Locally Advanced Cervical Cancer: Evolving Treatment Paradigms

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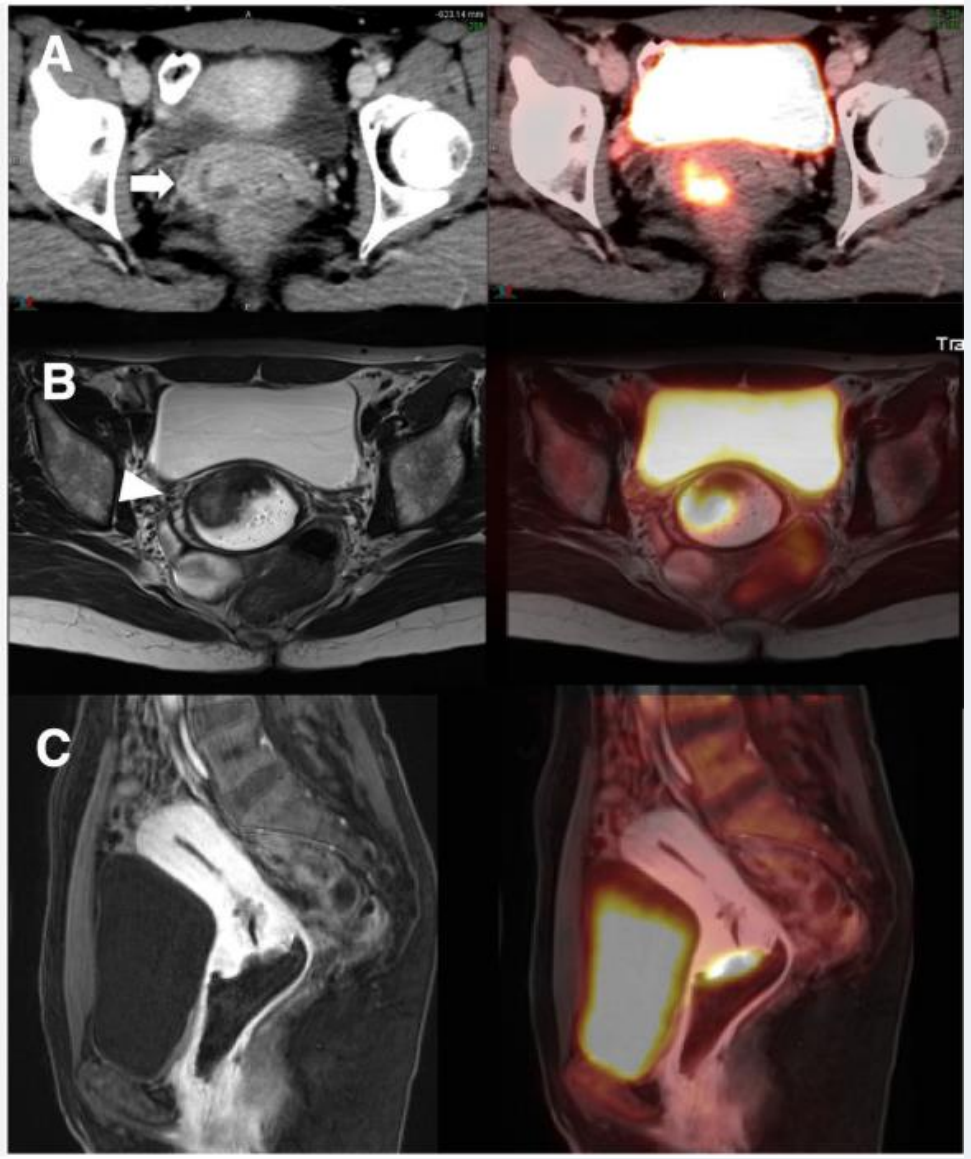
Disclosures

I have no financial disclosures

Outline

- Cervical cancer epidemiology
- Locally advanced cervical cancer (LACC)
- Immunotherapy in LACC
- Recent immunotherapy trials in LACC
- Second line options
- Conclusions
- LACC trials at Winship



Nguyen et al. J Nuclear Med Technology. 2020.

Cervical Cancer Epidemiology

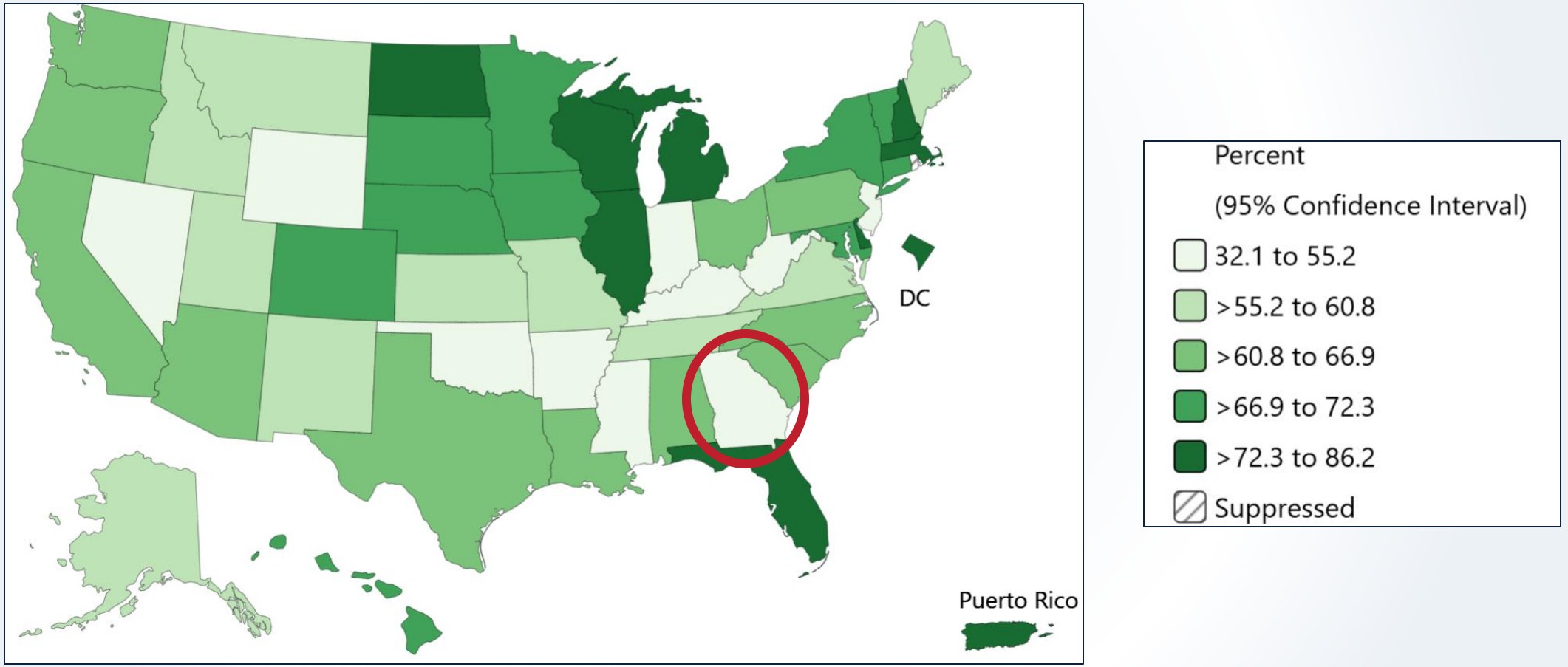
Cancer Facts & Figures, 2026

Adapted Table 1. Estimated Number of New Cancer Cases and Deaths by Sex, US, 2026

	Estimated New Cases			Estimated Deaths		
	Both sexes	**Male**	**Female**	**Both sexes**	**Male**	**Female**
Genital system	463,560	345,900	117,660	71,970	37,400	34,570
Uterine cervix	13,490		13,490	4,200		4,200
Uterine corpus	68,270		68,270	14,450		14,450
Ovary	21,010		21,010	12,450		12,450
Vulva	7,130		7,130	1,750		1,750
Vagina & other genital, female	7,760		7,760	1,720		1,720
Prostate	333,830	333,830		36,320	36,320	
Testis	9,810	9,810		630	630	
Penis & other genital, male	2,260	2,260		450	450	

Why are we still seeing a high incidence of cervical cancer?

Percent with Up-to-Date HPV Vaccination Coverage
All Races (includes Hispanic individuals), Female, Ages 13-17
(2023 National Immunization Survey)



Created by statecancerprofiles.cancer.gov on 06/15/2026

HPV Vaccination Helps Prevent against Cervical Cancer

HPV vaccination recommendations:

- Routine vaccination at age 11-12 (as early at age 9)
  - 2 doses (0, 6-12mo) if <15yo
  - 3 doses (0, 2, 6mo) if >15yo
  - Always 3 doses if immunocompromised
- Recommended to age 26
  - Up to age 45 after discussion with clinician

ACOG Committee Opinion. Number 809. Reaffirmed 2026.

New Updates to Cervical Cancer Screening Recommendations

July 2026

ACOG
American College of Obstetricians & Gynecologists

ACOG COMMITTEE STATEMENT

NUMBER 28

(REPLACES PRACTICE ADVISORY: UPDATED CERVICAL CANCER SCREENING GUIDELINES, APRIL 2021)

JULY 2026

Screening for Cervical Cancer

This Committee Statement was developed by the American College of Obstetricians & Gynecologists' Committee on Clinical Consensus–Gynecology
Nancy Sokkary, MD.

Table 1. - Summary of Recommendations for Cervical Cancer Screening for Patients at Average Risk

Age Group (y)	Recommendation
21–29	Cervical cytology every 3 years
30–65	Clinician-collected primary hrHPV every 5 y If primary clinician-collected hrHPV is not available: • Co-testing with hrHPV testing with cervical cytology every 5 y • Patient-collected primary hrHPV screening every 3 y* If primary hrHPV (clinician- or patient-collected) and co-testing are not available: • Cervical cytology alone every 3 y†
Older than 65	Routine screening not clinically indicated with adequate prior screening‡

hrHPV, high-risk human papillomavirus.

*Using clinician-ordered, U.S. Food and Drug Administration–approved testing kits.

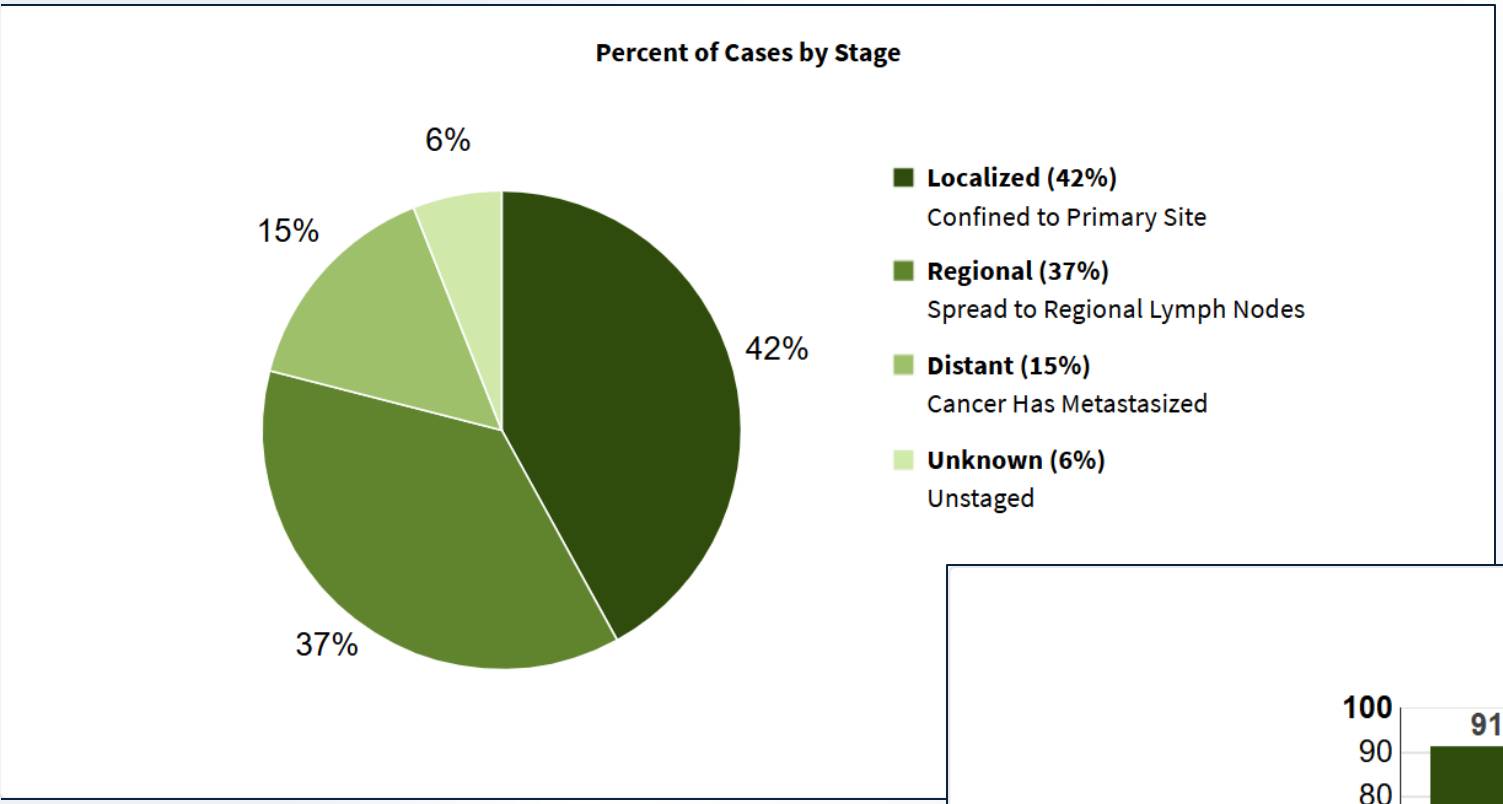
†Only in settings in which hrHPV primary testing or co-testing is not available or, if after counseling, the patient chooses cervical cytology alone and systems for appropriate follow-up are in place.

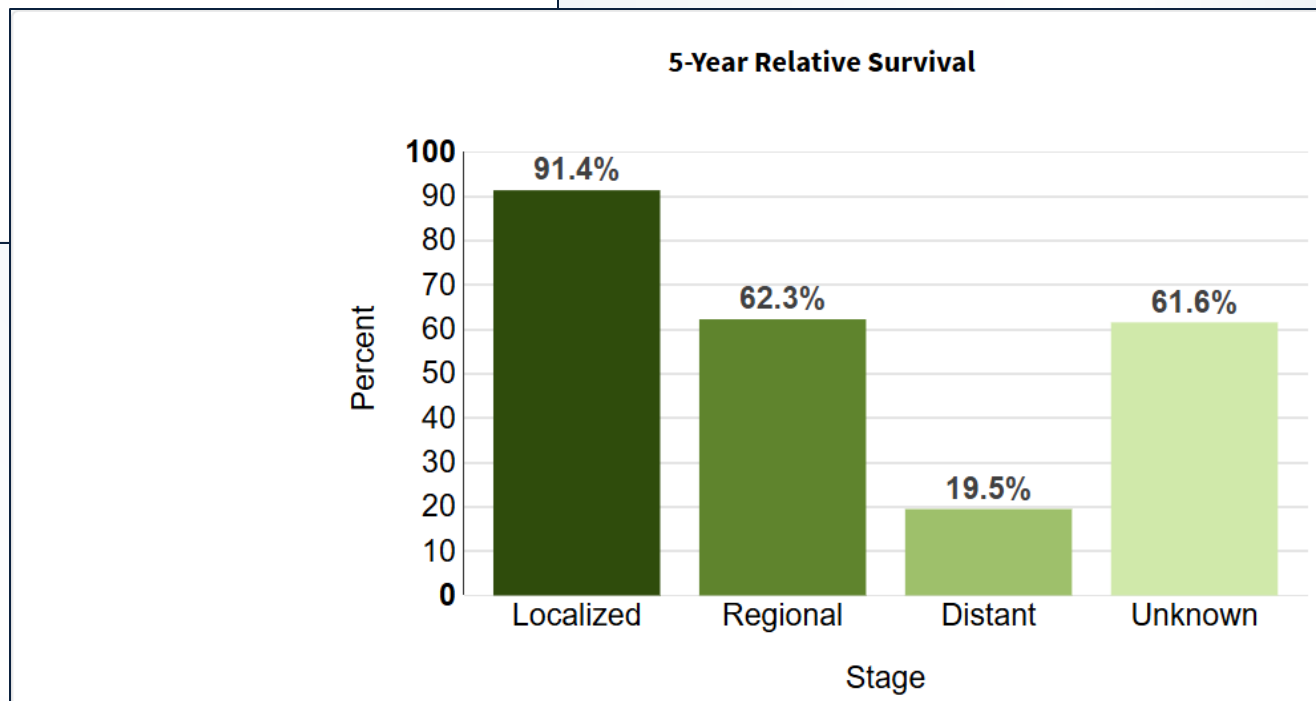
‡Defined as three consecutive negative cytology results or two consecutive negative co-testing results within 10 years before stopping screening, with the most recent test occurring within 3 years for cytology alone or 5 years for co-testing.

Risk Factors for Cervical Cancer

Factor	Relative Risk
HPV	4-150
Previous STD	2-10
No prior Pap	2-6
Multiple partners	2-5
Early coitarche	2-4
Smoking	2-4
Lower education/income	2-3
Black/Hispanic/Native American	2
Older age	2

Cervical Cancer by the Numbers





https://seer.cancer.gov/statfacts/html/cervix.html

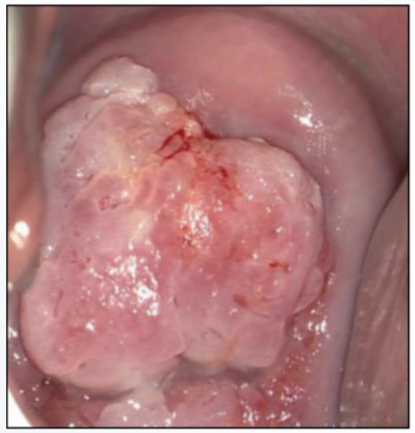
Locally Advanced Cervical Cancer

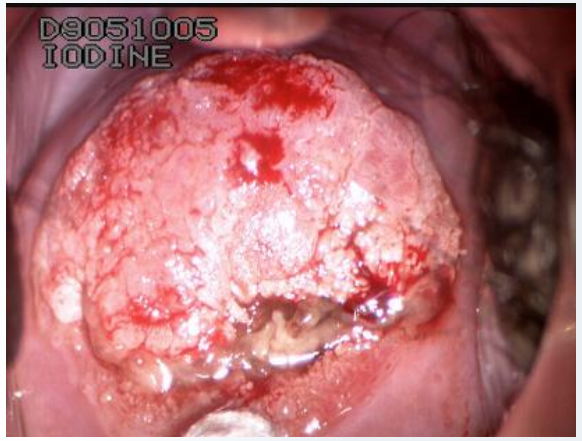
Locally Advanced Cervical Cancer (LACC)

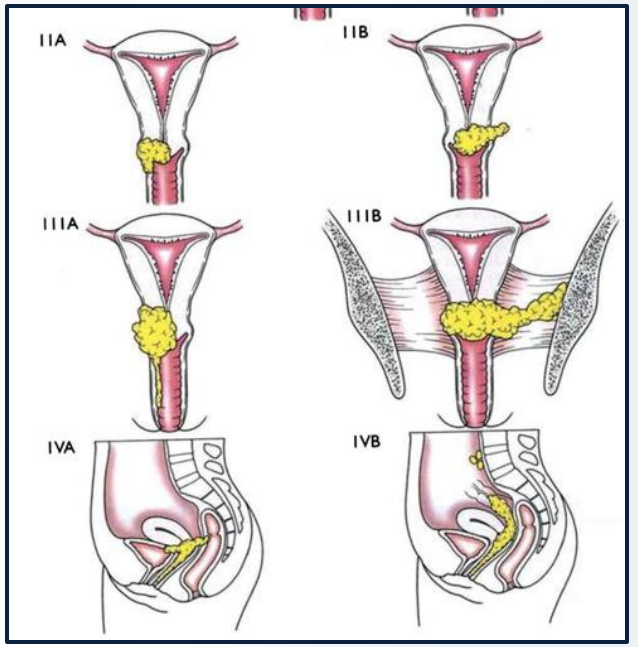
Table 4: Comparison of the 2009 and 2018 FIGO Staging Classifications

Stage	2009 FIGO Definition	2018 FIGO Definition
I	Confined to the cervix	Confined to the cervix
IA	≤5 mm depth and ≤7 mm width	≤5 mm depth*
IA1	≤3 mm depth	≤3 mm depth
IA2	>3 mm and not >5 mm depth	>3 mm and ≤5 mm depth
IB	>5 mm depth	>5 mm depth
IB1	≤4 cm maximum diameter	≤2 cm maximum diameter*
IB2	>4 cm maximum diameter	>2 cm and ≤4 cm maximum diameter*
IB3	...	>4 cm maximum diameter*
II	Beyond the uterus but not involving the lower one-third of the vagina or pelvic sidewall	Beyond the uterus but not involving the lower one-third of the vagina or pelvic sidewall
IIA	Upper two-thirds of the vagina	Upper two-thirds of the vagina
IIA1	Upper two-thirds of the vagina and ≤4 cm	Upper two-thirds of the vagina and ≤4 cm
IIA2	Upper two-thirds of the vagina and >4 cm	Upper two-thirds of the vagina and >4 cm
IIB	Parametrial invasion	Parametrial invasion
III	Lower vagina, pelvic sidewall, and ureters	Lower vagina, pelvic sidewall, ureters, and lymph nodes*
IIIA	Lower one-third of the vagina	Lower one-third of the vagina
IIIB	Pelvic sidewall	Pelvic sidewall
IIIC	...	Pelvic and para-aortic lymph node involvement*
IIIC1	...	Pelvic lymph node involvement*
IIIC2	...	Para-aortic lymph node involvement*
IV	Adjacent and distant organs	Adjacent and distant organs
IVA	Rectal or bladder involvement	Rectal or bladder involvement
IVB	Distant organs outside the pelvis	Distant organs outside the pelvis

Source.—Reference 18.
*Changes made in the 2018 FIGO staging classification.

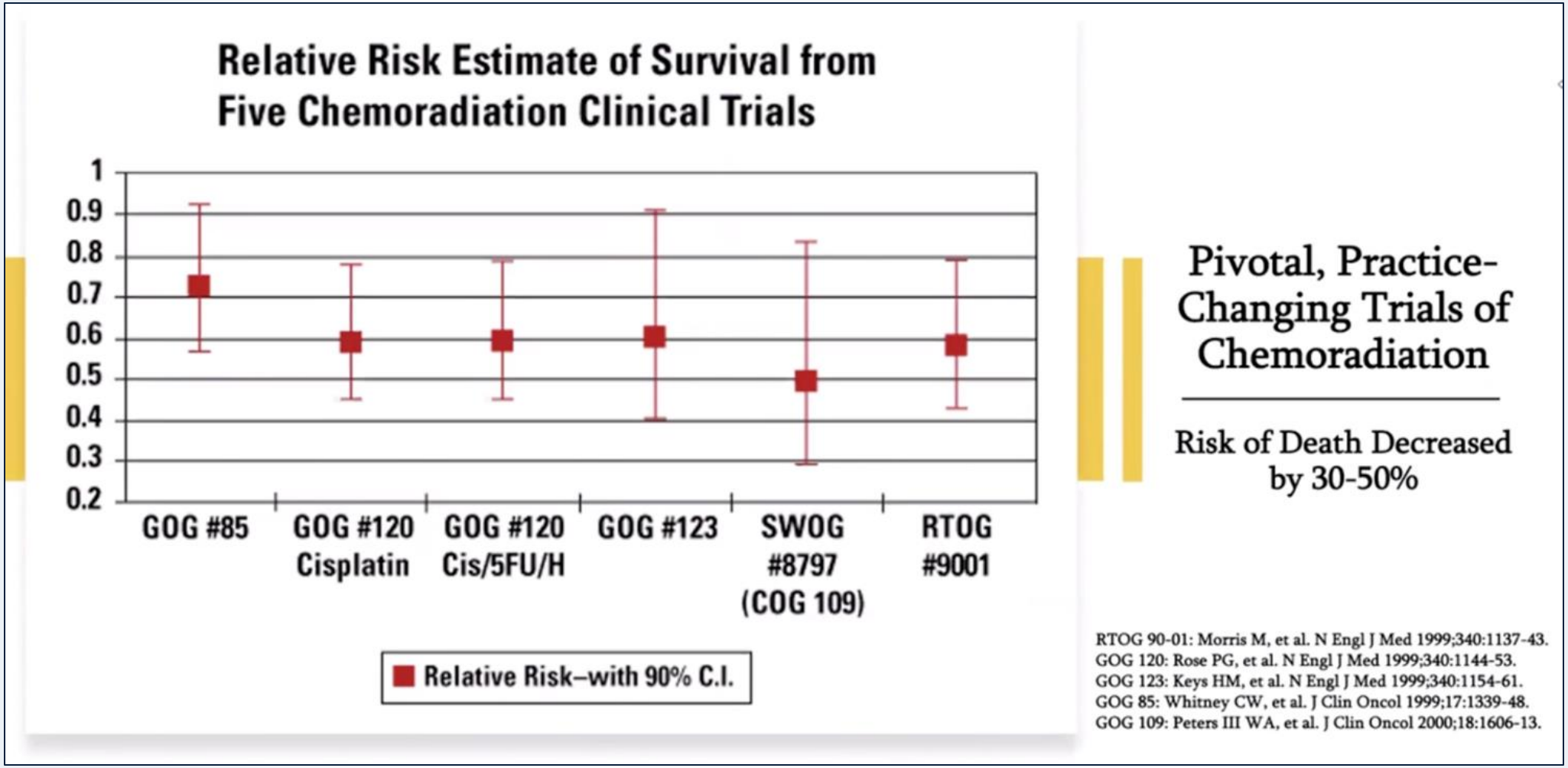






Montgomery et al. Obstet. Gynaecol. Reprod.Med. 2023.
Newton and Mould. Obstet. Gynaecol. Reprod.Med. 2017

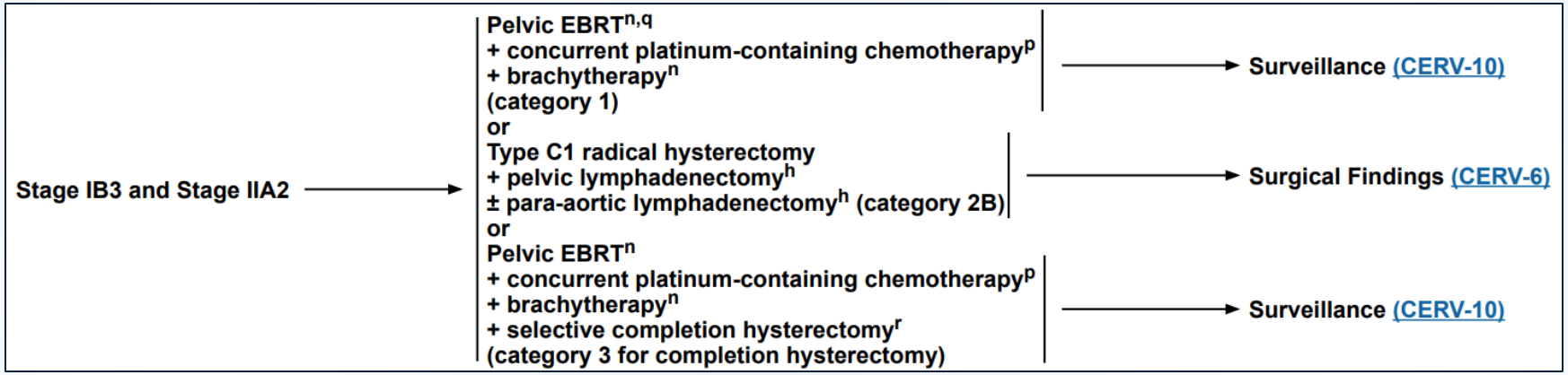
1999 NCI Alert: Use combination of chemotherapy + radiation therapy (RT) instead of radiation therapy alone to treat invasive cervical cancer

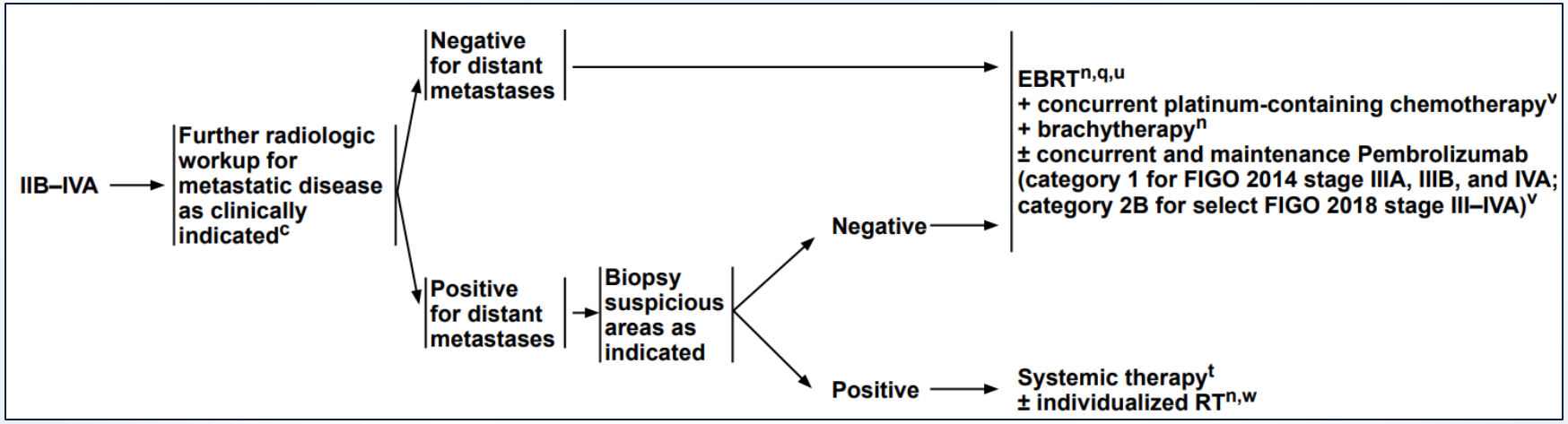


NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Cervical Cancer

Version 2.2026 — November 10, 2025





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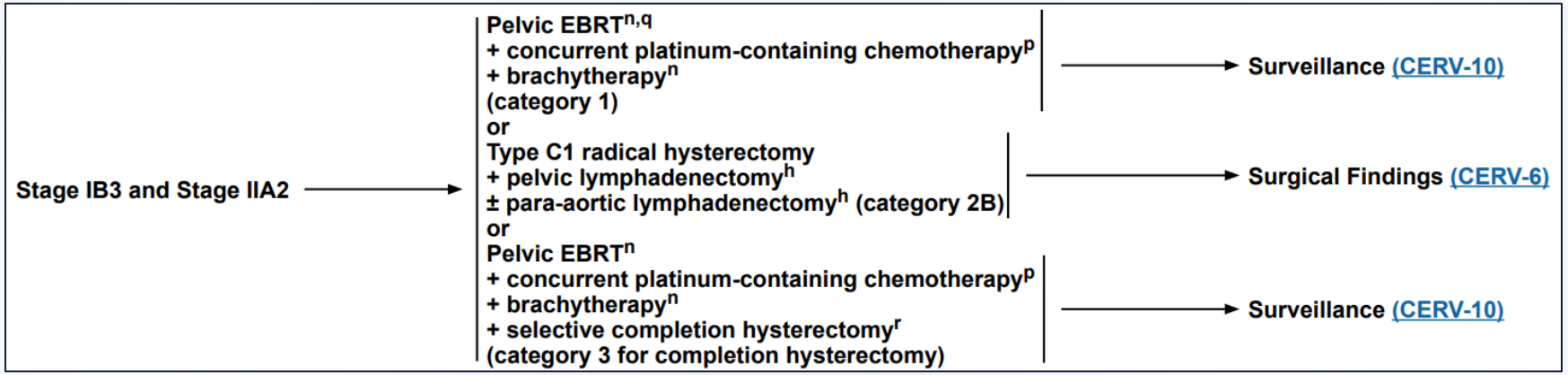
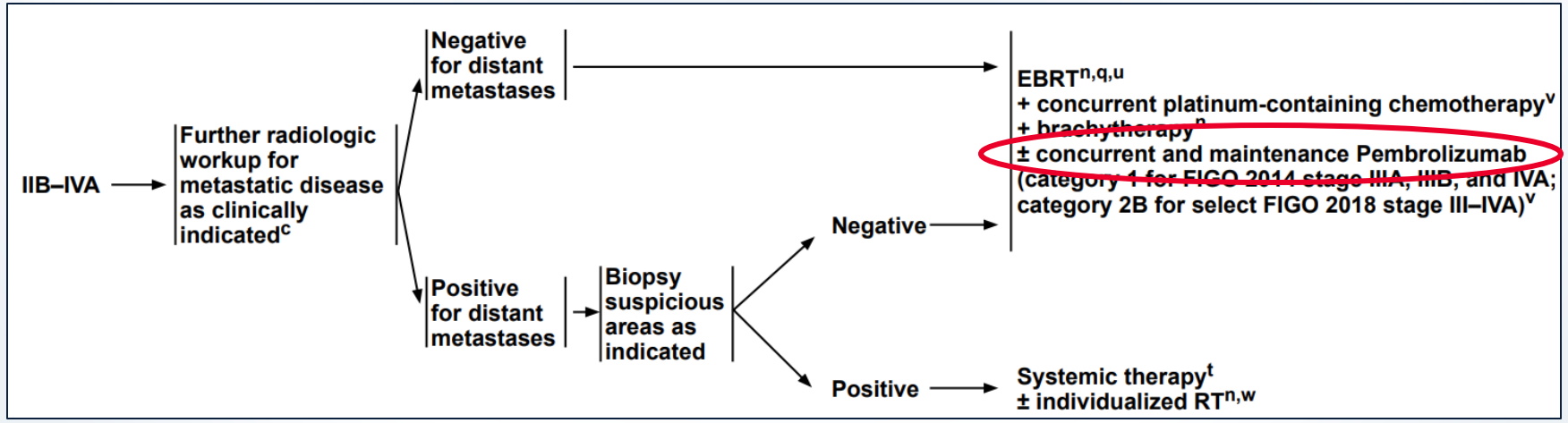
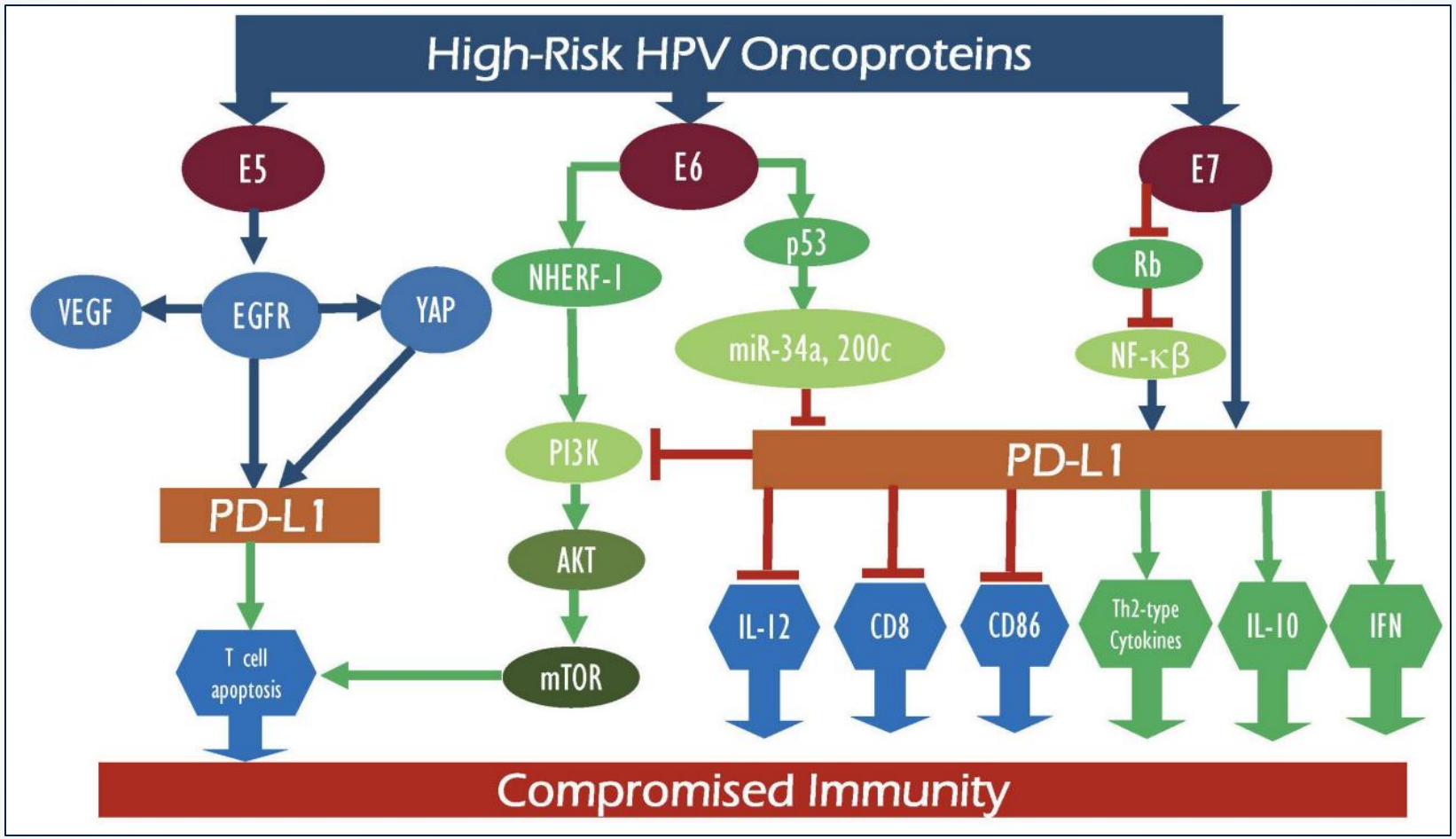




Is there benefit with immunotherapy in cervical cancer?



Allouch et al. Front Oncol. 2020.

Cervical Cancer has High PD-L1 Expression

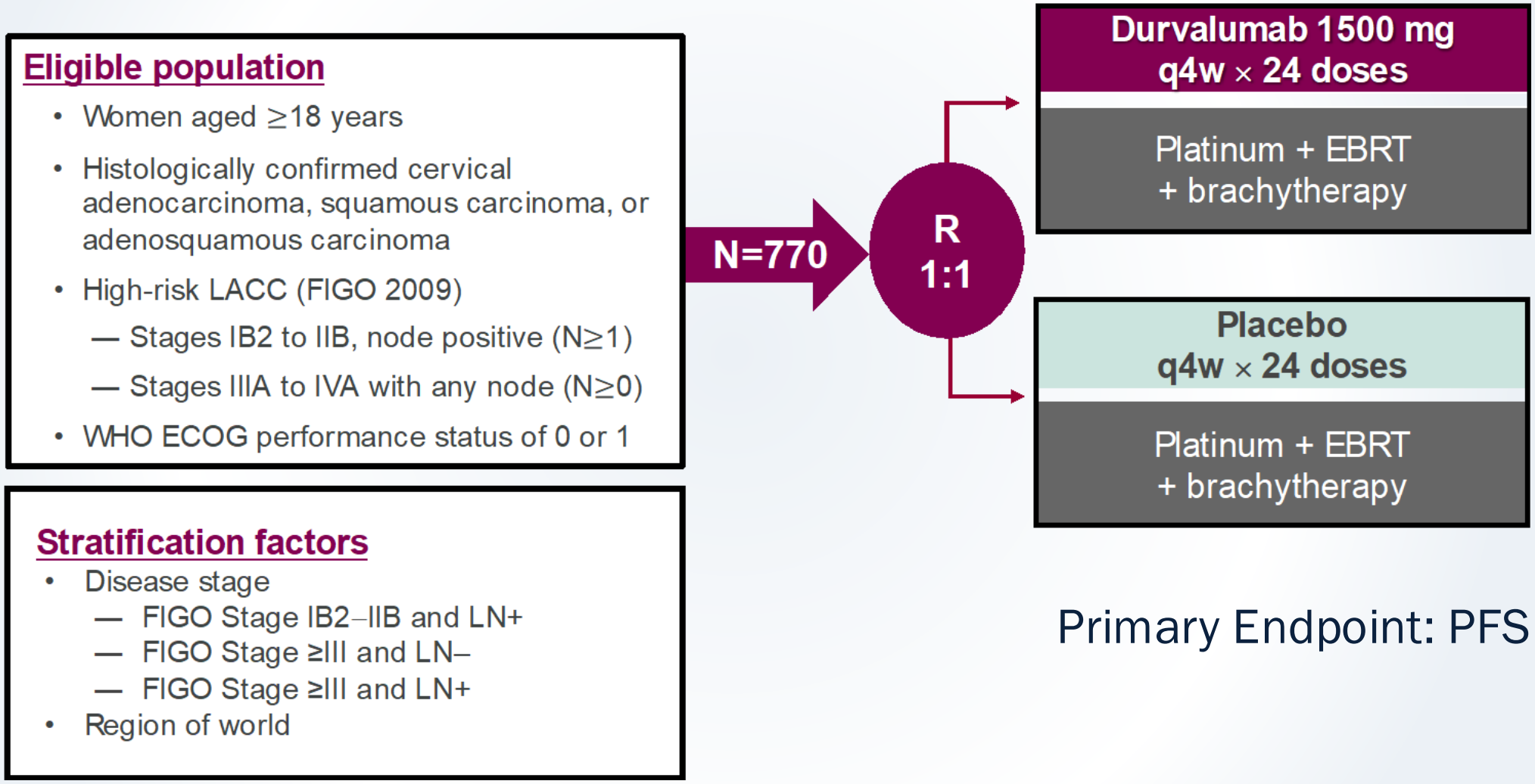
Adapted Table 3. Biomarkers by NGS across cancer types

(Vanderwalde et al. Cancer Med. 2018)

		MSI		TMB		PD-L1		MSI + TMB		MSI + PD-L1		TMB + PD-L1		MSI + TMB + PD-L1		None of these biomarkers	
	N	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Ovarian surface epithelial carcinomas	1517	17	1.1	24	1.6	291	19.2	13	0.9	6	0.4	10	0.7	6	0.4	1208	79.6
Endometrial carcinoma	879	155	17.6	110	12.5	142	16.2	89	10.1	24	2.7	22	2.5	15	1.7	592	67.3
Cervical cancer	168	6	3.6	13	7.7	74	44.0	2	1.2	3	1.8	10	6.0	1	0.6	89	53.0

Recent Immunotherapy Trials in LACC

CALLA: Durvalumab + ChemoRT vs. ChemoRT alone

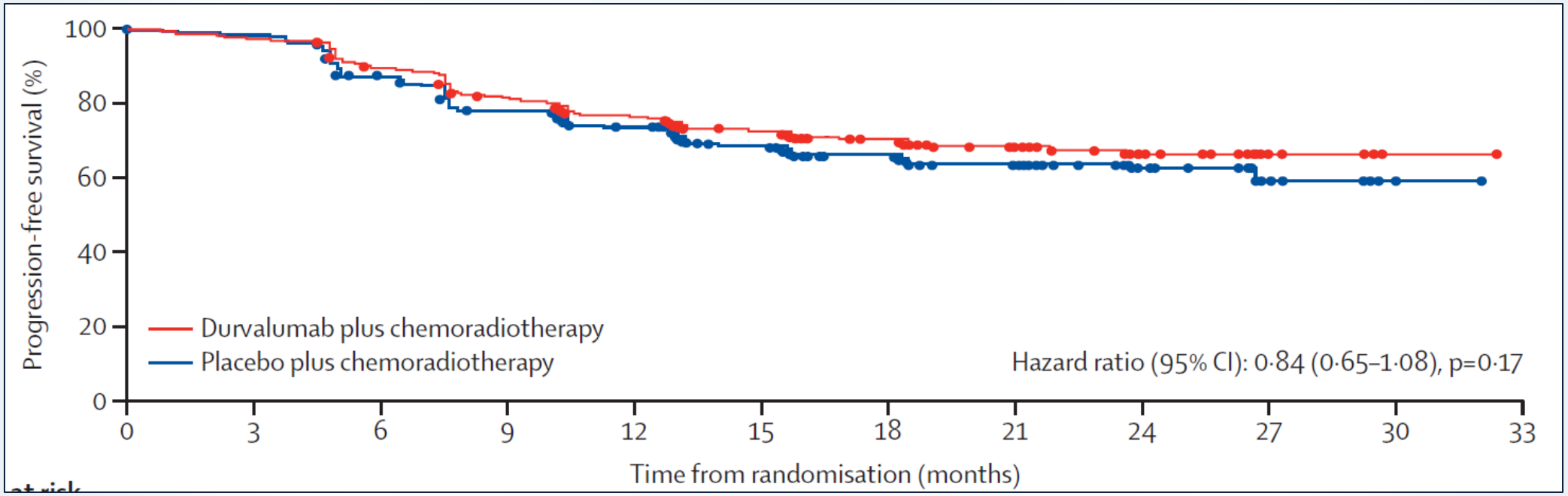


Primary Endpoint: PFS

Monk et al. The Lancet. 2023.

CALLA: Durvalumab + chemoRT vs ChemoRT alone

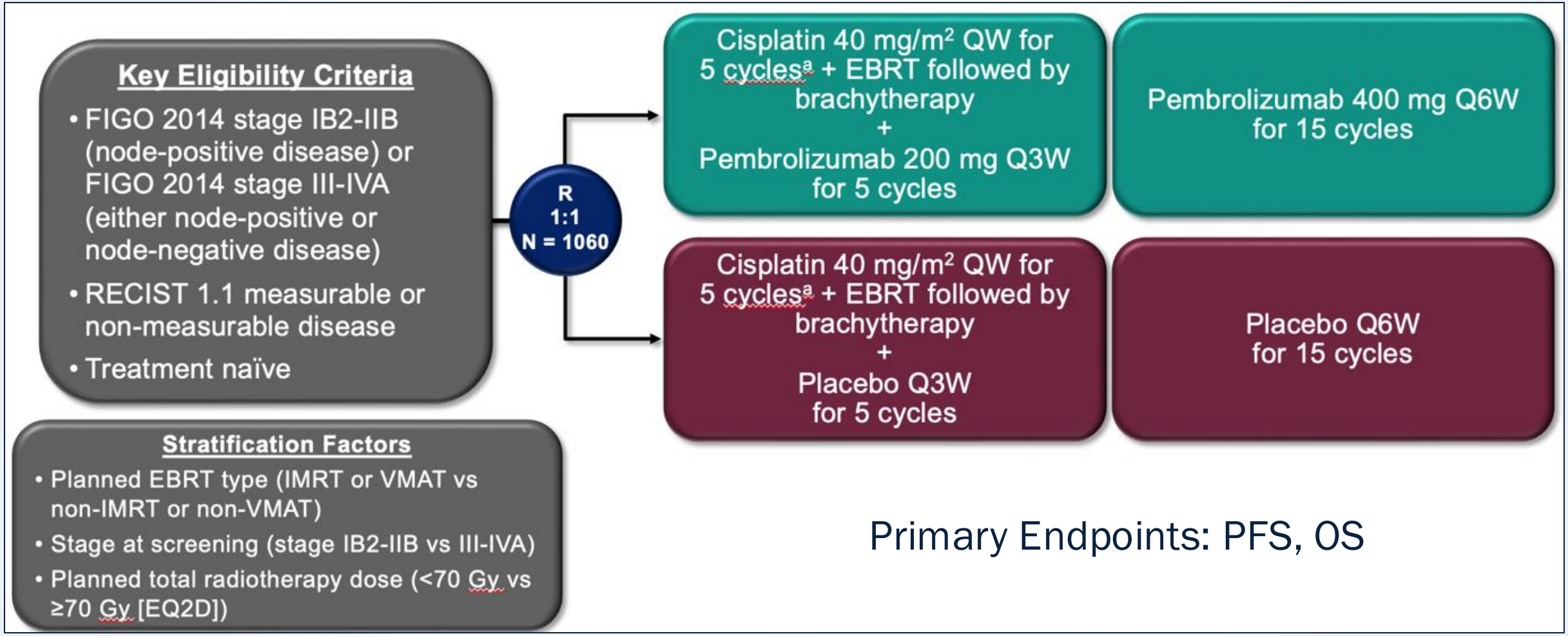
No significant difference in PFS between the two groups



Is there a role for immunotherapy in locally advanced cervical cancer?

Monk et al. The Lancet. 2023.

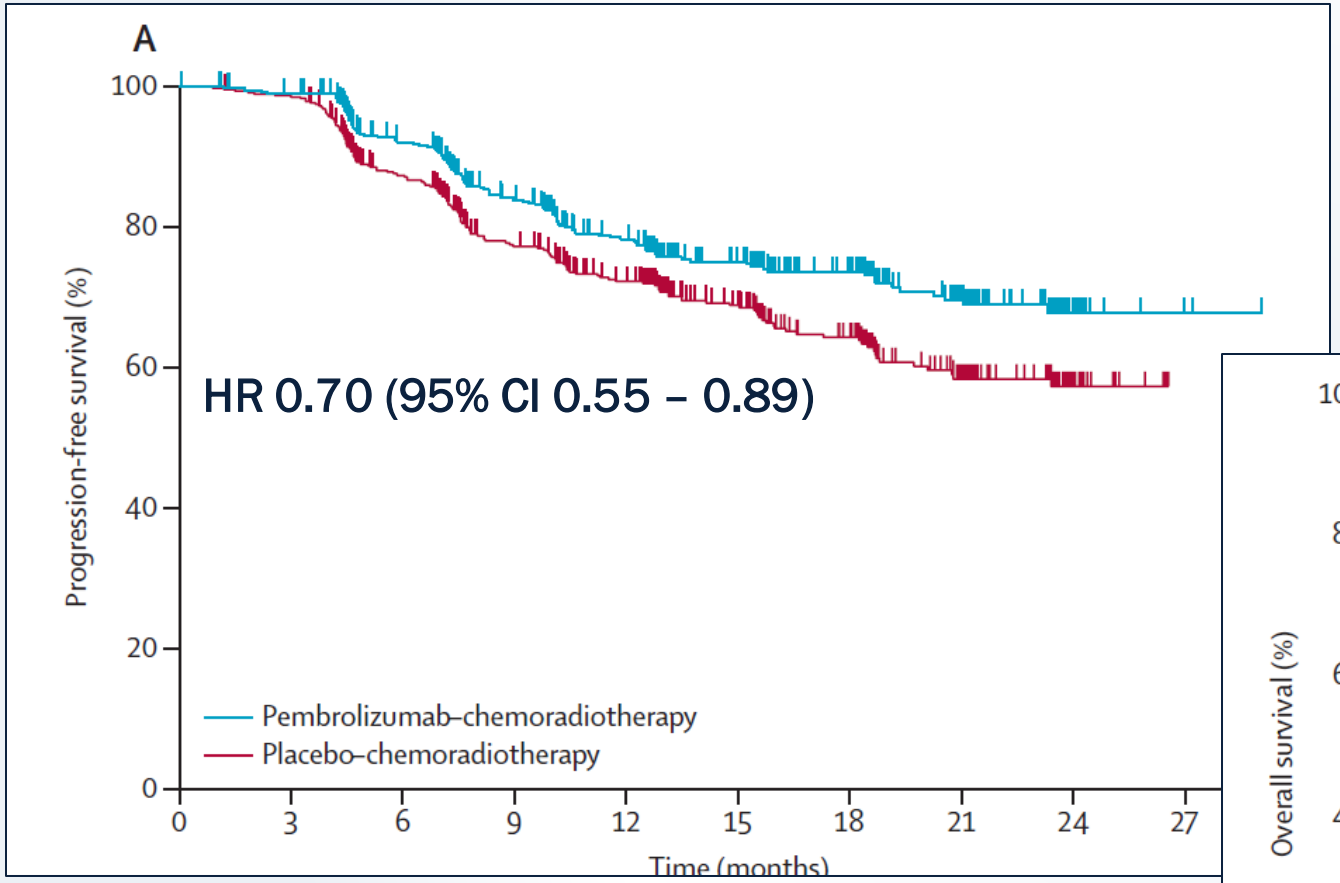
KEYNOTE A18: Pembrolizumab + ChemoRT vs. ChemoRT



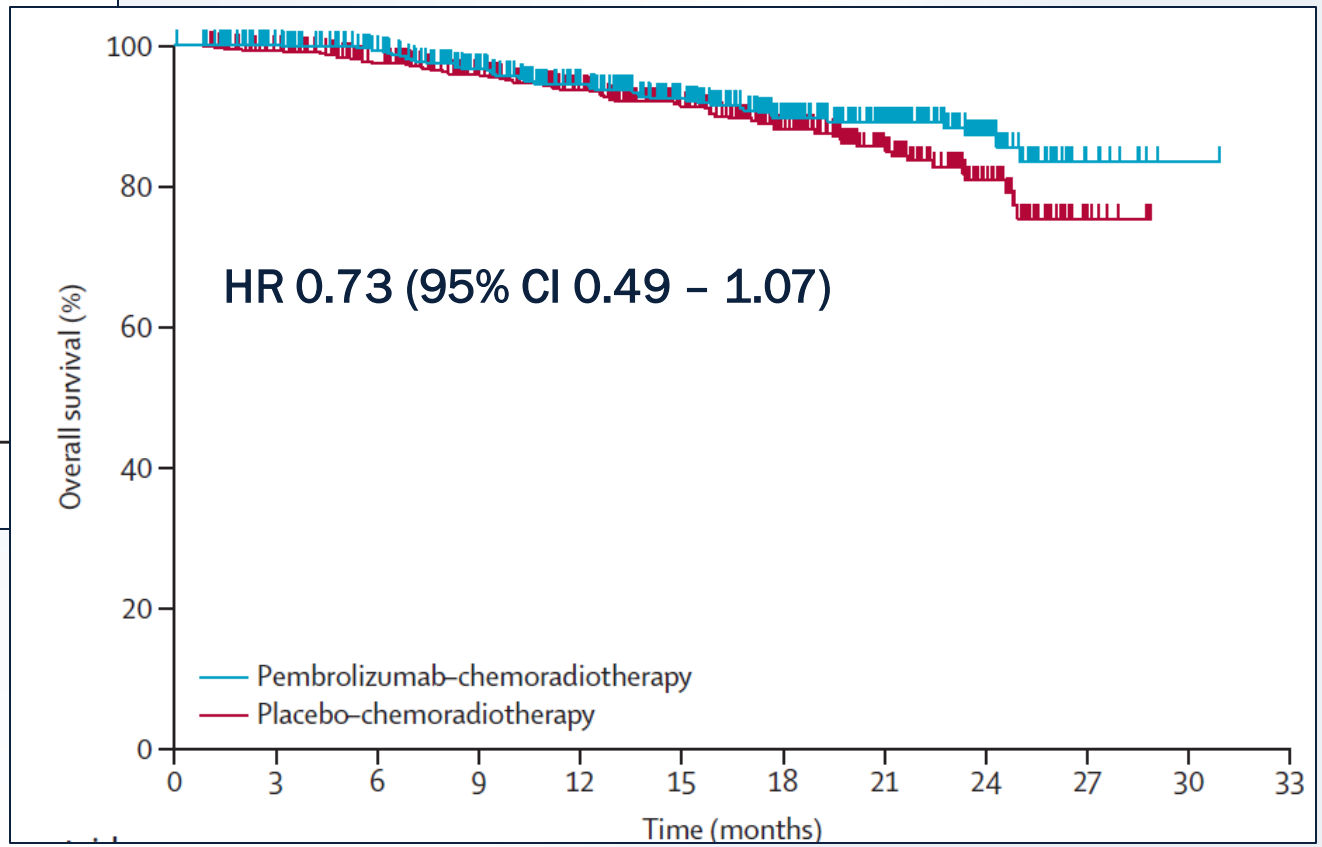
Lorusso et al. The Lancet. 2024.

KEYNOTE A18: Pembrolizumab + ChemoRT vs. ChemoRT

PFS



OS



Lorusso et al. The Lancet. 2024.

KEYNOTE A18 Adverse Events

	Pembrolizumab–chemoradiotherapy (n=528)		Placebo–chemoradiotherapy (n=530)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any adverse event*	525 (99%)	394 (75%)	526 (99%)	364 (69%)
Treatment-related adverse event†	507 (96%)	354 (67%)	509 (96%)	321 (61%)
Anaemia	313 (59%)	99 (19%)	292 (55%)	84 (16%)
Nausea	302 (57%)	7 (1%)	315 (59%)	9 (2%)
Diarrhoea	266 (50%)	22 (4%)	271 (51%)	23 (4%)
White blood cell count decreased	172 (33%)	102 (19%)	181 (34%)	111 (21%)
Neutrophil count decreased	153 (29%)	77 (15%)	148 (28%)	78 (15%)
Vomiting	132 (25%)	3 (<1%)	150 (28%)	7 (1%)
Leukopenia	125 (24%)	67 (13%)	92 (17%)	57 (11%)
Platelet count decreased	116 (22%)	25 (5%)	108 (20%)	13 (2%)
Neutropenia	113 (21%)	56 (11%)	92 (17%)	51 (10%)
Immune-mediated adverse event‡	167 (32%)	21 (4%)	54 (10%)	5 (<1%)
Hypothyroidism	102 (19%)	3 (<1%)	24 (5%)	0
Hyperthyroidism	60 (11%)	2 (<1%)	11 (2%)	0
Colitis	14 (3%)	4 (<1%)	9 (2%)	4 (<1%)
Thyroiditis	11 (2%)	1 (<1%)	1 (<1%)	0

Lorusso et al. The Lancet. 2024.

Updated KEYNOTE A18 Analysis

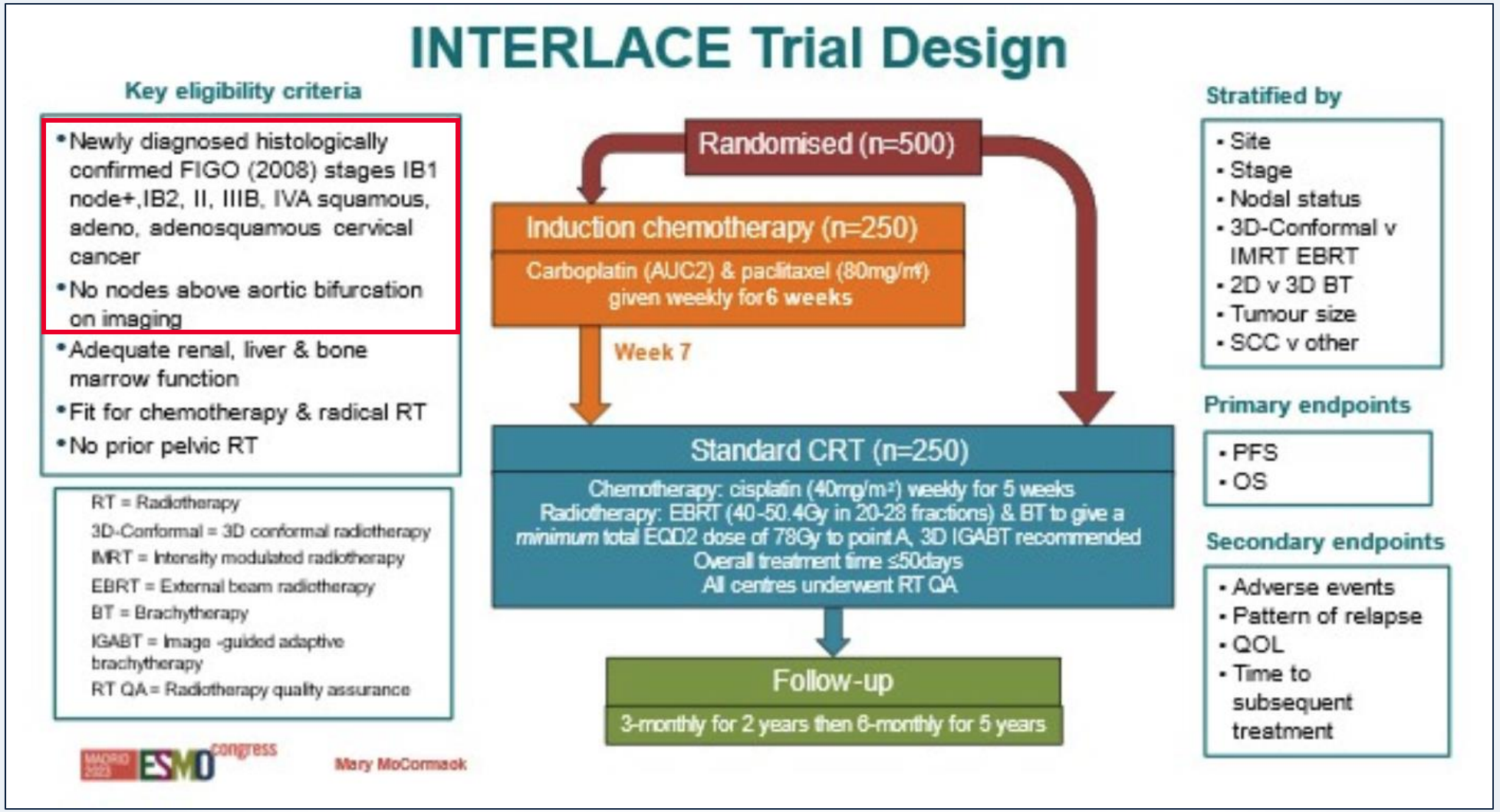
Summary of PFS and OS in ENGOT-cx11/GOG-3047/KEYNOTE-A18.

	Final Analysis 07JAN25		Interim Analysis 2 08JAN24		Interim Analysis 1 09JAN23	
	Pembro + CCRT	**Pbo + CCRT**	**Pembro + CCRT**	**Pbo + CCRT**	**Pembro + CCRT**	**Pbo + CCRT**
OS, median (95% CI)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)
36-mo OS	81.8%	74.4%	82.6%	74.8%	NR (NR-NR)	NR (NR-NR)
HR (95% CI)	0.73 (0.57-0.94)		0.67 (0.50-0.90); *P*=0.0040		0.73 (0.49-1.07); *P*=0.0541	
PFS, median (95% CI)	47.6 (47.6-NR)	47.5 (41.0-NR)	NR (NR-NR)	NR (32.0-NR)	NR (NR-NR)	NR (NR-NR)
24-mo PFS	70.6%	59.7%	70.6%	58.6%	67.8%	57.3%
HR (95% CI)	0.72 (0.59-0.87)		0.68 (0.56-0.84)		0.70 (0.55-0.89); *P*=0.0020	

NR=not reached.

Duska et al. 2025 ASCO Annual Meeting.

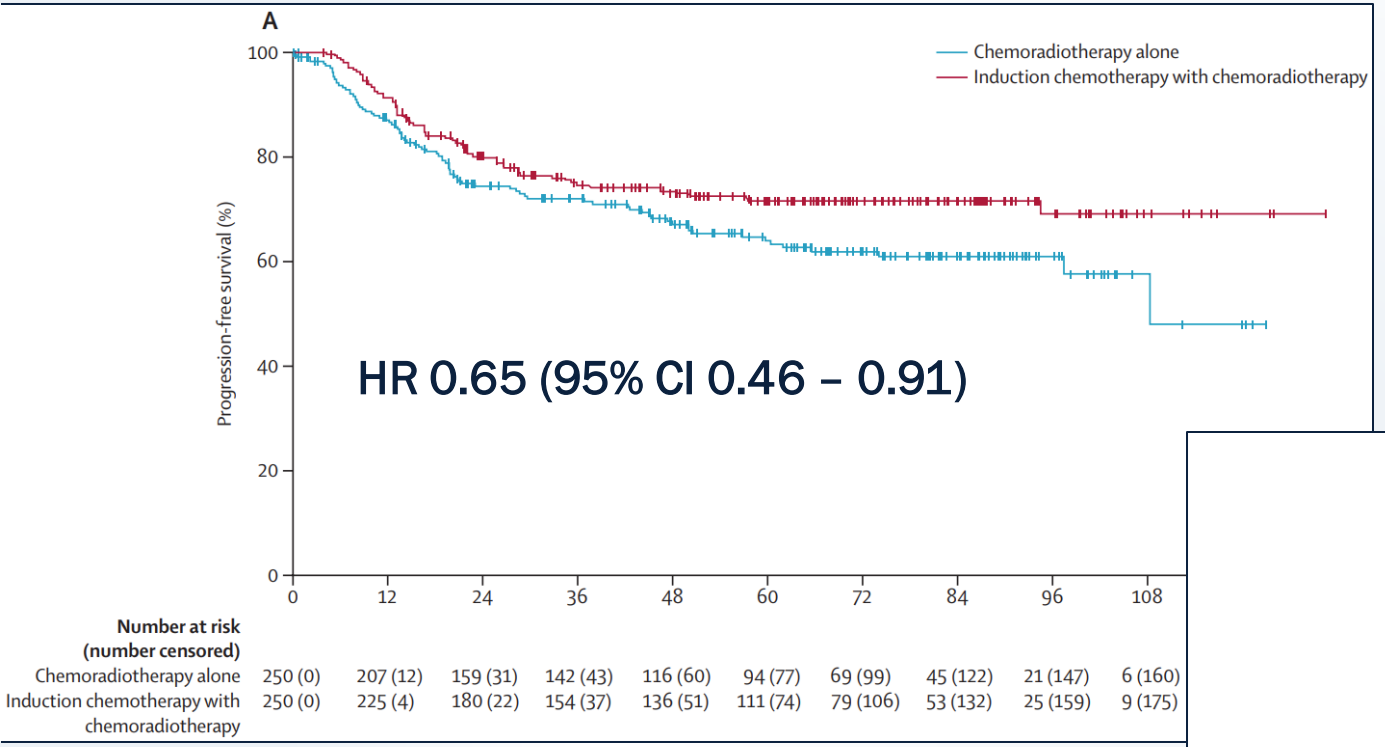
INTERLACE: Induction chemotherapy + ChemoRT vs. ChemoRT



McCormack et al. The Lancet. 2024.

INTERLACE: Induction chemotherapy + ChemoRT vs. ChemoRT

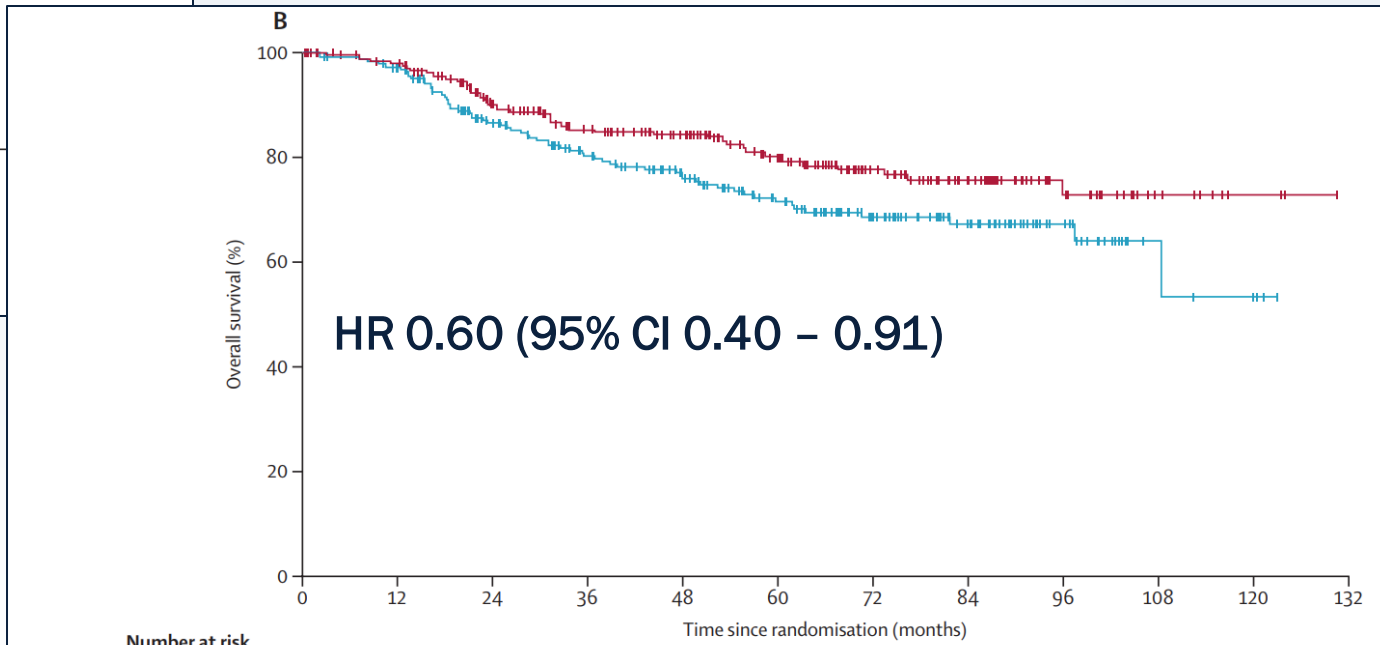
PFS



HR 0.65 (95% CI 0.46 – 0.91)

Number at risk (number censored)										
Chemoradiotherapy alone	250 (0)	207 (12)	159 (31)	142 (43)	116 (60)	94 (77)	69 (99)	45 (122)	21 (147)	6 (160)
Induction chemotherapy with chemoradiotherapy	250 (0)	225 (4)	180 (22)	154 (37)	136 (51)	111 (74)	79 (106)	53 (132)	25 (159)	9 (175)

OS



HR 0.60 (95% CI 0.40 – 0.91)

Number at risk (number censored)												
Chemoradiotherapy alone	250 (0)	230 (13)	186 (33)	157 (49)	132 (66)	105 (86)	75 (112)	48 (138)	24 (163)	6 (179)	3 (181)	0 (184)
Induction chemotherapy with chemoradiotherapy	250 (0)	240 (5)	196 (31)	169 (48)	150 (65)	118 (90)	83 (122)	55 (148)	26 (176)	9 (193)	4 (199)	0 (202)

McCormack et al. The Lancet. 2024.

INTERLACE Adverse Events

	Induction chemotherapy with chemoradiotherapy (n=250)		Chemoradiotherapy alone (n=250)
	Occurred at any time	Occurred after induction chemotherapy	
Any grade 3–4 event during induction chemotherapy	54 (22%)	NA	NA
Any adverse event	247 (99%)	243 (97%)	237 (95%)
Any grade 3–4 event	147 (59%)	131 (52%)	120 (48%)
Any haematological grade 3–4 event	74 (30%)	60 (24%)	32 (13%)
Neutropenia	48 (19%)	37 (15%)	13 (5%)
Anaemia	13 (5%)	9 (4%)	9 (4%)
Thrombocytopenia	13 (5%)	13 (5%)	5 (2%)
Any non-haematological grade 3–4 event	109 (44%)	98 (39%)	107 (43%)
Abdominal or pelvic pain	13 (5%)	11 (4%)	18 (7%)
Diarrhoea	20 (8%)	19 (8%)	31 (12%)
Fatigue, muscle weakness, or joint pain	28 (11%)	25 (10%)	14 (6%)
Infection	14 (6%)	12 (5%)	13 (5%)

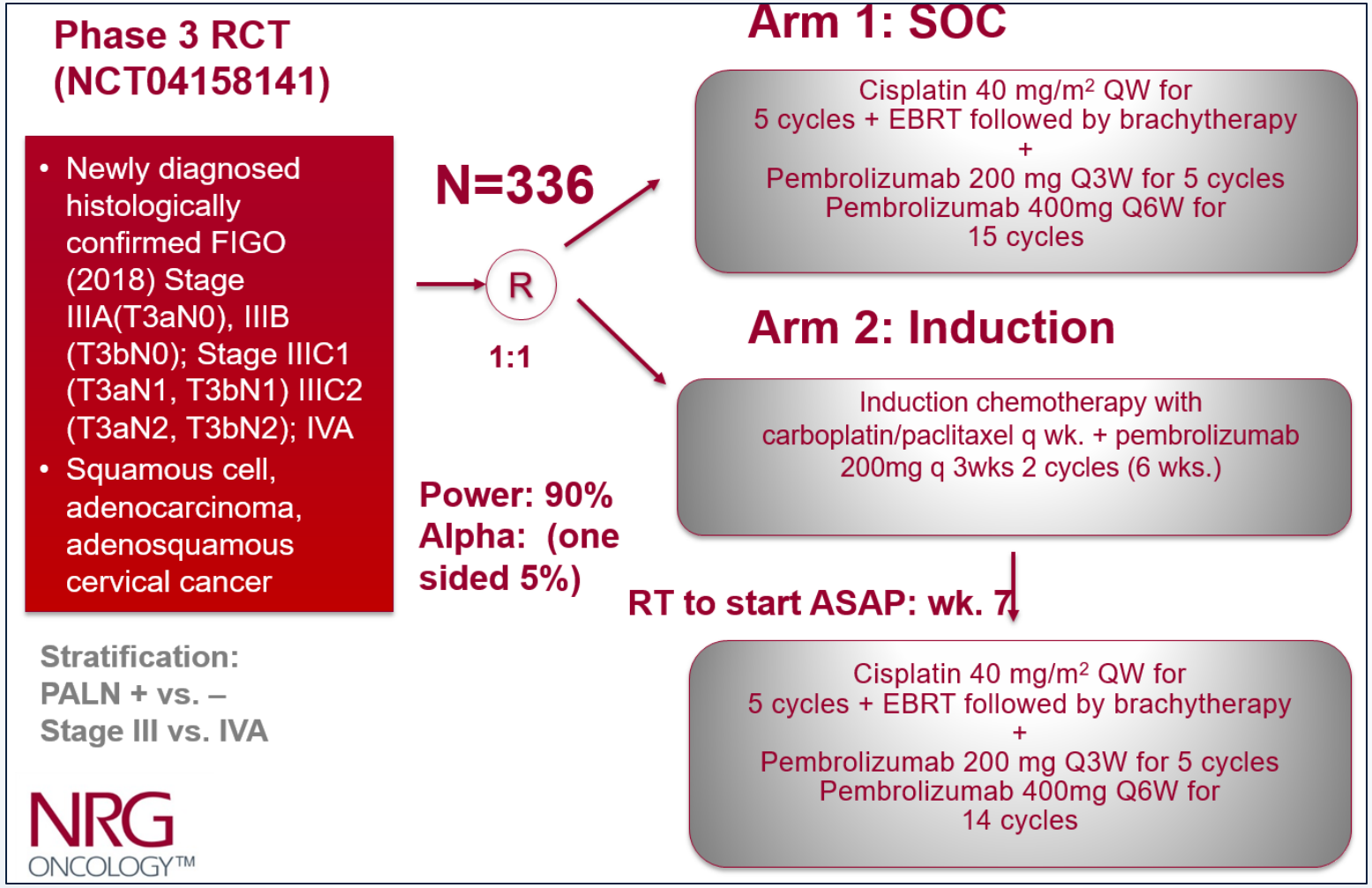
There were three deaths within 30 days of completing treatment, one (respiratory failure) in the induction chemotherapy with chemoradiotherapy group, and two in the chemoradiotherapy alone group (sepsis and pulmonary embolism); none were considered treatment-related. NA=not applicable.

Table 4: **Adverse events**

McCormack et al. The Lancet. 2024.

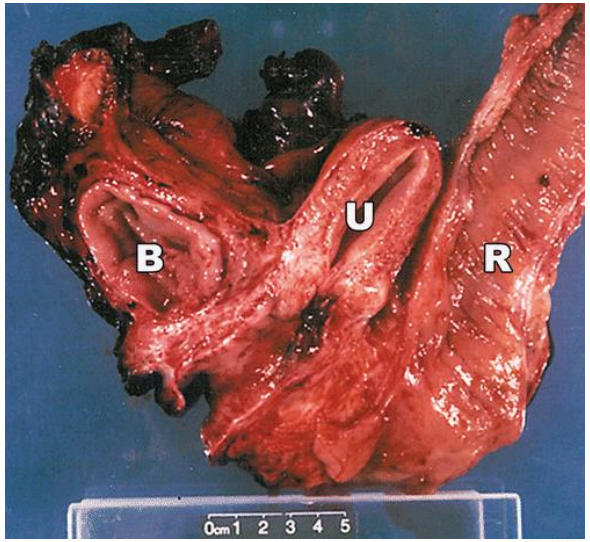
NRG GY037:
Induction chemotherapy + Pembrolizumab + ChemoRT vs. ChemoRT

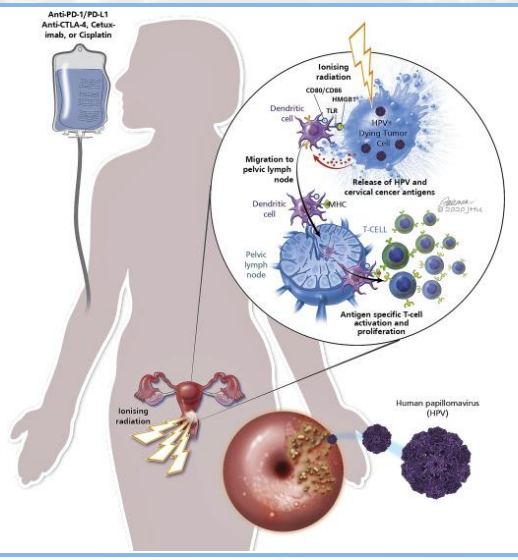
Currently open to accrual at Winship



Second Line Options

Second line treatment options are LIMITED, morbid, biomarker dependent





Pelvic exenteration

- 5-8% postop mortality rate
- Up to 100% complication rate
- Up to 50% cure rate in carefully selected population

Tisotumab Vedotin

- ORR **24%** (95% CI: 16%, 33%)
- Median duration of response was 8.3 months
- Ocular toxicities

Keynote 826

- Pembrolizumab + carboplatin + Taxol +/- bevacizumab
- Median OS 28.6 mo. (CPS ≥1)

Conclusions

- HPV vaccination ***is*** cancer prevention
- In LACC, chemoradiotherapy alone has been standard of care for nearly **27 YEARS**
- Cervical cancer survival rates have not changed over this time
- **Pembrolizumab + Chemoradiotherapy improves overall survival in locally advanced cervical cancer**
- Second line options are limited and can be morbid and toxic

Thank You