ASCO GUIDELINES

MANAGEMENT AND CARE OF WOMEN WITH INVASIVE CERVICAL CANCER: AMERICAN SOCIETY OF CLINICAL ONCOLOGY RESOURCE-STRATIFIED CLINICAL PRACTICE GUIDELINE				
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

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			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
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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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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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)

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	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

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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**		
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

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		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 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	**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

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		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

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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

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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			

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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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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
	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 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

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	Basic	Limited	Enhanced	Maximal
	feasible to perform in low-resource setting)	Prior RT plus noncentral disease: chemotherapy or best palliative care Type of recommendation: evidence-based Evidence: high Recommendation: strong	**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

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