Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

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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

INITIAL EVALUATION

STAGING1

STROMAL INVASION ≤ 3 mm

ECC results or margins positive?

No

Stage IA1

Observation (if fertility desired) or Simple hysterectomy

Yes

Repeat cone biopsy and ECC

ASSIGN STAGE BASED ON FINDINGS

Stage IA2: See Box A

Stage IB: See Page 2

PRIMARY TREATMENT

See Page 3 for Surveillance

High risk6

Post-operative radiation therapy with concurrent chemotherapy7

Intermediate risk6

Post-operative radiation therapy with or without concurrent chemotherapy7

Low risk

Radiation therapy

Surgical candidate?

Yes

Surgical candidate?

No

Consider MRI pelvis with and without contrast

Stromal invasion > 3 mm and ≤ 5 mm

No visible or palpable lesion

ECC = endocervical curettage

Visible or palpable lesion

See Page 2

1 See Appendix A: The International Federation of Gynecology and Obstetrics (FIGO) Staging

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

3 Positive margins includes dysplasia

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

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

6 High risk factors: positive nodes, positive margins, and/or parametrial involvement

7 Weekly cisplatin

8 Intermediate risk factors: stromal invasion, capillary lymphatic space involvement and/or large clinical tumor diameter. See Appendix B: Gynecological Oncology Group (GOG) Sedlis Criteria

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Department of Clinical Effectiveness V11

Approved by the Executive Committee of the Medical Staff on 04/21/2020
Invasive Cervical Cancer: Squamous Cell, Adenocarcinoma, Adenosquamous

CLINICAL PRESENTATION

Visible or palpable lesion

INITIAL EVALUATION

- Physical exam
- Cervical biopsy
- HIV screening
- Hepatitis screening
- PET/CT
- MRI of pelvis with and without contrast
- Cystoscopy/proctoscopy as indicated
- Lifestyle risk assessment

STAGING

Stage IB1 and IB2

Surgical candidate?

Yes

Stage IB3-IVA

Radiation therapy with or without concurrent chemotherapy

No

Stage IB3-IVB

Stage IVB or distant metastases on imaging

PRIMARY TREATMENT

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

High risk

Post-operative radiation therapy with concurrent chemotherapy

Intermediate risk

Post-operative radiation therapy with or without concurrent chemotherapy

Low risk

Radiation therapy with concurrent chemotherapy

See Page 3 for Surveillance

- Palliative chemotherapy and/or supportive care
- Palliative radiation
- Definitive management considered in rare cases with localized metastatic disease
- PD-L1 testing
- Consider clinical trials

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SURVEILLANCE

- Interval history and physical
- Cervical/vaginal cytology annually
- Imaging including chest x-ray as clinically indicated
- Recommended use of vaginal dilator after radiation treatment
- Consider vaginal estrogen cream\(^1\) and/or bone care for radiated patients
- Vitamin D level
- Exenteration surveillance based on clinical indications

\(\text{Recurrence?} \rightarrow \)

Yes

- PET
- Consider additional imaging as clinically indicated
- PD-L1 testing

No

- Continue surveillance

Recurrence in central pelvis

Recurrence in central pelvis

Prior radiation therapy

No prior radiation therapy

Isolated regional recurrence

Multiple sites of metastatic disease

\(\text{TREATMENT} \rightarrow \)

- Radiation therapy with concurrent chemotherapy\(^2\)
- 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\(^3\) and consideration of clinical trial participation

\(\text{DISPOSITION} \rightarrow \)

Individualized follow-up based on clinical indications and treatment plan

1 Long term use of vaginal estrogen requires progesterone
2 Weekly cisplatin
3 See Appendix C: Recurrent or Metastatic Chemotherapy Regimens
**APPENDIX A: The International Federation of Gynecology and Obstetrics (FIGO) Staging**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I</strong></td>
<td>Carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded)</td>
</tr>
<tr>
<td></td>
<td>IA: Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion &lt; 5 mm&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>IA1: Measured stromal invasion &lt; 3 mm in depth</td>
</tr>
<tr>
<td></td>
<td>IA2: Measured stromal invasion ≥ 3 mm and &lt; 5 mm in depth</td>
</tr>
<tr>
<td></td>
<td>IB: Invasive carcinoma with measured deepest invasion ≥ 5 mm (greater than stage IA), lesion limited to the cervix uteri&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>IB1: Invasive carcinoma ≥ 5 mm depth of stromal invasion and &lt; 2 cm in greatest dimension</td>
</tr>
<tr>
<td></td>
<td>IB2: Invasive carcinoma ≥ 2 cm and &lt; 4 cm in greatest dimension</td>
</tr>
<tr>
<td></td>
<td>IB3: Invasive carcinoma ≥ 4 cm in greatest dimension</td>
</tr>
<tr>
<td><strong>II</strong></td>
<td>Carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina</td>
</tr>
<tr>
<td></td>
<td>IIA: Involvement limited to the upper two-thirds of the vagina without parametrial invasion</td>
</tr>
<tr>
<td></td>
<td>IIA1: Invasive carcinoma &lt; 4 cm in greatest dimension</td>
</tr>
<tr>
<td></td>
<td>IIA2: Invasive carcinoma ≥ 4 cm in greatest dimension</td>
</tr>
<tr>
<td></td>
<td>IIB: With parametrial involvement but not up to the pelvic wall</td>
</tr>
<tr>
<td><strong>III</strong></td>
<td>The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>IIIA: Tumor involves lower third of the vagina, with no extension to the pelvic wall</td>
</tr>
<tr>
<td></td>
<td>IIIB: Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)</td>
</tr>
<tr>
<td></td>
<td>IIIC: Involvement of pelvic and/or paraaortic lymph nodes, irrespective of tumor size and extent (with r and p notations)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>IIIC1: Pelvic lymph node metastasis only</td>
</tr>
<tr>
<td></td>
<td>IIIC2: Paraaortic lymph node metastasis</td>
</tr>
<tr>
<td><strong>IV</strong></td>
<td>IVA: Spread or growth to adjacent organs</td>
</tr>
<tr>
<td></td>
<td>IVB: Spread to distant organs</td>
</tr>
</tbody>
</table>

<sup>1</sup> Imaging and pathology can be used, when available, to supplement clinical findings with respect to tumor size and extent, in all cases.

<sup>2</sup> The involvement of vascular/lymphatic spaces does not change the staging. The lateral extent of the lesion is no longer considered.

<sup>3</sup> Notation of r (imaging) and p (pathology) to indicate the findings that are used to allocate the cases to stage III. If imaging indicates pelvic node metastasis, r should be added to the stage allocation e.g., stage IIICr. If staging confirmed with pathological findings, p should be added to the stage allocation e.g., IIICp. The type of imaging modality or pathology technique should be documented. When in doubt, the lower staging should be assigned.
APPENDIX B: Gynecology Oncology Group (GOG) Sedlis Criteria

<table>
<thead>
<tr>
<th>LVSI</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>≥ 2 cm</td>
</tr>
<tr>
<td>Positive</td>
<td>Superficial third</td>
<td>≥ 5 cm</td>
</tr>
<tr>
<td>Negative</td>
<td>Deep or middle third</td>
<td>≥ 4 cm</td>
</tr>
</tbody>
</table>

LVSI = lymphovascular space invasion

APPENDIX C: Recurrent or Metastatic Chemotherapy Regimens

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

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SUGGESTED READINGS


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DEVELOPMENT CREDITS

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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