Where Science Becomes Hope

PRO: IMMUNOTHERAPY FOR LOCALLY ADVANCED CERVICAL CANCER

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DDHO 2024

EMORY WINSHIP CANCER INSTITUTE
National Cancer Institute-Designated Comprehensive Cancer Center

NCI Designated Comprehensive Cancer Center

Where Science Becomes Hope

No Disclosures

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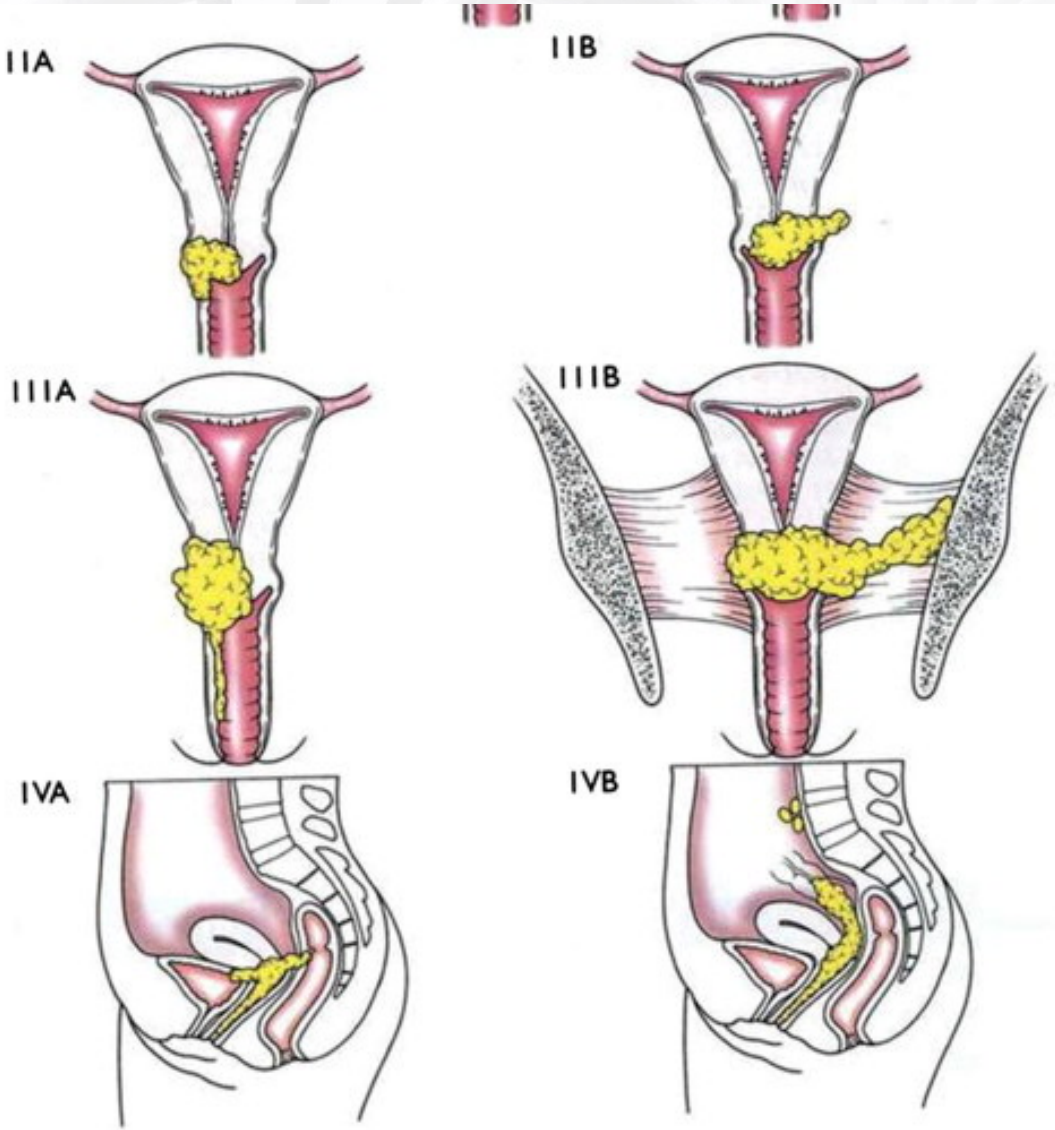
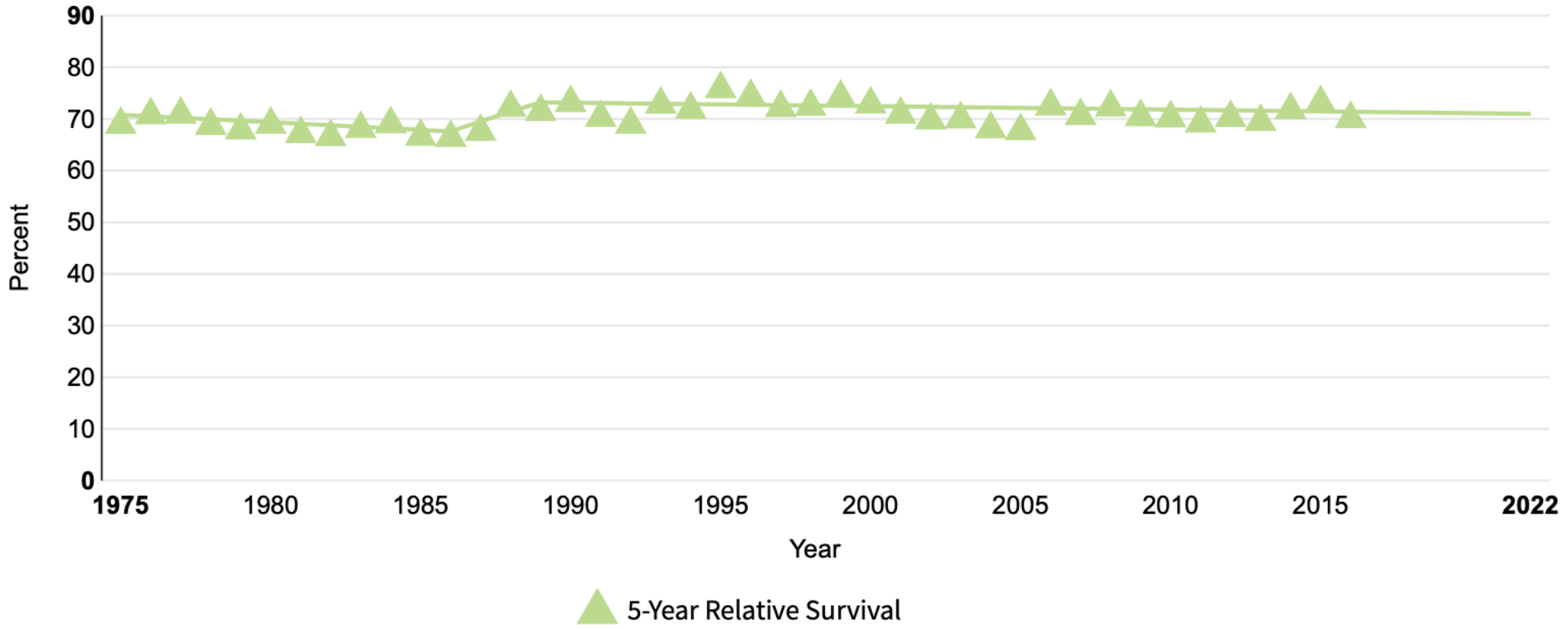
LOCALLY ADVANCED CERVICAL CANCER

- FIGO Stage IIA-IVA
- 40% of all cervical cancer
- 5-year survival: 25-60%
- Chemoradiation has been standard of care for 25 years
- Adjuvant chemotherapy did not improve survival (OUTBACK trial)



LOCALLY ADVANCED CERVICAL CANCER



SEER 8 5-Year Relative Survival Percent from 1975–2016, All Races, Females.

LOCALLY ADVANCED CERVICAL CANCER

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.

LOCALLY ADVANCED CERVICAL CANCER

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Cervical Cancer

NCCN Guidelines
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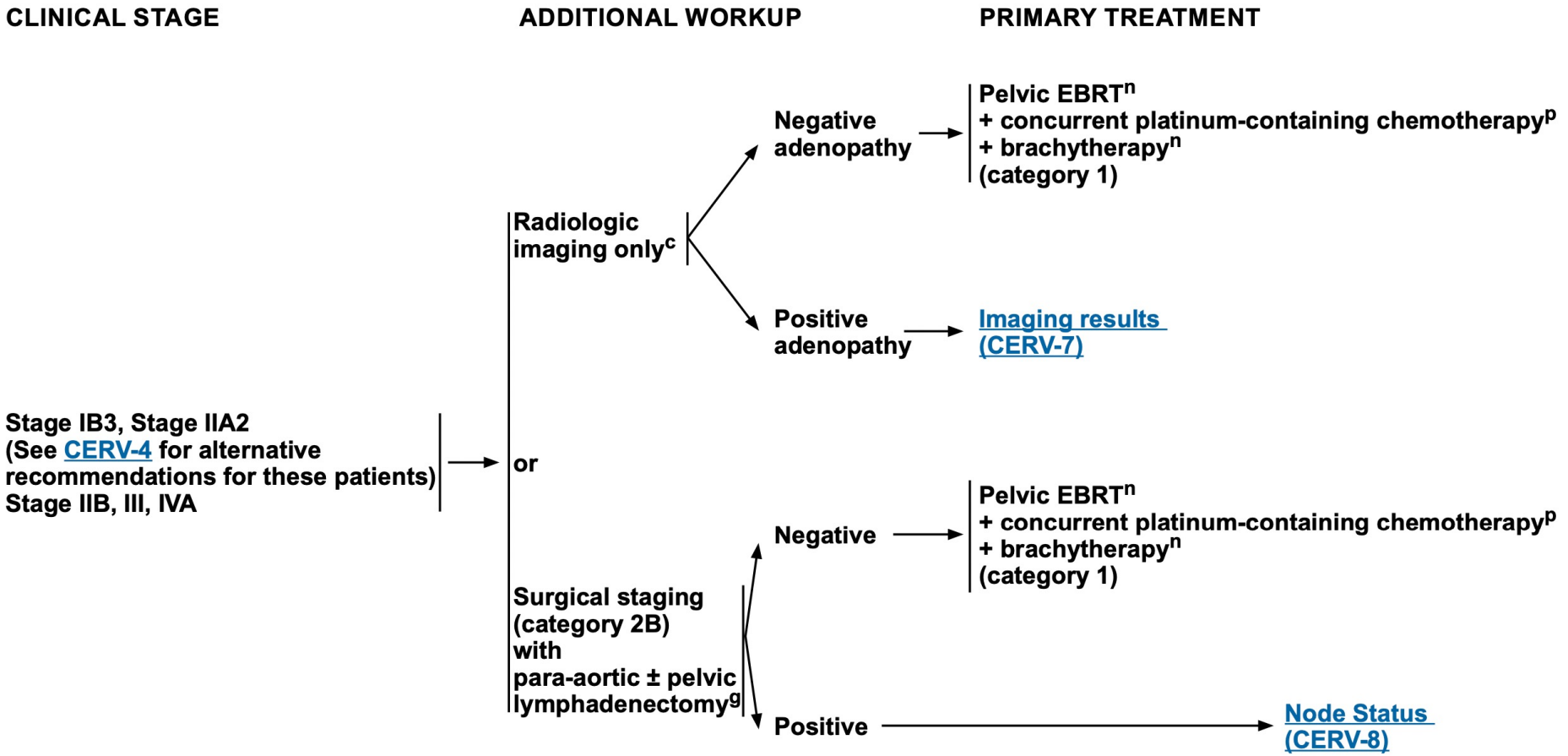

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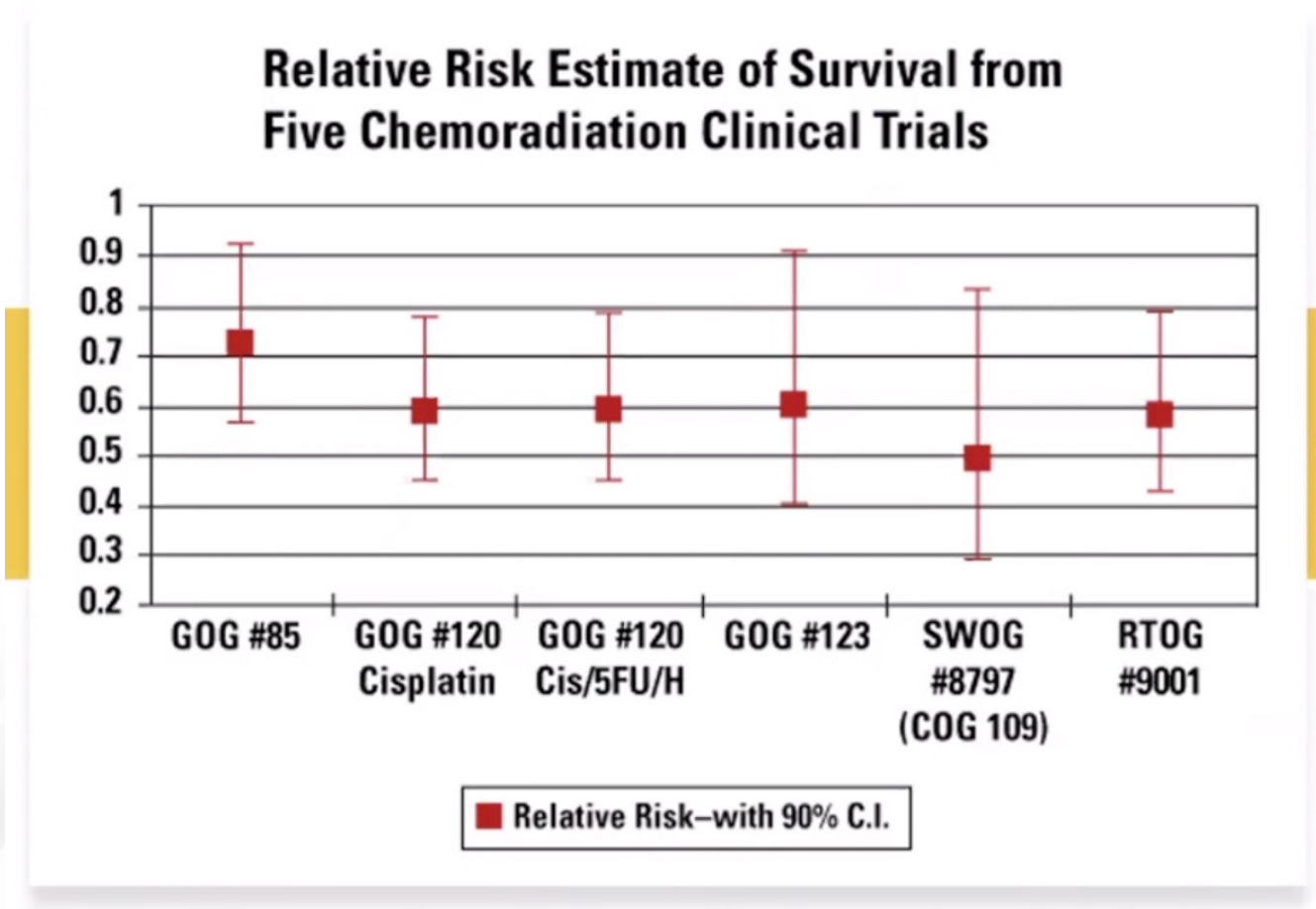


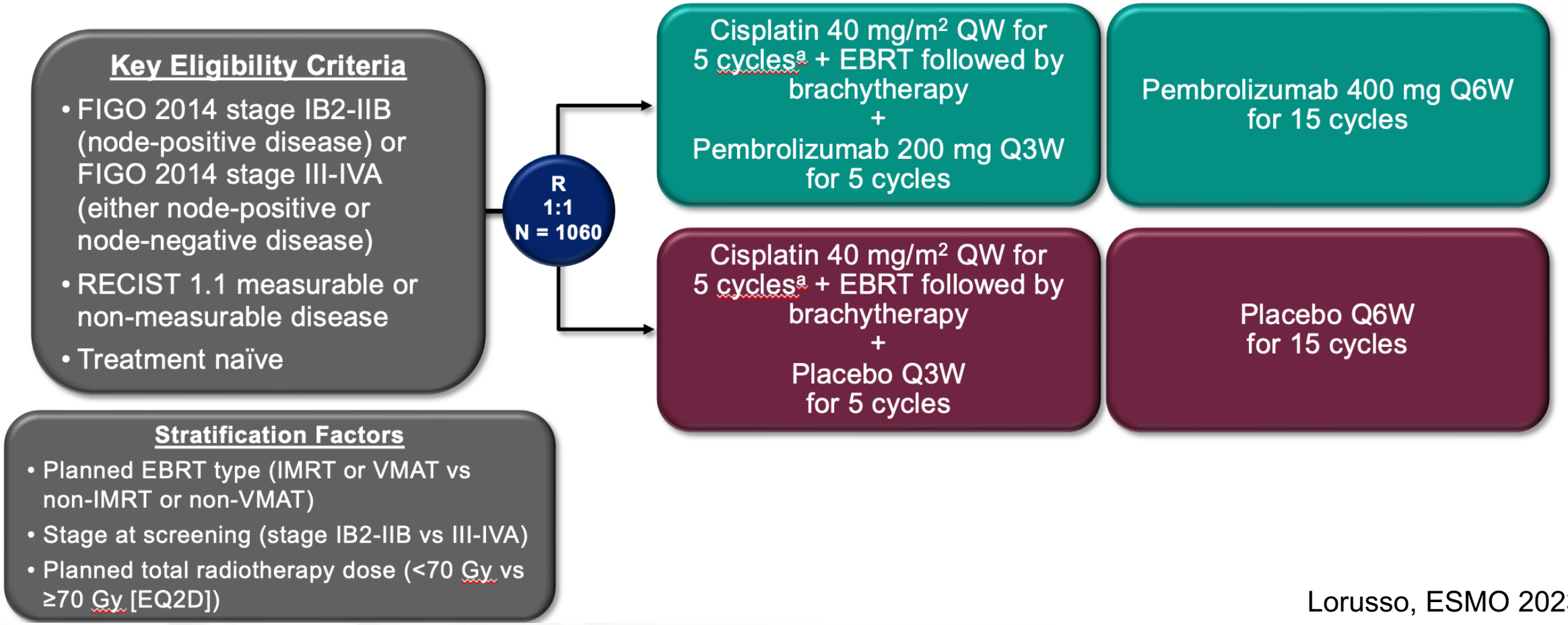
Pivotal, Practice-Changing Trials of Chemoradiation

Risk of Death Decreased by 30-50%

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.

1999 NCI Alert: use combination of chemo + RT instead of RT alone to treat invasive cervical cancer

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



Lorusso, ESMO 2023

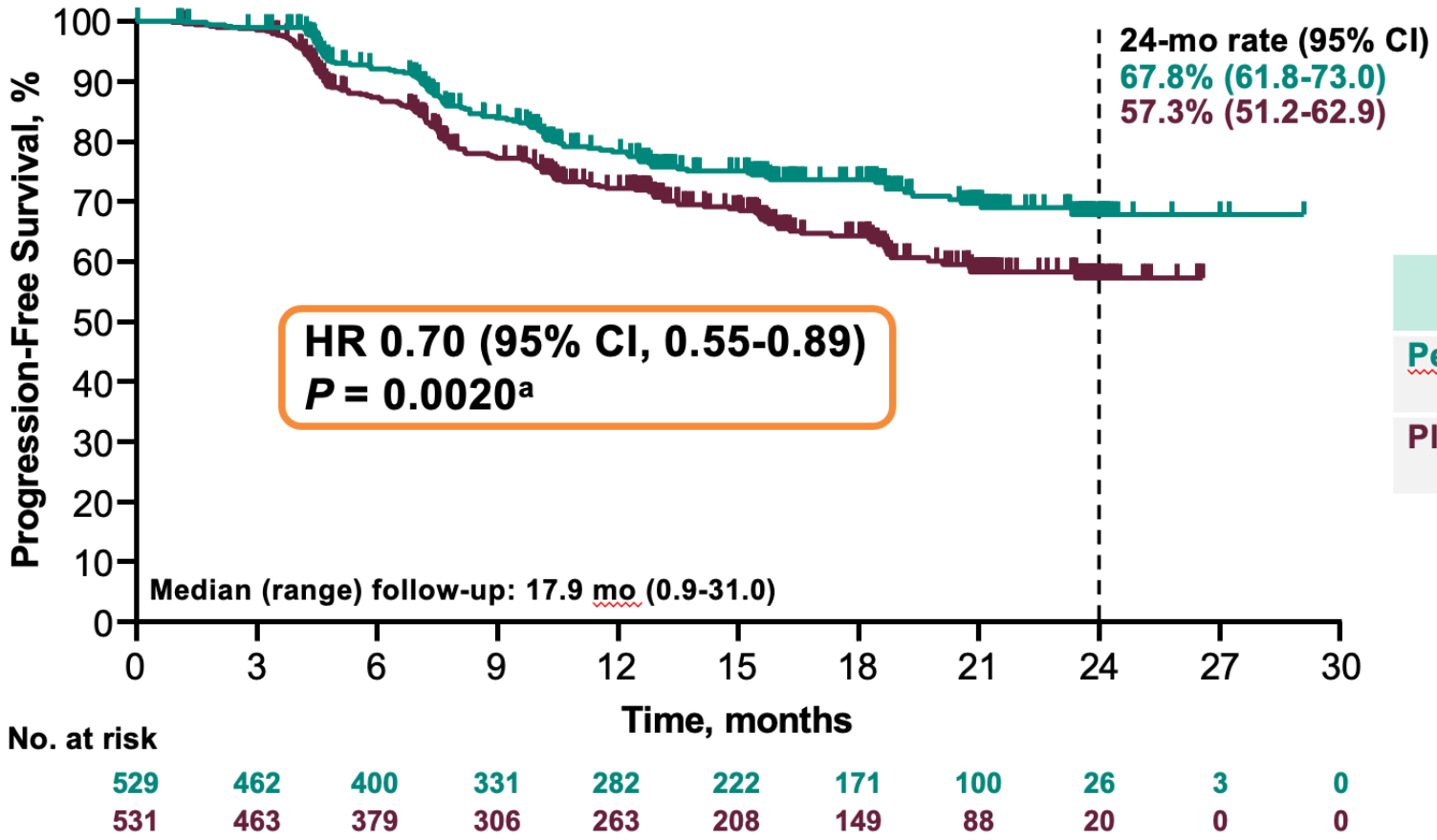
KEYNOTE A18

- FIGO 2014 stage IB2-IIB with + pelvic or para-aortic nodes or FIGO 2014 stage III-IVA with any nodal status
- 52% non-white race/ethnicity
- 95% PDL1 CPS ≥1

- High quality radiation therapy – rigorous plan evaluation process
- 1060 patients
- Accrued over <2 years (2020-2022)
- Co-primary endpoints: PFS and OS

Lorusso, Lancet 2024

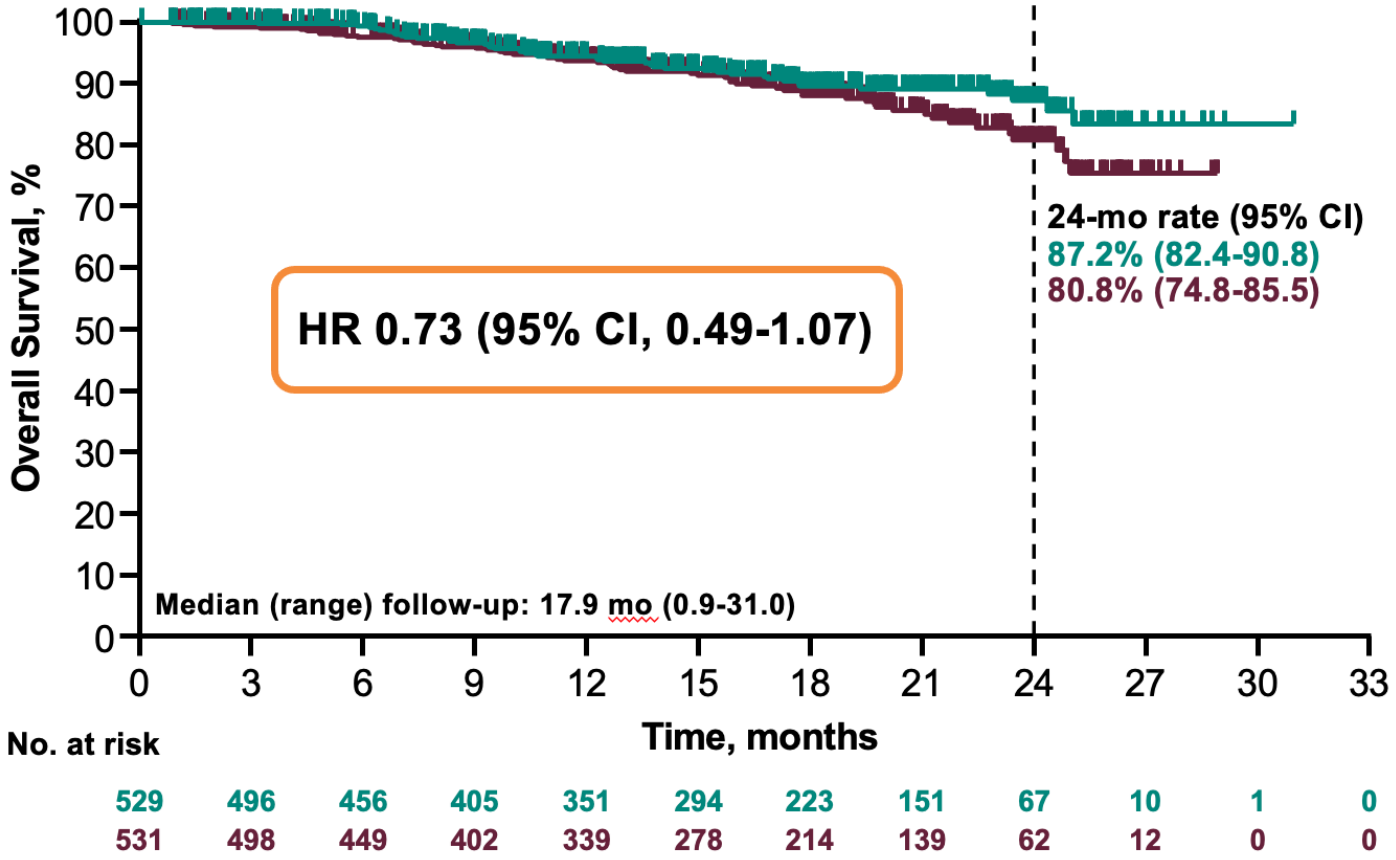
Primary Endpoint: Progression-Free Survival



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	21.7%	NR (NR-NR)
Placebo Arm	29.0%	NR (NR-NR)

Lorusso, ESMO 2023

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]

95% CI 0.49-1.07
BUT data not mature

KEYNOTE A18

January 12, 2024:
FDA approves pembrolizumab plus chemoradiotherapy as treatment for patients with ***FIGO 2014 Stage III-IVA*** *cervical cancer*

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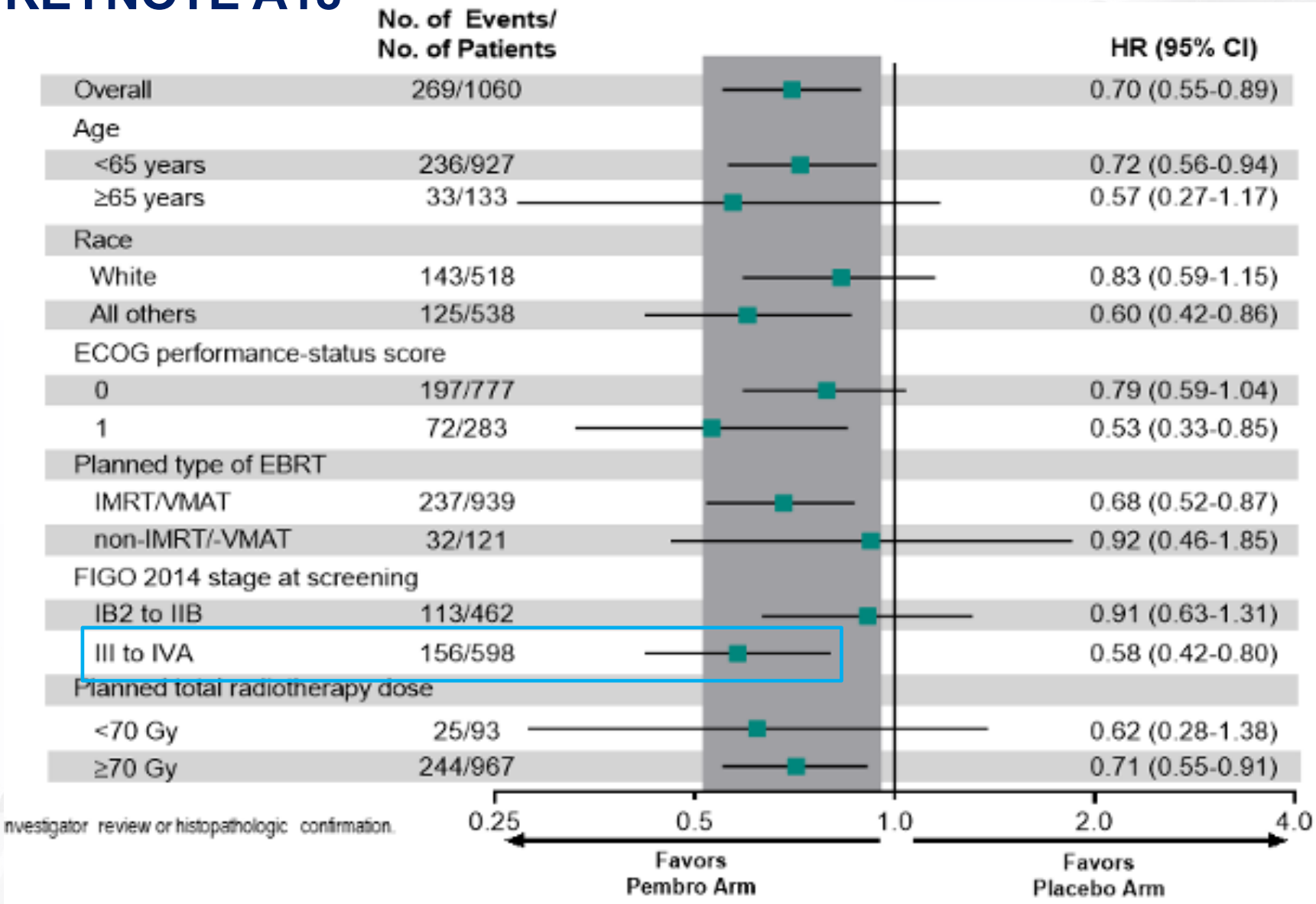


"hypothesis-generating subgroup analyses of both studies (*CALLA & A18*) showed that **patients at the highest risk of progression or death as defined by disease stage derived a greater treatment benefit** "

Lorusso, 2024

KEYNOTE A18

Media > News releases > News release

(pembrolizumab) Plus Chemoradiotherapy (CRT) Significantly Improved Overall Survival (OS) Versus CRT Alone in Patients With Newly Diagnosed High-Risk Locally Advanced Cervical Cancer

March 15, 2024 6:45 am ET

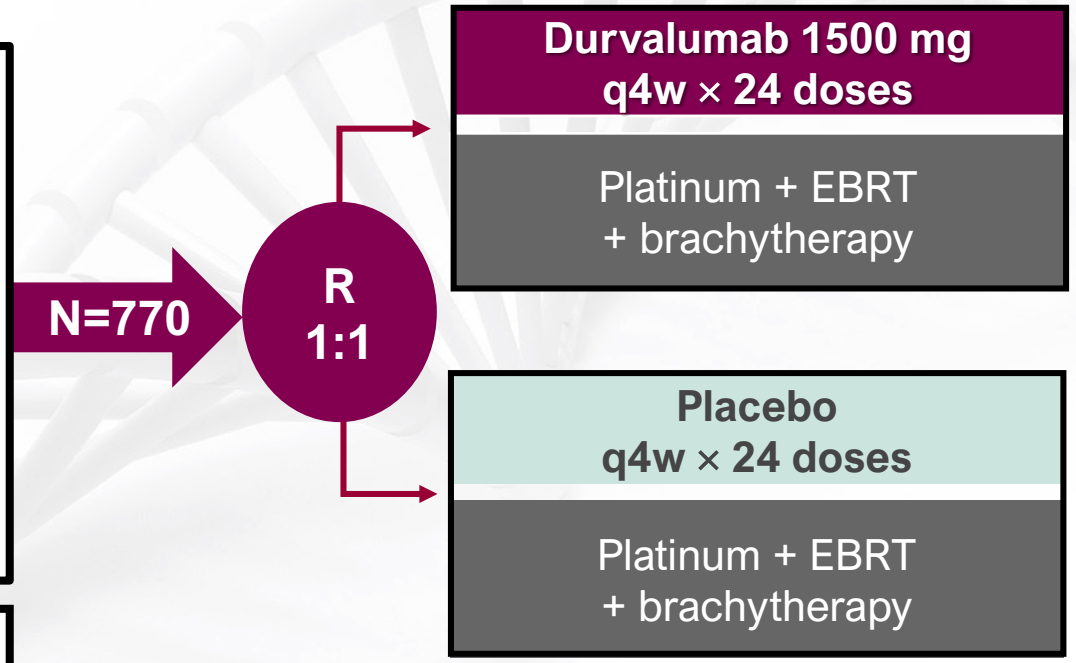
CALLA - CHEMORADIATION +/- DURVALUMAB

Eligible population

- Women aged ≥18 years
- Histologically confirmed cervical adenocarcinoma, squamous carcinoma, or adenosquamous carcinoma
- High-risk LACC (FIGO 2009)
  - Stages IB2 to IIB, node positive (N≥1)
  - Stages IIIA to IVA with any node (N≥0)
- WHO ECOG performance status of 0 or 1

Stratification factors

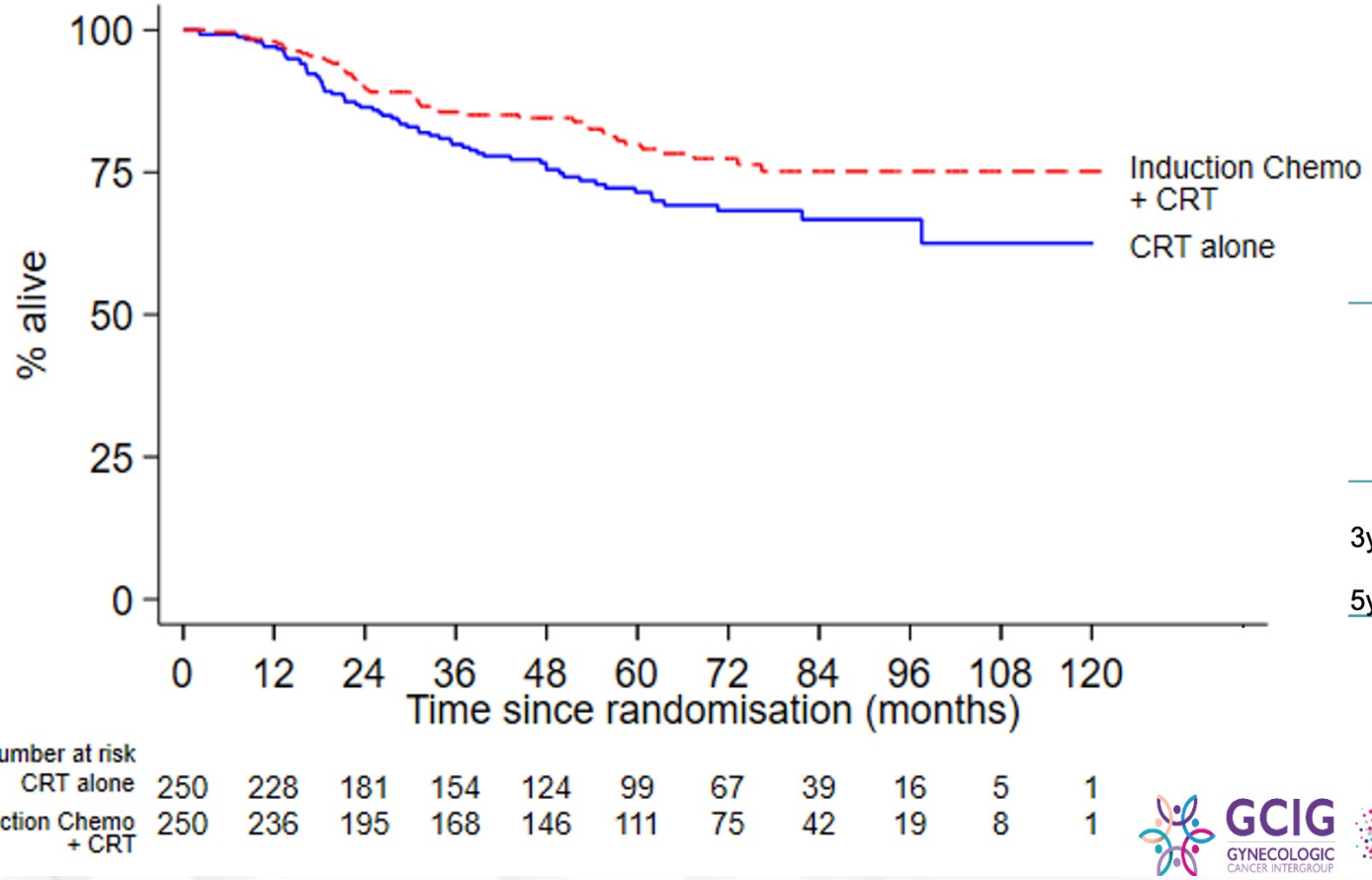
- Disease stage
  - FIGO Stage IB2–IIB and LN+
  - FIGO Stage ≥III and LN–
  - FIGO Stage ≥III and LN+
- Region of world



Negative trial
-PD-L1 inhibitor
-Lower risk population (1 pelvic node)
-Different geographic distribution
-N=770

INTERLACE - CHEMORADIATION +/- NACT

INTERLACE Overall Survival (median FU 64m)



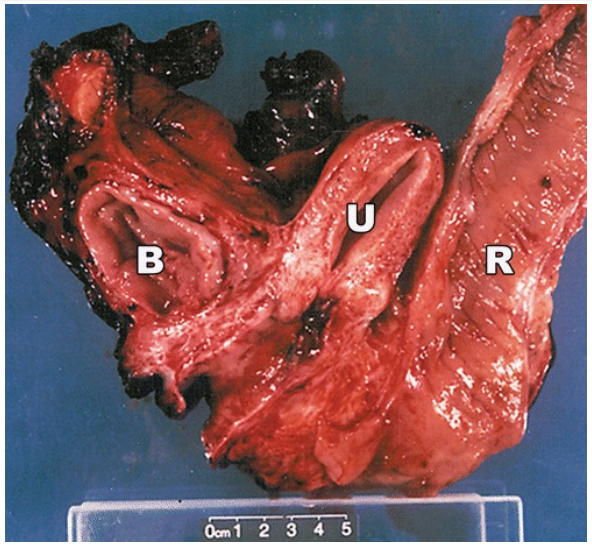
109 deaths
HR 0.61;95% CI: 0.40-0.91
P=0.04

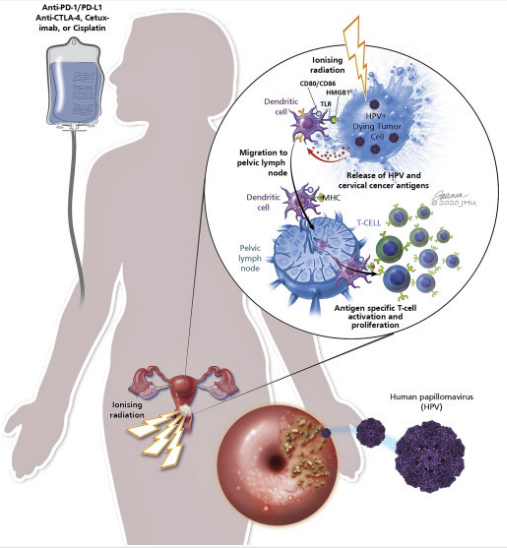
	Induction Chemo + CRT (n=250)	CRT alone (n=250)
3yr OS	86%	80%
5yr OS	80%	72%

- **IB1 node+, IB2,** II, IIIB, IVA (NO + PA nodes)
- Imrpoved OS with induction chemotherapy
- 500 patients **from 2012-2022**
- **Many did not get IMRT**
- Hasn't been published…

McCormack M et al. *ESMO* 2023

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 mos (CPS ≥1)

CONCLUSIONS

- Chemoradiation has been standard of care for **25 YEARS**
- Cervical cancer survival rates have not changed over this time
- pembrolizumab + chemoradiation improves overall survival

- Second line options are limited and can be morbid and toxic
  - (although now patients will not be IO-naïve…fewer options in second line?)
- May be most beneficial in patients with bulky disease - FDA approval
- Not all IO – CALLA trial
- Global implications – induction chemo may be more accessible