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

Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.*

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

STAGING[1]

PRIMARY TREATMENT

No visible or palpable lesion → • Cone biopsy with ECC • Chest X-ray • HIV screening • Hepatitis screening[2] • Lifestyle risk assessment[3]

Stromal invasion ≤ 3 mm → ECC results or positive margins[4]?

- Yes → Repeat cone biopsy and ECC → Assign stage based on findings
  - Stage IA1: See box A
  - Stage IA2: See box B
  - Stage IB: See Page 2
- No → Stage IA1 → **A** • Observation (if fertility desired) **or** • Simple hysterectomy → See Page 3 for Surveillance

Visible or palpable lesion → See Page 2

Stromal invasion > 3 mm and ≤ 5 mm → Consider PET (in addition to MRI pelvis with and without contrast) → **B** Surgical candidate?

- Yes → • Radical hysterectomy[5] and pelvic lymph node assessment[6] **or** • Radical trachelectomy (if fertility desired) and pelvic lymph node assessment[6] • Consideration of conservative surgery in select cases[7]
  - High[8] risk → Post-operative radiation therapy with concurrent chemotherapy[9]
  - Intermediate[10] risk → Post-operative radiation therapy with or without concurrent chemotherapy[9]
  - Low risk → See Page 3 for Surveillance
- No → Radiation therapy → See Page 3 for Surveillance

ECC = endocervical curettage

[1] For International Federation of Gynecology and Obstetrics (FIGO) Staging refer to: 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

[2] Refer to the Hepatitis B Virus (HB) Screening and Management algorithm

[3] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

[4] Positive margins includes high-grade dysplasia

[5] All procedures should be done open; minimally invasive surgery is no longer acceptable for radical hysterectomy or trachelectomy

[6] Lymphatic mapping with sentinel lymph node biopsy and/or lymph node dissection

[7] Criteria for conservative surgery include: ≤ 2 cm; squamous histology (any grade) or adenocarcinoma (grades 1 and 2 only); depth of invasion ≤ 10 mm invasion; no lymphovascular space invasion (LVSI)

[8] High risk factors: positive nodes, positive margins, and/or parametrial involvement

[9] Weekly cisplatin

[10] Intermediate risk factors: stromal invasion, lymphovascular space involvement (LVSI) and/or large clinical tumor diameter. For Gynecological Oncology Group (GOG) Sedlis Criteria refer to: 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

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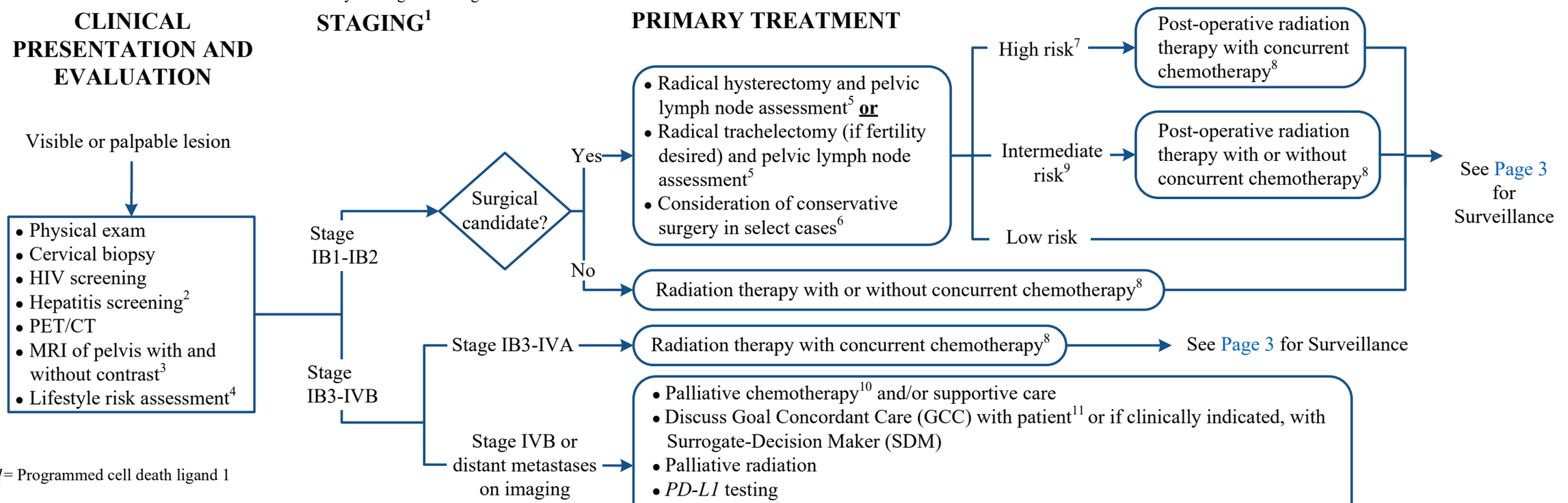

PD-L1= Programmed cell death ligand 1

[1] For International Federation of Gynecology and Obstetrics (FIGO) Staging refer to: 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

[2] Refer to the Hepatitis B Virus (HBV) Screening and Management algorithm

[3] MRI should be completed on **all** patients receiving definitive radiation and **all** patients undergoing trachelectomy

[4] See Physical Activity, Nutrition, and Tobacco Cessation algorithms. Ongoing reassessment of lifestyle risks should be a part of routine clinical practice.

[5] Lymphatic mapping with sentinel lymph node biopsy and/or lymph node dissection

[6] Criteria for conservative surgery include: ≤ 2 cm; squamous histology (any grade) or adenocarcinoma (grades 1and 2 only); depth of invasion ≤ 10 mm invasion; no LVSI

[7] High risk factors: positive nodes, positive margins, and/or parametrial involvement

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[10] See Appendix A: Recurrent or Metastatic Chemotherapy Regimens

[11] 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 SDM 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).

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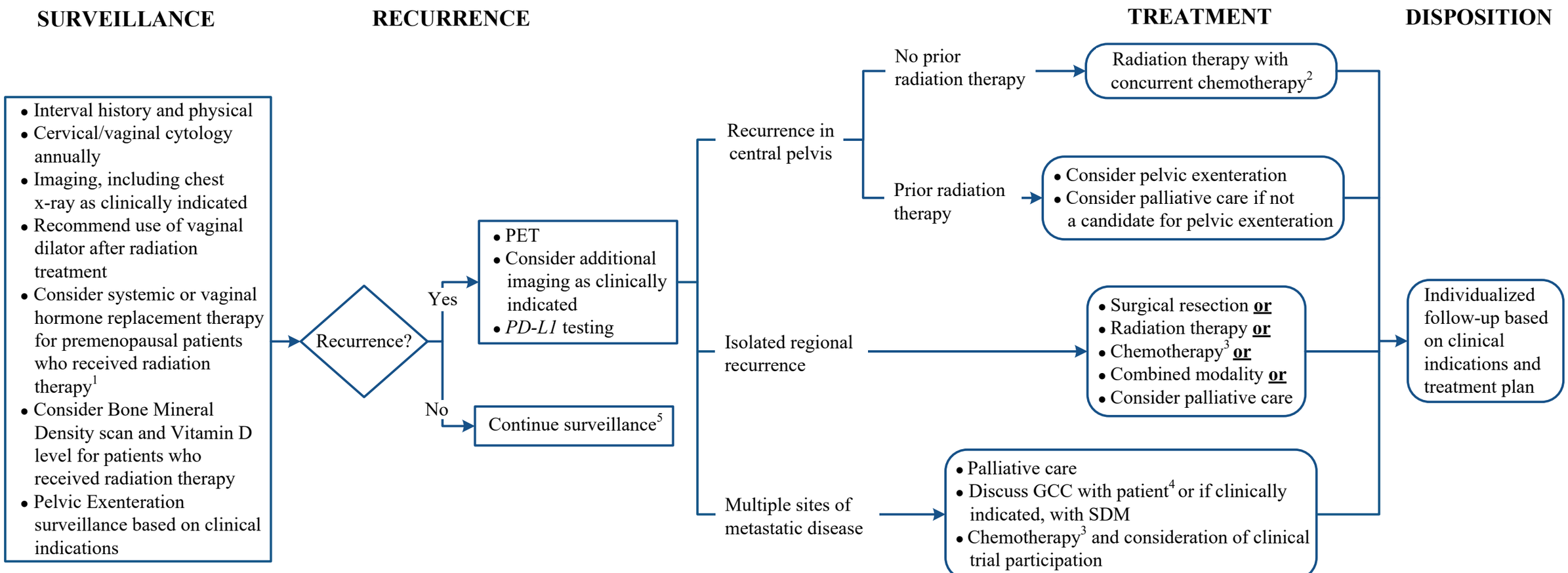

[1] Hormone replacement therapy includes estrogen and estrogen/progesterone if intact uterus
[2] Weekly cisplatin
[3] See Appendix A: Recurrent or Metastatic Chemotherapy Regimens
[4] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients or if clinically indicated the SDM 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

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APPENDIX A: 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) • 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 plus gemcitabine • Cisplatin • Carboplatin • Paclitaxel	• Bevacizumab • Docetaxel • Fluorouracil • Gemcitabine • Ifosfamide • Irinotecan • Mitomycin • Topotecan • Pemetrexed • Vinorelbine • Pembrolizumab (if *PD-L1* positive or *MSI*-high/dMMR) • Tisotumab vedotin-tftv • Larotrectinib (if *NTRK* gene fusion positive) • Entrectinib (if *NTRK* gene fusion positive) • Paclitaxel (protein-bound)

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

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