

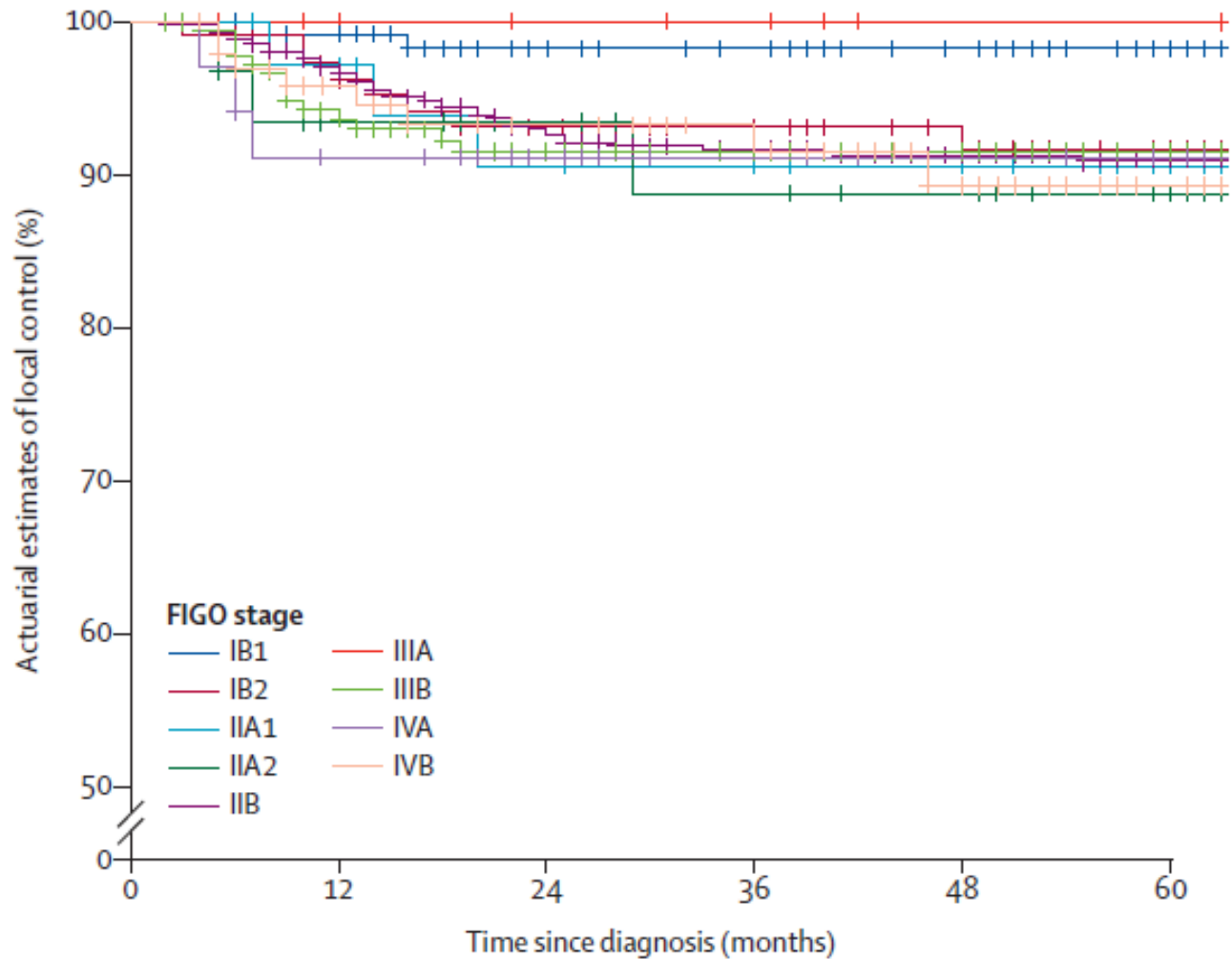
DISCUSSION for INTERLACE TRIAL

Hyun-Cheol Kang, MD, PhD

**Department of Radiation Oncology,
Seoul National University Hospital**



Results of EMBRACE-I



EXCELLENT LOCAL CONTROL BUT..

5-yr overall survival

IIB 78%

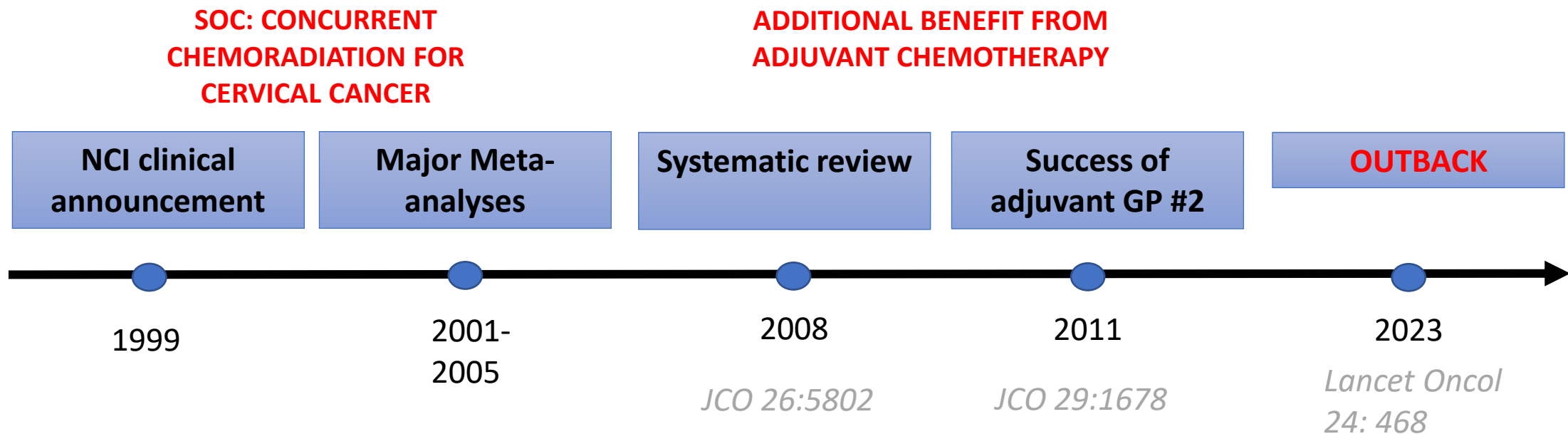
IIIA 76%

IIIB 64%

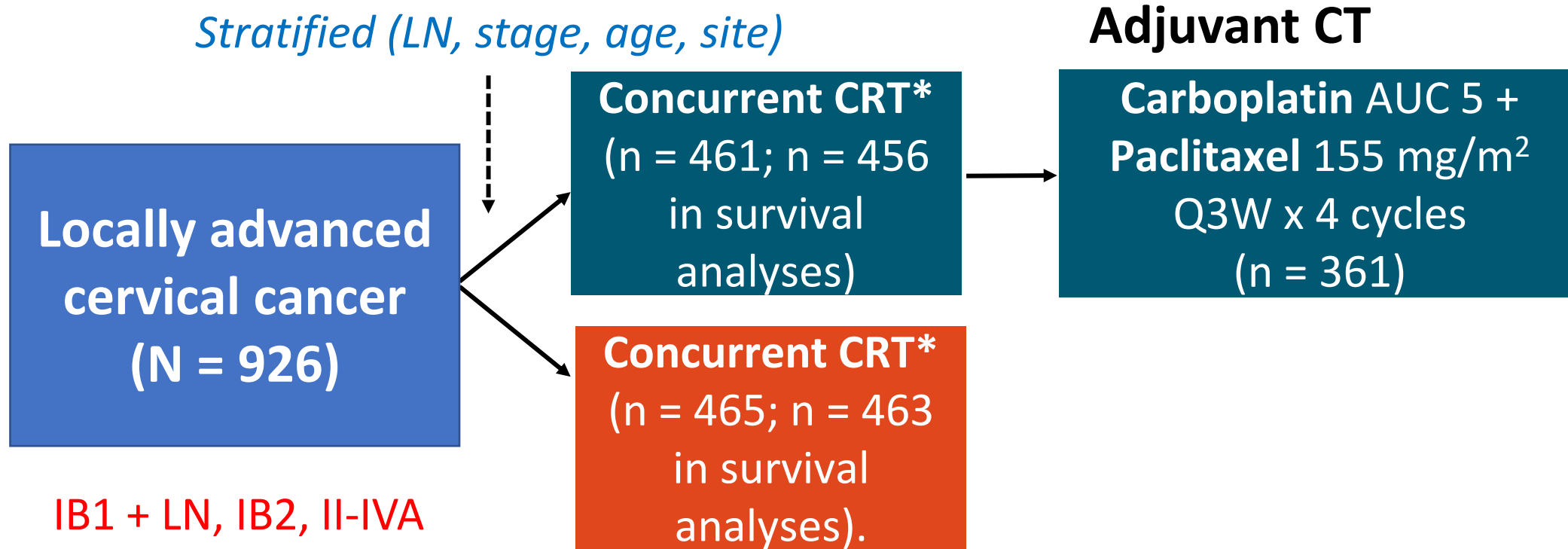
IVA 52%

Intensified treatment for locally advanced cervical cancer

- CRT + Adjuvant Chemotherapy?



OUTBACK trial (ASCO 2021)

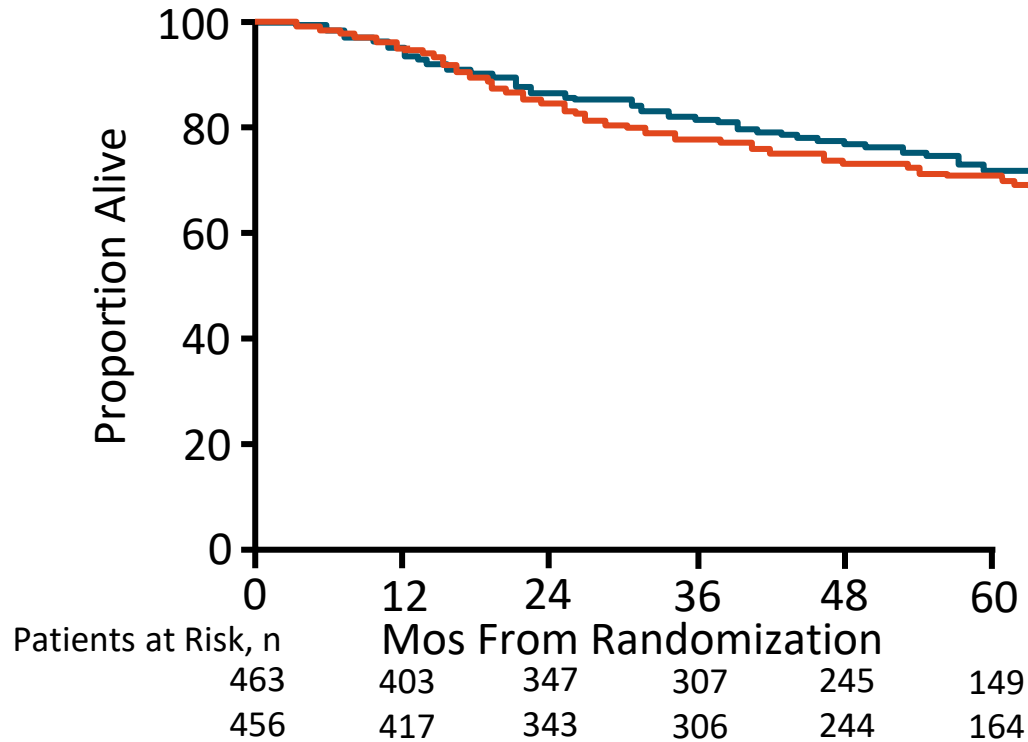


IB1 + LN, IB2, II-IVA
(FIGO 2008)
; ECOG PS 0-2

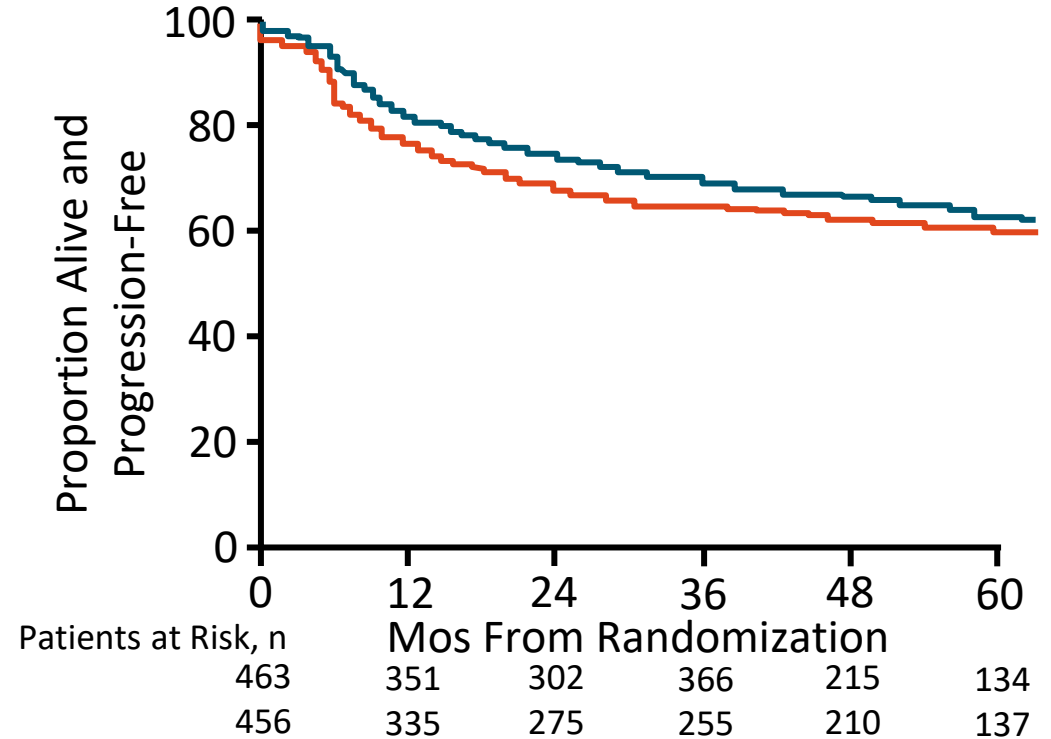
*40-45 Gy XRT + LN boost + brachytherapy
cisplatin 40 mg/m² weekly during XRT.

OUTBACK: OS and PFS

OS

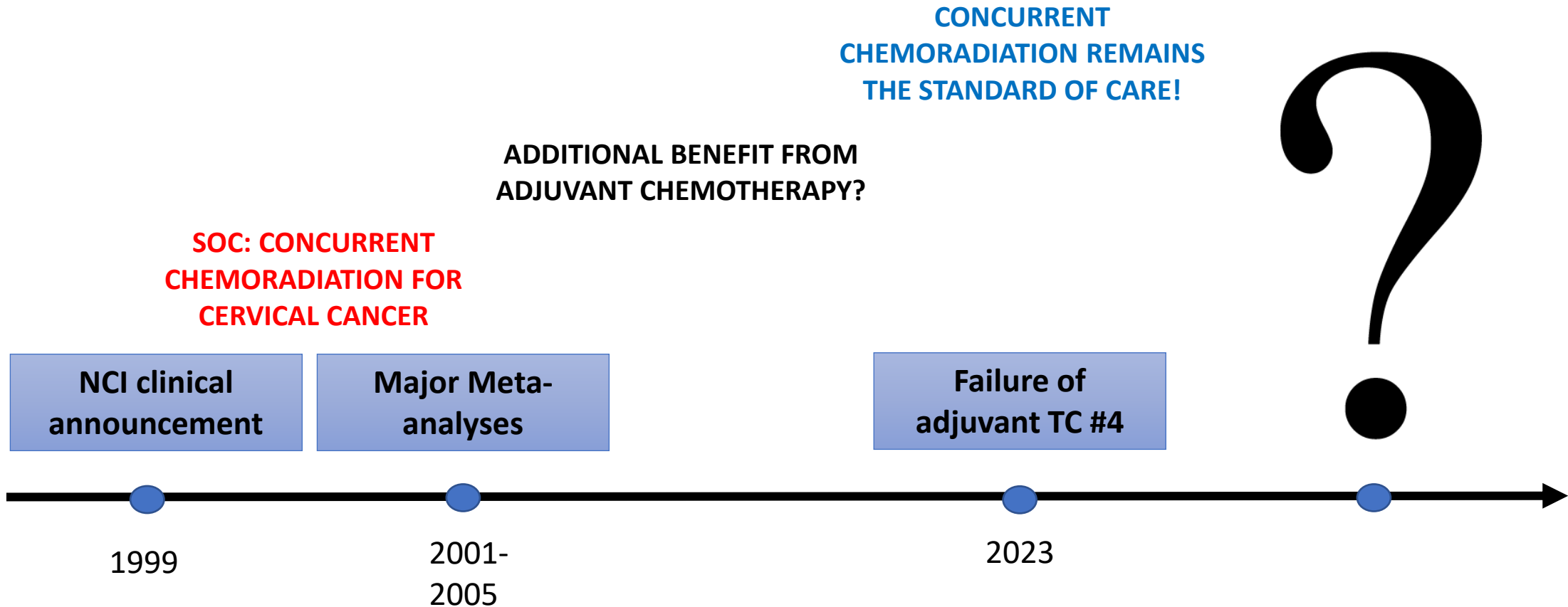


PFS

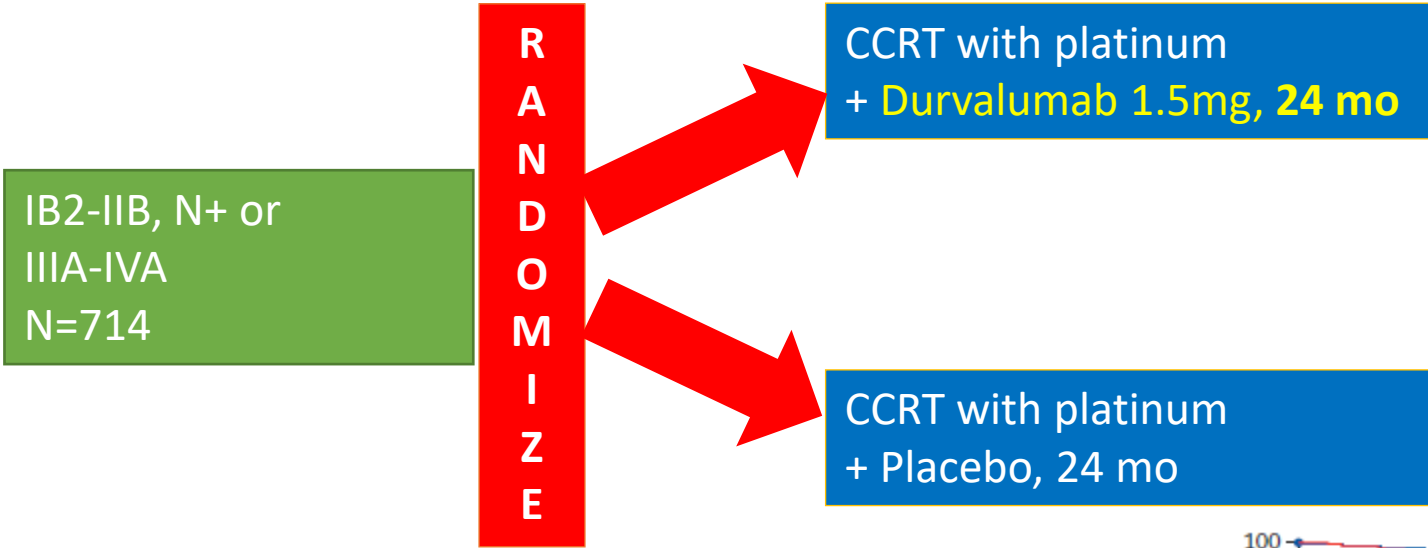


- Treatment effects consistent across subgroups **except for those aged < vs ≥60 yr**

What's NEXT?

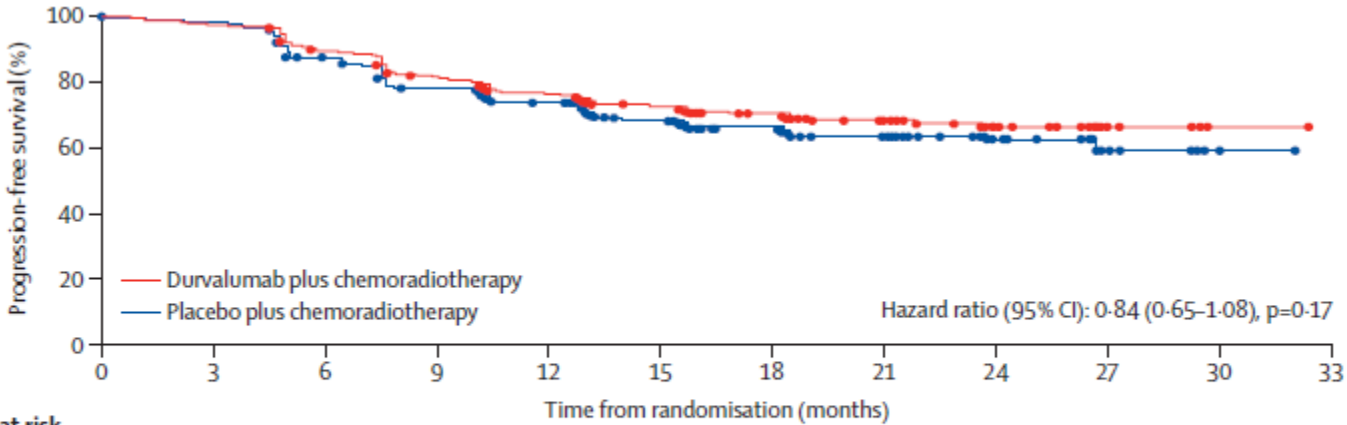


CALLA trial



NO SIGNIFICANT DIFFERENCE IN PFS

- ✓ Primary endpoint: PFS
- ✓ Secondary endpoint: OS, ORR, CR
- ✓ Exploratory endpoint: ctDNA, mR



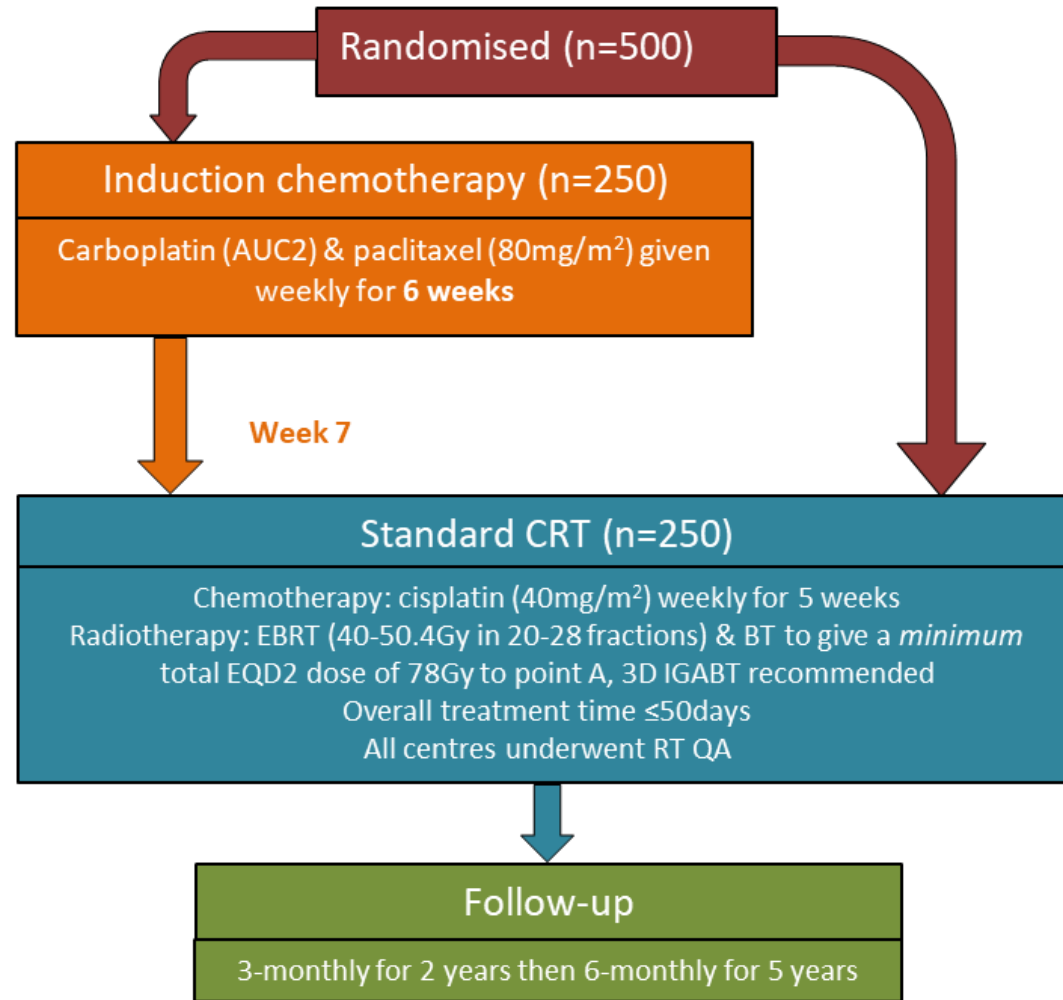
	0	3	6	9	12	15	18	21	24	27	30	33
Number at risk (number censored)												
Durvalumab plus chemoradiotherapy	385 (0)	363 (13)	330 (17)	294 (22)	270 (27)	215 (70)	163 (116)	110 (165)	43 (230)	11 (262)	1 (272)	0 (273)
Placebo plus chemoradiotherapy	385 (0)	368 (12)	318 (18)	282 (22)	257 (30)	203 (68)	146 (117)	109 (150)	49 (209)	14 (243)	2 (255)	0 (257)

INTERLACE trial

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
- Tumour size
- SCC v other

Primary endpoints

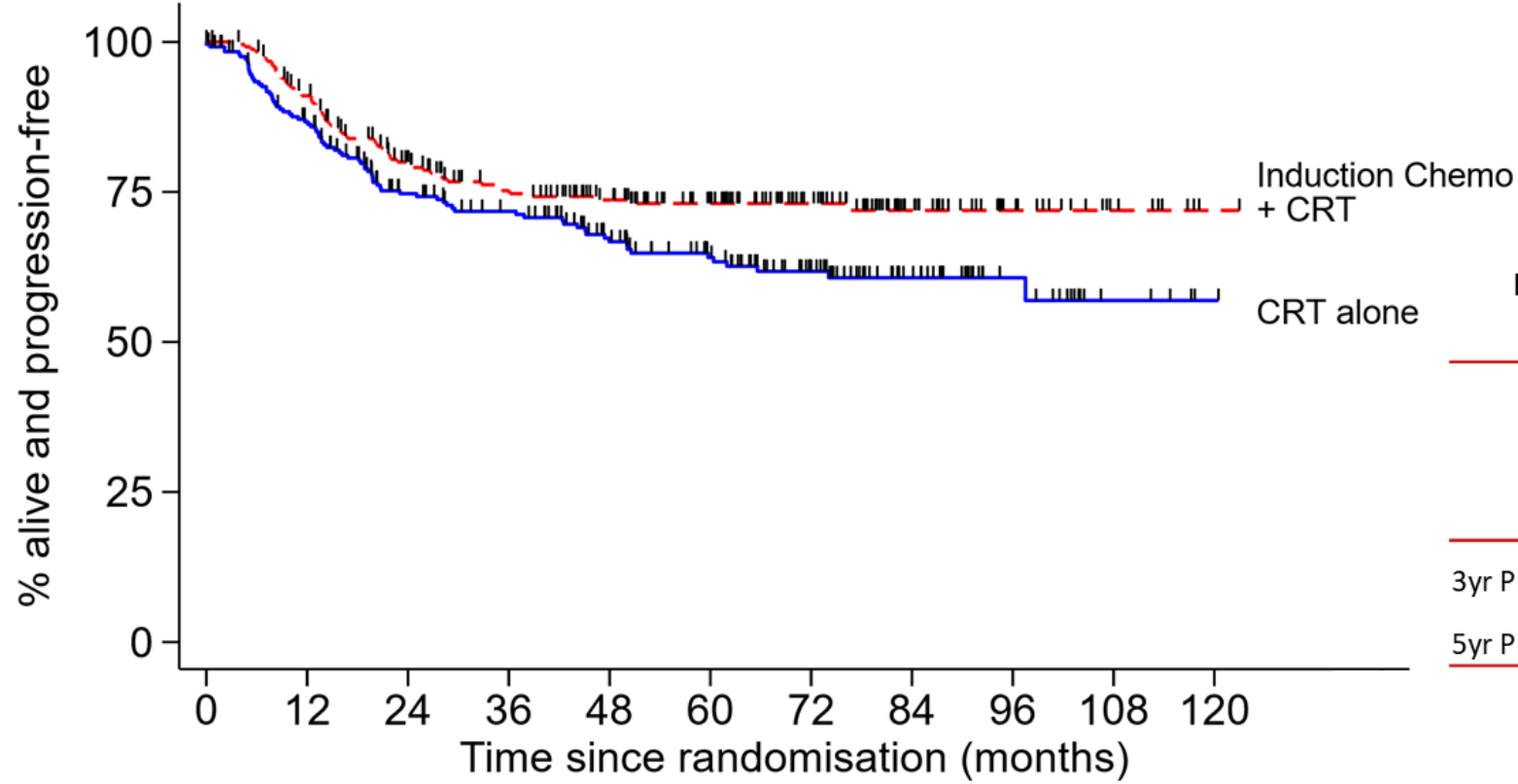
- PFS
- OS

Secondary endpoints

- Adverse events
- Pattern of relapse
- QOL
- Time to subsequent treatment

INTERLACE trial-Results (PFS)

INTERLACE Progression-Free Survival (median FU 64m)



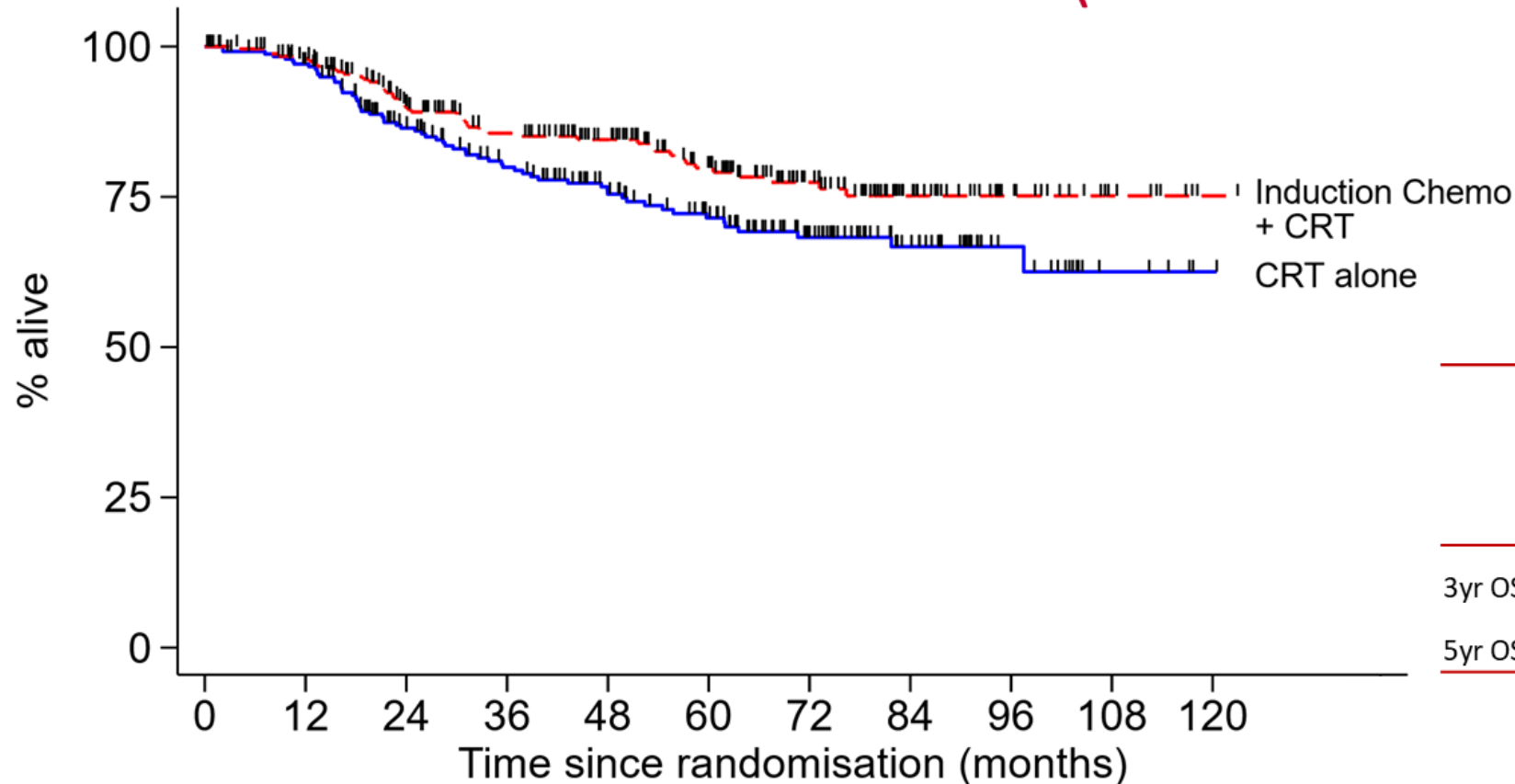
146 PFS events
 HR 0.65; 95% CI: 0.46-0.91
 P=0.013

	Induction Chemo + CRT (n=250)	CRT alone (n=250)
3yr PFS	75%	72%
5yr PFS	73%	64%

Number at risk	0	12	24	36	48	60	72	84	96	108	120
CRT alone	250	205	157	140	110	88	63	36	16	5	1
Induction Chemo + CRT	250	220	178	152	132	105	72	40	19	8	1

INTERLACE trial-Results (OS)

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	0	12	24	36	48	60	72	84	96	108	120
CRT alone	250	229	181	154	124	99	67	39	16	5	1
Induction Chemo + CRT	250	236	195	168	146	111	75	42	19	8	1

1. Both arms are well balanced given the nature of the disease characteristics.

However, details regarding radiation therapy are needed for an accurate assessment (e.g. RT QA).

INTERLACE trial-Adherence

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:		
Haematological	4	34
Non-haematological	25	20
Both	4	14
Other	20 (8)	13 (5)

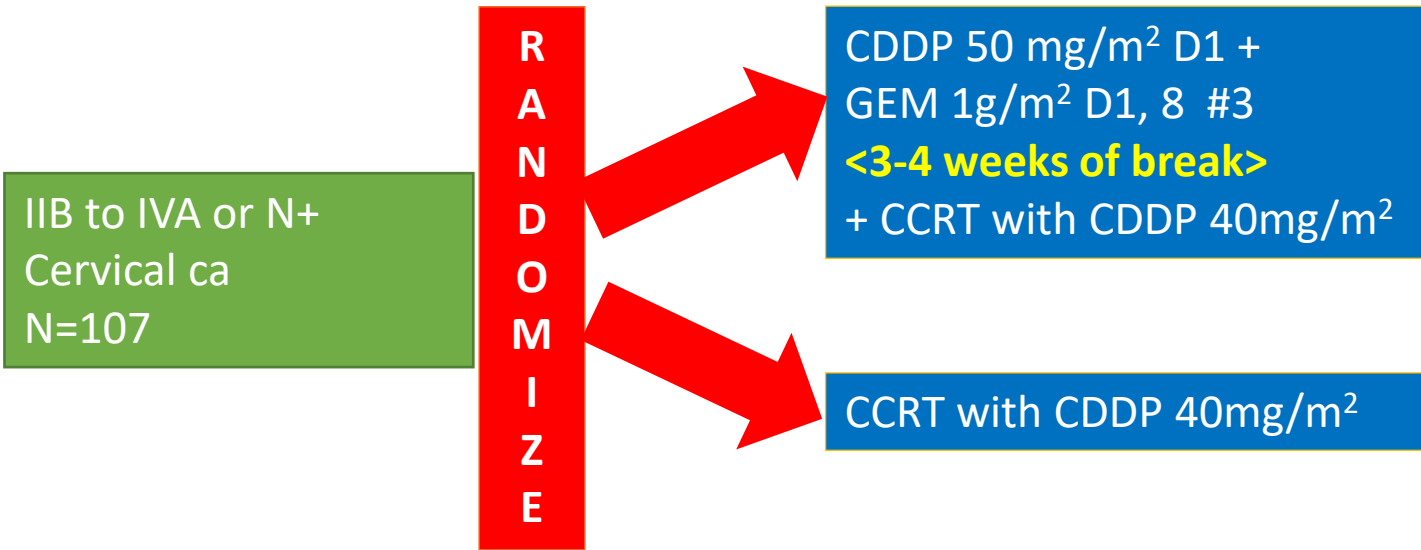
Adherence to Radiation

	CRT alone (n=250)	Induction Chemo + CRT (n=250)
	No. of patients (%)	
Received external beam radiotherapy	231 (92)	242 (97)
IMRT	93 (40)	102 (42)
3D conformal	138 (60)	140 (58)
Received brachytherapy	223 (97)	238 (98)
2D point A	49 (22)	46 (19)
3D point A	106 (48)	120 (51)
3D HRCTV D90	68 (30)	72 (30)
Median overall treatment time days (range)	45 (37-88)	45 (36-70)
<i>% completing treatment within 56 days</i>	95%	96%

19 patients (8%) did not received EBRT in CRT group.

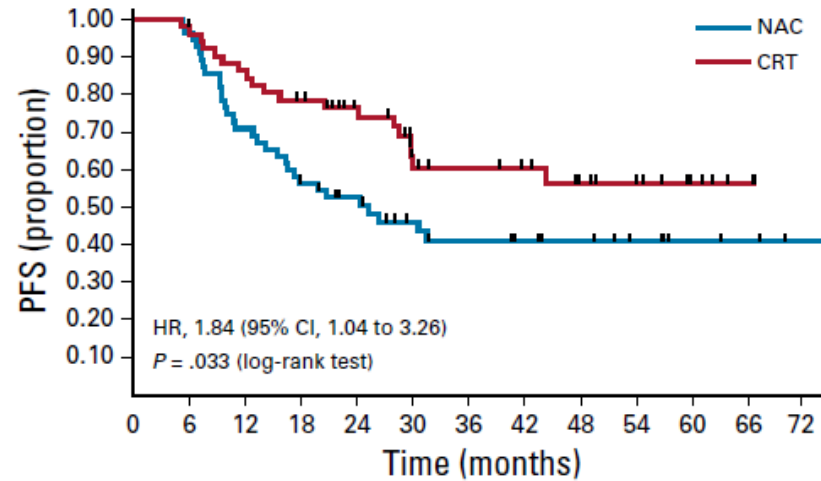
2. The delay before starting CCRT is detrimental, possibly because disease progression might occur during NAC., or because NAC compromised the delivery of CCRT.
→ "What is the best treatment regimen?"

CIRCE trial, A phase II study



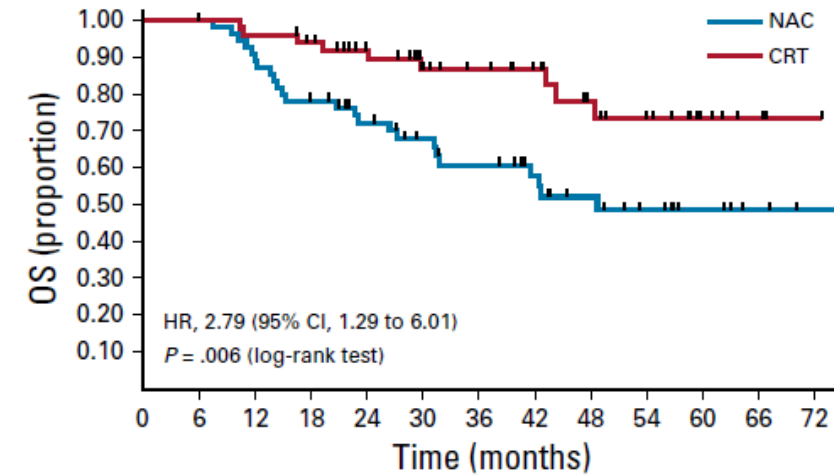
The addition of NAC is possibly inferior to CRT alone.

- ✓ Primary endpoint: 3-yr PFS
- ✓ Secondary endpoint: CRR, 3yr LR/OS, safety, QoL



No. at risk:

NAC	55	53	39	30	25	18	15	13	11	8	4	3	1
CRT	52	50	44	39	32	21	18	16	12	9	5	2	0



No. at risk:

NAC	55	55	49	42	35	29	25	20	15	11	6	3	1
CRT	52	51	49	46	39	29	26	22	16	12	6	3	1