THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (www.mdanderson.org/gynonctrials). Other co-morbidities are taken into consideration prior to treatment selection. All patients with invasive cervical cancer should be referred to a Gynecologic Oncologist.

CLINICAL PRESENTATION AND EVALUATION

No visible or palpable lesion →
- CKC with ECC
- Chest x-ray
- HIV screening
- Hepatitis screening[1]
- Lifestyle risk assessment[2]

Visible or palpable lesion → See Page 2

STAGING

Stage IA1 stromal invasion ≤ 3 mm with negative LVSI → ECC results or margins positive[3]?

Stage IA1 stromal invasion ≤ 3 mm with positive LVSI **or** Stage IA2 stromal invasion > 3 mm and ≤ 5 mm → Consider PET (in addition to MRI pelvis with and without contrast) → ECC results or margins positive[3]?

PRIMARY TREATMENT

ECC results or margins positive[3]?
- Yes → Repeat CKC with ECC → Treat based on stage:
  - Stage IA1: See Box A
  - Stage IA2: See Box B
  - Stage IB-IVB: See Page 2
- No — Stage IA1 → **A**
  - Observation (if fertility desired) **or**
  - Simple hysterectomy[4]

→ See Page 4 for Surveillance

ECC results or margins positive[3]?
- Yes → Repeat CKC with ECC → Treat based on stage:
  - Stage IA1-IA2: See Box B
  - Stage IB-IVB: See Page 2
- No → **B** Surgical candidate?
  - Yes →
    - Simple hysterectomy[4] and pelvic lymph node assessment[5] **or**
    - If fertility desired, CKC and pelvic lymph node assessment[5]
    - Consideration of conservative surgery in select cases[6]

    → High[7] risk → Post-operative radiation therapy with concurrent chemotherapy[8]
    → Intermediate[9] risk → Post-operative radiation therapy with or without concurrent chemotherapy[8]
    → Low risk
  - No → Radiation therapy

→ See Page 4 for Surveillance

SURVEILLANCE

CKC = cold knife conization
ECC = endocervical curettage
LVSI = lymphovascular space invasion

[1] Refer to the Hepatitis B Virus (HBV) Screening and Management and Hepatitis C Virus (HCV) Screening algorithms
[2] See Physical Activity, Nutrition, Obesity Screening and Management, and Tobacco Cessation Treatment algorithms. Ongoing reassessment of lifestyle risks should be a part of routine clinical practice.
[3] Positive margins includes high-grade dysplasia
[4] Minimally invasive hysterectomies are acceptable if ECC results and margins are negative. If margins remain positive, radical hysterectomy is preferred over simple hysterectomy.
[5] Lymphatic mapping with sentinel lymph node biopsy and/or lymph node dissection
[6] See Appendix A for Criteria for and Principles of Conservative Surgery
[7] High risk factors: positive nodes, positive margins, and/or parametrial involvement
[8] Weekly cisplatin or another platinum alternative (*e.g.,* carboplatin)
[9] Intermediate risk factors: stromal invasion, lymphovascular space involvement (LVSI) and/or large clinical tumor diameter

Department of Clinical Effectiveness V13
Approved by the Executive Committee of the Medical Staff on 10/21/2025

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (www.mdanderson.org/gynonctrials). Other co-morbidities are taken into consideration prior to treatment selection. All patients with invasive cervical cancer should be referred to a Gynecologic Oncologist.

CLINICAL PRESENTATION AND EVALUATION

Visible or palpable lesion

- Physical exam
- Cervical biopsy
- HIV screening
- Hepatitis screening[1]
- PET/CT
- MRI of pelvis with and without contrast[2]
- Lifestyle risk assessment[3]

STAGING

Clinical stage IB1 **and** a surgical candidate → Repeat CKC with ECC

- Stage IB1 stromal invasion < 10 mm on CKC
- Stage IB1 stromal invasion ≥ 10 mm on CKC

Clinical stage IB2 **and** a surgical candidate

Clinical stage IB1 or IB2 **and** not a surgical candidate

Clinical stage IB3-IVB → See Page 3

PRIMARY TREATMENT

- Simple hysterectomy[4] and pelvic lymph node assessment[5] **or**
- If fertility desired, conization and pelvic lymph node assessment[5]

- Radical hysterectomy and pelvic lymph node assessment[5] **or**
- If fertility desired, radical trachelectomy and pelvic lymph node assessment[5]
- Consideration of conservative surgery in select cases[6]

Radiation therapy with or without concurrent chemotherapy[8]

- High risk[7] → Post-operative radiation therapy with concurrent chemotherapy[8]
- Intermediate risk[9] → Post-operative radiation therapy with or without concurrent chemotherapy[8]
- Low risk

See Page 4 for Surveillance

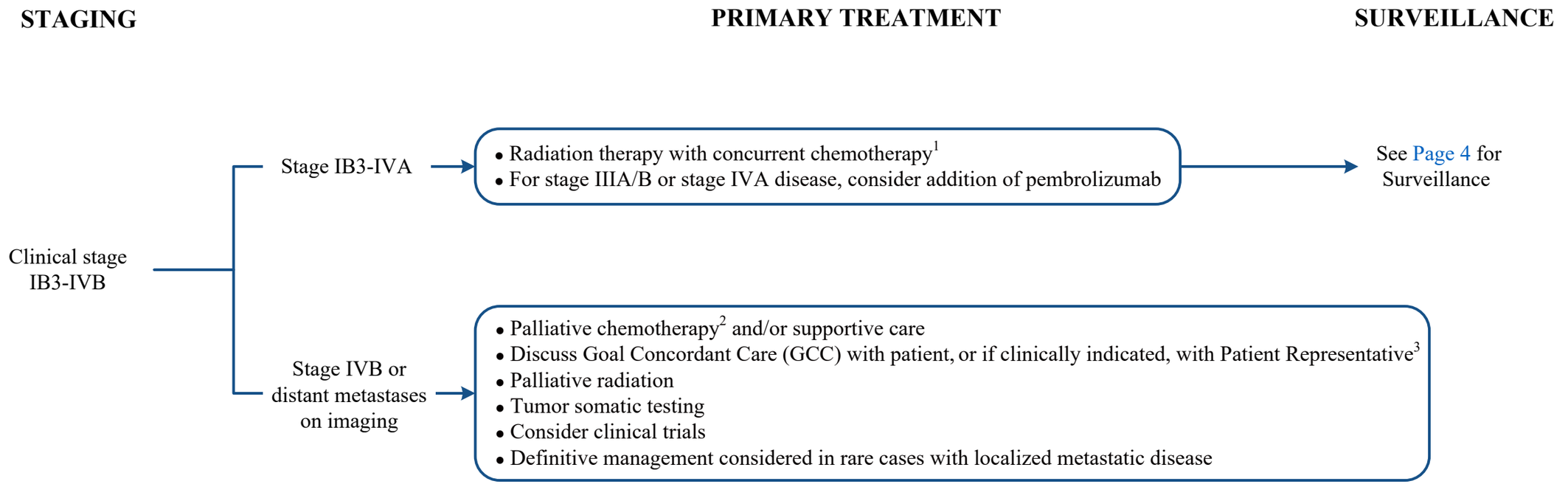
[1] Refer to the Hepatitis B Virus (HBV) Screening and Management and Hepatitis C Virus (HCV) Screening algorithms
[2] MRI should be completed on **all** patients receiving definitive radiation and **all** patients undergoing trachelectomy
[3] See Physical Activity, Nutrition, Obesity Screening and Management, and Tobacco Cessation Treatment algorithms. Ongoing reassessment of lifestyle risks should be a part of routine clinical practice.
[4] If margins remain positive, radical hysterectomy is preferred over simple hysterectomy
[5] Lymphatic mapping with sentinel lymph node biopsy and/or lymph node dissection
[6] See Appendix A for Criteria for and Principles of Conservative Surgery
[7] High risk factors: positive nodes, positive margins, and/or parametrial involvement
[8] Weekly cisplatin or another platinum alternative (*e.g.,* carboplatin)
[9] Intermediate risk factors: stromal invasion, LVSI and/or large clinical tumor diameter

Department of Clinical Effectiveness V13
Approved by the Executive Committee of the Medical Staff on 10/21/2025

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (www.mdanderson.org/gynonctrials). Other co-morbidities are taken into consideration prior to treatment selection. All patients with invasive cervical cancer should be referred to a Gynecologic Oncologist.



[1] Weekly cisplatin or another platinum alternative (*e.g.,* carboplatin)
[2] See Appendix B: Recurrent or Metastatic Chemotherapy Regimens
[3] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to the GCC home page (for internal use only).

Department of Clinical Effectiveness V13
Approved by the Executive Committee of the Medical Staff on 10/21/2025

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

Note: If available, clinical trials should be considered as preferred treatment options for eligible patients (www.mdanderson.org/gynonctrials). Other co-morbidities are taken into consideration prior to treatment selection. All patients with invasive cervical cancer should be referred to a Gynecologic Oncologist.

SURVEILLANCE

- Interval history and physical
- Cervical/vaginal cytology annually
- Imaging, including chest x-ray as clinically indicated
- Recommend use of vaginal dilator after radiation treatment
- Consider systemic or vaginal hormone replacement therapy for premenopausal patients who received radiation therapy[1]
- Consider Bone Mineral Density scan and Vitamin D level for patients who received radiation therapy
- Pelvic Exenteration surveillance based on clinical indications

RECURRENCE

Recurrence?

Yes

- PET/CT
- Consider additional imaging as clinically indicated
- Tumor somatic mutation testing

No

Continue surveillance[5]

TREATMENT

Recurrence in central pelvis

- No prior radiation therapy → Radiation therapy with concurrent chemotherapy[2]
- Prior radiation therapy →
  - Consider pelvic exenteration
  - Consider systemic chemotherapy or palliative care if not a candidate for pelvic exenteration

Isolated regional recurrence →

- Surgical resection **or**
- Radiation therapy **or**
- Chemotherapy[3] **or**
- Combined modality **or**
- Consider palliative care

Multiple sites of metastatic disease →

- Palliative care
- Discuss GCC with patient, or if clinically indicated, with Patient Representative[4]
- Chemotherapy[3] and consideration of clinical trial participation

DISPOSITION

Individualized follow-up based on clinical indications and treatment plan

[1] Hormone replacement therapy includes estrogen and estrogen/progesterone if intact uterus
[2] Weekly cisplatin or another platinum alternative (*e.g.,* carboplatin)
[3] See Appendix B: Recurrent or Metastatic Chemotherapy Regimens
[4] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to the GCC home page (for internal use only).
[5] For patients who are 5 years post-treatment and no evidence of disease, refer to Survivorship - Cervical Cancer algorithm

Department of Clinical Effectiveness V13
Approved by the Executive Committee of the Medical Staff on 10/21/2025

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

APPENDIX A: Criteria for and Principles of Conservative Therapy (conization and pelvic lymph node evaluation or simple hysterectomy with pelvic node evaluation)

Criteria	Principles
• Tumor ≤ 2 cm • Stromal invasion ≤10 mm on biopsy • Squamous, adenocarcinoma or adenosquamous of any grade • Lymphovascular space invasion positive or negative	• Prior to simple hysterectomy, perform conization and obtain negative margins for cancer (repeat conization if needed). Minimally-invasive simple hysterectomy is acceptable if conization is performed with negative margins. • For fertility-sparing procedure (*e.g.,* conization and lymph nodes), conization must have negative margins for cancer, cervical intraepithelial neoplasia grade 2 or 3 (CIN2/3), and adenocarcinoma in situ (AIS) • Performing conization and lymph node evaluation at the same time for fertility-sparing patients is acceptable

APPENDIX B: Recurrent or Metastatic Chemotherapy Regimens

First Line	Second Line or Subsequent
• Pembrolizumab plus cisplatin plus paclitaxel with or without bevacizumab (if *PD-L1* positive) • Pembrolizumab plus carboplatin plus paclitaxel with or without bevacizumab (if *PD-L1* positive) • Paclitaxel plus cisplatin or carboplatin plus bevacizumab plus atezolizumab (regardless of *PD-L1* testing)[1,2] • Cisplatin plus paclitaxel with or without bevacizumab • Carboplatin plus paclitaxel with or without bevacizumab • Topotecan plus cisplatin • Topotecan plus paclitaxel with or without bevacizumab • Cisplatin • Carboplatin • Paclitaxel	• Bevacizumab • Docetaxel • Fluorouracil • Gemcitabine • Ifosfamide • Irinotecan • Mitomycin • Topotecan • Pemetrexed • Vinorelbine • Pembrolizumab (if *PD-L1* positive or *MSI*-high/dMMR) • Tisotumab vedotin • Larotrectinib (if *NTRK* gene fusion positive) • Entrectinib (if *NTRK* gene fusion positive) • Paclitaxel (protein-bound) • Trastuzumab deruxtecan (if HER2 positive IHC 2+ or 3+) • Nivolumab • Refer to NCCN guidelines for additional useful therapies that are used in certain circumstances

[1] Not FDA approved
[2] Atezolizumab is indicated for resistant, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix. Refer to MD Anderson Cancer Center formulary.

Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

SUGGESTED READINGS

Bhatla, N., Berek, J., S., Fredes, M., C., Denny, L., A., Grenman, S., Karunaratne, K, … Sankaranarayanan, R. (2019). Revised FIGO staging for carcinoma of the cervix uteri. *International Journal of Gynecology and Obstetrics, 145*(1), 129-135. doi:10.1002/ijgo.12749

Huang, B., Cai, J., Xu, X., Guo, S., & Wang, Z. (2016). High-Grade Tumor Budding Stratifies Early-Stage Cervical Cancer with Recurrence Risk. *PLOS One*, *11*(11) doi:10.1371 journal.pone.0166311

Jung, P. S., Kim, D. Y., Lee, S. W., Park, J. Y., Suh, D. S., Kim, J. H., … Nam, J. H. (2015). Clinical role of adjuvant chemotherapy after radical hysterectomy for FIGO stage IB-IIA cervical cancer: Comparison with adjuvant RT/CCRT using inverse-probability-of-treatment weighting. *PLOS One*, *10*(7) doi:10.1371/journal.pone.0132298

Lorusso, D., Xiang, Y., Hasegawa, K., Scambia, G., Leiva, M., Ramos-Elias, P., … ENGOT-cx11/GOG-3047/KEYNOTE-A18 investigators (2024). Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): Overall survival results from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet, 404*(10460), 1321-1332. doi:10.1016/S0140-6736(24)01808-7

Monk, B. J., Colombo, N., Tewari, K. S., Dubot, C., Caceres, M. V., Hasegawa, K., … KEYNOTE-826 Investigators (2023). First-line pembrolizumab + chemotherapy versus placebo + chemotherapy for persistent, recurrent, or metastatic cervical cancer: Final overall survival results of KEYNOTE-826. *Journal of Clinical Oncology, 41*(36), 5505-5511. doi:10.1200/JCO.23.00914

Melamed, A., Margul, D. J., Chen, L., Keating, N. L., Del Carmen, M. G., Yang, J., … Wright, J. D. (2018). Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. *The New England Journal of Medicine, 379*(20), 1905-1914. doi:10.1056/NEJMoa1804923

National Comprehensive Cancer Network. (2025). *Cervical Cancer* (NCCN Guideline Version 3.2025). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf

Oaknin, A., Gladieff, L., Martínez-García, J., Villacampa, G., Takekuma, M., De Giorgi, U., … ENGOT-Cx10–GEICO 68-C–JGOG1084–GOG-3030 Investigators (2024). Atezolizumab plus bevacizumab and chemotherapy for metastatic, persistent, or recurrent cervical cancer (BEATcc): A randomised, open-label, phase 3 trial. *Lancet, 403*(10421), 31-43. doi:10.1016/S0140-6736(23)02405-4

Penninx, B. M. F., Samson, M. J., & Schnog, J. B. (2025). Pembrolizumab with chemoradiotherapy followed by pembrolizumab for stage III-IVa cervical cancer: is the ENGOT-cx11/GOG-3047/KEYNOTE-A18 trial practice changing? *Cancer, 131*(4), e35749. doi:10.1002/cncr.35749

Peters, W. A., 3rd, Liu, P. Y., Barrett, R. J., 2nd, Stock, R. J., Monk, B. J., Berek, J. S., … Alberts, D. S. (2000). Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. *Journal of Clinical Oncology, 18*(8), 1606-1613. doi:10.1200/JCO.2000.18.8.1606

Plante, M., Kwon, J. S., Ferguson, S., Samouëlian, V., Ferron, G., Maulard, A., … CX.5 SHAPE Investigators (2024). Simple versus radical hysterectomy in women with low-risk cervical cancer. *The New England Journal of Medicine, 390*(9), 819-829. doi:10.1056/NEJMoa2308900

Continued on next page

Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

SUGGESTED READINGS - continued

Ramirez, P. T., Frumovitz, M., Pareja, R., Lopez, A., Vieira, M., Ribeiro, R., … Isla, D. (2018). Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *The New England Journal of Medicine, 379*(20), 1895-1904. doi:10.1056/NEJMoa1806395

Salcedo, M. P., Sood, A. K., Jhingran, A., Eifel, P. J., Klopp, A. H., Iyer, R. B., … Schmeler, K. M. (2020). Pelvic fractures and changes in bone mineral density after radiotherapy for cervical, endometrial, and vaginal cancer: A prospective study of 239 women. *Cancer, 126*(11), 2607-2613. doi:10.1002/cncr.32807

Salvo, G., Ramirez, P. T., Levenback, C. F., Munsell, M. F., Euscher, E. D., Soliman, P. T., & Frumovitz, M. (2017). Sensitivity and negative predictive value for sentinel lymph node biopsy in women with early-stage cervical cancer. *Gynecologic Oncology, 145*(1), 96-101. doi:10.1016/j.ygyno.2017.02.005

Schmeler, K. M., Pareja, R., Blanco, A. L., Fregnani, J. H., Lopes, A., Perrotta, M., … Ramirez, P. T. (2021). ConCerv: A prospective trial of conservative surgery for low-risk early-stage cervical cancer. *International Journal of Gynecologic Cancer, 31*(10). doi:10.1136/ijgc-2021-002921

Sedlis, A., Bundy, B. N., Rotman, M. Z., Lentz, S. S., Muderspach, L. I., & Zaino, R. J. (1999). A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A gynecologic oncology group study. *Gynecologic Oncology, 73*(2), 177-183. doi:10.1006/gyno.1999.5387

Tewari, K. S., Sill, M. W., Long III, H. J., Penson, R. T., Huang, H., Ramondetta, L. M., … Michael, H. E. (2014). Improved survival with bevacizumab in advanced cervical cancer. *The New England Journal of Medicine, 370*(8), 734-743. doi:10.1056/NEJMoa1309748

Vergote, I., González-Martín, A., Fujiwara, K., Kalbacher, E., Bagaméri, A., Ghamande, S., … innovaTV 301/ENGOT-cx12/GOG-3057 Collaborators (2024). Tisotumab vedotin as second- or third-line therapy for recurrent cervical cancer. *The New England Journal of Medicine, 391*(1), 44-55. doi:10.1056/NEJMoa2313811

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Gynecologic Oncology Center providers at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

Core Development Team Leads

Jeffrey How, MD (Gynecologic Oncology & Reproductive Medicine)
Anuja Jhingran, MD (Radiation Oncology)
Roni Wilke, MD (Gynecologic Oncology & Reproductive Medicine)

Workgroup Members

Alexandra S. Bercow, MD (Gynecologic Oncology & Reproductive Medicine)
Michael W. Bevers, MD (Gynecologic Oncology & Reproductive Medicine)
Diane C. Bodurka, MD (Gynecologic Oncology & Reproductive Medicine)
Lauren Colbert, MD (Radiation Oncology)
Olga N. Fleckenstein, BS♦
David M. Gershenson, MD (Gynecologic Oncology & Reproductive Medicine)
Donyika Joseph, PharmD (Pharmacy Clinical Programs)
Ann Klopp, MD, PhD (Radiation Oncology)
Lilie Lin, MD (Radiation Oncology)
Larissa Meyer, MD (Gynecologic Oncology & Reproductive Medicine)
Shrina Patel, PharmD (Pharmacy Clinical Programs)
Lois M. Ramondetta, MD (Gynecologic Oncology & Reproductive Medicine)
Jose A. Rauh-Hain, MD (Gynecologic Oncology & Reproductive Medicine)
Kathleen M. Schmeler, MD (Global Oncology, Gynecologic Oncology & Reproductive Medicine)
Pamela T. Soliman, MD (Gynecologic Oncology & Reproductive Medicine)
Anil K. Sood, MD (Gynecologic Oncology & Reproductive Medicine)
Mary Lou Warren, DNP, APRN, CNS-CC♦
Shannon N. Westin, MD (Gynecologic Oncology & Reproductive Medicine)

♦Clinical Effectiveness Development Team