UC San Diego Health

Updates on the Cervical Cancer Landscape

Pratibha Sareen Binder

Wednesday, January 15, 2024

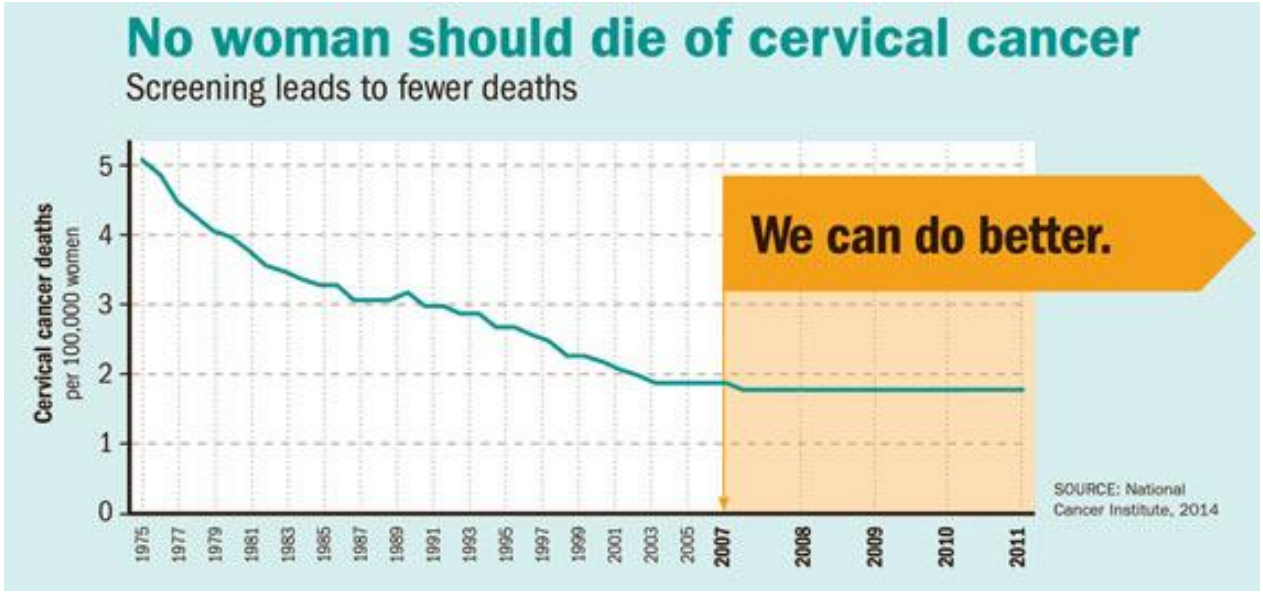
Our Agenda

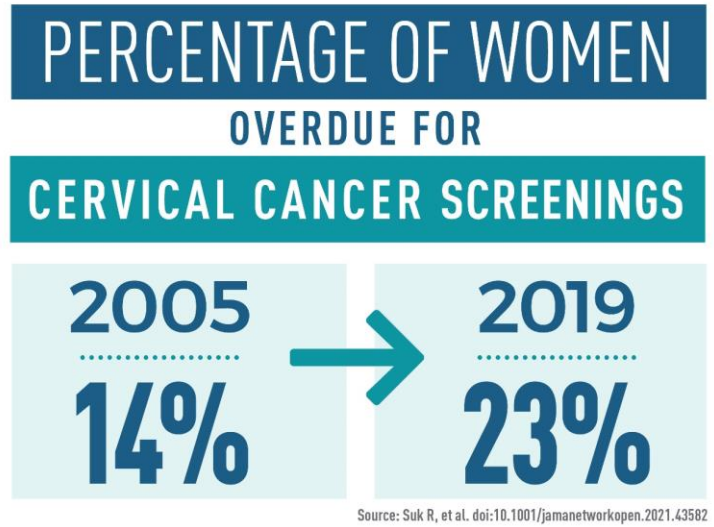
- *Happy Cervical Cancer Awareness Month!*
- Overview
  - The Cervical Cancer Landscape
  - The Cervical Cancer Burden in San Diego County
- Treating Cervical Cancer in 2025
  - Updates to Treatment: New Standards of Care
  - Promising Clinical Trials
- Q&A
- Closing and Thank You!

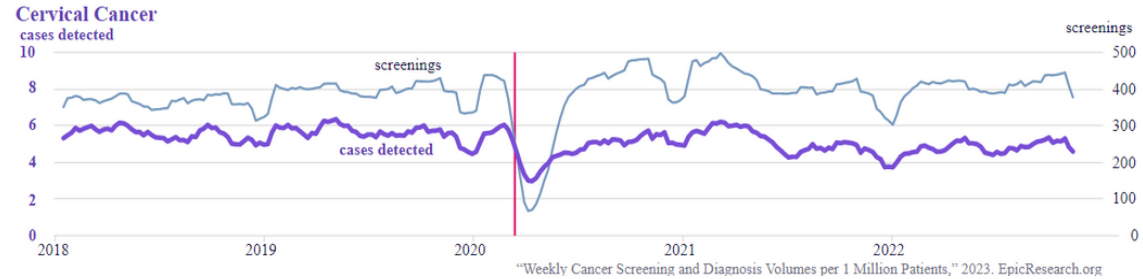
Overview: The Cervical Cancer Landscape

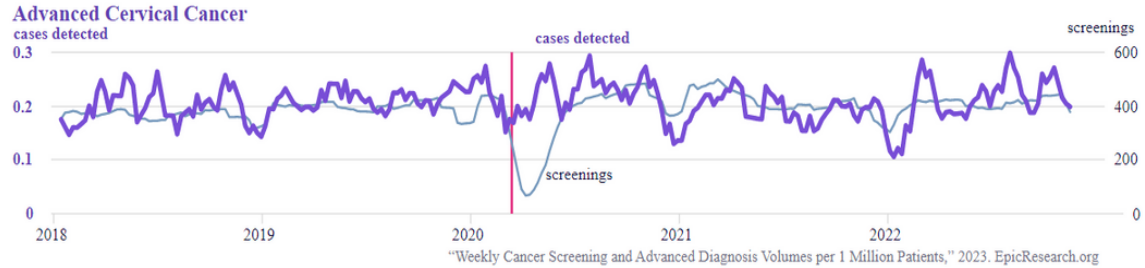
Happy Cervical Cancer Awareness Month 2025!

- Death rates from cervical cancer (CC) have dropped significantly in the last 40 years due to regular Pap tests - finding cervical pre-cancer before it turns into cancer.
- But concerningly, CC incidence and death rates in the US have stagnated, and in some regions, increased, in recent years
- In a study published in the *International Journal of Gynecological Cancer*, almost **30,000** individuals were diagnosed with late-stage cervical cancer between 2001 to 2018
    - **Estimated 2024 Diagnoses**: 13,820 [ACS] (13,960 in 2023)
    - **Estimated 2024 Deaths**: 4,360 [ACS] (4310 in 2023)









"IT MIGHT TAKE YEARS TO FULLY REALIZE THE IMPACT OF MISSED SCREENINGS"

Alban C, Sahakian S, Allen S, Stamp T. Missed Cancer Screenings Not Yet Associated with Increased Cancer Rates or Severity. Epic Research. https://epicresearch.org/articles/missed-cancer-screenings-not-associated-with-increased-cancer-rates-or-severity. Accessed on January 15, 2025.

Overview: The Cervical Cancer Burden in San Diego County

2020 Statistics [California Cancer Registry]

- 111 cases diagnosed in 2020
- 38% of cases in Hispanic/Latine individuals
- 15% in Asian/Pacific Islander individuals
- 74% of cases were in individuals aged 18-64; 26% were aged 65+

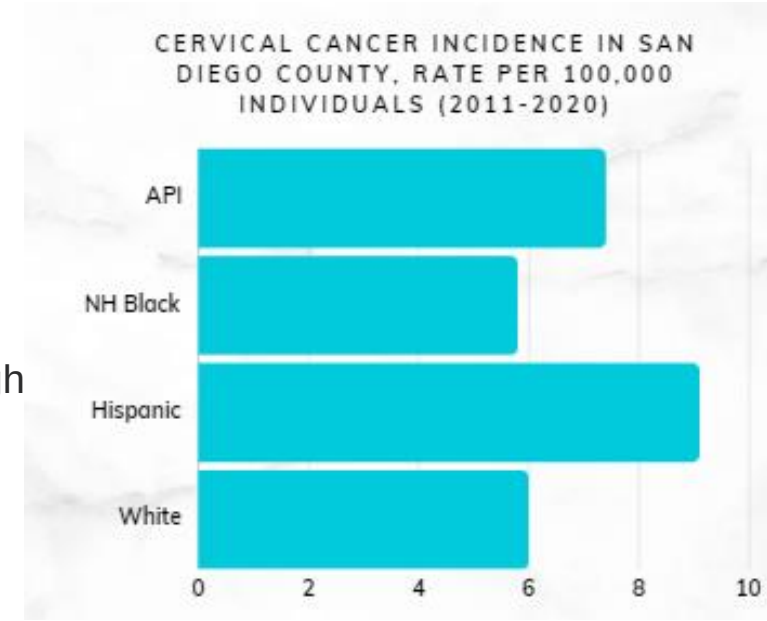
2021 Statistics

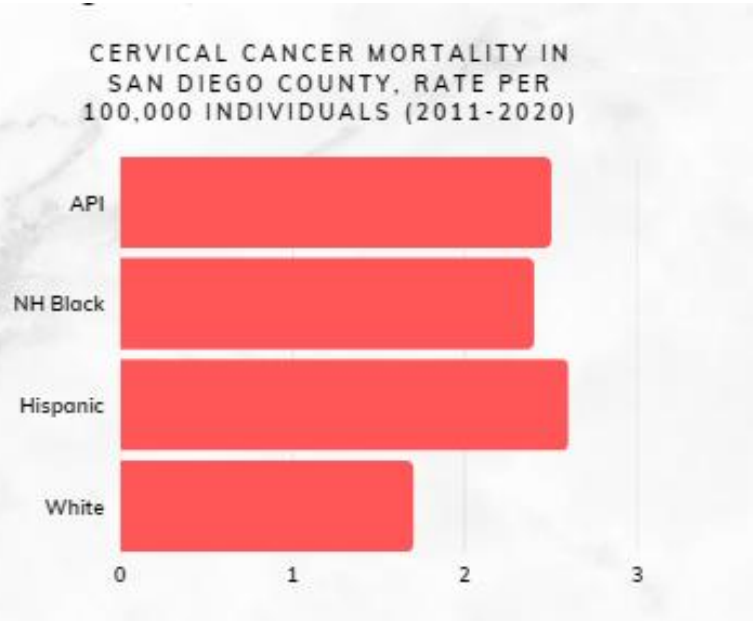
- 115 cases in 2021
- 45% of cases in Hispanic/Latine individuals (up from 38%)
- 11% in Asian/Asian American individuals (down from 15%)
- **85% of cases were in ages 18-64**; 15% were aged 65+

California Cervical Cancer Screening Rate: 82%

NHC 2022 Cervical Cancer Screening Rate: 62%

*Although cases were not high enough to determine local incidence and mortality rates, national data shows American Indian and Alaska Natives are nearly 2x as likely to develop cervical cancer compared to white women and 4x as likely to die from it.





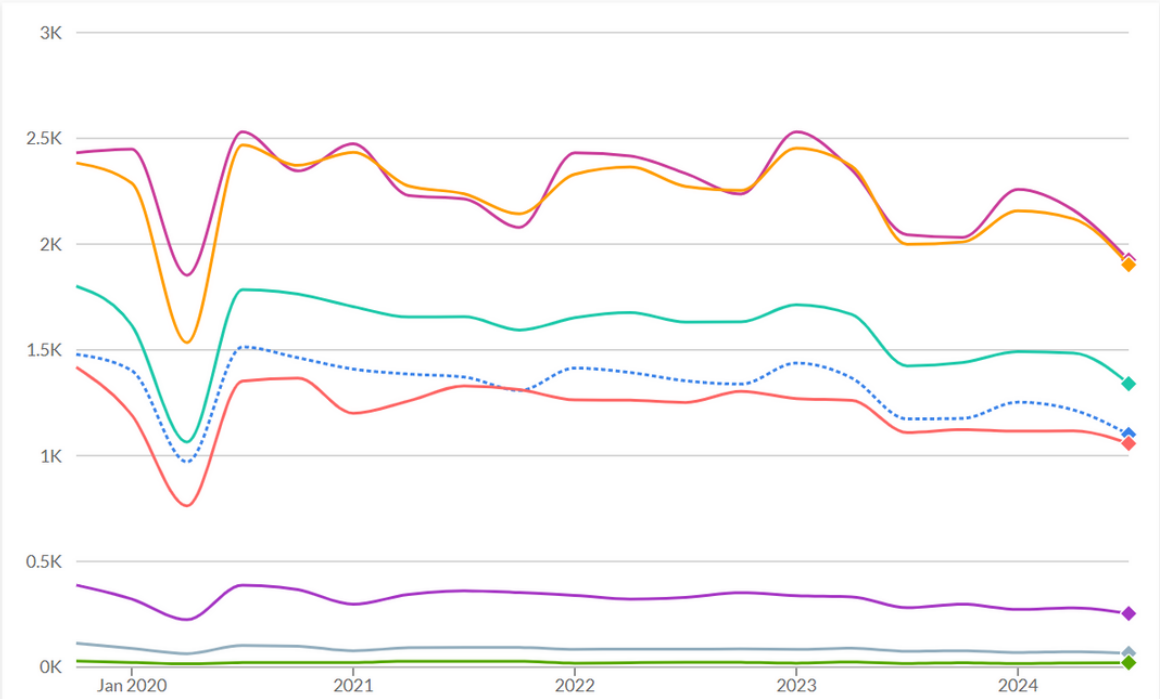
*Current data sets do not have a Middle East and North African ethnicity designation, potentially masking disparities.

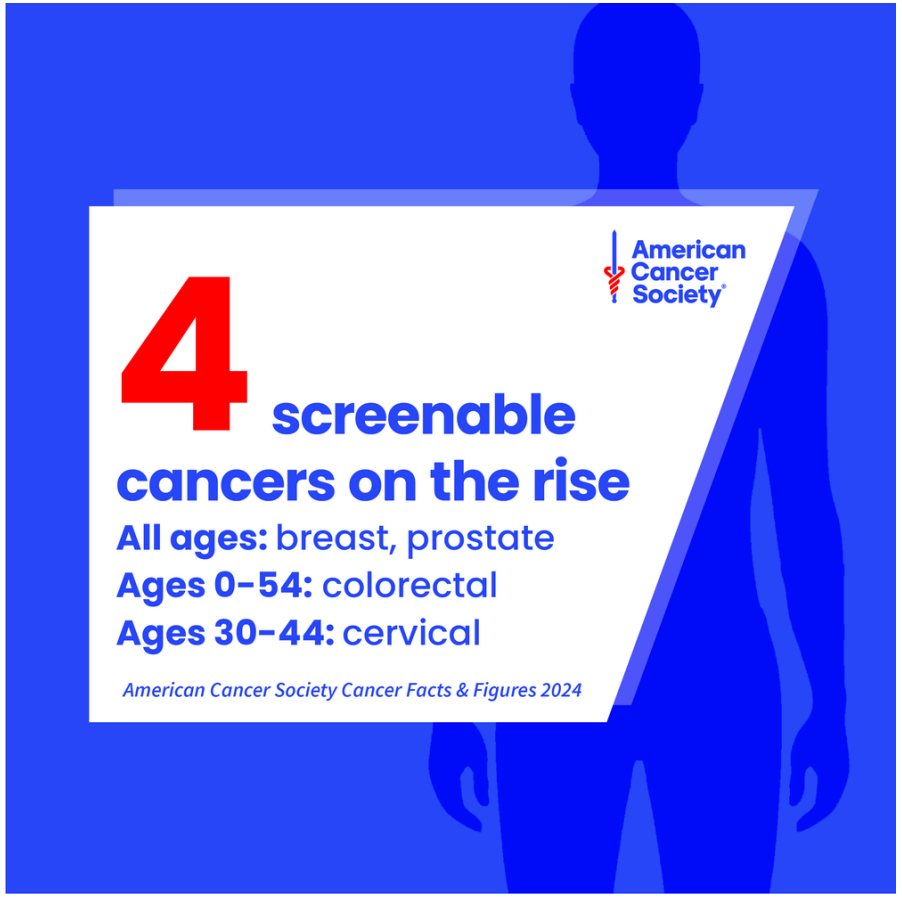
Overview: Cervical Cancer screening rate is decreasing

Cervical Cancer Screenings
Q3 2024

1.1k 18-85+	1.93k 18-34
1.9k 35-44	1.34k 45-54
1.06k 55-64	254 65-74
65.7 75-84	21.4 85+

Quarterly rates of screenings per 100,000 patients.





Agenda

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- Cervical Cancer
  - Is conservative surgery acceptable? SHAPE and ROCC trials
  - Immunotherapy in front line treatment of metastatic or recurrent cervical cancer
  - Introduction of Antibody Drug Conjugates to the treatment of cervical cancer
  - Clinical trials at UC San Diego

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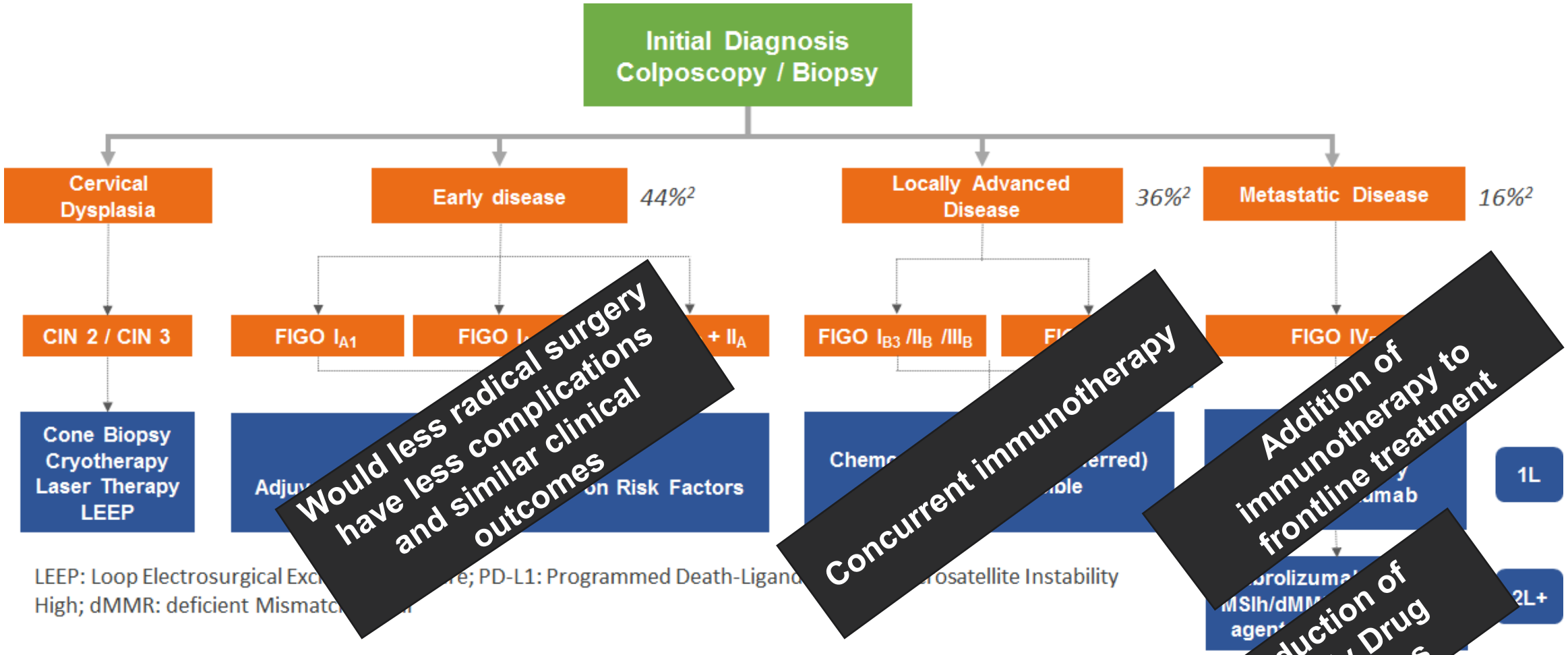
Cervical cancer treatment paradigm



LEEP: Loop Electrosurgical Exci e; PD-L1: Programmed Death-Ligand rosatellite Instability High; dMMR: deficient Mismatc

[1] NCCN Cervical Cancer Guidelines v2.2019
[2] SEER Cancer Stat Facts: Cervical Cancer. National Cancer Institute. Bethesda, MD

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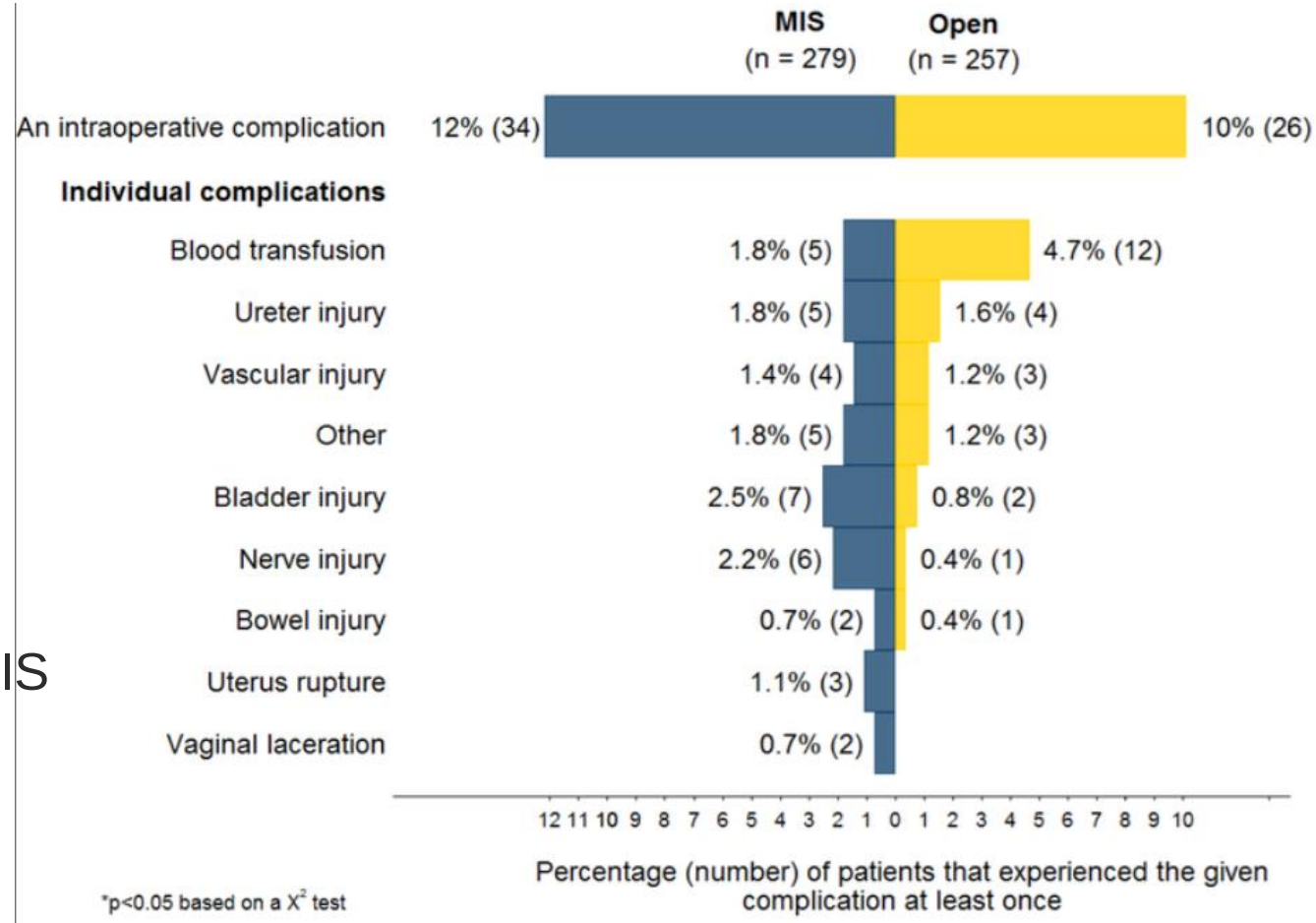
Radical Hysterectomy – complication rates (LACC trial: open vs. MIS)

- Intra-operative (1-5%):
  - Blood transfusion 2-5%
  - Ureteral injury 1-2%
  - Bladder injury 0.8-2.5%, higher in MIS
  - Nerve injury 0.4-2.2%, higher in MIS
  - Vascular injury 1-2%
- Post-operative (1-5%):
  - Pain 6.8-9.3%, higher in open
  - Anemia 6%
  - Delayed bladder function 5%
  - Vaginal vault complication 0.8-4%, higher in MIS
  - GU fistula/stricture 2-3%
  - Neuropathy 0.8-2.2%
  - SSI 1-2%
  - Wound complication: 1-6%, higher in open
  - Lymphedema/lymphocele 1%



Obermair et al. AJOG 2020;223(5):757

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Defining a low-risk group

Author	Year	Low-risk criteria	N	Parametrial involvement in low-risk group (%)
Kinney [13]	1995	Squamous histology only, tumor <2 cm, no LVSI*	83	0.0%
Covens [14]	2002	All histologies, tumor <2 cm, DOI** <10 mm, negative pelvic lymph nodes	536	0.6%
Stegeman [15]	2007	Squamous, adenocarcinoma, adenosquamous or clear cell histology, tumor <2 cm, DOI** <10 mm, no LVSI*, negative pelvic lymph nodes	103	0.0%
Wright [16]	2008	All histologies, tumor <2 cm, no LVSI*, negative pelvic lymph nodes	270	0.4%
Frumovitz [19]	2009	Squamous, adenocarcinoma or adenosquamous histology, tumor <2 cm, no LVSI*	125	0.0%

*LVSI: lymphvascular space involvement
**DOI: depth of invasion

Retrospective studies **N=1117** **< 1%**

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Defining a low-risk group

- Covens et al 2002 (PMID 11748991)
  - –842 pts w/ radical sx for clinical stage IA1/2 and IB1 cervical cancer
  - –6% positive LN rate; 4% positive parametrial rate
  - **–Subgroup n=536 w/ neg LN, <2cm tumor, DOI < 10 mm -> 0.6% +parametria**
- Wright et al 2007 (PMID – 17654664)
  - –594 pts w/ radical sx +PND from 1989-2005
  - –11% +parametria: assoc w/ hist, adv gr, deep invasion, LVSI, large tumor, adv stage, uterine/vag involvement, +P/PALN AND assoc w/ incr recurr & decre DFS/OS
  - **–Subgroup of neg nodes, no LVSI, tumor <2cm -> 0.4% +parametria**
- Frumovitz et al 2009 (PMID – 19546764)
  - –350 pts w/ radical sx +PND from 1990-2006
  - –7.7% +parametria: assoc w/ >2cm tumor, higher gr, LVSI and +PLN
  - **–Subgroup n=125 w/ no LVSI, tumor <=2cm, any hist, all gr -> 0% +parametria**

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SHAPE trial (Canadian Cancer Trials Group)

- **CCTG CX.5-SHAPE** trial enrolled 700 patients with low-risk SCC, AC, ASC of the cervix and randomly assigned them to RH or SH plus PLND
- **Population:** Low-risk disease = stage IA2 and IB1 with lesions < 2 cm of HPV-related cervical cancer histology. Limited stromal invasion was allowed (< 10 mm on LEEP/cone and < 50% depth on MRI)
- **Primary outcome:** 3-yr Pelvic recurrence rate
- **Secondary outcome:** Acute surgery-related adverse events within 4 weeks of surgery and >/= 4 weeks after surgery
- Other outcomes: 3-year extra-pelvic recurrence-free survival and overall survival

SCC: squamous cell carcinoma; AC: adenocarcinoma; ASC: adenosquamous carcinoma.
RH: radical Hysterectomy; SH: simple hyst; PLND: Pelvic lymph node dissection

Plante M, et al. 2023 ASCO annual meeting

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SHAPE trial (Canadian Cancer Trials Group)

Low-risk cervical cancer as defined by:

- squamous cell, adenocarcinoma, adenosquamous carcinoma
- Stage IA2 and modified IB1
- < 10mm stromal invasion on LEEP/cone
- < 50% stromal invasion on MRI
- max dimension of ≤ 20 mm
- Grade 1-3 or not assessable

RANDOMIZE

↗ ARM 1 (Control)
Radical Hysterectomy*

↘ Arm 2 (Experimental)
Simple Hysterectomy*

→→Pelvic relapse

* Regardless of treatment assignment, surgery will include pelvic lymph node dissection with optional sentinel lymph node (SN) mapping. If SN mapping is to be done, the mode is optional, but the laparoscopic approach is preferred.

Planned sample size: 700 (non-inferiority at 0.05 level with 80% power)

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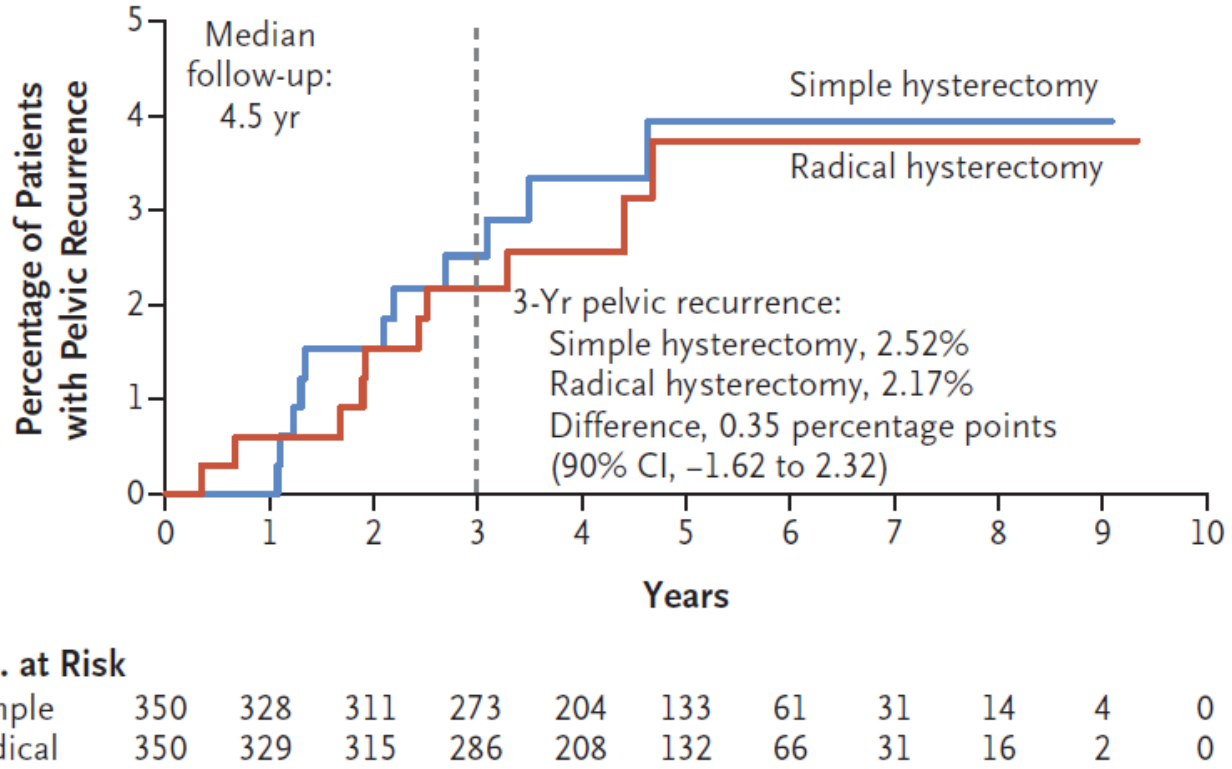
SHAPE trial (Canadian Cancer Trials Group)



No. at Risk

Simple	350	328	311	273	204	133	61	31	14	4	0
Radical	350	329	315	286	208	132	66	31	16	2	0

Figure 1. Kaplan–Meier Curves for Pelvic Recurrence.

- Among 700 patients included in the intent-to-treat analysis, 11 pelvic recurrences occurred in the simple hysterectomy group and 10 in the radical hysterectomy group after median follow-up times of 4.5 and 4.6 years, respectively.
- The incidence of pelvic recurrence at 3 years was 2.52% in the simple hysterectomy group and 2.17% in the radical hysterectomy group.
- The difference was 0.35 percentage points (90% confidence interval, −1.62 to 2.32); the upper limit of the confidence interval (2.32) was consistent with noninferiority of simple hysterectomy.
- 3-year extra-pelvic recurrence-free survival (98.1% vs 99.7%) and overall survival (99.1% vs 99.4%) were also similar between the simple and radical hysterectomy approaches

Plante M, et al. NEJM 2024;390:819-29.

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SHAPE trial (Canadian Cancer Trials Group)

Table 3. Sites of Disease Recurrence and Causes of Death.*

Event	Intention-to-Treat Analysis			Per-Protocol Analysis		
	Simple Hysterectomy (N=350)	Radical Hysterectomy (N=350)	Hazard Ratio (95% CI)	Simple Hysterectomy (N=317)	Radical Hysterectomy (N=312)	Hazard Ratio (95% CI)
	number (percent)			*number (percent)*		
Disease recurrence†	15 (4.3)	10 (2.9)	1.54 (0.69–3.45)	12 (3.8)	10 (3.2)	1.19 (0.51–2.77)
Pelvic recurrence	11 (3.1)	10 (2.9)	1.12 (0.47–2.67)	10 (3.2)	10 (3.2)	1.01 (0.42–2.44)
Vaginal vault	9 (2.6)	8 (2.3)		9 (2.8)	8 (2.6)	
Parametrium	1 (0.3)	0		1 (0.3)	0	
Lower paraaortic and common iliac lymph nodes	1 (0.3)	0		0	0	
Central pelvis	0	1 (0.3)		0	1 (0.3)	
Pelvic sidewall	0	1 (0.3)		0	1 (0.3)	
Extrapelvic recurrence	7 (2.0)	2 (0.6)	3.82 (0.79–18.4)	4 (1.3)	2 (0.6)	2.03 (0.37–11.2)
Abdomen	2 (0.6)	0		0	0	
Paraaortic lymph nodes	2 (0.6)	2 (0.6)		1 (0.3)	2 (0.6)	
Supraclavicular lymph nodes	1 (0.3)	0		1 (0.3)	0	
Interaortocaval and obturator lymph nodes and vaginal vault	1 (0.3)	0		1 (0.3)	0	
Vaginal introitus	1 (0.3)	0		1 (0.3)	0	
Death	7 (2.0)	7 (2.0)	1.09 (0.38–3.14)	3 (0.9)	4 (1.3)	0.71 (0.16–3.21)
Cervical cancer	4 (1.1)	1 (0.3)		2 (0.6)	1 (0.3)	
Other primary cancer	1 (0.3)	3 (0.9)		0	2 (0.6)	
Other medical condition	2 (0.6)	3 (0.9)		1 (0.3)	1 (0.3)	

- Hazard ratios are from stratified proportional-hazards models for secondary time-to-event outcomes (tests for superiority).

- The intention-to-treat analysis included all patients who underwent randomization; the per-protocol analysis included all patients who met the eligibility criteria at the time of randomization, underwent randomization, underwent surgery, and had postsurgical findings that did not meet criteria for exclusion on the basis of disease severity.

Plante M, et al. NEJM 2024;390:819-29.

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SHAPE trial (Canadian Cancer Trials Group)

Outcome	Simple Hysterectomy (N=338)	Radical Hysterectomy (N=344)	P Value
	number (percent)		
Intraoperative injury			
Any intraoperative injury	24 (7.1)	22 (6.4)	0.77
Bladder	3 (0.9)	9 (2.6)	0.14
Ureter	3 (0.9)	5 (1.5)	0.73
Nerve	5 (1.5)	2 (0.6)	0.28
Bowel	2 (0.6)	2 (0.6)	1.00
Vein	4 (1.2)	1 (0.3)	0.21
Other	7 (2.1)	3 (0.9)	0.22
Surgery-related adverse event >4 wk after surgery†			
Any adverse event	181 (53.6)	208 (60.5)	0.08
Abdominal pain	36 (10.7)	47 (13.7)	0.24
Constipation	13 (3.8)	19 (5.5)	0.37
Fatigue	19 (5.6)	28 (8.1)	0.23
Paresthesia	17 (5.0)	22 (6.4)	0.51
Peripheral sensory neuropathy	21 (6.2)	13 (3.8)	0.16
Urinary incontinence	16 (4.7)	38 (11.0)	0.003
Urinary retention	2 (0.6)	34 (9.9)	<0.001
Dyspareunia	21 (6.2)	19 (5.5)	0.75
Pelvic pain	23 (6.8)	17 (4.9)	0.33
Lymphedema	35 (10.4)	36 (10.5)	1.00
Hot flashes	14 (4.1)	20 (5.8)	0.38

SH had significantly less acute surgery-related adverse events within 4 weeks of surgery compared with RH (42.6% vs 50.6%; *P* = .04).

Plante M, et al. NEJM 2024;390:819-29.

ROCC trial

ROCC/GOG-3043: A randomized non-inferiority trial of robotic versus open radical hysterectomy for early-stage cervical cancer.

ROCC is a multi-center, prospective, randomized, non-inferiority trial. The primary objective is to determine whether robotic-assisted (RBT) radical hysterectomy is not inferior to abdominal (OPEN) approach with respect to 3-year disease-free survival (DFS). Secondary objectives include DSS, OS, patterns of recurrence, peri- and postoperative complications, long-term morbidity, impact on patient-reported outcome (PRO) measures and development of lower extremity lymphedema (LEL).

Key inclusion criteria include patients with histologically confirmed adenocarcinoma, squamous cell, and adenosquamous cell carcinoma of FIGO 2018 stage IA2-IB2

OPEN AND ENROLLING AT UCSD

Bixel KL, et al. 2022 ASCO annual meeting

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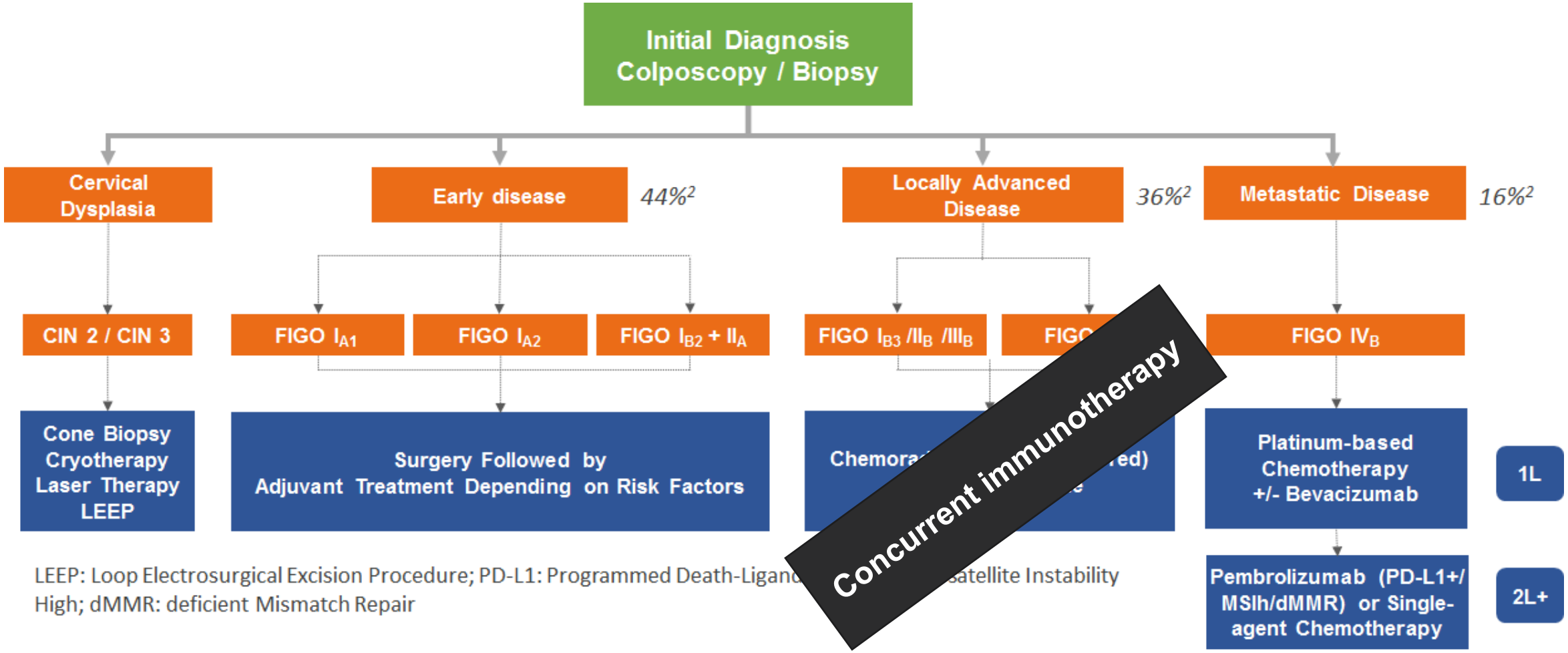
Cervical cancer treatment paradigm



LEEP: Loop Electrosurgical Excision Procedure; PD-L1: Programmed Death-Ligand ... Satellite Instability High; dMMR: deficient Mismatch Repair

[1] NCCN Cervical Cancer Guidelines v2.2019
[2] SEER Cancer Stat Facts: Cervical Cancer. National Cancer Institute. Bethesda, MD

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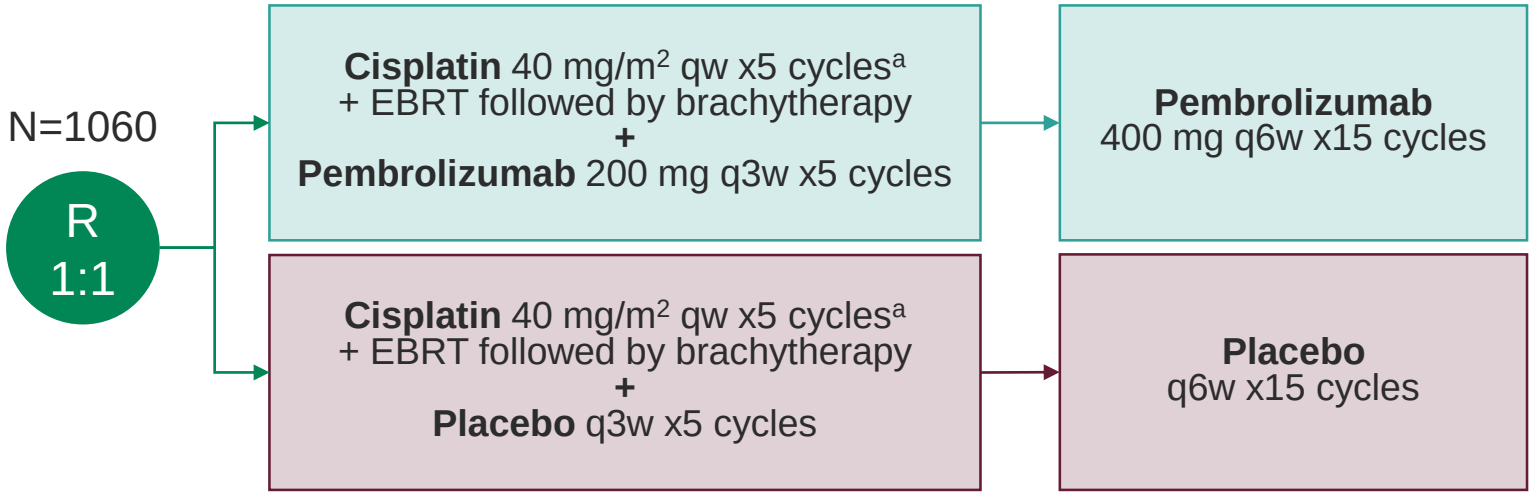
KEYNOTE-A18: Phase 3 Trial of Pembrolizumab + Chemoradiotherapy for High-Risk Locally Advanced Cervical Cancer

- FIGO 2014 stage IB2-IIB (node-positive) or stage III-IVA (node-positive or node-negative)
- RECIST 1.1 measurable or non-measurable disease
- Treatment naïve



- Stratification factors: planned EBRT type (IMRT or VMAT vs non-IMRT or non-VMAT), stage at screening (stage IB2-IIB vs III-IVA), and planned total radiotherapy dose (<70 Gy vs ≥70 Gy [EQ2D])

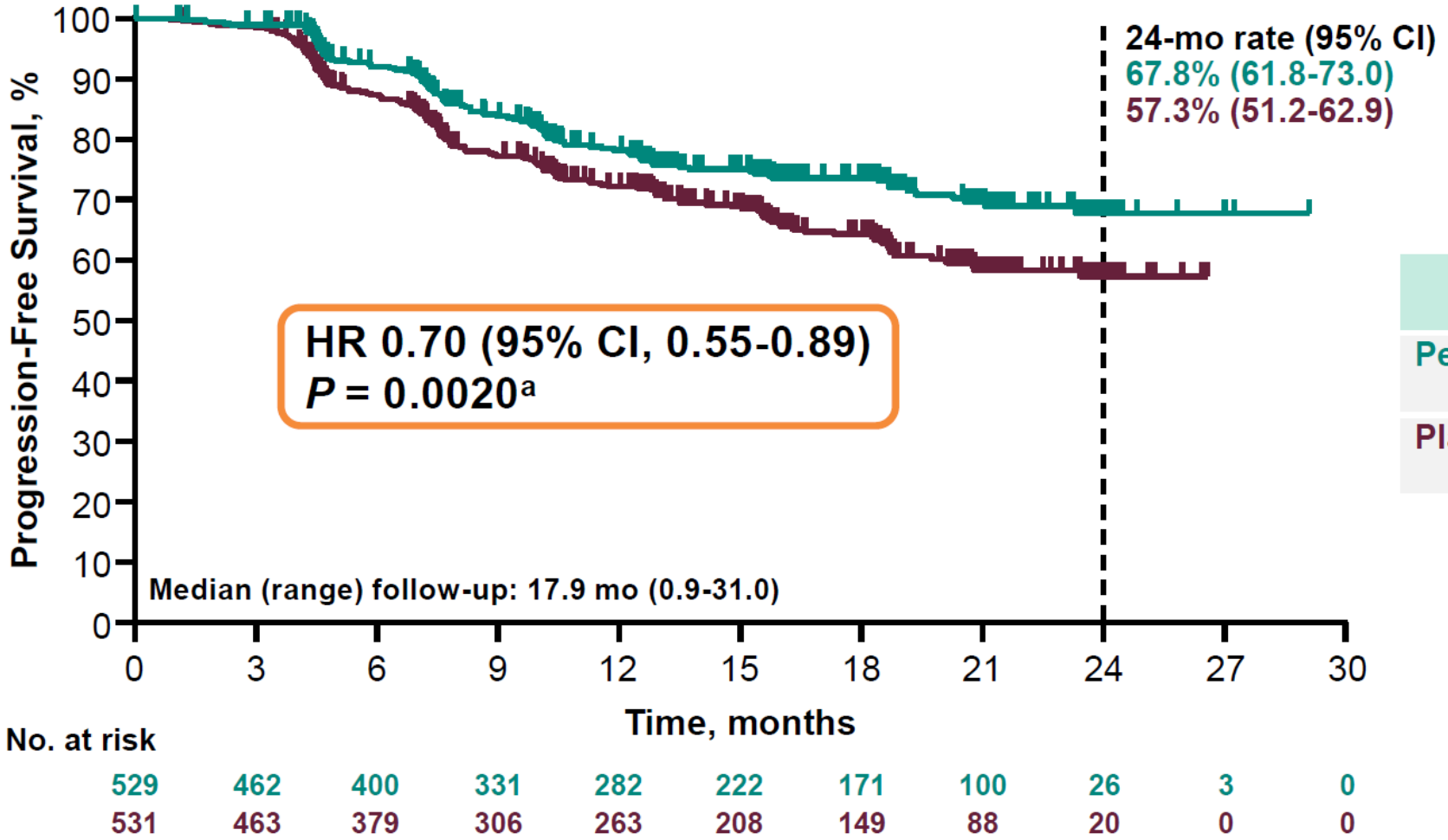
Endpoints
- Primary: PFS and OS
- Key secondary: 24-mo PFS, ORR, PROs, and safety

Pembrolizumab is not FDA approved for the treatment of locally advanced cervical cancer at this time

[a] A sixth cycle was allowed per investigator discretion.

Lorusso D, et al. 2023 Annual ESMO Meeting. Abstract LBA38.

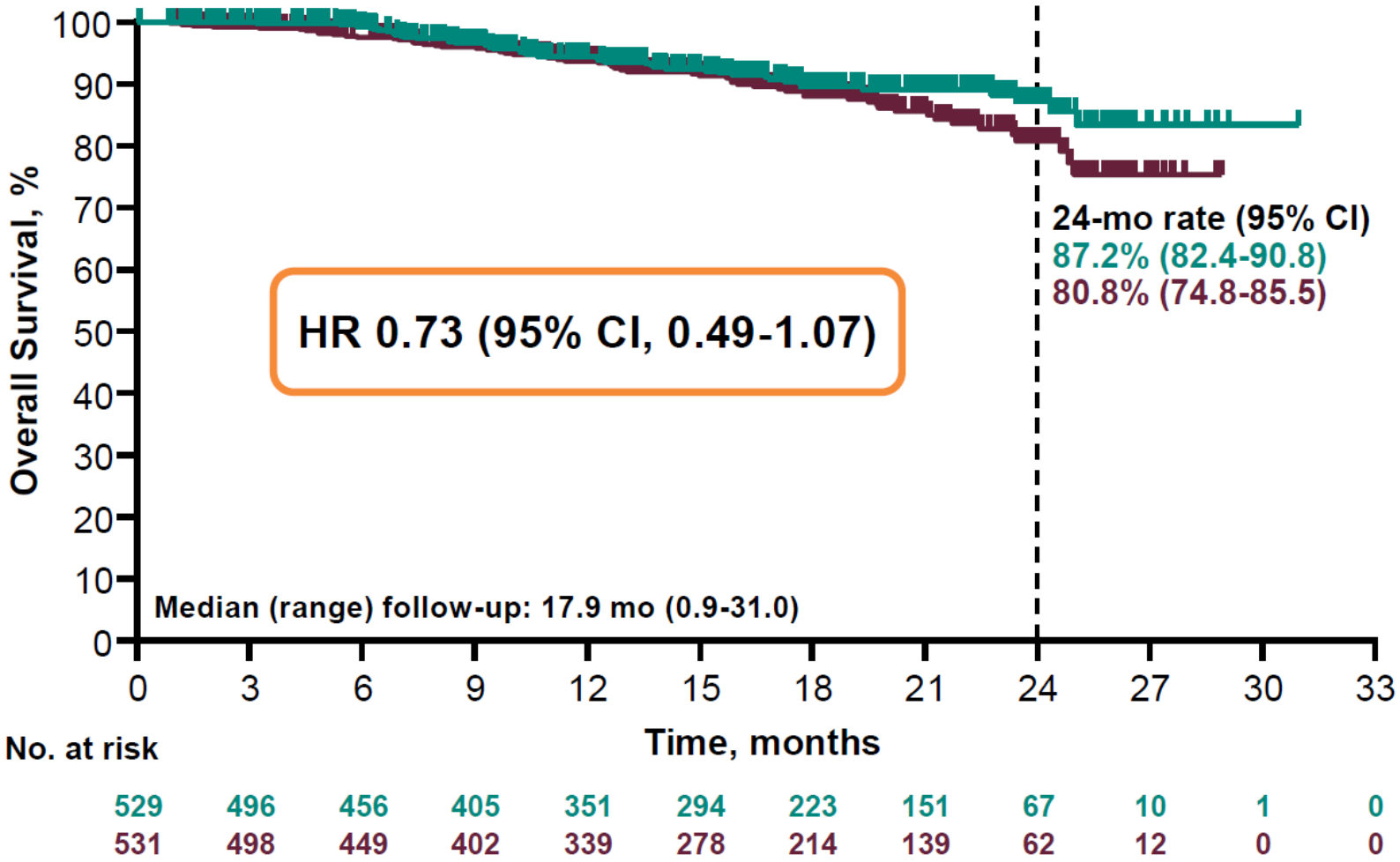
KEYNOTE-A18: PFS



	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.

KEYNOTE-A18: OS



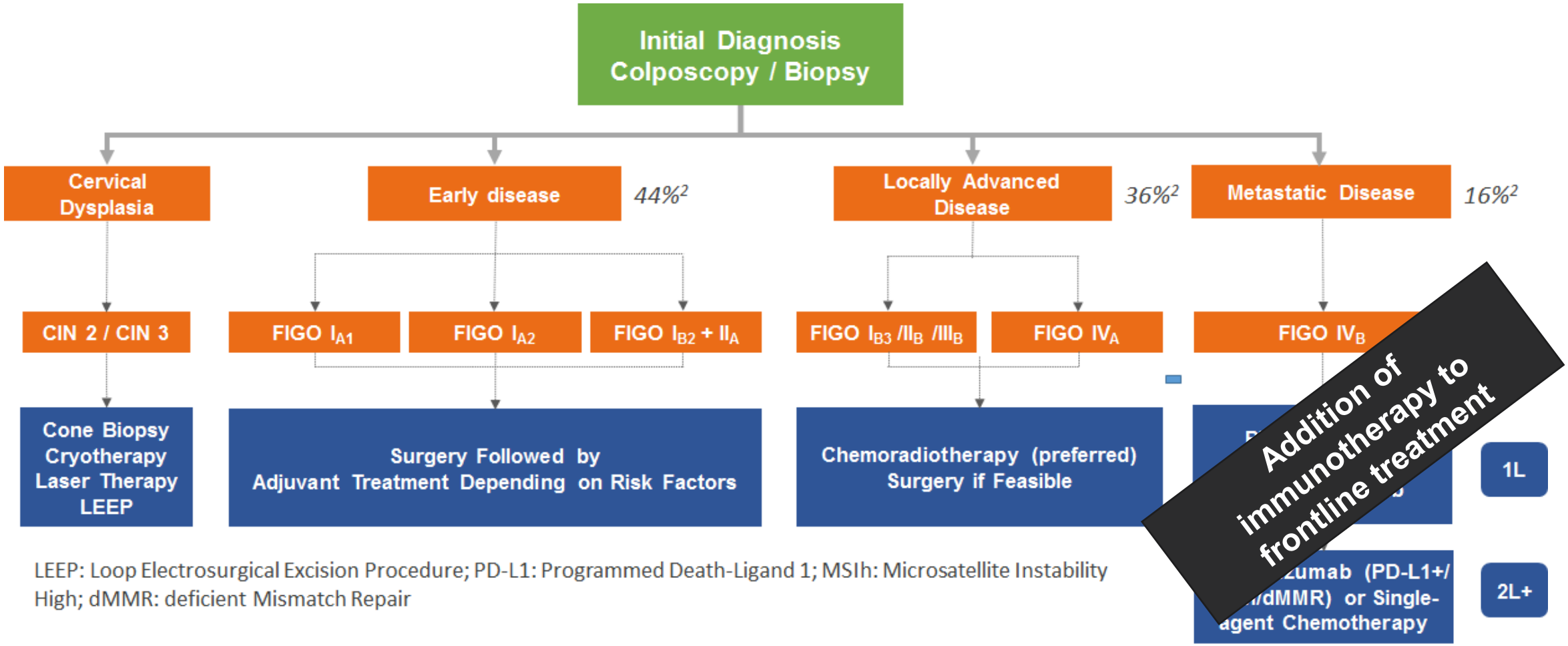
	Pts w/ Event*	Median, mo (95% CI)
Pembro Arm	8.3%	NR (NR-NR)
Placebo Arm	11.1%	NR (NR-NR)

*42.9% information fraction[a]

[a] At this analysis, 103 of the 240 deaths expected at the final analysis had occurred.

Lorusso D, et al. 2023 Annual ESMO Meeting. Abstract LBA38.

Cervical cancer treatment paradigm



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[2] SEER Cancer Stat Facts: Cervical Cancer. National Cancer Institute. Bethesda, MD

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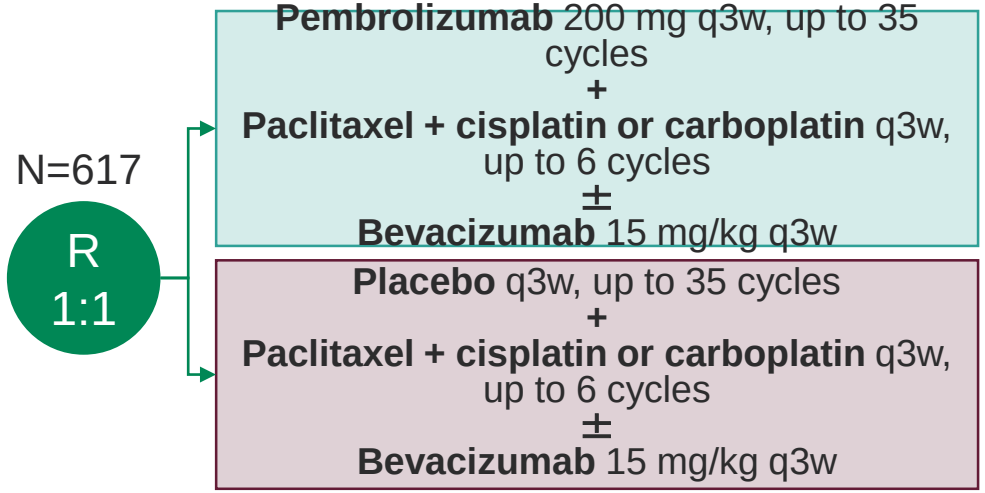
KEYNOTE 826: Phase 3 Trial of Pembro + Chemo ± Bev

- Persistent, recurrent, or metastatic cervical cancer not amenable to curative treatment
- No prior systemic chemotherapy
- ECOG PS 0-1



- Stratification factors: metastatic disease at diagnosis (yes vs no); PD-L1 CPS (<1 vs 1 to <10 vs ≥10); planned Bev use (yes vs no)

Endpoints
- Dual primary: OS and PFS
- Secondary: ORR, DOR, 12-mo PFS, and safety

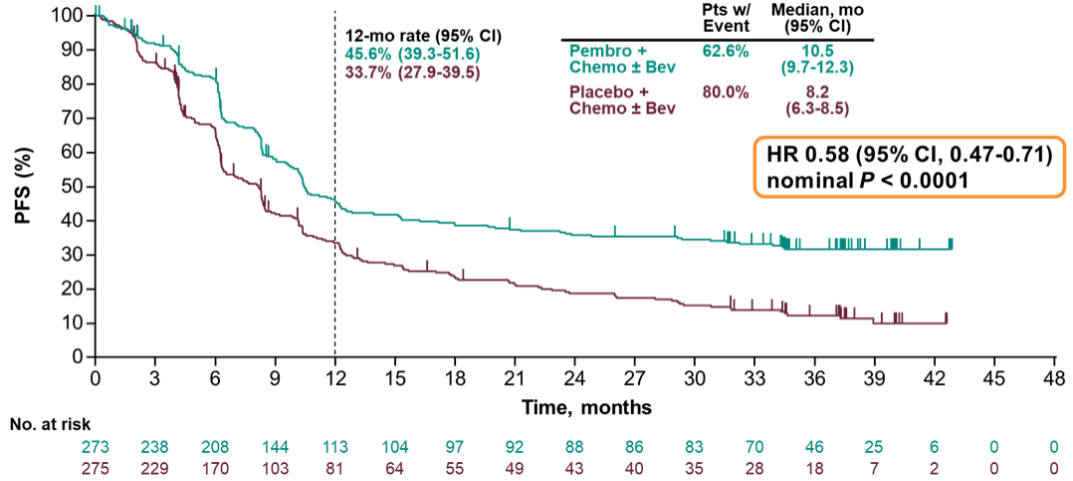
	Pembro + Chemo ± Bev (n=308)	Placebo + Chemo ± Bev (n=309)
Median age (range), y	51 (25-82)	50 (22-79)
ECOG PS 1, no. (%)	128 (42)	139 (45)
SCC, no. (%)	235 (76)	211 (68)
PD-L1 CPS, no. (%)		
<1	35 (11)	34 (11)
1 to <10	115 (37)	116 (38)
≥10	158 (51)	159 (51)
Bevacizumab use during trial, no. (%)	196 (64)	193 (62)

FDA approved October 2021 **in combination with chemotherapy, with or without bevacizumab**, for patients with persistent, recurrent, or metastatic cervical cancer **whose tumors express PD-L1 (CPS ≥1)**

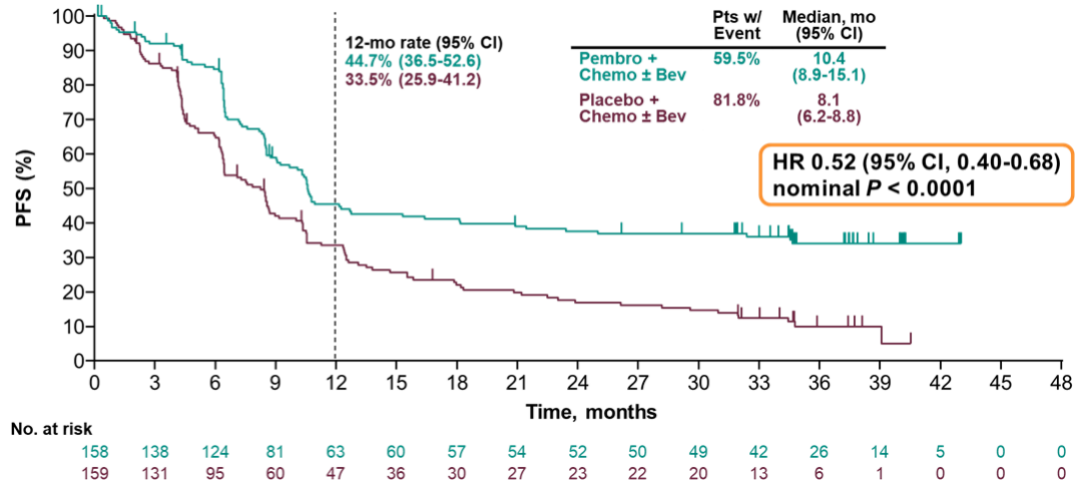
Monk BJ, et al. 2023 Annual ASCO Meeting. Abstract 5500.

KEYNOTE 826: PFS

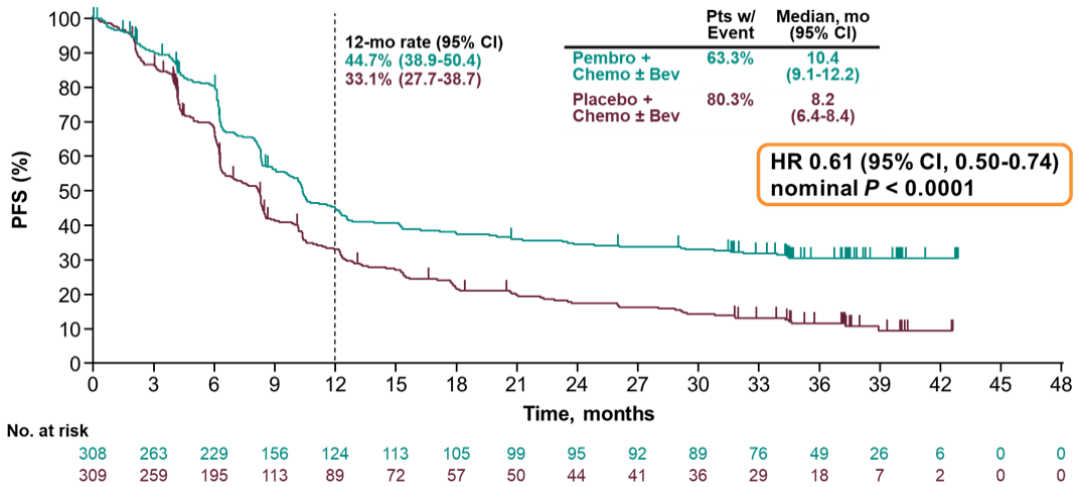
PD-L1 CPS ≥1 Population



PD-L1 CPS ≥10 Population



ITT Population



Pembrolizumab

Placebo

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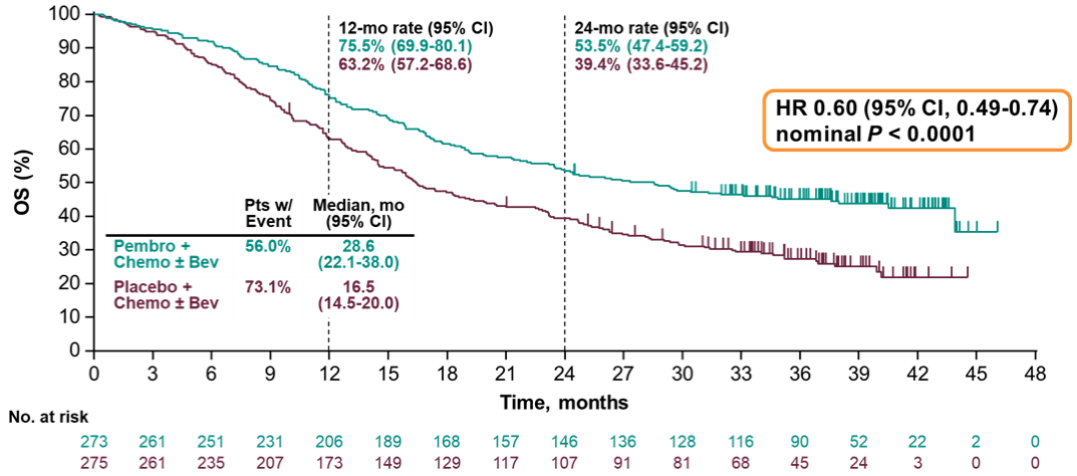
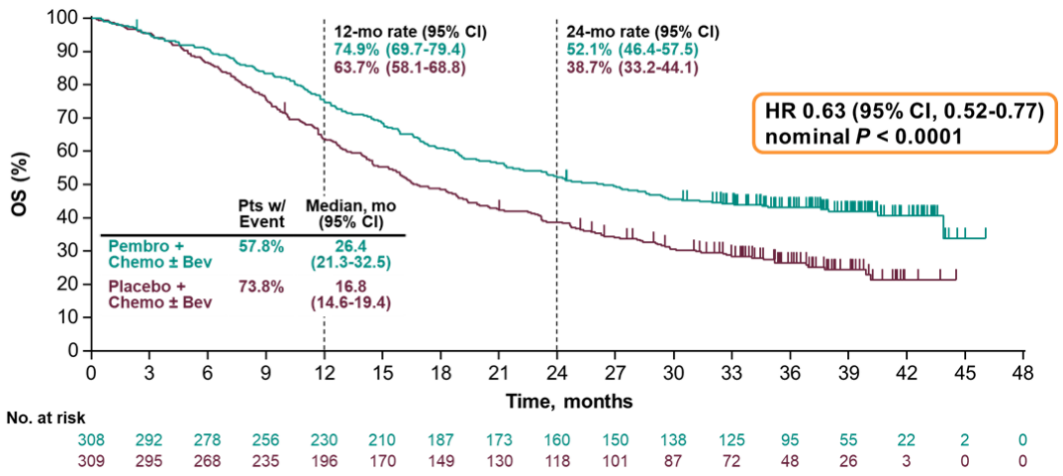
KEYNOTE 826: OS

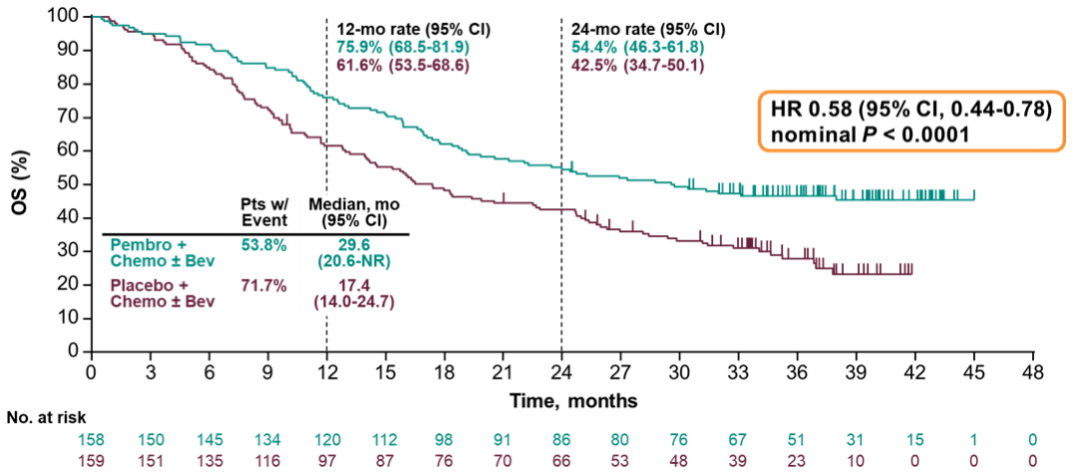
PD-L1 CPS ≥1 Population



ITT Population



PD-L1 CPS ≥10 Population



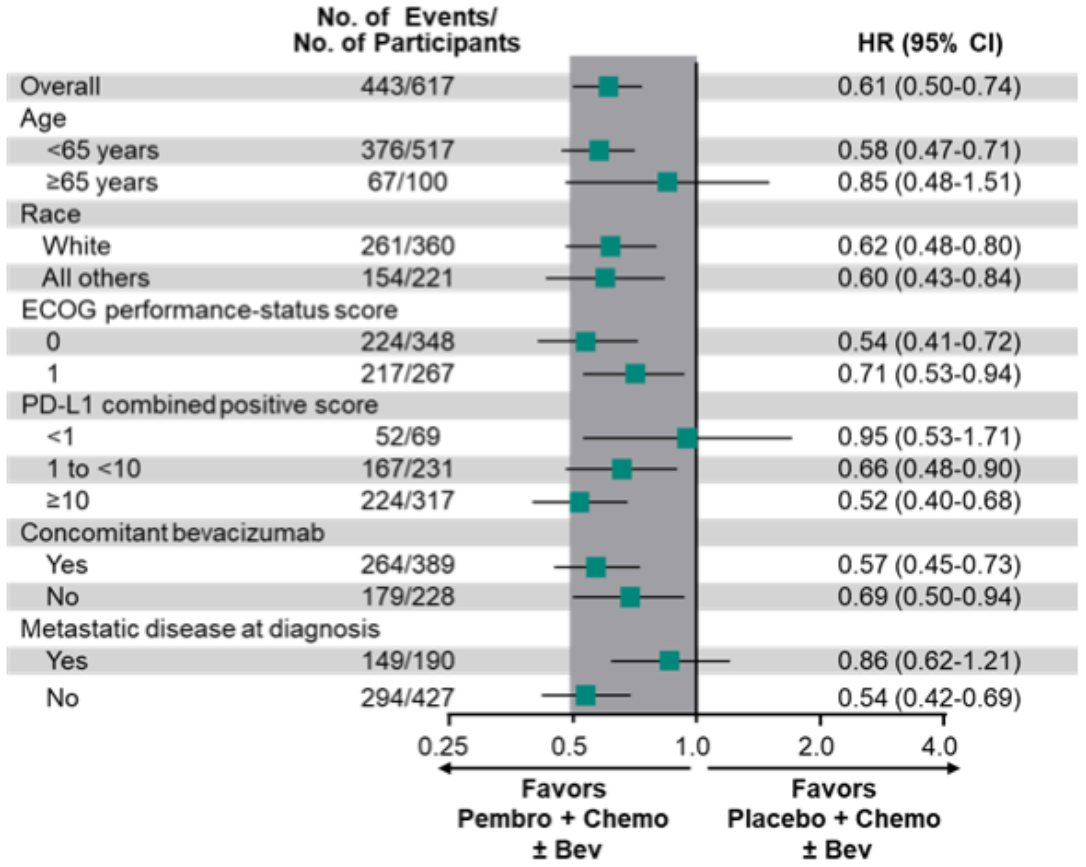
Pembrolizumab

Placebo

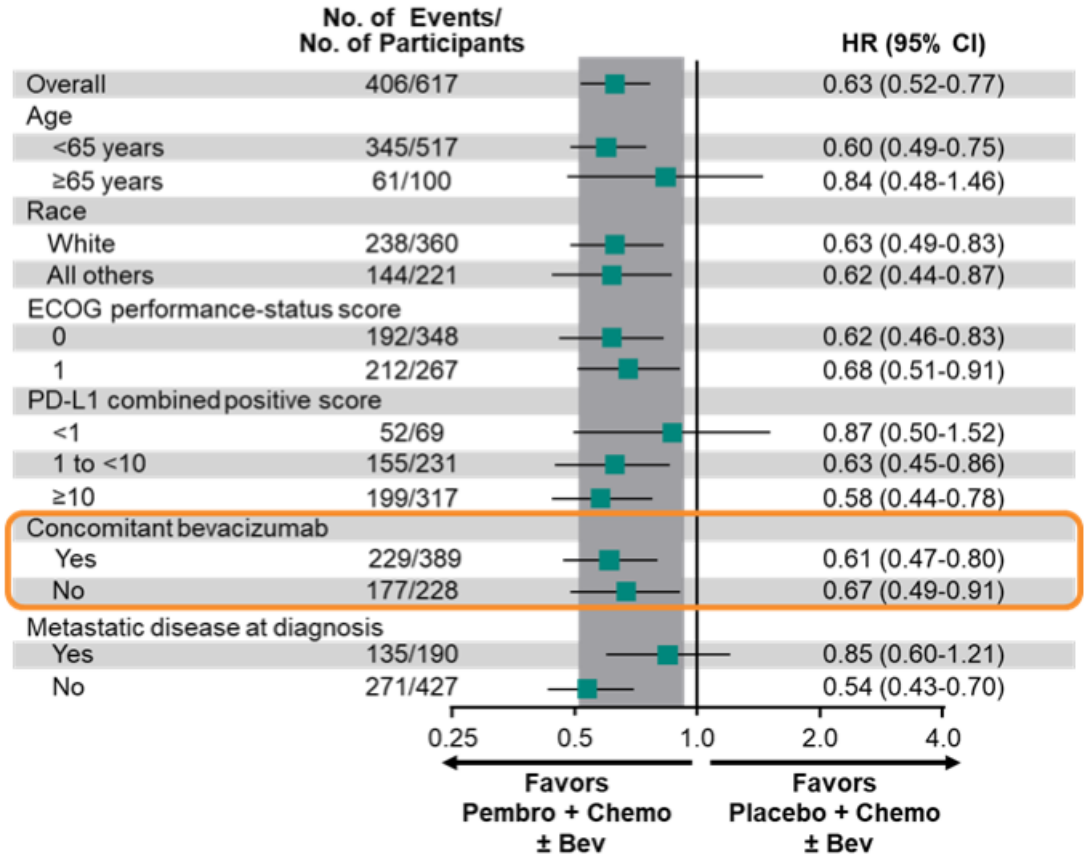
Monk BJ, et al. 2023 Annual ASCO Meeting. Abstract 5500.

KEYNOTE 826: ITT Population Subgroup Analysis

PFS

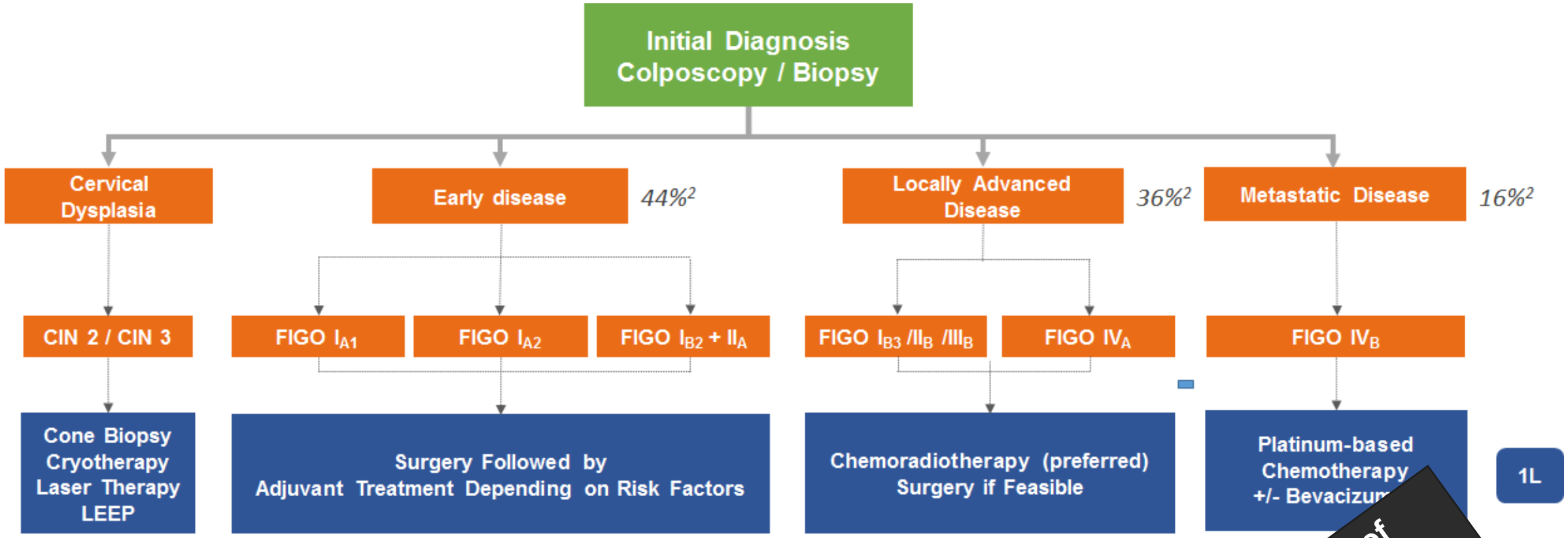


OS



Monk BJ, et al. 2023 Annual ASCO Meeting. Abstract 5500.

Cervical cancer treatment paradigm



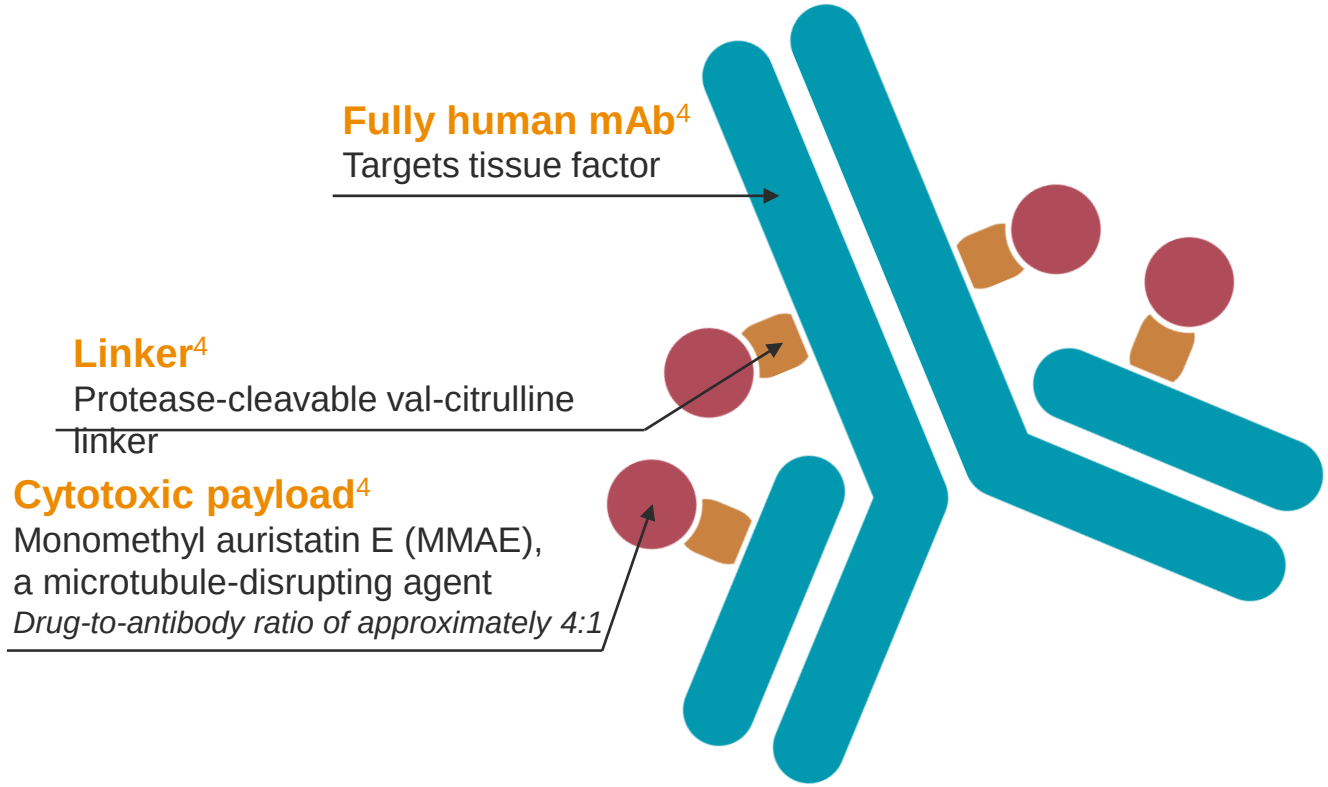
LEEP: Loop Electrosurgical Excision Procedure; PD-L1: Programmed Death-Ligand 1; MSIh: Microsatellite Instability High; dMMR: deficient Mismatch Repair

[1] NCCN Cervical Cancer Guidelines v2.2019
[2] SEER Cancer Stat Facts: Cervical Cancer. National Cancer Institute. Bethesda, MD

UC San Diego Health

Tisotumab Vedotin (TV): A Tissue Factor-Directed ADC

- Tissue factor
  - Transmembrane protein that is the primary initiator of coagulation[1]
  - Involved in angiogenesis and metastasis of cancer[1]
  - Highly expressed in cervical cancer[2,3]



1. Versteeg HH, et al. *Semin Thromb Hemost*. 2015;41(7):747-755. **2.** Cocco E, et al. *BMC Cancer*. 2011;11:263. **3.** Zhao X, et al. *Exp Ther Med*. 2018;16(5):4075-4081. **4.** Tisotumab vedotin. Package insert. Seagen Inc.; 2023.

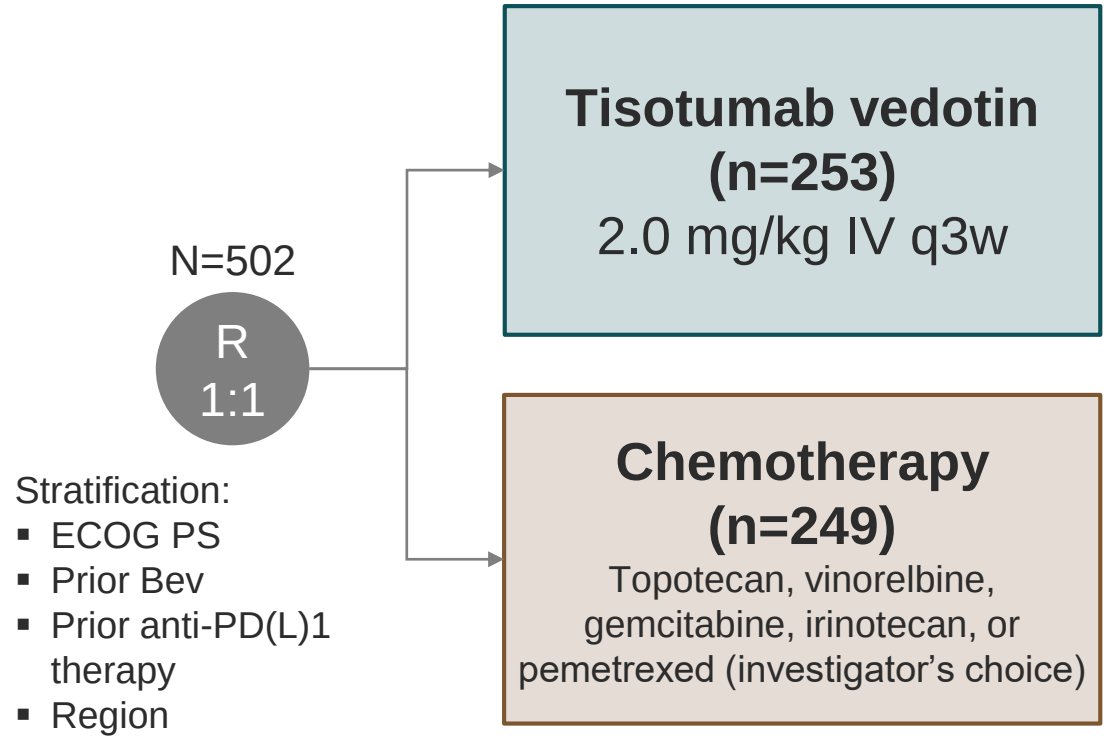
InnovaTV 301/ENGOT-cx12/GOG-3057: Phase 3 Trial of Tisotumab Vedotin vs Chemotherapy[1,2]

Key eligibility criteria

- Recurrent or metastatic cervical cancer
- Disease progression on or after chemotherapy doublet ± Bev and an anti-PD-(L)1 agent, if eligible and available
- ≤2 prior therapies for recurrent/metastatic disease
- ECOG PS 0-1

Primary endpoint: OS

Key secondary endpoints: PFS, ORR, safety



FDA approved September 2021 for the treatment of adult patients with recurrent or metastatic cervical cancer **with disease progression on or after chemotherapy**

Vergote I, et al. 2023 Annual ESMO Meeting. Abstract LBA9.

InnovaTV 301: Baseline Characteristics

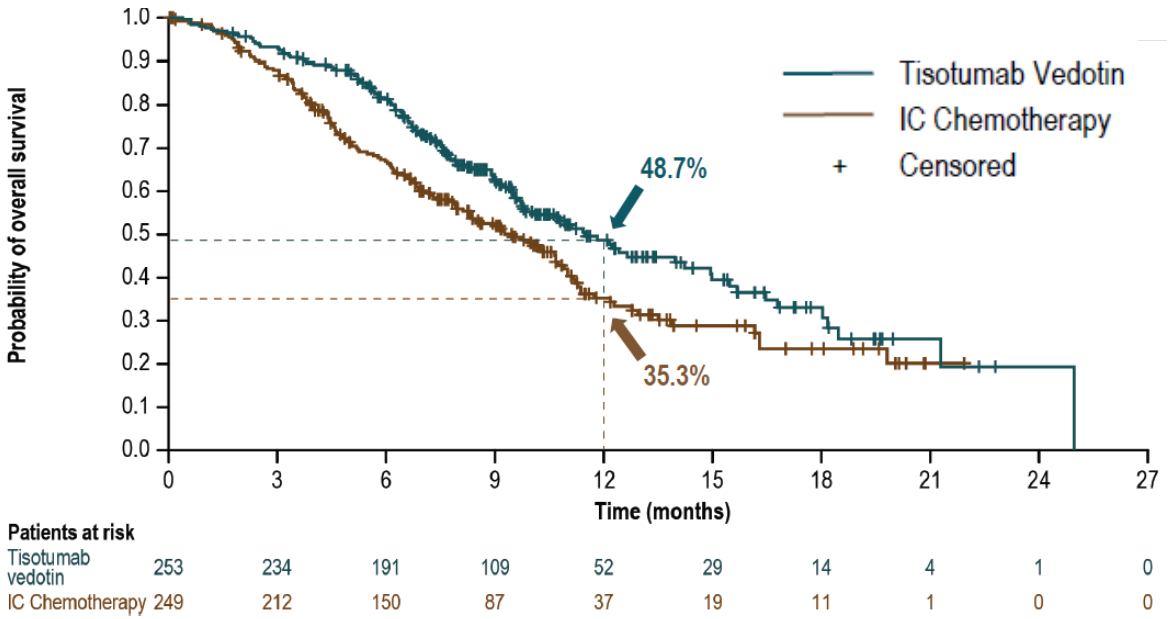
	TV (N=253)	Chemo (N=249)
Median age, yrs (range)	51 (26-80)	50 (27-78)
ECOG PS, no. (%)		
0	137 (54.2)	136 (54.6)
1	116 (45.8)	113 (45.4)
Region, no. (%)		
United States	16 (6.3)	14 (5.6)
Europe	106 (41.9)	104 (41.8)
Asia	85 (33.6)	88 (35.3)
Other	46 (18.2)	43 (17.3)
Histology, no. (%)		
SCC	160 (63.2)	157 (63.1)
AC	85 (33.6)	75 (30.1)
ASC	8 (3.2)	17 (6.8)

	TV (N=253)	Chemo (N=249)
Disease status at study entry, no. (%)		
Pelvic recurrent only	27 (10.7)	24 (9.6)
Extra-pelvic metastatic	226 (89.3)	225 (90.4)
Number of prior r/m systemic regimens, no. (%)		
0	159 (62.8)	149 (59.8)
1	93 (36.8)	100 (40.2)
Unknown	1 (0.4)	0
Prior Bev, no. (%)	164 (64.8)	157 (63.1)
Prior anti-PD-(L)1 therapy, no. (%)	71 (28.1)	67 (26.9)
Prior radiation therapy for cervical cancer, no. (%)	205 (81.0)	203 (81.5)
Biopsy evaluable, no. (%)	210 (83.0)	194 (77.9)
Positive membrane TF expression[a]	194 (92.4)	183 (94.3)

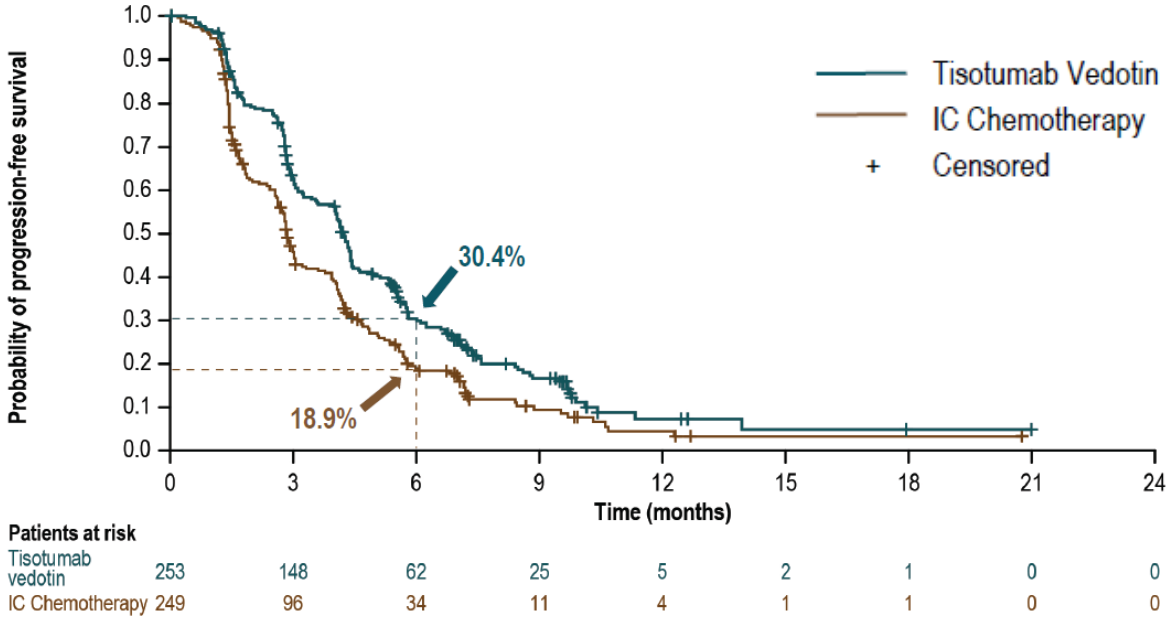
[a] TF expression is defined as TF membrane expression ≥1% with immunohistochemistry; percentages are calculated based on number of evaluable biopsies.

InnovaTV 301: OS and PFS

	Events/ Total	mOS (95% CI)	HR (95% CI)	Stratified log-rank P value[a]
TV	123/253	**11.5** (9.8-14.9)	**0.70** (0.54-0.89)	0.0038
Chemo	140/249	**9.5** (7.9-10.7)		



	Events/ Total	mPFS (95% CI)	HR (95% CI)	Stratified log-rank P value[b]
TV	198/253	**4.2** (4.0-4.4)	**0.67** (0.54-0.82)	<0.0001
Chemo	194/249	**2.9** (2.6-3.1)		



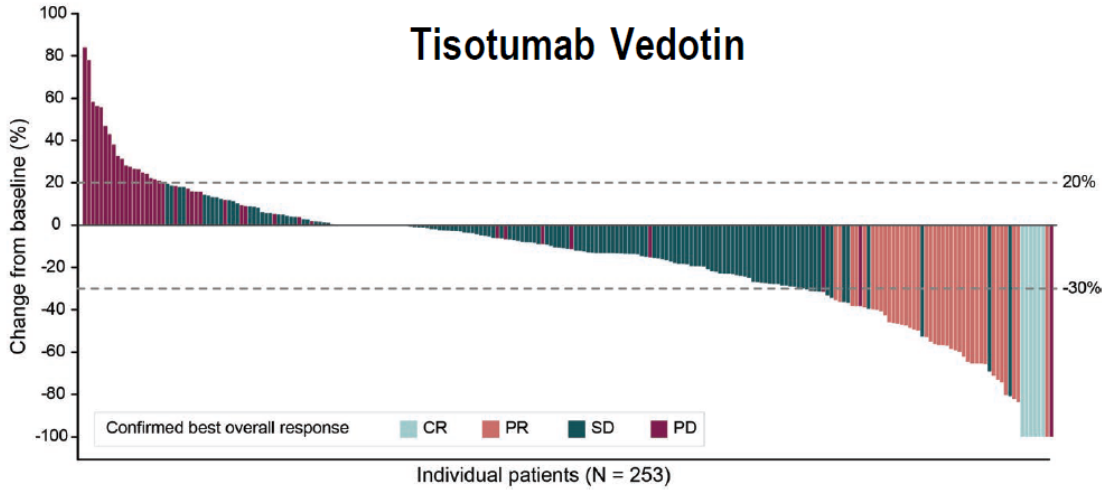
[a] The threshold for statistical significance is 0.0226 (2-sided), based on the actual number of OS events at interim analysis.

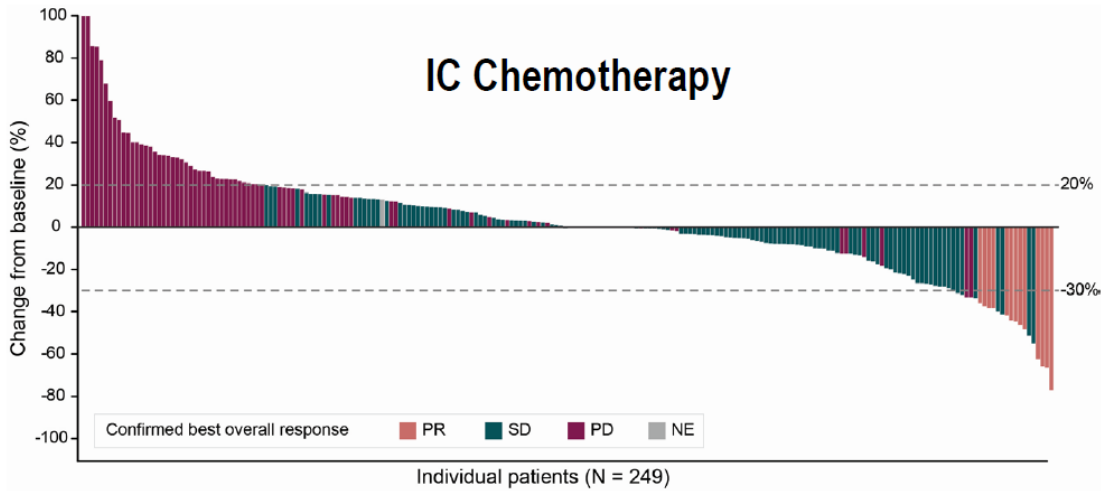
[b] The threshold for statistical significance is 0.0453 (2-sided), based on the actual number of PFS events at interim analysis.

Vergote I, et al. 2023 Annual ESMO Meeting. Abstract LBA9.

InnovaTV 301: Antitumor Activity

	TV (N=253)	Chemo (N=249)
ORR, % (95% CI)	**17.8** (13.3-23.1)	**5.2** (2.8-8.8)
Odds ratio (95% CI)	4.0 (2.1-7.6)	
P value	<0.0001	
Best overall response, no. (%)		
CR	6 (2.4)	0
PR	39 (15.4)	13 (5.2)
SD	147 (58.1)	132 (53.0)
PD	46 (18.2)	74 (29.7)
Not evaluable	15 (5.9)	30 (12.0)
DCR[a], % (95% CI)	**75.9** (70.1-81.0)	**58.2** (51.8-64.4)
mDOR (95% CI)	**5.3** (4.2-8.3)	**5.7** (2.8-NR)





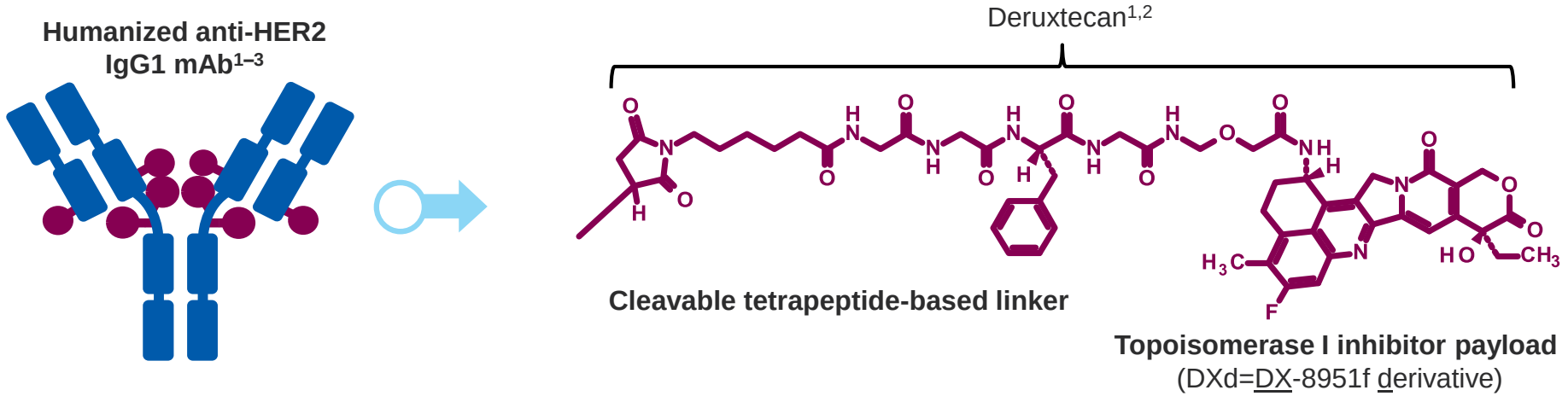
[a] DCR defined as CR+PR+SD; CR and PR were confirmed responses. The minimum criteria for SD duration was ≥5 weeks after the date of randomization.

Vergote I, et al. 2023 Annual ESMO Meeting. Abstract LBA9.

Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: DESTINY-PanTumor02 interim results

T-DXd is an ADC with three components:

1. A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
2. A topoisomerase I inhibitor payload, an exatecan derivative
3. A tetrapeptide-based cleavable linker



[a]The clinical relevance of these features is under investigation. ADC, antibody–drug conjugate; HER2, human epidermal growth factor receptor 2; IgG1, immunoglobulin G1; mAb, monoclonal antibody; T-DXd, trastuzumab deruxtecan.

1. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173–185. 2. Ogitani Y, et al. *Clin Cancer Res.* 2016;22(20):5097–5108. 3. Trail PA, et al. *Pharmacol Ther*. 2018;181:126–142.
4. Okamoto H, et al. *Xenobiotica*. 2020;50(10):1242–1250. 5. Nagai Y, et al. *Xenobiotica*. 2019;49(9):1086–1096.

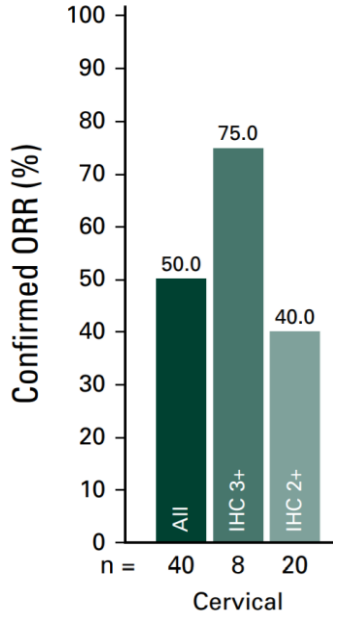
DESTINY-PanTumor02: Phase 2 Trial of T-DXd for Previously Treated HER2-Expressing Solid Tumors

Key eligibility criteria
- Locally advanced, unresectable, or metastatic solid cancers
- ≥1 prior systemic treatment
- HER2 IHC 3+ or 2+ (gastric scoring)
- ECOG PS 0-1

T-DXd
5.4 mg/kg q3w IV
(n=40 cervical)
(N=268 all cohorts)

Primary endpoint: Investigator-assessed ORR
Secondary endpoints: DOR, DCR, PFS, OS, safety

Median follow-up duration (all cohorts):
12.75 mo (range, 0.4-31.6)



	Cervical
	Total (N=40)
Best overall response, no. (%)	
CR	2 (5)
PR	18 (45)
SD	11 (27.5)
PD	7 (17.5)
NE	1 (2.5)

	Cervical		
	Total (N=40)	**IHC 3+** (n=8)	**IHC 2+** (n=20)
mDOR[a], mo (95% CI)	**14.2** (4.1-NR)	-	-
mPFS, mo (95% CI)	**7.0** (4.2-11.1)	**NR** (3.9-NR)	**4.8** (2.7-5.7)
mOS, mo (95% CI)	**13.6** (11.1-NR)	**NR** (3.9-NR)	**11.5** (5.1-NR)

Safety summary (N=267, all tumor cohorts)
- Grade ≥3 drug-related AE: 40.8%
- Drug-related ILD/pneumonitis: 10.5% [3 (1.1%) fatal]
- Drug-related AE resulting in death: 4 (1.5%)
- Drug-related AE leading to discontinuation: 8.6%

T-DXd is not FDA approved for cervical cancer; it is included in the **NCCN Guidelines®** for HER2-positive tumors **IHC 3+ or 2+**

[a] DOR includes only patients with an objective response.

Meric-Bernstam F, et al. J Clin Oncol. 2023. DOI: 10.1200/JCO.23.02005

OTHER CLINICAL TRIALS OPEN AT UCSD

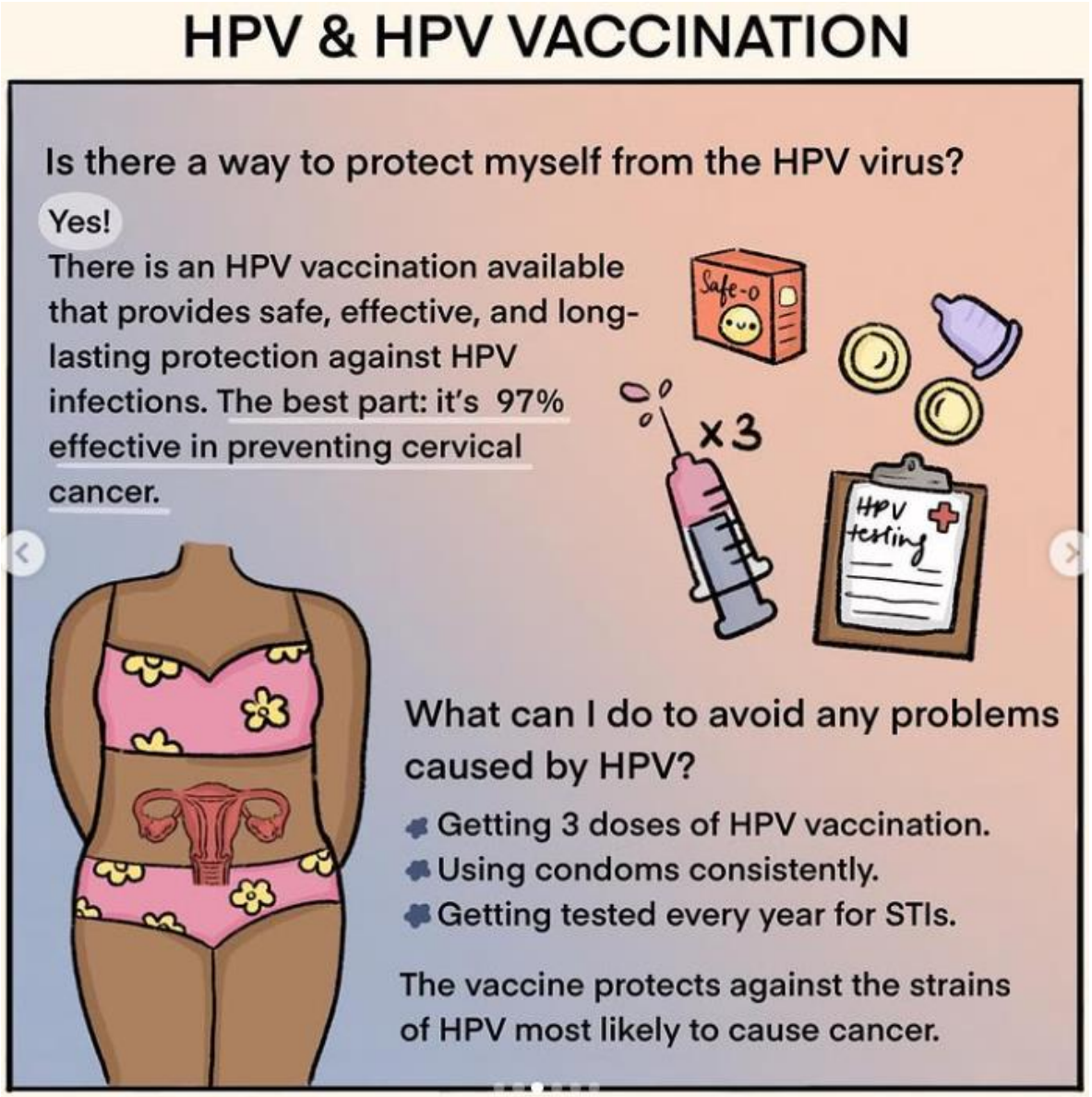
- **Varian/ARTIA IRB 801727** Daily Adaptive External Beam Radiation Therapy in the Treatment of Carcinoma of the Cervix: A Phase II Trial of an Individualized Approach for Intestinal Toxicity Reduction (ARTIA-Cervix)
  - Main inclusions: Histologically confirmed, newly diagnosed advanced cervical cancer: FIGO 2018 clinical stages IB2-IVA without positive LN with plan for definitive chemoradiation treatment for cervix cancer.

- **GOG-3092 EVOLVE AstraZeneca IRB 810096** This is a phase III, randomized, double-blind, placebo-controlled, multicenter, global study of volrustomig in women with high risk locally advanced cervical cancer, who have not progressed following platinum-based, concurrent chemoradiation therapy (eVOLVE-Cervical)
  - Main inclusions: Participants must have completed concurrent chemoradiotherapy within 1 to 56 days prior to randomization. Received weekly cisplatin 40 mg/m2 for 5 to 6 cycles as concurrent chemotherapy with radiation therapy. Participants must not have progressed following CCRT

- **ROCC GOG-3043 IRB 804088** A Randomized Controlled Trial of Robotic versus Open Radical Hysterectomy for Cervical Cancer.

- **GOG-3101:** Merck Sharp & Dohme LLC MK2870-020-00/GOG-3101/ENGOT-cx20: A Phase 3 Randomized, Active-controlled, Open-label, Multicenter Study to Compare the Efficacy and Safety of MK-2870 Monotherapy **(anti-TROP2 ADC)** Versus Treatment of Physician's Choice as Second-line Treatment for Participants with Recurrent or Metastatic Cervical Cancer (TroFuse-020/GOG-3101/ENGOT-cx20).

PREVENTION IS KEY: Only gynecologic cancer with well studied screening test and vaccine



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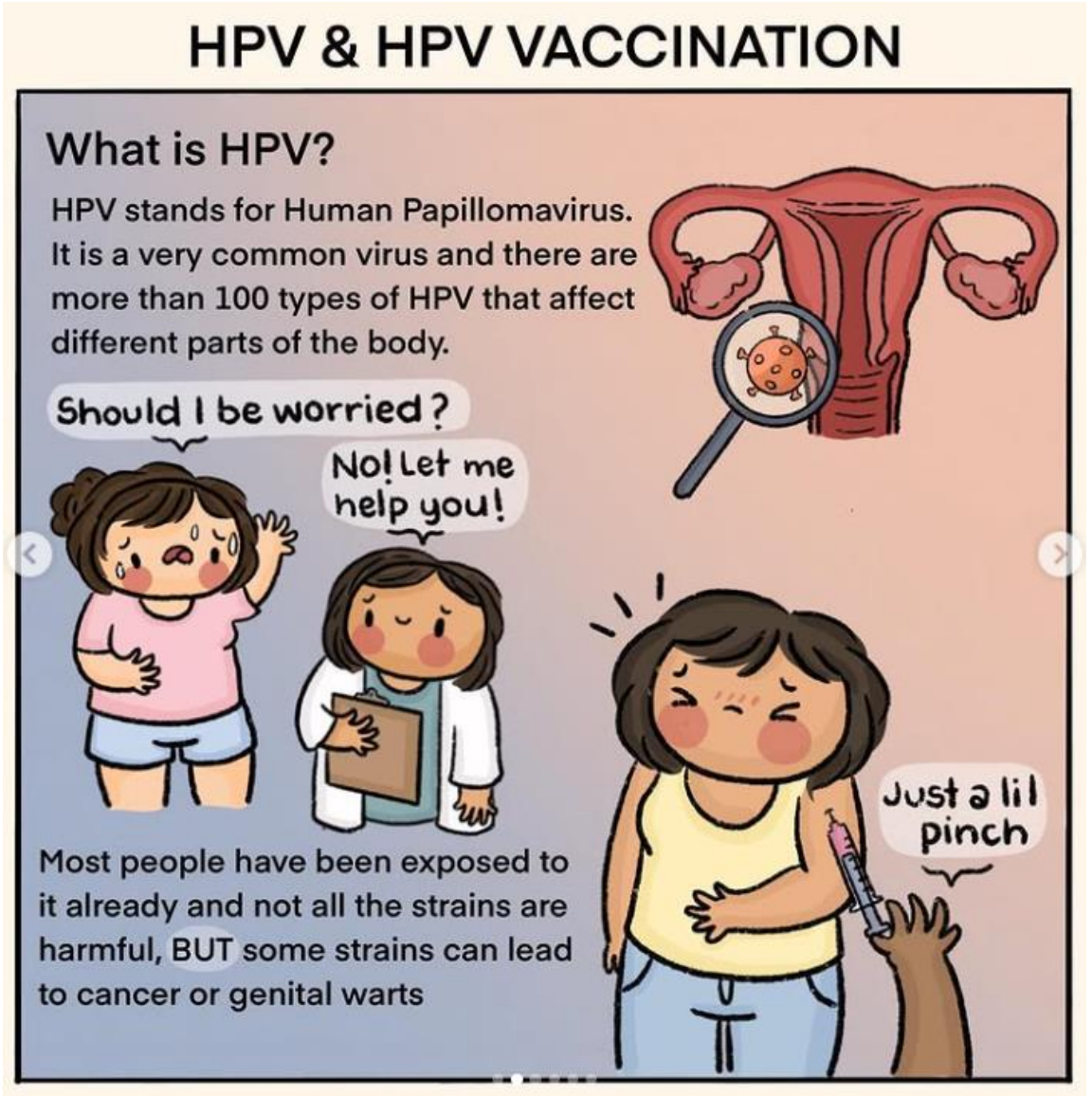

Questions?

Thank you!

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