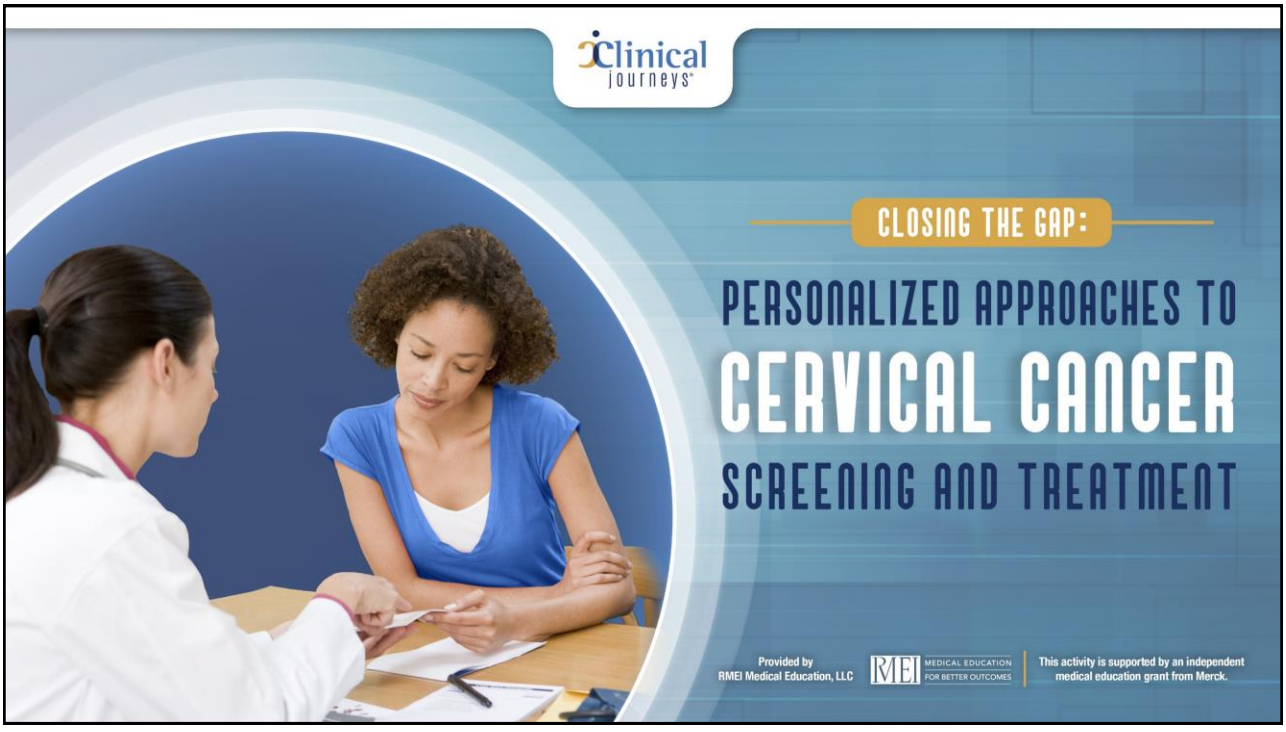

1

Burden of Cervical Cancer

Incidence in the United States in 2023[1]

An estimated 13,960 women will be diagnosed with invasive cervical cancer

Mortality in the United States in 2023[1]

An estimated 4,310 women will die from cervical cancer

5-Year Relative Survival Rates[2]

91% Localized disease

60% Regional disease

19% Distant/metastatic disease

1. American Cancer Society. Cancer Facts & Figures 2023. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf
2. SEER, National Cancer Institute, 2023. https://bit.ly/3FfxOUk

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Patient Story: Tina

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USPSTF Recommendations for Routine Cervical Cancer Screening

Population*	Recommendation
Aged less than 21 years	No screening
Aged 21–29 years	Cytology alone every 3 years‡
Aged 30–65 years	Any one of the following: • Cytology alone every 3 years • FDA-approved primary hrHPV testing alone every 5 years • Cotesting (hrHPV testing and cytology) every 5 years
Aged greater than 65 years	No screening after adequate negative prior screening results§
Hysterectomy with removal of the cervix	No screening in individuals who do not have a history of high-grade cervical precancerous lesions or cervical cancer

- Recommendations apply to individuals with a cervix who do not have any signs or symptoms of cervical cancer, regardless of sexual history or HPV vaccination status
- Recommendations do not apply to individuals who are at high risk, including those who have previously had a high-grade precancerous lesion diagnosis or are immunocompromised

FDA, US Food and Drug Administration; hrHPV, high-risk human papillomavirus testing; USPSTF, US Preventive Services Task Force

US Preventive Services Task Force. *JAMA.* 2018;320(7):674-686.
ACOG. Updated Cervical Cancer Screening Guidelines. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2021/04/updated-cervical-cancer-screening-guidelines#practice-bulletin-figures-1

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Racial/Ethnic Disparities in Cervical Cancer

Screening

Women from racial/ethnic minority groups are significantly more likely to have never been screened for cervical cancer than non-Hispanic White women.[1]

Follow-up

Black women are[2]

- Less likely to be informed of an abnormal Pap test
- Less likely to be contacted for follow-up treatment

Stage at Diagnosis

Black women and Hispanic women are significantly more likely to be diagnosed with advanced-stage cervical cancer than White women.[3]

1. Datta GD, et al. *Prev Med.* 2022;159:107055.
2. Ford S, et al. *Gynecol Oncol.* 2021;160(2):369-374.
3. Holt HK, et al. *JAMA Netw Open.* 2023;6(3):e232985.

Symptoms of Cervical Cancer

Possible Symptoms at Earlier Stages

- Abnormal vaginal bleeding
  - After sexual intercourse
  - After menopause
  - Between menstrual periods
  - Periods that are longer or heavier than usual
- Unusual vaginal discharge (may contain blood)
- Pain
  - During sexual intercourse
  - In the pelvic region

Symptoms of More Advanced Disease

- Swelling of Legs
- Problems urinating
- Problems having a bowel movement
- Blood in urine

American Cancer Society. Signs and Symptoms of Cervical Cancer. January 3, 2020.
https://www.cancer.org/cancer/types/cervical-cancer/detection-diagnosis-staging/signs-symptoms.html

Tina: Medical History

Symptoms

- ❑ Vaginal bleeding and spotting between menstrual periods and after sexual intercourse for past year
- ❑ Leg swelling and problems urinating started 6 weeks ago

Diagnosis

- ❑ Large cervical mass
- ❑ HPV 16 positive
- ❑ Metastasized to liver and lungs
- ❑ Stage IVB cervical cancer

NCCN-Recommended Biomarker Testing

Line of Therapy	Type of Cervical Cancer	Recommended Testing
First	Recurrent, progressive, or metastatic	PD-L1 as determined by an FDA-approved test (combined positive score ≥1)
Second	Recurrent, progressive, or metastatic	Mismatch repair/microsatellite instability testing
Second	Cervical sarcoma	*NTRK* gene fusion
Second	Unresectable or metastatic tumor	Consider tumor mutational burden through a validated and/or FDA-approved assay
Second	Locally advanced or metastatic	Consider *RET* gene fusion

NCCN, National Comprehensive Cancer Network
NCCN Clinical Practice Guidelines, Cervical Cancer. Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf

Tina

- ❑ Metastatic cervical cancer
- ❑ Primary tumor is PD-L1 positive
- ❑ Optimal candidate for first-line treatment with the NCCN guideline-preferred anti-PD-1 therapy

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NCCN-recommended First-line Treatment Options for Cervical Cancer

Preferred Regimens for PD-L1-positive Tumors

- Pembrolizumab + cisplatin/paclitaxel ± bevacizumab
- Pembrolizumab + carboplatin/paclitaxel ± bevacizumab

Preferred Regimens for PD-L1-negative Tumors

- Cisplatin / paclitaxel / bevacizumab
- Carboplatin / paclitaxel / bevacizumab

Other Recommended Regimens

- Cisplatin / paclitaxel
- Carboplatin / paclitaxel
- Topotecan / paclitaxel / bevacizumab
- Topotecan / paclitaxel
- Cisplatin / topotecan
- Cisplatin
- Carboplatin

NCCN Clinical Practice Guidelines, Cervical Cancer. Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf

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KEYNOTE-826: Phase 3 Study

- n=617
- ≥18 years of age
- Persistent, recurrent, or metastatic adenocarcinoma, adenosquamous carcinoma, or squamous-cell carcinoma of the cervix
- No prior systemic therapy

R

Pembrolizumab: 200 mg every 3 weeks
Platinum-based chemotherapy
± Bevacizumab

Placebo every 3 weeks
Platinum-based chemotherapy
± Bevacizumab

1° Endpoints

- PFS
- OS

2° Endpoints

- % patients with confirmed complete or partial response
- Duration of response
- % patients alive without disease progression at 12 months

PFS, progression-free survival; OS, overall survival

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

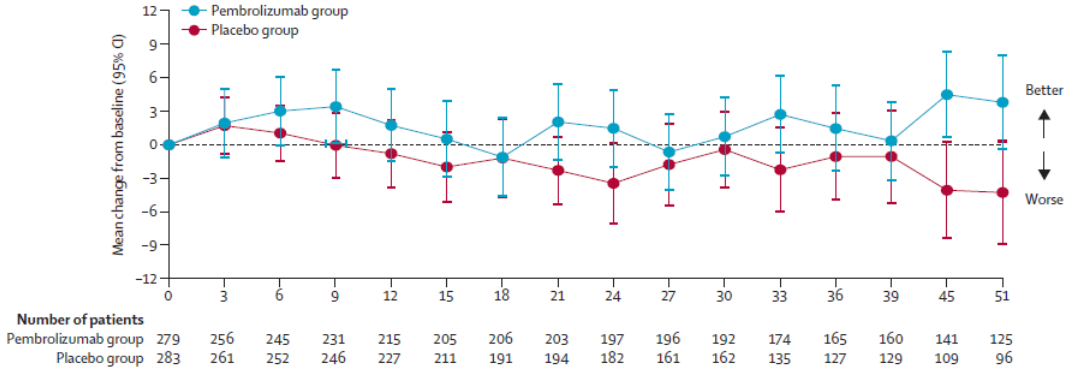
KEYNOTE-826: Final Survival Results

	PD-L1 CPS ≥1		All-Comer		PD-L1 CPS ≥10	
	Pembro + Chemo n = 273	Pbo + Chemo n = 275	Pembro + Chemo n = 308	Pbo + Chemo n = 309	Pembro + Chemo n = 158	Pbo + Chemo n = 159
OS, median, mo	28.6	16.5	26.4	16.8	29.6	17.4
24-mo OS rate, %	53.5	39.4	52.1	38.7	54.4	42.5
OS, HR (95% CI)	0.60 (0.49-0.74); *P*< 0.0001		0.63 (0.52-0.77); *P*< 0.0001		0.58 (0.44-0.78); *P*< 0.0001	
PFS, median, mo	10.5	8.2	10.4	8.2	10.4	8.1
12-mo PFS rate, %	45.6	33.7	44.7	33.1	44.7	33.5
PFS, HR (95% CI)	0.58 (0.47-0.71); *P*< 0.0001		0.61 (0.50-0.74); *P*< 0.0001		0.52 (0.40-0.68); *P*< 0.0001	

The benefit of pembrolizumab + chemo was observed regardless of bevacizumab use

Monk BJ, et al. *J Clin Oncol.* 2023;41(suppl 16):Abstract 5500.

KEYNOTE-826: Health-Related Quality of Life



The survival benefit achieved by adding pembrolizumab to chemotherapy with or without bevacizumab was not accompanied by a decrease in health-related quality of life.

Monk BJ, et al. *Lancet Oncol.* 2023;24(4):392-402.

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KEYNOTE-826: Safety Data

Most Common Grade ≥3 AEs	Pembro + Chemo Percent of Patients	Placebo + Chemo Percent of Patients
Anemia	30.3%	27.8%
Neutropenia	12.4%	9.7%
Hypertension	10.4%	11.7%

Incidence of grade ≥3 AEs was 82.4% in the pembrolizumab + chemo arm and 75.4% in the placebo + chemo arm

AE, adverse event

Monk BJ, et al. *J Clin Oncol.* 2023;41(suppl 16):Abstract 5500.

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KEYNOTE-826: Potential irAEs

irAE	Pembro + Chemo (N=307)		Placebo + Chemo (N=309)	
	Any Grade	Grade 3-5	Any Grade	Grade 3-5
	Number of patients (percent)			
Any Event	104 (33.9)	35 (11.4)	47 (15.2)	9 (2.9)
Hypothyroidism	56 (18.2)	4 (1.3)	28 (9.1)	1 (0.3)
Hyperthyroidism	23 (7.5)	0	9 (2.9)	1 (0.3)
Colitis	16 (5.2)	5 (1.6)	5 (1.6)	5 (1.6)
Severe Skin Reactions	14 (4.6)	12 (3.9)	1 (0.3)	1 (0.3)
Thyroiditis	11 (3.6)	2 (0.7)	1 (0.3)	0
Pneumonitis	6 (2.0)	1 (0.3)	1 (0.3)	0
Hepatitis	5 (1.6)	4 (1.3)	1 (0.3)	1 (0.3)
Adrenal Insufficiency	4 (1.3)	3 (1.0)	0	0

irAE	Pembro + Chemo (N=307)		Placebo + Chemo (N=309)	
	Any Grade	Grade 3-5	Any Grade	Grade 3-5
	Number of patients (percent)			
Pancreatitis	3 (1.0)	2 (0.7)	1 (0.3)	0
Myositis	2 (0.7)	1 (0.3)	0	0
Type 1 Diabetes Mellitus	2 (0.7)	2 (0.7)	0	0
Vasculitis	2 (0.7)	0	0	0
Cholangitis Sclerosing	1 (0.3)	1 (0.3)	0	0
Encephalitis	1 (0.3)	1 (0.3)	0	0
Hypophysitis	1 (0.3)	1 (0.3)	1 (0.3)	0
Myocarditis	1 (0.3)	1 (0.3)	0	0
Nephritis	1 (0.3)	0	0	0

irAE, immune-related adverse event

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

Strategies to Mitigate Potential irAEs

Patient education can improve rapid identification and management of irAEs

- Instruct patients to notify the oncology healthcare team if any new symptoms develop, including severe fatigue, rash, cough, shortness of breath, chest pain, abdominal bloating, change in bowel pattern, weight loss, severe muscle weakness, and/or severe muscle or joint pains
- Instruct patients to carry a wallet card with the type of immunotherapy they are receiving, potential irAEs, and contact numbers for their oncology healthcare team

Laboratory tests should be obtained prior to each treatment and at regular intervals after completion of pembrolizumab to assess for organ function (eg, complete metabolic panel; kidney, liver, thyroid, pancreas)

NCCN Clinical Practice Guidelines, Management of Immunotherapy-Related Toxicities. Version 2.2023.
https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf

Tina

- Develops symptomatic immune-related hypothyroidism
- Referred to an endocrinologist
- Thyroid hormone supplementation with levothyroxine relieves her fatigue and the constant feeling of being cold

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Summary

- **Tina's story highlights the importance of:**
  - Guideline-recommended cervical cancer screening to catch cancer early or before it develops
  - Biomarker testing to guide cervical cancer treatment decisions
  - Immunotherapeutic strategies for treating persistent, recurrent, or metastatic cervical cancer

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and evaluation to receive CE credit