CECONCOLOGY

ADVANCING CERVICAL CANCER CARE

Navigating New Therapies, Guidelines, and Patient-Centric Approaches

OVERVIEW

Delayed diagnosis of cervical cancer often leads to poor prognosis and lower survival rates, especially in advanced stages. Recent therapeutic advancements, including immune-checkpoint inhibitors and antibody-drug conjugates (ADCs), offer new hope for managing advanced cervical cancer. However, there are significant gaps in knowledge and practice, especially in the community setting, which increase the risk of suboptimal treatment decisions and missed opportunities to enhance patient outcomes.

In this CE Concepts Grand Rounds series, expert faculty will examine the evolving treatment landscape for advanced cervical cancer and discuss how they develop individualized treatment plans that apply current guideline recommendations, consider new treatment methods, and respect the unique needs of each patient.

TARGET AUDIENCE

Community-based gynecologic oncologists, OB/GYNs, physician associates (PAs), pharmacists, nurse practitioners (NPs), and nurses caring for patients with recurrent/metastatic cervical cancer

LEARNING OBJECTIVES

- Evaluate the evolving treatment landscape for advanced cervical cancer, including the use of chemotherapy, radiation therapy, immunotherapy, antibody-drug conjugates (ADCs), and insights from ongoing clinical trials
- Develop individualized treatment plans for advanced cervical cancer by applying guideline recommendations and therapy knowledge, considering both clinical and non-clinical patient-specific factors

AGENDA

50 minutes	Presentation
10 minutes	Q&A

FACULTY

Bradley J. Monk, MD, FACS, FACOG (Chair)
Florida Cancer Specialists and Research Institute
Medical Director, Late-Phase Clinical Research
West Palm Beach, FL
Vice President and Member of Board of Directors, GOG-Foundation
Director, GOG-Partners
West Palm Beach, Florida

Bradley J. Monk, MD, FACS, FACOG, graduated from the University of Arizona College of Medicine–Tucson and completed a residency in obstetrics and gynecology at the University of California–Los Angeles. He completed his fellowship in gynecologic oncology at the University of California–Irvine.

In 1995, Dr. Monk was appointed Director of Gynecologic Oncology at Texas Tech University Health Services Center in Lubbock. From 1998 until 2010, he was an associate professor in the Division of Gynecologic Oncology, Department of Obstetrics and Gynecology at the Chao Family Comprehensive Cancer Center, University of California Irvine Medical Center, and was the director of research in the Department of Obstetrics and Gynecology.

After moving to Arizona, Dr. Monk was appointed director and professor in the Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Creighton University School of Medicine at St. Joseph's Hospital and Medical Center in Phoenix. Dr. Monk also became a professor on the clinical scholar track at the University of Arizona College of Medicine, Phoenix. In 2016, he transitioned to Arizona Oncology and was part of the US Oncology Network. He was chair of the Gynecologic Cancer Committee for US Oncology Research until 2022, when his practice was acquired by HonorHealth. He served as director and principal investigator at the Virginia G. Piper Cancer Center at HonorHealth, where he was also the site research leader for the Sarah Cannon Research Institute.

In 2024, Dr. Monk moved to West Palm Beach, Florida, and joined the Florida Cancer Specialists and Research Institute. He was appointed the medical director of the Late-Phase Clinical Research Program across the state network and is accountable for all cancer types.

Dr. Monk's research interests include the prevention and treatment of gynecologic cancers. He was the first to report the activity of anti-vascular growth factor (VEGF) therapy in ovarian and cervical cancers; his papers in the *New England Journal of Medicine* led to the global approval of anti-VEGF therapy in recurrent cervical cancer in 2014 and advanced ovarian in 2018. He was also the lead author on the pivotal trial of trabectedin in recurrent ovarian cancer as well as many other studies that have met their primary endpoints. Additionally, his other papers in the *New England Journal of Medicine, Journal of Clinical Oncology* and *Lancet Oncology* have led to multiple FDA/EMA approvals of PARP inhibitors in ovarian cancer plus immunotherapy in advanced and recurrent cervical and endometrial cancer.

Dr. Monk was chair of the Cervical Cancer Sub-Committee for NRG Oncology for 11 years and is a prior chair of the Cervical Cancer Committee for the Gynecologic Cancer Intergroup. He is a fellow of the American College of Surgeons, the American College of Obstetricians and Gynecologists, and the American Society for Colposcopy and Cervical Pathology as well as being an active member of the Society of Gynecologic Oncology, International Gynecologic Cancer Society, and American Society of Clinical Oncology. He has authored more than 400 peer-reviewed articles along with over 35 book chapters that deal predominantly with the prevention and treatment of gynecologic malignancies and patient-reported outcomes. He is on the editorial board for multiple peer-review oncology journals and is the gynecologic cancer section co-editor for *Annals of Oncology*. Finally, he is vice president and on the board of directors for the GOG-Foundation and directs the GOG-Partners Research consortium, which he co-founded in 2010.

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Sandra Caballero, PharmD (Planning Committee)

Sharon Tordoff (Planning Committee)

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Alaa Bawaneh, MD, PhD—no disclosures to report.

Margaret Wright, BSN, RN—no disclosures to report.

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This activity is designated for 1.0 contact hour.

Note to Nurse Practitioners: the content of this CNE activity pertains to Pharmacology.

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This activity is designated for 1.0 contact hours.

The program content has been reviewed by the Oncology Nursing Certification Corporation (ONCC) and is acceptable for recertification points in the following ILNA subject areas:

OCN

- Care Continuum
- Oncology Nursing Practice
- Symptom Management, Palliative Care, Supportive Care
- Treatment

CBCN

- Care Continuum
- Treatment

CPHON

- Care Continuum
- Oncologic Nursing Practice
- Treatment

AOCNP

- Care Continuum
- Oncology Nursing Practice
- Treatment

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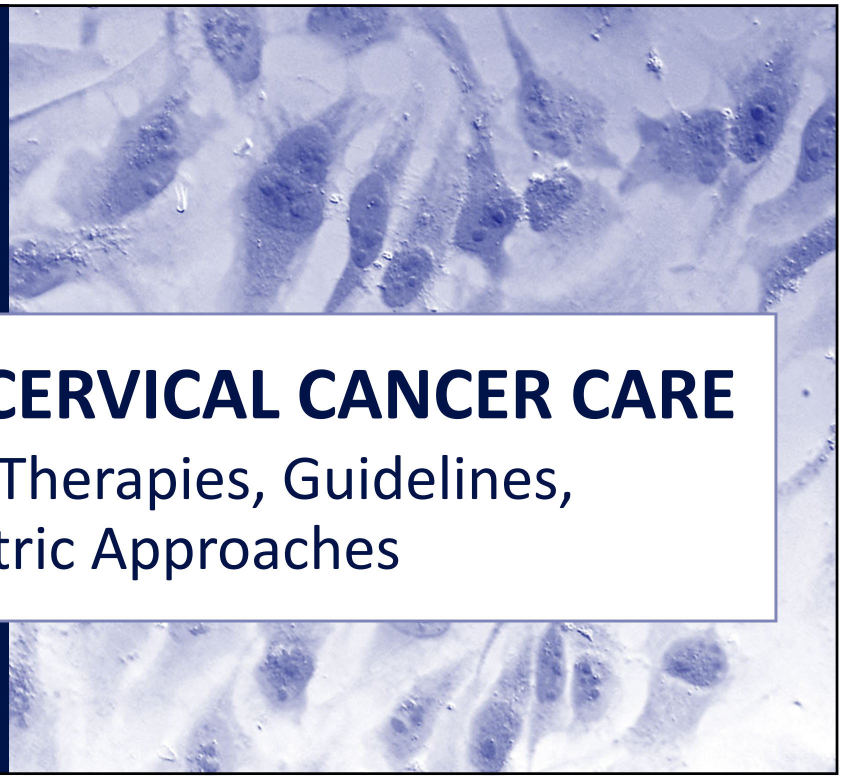

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This program is supported by an independent educational grant from Pfizer Inc.

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Activity Credit Types

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Nurses (ANCC)
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  - Treatment

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To Ask a Question

To submit a question, please go to the *Ask Question* tab at the bottom of the screen.

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Bradley J. Monk, MD, FACS, FACOG

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Director, GOG-Partners

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LEARNING OBJECTIVE

Evaluate the evolving treatment landscape for advanced cervical cancer, including the use of chemotherapy, radiation therapy, immunotherapy, antibody-drug conjugates (ADCs), and insights from ongoing clinical trials

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LEARNING OBJECTIVE

Develop individualized treatment plans for advanced cervical cancer by applying guideline recommendations and therapy knowledge, considering both clinical and non-clinical patient-specific factors

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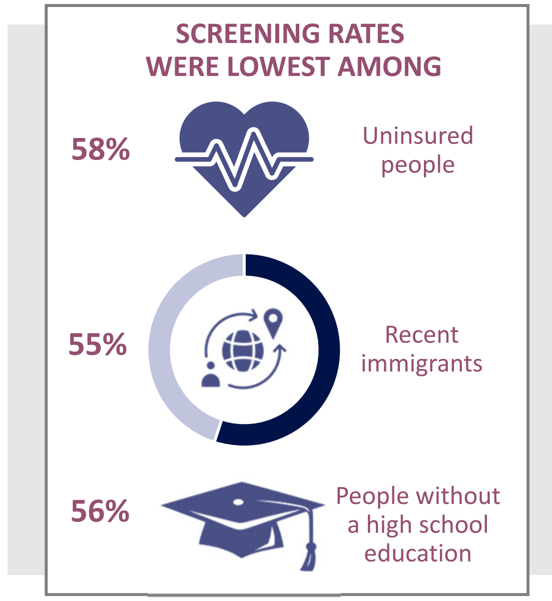
Cervical Cancer Incidence/Mortality in the United States

- Over 50% of all new cervical cancer cases are among individuals who have never been screened or who have received screening infrequently
- Increases in HPV vaccination among adolescents ages 13–17 has contributed to declining cervical cancer rates
- Having health insurance is associated with earlier stage at diagnosis
- Research shows that those who are uninsured and underinsured have lower cervical cancer screening rates, resulting in a greater risk of being diagnosed at a later, more advanced stage of disease



HPV, human papillomavirus.

American Cancer Society Cancer Action Network (ACS CAN). ACS CAN website. Published February 21, 2024. https://www.fightcancer.org/policy-resources/just-facts-cervical-cancer-disparities.

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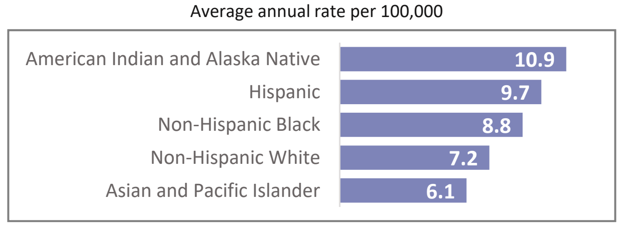
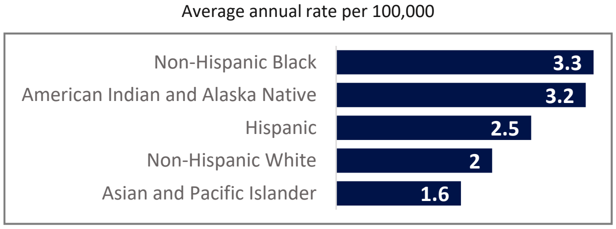
Cervical Cancer Incidence/Mortality in the United States

- Localized-stage disease was diagnosed in 37% of Non-Hispanic Black women vs 46% of White women with cervical cancer
- 5-year relative survival rate for cervical cancer is 67% overall and 67% in Non-Hispanic White people, but 56% in Non-Hispanic Black people

Incidence, 2015–2019, by Ethnicity
Average annual rate per 100,000



Mortality, 2016–2020, by Ethnicity
Average annual rate per 100,000



Henrietta Lacks (born Loretta Pleasant; August 1, 1920–October 4, 1951) was an African-American woman whose cervical cancer cells are the source of the HeLa cell line, the first immortalized human cell line. HeLa cells were grown from a tumor biopsy obtained during treatment for cervical cancer at Johns Hopkins Medical Center, at the time, the only hospital in the area to treat poor Black patients. As was then the practice, no consent was required to culture the cells, and neither she nor her family received compensation.

American Cancer Society Cancer Action Network (ACS CAN). ACS CAN website. Published February 21, 2024. https://www.fightcancer.org/policy-resources/just-facts-cervical-cancer-disparities.
Johns Hopkins Medicine. Johns Hopkins Medicine website. 2025. https://www.hopkinsmedicine.org/henrietta-lacks.

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Cervical Cancer Prevention

- HPV vaccination protects against the types of HPV that most often cause cervical, vaginal, and vulvar cancers
- HPV vaccination is recommended for
  - Preteens age 11–12, but can be given starting at age 9 (2 doses, 6 months apart)
  - Everyone through age 26 if they are not vaccinated already (3 doses for people who start the series after their 15th birthday)
- Some adults ages 27–45 who are not already vaccinated may benefit from HPV vaccination
- HPV vaccination prevents new HPV infections but does not treat existing infections or diseases

Centers for Disease Control and Prevention (CDC). CEC website. 2023. https://www.cdc.gov/cervical-cancer/prevention/index.html.

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Cervical Cancer Screening Guidelines

	2020 ACS	2018 USPSTF
Age 21–24	No screening	Pap test every 3 years
Age 25–29	HPV test every 5 years (preferred) HPV/Pap co-test every 5 years (acceptable) Pap test every 3 years (acceptable)	Pap test every 3 years
Age 30–65	HPV test every 5 years (preferred) HPV/Pap co-test every 5 years (acceptable) Pap test every 3 years (acceptable)	Pap test every 3 years, HPV test every 5 years, or HPV/Pap co-test every 5 years
Age ≥65	No screening if a series of prior tests were normal	No screening if a series of prior tests were normal and not at high risk for cervical cancer

ACS, American Cancer Society; HPV, human papillomavirus; USPSTF, U.S. Preventive Services Task Force.

National Cancer Institute (NCI). NCI website. 2020.
https://www.cancer.gov/news-events/cancer-currents-blog/2020/cervical-cancer-screening-hpv-test-guideline.

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Cervical Cancer Staging

Stage	2014 FIGO	2018 FIGO
I	**Confined to the cervix**	
IA	≤5 mm depth and ≤7 mm width	≤5 mm depth*
IA1	≤3 mm in depth and ≤7 mm width	≤3 mm depth
IA2	>3 mm and <5 mm in depth and ≤7 mm width	>3 mm and ≤5 mm depth
IB	Confined to the cervix, or preclinical lesions greater than stage IA	>5 mm depth
IB1	Clinical lesions ≤4 cm in size	≤2 cm maximum diameter*
IB2	Clinical lesions >4 cm in size	>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**	
IIA	Upper 2/3 of the vagina without obvious parametrial involvement	Upper 2/3 of the vagina
IIA1	Clinically visible lesion ≤4 cm	Upper 2/3 of the vagina and ≤4 cm
IIA2	Clinically visible lesion <4 cm	Upper 2/3 of the vagina and >4 cm
IIB	Obvious parametrial involvement but not onto the pelvic sidewall	Parametrial invasion
III	**Pelvic sidewall; lower third of the vagina; Hydronephrosis/non-functioning kidney**	**Lower vagina, pelvic sidewall, ureters and lymph nodes***
IIIA	Involvement of the lower vagina but no extension onto pelvic sidewall	Lower 1/3 of the vagina
IIIB	Extension onto the pelvic sidewall, or hydronephrosis/non-functioning kidney	Extension onto the 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**	
IVA	Spread to adjacent pelvic organs	Rectal or bladder involvement
IVB	Spread to distant organs	Distant organs outside the pelvis

*New to 2018 staging criteria

FIGO, Fédération Internationale de Gynécologie et d'Obstétrique.

FIGO Committee on Gynecologic Oncology. *Int J Gynaecol Obstet*. 2014;125(2):97–98.
Bhatla N, et al. *Int J Gynecol Obstet*. 2019;145(1):129–135.

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Patient Case

A 58-year-old post-menopausal female was referred to gynecologic oncology service after experiencing repeated abnormal vaginal bleeding.

Her last menstrual period was at age 52. She is single and without consistent medical insurance, and she is non-compliant with all recommended cancer screenings.

Examination and biopsy of the cervix demonstrated invasive adenocarcinoma. PET-CT imaging confirmed an oblong cervical lesion, 6 cm in the longest dimension; invasion of upper 1/3 of the anterior vaginal wall; invasion of left parametrium, not involving the pelvic side wall or other organs; and no metastases observed.

She was diagnosed with FIGO stage IIB cervical cancer.

What would you recommend for this patient?

PET-CT, positron emission tomography/computed tomography.

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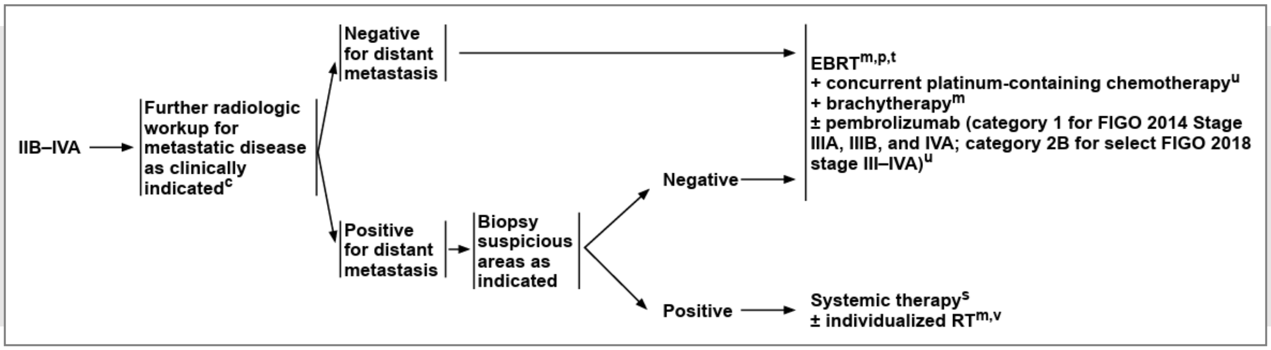
NCCN Recommended Cervical Cancer Primary Treatment



[p] Induction chemotherapy (carboplatin/paclitaxel) followed by single agent cisplatin (or carboplatin) and radiation given according to the INTERLACE protocol could be considered. (McCormack M, et al. *Lancet.* 2024;404:1525–1535.)

[t] Extended field RT is recommended when para-aortic nodes are involved by imaging or confirmed on pathology. This may also be added in select patients with positive pelvic nodes, such as common iliac metastasis.

[u] Concurrent platinum-containing chemotherapy with EBRT utilizes cisplatin as a single agent (or carboplatin if cisplatin intolerant). Pembrolizumab may be added as follows: cisplatin (or carboplatin)/RT and pembrolizumab (for FIGO 2014 stage IIIA, IIIB, and IVA: category 1); cisplatin (or carboplatin)/RT and pembrolizumab (for select FIGO 2018 stage III–IVA: category 2B). Category 2B is for FIGO 2018 stage IIIC purely on nodal metastasis without concomitant tumor characteristics defined in 2014 FIGO stage IIIA–IIIB. If the FIGO 2018 staging of stage III overlaps with FIGO 2014 IIIA/IIIB staging, category 1 can be applied to cisplatin (or carboplatin) + pembrolizumab.

EBRT, external beam radiation therapy; RT, radiation therapy.

National Comprehensive Cancer Network (NCCN). NCCN website. Version 4.2025. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf.

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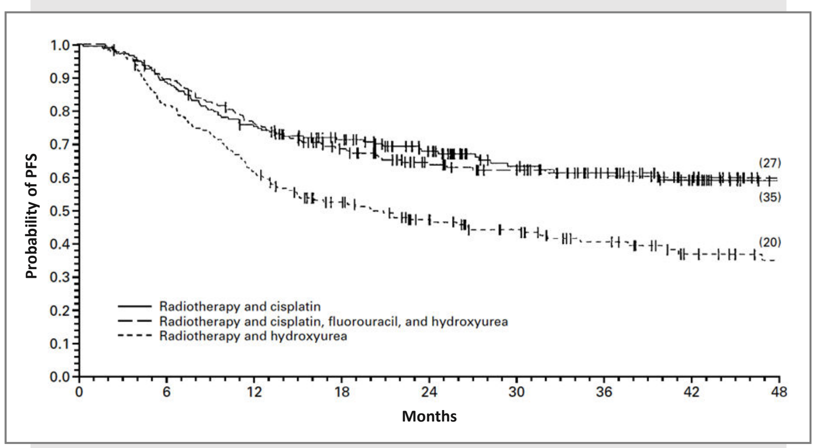
GOG 120 Established the Standard of Care in 1999

Cisplatin Plus RT in Locally Advanced Cervical Cancer (LACC)

- N=526 women
- Median duration of follow up was 35 months
- Both groups that received cisplatin had a higher rate of progression-free survival (PFS) and overall survival (OS)
- At 2 years, 67% of patients were alive and progression-free with cisplatin compared to 46% with hydroxyurea



Rose PG, et al. *N Engl J Med*. 1999;340(15):1144.

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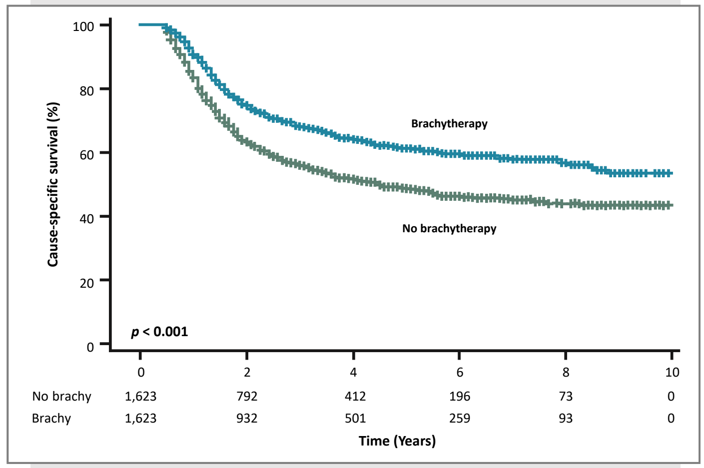
Brachytherapy

- Brachytherapy (BT) is the only method demonstrated to provide the high dose of radiation needed to control cervical cancer while minimizing adverse effects on normal tissue
- SEER data shows BT utilization **decreased from 83% in 1988 to 58% in 2009** (*P*<0.001)
- BT was associated with higher 4-year cause-specific survival (64.3% vs 51.5%, *P*<0.001) and OS (58.2% vs 46.2%, *P*<0.001)



Banerjee R, Kamrava M. *Int J Women's Health*. 2014;6:555–564.
Han K, et al. *Int J Radiat Oncol Biol Phys*. 2013;87:111–119. Holschneider CH, et al. *Gynecol Oncol*. 2019;152:540–547.

Patient Case (…continued)

The patient underwent surgery (radical hysterectomy, bilateral salpingo-oophorectomy, lymph node dissection, and exploratory laparotomy). She also receives 5 cycles of adjuvant cisplatin + EBRT, followed by brachytherapy.

At 22 months post surgery, MRI and PET-CT confirm recurrence within the original radiation field.

What would you recommend for this patient?

MRI, magnetic resonance imaging.

ENGOT-cx11/GOG-3047/KEYNOTE-A18

Randomized, Double-Blind, Phase III Study

Key Eligibility Criteria

- FIGO 2014 stage IB2-IIB (node-positive disease) or FIGO 2014 stage III-IVA (either node-positive or node-negative disease)
- 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)
- Planned total radiotherapy dose (<70 Gy vs ≥70 Gy [EQD2])

R
1:1
N=1,060

Cisplatin 40 mg/m² QW for 5 cycles[a] + EBRT followed by brachytherapy
+
Pembrolizumab 200 mg Q3W for 5 cycles

Pembrolizumab 400 mg Q6W for 15 cycles

Cisplatin 40 mg/m² QW for 5 cycles[a] + EBRT followed by brachytherapy
+
Placebo Q3W for 5 cycles

Placebo Q6W for 15 cycles

Endpoints

- Primary: PFS (per RECIST v1.1) by investigator or histopathologic confirmation and OS
- Secondary: 24-month PFS, 36-month OS, ORR, patient-reported HRQoL, and safety

[a]A 6th cycle was allowed per investigator discretion.

EQD2, equivalent dose in 2 Gy; Gy, gray (radiation dose); HRQoL, health-related quality of life; IMRT, intensity-modulated radiation therapy; ORR, overall response rate; Q#W, every # week(s); RECIST, Response Evaluation Criteria in Solid Tumors; VMAT, volumetric-modulated arc therapy.

Lorusso D, et al. *Lancet*. 2024;403(10434):1341–1350. Lorusso D, et al. *Ann Oncol*. 2023;34:S1279–S1280.

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KEYNOTE-A18: Baseline Characteristics

	Pembro Arm (N=529)	Placebo Arm (N=531)
Age, median (range)	49 years (22–87)	50 years (22–78)
Race[a]		
White	254 (48.0%)	264 (49.7%)
Asian	156 (29.5%)	148 (27.9%)
Multiple	78 (14.7%)	86 (16.2%)
American Indian or Alaska Native	24 (4.5%)	22 (4.1%)
Black or African American	14 (2.6%)	8 (1.5%)
Native Hawaiian or Other Pacific Islander	2 (0.4%)	1 (0.2%)
PD-L1 CPS		
<1	22 (4.2%)	28 (5.3%)
≥1	502 (94.9%)	498 (93.8%)
Missing	5 (0.9%)	5 (0.9%)
ECOG PS 1	149 (28.2%)	133 (25.0%)
Squamous cell carcinoma	434 (82.0%)	451 (84.9%)

	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 (2.6%)	10 (1.9%)
Positive pelvic and para-aortic	104 (19.7%)	104 (19.6%)
No positive pelvic or para-aortic	84 (15.9%)	93 (17.5%)
Planned type of EBRT		
IMRT or VMAT	469 (88.7%)	470 (88.5%)
Non-IMRT and non-VMAT	60 (11.3%)	61 (11.5%)
Planned total radiotherapy dose (EQD2)		
<70 Gy	47 (8.9)	46 (8.7)
≥70 Gy	482 (91.1)	485 (91.3)

[a]3 patients (0.3%) had missing information for race, 1 (0.2%) in the pembro arm and 2 (0.4%) in the placebo arm.
[b]Per protocol, a positive lymph node is defined as ≥1.5 cm shortest dimension by MRI or CT. Data cutoff date: January 8, 2024.

CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PD-L1, programmed cell death ligand 1.
Lorusso D, et al. *Lancet*. 2024;403(10434):1341–1350. Lorusso D, et al. *Ann Oncol*. 2023;34:S1279–S1280.

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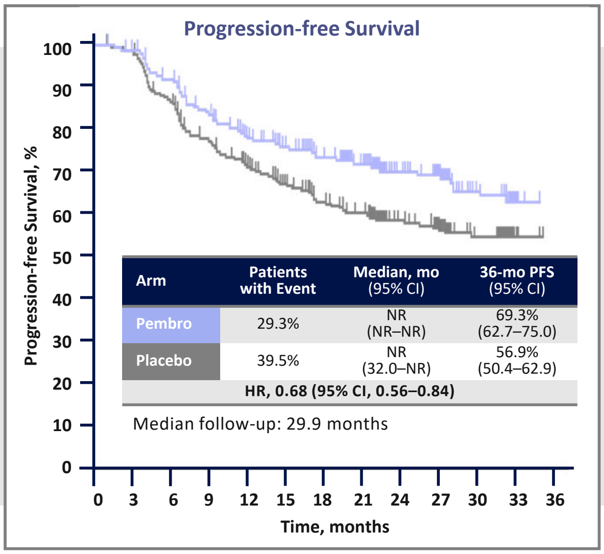
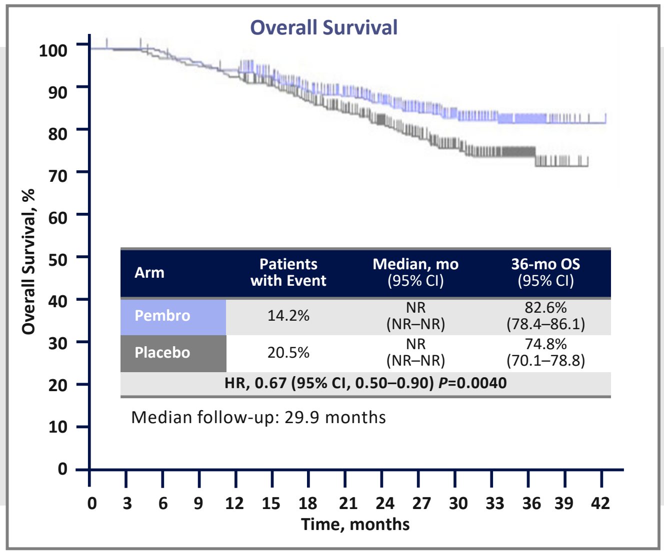
KEYNOTE-A18

Updated PFS and OS



Arm	Patients with Event	Median, mo (95% CI)	36-mo PFS (95% CI)
Pembro	29.3%	NR (NR–NR)	69.3% (62.7–75.0)
Placebo	39.5%	NR (32.0–NR)	56.9% (50.4–62.9)
HR, 0.68 (95% CI, 0.56–0.84)			



Arm	Patients with Event	Median, mo (95% CI)	36-mo OS (95% CI)
Pembro	14.2%	NR (NR–NR)	82.6% (78.4–86.1)
Placebo	20.5%	NR (NR–NR)	74.8% (70.1–78.8)
HR, 0.67 (95% CI, 0.50–0.90) *P*=0.0040			

CI, confidence interval; HR, hazard ratio; NR, not reached.

Lorusso D, et al. *Lancet*. 2024;404(10460):1321–1332. Lorusso D, et al. *Lancet*. 2024;403(10434):1341–1350.

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KEYNOTE-826

Randomized, Double-Blind, Phase III Study

Key Eligibility Criteria

- Persistent, recurrent, or metastatic cervical cancer not amenable to curative treatment
- No prior systemic chemotherapy (prior radiotherapy and chemoradiotherapy permitted)
- ECOG PS 0 or 1

R 1:1

Pembrolizumab 200 mg IV Q3W for up to 35 cycles + Paclitaxel + Cisplatin or Carboplatin IV Q3W for up to 6 cycles[a] ± Bevacizumab 15 mg/kg IV Q3W

Placebo IV Q3W for up to 35 cycles + Paclitaxel + Cisplatin or Carboplatin IV Q3W for up to 6 cycles[a] ± Bevacizumab 15 mg/kg IV Q3W

Stratification Factors

- Metastatic disease at diagnosis (yes vs no)
- PD-L1 CPS (<1 vs 1 to <10 vs ≥10)
- Planned bevacizumab use (yes vs no)

Endpoints

- Dual primary: OS and PFS per RECIST v1.1 by investigator
- Secondary: ORR, DoR, 12-month PFS, and safety
- Exploratory: PROs assessed per EuroQol EQ-5D-5L VAS

[a]Paclitaxel: 175 mg/m^2. Cisplatin: cisplatin 50 mg/m^2. Carboplatin: AUC 5 mg/mL/min. The 6-cycle limit was introduced with protocol amendment 2; although, participants with ongoing clinical benefit who were tolerating chemotherapy could continue beyond 6 cycles after sponsor consultation.

DoR, duration of response; PRO, patient-reported outcomes; VAS, visual analog scale.

Colombo N, et al. *N Engl J Med*. 2021;385(20):1856–1867.

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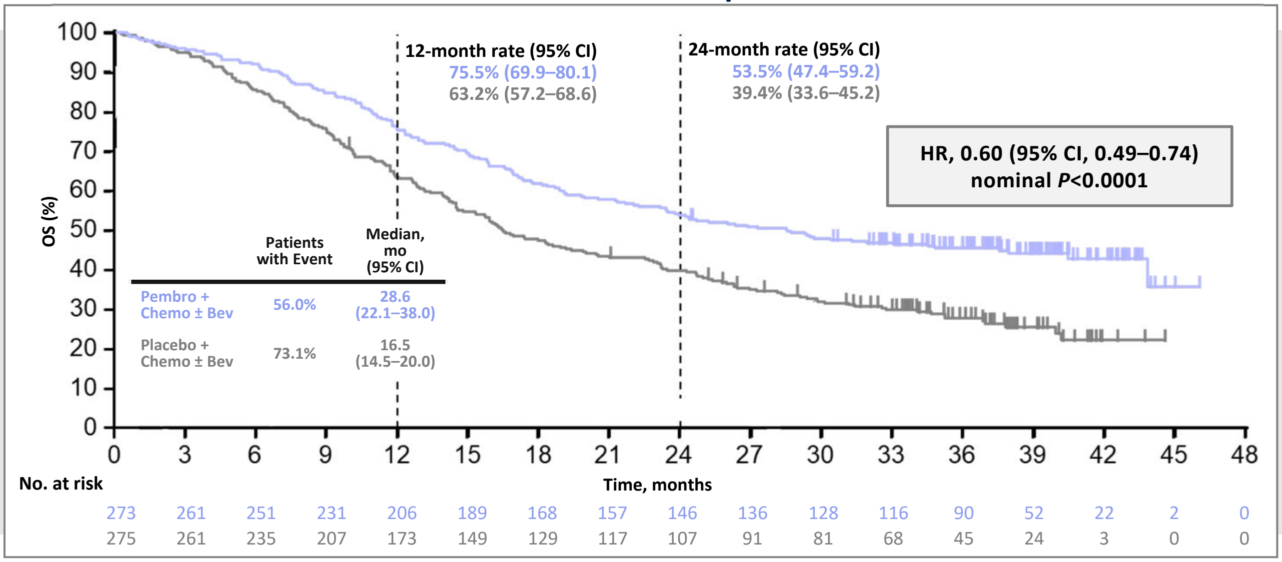
KEYNOTE-826: Protocol-specified Final OS

PD-L1 CPS ≥1 Population



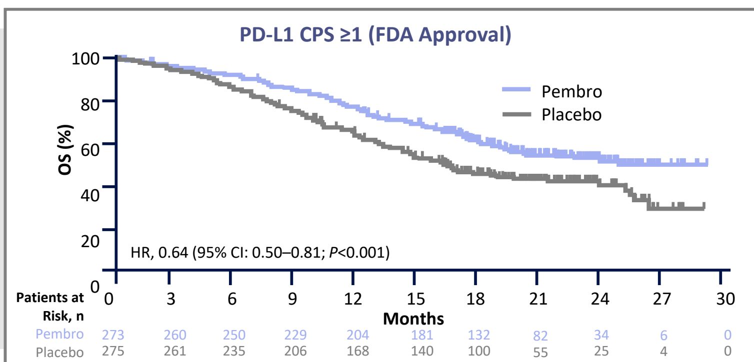
Data cutoff date: October 3, 2022.

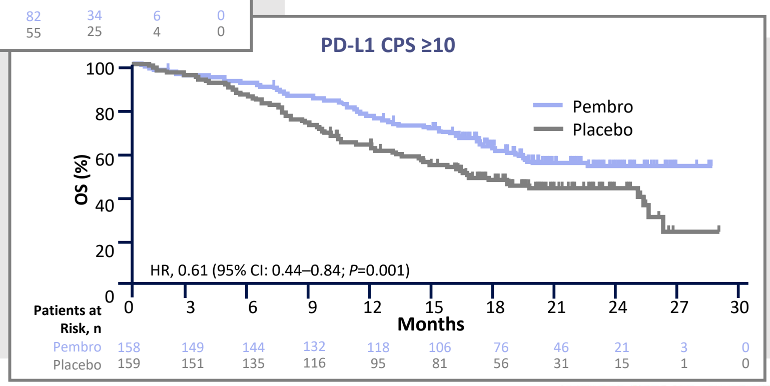
Bev, bevacizumab; Chemo, chemotherapy.

Monk BJ, et al. *J Clin Oncol*. 2023;41(36):5505–5511.

KEYNOTE-826

Interim OS





Pembro, pembrolizumab.

Colombo N, et al. *N Engl J Med*. 2021;385(20):1856–1867.

BEATcc

Study Design

- Primary stage IVB, persistent or recurrent carcinoma of the cervix
- Measurable disease by RECIST v1.1
- ECOG-PS: 0–1
- No previous systemic chemotherapy for advanced or recurrent disease
- Available tissue (archival or fresh)
- N=404 patients

R 1:1

Control Arm

Cisplatin or carboplatin + paclitaxel + bevacizumab (GOG 240) until disease progression, unacceptable toxicity, death, or withdrawal of consent

Experimental Arm

Cisplatin or carboplatin + paclitaxel + bevacizumab + atezolizumab until disease progression, unacceptable toxicity, death, or withdrawal of consent

Primary Endpoint
- OS

Secondary Endpoints
- PFS
- ORR
- DoR
- Safety
- HRQoL

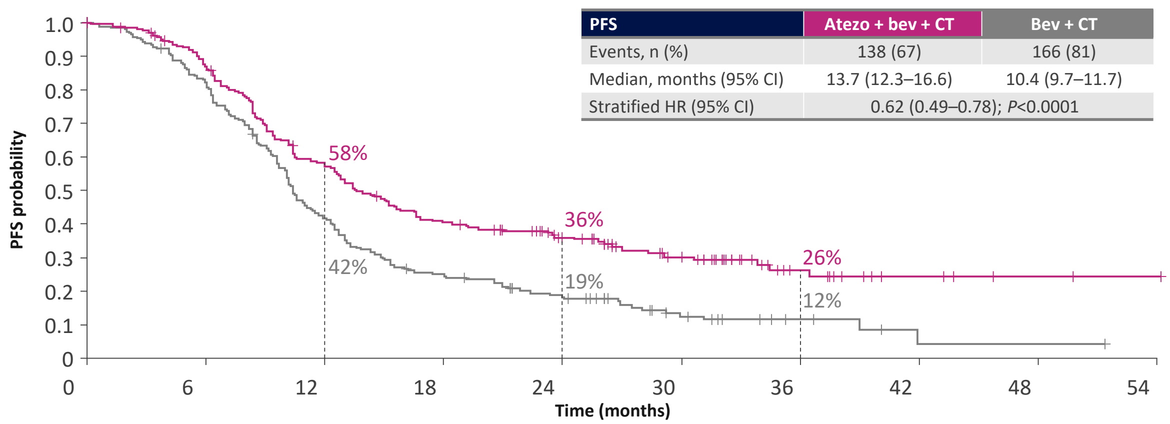
Stratification Factors
- Prior ChemoRT
- Histology: SCC vs Adeno (including adenosquamous)
- Chemotherapy backbone: cisplatin vs carboplatin

Atezolizumab is not FDA-approved for the treatment of cervical cancer.
Adeno, adenocarcinoma; ChemoRT, chemotherapy + radiation therapy; SCC, squamous cell carcinoma.

Grau JF, et al. *Int J Gynecol Cancer*. 2020;30(1):139–143.

BEATcc

Dual Primary Endpoint, PFS



PFS	Atezo + bev + CT	Bev + CT
Events, n (%)	138 (67)	166 (81)
Median, months (95% CI)	13.7 (12.3–16.6)	10.4 (9.7–11.7)
Stratified HR (95% CI)	0.62 (0.49–0.78); *P*<0.0001	

No. at risk										
Atezo + bev + CT	206	174	114	79	58	37	13	5	2	1
Bev + CT	204	159	80	47	31	13	5	1	1	0

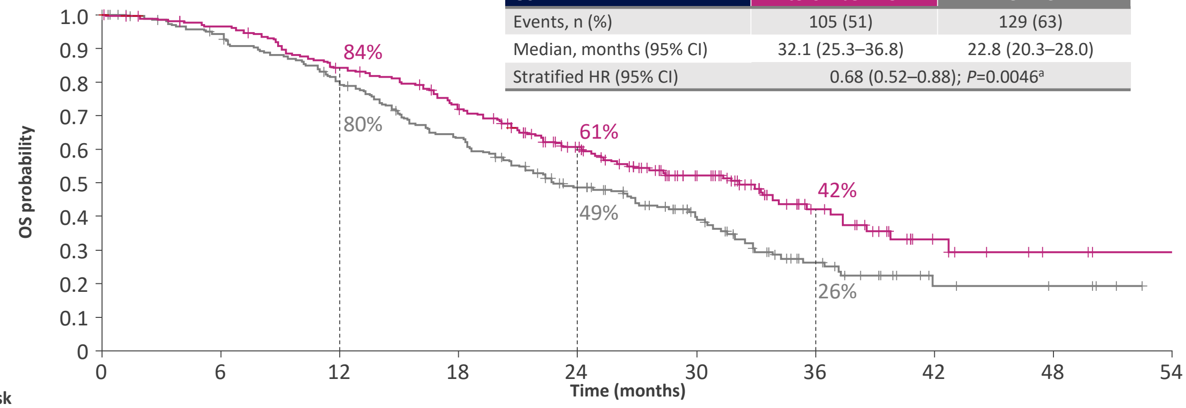
Data cut-off: July 17, 2023 (median follow-up: 32.9 months; 95% CI, 31.2–34.6 months).

Oaknin A, et al. *Lancet*. 2024;403(10421):31–43.

BEATcc: Dual Primary Endpoint, OS

Interim Analysis

OS	Atezo + bev + CT	Bev + CT
Events, n (%)	105 (51)	129 (63)
Median, months (95% CI)	32.1 (25.3–36.8)	22.8 (20.3–28.0)
Stratified HR (95% CI)	0.68 (0.52–0.88); *P*=0.0046[a]	



No. at risk										
Atezo + bev + CT	206	194	167	140	103	64	27	9	3	1
Bev + CT	204	182	152	119	83	50	22	6	4	0

[a]Interim OS was statistically significant, crossing the boundary of *P*=0.0238.
Data cut-off: July 17, 2023 (median follow-up: 32.9 months; 95% CI, 31.2–34.6 months).

Atezolizumab is not FDA-approved for the treatment of cervical cancer.

Atezo, atezolizumab.

Oaknin A, et al. *Lancet*. 2024;403(10421):31–43.

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Patient Case (…continued)

She receives comprehensive molecular testing. Findings include: PD-L1 CPS 6; HER2 IHC 1+; and negative for other actionable molecular alterations.

She receives pembrolizumab + cisplatin/paclitaxel + bevacizumab and achieves a complete response lasting for 12 months, until her cancer recurs.

What would you recommend for this patient in the second line of therapy?

IHC, immunohistochemistry.

National Comprehensive Cancer Network (NCCN). NCCN website. Version 4.2025. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf.

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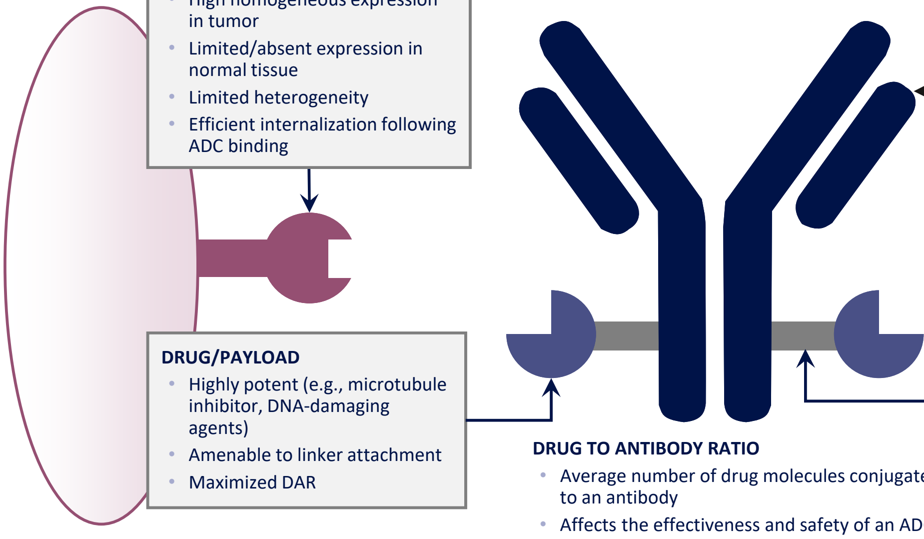
ADVANCING CERVICAL CANCER CARE

Navigating New Therapies, Guidelines, and Patient-Centric Approaches

ADCs: Understanding Their Composition and Structure



ANTIGEN TARGET/RECEPTOR
- High homogeneous expression in tumor
- Limited/absent expression in normal tissue
- Limited heterogeneity
- Efficient internalization following ADC binding

ANTIBODY
- High affinity and avidity for target antigen
- Long half-life
- Conjugation sites with minimal impact on ADC stability, internalization, and pharmacokinetics (e.g., cysteine, lysine)
- Chimeric or humanized (decreasing immunogenicity)

DRUG/PAYLOAD
- Highly potent (e.g., microtubule inhibitor, DNA-damaging agents)
- Amenable to linker attachment
- Maximized DAR

DRUG TO ANTIBODY RATIO
- Average number of drug molecules conjugated to an antibody
- Affects the effectiveness and safety of an ADC

LINKER
- Controlled release of payload
  - Non-cleavable (e.g., lysosomal degradation of mAb)
  - Cleavable (e.g., acid/redox/lysosomal sensitive)

ADC, antibody-drug conjugate; DAR, drug to antibody ratio, mAb, monoclonal antibody.

Koster KL, et al. *Explor Target Antitumor Ther*. 2022;3(1):27–36. Trail PA. *Antibodies*. 2013;2(1):113–129.

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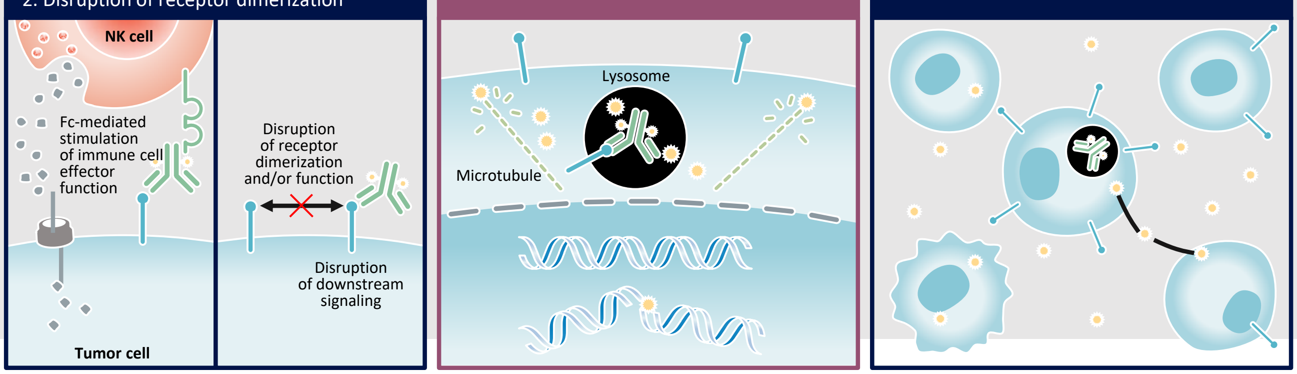
ADC Mechanisms of Action

Antibody engagement leads to payload-independent antitumor activity via several mechanisms:
1. Fc-mediated stimulation of immune cell
2. Disruption of receptor dimerization

Most ADCs are internalized in tumor cells
The payload is released from endosomes and/or lysosomes and takes its effect on cells, leading to cell death

Membrane-permeable payloads enter neighboring cells regardless of target expression and can also kill these cells (bystander effect)



Fc region of the mAb component of ADCs can orchestrate antibody-dependent cellular cytotoxicity (ADCC)

Drago JZ, et al. *Nat Rev Clin Oncol*. 2021;18:327–344.

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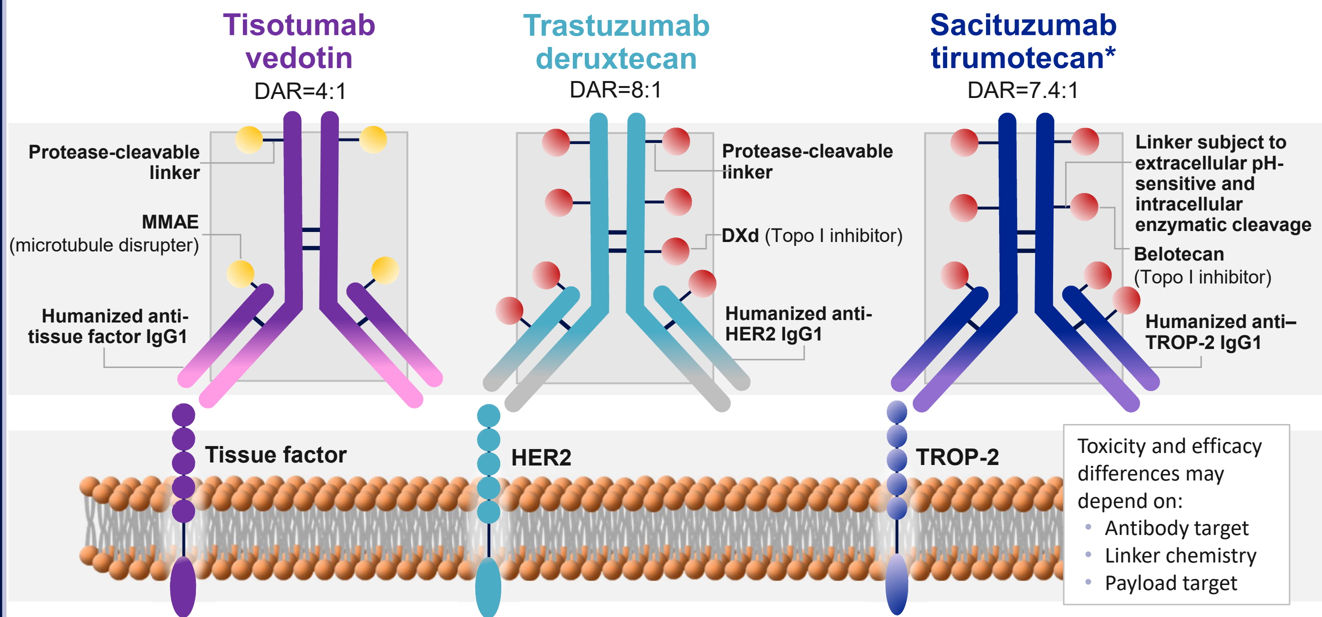
Comparison of ADCs for Cervical Cancer



Toxicity and efficacy differences may depend on:

- Antibody target
- Linker chemistry
- Payload target

DXd, deruxtecan; IgG, immunoglobulin G; MMAE, monomethyl auristatin E.

*Sacituzumab tirumotecan is not FDA approved for any indication.

Xu B, et al. *J Clin Oncol*. 2024;42(Suppl 16):104.
Tisotumab vedotin-tftv (package insert). Revised April 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761208s007lbl.pdf.
Fam-trastuzumab deruxtecan-nxki (package insert). Revised April 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761139s028lbl.pdf.

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Optimal ADC Targets in Gynecologic Cancers

Tissue factor (TF) is a transmembrane receptor for coagulation factor VII/VIIa

- Under normal conditions, it is involved in the coagulation cascade
- Under oncogenic conditions, it is involved in tumor angiogenesis, proliferation, and thrombosis
- It is highly expressed in squamous cell and adenocarcinoma of the cervix

Unmet need in recurrent or metastatic cervical cancer

- Associated with a poor prognosis and a high mortality rate globally
- Fourth most deadly cancer in female patients worldwide
- Despite the addition of immunotherapy, patients who progress on/after first-line therapy continue to have a high unmet need

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Phase II innovaTV-204/GOG-3023/ENGOT-cx6
Tisotumab Vedotin in Cervical Cancer

Key Eligibility Criteria
- Recurrent or metastatic cervical cancer
- Disease progression on or after chemotherapy doublet + bevacizumab, if eligible
- ≤2 prior lines
- Measurable disease per RECIST v1.1
- ECOG PS 0–1

→ **Tisotumab vedotin** 2 mg/kg IV Q3W (n=253) →

Primary Endpoint
- ORR

Key Secondary Endpoints
- DoR, PFS, safety

[a]Chemotherapy regimens were given at the following doses: topotecan: 1 or 1.25 mg/m^2 IV on days 1 to 5, every 21 days; vinorelbine: 30 mg/m^2 IV on days 1 and 8, every 21 days; gemcitabine: 1,000 mg/m^2 IV on days 1 and 8, every 21 days; irinotecan: 100 or 125 mg/m^2 IV weekly for 28 days, every 42 days; pemetrexed: 500 mg/m^2 on day 1, every 21 days.

Coleman RL, et al. *Lancet Oncol*. 2021;22(5):609–619.

CECONCOLOGY

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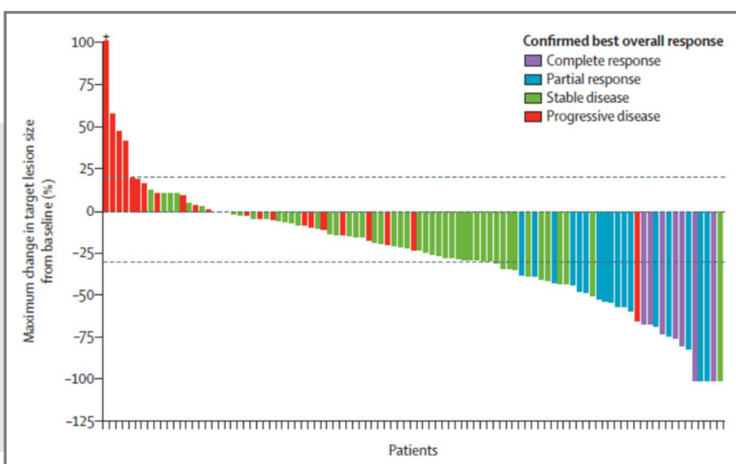
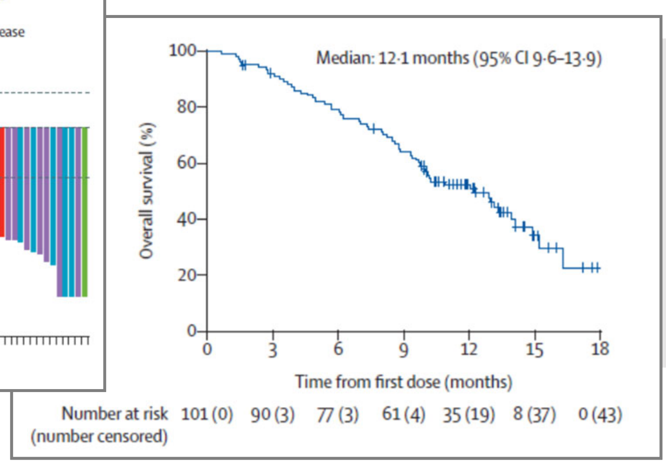
Phase II innovaTV-204/GOG-3023/ENGOT-cx6
Tisotumab Vedotin in Cervical Cancer





Coleman RL, et al. *Lancet Oncol*. 2021;22(5):609–619.

CECONCOLOGY

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Phase III innovaTV 301
Tisotumab Vedotin in Cervical Cancer

- **2021:** Received accelerated FDA approval for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy, based on the phase II innovaTV 204/GOG-3023/ENGOT-cx6 study
- **2024:** Under FDA priority review for full approval based on data from the phase III confirmatory innovaTV301/ENGOT-cx12/GOG-3057 trial

Key Eligibility Criteria
- Recurrent or metastatic cervical cancer
- Disease progression on or after chemotherapy doublet ± bevacizumab and an anti–PD-L1 agent, if eligible and available
- ≤2 prior lines
- Measurable disease per RECIST v1.1
- ECOG PS 0–1

Stratification
- ECOG PS (0 vs 1)
- Prior bevacizumab (yes vs no)
- Prior anti–PD-L1 therapy (yes vs no)
- Geographic region (U.S., Europe, other)

R 1:1

Tisotumab vedotin
2 mg/kg IV Q3W
(n=253)

IC chemotherapy[a]
(n=249)

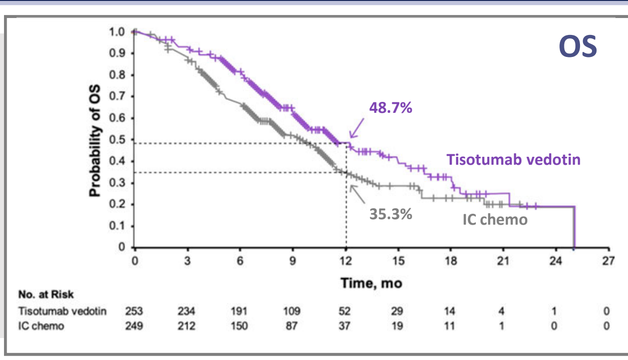
Primary Endpoint
- OS

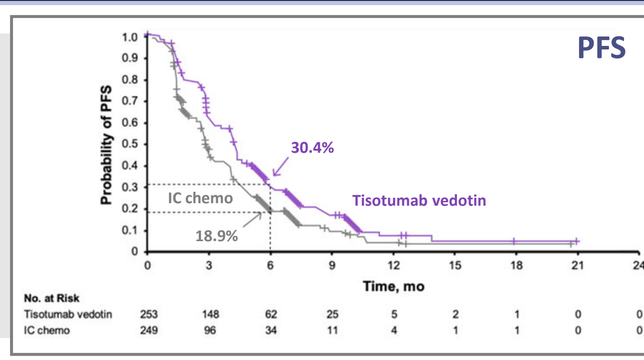
Key Secondary Endpoints
- INV-PFS, INV-ORR, safety

[a]Chemotherapy regimens were given at the following doses: topotecan: 1 or 1.25 mg/m² IV on days 1 to 5, every 21 days; vinorelbine: 30 mg/m² IV on days 1 and 8, every 21 days; gemcitabine: 1,000 mg/m² IV on days 1 and 8, every 21 days; irinotecan: 100 or 125 mg/m² IV weekly for 28 days, every 42 days; pemetrexed: 500 mg/m² on day 1, every 21 days.

INV, investigator.
Vergote I, et al. *N Engl J Med.* 2024;391(1):44–55.

Phase III innovaTV 301
Tisotumab Vedotin in Cervical Cancer





	Events/Total, n	Median OS, mo (95% CI)
Tisotumab vedotin	123/253	11.5 (9.8–14.9)
IC chemo	140/249	9.5 (7.9–10.7)
Stratified log-rank P^a=0.0038		
HR, 0.70 (95% CI, 0.54–0.89)		

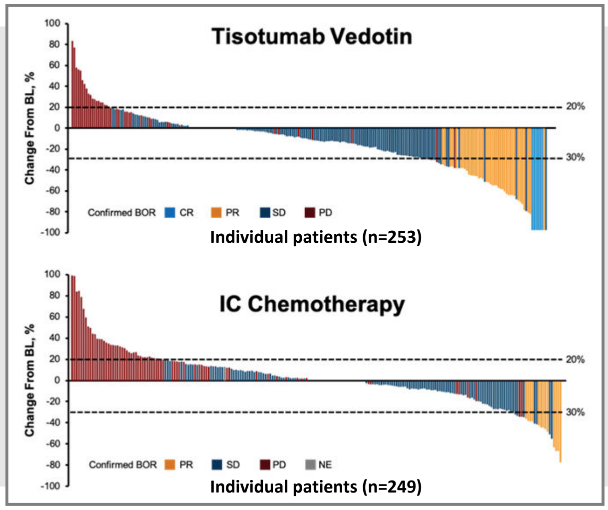
	Events/Total, n	Median PFS, mo (95% CI)
Tisotumab vedotin	198/253	4.2 (4.0–4.4)
IC chemo	194/249	2.9 (2.6–3.1)
Stratified log-rank P^b<0.0001		
HR, 0.67 (95% CI, 0.54–0.82)		

[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. *N Engl J Med.* 2024;391(1):44–55.

innovaTV 301
Tisotumab Vedotin in Cervical Cancer

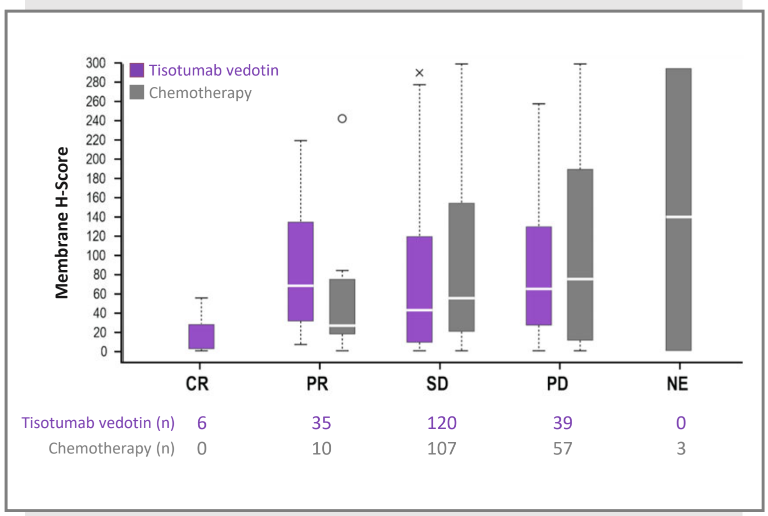
	Tisotumab Vedotin (n=253)	IC Chemotherapy (n=249)
ORR, % (95% CI)	17.8 (13.3–23.1)	5.2 (2.8–8.8)
Odds ratio (95% CI)	4.0 (2.1–7.6) *P*<0.0001	
BOR, n (%)		
CR	6 (2.4)	0
PR	39 (15.4)	13 (5.2)
SD	147 (58.1)	132 (53.0)
PD	46 (18.2)	74 (29.7)
NE/NA	15 (5.9)	30 (12.0)
DCR,[a] % (95% CI)	75.9 (70.1–81.0)	58.2 (51.8–64.4)
Median DoR (95% CI)	5.3 (4.2–8.3)	5.7(2.8–NR)



BOR, best overall response; CR, complete response; DCR, disease control rate; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.
Vergote I, et al. *N Engl J Med*. 2024;391(1):44–55.

innovaTV 301
Confirmed ORR Trends Were Consistent Regardless of Tissue Factor (TF) Expression

- 210 (83.0%) tisotumab vedotin patients and 194 (77.9%) chemotherapy patients had biopsies evaluable for TF expression
  - Of these, positive membrane TF expression was observed in 194 (92.4%) and 183 (94.3%) patients, respectively
- Comparable distribution of TF expression was observed among different confirmed best overall response groups



Vergote I, et al. *N Engl J Med*. 2024;391(1):44–55.

Patient Case (...continued)

The patient receives tisotumab vedotin, but prior to initiation, she has an eye exam to determine baseline BCVA.

In the second cycle, she develops dry eye.

What additional steps would you take?

BCVA, best-corrected visual acuity.

National Comprehensive Cancer Network (NCCN). NCCN website. Version 4.2025. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf.

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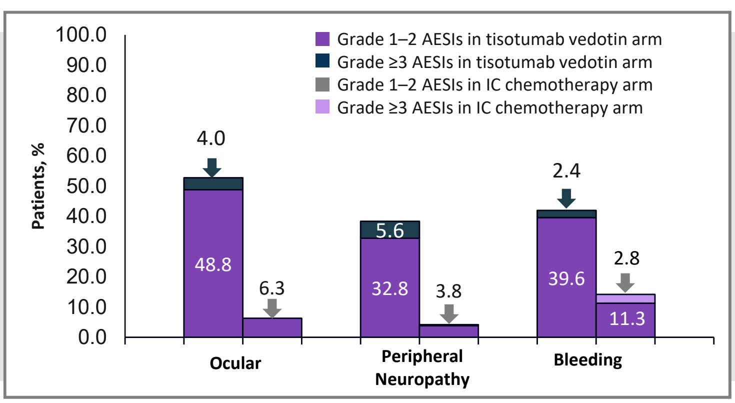
innovaTV 301

Treatment-Related Adverse Events of Special Interest (AESIs) for Tisotumab Vedotin



- There were no grade 4 or 5 AESIs
- Dose discontinuation because of ocular and peripheral neuropathy events occurred in 5.6% of patients for each arm

Most Common Preferred Terms for Each AESI

- **Ocular:** conjunctivitis (31.2%), keratitis (15.6%), dry eye (13.2%)
- **Peripheral neuropathy:** peripheral sensory neuropathy (28.4%), paresthesia (3.0%), muscular weakness (2.8%), peripheral sensorimotor neuropathy (3.2%)
- **Bleeding:** epistaxis (26.0%), hematuria (7.2%), vaginal hemorrhage (10.0%)

AESI, adverse event of special interest.

Vergote I, et al. *N Engl J Med.* 2024;391(1):44–55.

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Expert Insights on the Effective Implementation of Tisotumab Vedotin and Practical Tips for Its Use

Important Provider/Patient Discussion Points

- Treatment schedule and dosing
- Management of AEs
  - Potential for dose holds or reductions
- Ocular AEs—focus on expectations, prevention, plan for eye drops/regimens
  - Timeline of eye drops (prior to infusion/day of infusion/days after infusion)
  - Types of eye drops
  - Patient reminder tools
  - Educate eye care specialists

Ophthalmic Examination
This will include visual acuity and slit lamp testing by an eye care provider

Corticosteroid Eye Drop
For 72 hours after infusion, administer 1 drop dexamethasone 0.1% per eye 3× day

Prior to infusion day → Day of infusion (day 1) → Days 2 and 3

10 minutes before infusion → During ADC infusion (30 minutes) → For 20 minutes after infusion

Corticosteroid and Vasoconstrictor Eye Drops
Administer 1 drop of dexamethasone 0.1% per eye and 3 drops of brimonidine tartrate 0.2% per eye

Cold Packs
Change as needed to ensure eye area remains cold

THROUGHOUT TREATMENT

Use lubricating eye drops multiple times every day throughout treatment and for 30 days after last dose

Avoid contact lens use throughout treatment unless directed by an eye care provider

Kim SK, et al. *Gynecol Oncol*. 2022;165:385–392. Richardson DL, et al. *Gynecol Oncol Rep*. 2023;46:101148.

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Cryotherapy for Stomatitis Prevention

- Oral mucositis is a common complication of cancer treatment, leading to atrophy and destruction of the mucosal lining of the mouth and pain, swelling, and ulcers
  - Grade I: painless ulcerations, erythema, or mild discomfort with no lesions
  - Grade II: painful ulcerations or erythema that do not impose on the patient's eating abilities
  - Grade III: painful confluent pseudomembranous ulcerations or erythema that impact the patient's ability to eat and drink
  - Grade IV: severe deep and/or necrotic ulcerations that require enteral or parenteral support
- Cryotherapy cools the mouth, promotes vasoconstriction, reduces local drug concentrations during infusion of mucotoxic agents with short half-lives
  - Ice chips, frozen mouth guards, commercial devices

Oncology Nursing Society (ONS). ONS website. https://congress.ons.org/clinical-tools/pep/mucositis/cryotherapy.
Al-Rudayni AHM, et al. *Curr Oncol*. 2021;28(4):2852–2867.

CECONCOLOGY

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DESTINY-PanTumor02

T-DXd for HER2-expressing Solid Tumors

Tumor types were selected based on epidemiological frequency, prevalence of HER2 expression, and unmet medical need.

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer guidelines)
- Prior HER2-targeting therapy
- ECOG/WHO PS 0–1 restricted in strenuous activity

T-DXd
5.4 mg/kg
Q3W

n=40 per cohort planned
(*cohorts with no objective responses in the first 15 patients were to be closed*)

- Cervical cancer
- Endometrial cancer
- Ovarian cancer
- Biliary tract cancer
- Pancreatic cancer
- Bladder cancer
- Other tumors[a]

Primary endpoint
- Confirmed ORR (investigator)

Secondary endpoints
- DoR
- DCR
- PFS
- OS
- Safety

Data cut-off for analysis
- June 8, 2023
- FDA approved April 5, 2024

[a]Other tumors cohort: salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget disease (n=3), cutaneous melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, head and neck cancer, lip and/or oral cavity cancer, esophageal adenocarcinoma, intestinal adenocarcinoma, appendiceal adenocarcinoma, esophageal squamous cell carcinoma, testicular cancer, and vulvar carcinoma (all n=1).

ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; WHO, World Health Organization.
Meric-Bernstam F, et al. *J Clin Oncol*. 2024;42:47–58. Clinicaltrials.gov. Identifier: NCT04482309. Last updated March 18, 2025.

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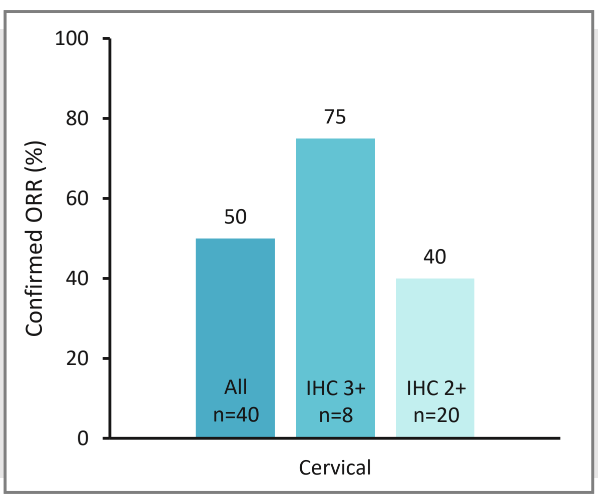
DESTINY-PanTumor02 Study

ORR by HER2 Status: Primary Analysis, Cervical Cancer



Median follow-up: 12.75 months

Efficacy by Tumor Cohort	Cervical Cancer
Median PFS, months	7.0
PFS, 6 months	51.3
PFS, 12 months	29.9
Median OS, months	13.6
OS, 6 months	80.0
OS, 12 months	59.1

Meric-Bernstam F, et al. *J Clin Oncol*. 2024;42:47–58.

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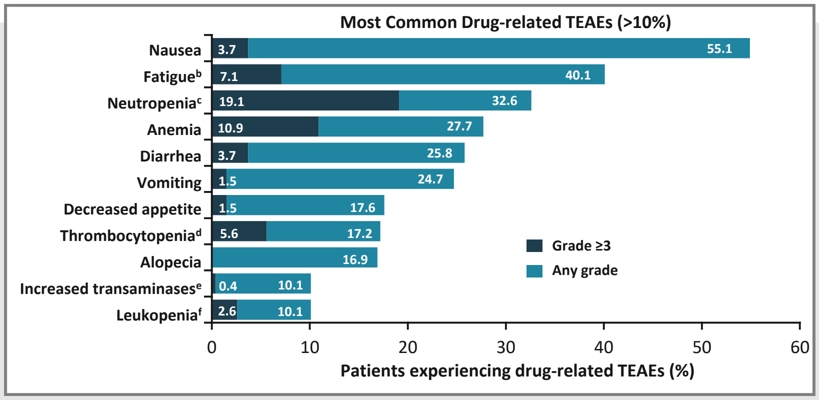
DESTINY-PanTumor02: Safety Summary

n (%)	All Patients, All Tumor Types (N=267)
Any drug-related TEAEs	226 (84.6)
Drug-related TEAEs grade ≥3	109 (40.8)
Serious drug-related TEAEs	36 (13.5)
Drug-related TEAEs-associated with dose discontinuations	23 (8.6)
Drug-related TEAEs-associated with dose interruptions	54 (20.2)
Drug-related TEAEs-associated with dose reductions	54 (20.2)
Drug-related TEAEs-associated with deaths	4 (1.5)[a]



ILD/Pneumonitis Adjudicated as T-DXd related, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
All patients, all tumor types (N=267)	7 (2.6)	17 (6.4)	1 (0.4)	0	3 (1.1)	28 (10.5)

Analyses were performed in patients who received ≥1 dose of T-DXd (N=267); median total treatment duration 5.6 months (range 0.4–31.1).[a]Included pneumonia (n=1), organizing pneumonia (n=1), pneumonitis (n=1), and neutropenic sepsis (n=1). [b]Category includes the preferred terms fatigue, asthenia, and malaise. [c]Category includes the preferred terms neutrophil count decreased and neutropenia. [d]Category includes the preferred terms platelet count decreased and thrombocytopenia. [e]Category includes the preferred terms aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyl transferase increased, hypertransaminasemia. [f]Category includes the preferred terms white blood cell count decreased and leukopenia.

ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event.
Meric-Bernstam F, et al. *J Clin Oncol*. 2024;42:47–58.

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Components of Care Utilizing Immunotherapies

- Team approach
- Regular (weekly) contact with patient
- Identify AEs early
- Patient education and patient-empowered AE monitoring
- Several PROMs are available for monitoring AEs
  - May identify non-treatment-related barriers to care (i.e., transportation, food/housing security)
- Multidisciplinary/multispecialty care

Emphasize to patients that it is extremely important for them to inform their medical care team as soon as possible if they experience any unusual symptoms during or after treatment with cancer immunotherapy.

AEs, adverse events; PROMs, patient-reported outcome measures.
Mendoza T, et al. *J Immunother Cancer*. 2020;8(2). Makker V, et al. *N Engl J Med*. 2022;386(5):437–448.

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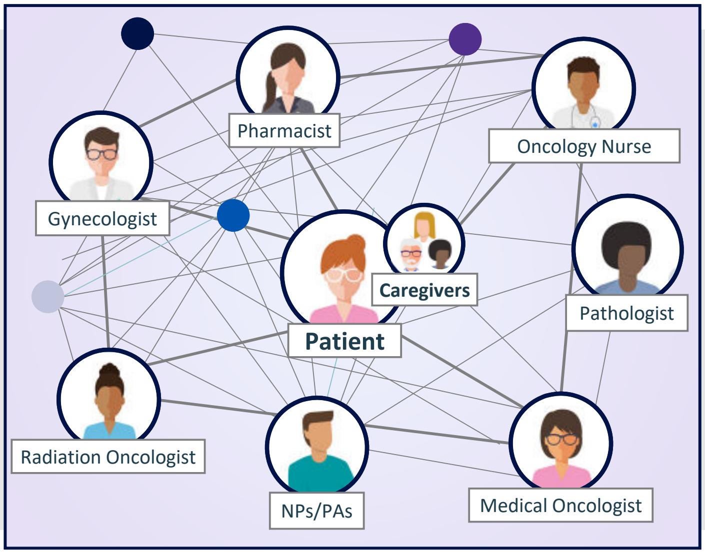
Team-based Approach for the Management of Patients with Cancer



In general, treatment recommendations should be made by a multidisciplinary team (MDT).

MDTs increase treatment personalization, improve outcomes, preserve quality of life, and increase overall patient satisfaction.

Each person on the care team should:

- Encourage use of comprehensive molecular biomarker testing
- Ensure guideline-concordant care
- Be available to answer questions

Cornelius LA, et al. *Oncologist*. 2021;26(9):e1644–e1651. Daly ME, et al. *J Clin Oncol*. 2022:40(12).

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Put information into action!

Takeaways from this program can be implemented into your practice to improve patient care.

- Encourage use of HPV vaccination as a tool to reduce cervical cancer incidence
- Document delivery of guideline-concordant care in EHR charts
- Recognize challenges to receipt of care faced by patients
- Discuss emerging therapy options and clinical trial participation with patients with cervical cancer

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2. Complete the post-test and evaluation at the conclusion of the webcast
3. Enter your **ABIM ID number** and **DOB** (MM/DD) on the evaluation, so credit can be submitted to ABIM

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- In approximately 3 months, complete the follow-up survey from Creative Educational Concepts

CME for MIPS IMPROVEMENT ACTIVITY

CEC will send you confirmation of your participation to submit to CMS attesting to your completion of a CME for MIPS Improvement Activity.

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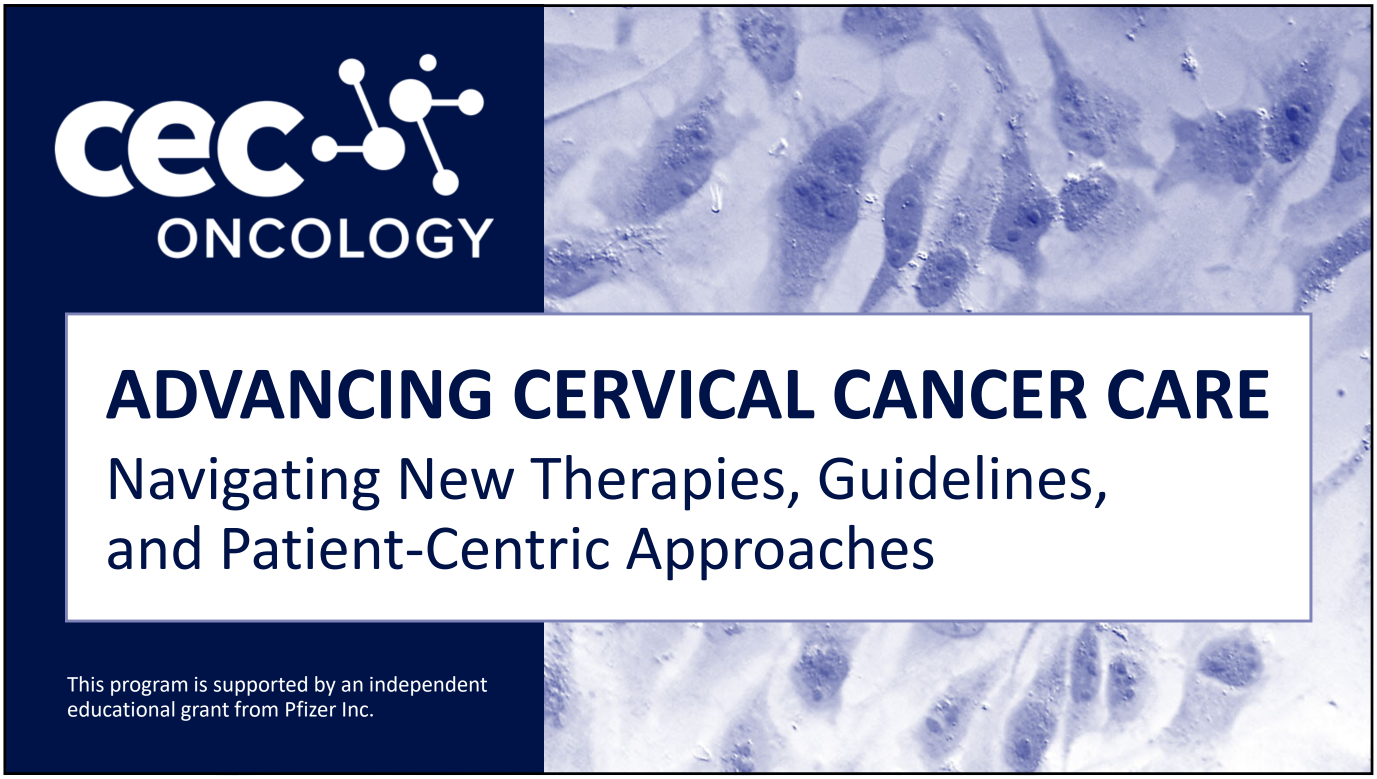
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ADVANCING CERVICAL CANCER CARE
Navigating New Therapies, Guidelines, and Patient-Centric Approaches
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