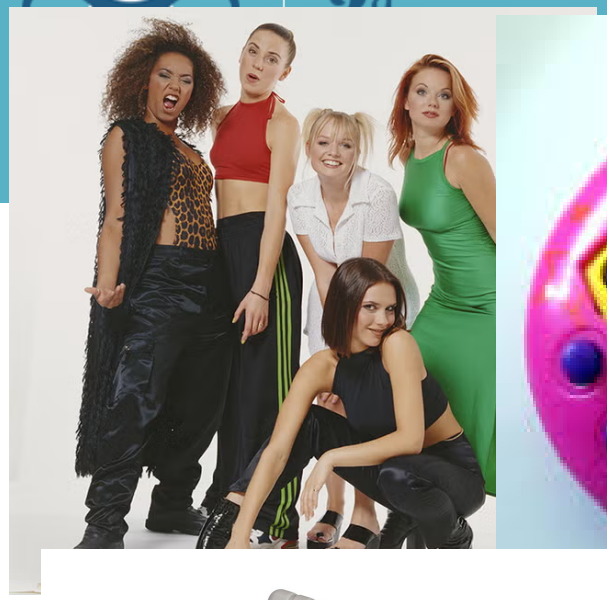
3ª Jornada de Actualización EN CÁNCER GINECOLÓGICO

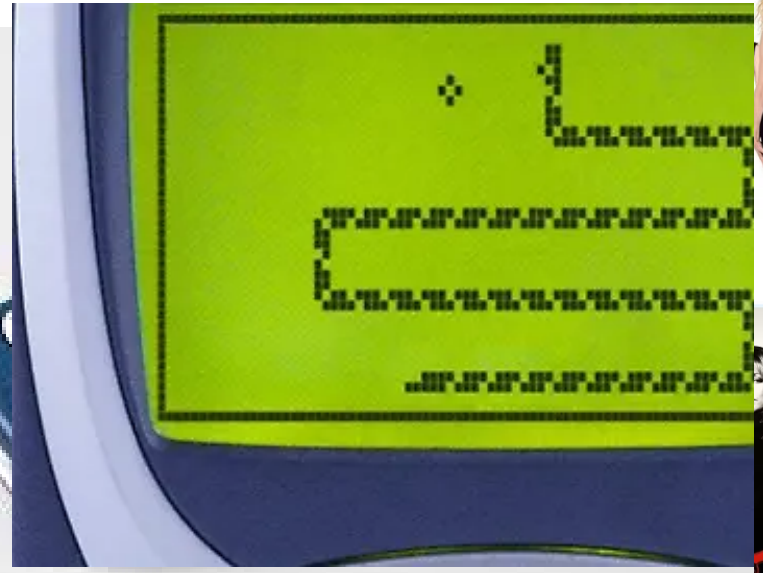
Bilbao
12-13 junio 2025

Mesa cáncer de cérvix. Enfermedad localmente avanzada.

Ane Zumarraga Cuesta
Hospital Universitario Basurto
13/06/2025

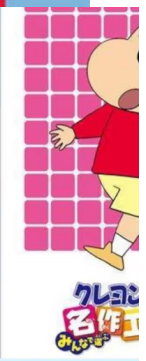



Nintendo GAME BOY
SELECT
START
B
A

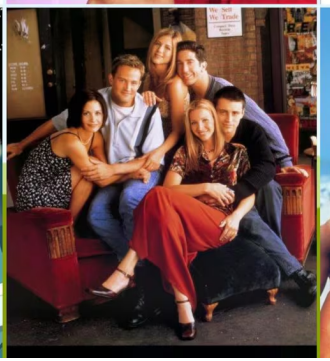



THE SIMPSONS


The Fresh Prince of Bel-Air

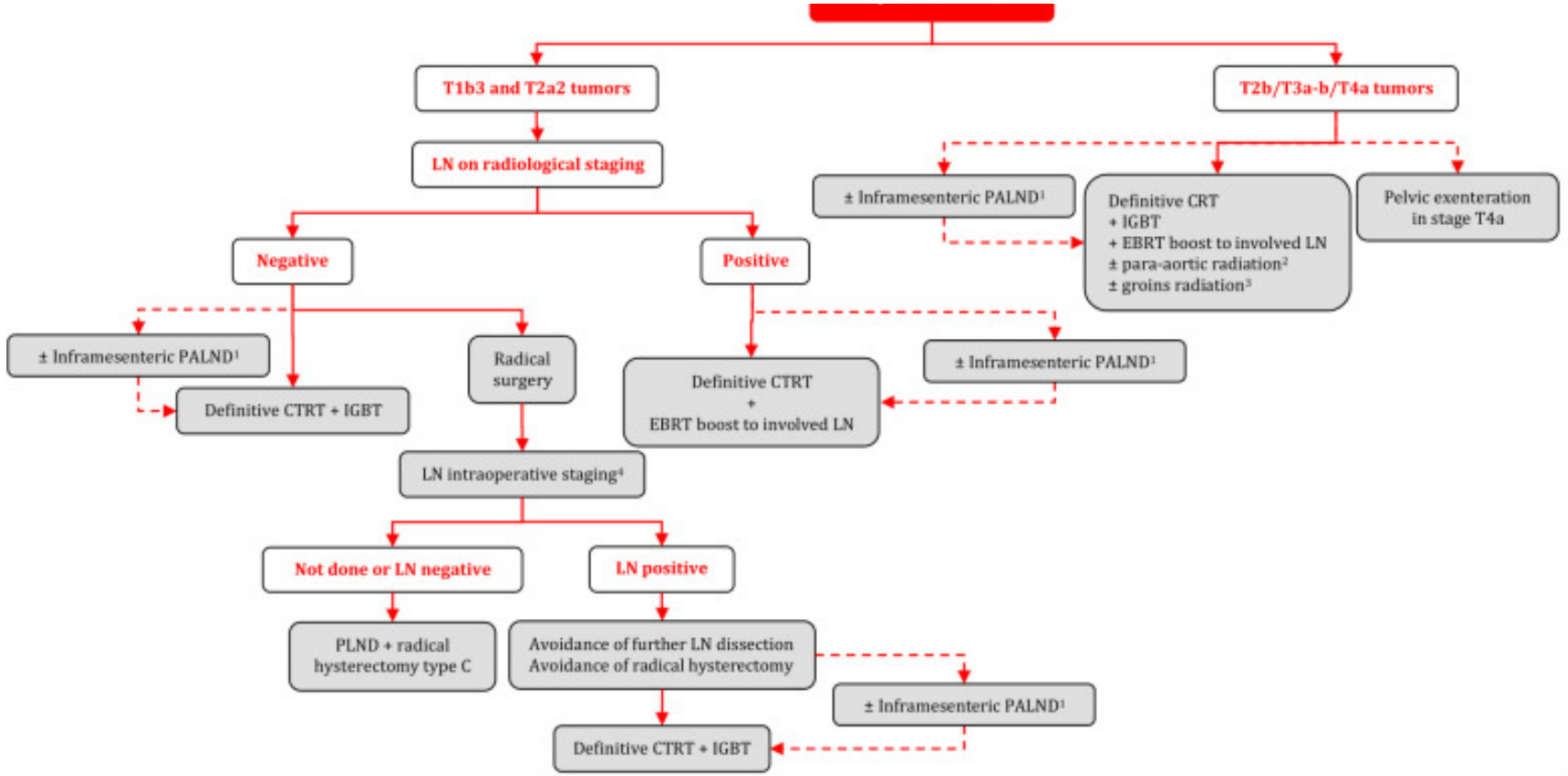



FUTURAMA



Int J Gynecol Cancer. 2023 May 1;33(5):649-666. doi: 10.1136/ijgc-2023-004429.

ESGO/ESTRO/ESP Guidelines for the management of patients with cervical cancer – Update 2023



CTRT chemoradiotherapy; EBRT external beam radiotherapy; IGBT image-guided brachytherapy; LN lymph node; PALND paraaortic lymph node dissection; PLND pelvic lymph node dissection.

¹PALND at least up to inferior mesenteric artery may be considered for staging purposes; ²The indication for elective para-aortic irradiation can be based on the number of level 1 positive nodes (external iliac, interiliac, internal iliac) on imaging (e.g.>2 positive nodes). It should always be applied in patients who on imaging have even one positive node on imaging at level 2 (common iliac) and above. ³The groins should also be included in the elective target for patients with tumour involvement of the lower third of the vagina; ⁴LN staging should follow the same principles as in T1b1-2 tumors.

TRIAL	INTERVENTION	OUTCOME
GOG 109	Adjuvant RT vs CDDP based RT	Superiority of Adjuvant
GOG 85	CDDP-bas RT	
GOG 120	CDDP-bas RT	
GOG 123	CDDP-bas alone	
RTOG 9001	CDDP+5FU alone	

e-Year Overall Survival Rate by Stage

	FIGO 2018	
	Total Patients (N = 62,212)	5-Year Survival (n=55,490)
IB2	4,120 (6.6)	83.3 (81.8–84.8)
IB3	3,790 (6.1)	76.1 (74.3–77.8)
II	617 (1.0)	56.1 (51.4–60.5)
IIA	796 (1.3)	63.4 (59.5–67.0)
IIA1	742 (1.2)	70.3 (65.9–74.3)
IIA2	1,101 (1.8)	65.3 (61.6–68.6)
IIB	8,904 (14.3)	63.9 (62.7–65.0)
III	407 (0.7)	39.3 (33.9–44.7)
IIIA	954 (1.5)	40.7 (37.1–44.3)
IIIB	5,177 (8.3)	41.4 (39.9–42.9)
IIIC	5,350 (8.6)	46.3 (44.8–47.8)
IIIC1	4,625 (7.4)	60.8 (58.7–62.8)
IIIC2	1,114 (1.8)	37.5 (33.3–41.7)
IVA	1,890 (3.0)	24.0 (21.7–26.3)

Wright J et al, Obstet Gynecol 2019

Chemoradiotherapy for Cervical Cancer Meta-analysis Collaboration (CCCMAC).Cochrane Database Syst Rev 2010
Gynaecological Tumours Essentials for Clinicians, ESMO 2024
Kim YS et al. Gynecol Oncol 108:195-200, 2008

- El cáncer de cérvix es un tumor quimiosensible: TRO 48-93%

- Beneficio por estadios con QRT
  - Metaanálisis 2010: beneficio en SG en E.IA-IIA 10%, IIB 7% y III-IV 3%

- Fallos a distancia con QRT
  - QRT 15-20%
  - Dueñas et al. Con doblete 16 vs 8%

- Around 30% of recurrence
- 5y OS = 17%

Metaanálisis Ye Q et al. J Cancer Res Clin Oncol 2013

DOBLETES CDDP CONCOMITANTES CON RT

QTNA → RTQT

QTNA → CIRUGÍA

QTRT → CIRUGÍA

RT-QT + BRAQUI

QTRT → QT

QTRT → IT mantenimiento

CIRUGÍA → RT

RT-QT + BRAQUI

DOBLETE DE CDDP

F. Petrelli et al. / Gynecologic Oncology 134 (2014) 166–171

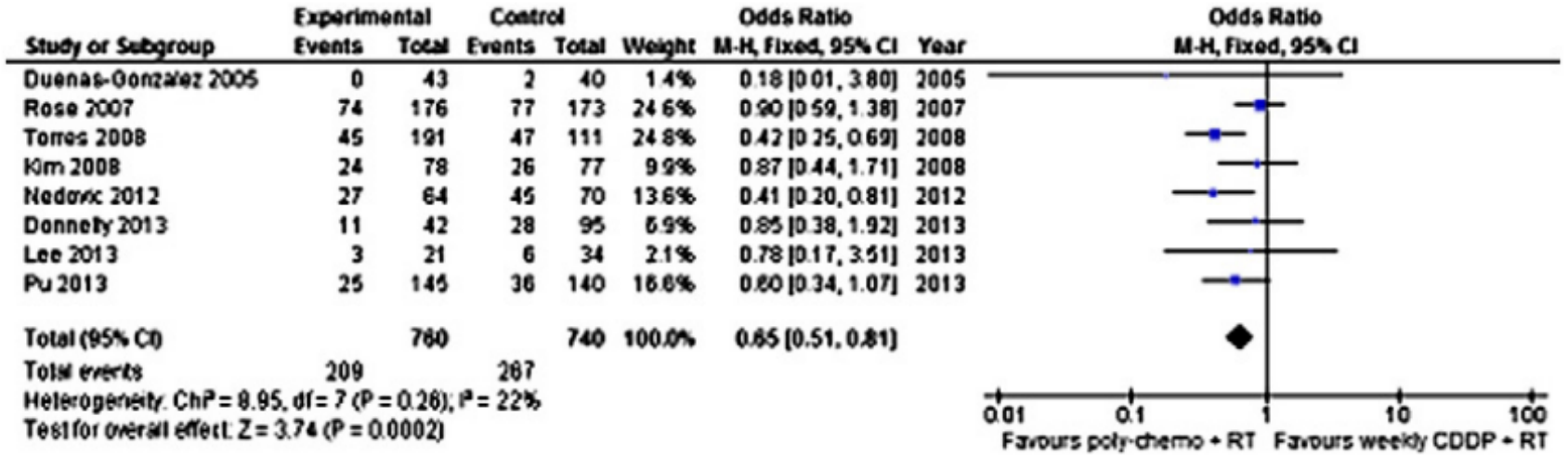


Fig. 2. Meta-analysis of OS for all studies.

Radiotherapy with concurrent cisplatin-based doublet or weekly cisplatin for cervical cancer: A systematic review and meta-analysis. Petrelli et al. Gynecologic Oncology. https://doi.org/10.1016/j.ygyno.2014.04.049

DOBLETES CDDP CONCOMITANTES CON RT

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RT-QT + BRAQUI

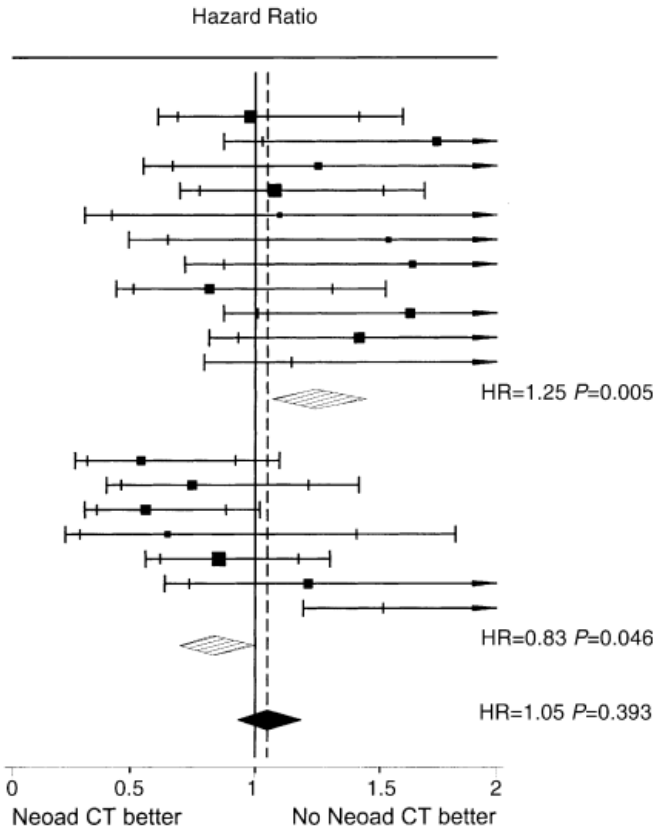
QMT NEOADYUVANTE

Neoadjuvant chemotherapy for locally advanced cervical cancer: a systematic review and meta-analysis of individual patient data from 21 randomised trials

Neoadjuvant Chemotherapy for Cervical Cancer Meta-analysis Collaboration*,[1]

Received 26 February 2003; accepted 10 March 2003

Trial	Neoad CT (no. events/no. entered)	No Neoad CT	O-E	Variance
>14 day cycles				
Chauvergne, 1993	57/92	54/90	−0.47	27.66
Souhami, 1991	29/48	31/55	7.64	13.64
Tattersall, 1992	20/34	18/37	2.17	9.41
Herod, 2001	68/89	62/88	2.60	32.39
Cardenas, 1991	7/13	9/18	0.37	3.84
Cardenas, 1993	12/14	8/16	2.16	4.91
Chiara, 1994	22/32	16/32	4.68	9.33
Sundfor, 1996	31/48	35/48	−3.41	16.40
CCSG AOCOA	38/129	28/131	8.08	16.31
Kumar, 1998	49/88	34/85	7.43	20.73
LGOG	9/15	2/12	3.61	2.73
Sub-total	342/602	297/612	34.85	157.36
≤14 day cycles				
Sardi, 1997	19/104	32/106	−7.97	12.69
Sardi, 1998	30/73	33/74	−4.61	15.56
Sardi, 1996	34/54	41/54	−10.61	17.89
PMB	9/16	15/19	−2.68	5.94
Symonds, 2000	68/105	76/110	−5.86	35.84
Leborgne, 1997	32/48	28/49	2.98	14.94
MRC CeCa	19/24	9/24	7.86	6.64
Sub-total	211/424	234/436	−20.89	109.48
Total	553/1026	531/1048	13.96	266.85



- > 1000 Pts in 18 published studies
- Small numbers / plethora regimens / most failed to show a benefit
- Suggestion of benefit with short cycle schedules….

Results from neoadjuvant chemotherapy followed by surgery compared to chemoradiation for stage Ib2-IIb cervical cancer EORTC GCG 55994

Estudio EORTC 5594

EORTC

Trial Design

Cervical carcinoma of squamous or adeno(squamous) cell type

FIGO stage Ib2, IIa >4cm, or IIb

R

Arm 1: NACT + Sy → Neoadjuvant cisplatin-based chemotherapy* (≥225 mg/m²) followed by radical hysterectomy — N=314

Arm 2: CTRTx → Concomitant radiation and chemotherapy 45-50 Gy plus boost + weekly ≥40mg/m² cisplatin — N=312

\+ N=626

Endpoints:

- Primary: overall survival (OS) at 5 years
- Secondary: PFS, toxicity & QoL

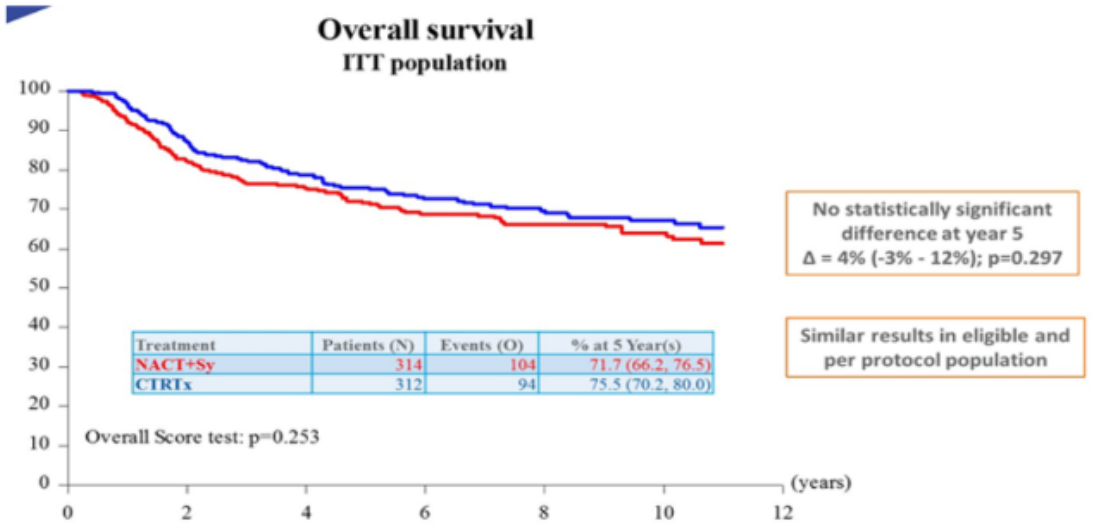
Stratification:

- Age (<50 vs >50), Cell type, FIGO stage (1994), and Institution

Seguimiento mediano 8 años

* Chemotherapy:

- Cisplatin mono: 46%
- Cisplatin + PT: 20%
- Cisplatin + PT + Ifos: 19%
- Cisplatin + Other: 15%



Treatment	Patients (N)	Events (O)	% at 5 Year(s)
NACT+Sy	314	104	71.7 (66.2, 76.5)
CTRTx	312	94	75.5 (70.2, 80.0)

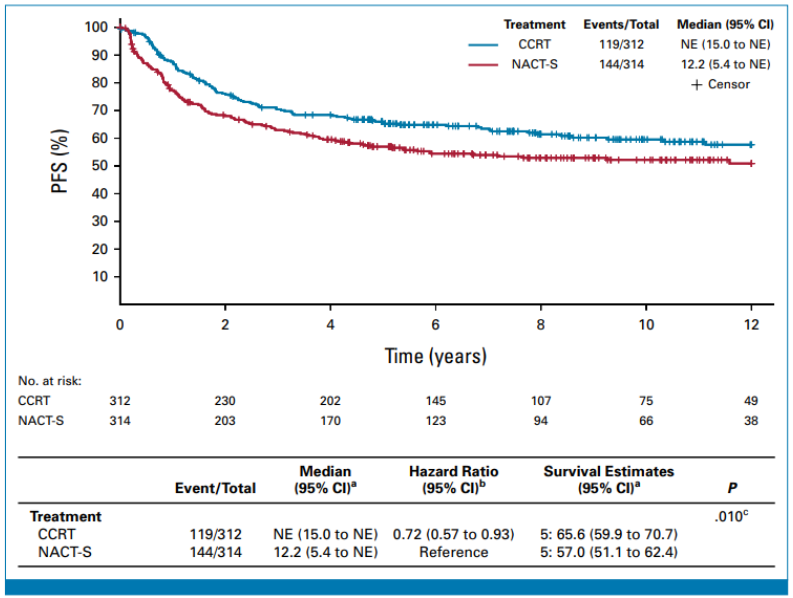
No statistically significant difference at year 5
Δ = 4% (-3% - 12%); p=0.297

Similar results in eligible and per protocol population

Kenter G et al, J Clin Oncol 2018

TABLE 1. Baseline Characteristics

Characteristic	NACT-S (n = 314)	CCRT (n = 312)
Age, years, median (range)	46 (23-73)	47 (23-75)
ECOG PS 0/1, No. (%)	277 (88)/36 (12)	273 (88)/39 (12)
FIGO stage, No. (%)		
IB2	83 (26)	86 (28)
IIA2	48 (15)	47 (15)
IIB	179 (57)	178 (57)
III	3 (1)	0 (0)
IV	0 (0)	1 (0.3)
Missing	1 (0.3)	0 (0)
Histologic type of carcinoma, No. (%)		
Squamous cell	266 (85)	264 (85)
Adenocarcinoma	31 (10)	35 (11)
Adenosquamous cell	16 (5)	11 (4)
BMI, No. (%)		
≤25/25-30/>30	119 (38)/86 (27)/73(23)	126 (40)/98 (31)/47 (15)



	Event/Total	Median (95% CI)[a]	Hazard Ratio (95% CI)[b]	Survival Estimates (95% CI)[a]	P
Treatment					.010[c]
CCRT	119/312	NE (15.0 to NE)	0.72 (0.57 to 0.93)	5: 65.6 (59.9 to 70.7)	
NACT-S	144/314	12.2 (5.4 to NE)	Reference	5: 57.0 (51.1 to 62.4)	

FIG 3. Primary analysis: PFS in the ITT population. [a]Kaplan-Meier method. [b]Cox model. [c]Log-rank test. CCRT, concomitant chemoradiotherapy; ITT, intention-to-treat; NACT-S, neoadjuvant chemotherapy followed by surgery; NE, not estimable; PFS, progression-free survival.

Estudio Hindú

Study Design

- Squamous carcinoma
- Stage IB2,IIA, or IIB
- ECOG 0-1
- No prior treatment
- Adequate hematological & renal function

Stratify by stage → 1:1 → N=633

- **Experimental** (N = 317): NACT X 3 cycles followed by surgery
- **Control** (N = 318): Concurrent chemoradiation.

- **Planned cross-over from NACT-Surgery to CTRT**
  - Unresectable disease after 2nd or 3rd cycle NACT
  - Intraoperative unresectability
  - Lymph node positive on frozen section intraoperative
- **Postoperative adjuvant RT**
  - T > 4 cm, LVI +, deep cervical stromal invasion, *(any two)*
- **Postoperative adjuvant CTRT**
  - LN +, parametrium +, surgical margin +, *(any one)*

- **Neoadjuvant chemotherapy**
  Paclitaxel (175 mg/m2) + Carboplatin: (AUC 5-6) every 3 weeks X 3 cycles
- **Concomitant chemotherapy**
  Cisplatin (40/m2/week) X 5 weeks
- **Radiation therapy**
  EBRT: 40 Gy/20 fr/5 weeks + HDR: 7Gy/5 application

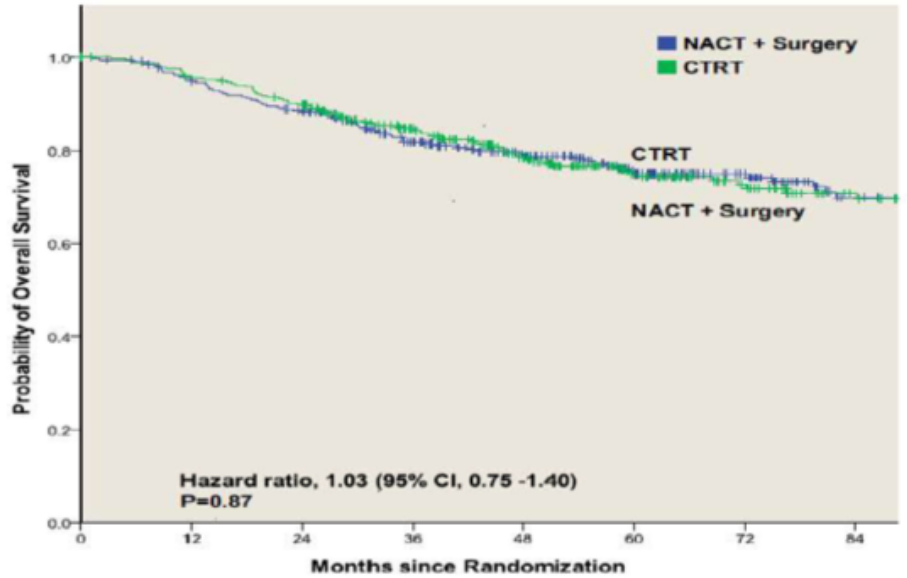


Table 1. Baseline Patients Characteristics

Characteristic	NACT Plus Surgery (n = 316)	CTRT (n = 317)
Median age, years (range)	50 (27-65)	48 (26-65)
Median hemoglobin, g/dL (range)	11.5 (7.6-15.6)	11.5 (7.4-15.5)
Median body mass index, kg/m^2 (range)	22.6 (12.8-44.2)	22.5 (14.5-38.4)
Comorbidities		
Yes	67 (21.2)	61 (19.2)
No	249 (78.8)	256 (80.8)
Eastern Cooperative Oncology Group performance status		
0	290 (91.8)	293 (92.4)
1	26 (8.2)	24 (7.6)
FIGO stage		
IB2	57 (18.0)	56 (17.7)
IIA	80 (25.3)	78 (24.6)
IIB	179 (56.7)	183 (57.7)
Radiologic pelvic lymph node status		
Positive	46 (14.6)	45 (14.2)
Negative	270 (85.4)	272 (85.8)

NOTE. Data presented as No. (%) unless otherwise indicated.
Abbreviations: CTRT, concomitant chemotherapy and radiotherapy; FIGO, International Federation of Gynecology and Obstetrics; NACT, neoadjuvant chemotherapy.

Gupta S et al , J Clin Oncol 2018

DOBLETES CDDP CONCOMITANTES CON RT

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RT-QT + BRAQUI

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RT-QT + BRAQUI

QT ADYUVANTE

DESIGN

Patients with cervical cancer suitable for chemoradiation with curative intent:

- **FIGO 2008 Stage IB1+LN, IB2, II, IIIB, IVA**
- **ECOG 0-2**
- **Squamous cell ca adenocarcinoma or adenosquamous ca**
- **No nodal disease above L3/4**

R

1 → **Concurrent Chemoradiation (CRT)**

1 → **Concurrent Chemoradiation (CRT)** → **Adjuvant Chemo (ACT) Carboplatin + Paclitaxel**

Primary End point

Overall Survival

Secondary End points

Progression-free Survival

Adverse Events

Sites of disease recurrence

Radiation protocol compliance

Patient-reported outcomes

Stratification Factors

- Pelvic or common iliac nodal involvement
- Requirement for extended-field radiotherapy
- FIGO 2008 stage: IB/IIA or IIB or IIIB/IVA
- Age <60 or ≥60 years
- Hospital/site

926 patients

	Chemoradiotherapy only group (n=456)	Adjuvant chemotherapy group (n=463)
Age, years	45 (38–54)	46 (37–55)
ECOG performance status		
0	344 (75%)	337 (73%)
1	94 (21%)	117 (25%)
2	18 (4%)	9 (2%)
Race*		
White	326 (71%)	337 (73%)
Black or African American	68 (15%)	53 (11%)
Asian	22 (5%)	31 (7%)
Aboriginal or Pacific Islander	11 (2%)	13 (3%)
Other	28 (6%)	29 (6%)
Geographical region		
Australia and New Zealand	84 (18%)	81 (17%)
USA and Canada	366 (80%)	373 (81%)
China, Saudi Arabia, and Singapore	6 (1%)	9 (2%)
Tobacco smoking		
Never smoker	237 (52%)	224 (48%)
Current or former smoker or unknown	219 (48%)	239 (52%)
Histological type		
Squamous cell carcinoma	358 (79%)	383 (83%)
Adenocarcinoma	79 (17%)	68 (15%)
Adenosquamous cell carcinoma	19 (4%)	12 (3%)
FIGO 2008 stage		
IB1 (all node positive), IB2, or IIA	152 (33%)	154 (33%)
IIB	196 (43%)	197 (43%)
IIIB or IVA	108 (24%)	112 (24%)
Maximum tumour diameter, cm	5·0 (4·0–6·0)	5·0 (4·0–6·0)
Nodal involvement		
Pelvic alone	144 (32%)	149 (32%)
Common iliac alone	33 (7%)	31 (7%)
Pelvic and common iliac	44 (10%)	44 (10%)
Neither	225 (49%)	231 (50%)
Unknown	10 (2%)	8 (2%)
Extended field radiotherapy planned		
No	397 (87%)	404 (87%)
Yes	59 (13%)	59 (13%)

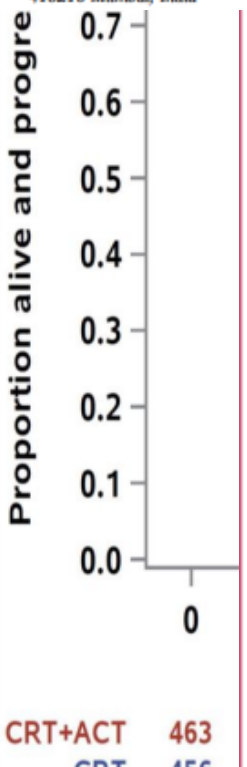
Data are median (IQR) or n (%). ECOG=Eastern Cooperative Oncology Group. FIGO=International Federation of Gynecology and Obstetrics. *Self-reported.

Table 1: **Baseline demographic and disease characteristics, intention-to-treat population**

A systematic review and meta-analysis of adjuvant chemotherapy after chemoradiation for locally advanced cervical cancer

Nanda Horeweg [a,*,1], Prachi Mittal [b], Patrycja L. Gradowska [c], Ingrid Boere [d], Remi A. Nout [e,2], Supriya Chopra [f,2]

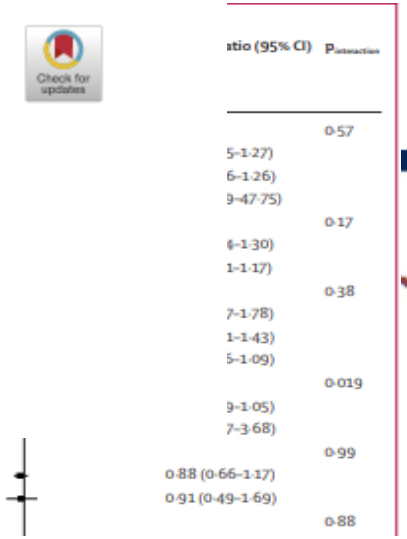
[a] Department of Radiation Oncology, Leiden University Medical Center, 2333ZA Leiden, The Netherlands
[b] Department of Radiation Oncology, Tata Memorial Hospital, Tata Memorial Centre, Parel, Homi Bhabha National Institute, 400012 Mumbai, India
[c] Department of Hematology – HOVON Data Center, Erasmus MC Cancer Institute, P.O. Box 2040, 3000CA Rotterdam, The Netherlands
[d] Department of Medical Oncology, Erasmus Medical Center Cancer Institute, P.O. Box 2040, 3000CA Rotterdam, The Netherlands
[e] Department of Radiotherapy, Erasmus MC Cancer Institute, University Medical Center, P.O. Box 2040, 3000CA Rotterdam, The Netherlands
[f] Department of Radiation Oncology, Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, Homi Bhabha National Institute, Parel, 410210 Mumbai, India

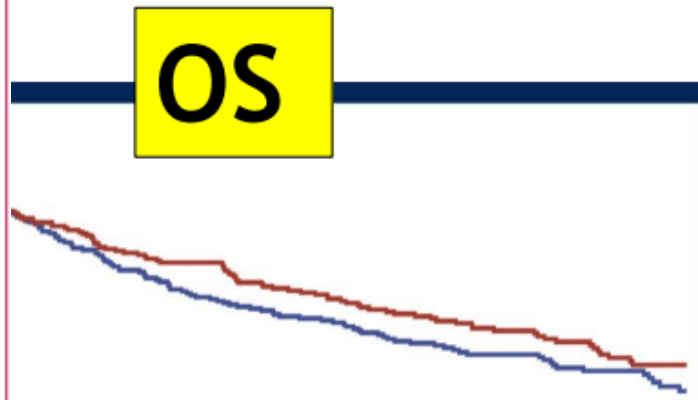


Country					
USA and Canada	102/366	88/373	70 (64–75)	71 (65–76)	0·88 (0·66–1·17)
Australia and New Zealand	21/84	19/81	75 (64–83)	77 (66–85)	0·91 (0·49–1·69)
Smoking					
Never smoked	60/237	49/2			
Current or former smoker, or unknown	63/219	60/2			
Tumour histology (post hoc)					
Squamous or adenosquamous cell carcinoma	102/377	91/3			
Adenocarcinoma	21/79	18/6			
Overall	**123/456**	**109/4**			

B

	Events/total				
	Chemoradiotherapy only group	Adjuv chem			
Pelvic or common iliac nodal involvement, or both					
Yes	93/221	84/2			
No	72/225	65/2			
Unknown	3/10	2/8			
Requirement for EFRT					
No	138/397	130/4			
Yes	30/59	21/5			
FIGO 2008 stage					
Stage IB1 and node positive, stage IB2, or stage IIA	46/152	40/1			
Stage IIB	68/196	60/1			
Stage IIIB or stage IVA	54/108	51/1			
Age (years)					
<60	148/390	121/3			
≥60	20/66	30/7			
Country					
USA and Canada	142/366	127/3			
Australia and New Zealand	26/84	22/81	68 (57–77)	74 (63–82)	0·79 (0·45–1·40)
Smoking					
Never smoked	82/237	71/224	64 (57–70)	64 (56–70)	0·90 (0·65–1·23)
Current or former smoker, or unknown	86/219	80/239	59 (51–65)	63 (56–69)	0·83 (0·61–1·13)
Tumour histology (post hoc)					
Squamous or adenosquamous cell carcinoma	135/377	122/395	63 (58–68)	65 (60–70)	0·86 (0·68–1·10)
Adenocarcinoma	33/79	29/68	53 (40–65)	54 (41–66)	0·90 (0·55–1·48)
Overall	**168/456**	**151/463**	**62 (57–66)**	**63 (58–68)**	**0·86 (0·69–1·08)**





J Gynecol Oncol. 2019 Jul;30(4):e82
https://doi.org/10.3802/jgo.2019.30.e82
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Original Article

Check for updates

A randomized controlled trial comparing concurrent chemoradiation versus concurrent chemoradiation followed by adjuvant chemotherapy in locally advanced cervical cancer patients: ACTLACC trial

343 306 244 164

DOBLETES CDDP CONCOMITANTES CON RT

QTNA → RTQT

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RT-QT + BRAQUI

QTRT → QT

QTRT → IT mantenimiento

CIRUGÍA → RT

RT-QT + BRAQUI

QMT INDUCCIÓN

TABLE 1. Patient Demographics and Baseline Clinical Characteristics of the Modified Intention-to-Treat Population

Characteristic	No. of Patients (%) NAC (n = 55)	CRT (n = 52)	P
Age, years			.224*
Median	48	45	
Range	22-69	20-67	
ECOG PS			.769†
0	25 (45.5)	25 (48.0)	
1	30 (54.5)	26 (50.0)	
2	0 (0)	1 (1.9)	
			.654†
	(87.2)	46 (88.4)	
	(12.7)	5 (9.6)	
	—	1 (1.9)	
			.745†
	(43.6)	22 (42.3)	
	(0)	1 (1.9)	
	(47.2)	22 (42.3)	
	(9.0)	7 (13.4)	
			.557†
	(41.8)	22 (42.3)	
	(58.2)	30 (57.6)	
			.471*
	1.4	11.9	
	-12.3	10.6-13.1	

rapy; ECOG PS, Eastern Cooperative
hemoglobin; IQR, interquartile range;

and Obstetrics 2009 staging

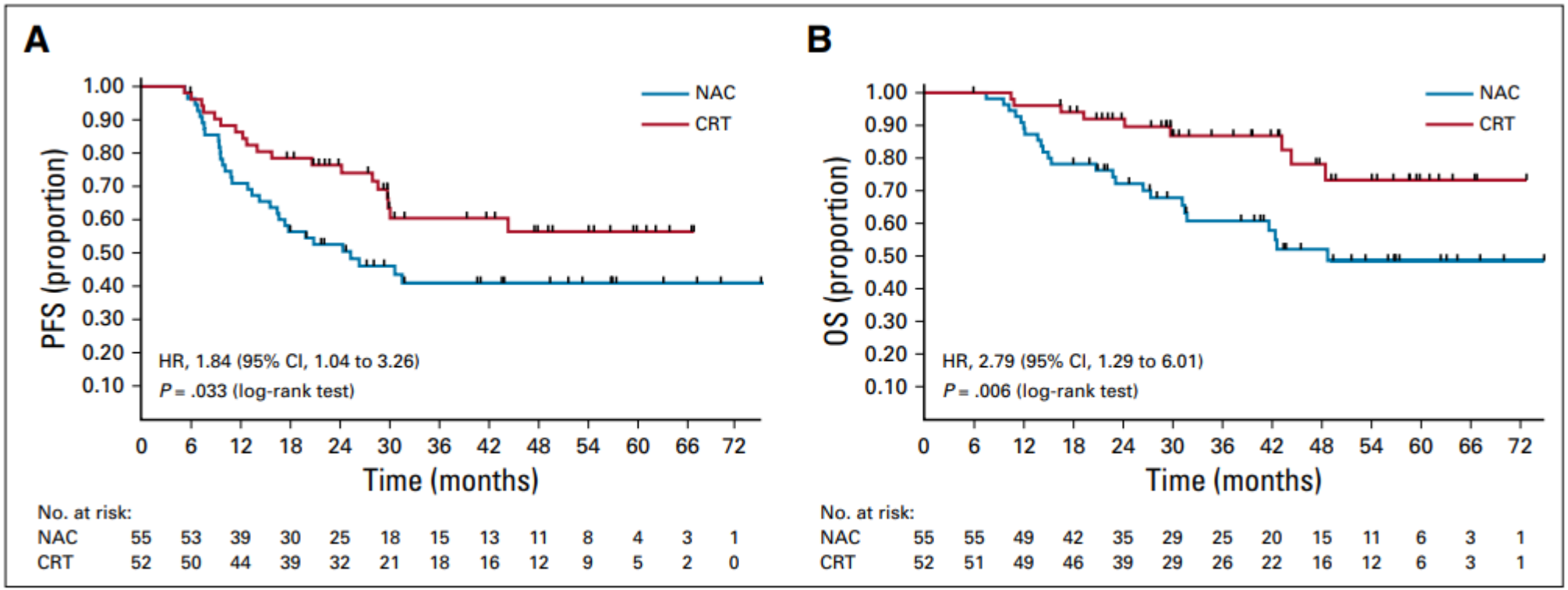


FIG 2. Kaplan-Meier curves for (A) progression-free survival (PFS) and (B) overall survival (OS). The results presented in the curves refer to the comparison between survival curves. CRT, chemoradiation therapy; HR, hazard ratio; NAC, neoadjuvant chemotherapy.

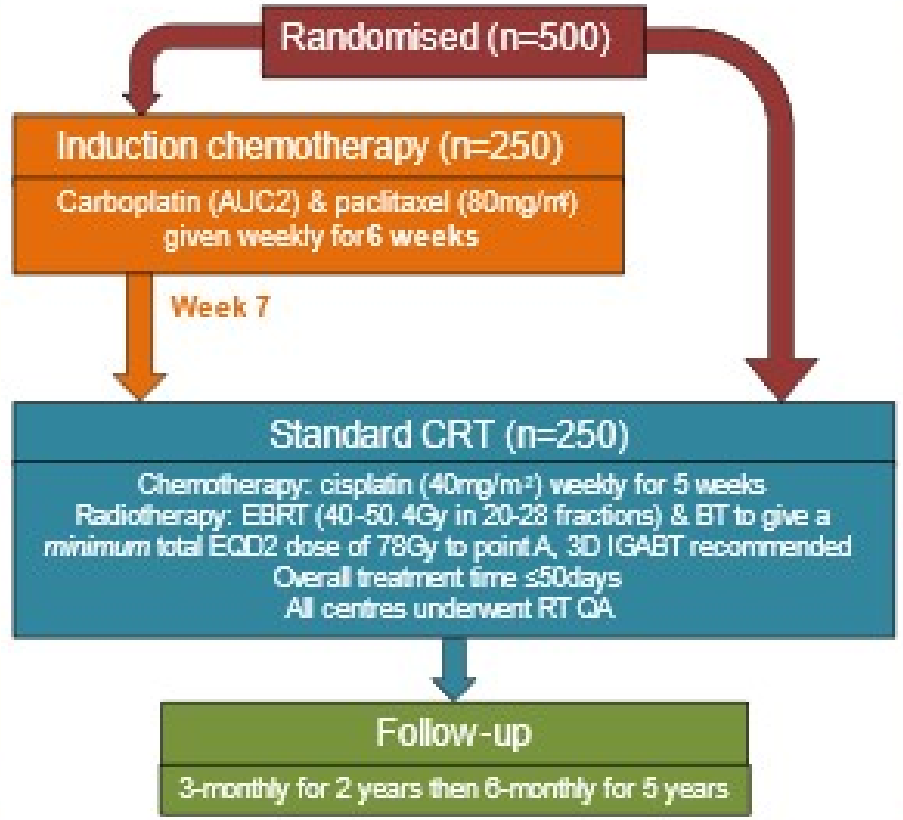
INTERLACE

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 2022 ESMO congress

Mary McCormack

INTERLACE: demographics and adherence to therapy

Disease Characteristic	CRT (n = 250)	Induction CT + CRT (n = 250)
FIGO stage, n (%)		
▪ 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, n (%)		
▪ Nonsquamous	45 (18)	44 (18)
▪ Squamous	205 (82)	206 (82)
Nodal status, n (%)		
▪ Negative	142 (57)	44 (18)
▪ Positive	108 (43)	206 (82)
Median longest tumor diameter, cm (range)	4.9 (1.8-12.8)	4.8 (1.3-13.5)

Adherence to Induction Chemotherapy	Paclitaxel and Carboplatin (n = 250)
Completed 6 weekly cycles, n (%)	211 (84)
Completed at least 5 cycles, n (%)	230 (92)
Main reasons for fewer than 6 cycles, n (%)	
▪ AEs leading to d/c	29 (11)
▪ Hematologic AEs	9 (31)
▪ Nonhematologic AEs	17 (59)
▪ Hematologic and nonhematologic AEs	3 (10)
Withdrawal/other, n (%)	10 (4)
Median interval from induction CT to radiotherapy, days (range)	7 (5-53)

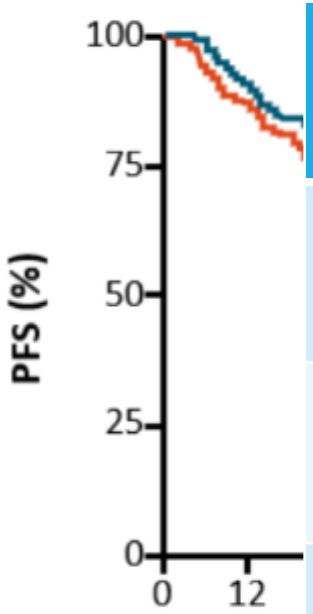
Adherence to Cisplatin, n (%)	CRT (n = 250)	Induction CT + CRT (n = 250)
Completed 5 weekly cycles	197 (79)	169 (68)
		212 (85)
FIGO stage (2018)		
I and II	128 (51%)	126 (50%)
IIIB and IVA	22 (9%)	16 (6%)
IIIC	100 (40%)	108 (43%)
		68 (27)
		34 (50)
		20 (29)
▪ Hematologic and nonhematologic AEs	4 (12)	14 (21)
▪ Other	20 (8)	13 (5)

Adherence to Radiation	CRT (n = 250)	Induction CT + CRT (n = 250)
Received EBRT, n (%)	321 (92)	242 (97)
▪ IMRT	93 (40)	102 (42)
▪ 3D conformal	138 (60)	140 (58)
Received brachytherapy, n (%)	223 (97)	238 (98)
▪ 2D point A	49 (22)	46 (19)
▪ 3D point A	106 (48)	120 (51)
▪ 3D HR-CTV D90	68 (30)	72 (30)
Overall median treatment time, days (range)	45 (37-88)	45 (36-70)

Accrual 2012-2022, diverse RT technics

INTERLACE: PFS & OS (Coprimary Endpoints)

Median follow-up: 64 mo



	QMT NA + QRT	QRT
Recaídas pélvicas / locales	11%	9%
Recaídas a distancia	7%	12%
Tox. G3/4	59%	48%

	CRT (n = 250)	Induction CT + CRT (n = 250)
PFS events	146	
HR (95% CI); *P* value	0.65 (0.46-0.91); 0.013	
3-yr PFS rate, %	72	75
5-yr PFS rate, %	64	73

	CRT (n = 250)	Induction CT + CRT (n = 250)
OS events	109	
HR (95% CI); P value	0.61 (0.40-0.91); 0.04	
3-yr OS rate, %	80	88
5-yr OS rate, %	72	80

Falta de inclusión de pacientes de alto resigo
Solo 40% tratadas con IMRT

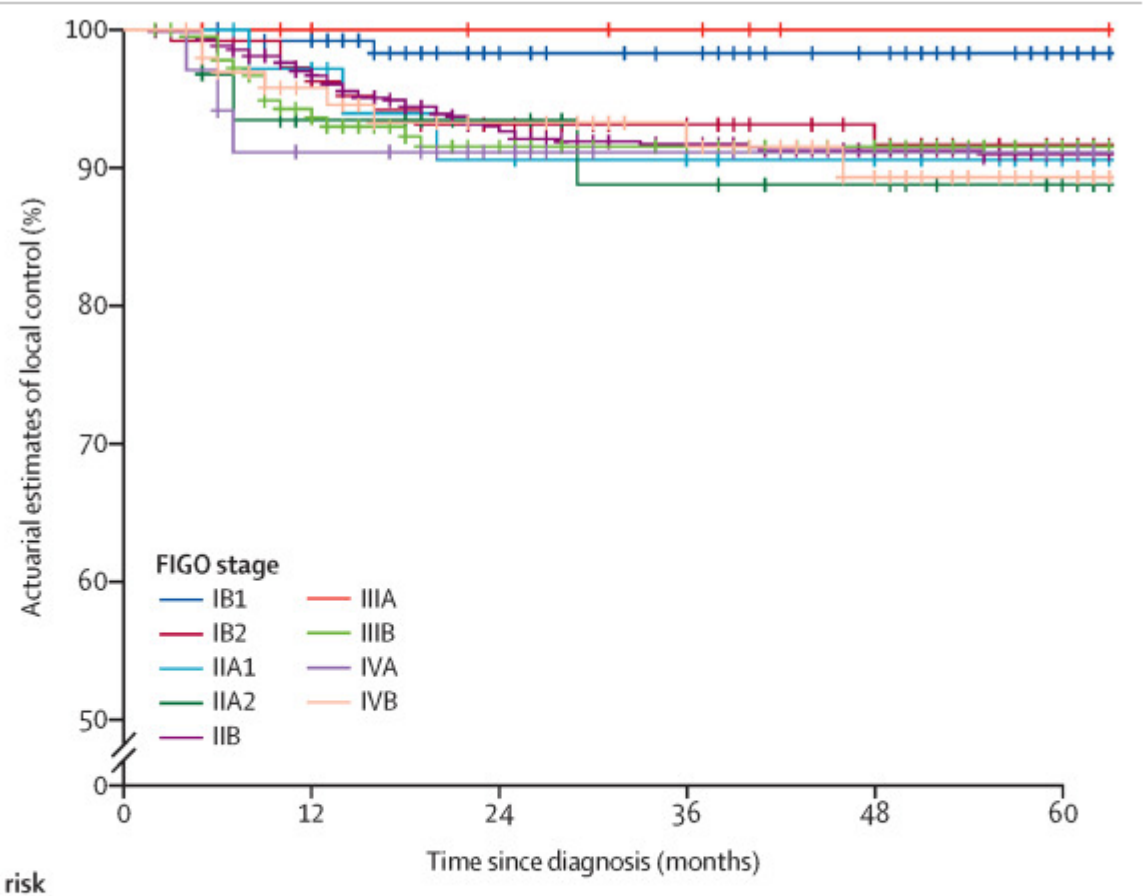
OS 5y: 80% vs 72%.

OS EMBRACE ESTADIOS I – III
83 – 73 % (N0-N1)

SLE 5y: 72% vs 64%.

SLE EMBRACE ESTADIOS I – III
73 – 65 % (N0-N1)

TRA
- R
- R
- IC
- G
- IC
- Ti
- M
- D
- A



Number at risk (number censored)						
IB1	124 (0)	117 (6)	101 (21)	92 (30)	79 (43)	56 (66)
IB2	119 (0)	98 (18)	83 (29)	73 (39)	63 (49)	52 (59)
IIA1	38 (0)	32 (5)	27 (8)	26 (9)	24 (11)	19 (16)
IIA2	31 (0)	26 (3)	22 (7)	19 (9)	15 (13)	11 (17)
IIB	693 (0)	612 (61)	519 (130)	459 (183)	378 (262)	285 (354)
IIIA	13 (0)	10 (3)	8 (5)	7 (6)	4 (9)	4 (9)
IIIB	190 (0)	146 (34)	120 (56)	106 (70)	96 (80)	80 (96)
IVA	34 (0)	28 (3)	22 (9)	17 (14)	15 (16)	12 (19)
IVB	98 (0)	78 (16)	62 (30)	54 (38)	39 (51)	28 (62)

l adaptive brachytherapy in locally advanced cer (EMBRACE-I): a multicentre prospective ly

*up, Maximilian Paul Schmid, Ina Jürgenliemk-Schulz, Christine Haie-Meder, Lars Ulrik Fokdal, Alina Emiliana Sturdza, ntshetty, Barbara Segedin, Kjersti Bruheim, Fleur Huang, Bhavana Rai, Rachel Cooper, Elzbieta van der Steen-Banasik, Rumwell Pieters, Li-Tee Tan, Remi Abubakar Nout, Astrid Agatha Catharina De Leeuw, Robin Ristl, Primoz Petric, chheiner, Christian Kirisits, Jacob Christian Lindegaard, EMBRACE Collaborative Group**

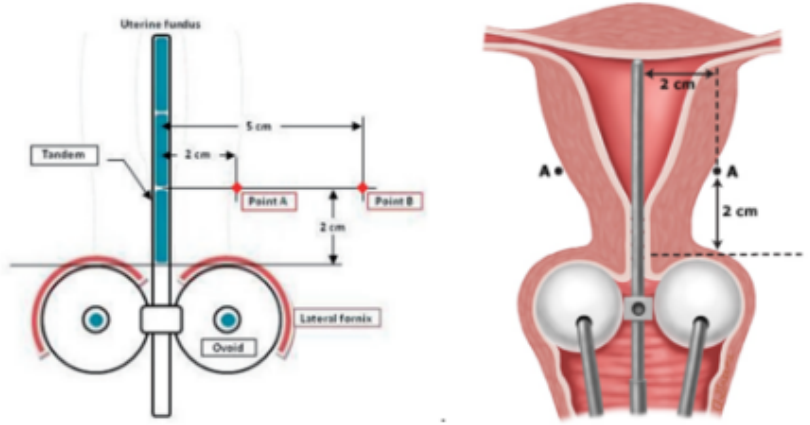


Figura 6: *Localización del punto A para un aplicador tándem y ovoide [33, 32]*

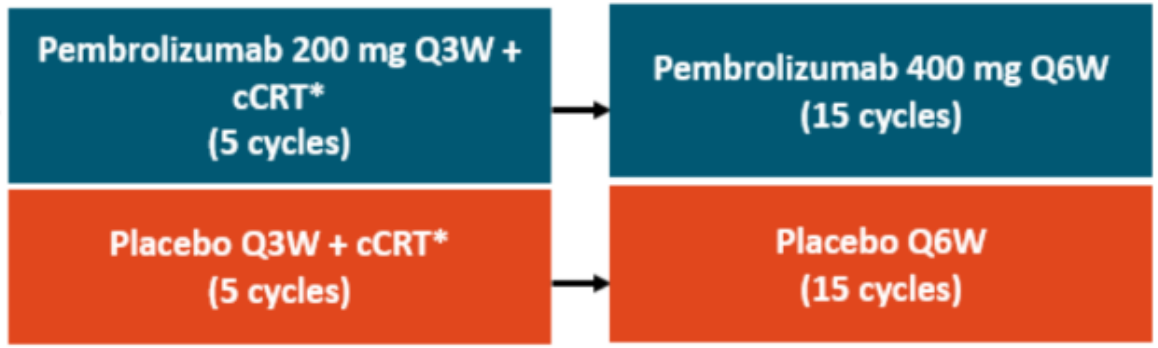
KEYNOTE A-18

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

Stratified by planned EBRT (IMRT or VMAT vs non-IMRT or non-VMAT); stage (IB2-IIB vs III-IVA); and planned total radiotherapy dose (<70 Gy vs ≥70 Gy [EQ2D])

Median follow-up IA1 17.9 m e IA2 29.9 m

Patients with newly diagnosed, previously untreated, high-risk locally advanced cervical cancer FIGO 2014 stage IB2-IIB node positive; or stage III-IVA; ECOG PS ≤1 (N = 1060)



Protocol Amendments
- Jan 6, 2021: change of PFS by BICR to per investigator
- **Nov 8, 2022: change of multiplicity strategy in SAP;** prespecified α to be passed to another hypothesis (PFS, 1-sided α = 0.025 to OS, 1-sided α = 0).

*cCRT regimen included 5 cycles (with optional sixth dose) of cisplatin 40 mg/m² QW with EBRT, then followed by brachytherapy

Statistical Considerations (IA1)
- Interim analysis after ~237 PD or deaths
- Cutoff date: January 9, 2023
- Interim analysis database lock: Feb 17, 2023
- Efficacy assessment in all randomized participants and safety in all participants who received 1 dose of study drug

- **Primary endpoints:** PFS per RECIST v1.1 by investigator (histopathologic confirmation) and OS
- **Key secondary endpoints:** 24-mo PFS, ORR, PRO, and safety

Lorusso, ESMO 2023, 2024 & The Lancet 2024

Baseline Characteristics

134	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Stage at screening (FIGO 2014 criteria)		
IB2-IIB	233 (44.0%)	226 (42.6%)
III-IVA	296 (56.0%)	305 (57.4%)
Lymph node involvement[b]		
Positive pelvic only	327 (62.2%)	324 (61.0%)
Positive para-aortic only	14	
Positive pelvic and para-aortic	104	
No positive pelvic or para-aortic	84	
Planned type of EBRT		
IMRT or VMAT	469	
Non-IMRT and non-VMAT	60	
Planned total radiotherapy dose (EQD2)		
<70 Gy	47	
≥70 Gy	482	
PD-L1 CPS		
<1	22	
≥1	502	
Missing	5	

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)

Domenica Lorusso, Yang Xiang, Kosei Hasegawa, Giovanni Scambia, Manuel Leiva, Pier Ramos-Elias, Alejandro Acevedo, Jakub Cvek, Leslie Randall, Andrea Juliana Pereira de Santana Gomes, Fernando Contreras Mejía, Limor Helpman, Hüseyin Akılı, Jung-Yun Lee, Valeriya Saevets, Flora Zagouri, Lucy Gilbert, Jalid Sehouli, Ekkasit Tharavichitkul, Kristina Lindemann, Nicoletta Colombo, Chih-Long Chang, Marketa Bednarikova, Hong Zhu, Ana Oaknin, Melissa Christiaens, Edgar Petru, Tomoka Usami, Peng Liu, Karin Yamada, Sarper Toker, Stephen M Keefe, Sandro Pignata*, Linda R Duska*, on behalf of the ENGOT-cx11/GOG-3047/KEYNOTE-A18 investigators†

PROTOCOL AMENDMENT NO.: A18-00 / ENGOT-cx11

10.7.2.5 Japan

Study Intervention(s)

normal tissue damage. The
CTV should be higher than

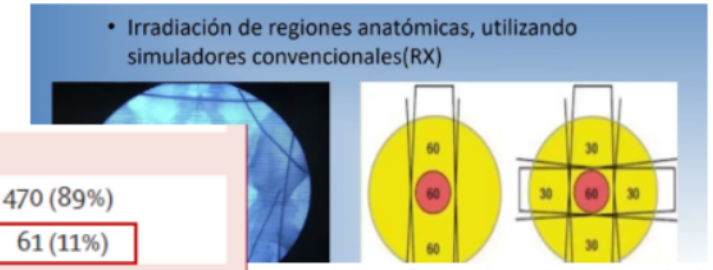
Planned type of external beam radiotherapy		
IMRT or VMAT	469 (89%)	470 (89%)
Non-IMRT and non-VMAT	60 (11%)	61 (11%)
Planned total radiotherapy dose		
<70 Gy	47 (9%)	46 (9%)
≥70 Gy	482 (91%)	485 (91%)

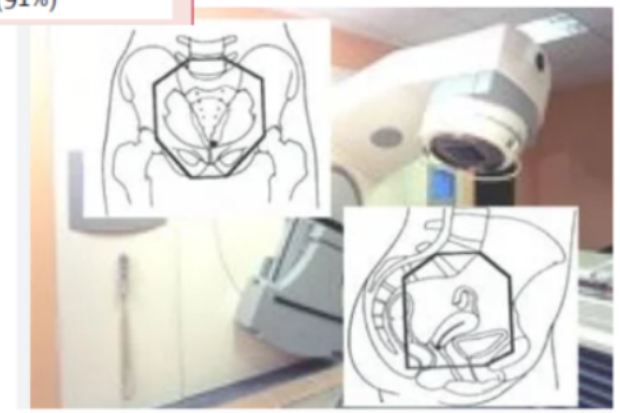
I B1, II A1 (small tumor size)	20 Gy	30 Gy	24 Gy/4 fractions
I B2, II (large tumor size), III	30 Gy	20 Gy	24 Gy/4 fractions
	40 Gy	10 Gy	18 Gy/3 fractions
IVA	40 Gy	10 Gy	18 Gy/3 fractions
	50 Gy	0 Gy	12 Gy/3 fractions

EBRT = external beam radiotherapy; EQD2 = total equieffective dose; FIGO = Federation of Gynecologists and Obstetricians; HDR = high dose rate.
a 1.8-2.0 Gy per fraction, 5 days during a week. Boost EBRT of 6-10 Gy will be indicated for participants with nodular parametrium involvement to the pelvic walls and/or nodal metastases.
b 5-6 Gy per fraction, 1-2 days during a week.

Note: Weekly cisplatin (40 mg/m²) is to be administered for 5 administrations during the radiotherapy period. An optional, 6th infusion of cisplatin may be administered according to local practice.
Total Radiation Dose:
1. Cervical lesion: EBRT (**1**) + intracavitary brachytherapy (**3**) → 62-66 Gy (EQD2)
2. Pelvic lymph node, parametrium: EBRT (**1 + 2**) only → 50 Gy

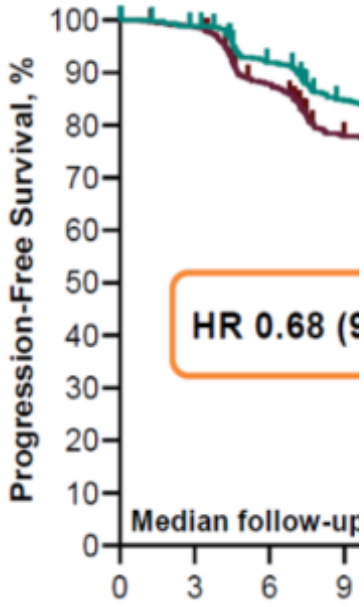
he D90 for the high-risk
ed interruptions may be





KN-A18:

Updated Prog



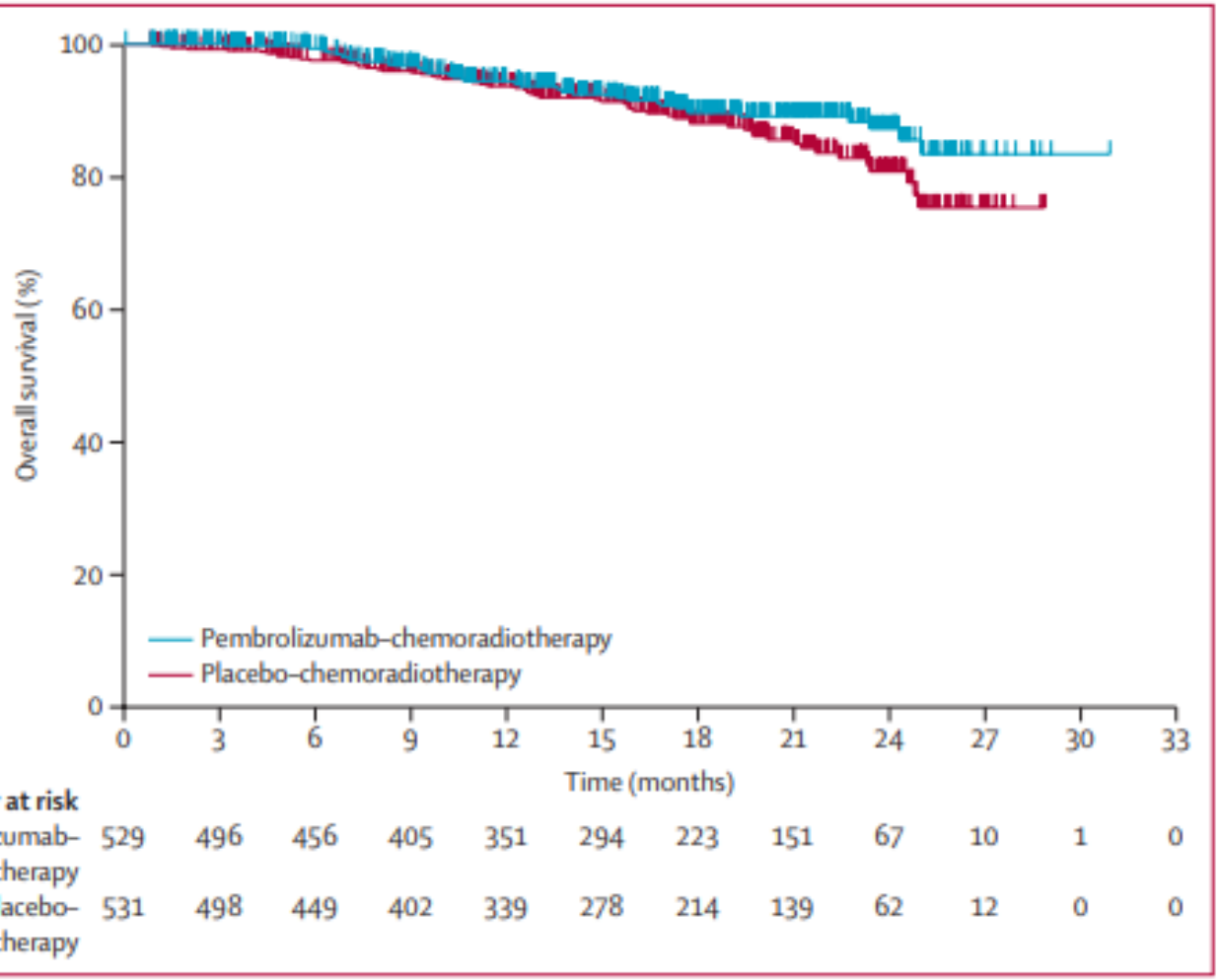
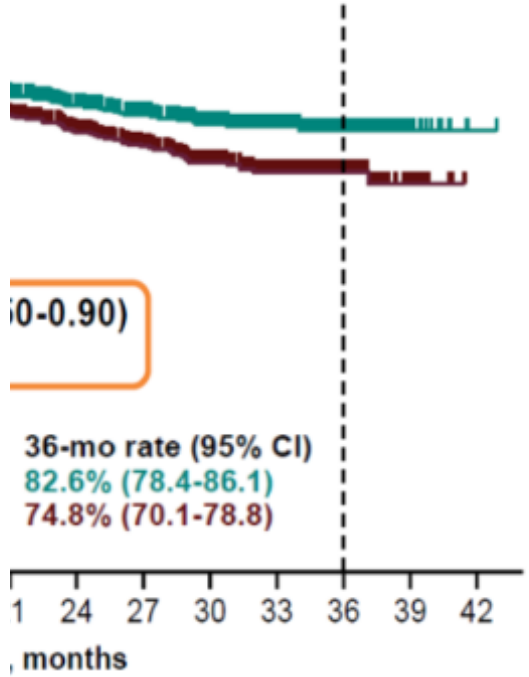


Figure 3: **Overall survival**
Kaplan–Meier estimates of overall survival in the intention-to-treat population. Tick marks indicate censoring of data.

val at IA2



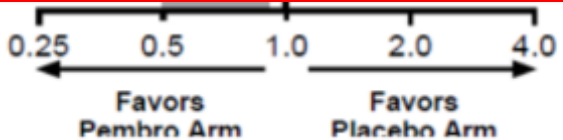
Pembr			
Placebo Arm	39.5%	NR (32.0-NR)	(NR-NR)

76.7% information fraction[3]

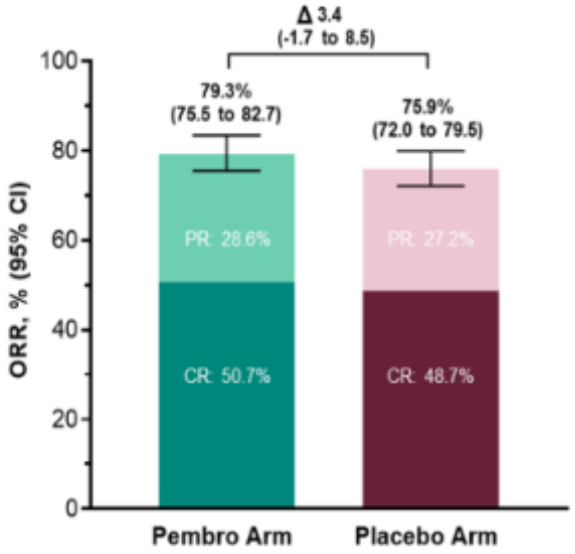
At this time, 66 patients had received immunotherapy as post-progression treatment, including 10.9% in the pembro arm and 26.4% in the placebo arm

Overall Survival in Protocol-Specified Subgroups

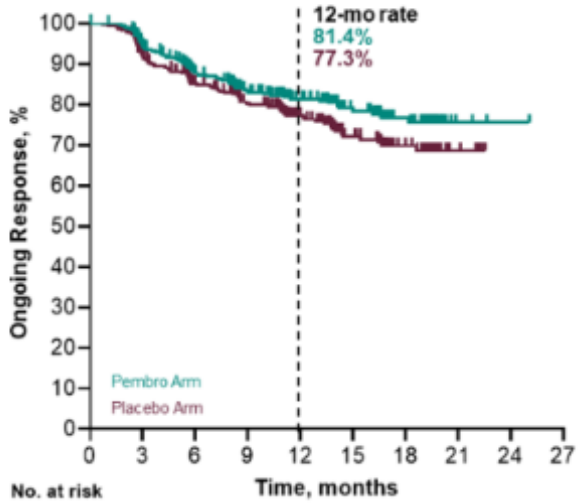
IA2	No. of Events/ No. of Patients	HR (95% CI)
Overall	184/1060	0.67 (0.50-0.90)
Age		
<65 years	162/927	0.61 (0.44-0.83)
≥65 years	22/133	1.35 (0.58-3.11)
Race		
White	96/518	0.92 (0.61-1.37)
All others	88/539	0.48 (0.31-0.74)
ECOG PS score		
0	134/778	0.67 (0.47-0.94)
1	50/282	0.68 (0.39-1.20)
Planned EBRT		
IMRT/VMAT	164/939	0.67 (0.49-0.92)
non-IMRT/-VMAT	20/121	0.69 (0.28-1.69)
FIGO 2014 stage		
IB2 to IIB	68/459	0.89 (0.55-1.44)
III to IVA	116/601	0.57 (0.39-0.83)
Planned total RT dose		
<70 Gy	16/93	0.64 (0.23-1.75)
≥70 Gy	168/967	0.68 (0.50-0.92)

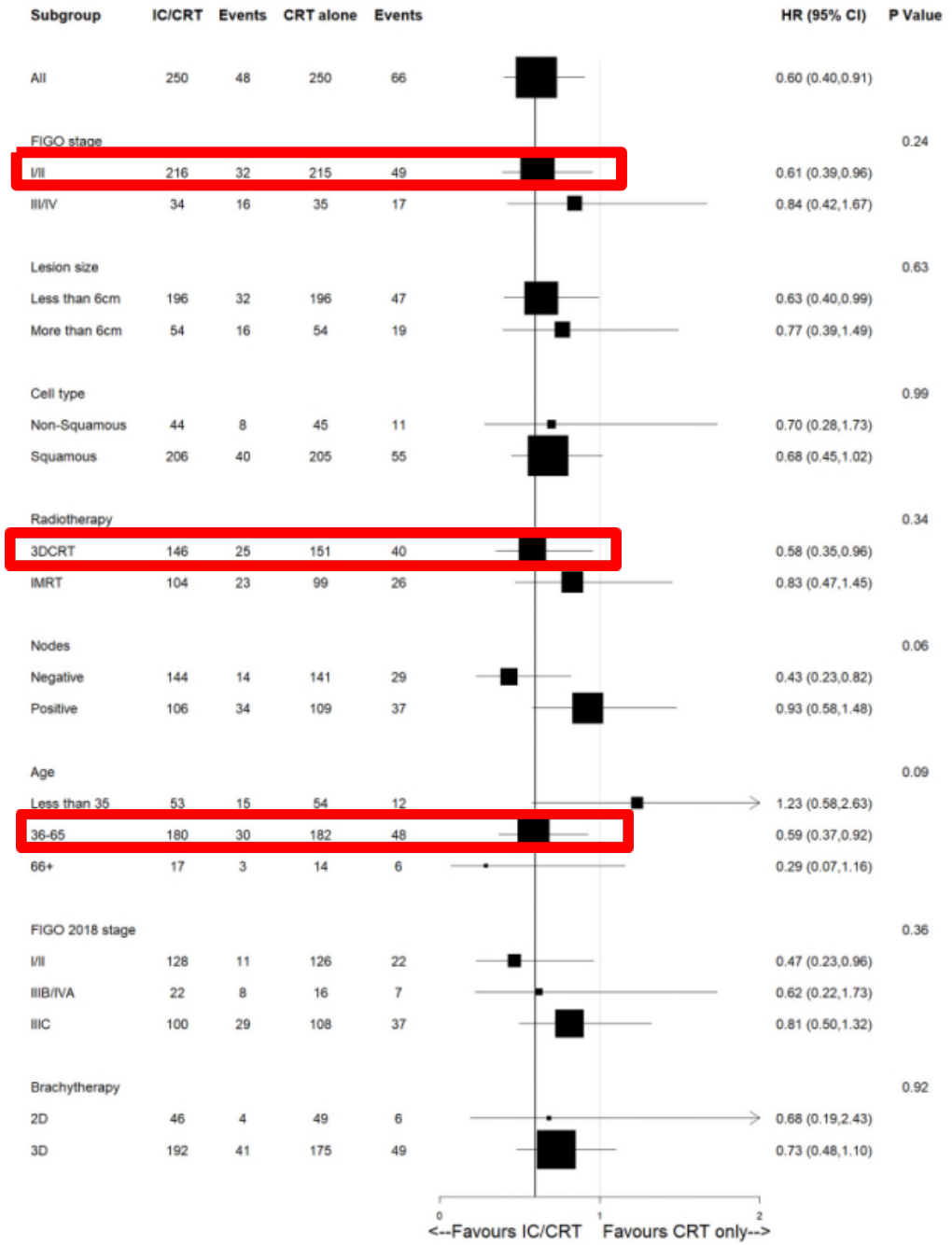


Secondary End Points: Best Objective Response

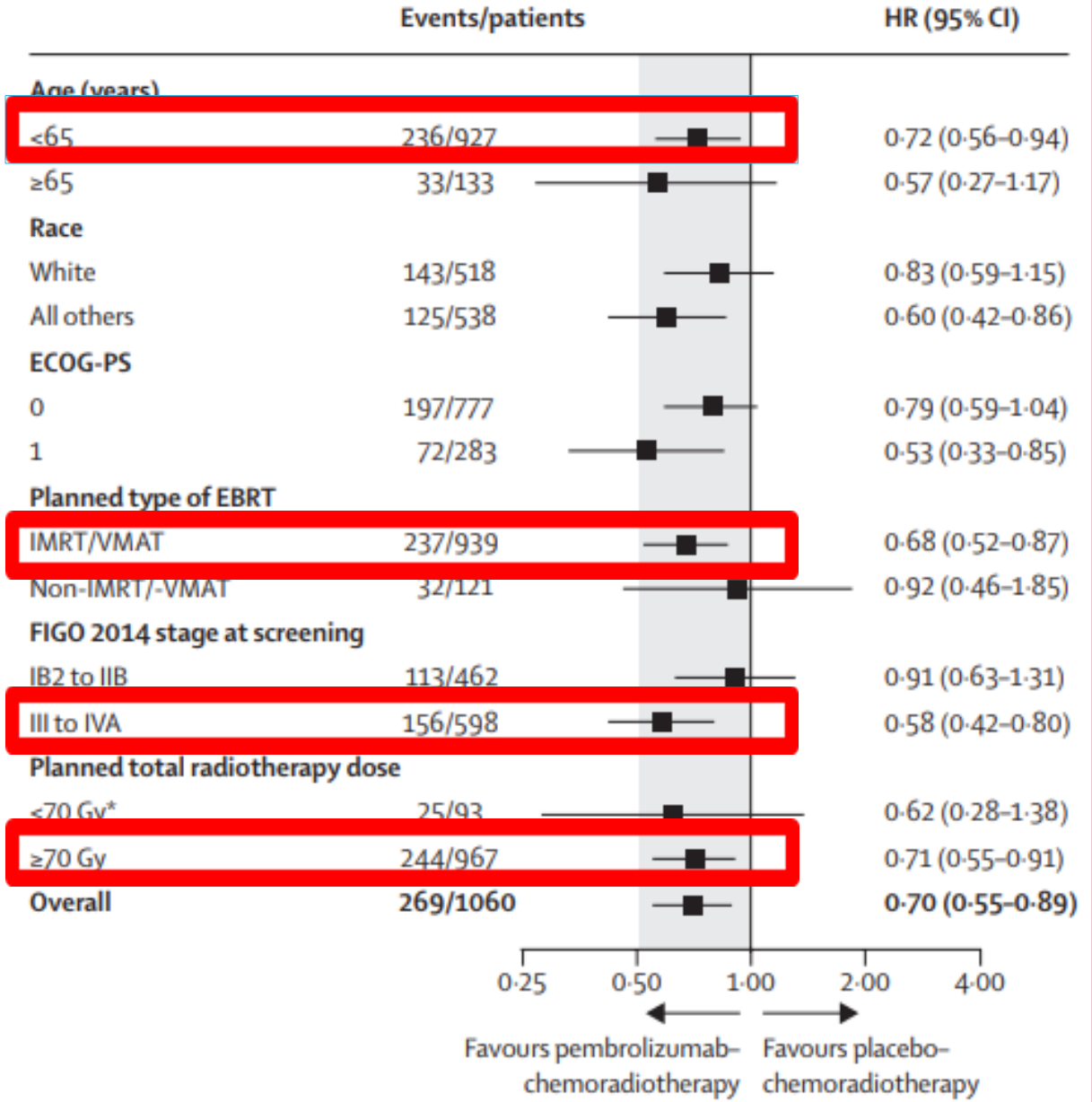


Duration of Response

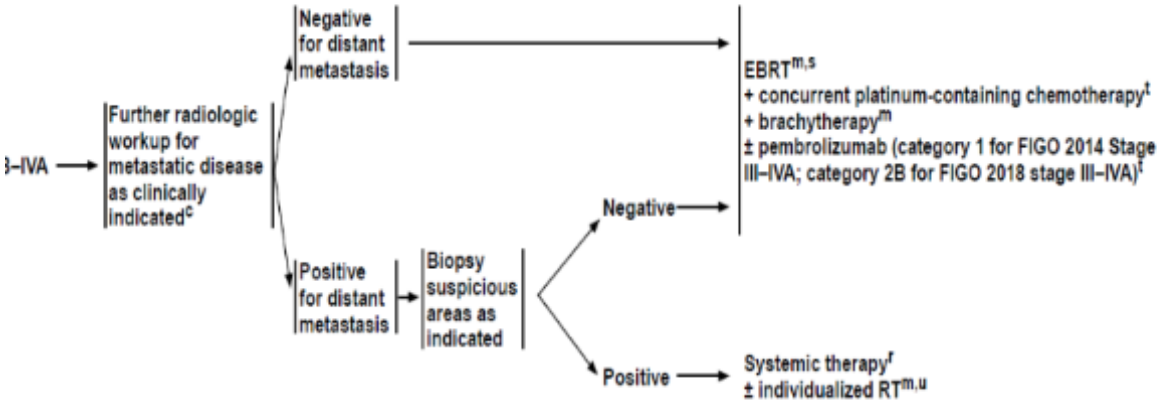



Subgroup
IC/CRT
Events
CRT alone
Events
HR (95% CI)
P Value
All 250 48 250 66 0.60 (0.40,0.91)
FIGO stage 0.24
I/II 216 32 215 49 0.61 (0.39,0.96)
III/IV 34 16 35 17 0.84 (0.42,1.67)
Lesion size 0.63
Less than 6cm 196 32 196 47 0.63 (0.40,0.99)
More than 6cm 54 16 54 19 0.77 (0.39,1.49)
Cell type 0.99
Non-Squamous 44 8 45 11 0.70 (0.28,1.73)
Squamous 206 40 205 55 0.68 (0.45,1.02)
Radiotherapy 0.34
3DCRT 146 25 151 40 0.58 (0.35,0.96)
IMRT 104 23 99 26 0.83 (0.47,1.45)
Nodes 0.06
Negative 144 14 141 29 0.43 (0.23,0.82)
Positive 106 34 109 37 0.93 (0.58,1.48)
Age 0.09
Less than 35 53 15 54 12 1.23 (0.58,2.63)
36-65 180 30 182 48 0.59 (0.37,0.92)
66+ 17 3 14 6 0.29 (0.07,1.16)
FIGO 2018 stage 0.36
I/II 128 11 126 22 0.47 (0.23,0.96)
IIIB/IVA 22 8 16 7 0.62 (0.22,1.73)
IIIC 100 29 108 37 0.81 (0.50,1.32)
Brachytherapy 0.92
2D 46 4 49 6 0.68 (0.19,2.43)
3D 192 41 175 49 0.73 (0.48,1.10)
0
1
2
<--Favours IC/CRT
Favours CRT only-->

B


Events/patients
HR (95% CI)
Age (years)
<65 236/927 0·72 (0·56–0·94)
≥65 33/133 0·57 (0·27–1·17)
Race
White 143/518 0·83 (0·59–1·15)
All others 125/538 0·60 (0·42–0·86)
ECOG-PS
0 197/777 0·79 (0·59–1·04)
1 72/283 0·53 (0·33–0·85)
Planned type of EBRT
IMRT/VMAT 237/939 0·68 (0·52–0·87)
Non-IMRT/-VMAT 32/121 0·92 (0·46–1·85)
FIGO 2014 stage at screening
IB2 to IIB 113/462 0·91 (0·63–1·31)
III to IVA 156/598 0·58 (0·42–0·80)
Planned total radiotherapy dose
<70 Gy* 25/93 0·62 (0·28–1·38)
≥70 Gy 244/967 0·71 (0·55–0·91)
Overall 269/1060 0·70 (0·55–0·89)
0·25
0·50
1·00
2·00
4·00
Favours pembrolizumab–chemoradiotherapy
Favours placebo–chemoradiotherapy

NCCN Guidelines Version 1.2025 Cervical Cancer



Chemoradiation[c]

Preferred Regimens
- Cisplatin + pembrolizumab[d,e,f,1]
  - category 1: FIGO 2014 Stage III–IVA
  - category 2B: FIGO 2018 stage III–IVA
- Carboplatin + pembrolizumab[d,e,f,1] if cisplatin intolerant
  - category 1: FIGO 2014 Stage III–IVA
  - category 2B: FIGO 2018 stage III–IVA
- Cisplatin
- Carboplatin if cisplatin intolerant

Other Recommended Regimens (if single agent cisplatin and carboplatin are unavailable)
- Capecitabine/mitomycin[2]
- Gemcitabine[3]
- Paclitaxel[4,5]

Concurrent platinum-containing chemotherapy with EBRT utilizes cisplatin as a single agent (or carboplatin if cisplatin intolerant).

Pembrolizumab may be added with CRT as follows:
- Cisplatin (or carboplatin)/RT and pembrolizumab (FIGO 2014 stage III–IVA: category 1)
- Cisplatin (or carboplatin)/RT and pembrolizumab (FIGO 2018 stage III–IVA: category 2B).

Checkpoint inhibitors and/or monoclonal antibodies included in this regimen may be continued as maintenance therapy. Refer to the original study protocol for
maintenance therapy dosing schedules.

SEOM-GEICO Clinical Guidelines on cervical cancer (2023)

Luis Manso[1] · Avinash Ramchandani-Vaswani[2] · Ignacio Romero[3] · Luisa Sánchez-Lorenzo[4] · María José Bermejo-Pérez[5] · Purificación Estévez-García[6] · Lorena Fariña-Madrid[7] · Yolanda García García[8] · Marta Gil-Martín[9] · María Quindós[10]

Clinical and Translational Oncology
https://doi.org/10.1007/s12094-024-03604-3

Recommendations

- Primary weekly cisplatin-based (40 mg/m^2) CRT remains the standard of care for LACC until immunotherapy is approved **[I, A]**.
- Induction chemotherapy with the INTERLACE regimen before definitive CRT might be an option for selected patients **[I, B]**.
- Adjuvant ChT after CRT is not recommended **[I, D]**.
- Neoadjuvant ChT before radical surgery is not a standard approach in LACC **[I, D]**.
- The addition of pembrolizumab to CRT will likely become the standard treatment for LACC **[I, A]**.

INMUNOTERAPIA

Ensayo	Población	Fármaco en investigación Duración	Diseño	Objetivos primarios
CALLA (1)	FIGO 2009: IB2 to IIB N+, IIIA-IVA	**Durvalumab (anti-PDL1)** Durante QT-RT + 24 meses	Fase 3 QT-RT control (n=714)	**PFS** **HR 0.84** [95% CI, 0.65–1.08]; P=0.174)
ENGOT cx11 /GOG3047/ KEYNOTE-A18 (2) APROBACIÓN EMA Estadios III-IVa	FIGO 2014 • IB2-IIB N+ • IIA-IVA	**Pembrolizumab (anti-PD1)** Durante QT-RT + 24 meses	Fase 3 QT-RT control (n=980)	**PFS/OS** **- PFS: HR 0.68** (95% CI, 0.56-0.84; p=0.002) **- OS: HR 0.67** (95% CI, 0.50-0.90; p=0.004)
ATEZOLACC (3)		**Atezolizumab** Durante QT-RT + 14 meses	Fase 2 randomizado QT-RT control (n=189)	PFS
GEICO78-C /ATOMICC (4)		**Dostarlimab** Tras QT-RT 24 meses	Fase 2 randomizado QT-RT control (n=132)	PFS
COLIBRI (5)	FIGO 2018: IB3-IVA (50% III-IV)	**Nivolumab+Ipilimumab neoady** QT-RT Nivo adyuvante 6 meses	Fase 2 (n=40)	Cambios en el ratio CD8+/FOXP3+ en biopsias antes y después de inmunoterapia TR 82%

(1) Monk B. et al; Int J Gynecol Cancer 2022;32(Suppl 3); (2) Lorusso D. et al. ESMO 2023, Abstract - LBA38; (3) NCT03612791 PI C. Chargani ; (4) NCT03833479 PI A. Oaknin; (5) NCT03298893 PI M.Rodrigues

S. Varela, SOG-GIN 2024

Muchas gracias por la atención