Management and Care of Women with Invasive Cervical Cancer: American Society of Clinical Oncology Resource-Stratified Clinical Practice Guideline

Introduction

- The purpose of this guideline is to provide expert guidance to clinicians and policymakers in all resource settings on the workup, treatment, and palliative care for women diagnosed with invasive cervical cancer.

- Treatment of cervical cancer is dependent on the stage of disease. Treatment may include surgical treatments such as conization, hysterectomy or radical hysterectomy, radiation therapy, and/or chemotherapy.

- Different regions of the world, both among and within countries, differ with respect to access to these treatments. In particular, regions with lower resources tend to have poorer screening programs, and patients present with more advanced disease that requires either radical surgery or chemoradiotherapy, neither of which is readily available in these areas.

- For this reason, standard guidelines that assume ideal availability of surgery and radiotherapy may not be applicable. The goal of this guideline is to recommend options in settings in which ideal treatment regimens may not be available.

ASCO Guideline Development Methodology

The ASCO Clinical Practice Guidelines Committee (CPGC) guideline process includes:

- a systematic literature review by ASCO guidelines staff
- an expert panel provides critical review and evidence interpretation to inform guideline recommendations
- final guideline approval by ASCO CPGC

The full ASCO Guideline methodology supplement can be found at:

www.asco.org/rs-cervical-cancer-treamtent-guideline

Clinical Questions

This clinical practice guideline addresses four overarching clinical questions:

- In the basic, limited, enhanced, and maximal resource settings, what are the appropriate care options for women with invasive cervical cancer in

  (1) Workup

  (2) Treatment

  (3) Follow-up and post-treatment surveillance

  (4) Palliative care

Target Population and Audience

Target Population

Women at all levels of resource settings diagnosed with invasive cervical cancer.

Target Audience

This clinical practice guideline globally targets health care providers (including gynecologic oncologists, medical oncologists, radiation oncologists, obstetricians and gynecologists, surgeons, nurses, and palliative care clinicians), policymakers, patients, and caregivers.

Summary of Recommendations

Workup

The purpose of workup is to assess the patient's overall health status and gather data to inform treatment. Modalities include history and physical examination, biopsies, blood tests, and imaging. Tests available in maximal settings, such as magnetic resonance imaging or positron emission tomography (PET) – computed are optional.

Treatment

The treatment for invasive cervical cancer consists of surgery, chemotherapy, and radiation therapy, sometimes in combination.

Treatment Capacity

Treatment	Setting			
	Basic	Limited	Enhanced	Maximal
Surgery	Simple (extrafascial) hysterectomy or more extensive hysterectomy can be performed*	**Modified radical and radical hysterectomy**	**Capable of performing most major surgeries,** including radical hysterectomy, **radical trachelectomy,† pelvic and para-aortic LN sampling, and pelvic exenteration†** Following are not available: PET scan, interventional radiology, sentinel node biopsy/IORT, and bevacizumab	Radical hysterectomy, radical trachelectomy, pelvic and para-aortic LN sampling, **sentinel node biopsy**, and pelvic exenteration; radiation therapy, chemotherapy, **interventional radiology, palliative care service, and bevacizumab are all available**
Chemotherapy	Availability of chemotherapy drugs is unpredictable	**Chemotherapy may be available**	**Chemotherapy available**; bevacizumab not available	Chemotherapy available; **bevacizumab is available**
Radiation therapy	No radiation therapy available	**Limited external RT with no brachytherapy available;** in some areas where there are only brachytherapy and no external RT, this will be considered as basic level	**RT including external beam and brachytherapy available;** interventional radiology not available	RT including external beam and brachytherapy available; interventional radiology available

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Treatment Capacity

Treatment	Setting			
	Basic	Limited	Enhanced	Maximal
Pathology	Pathology services are not available; if there is a way to send pathology for review when needed, that should occur. (Basic pathology may be available, but diagnosis is often delayed for more than one month. There are no frozen sections or pathology consultations in the region.)	**Pathology services in development** (There are basic pathology and **frozen section** services. Consultations are not readily available.)	Pathology services in development or not always available (Pathology services including frozen sections are available. Tumor registry and regular multidisciplinary conferences are not consistently available in the region.)	**Pathology available** **(Full pathology services including diagnosis, consultation, tumor registry, and multidisciplinary conferences are available.)**
Palliative care	Palliative care service is in development; basic palliative care, including pain and symptom management, should be provided‡	**Pain and symptom management available**; palliative care service is in development	Palliative care service not always available	**Palliative care service available**

*Where medical facilities exist to take care of women who are at high risk for postoperative complications
†Can be performed in some enhanced levels
‡Palliative care is multifaceted and in some contexts can be provided concurrently with tumor-directed therapy. Pain management and best supportive care are necessary but insufficient parts of palliative care in all settings. Women with advanced cervical cancer with or without access to tumor-directed therapy may have specific late-stage symptoms that require clinicians to perform or offer urogenital-specific interventions. See the Special Commentary section.

Work Up

Setting			
Basic	Limited	Enhanced	Maximal
History and physical examination, CBC, cervical biopsy, cone biopsy, and LFT/renal function studies Imaging (optional in ≤ stage IB1 disease): chest x-ray Smoking cessation and counseling; may offer HIV testing	History and physical examination, CBC, cervical biopsy, **pathologic review,** cone biopsy, and LFT/renal function studies Imaging (optional in ≤ stage IB1): chest x-ray, **CT (specifically CT of abdomen and pelvis for women with advanced-stage disease for treatment planning purposed)** Smoking cessation and counseling; may offer HIV testing	History and physical examination, CBC, cervical biopsy, pathologic review, cone biopsy, and LFT/renal function studies Imaging (optional in ≤ stage IB1): chest x-ray, CT **or MRI** Smoking cessation and counseling; may offer HIV testing Optional: **EUA cystoscopy/proctoscopy only if suspicion of bladder or rectum invasion by CT or MRI**	History and physical examination, CBC, cervical biopsy, pathologic review, cone biopsy, and LFT/renal function studies Imaging (optional ≤ stage IB1): chest x-ray, CT, or MRI **or PET-CT** Smoking cessation and counseling; may offer HIV testing Optional: EUA cystoscopy/proctoscopy only if suspicion of bladder or rectum invasion by CT or MRI

NOTE. Bold indicates addition of a recommended action over a previous resource level (eg, in limited setting, a bold action is one that was not recommended in basic).

Abbreviations: CBC, complete blood count; CT, computed tomography; EUA, examination under anesthesia; LFT, liver function test; MRI, magnetic resonance imaging; PET, positron emission tomography

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Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IA1, LVSI negative, FS	1A1 (negative margins): cone biopsy[1] (with scalpel) Repeat cone biopsy or extrafascial hysterectomy for positive margins Type of recommendation: evidence-based Evidence: high Recommendation: strong	1A1 (negative margins): cone biopsy Repeat cone biopsy or extrafascial hysterectomy for positive margins Type of recommendation: evidence-based Evidence: high Recommendation: strong	1A1 (negative margins): cone biopsy Repeat cone biopsy, or extrafascial hysterectomy for positive margins. Type of recommendation: evidence-based Evidence: high Recommendation: strong	1A1 (negative margins): cone biopsy Repeat cone biopsy or extrafascial hysterectomy for positive margins Type of recommendation: evidence-based Evidence: high Recommendation: strong
IA1, LVSI positive, FS	Cone biopsy in selected cases, if follow-up possible Type of recommendation: consensus-based Evidence: intermediate Recommendation: weak	Cone biopsy Type of recommendation: consensus-based Evidence: intermediate Recommendation: weak	Cone biopsy **plus PLND** (see Discussion regarding current evidence on FS sparing for women desiring fertility preservation) Type of recommendation: evidence and consensus-based Evidence: high Recommendation: strong	Cone biopsy plus PLND Type of recommendation: evidence and consensus-based Evidence: high Recommendation: strong
			OR **radical trachelectomy plus pelvic LND** Type of recommendation: evidence and consensus-based Evidence: intermediate Recommendation: moderate	OR radical trachelectomy plus PLND **(may offer ± SLN)** Type of recommendation: evidence and consensus-based Evidence: intermediate Recommendation: moderate

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Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IA1, non-FS (no LVSI)	Cone biopsy (if follow-up possible) OR extrafascial hysterectomy,[2] then observe after initial cone biopsy, repeat cone, or extrafascial hysterectomy if margins are positive Type of recommendation: evidence and consensus-based Evidence: high Recommendation: strong	Cone biopsy (if follow-up possible); observe (after cone biopsy)[3] OR extrafascial hysterectomy[2] (extrafascial hysterectomy OR modified **radical hysterectomy plus PLND** OR if positive margins repeat conization[4]) Type of recommendation: evidence and consensus-based Evidence: high Recommendation: strong	Cone biopsy[3] OR extrafascial hysterectomy[2] (extrafascial hysterectomy OR modified radical hysterectomy plus pelvic LND OR if positive margins repeat conization[4]) Type of recommendation: evidence-based Evidence: high Recommendation: strong	Cone biopsy[3] OR extrafascial hysterectomy[2] (extrafascial hysterectomy OR modified radical hysterectomy plus **pelvic LN sampling** if positive margins **[may offer ± SLN]** OR repeat conization[4]) Type of recommendation: evidence-based Evidence: high Recommendation: strong
IA1, non-FS (with LVSI)	As above Type of recommendation: consensus-based Evidence: low Recommendation: weak	Stage IA1 (with LVSI) and stage IA2: modified radical hysterectomy Type of recommendation: consensus-based Evidence: low Recommendation: weak	Stage IA1 (with LVSI) and stage IA2: modified radical hysterectomy (when positive margins on repeat cone) **plus PLND ± PANB (pelvic irradiation plus brachytherapy [with LVSI] if patient is not eligible for surgery)** Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate	Stage IA1 (with LVSI) and stage IA2: modified radical hysterectomy plus pelvic LND ± para-aortic (**may offer ± SLN** OR pelvic irradiation plus brachytherapy [if patient is not eligible for surgery]) Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate

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Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IA2 FS	Cone biopsy (if follow-up possible) Type of recommendation: consensus-based Evidence: low Recommendation: weak	Cone biopsy (if follow-up possible) Type of recommendation: consensus-based Evidence: low Recommendation: weak	Cone biopsy **plus PLND ± para-aortic LN sampling**[3] Type of recommendation: evidence-based Evidence: low Recommendation: weak	Cone biopsy plus pelvic LND ± para-aortic LN sampling[3] Type of recommendation: evidence-based Evidence: low Recommendation: weak
			Radical trachelectomy plus PLND Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate	Radical trachelectomy plus PLND Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate
IA2, non-FS	Cone biopsy (if follow-up possible) or extrafascial hysterectomy (non-FS) Type of recommendation: evidence and consensus-based Evidence: low Recommendation: weak	Cone biopsy **plus PLND ± para-aortic LN sampling**[3] Type of recommendation: evidence-based Evidence: low Recommendation: weak	Cone biopsy plus PLND ± para-aortic LN sampling[3] Type of recommendation: evidence-based Evidence: low Recommendation: weak	See above
	Extrafascial hysterectomy Type of recommendation: evidence-based Evidence: low Recommendation: weak	**Modified radical hysterectomy plus PLND ± para-aortic LN sampling**[4] Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate	Modified radical hysterectomy plus PLND ± para-aortic LN sampling[4] Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate	Modified radical hysterectomy plus PLND ± para-aortic LN sampling[4] Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate
			OR pelvic RT and brachytherapy Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate	OR pelvic RT and brachytherapy Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate

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Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IB1, FS	No recommendation	No recommendation	**Radical trachelectomy plus PLND** (if adding trachelectomy > 2 cm) Adjuvant therapy may be needed for patients with tumors > 2 cm with risk factors Type of recommendation: evidence and consensus-based Evidence: intermediate Recommendation: moderate	Radical trachelectomy plus pelvic LN sampling; **may offer SLN** Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate
IB1, Non-FS	Extrafascial hysterectomy Type of recommendation: consensus-based Evidence: insufficient Recommendation: weak	**Radical hysterectomy plus PLND or radical hysterectomy (see Note) with adjuvant RT or RT with concurrent low-dose chemotherapy (concurrent chemoRT), if needed** Type of recommendation: evidence and consensus-based Evidence: high Recommendation: moderate to strong	Radical hysterectomy plus pelvic LND Type of recommendation: evidence-based Evidence: high Recommendation: strong	Radical hysterectomy plus PLND; **may offer SLN** Type of recommendation: evidence-based Evidence: high (SLN option, low) Recommendation: strong (weak)

Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IB1, Non-FS	NACT if available, then extrafascial hysterectomy Type of recommendation: consensus-based Evidence: insufficient Recommendation: weak	**ChemoRT or RT followed by extrafascial or radical hysterectomy (see Note) ± PLND ± PANB**[5] If no RT is available but chemotherapy is available, **NACT may be used to shrink the tumor to make it removable by surgery (extrafascial or modified radical hysterectomy [see Note] ± PLND ± PANB**[5]**)** If the patient's tumor does not shrink and is not resectable with negative margins, palliative measures, including best supportive care, ± chemotherapy should be offered Type of recommendation: evidence and consensus-based Evidence: low Recommendation: weak	**Pelvic RT plus brachytherapy plus concurrent low-dose platinum-based chemotherapy** Type of recommendation: evidence-based Evidence: high Recommendation: strong	Pelvic RT plus brachytherapy plus concurrent low-dose platinum-based chemotherapy Type of recommendation: evidence-based Evidence: high Recommendation: strong
Note		Wherever radical hysterectomy with concurrent chemoRT listed as a surgical option above, **extrafascial hysterectomy is recommended if there is residual disease after RT or chemoRT with a boost of 68 Gy or initial tumor > 6 cm.** **Radical hysterectomy may be used following RT or chemoRT to a dose of 50 Gy**		

Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IB2 and IIA2	If chemotherapy is available, use NACT followed by extrafascial hysterectomy; if chemotherapy is not available, extrafascial hysterectomy (modification as deemed necessary) may be performed if the surgical capacity is present Type of recommendation: consensus-based Evidence: low Recommendation: weak	If chemotherapy is available, NACT **followed by radical hysterectomy (see Note) plus PLND ± para-aortic LN sampling may be an option**[4,6] Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate	**Pelvic RT plus concurrent low-dose platinum-based chemotherapy plus brachytherapy** Type of recommendation: evidence-based Evidence: high Recommendation: strong	Pelvic RT plus concurrent low-dose platinum-based chemotherapy plus brachytherapy Type of recommendation: evidence-based Evidence: high Recommendation: strong
		If EBRT is available, but not brachytherapy, then chemoRT followed by extrafascial hysterectomy or RT (if chemotherapy not available) followed by extrafascial hysterectomy (see Note) Type of recommendation: consensus-based Evidence: low Recommendation: weak	**Pelvic RT plus** concurrent low-dose platinum-based chemotherapy **plus brachytherapy plus adjuvant hysterectomy**; adjuvant hysterectomy is not recommended except if evidence of presence of residual disease Type of recommendation: evidence-based Evidence: intermediate Recommendation: weak	Pelvic RT plus concurrent low-dose platinum-based chemotherapy plus brachytherapy plus adjuvant hysterectomy; adjuvant hysterectomy is not recommended except if evidence of presence of residual disease Type of recommendation: evidence-based Evidence: intermediate Recommendation: weak

Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IB2 and IIA2		OR **if no EBRT is available, then brachytherapy and concurrent low-dose platinum-based chemotherapy followed by radical hysterectomy (see Note)**[6] **When brachytherapy is not available, extrafascial or radical hysterectomy is recommended only when there is persistent central pelvic disease and selective lymphadenectomy or LN biopsy for suspicious lesions** Type of recommendation: evidence and consensus-based Evidence: low/intermediate Recommendation: weak/moderate		
		Radical hysterectomy plus PLND ± para-aortic LN sampling Type of recommendation: evidence-based Evidence: low Recommendation: weak	Radical hysterectomy plus pelvic LND ± para-aortic LND sampling[3] **and adjuvant RT or chemoRT if needed** Type of recommendation: evidence-based Evidence: low Recommendation: weak	Radical hysterectomy plus pelvic LND ± para-aortic LN sampling and adjuvant RT or chemoRT if needed **(plus RT ± concurrent low-dose platinum-based chemotherapy after hysterectomy if risk factors)**[3] Type of recommendation: evidence and consensus-based Evidence: low Recommendation: weak

Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
Note	With risk factors on pathology specimen: adjuvant chemotherapy after hysterectomy Type of recommendation: evidence and consensus-based Evidence: insufficient Recommendation: weak	With risk factors on pathology specimen: **adjuvant RT ± chemotherapy after hysterectomy** **Adjuvant RT (intermediate risk) or with concurrent low-dose platinum-based chemotherapy (high risk) in a referral center** Wherever radical hysterectomy with concurrent chemoRT listed as a surgical option above, **extrafascial hysterectomy is recommended if there is residual disease after RT or chemoRT with a boost of 68 Gy or initial tumor > 6 cm.** **Radical hysterectomy may be used following RT or chemoRT to a dose of 50 Gy** Type of recommendation: evidence and consensus-based Evidence: low Recommendation: weak	With risk factors on pathology specimen: adjuvant RT ± concurrent low-dose platinum-based chemotherapy after hysterectomy Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate	With risk factors on pathology specimen: adjuvant RT ± concurrent low-dose platinum-based chemotherapy after hysterectomy Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate
IIA1	See IB1	See IB1	See IB1	See IB1
IIA2	See IB2	See IB2	See IB2	See IB2

Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IIB and IIIA	NACT followed by extrafascial hysterectomy (modification as deemed necessary) Type of recommendation: consensus-based Evidence: insufficient Recommendation: weak	**ChemoRT or RT[6] followed by extrafascial or modified hysterectomy ± PLND[7] ± PANB** **NACT followed by extrafascial or modified hysterectomy ± PLND[7] ± PANB[6]** Type of recommendation: consensus-based Evidence: low/intermediate Recommendation: weak/moderate	**Pelvic RT plus** concurrent low-dose platinum-based chemotherapy **plus brachytherapy** **Adjuvant hysterectomy is an option only if residual disease after chemoRT** Type of recommendation: evidence-based Evidence: high Recommendation: strong	Pelvic RT plus concurrent low-dose platinum-based chemotherapy plus brachytherapy Adjuvant hysterectomy is an option only if residual disease after chemoRT Type of recommendation: evidence-based Evidence: high Recommendation: strong
	Extrafascial hysterectomy when chemotherapy is not consistently available Type of recommendation: consensus-based Evidence: insufficient Recommendation: weak	**Extrafascial or modified hysterectomy plus pelvic LND ± para-aortic LN sampling[4] plus adjuvant therapy** Type of recommendation: consensus-based Evidence: insufficient Recommendation: weak		
	Palliative care Type of recommendation: consensus-based Evidence: intermediate Recommendation: strong			

Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IIIB to IVA	Palliative care Type of recommendation: evidence-based Evidence: intermediate Recommendation: strong	**ChemoRT or RT[6] followed by extrafascial or radical hysterectomy (see Note) ± PLND[7] ± PANB** **NACT (followed by radical hysterectomy plus PLND[7] ± PANB may be an option] and/or palliative care** Type of recommendation: consensus-based Evidence: low/intermediate Recommendation: weak/moderate	**Pelvic RT plus brachytherapy plus** concurrent low-dose platinum-based chemotherapy **(in some cases extended-field RT)** AND/OR palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong	Pelvic RT plus brachytherapy plus concurrent low-dose platinum-based chemotherapy (in some cases extended-field RT) AND/OR palliative care (Options before palliative care alone include: **RT boost, salvage surgery,** or chemotherapy) Type of recommendation: evidence and consensus-based Evidence: high Recommendation: strong
	NACT followed by extrafascial hysterectomy Type of recommendation: consensus-based Evidence: insufficient Recommendation: weak	**RT ± concurrent low-dose platinum-based chemotherapy (may offer systemic adjuvant chemotherapy)** Type of recommendation: evidence-based Evidence: intermediate Recommendation: moderate	RT + **brachytherapy** ± concurrent low-dose platinum-based chemotherapy (may offer systemic adjuvant chemotherapy) Type of recommendation: evidence-based Evidence: intermediate Recommendation: weak	RT + brachytherapy ± concurrent low-dose platinum-based chemotherapy (may offer systemic adjuvant chemotherapy) Type of recommendation: evidence-based Evidence: intermediate Recommendation: weak
Note		Wherever radical hysterectomy with concurrent chemoRT listed as a surgical option above, **extrafascial hysterectomy is preferred if there is residual disease or initial tumor > 6 cm** Type of recommendation: consensus-based Evidence: intermediate Recommendation: weak		

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Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IVB	Palliative care and chemotherapy (if available) Type of recommendation: evidence-based Evidence: high Recommendation: strong	Palliative care **and/or chemotherapy ± individualized RT** (palliative care may include palliative RT) Type of recommendation: evidence-based Evidence: high Recommendation: strong	Chemotherapy ± individualized RT AND/OR palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong	Chemotherapy **± bevacizumab** ± individualized RT AND/OR palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong
Recurrent	Palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong	**Depending on previous RT and either "no prior RT or failure outside of previously treated field"*** (CERV-11) **then may offer tumor-directed RT plus platinum-based chemotherapy** Type of recommendation: evidence-based Evidence: high Recommendation: strong	**Depending on previous RT and central *v* noncentral disease:** **Central disease: chemoRT or RT ± brachytherapy if no prior RT** **If central and prior RT: exenteration** **Noncentral: chemotherapy, tumor-directed RT,** and palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong	**Depending on previous RT and central *v* noncentral disease:** Central disease: chemoRT or RT ± brachytherapy if no prior RT If central and prior RT: exenteration Noncentral: chemotherapy, tumor-directed RT, and palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong
			Prior RT plus central disease: pelvic exenteration OR radical hysterectomy OR brachytherapy (latter two "in carefully selected patients with small (< 2 cm) lesions"** (CERV-11)**)** Type of recommendation: evidence-based Evidence: high Recommendation: strong	Prior RT plus central disease: pelvic exenteration ± intraoperative RT OR radical hysterectomy OR brachytherapy (latter two "in carefully selected patients with small (< 2 cm) lesions" ** (CERV-11) Type of recommendation: evidence-based Evidence: high Recommendation: strong

Summary of Recommendations

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
Recurrent	AND/OR central disease: chemotherapy Type of recommendation: consensus-based Evidence: insufficient Recommendation: weak NOTE. this is best managed with exenteration (type of surgery that is not	Prior RT plus noncentral disease: chemotherapy or best palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong	**Pelvic RT plus brachytherapy plus** concurrent low-dose platinum-based chemotherapy **(in some cases extended-field RT)** AND/OR palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong	Pelvic RT plus brachytherapy plus concurrent low-dose platinum-based chemotherapy (in some cases extended-field RT) AND/OR palliative care (Options before palliative care alone include: **RT boost, salvage surgery,** or chemotherapy) Type of recommendation: evidence and consensus-based Evidence: high Recommendation: strong
	AND/OR central disease: chemotherapy Type of recommendation: consensus-based Evidence: insufficient Recommendation: weak NOTE. this is best managed with exenteration (type of surgery that is not		**Prior RT plus noncentral disease: tumor-directed RT ± chemotherapy** or best palliative care NOTE. Before palliative care alone, try options such as **RT boost, salvage surgery**, or chemotherapy Type of recommendation: evidence-based Evidence: high Recommendation: strong	Prior RT plus noncentral disease: tumor-directed RT ± chemotherapy OR **resection with intraoperative RT for close or positive margins OR clinical trial OR chemotherapy plus bevacizumab** AND/OR palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong
				If recurrence after any of the above, then clinical trial OR chemotherapy OR best supportive care Type of recommendation: evidence-based Evidence: high Recommendation: strong

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Summary of Recommendations

NOTE. Bold indicates addition of a recommended action over a previous resource level (eg, in limited setting, a bold action is one that was not recommended in basic). Additional recommendations regarding settings with limited radiotherapy resources are provided in the main article.

Abbreviations: chemoRT, chemotherapy plus radiotherapy; EBRT, external-beam radiation therapy; FS, fertility sparing; LN, lymph node; LND, lymph node dissection; LVSI, lymphovascular space invasion; NACT, neoadjuvant chemotherapy; PANB, para-aortic node biopsy; PLND, pelvic lymph node dissection; RT, radiotherapy.

[1]This option in basic level only if follow-up is available; [2]For negative margins or operable tumor or positive margins for dysplasia or carcinoma; [3]For negative margins or inoperable tumor; [4]Margins for dysplasia or carcinoma;[5]Selective lymphadenectomy or LN biopsy for suspicious lesions [6]Recommended in setting where chemotherapy is not consistently available; [7]When brachytherapy is not available, extrafascial or radical hysterectomy is recommended only when there is persistent central pelvic disease and selective lymphadenectomy or LN biopsy for suspicious lesions

References

*Koh WJ, Greer BE, Abu-Rustum NR, et al: NCCN Guidelines Version 2.2015: Cervical Cancer Preliminary Resource Stratification—Limited Level. Fort Washington, PA, National Comprehensive Cancer Network, 2015

**Koh WJ, Greer, B.E., Abu-Rustum, NR, et. al.: NCCN guidelines version 2.2015: Cervical cancer preliminary resource stratification: Maximal level, National Comprehensive Cancer Network, Fort Washington, PA, 2015

Chemotherapy Regimens for Stage IV or Recurrent Disease

Setting			
Basic	Limited	Enhanced	Maximal
Single-agent platinum-based therapy (cisplatin or carboplatin)	Cisplatin or carboplatin, **cisplatin plus paclitaxel, or carboplatin plus paclitaxel**	Cisplatin plus paclitaxel or Carboplatin plus paclitaxel (highest-level evidence for cisplatin: CCO)	Cisplatin plus paclitaxel **plus bevacizumab** or carboplatin plus paclitaxel **plus bevacizumab**

Options for Follow-Up for All Settings

- **Follow-up should be based on each individual's risk of cervical cancer recurrence; high-quality evidence is lacking on the best methods of post-treatment surveillance; some guidance is offered in other guidelines and is provided here as guidance rather than as recommendations:**
  - After 1 to 2 years, every 3 to 6 months
  - After 3 to 5 years: every 6 to 12 months
  - After ≥ 5 years, every year based on risk of recurrence
- Pelvic and physical examination
- Imaging and laboratory tests based on symptoms or suspicion
- Patient education
- Cytology may be offered, if available, every 3 years after cone biopsy, radical hysterectomy, or trachelectomy; cytology should not be performed after RT
- In patients at high risk for locoregional failure, PET-CT 3 months after therapy is optional

Special Commentary

Palliative Care for Women with Advanced Cervical Cancer

- Palliative care and pain management are part of the treatment for cancers, including cervical cancer, to avoid unnecessary suffering during the final stages of the disease.

- Pain control is a vital component of palliative care; it is a basic human right often neglected in cancer control programs.

- Patients with advanced or recurrent cervical cancer may have any of the following symptoms:
  - Vaginal bleeding or discharge
  - Pelvic or back pain
  - Urinary or bowel fistulas
  - Lower-extremity edema
  - Deep-venous thrombosis
  - Dyspnea resulting from anemia or pulmonary involvement or
  - Uremia from ureteral obstruction

Special Commentary

- In limited resource settings where radiation therapy is limited, providers may have to prioritize its use to treat selective patients with advanced-stage disease and to palliate symptoms in other patients who normally receive antitumor treatment in maximal-level settings.

- Interventions to control vaginal bleeding include radiation therapy or brachytherapy, embolization of the uterine arteries, surgical resection, and arterial ligation. Vaginal packing is usually a temporary measure.

- Pain is often a disabling symptom of advanced or recurrent cervical cancer. Narcotic analgesics may be prepared for oral, rectal, vaginal, sublingual, intravenous, intramuscular, epidural, or topical administration.

- When pain is directly attributable to specific foci of disease a brief course of palliative radiation therapy yields substantial pain reduction in a high percentage of patients. However, pain relief may not be maximally achieved until weeks after the palliative radiation therapy ends.

Cost Implications

- There are very few studies of the cost effectiveness of treatment in low- and middle-income countries.
- Concentrating surgical volume in high-risk centers and by high-risk surgeons has been shown in many clinical settings to improve outcome.
- Thus, even in countries without trained gynecologic oncologists or access to ideal radiation therapy facilities, surgical outcomes could be improved by concentrating resources and designating experts.
- These types of changes may be cost effective both by improving clinical outcomes and by optimally using existing resources.

Limitations of Research

- There were several areas where evidence was lacking to make strong recommendations.
  - Optimal post-treatment surveillance for women with cervical cancer at risk for recurrence, including the role of PET scans in maximal resource settings
  - Using squamous cell carcinoma antigen and/or high-sensitivity C-reactive protein
  - Optimal dose fractionation of brachytherapy
  - Surgery for women with stage IA2 or IB1 disease with tumors smaller than 2 cm in size and 1 cm in depth in the non–fertility-sparing setting
  - Optimal treatment of patients with stage IB1 cervical cancer with tumor size between 2 and 4 cm
  - Optimal fertility-sparing procedures for women with stage IA1 or IA2 disease
  - Treatment of women with invasive cervical cancer in basic settings, including regarding chemotherapy and radiation therapy
- ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate.

Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at

www.asco.org/rs-cervical-cancer-treatment-guideline

Patient information is available at www.cancer.net

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