Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. 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/gynonc_trials). 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

INITIAL EVALUATION

STAGING

PRIMARY TREATMENT

Stage IA2 – see Box A
Stage IB – see Page 2
Surveillance, see Page 4

Surgical candidate?

Yes

Radical hysterectomy or pelvic lymph node dissection
Radical trachelectomy (if fertility desired) and pelvic lymph node dissection
Consideration of clinical trial participation to include possible conservative surgery
Lymphatic mapping and sentinel lymph node biopsy

High risk
Post-operative radiation therapy with concurrent chemotherapy
Intermediate risk
Post-operative radiation therapy with or without concurrent chemotherapy
Low risk

No

Radical hysterectomy

Repeat cone biopsy and ECC
Assign stage based on findings

Yes

No

Stage IA1

ECC or margins positive?

Yes

No

Cone biopsy with ECC
Chest X-ray
Testing for HIV
Hepatitis screening
Rapid plasma reagin test
Lifestyle risk assessment

Less than or equal to 3 mm of stromal invasion with an extension of less than or equal to 7 mm

Greater than 3 mm and less than or equal to 5 mm of stromal invasion with an extension of less than or equal to 7 mm

ECC = endocervical curettage

1 See Physical Activity, Nutrition, and Tobacco Cessation Algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
2 See Appendix A for FIGO Staging
3 Hysterectomy may be performed through open or minimally invasive techniques based on surgeon/patient discretion
4 High risk factors are positive nodes, positive margins, or parametrical involvement
5 Weekly cisplatin
6 Intermediate risk factors: stromal invasion, capillary lymphatic space involvement and large clinical tumor diameter. Refer to Appendix B for GOG Sedlis Criteria.

Department of Clinical Effectiveness V10
Approved by the Executive Committee of the Medical Staff on 03/27/2018

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CLINICAL PRESENTATION

INITIAL EVALUATION

STAGING

STAGING

PRIMARY TREATMENT

Visible lesion

Stage IB1

 Imaging as indicated:
  • Physical exam
  • Cervical biopsy
  • Chest X-ray
  • Testing for HIV

Stage IB2-IVB

 Imaging as indicated:
  • PET
  • CT
  • MRI of pelvis
  • Cystoscopy
  • Proctoscopy

Surgical candidate?

Yes

Radical hysterectomy and pelvic node dissection or Radical trachelectomy (if fertility desired) and pelvic lymph node dissection

Lymphatic mapping and sentinel lymph node biopsy

No

Radiation therapy with or without concurrent chemotherapy

High risk

Post-operative radiation therapy with concurrent chemotherapy

Intermediate risk

Post-operative radiation therapy with or without concurrent chemotherapy

Low risk

Surveillance, see Page 4

Stage IIA

Stage IIB

Stage IIIA/B

Stage IVA

Stage IVB or distant metastases on imaging

• Radiation therapy with concurrent chemotherapy
  • Consider extraperitoneal surgical staging

Surveillance, see Page 4

Palliative treatment

• Definitive management considered in rare cases with localized metastatic disease

Stage IVA

1 Relative indications in favor of primary radiation therapy are: positive nodes, extensive lymphovascular space involvement, deep stromal invasion

2 See Appendix A for FIGO Staging

3 All trachelectomy patients should get MRI

4 Weekly cisplatin

5 High risk factors are positive nodes, positive margins, or parametrial involvement

6 Intermediate risk factors: stromal invasion, capillary lymphatic space involvement and large clinical tumor diameter. Refer to Appendix B for GOG Sedlis Criteria.

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**RECURRENT**

- Imaging:
  - PET
  - Consider additional imaging as clinically indicated

- No prior radiation therapy
  - Recurrence in central pelvis
  - Prior radiation therapy
  - Isolated regional recurrence
  - Multiple sites of metastatic disease

**TREATMENT**

- Radiation therapy with concurrent chemotherapy
  - Consider palliative care

- Consider pelvic exenteration
  - Consider palliative care if not a candidate for pelvic exenteration

- Surgical resection or
  - Radiation therapy or
  - Chemotherapy or
  - Combined modality or
  - Consider palliative care

- Palliative care
  - Chemotherapy and consideration of clinical trial participation

**Individualized follow-up based on clinical indications and treatment plan**

---

1 Weekly cisplatin
2 See Appendix C for Chemotherapy Regimens
Surveillance:

- Interval history and physical
- Cervical/vaginal cytology annually
- Laboratory assessment (CBC, BUN, creatinine) as clinically indicated
- Imaging including chest x-ray as clinically indicated
- Recommended use of vaginal dilator after radiation treatment
- Consider vaginal estrogen cream and/or bone care for radiated patients
- Exenteration surveillance based on clinical indications

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

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
</table>
| I     | Carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded)  
IA: Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion less than or equal 5 mm and largest extension less than or equal 7 mm  
IA1: Measured stromal invasion less than or equal 3 mm in depth and extension of less than or equal 7 mm  
IA2: Measured stromal invasion greater than 3 mm and less than or equal 5 mm with an extension of less than or equal 7 mm  
IB: Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA  
IB1: Clinically visible lesion less than or equal 4 cm in greatest dimension  
IB2: Clinically visible lesion greater than 4 cm in greatest dimension |
| II    | Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina  
IIA: Without parametrial invasion  
IIA1: Clinically visible lesion less than or equal 4 cm in greatest dimension  
IIA2: Clinically visible lesion greater than 4 cm in greatest dimension  
IIB: Without obvious parametrial invasion |
| III   | Tumor extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or non-functioning kidney  
III A: Tumor involves lower third of the vagina, with no extension to the pelvic wall  
III B: Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney |
| IV    | IVA: Spread or growth to adjacent organs  
IVB: Spread to distant organs |

1 All macroscopically visible lesions even with superficial invasion are allotted to stage IB carcinomas. Invasion is limited to a measured stromal invasion with a maximal depth of 5 mm and a horizontal extension of less than or equal to 7 mm. Depth of invasion should not be greater than 5 mm taken from the base of the epithelium of the original tissue superficial or glandular. The depth of invasion should always be reported in mm, even in those cases with “early (minimal) stromal invasion” (~1 mm). The involvement of vascular/lymphatic spaces should not change the stage allotment.

2 On rectal examination, there is no cancer-free space between the tumor and the pelvic wall. All cases with hydronephrosis or non-functioning kidney are included, unless they are known to be due to another cause.

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APPENDIX C: Chemotherapy Regimens

<table>
<thead>
<tr>
<th>Recurrence or Metastatic Therapy</th>
<th>First Line</th>
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</thead>
<tbody>
<tr>
<td>Positive</td>
<td>● Paclitaxel, cisplatin and bevacizumab</td>
</tr>
<tr>
<td>Positive</td>
<td>● Paclitaxel and cisplatin</td>
</tr>
<tr>
<td>Positive</td>
<td>● Paclitaxel and carboplatin</td>
</tr>
<tr>
<td>Positive</td>
<td>● Topotecan and cisplatin</td>
</tr>
<tr>
<td>Positive</td>
<td>● Cisplatin and gemcitabine</td>
</tr>
<tr>
<td>Positive</td>
<td>● Cisplatin</td>
</tr>
<tr>
<td>Positive</td>
<td>● Carboplatin</td>
</tr>
<tr>
<td>Positive</td>
<td>● Paclitaxel</td>
</tr>
<tr>
<td>Positive</td>
<td>● Paclitaxel (protein-bound)</td>
</tr>
<tr>
<td>Second Line</td>
<td>● Bevacizumab</td>
</tr>
<tr>
<td>Second Line</td>
<td>● Docetaxel</td>
</tr>
<tr>
<td>Second Line</td>
<td>● Fluorouracil</td>
</tr>
<tr>
<td>Second Line</td>
<td>● Gemcitabine</td>
</tr>
<tr>
<td>Second Line</td>
<td>● Ifosfamide</td>
</tr>
<tr>
<td>Second Line</td>
<td>● Irinotecan</td>
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<tr>
<td>Second Line</td>
<td>● Mitomycin</td>
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<tr>
<td>Second Line</td>
<td>● Topotecan</td>
</tr>
<tr>
<td>Second Line</td>
<td>● Pemetrexed</td>
</tr>
<tr>
<td>Second Line</td>
<td>● Vinorelbine</td>
</tr>
</tbody>
</table>

APPENDIX B: Gynecology Oncology Group Sedlis Criteria

<table>
<thead>
<tr>
<th>LVSİ</th>
<th>Stromal Invasion</th>
<th>Tumor Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Deep third</td>
<td>Any</td>
</tr>
<tr>
<td>Positive</td>
<td>Middle third</td>
<td>greater than or equal to 2 cm</td>
</tr>
<tr>
<td>Positive</td>
<td>Superficial third</td>
<td>greater than or equal to 5 cm</td>
</tr>
<tr>
<td>Negative</td>
<td>Deep or middle third</td>
<td>greater than or equal to 4 cm</td>
</tr>
</tbody>
</table>
SUGGESTED READINGS


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:

Michael W. Bevers, MD (Surgery)
Diane C. Bodurka, MD (Gyn Onc)
Jennifer K. Burzawa, MD (Surgery)
Robert L. Coleman, MD (Gyn Onc & Reproductive Med)
Patricia Eifel, MD (Radiation Oncology)¹
Nicole Fleming, MD (Gyn Onc)
Michael M. Frumovitz, MD (Gyn Onc & Reproductive Med)
David M. Gershenson, MD (Gyn Onc & Reproductive Med)
Shonice Holdman, MBA*  
Anuja Jhingran, MD (Radiation Oncology)¹

Ann Klopp, MD (Radiation Oncology)
Lillie Lin (Radiation Oncology Department)
Karen H. Lu, MD (Gyn Onc)
Larissa Meyer, MD (Gyn Onc & Reproductive Med)
Amy Pai, PharmD*  
Pedro T. Ramirez, MD (Gyn Onc & Reproductive Med)
Lois M. Ramondetta, MD (Gyn Onc & Reproductive Med)
Kathleen M. Schmeler, MD (Gyn Onc & Reproductive Med)¹  
Pamela T. Soliman, MD (Gyn Onc & Reproductive Med)
Anil K. Sood, MD (Gyn Onc & Reproductive Med)
Shannon N. Westin, MD (Gyn Onc & Reproductive Med)

¹ Core Development Team  
* Clinical Effectiveness Development Team