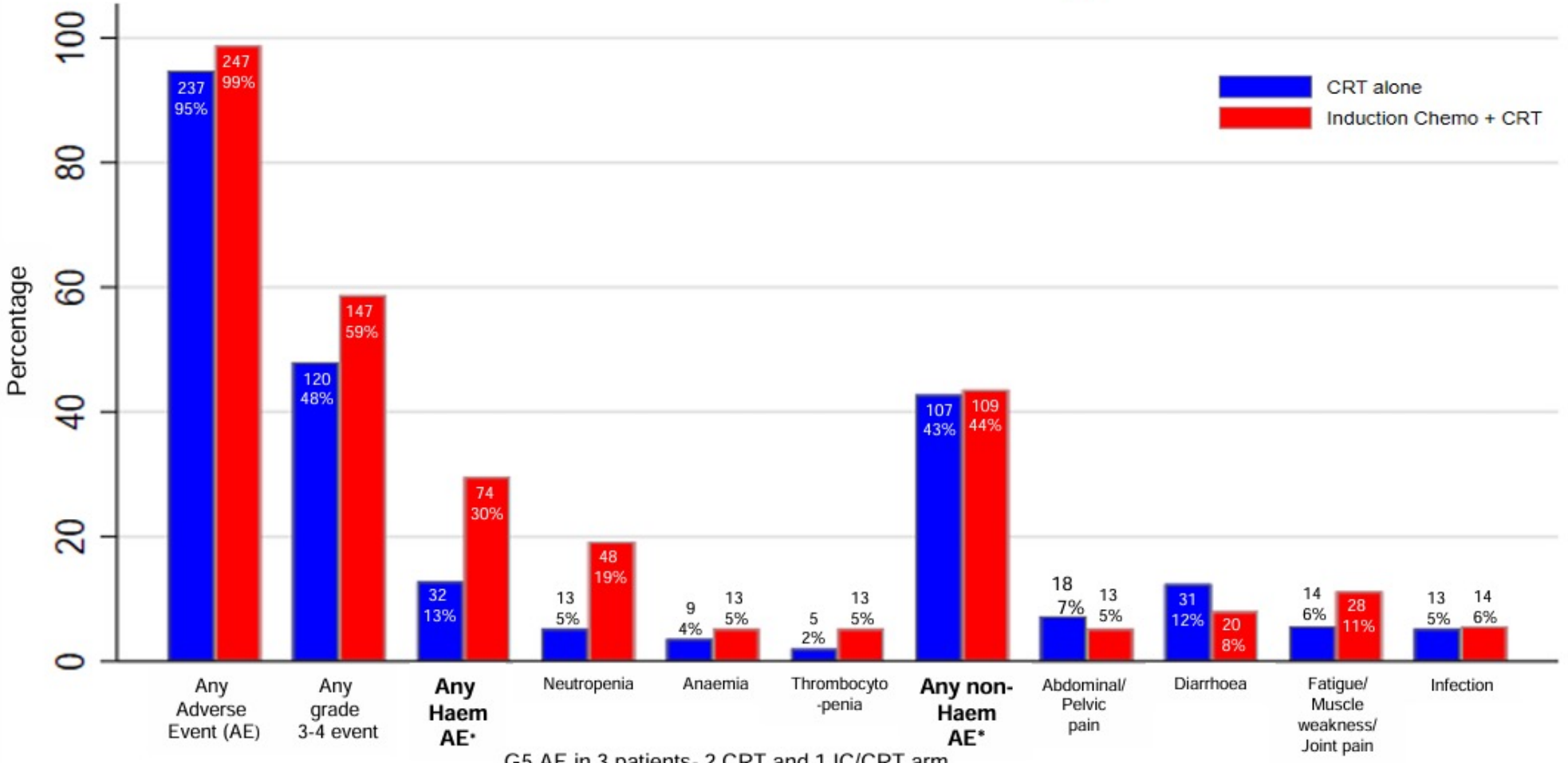
Adverse Events at any time



G5 AE in 3 patients- 2 CRT and 1 IC/CRT arm

*Grade 3-4 only . *106 people (42%) reported grade 2 alopecia in the IC/CRT*

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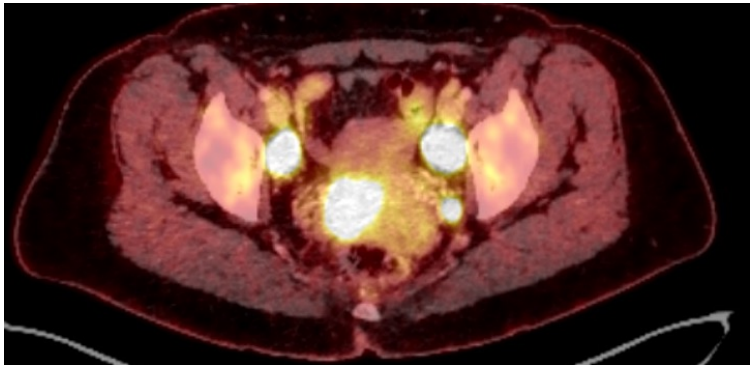
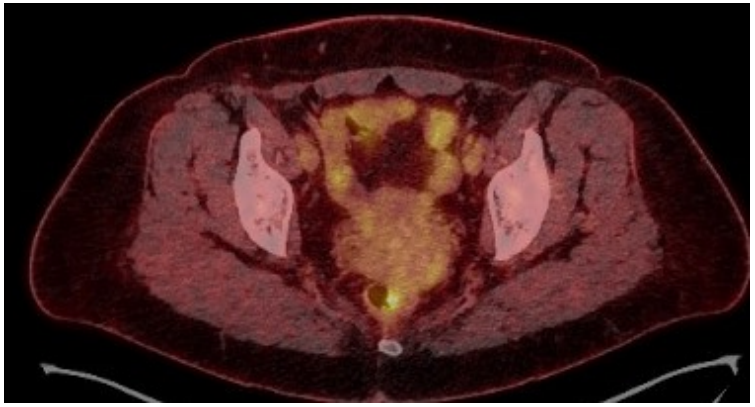
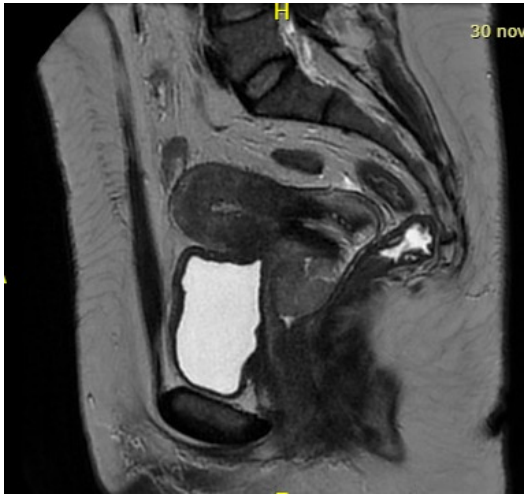
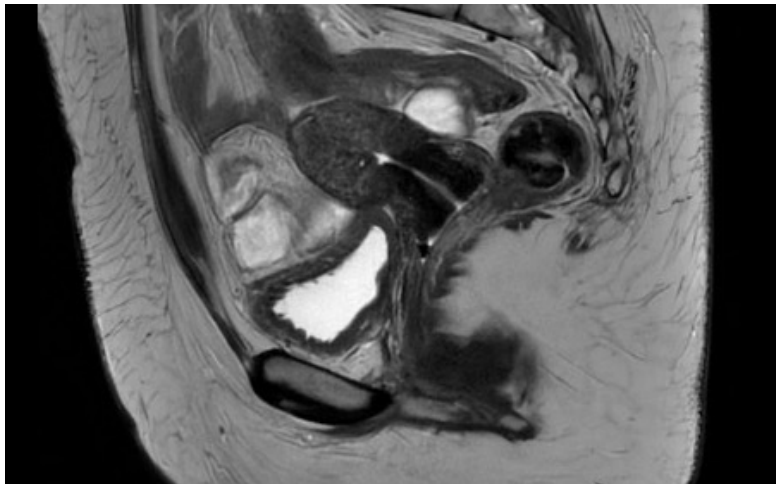
Cas clinique: bilan juin 2024 après CT et RCT curie

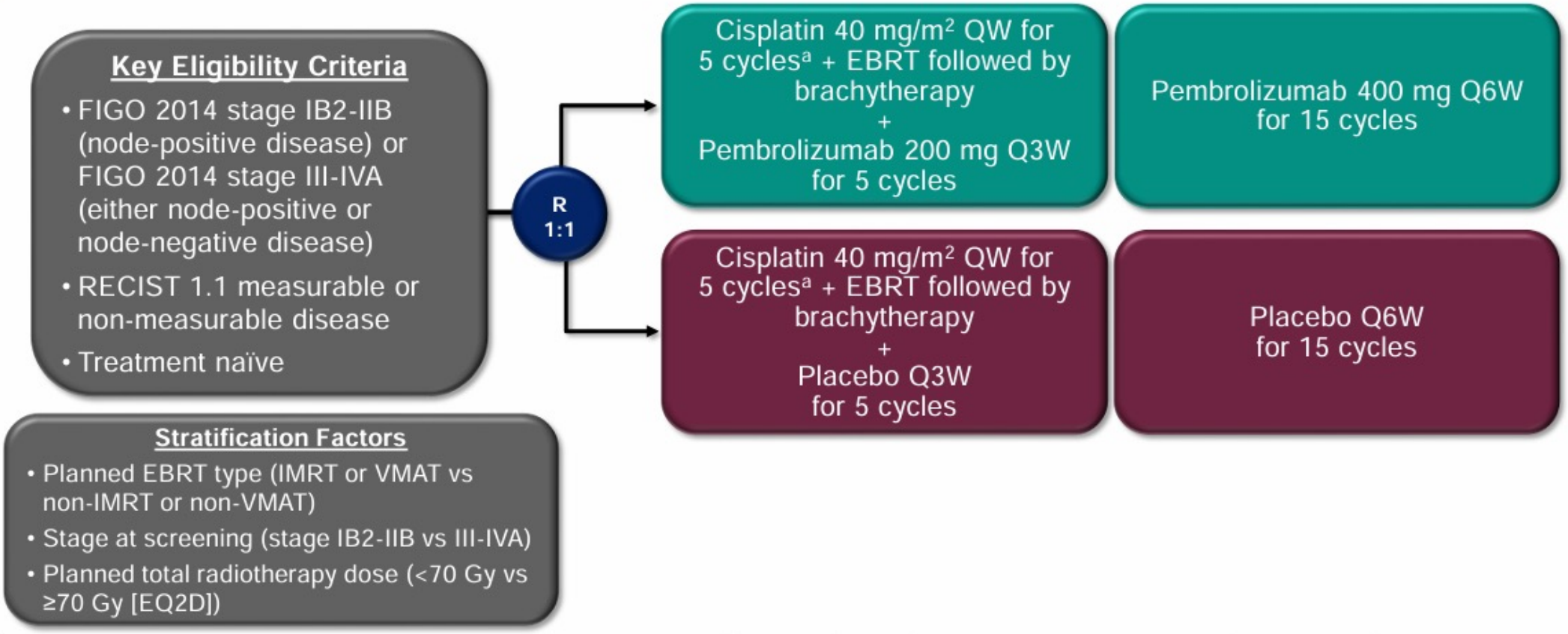








ENGOT-cx11/GOG-3047/KEYNOTE-A18: Randomized, Double-Blind, Phase 3 Study



[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.

MADRID 2023 ESMO congress

Lorusso D, Xiang Y, Hasegawa K, et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial. *Lancet.* 2024;403(10434):1341-1350. https://www.ncbi.nlm.nih.gov/pubmed/38521086

Presented by: Domenica Lorusso

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.

MADRID 2023 ESMO congress

Lorusso D, Xiang Y, Hasegawa K, et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial. *Lancet.* 2024;403(10434):1341-1350. https://www.ncbi.nlm.nih.gov/pubmed/38521086

Presented by: Domenica Lorusso

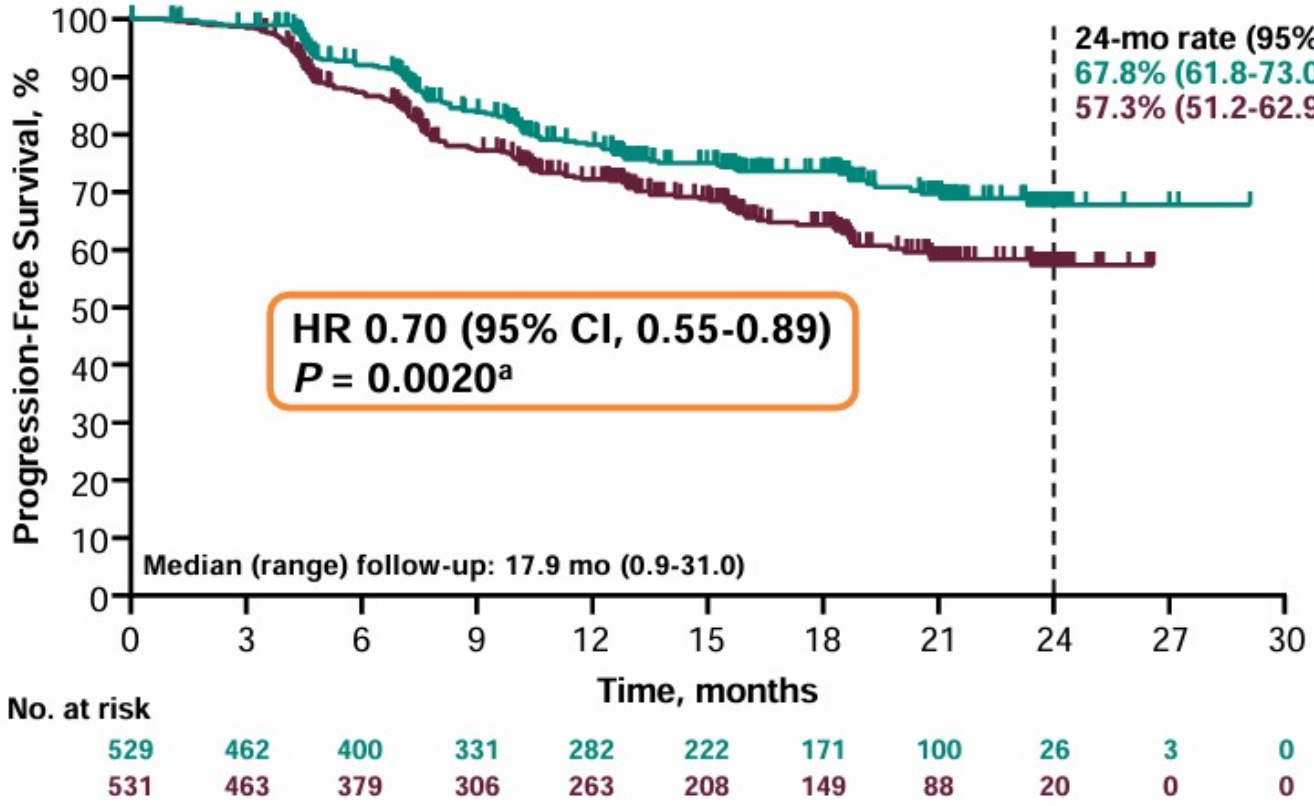
Summary of Treatment Exposure

	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.

Lorusso D, Xiang Y, Hasegawa K, et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial. *Lancet.* 2024;403(10434):1341-1350. https://www.ncbi.nlm.nih.gov/pubmed/38521086

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)

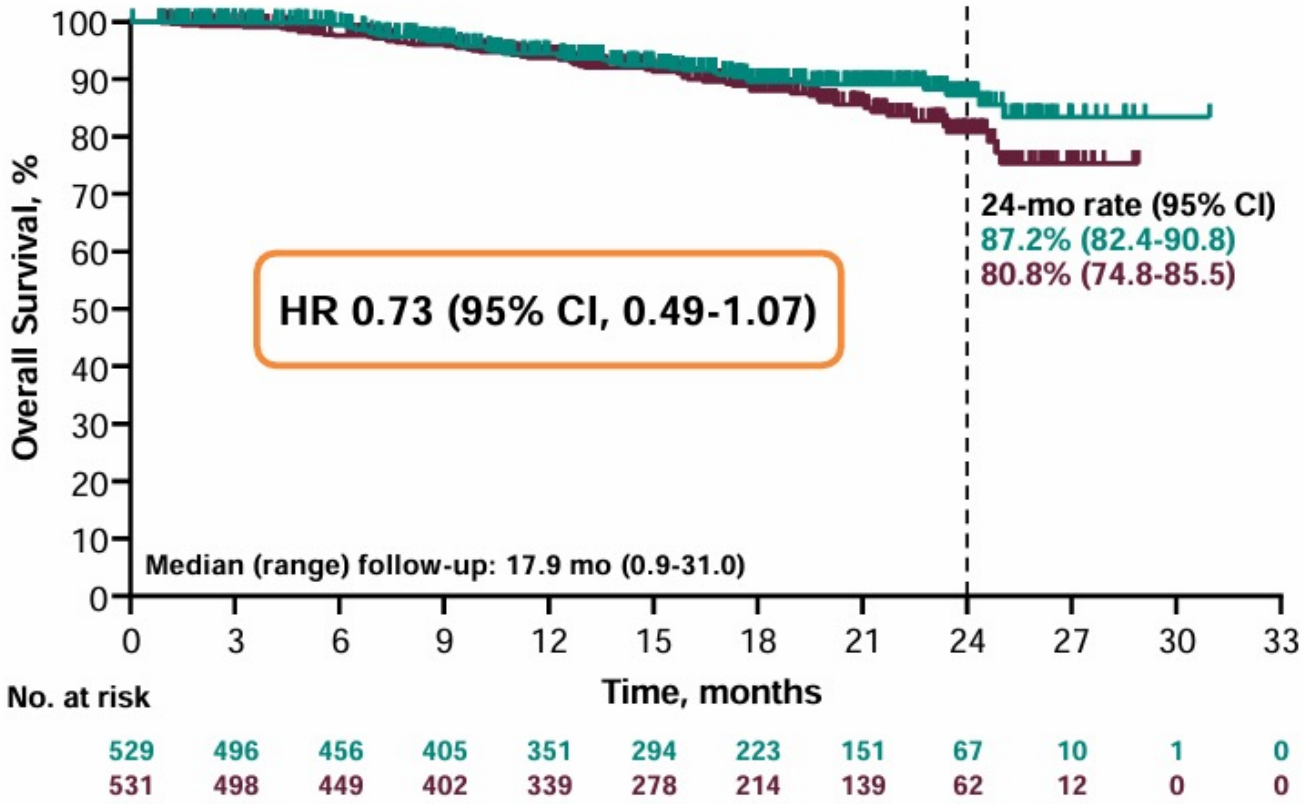
Response assessed per RECIST v1.1 by investigator review or histopathologic confirmation. [a]With 269 events (88.5% information fraction), the observed *P* = 0.0020 (1-sided) crossed the prespecified nominal boundary of 0.0172 (1-sided) at this planned first interim analysis. The success criterion of 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.

MADRID 2023 ESMO congress

Lorusso D, Xiang Y, Hasegawa K, et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial. *Lancet.* 2024;403(10434):1341-1350. https://www.ncbi.nlm.nih.gov/pubmed/38521086

Presented by: Domenica Lorusso

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.

Lorusso D, Xiang Y, Hasegawa K, et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial. *Lancet.* 2024;403(10434):1341-1350. https://www.ncbi.nlm.nih.gov/pubmed/38521086

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.

Lorusso D, Xiang Y, Hasegawa K, et al. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial. *Lancet.* 2024;403(10434):1341-1350. https://www.ncbi.nlm.nih.gov/pubmed/38521086

En 2025 comment allons-nous choisir ?

- Selon le stade ?

Stades I/II: Chimiothérapie néoadjuvante

Stades III/IV: Immunothérapie

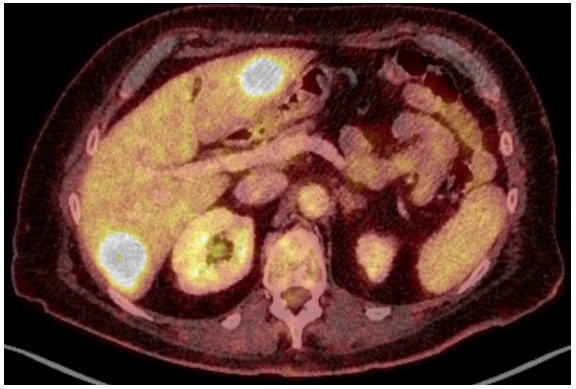
- Selon le coût ?

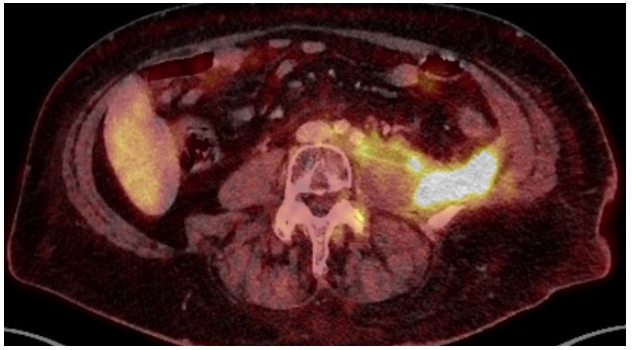
- Selon le type histologique?

- Combiner les 2 attitudes ?

ME LA N 58 ans

Tabagisme 40 pquets/année, DNID
Métrorragies depuis juin 2022
Diagnostic janv 2023 adénocarcinome col utérin
Clinique: lésion ulcérée avec disparition col envahissement vaginal 1/3 inf; envahissement paramétrial au TR
Bilan PET TDM /IRM pelvienne: IIIC1
Traitement RCT et curie thérapie de fev à mars 2023
mars 2023: récidive métastatique asymptomatique



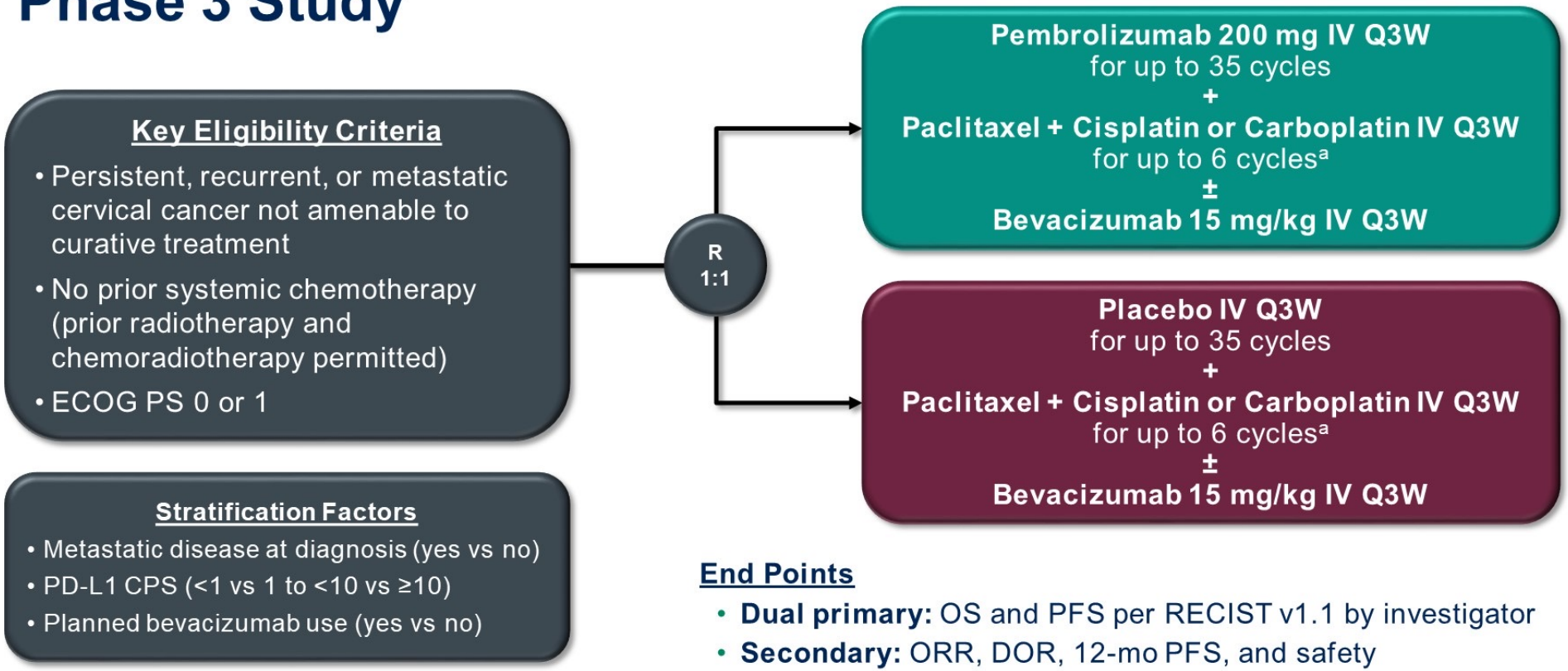


Progrès Cancer cervical récidivant/métastatique

	FIRST-LINE RECURRENT/METASTATIC			SECOND-LINE RECURRENT
	GOG 204 CDDP+Paclitaxel	GOG 240 Doublet + Bevacizumab	KN-826 ChemoRx + Pembrolizumab with or without Bevacizumab	EMPOWER Cemiplimab
Median OS	12.0m	17.0m, HR 0.71	24.4m, HR 0.64	12.0m, HR 0.69
ORR.	29.1%	48%	68.1% in PD-L1+ $\geq$1%	18% in PD-L1+ $\geq$1%

GOG-0204: Monk BJ, et al. J Clin Oncol 2009;27:4649-55.
GOG-0240: Tewari KS, et al. N Engl J Med 2014;370:734-43.
Keynote-826: Colombo N, et al. N Engl J Med 2021;385:1856-67.
EMPOWER: Tewari KS, et al. N Engl J Med 2022;386:544-55.

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



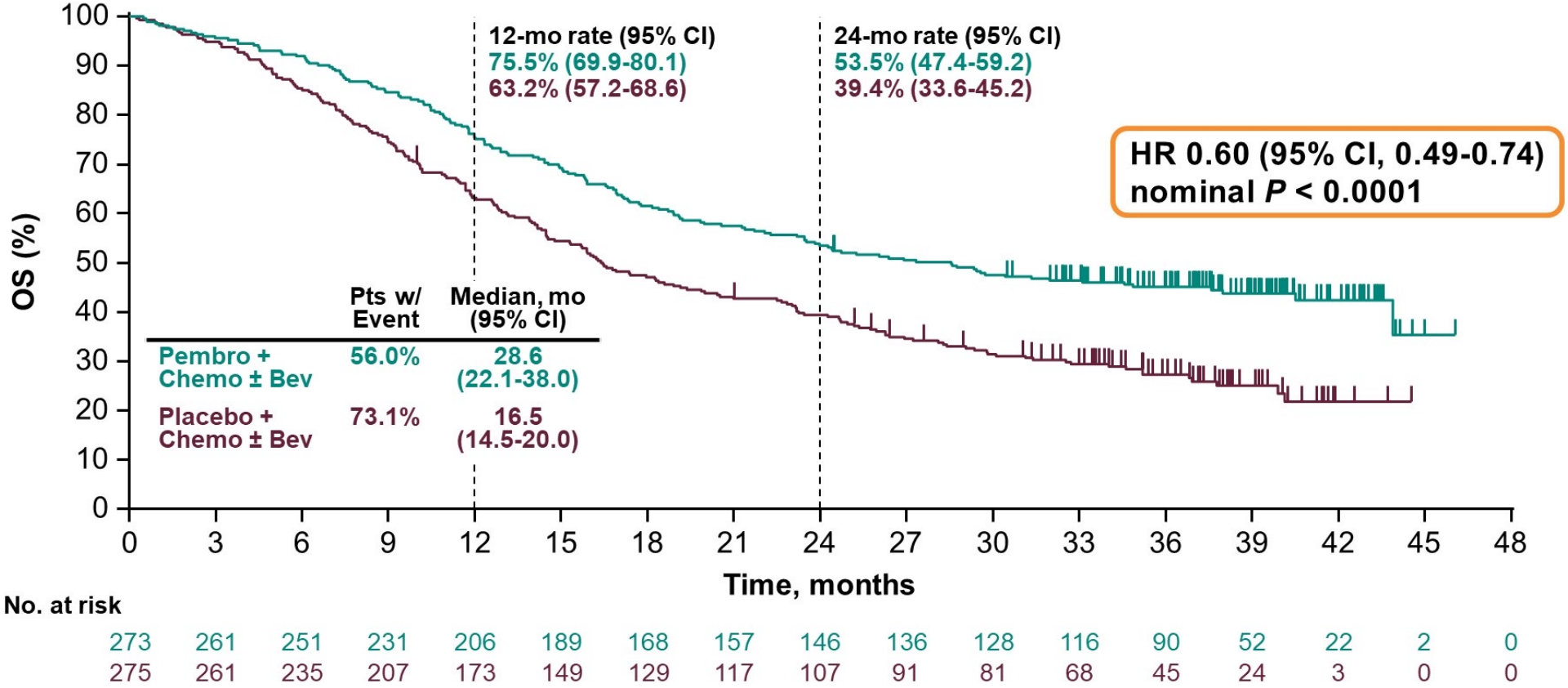
End Points

- **Dual primary:** OS and PFS per RECIST v1.1 by investigator
- **Secondary:** ORR, DOR, 12-mo PFS, and safety

[a]Paclitaxel: 175 mg/m^2. Cisplatin: cisplatin 50 mg/m^2. 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). KEYNOTE-826 ClinicalTrials.gov identifier, NCT03635567.

Monk et al. First-Line Pembrolizumab + Chemotherapy Versus Placebo + Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Final Overall Survival Results of KEYNOTE-826 ; J Clin Oncol. 2023 Dec 20;41(36):5505-5511

Protocol-Specified Final OS: PD-L1 CPS ≥1 Population



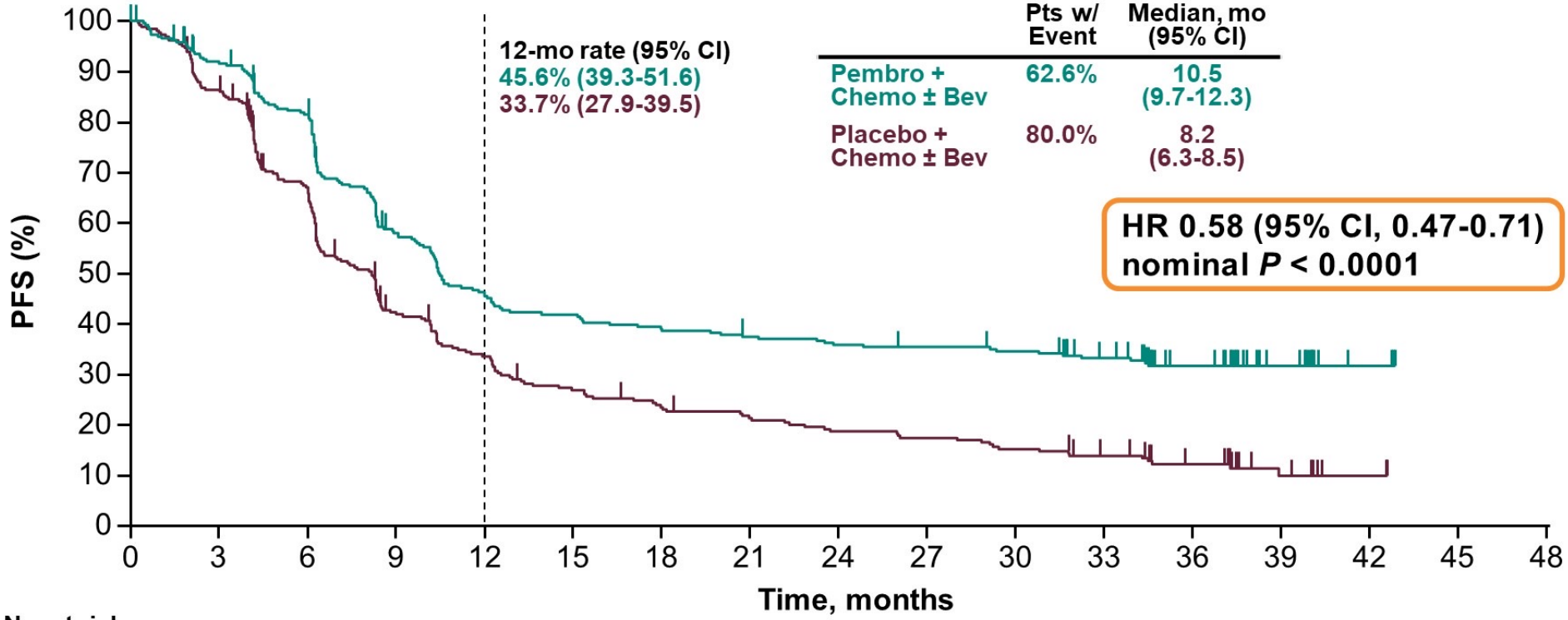
No. at risk

273	261	251	231	206	189	168	157	146	136	128	116	90	52	22	2	0
275	261	235	207	173	149	129	117	107	91	81	68	45	24	3	0	0

Data cutoff date: October 3, 2022.

Monk et al. First-Line Pembrolizumab + Chemotherapy Versus Placebo + Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Final Overall Survival Results of KEYNOTE-826 ; J Clin Oncol. 2023 Dec 20;41(36):5505-5511

Protocol-Specified Final PFS: PD-L1 CPS ≥1 Population



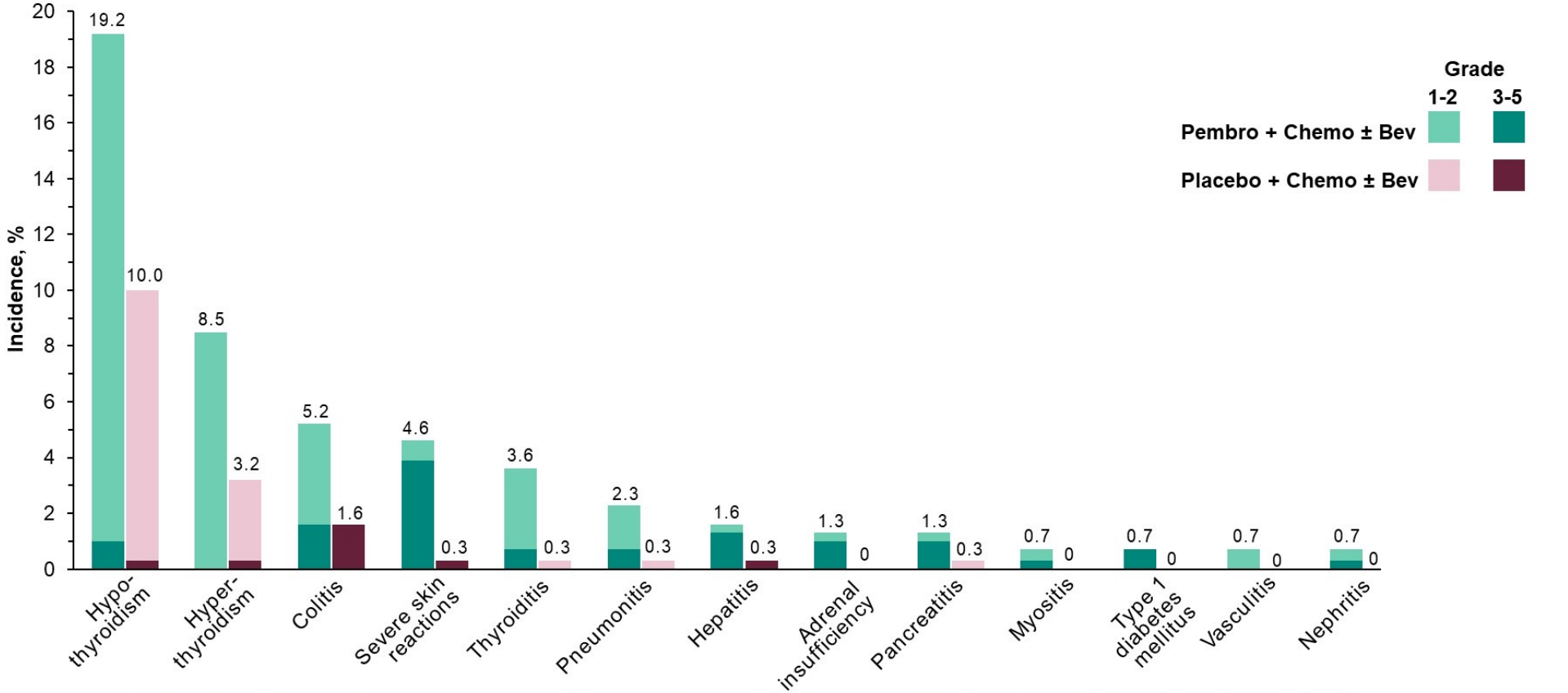
No. at risk

273	238	208	144	113	104	97	92	88	86	83	70	46	25	6	0	0
275	229	170	103	81	64	55	49	43	40	35	28	18	7	2	0	0

Response assessed per RECIST v1.1 by investigator review. Data cutoff date: October 3, 2022.

Monk et al. First-Line Pembrolizumab + Chemotherapy Versus Placebo + Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Final Overall Survival Results of KEYNOTE-826 ; J Clin Oncol. 2023 Dec 20;41(36):5505-5511

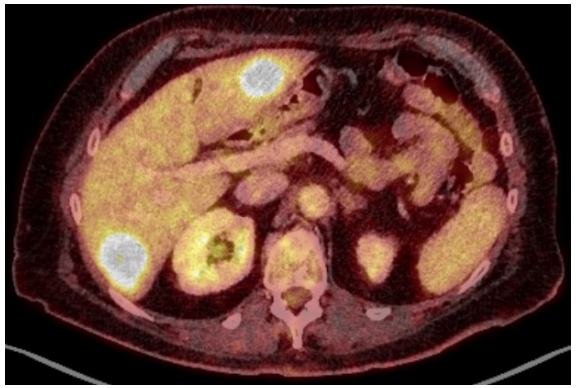
Updated Immune-Mediated AEs, Incidence ≥2 Patients in Either Arm

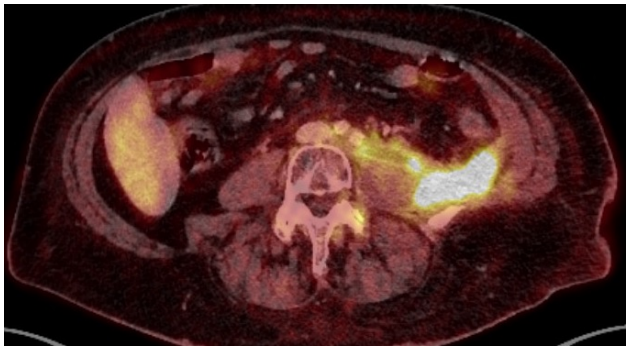


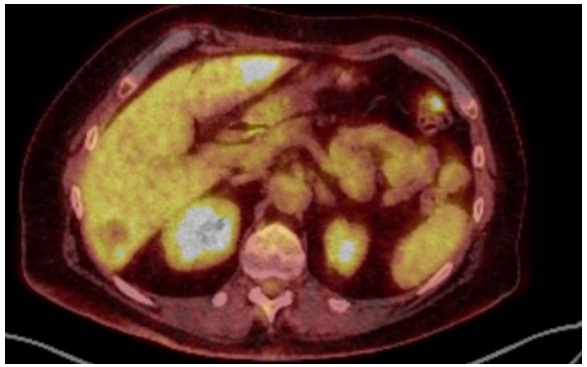
Events were considered regardless of attribution to treatment by the investigator. Related terms were included in addition to the specific terms listed. Data cutoff date: October 3, 2022.

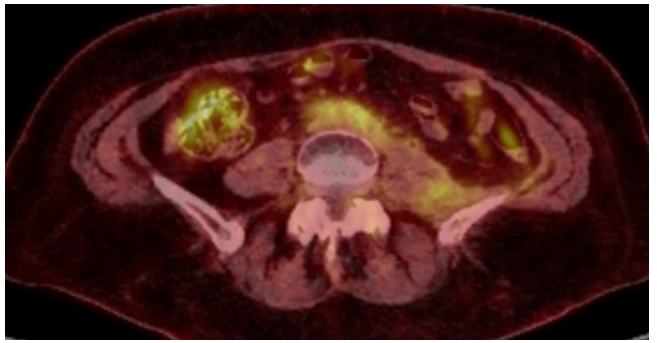
Monk et al. First-Line Pembrolizumab + Chemotherapy Versus Placebo + Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Final Overall Survival Results of KEYNOTE-826 ; J Clin Oncol. 2023 Dec 20;41(36):5505-5511

Cas clinique: carboplatine paclitaxel bevacizumab pembrolizumab 3 mois









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 R/M CC
- In patients with pelvic disease, no bladder or rectal mucosa involvement
- Available archival or fresh tumour sample for PD-L1 expression

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)
- OS

Key secondary endpoints

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

Stratification factors:

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

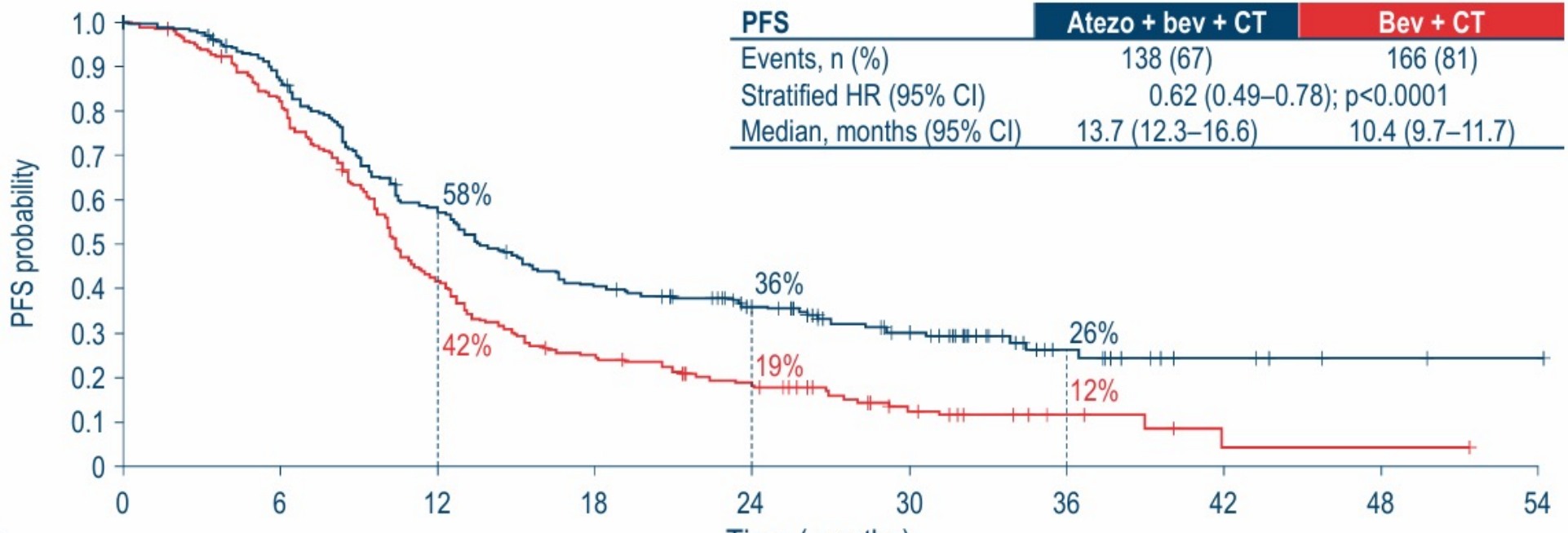
[a]Paclitaxel 175 mg/m² day 1 + platinum (cisplatin 50 mg/m² or carboplatin AUC5) day 1; [b]Capped at 20% of the overall population
CR = complete response; DoR = duration of response; ECOG = Eastern Cooperative Oncology Group; ORR = objective response rate; PFS2 = time from randomisation to second progression or death; PS = performance status; q3w = every 3 weeks; TFST = time from randomisation to first subsequent therapy or death

Oaknin A et al. Atezolizumab plus bevacizumab and chemotherapy for metastatic, persistent, or recurrent cervical cancer (BEATcc): a randomised, open-label, phase 3 trial; Lancet. 2024 Jan 6;403(10421):31-43

Dual primary endpoint: PFS

Statistically significant 38% reduction in risk of progression or death

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



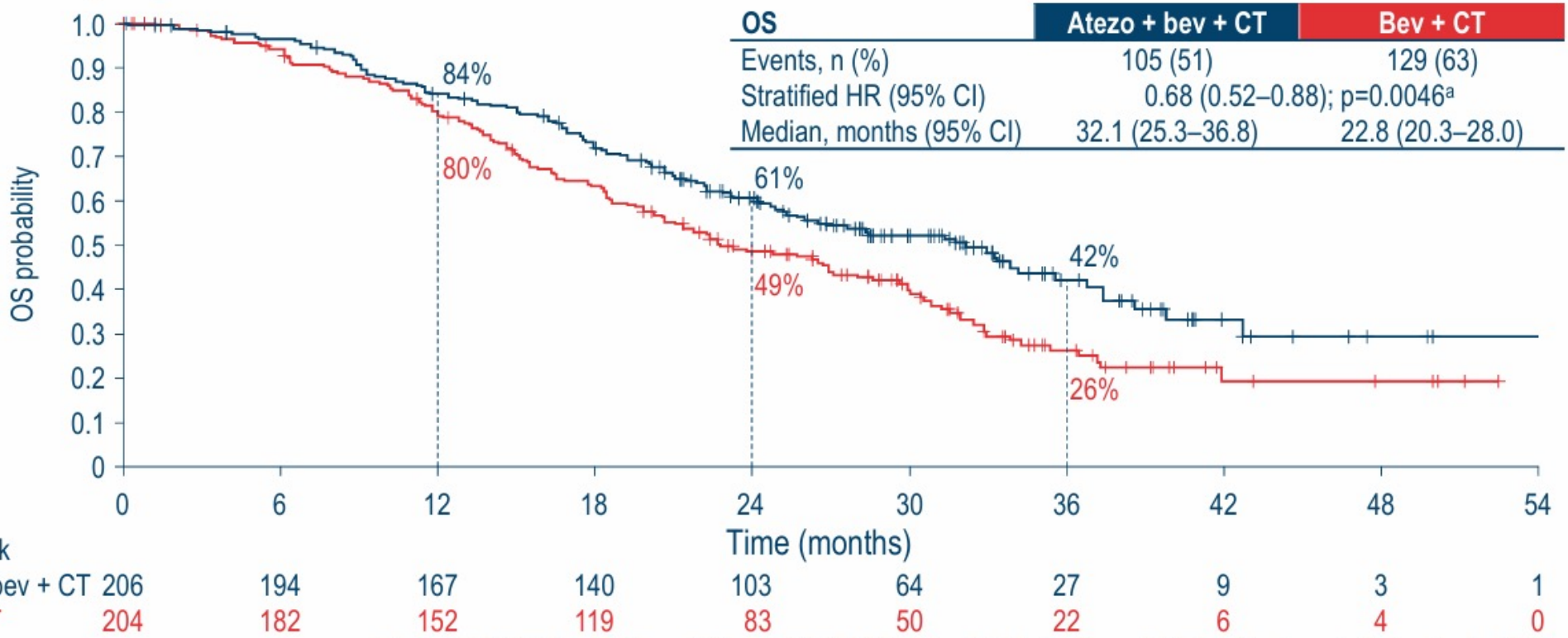
No. at risk										
Atezo + bev + CT	206	174	114	79	58	37	13	5	2	1
Bev + CT	204	159	80	47	31	13	5	1	1	0

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

Oaknin A et al. Atezolizumab plus bevacizumab and chemotherapy for metastatic, persistent, or recurrent cervical cancer (BEATcc): a randomised, open-label, phase 3 trial; Lancet. 2024 Jan 6;403(10421):31-43

Dual primary endpoint: OS (interim analysis)

Statistically significant 32% reduction in risk of death



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

No. at risk										
Atezo + bev + CT	206	194	167	140	103	64	27	9	3	1
Bev + CT	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]Interim OS was statistically significant, crossing the boundary of p=0.0238

Oaknin A et al. Atezolizumab plus bevacizumab and chemotherapy for metastatic, persistent, or recurrent cervical cancer (BEATcc): a randomised, open-label, phase 3 trial; Lancet. 2024 Jan 6;403(10421):31-43

Que faire après immunothérapie ?

Chimiothérapie ?

Essai thérapeutique ?

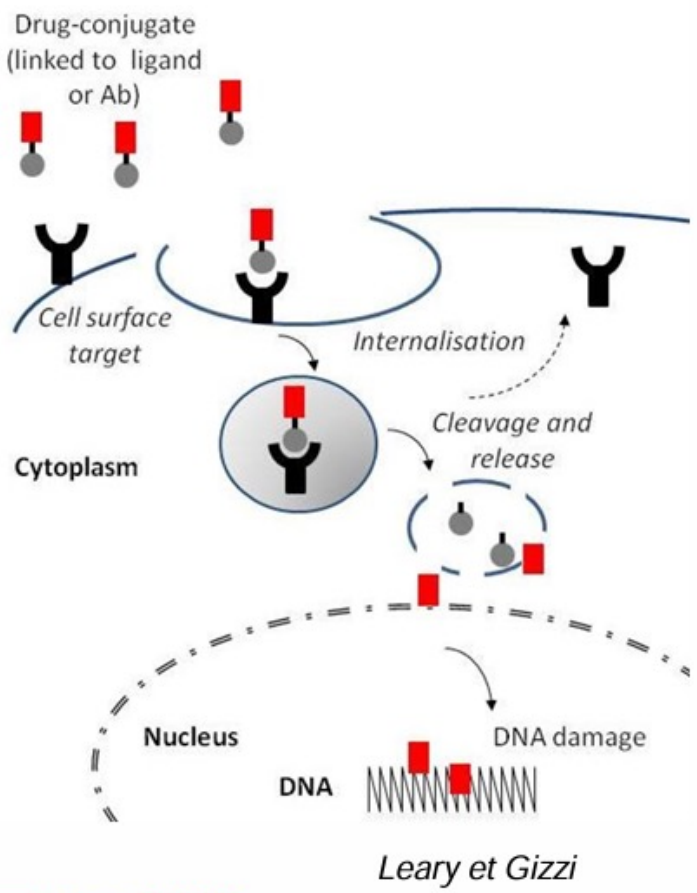
COURS ST-PAUL
RPC 2023

Cancer du col : efficacité des chimio en 2ème ligne

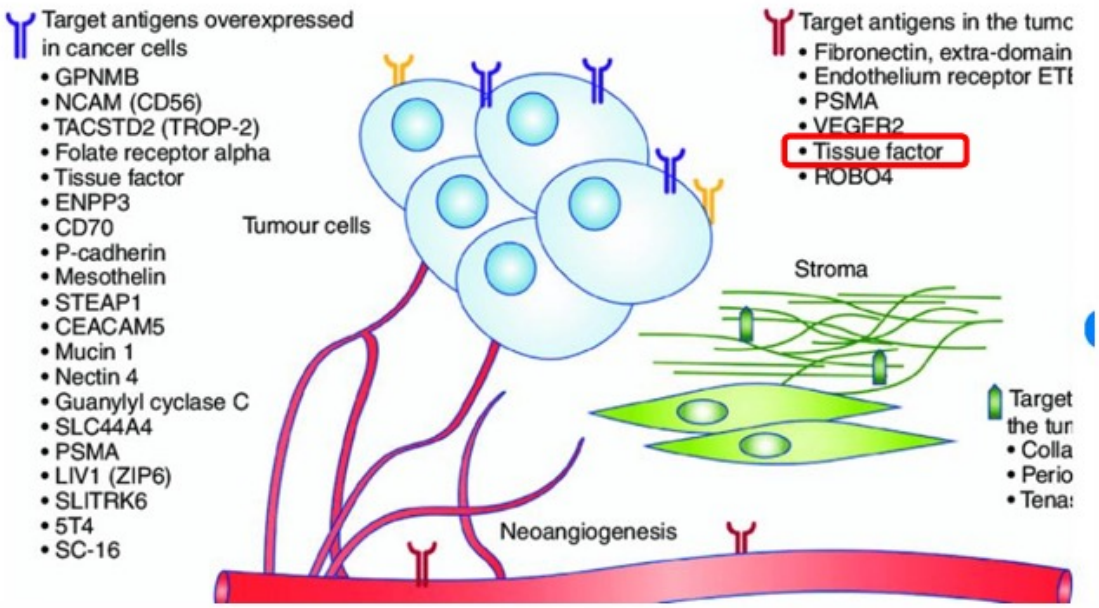
	N	Taux de Réponse (%)	Survie Sans Rechute (mois)	Survie Globale (mois)
Topotecan*	45	12,5	2,1	6,6
Vinorelbine*	44	13,7	-	-
Pemetrexed*	43	13,9	2,3	8
Docetaxel*	27	8,7	3,8	7
Gemcitabine*	22	4,5	2,1	6,5
Capecitabine***	23	0	-	5,7
Irinotecan**	42	21	-	6,4

* Yu et al Am J Hematol Oncol 2015
** Verschraegen et al J Clin Oncol 1997
*** Jenkins AD Gynecol Oncol 2005

Antibody-Drug Conjugates



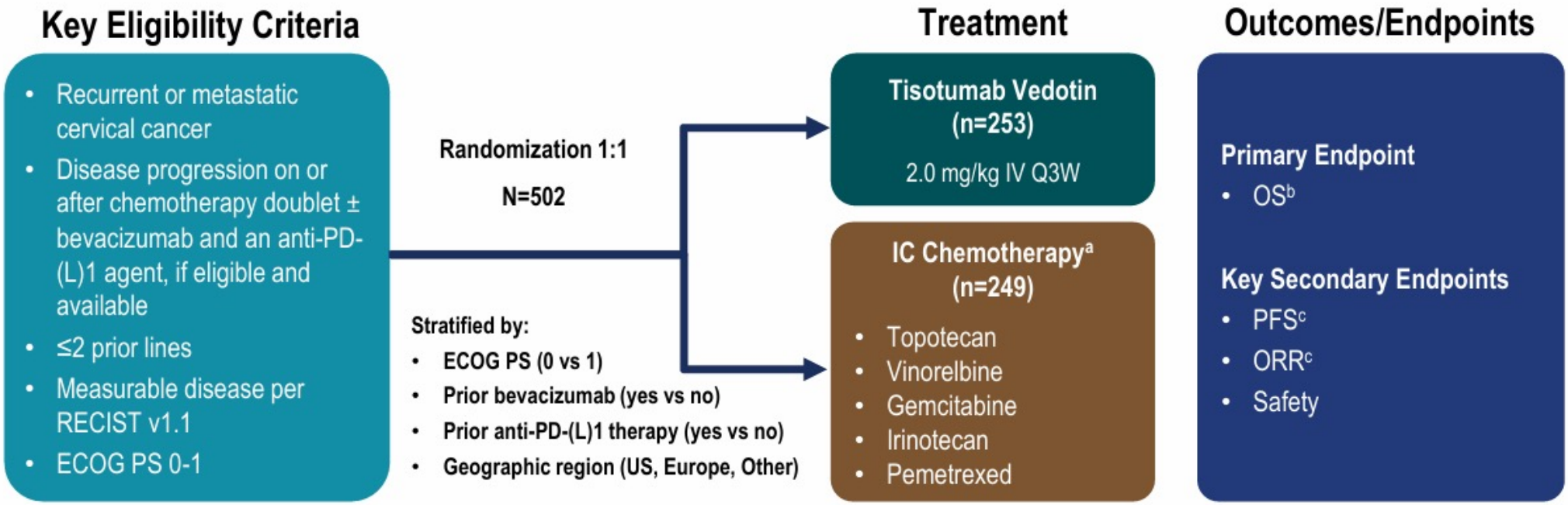
Leary et Gizzi



MADRID 2023 ESMO congress

Alexandra Leary, MD, PhD

innovaTV 301: A Randomized, Open-Label, Phase 3 Trial



- Data presented herein are a planned interim analysis

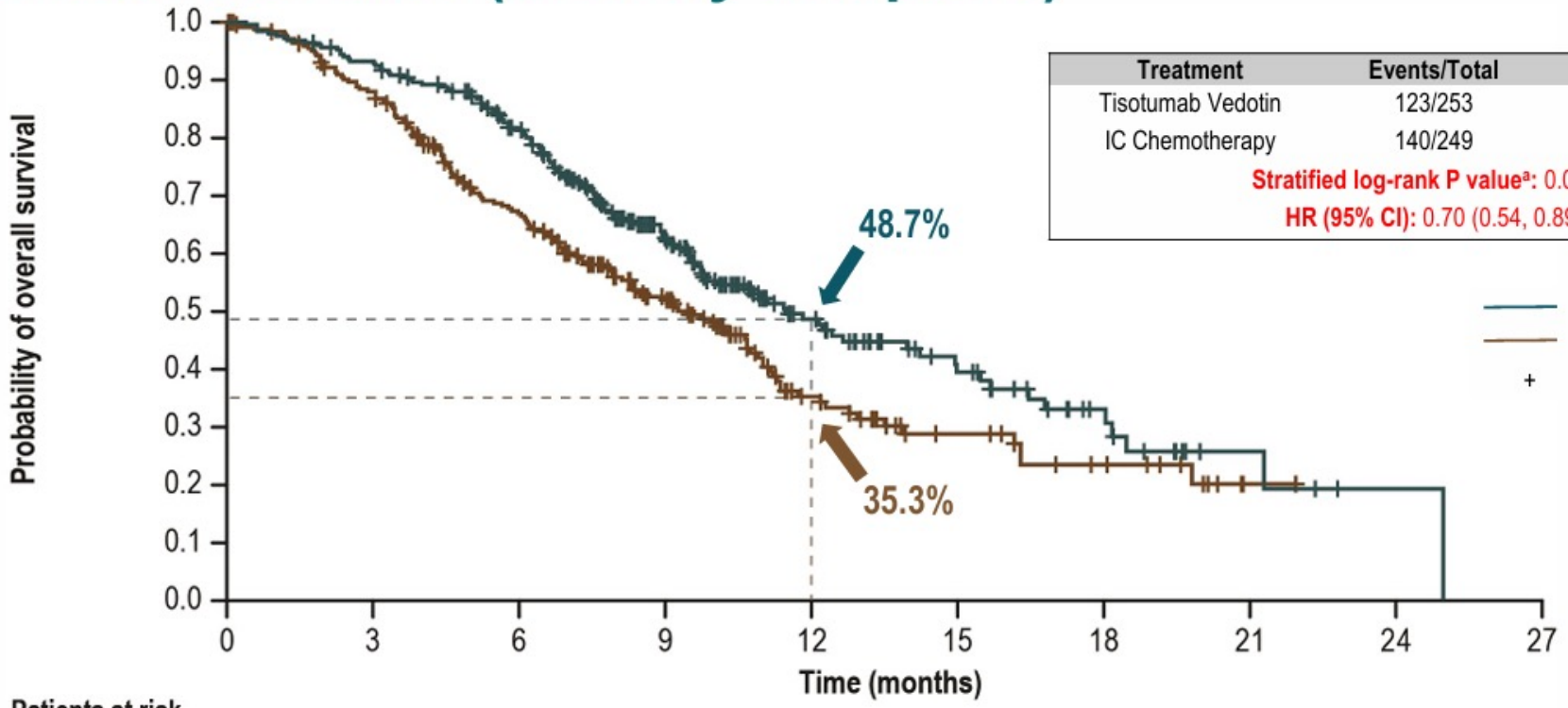
IC, investigator's choice
End of treatment visit occurred 30 days after the last dose of treatment. Survival follow-up occurred every 60 days after the last dose of treatment.
[a]Chemotherapy regimens were given at the following doses: topotecan: 1 or 1.25 mg/m^2 IV on Days 1 to 5, every 21 days; vinorelbine: 30 mg/m^2 IV on Days 1 and 8, every 21 days; gemcitabine: 1000 mg/m^2 IV on Days 1 and 8, every 21 days; irinotecan: 100 or 125 mg/m^2 IV weekly for 28 days, every 42 days; pemetrexed: 500 mg/m^2 on Day 1, every 21 days; [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.

MADRID 2023 ESMO congress

Prof. Ignace Vergote

Vergote I et al. Presented at: European Society for Medical Oncology Congress; 20–24 October 2023; Madrid, Spain. Abstract LBA9

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)

Patients at risk

Tisotumab vedotin	253	234	191	109	52	29	14	4	1	0
IC Chemotherapy	249	212	150	87	37	19	11	1	0	0

[a]The threshold for statistical significance is 0.0226 (2-sided), based on the actual number of OS events at interim analysis.

MADRID 2023 ESMO congress

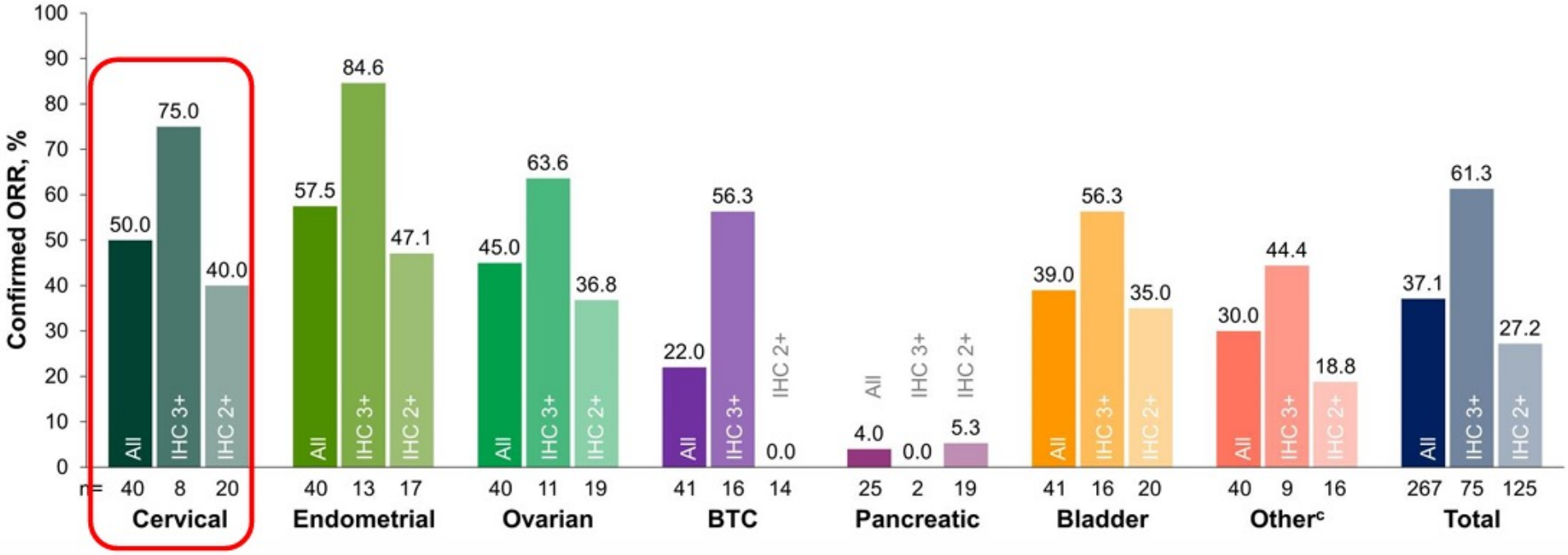
Prof. Ignace Vergote

Vergote I et al. Presented at: European Society for Medical Oncology Congress; 20–24 October 2023; Madrid, Spain. Abstract LBA9

DESTINY-PanTumor02: Trastuzumab Deruxtecan (T-DXt)

DESTINY-PanTumor02

Objective Response Rate by HER2 status



Meric Berstam et al ASCO 2023

MADRID 2023 ESMO congress

Alexandra Leary, MD, PhD

Meric-Bernstam F et al. Presented at: European Society for Medical Oncology Congress; 20–24 October 2023; Madrid, Spain. Abstract LBA34

Pour les cancers du col récidivants/métastatiques

- L'immunothérapie est un standard associé à la chimiothérapie en première ligne
- Permet de contrôler à 2 ans plus de 1/3 des patientes
- Rajout du Bevacizumab en l'absence de risque de fistule évident
- Les ADC seront prochainement un standard en seconde ligne
- Éviter mono-chimiothérapie en seconde ligne et au-delà
- Privilégier inclusion essai thérapeutique