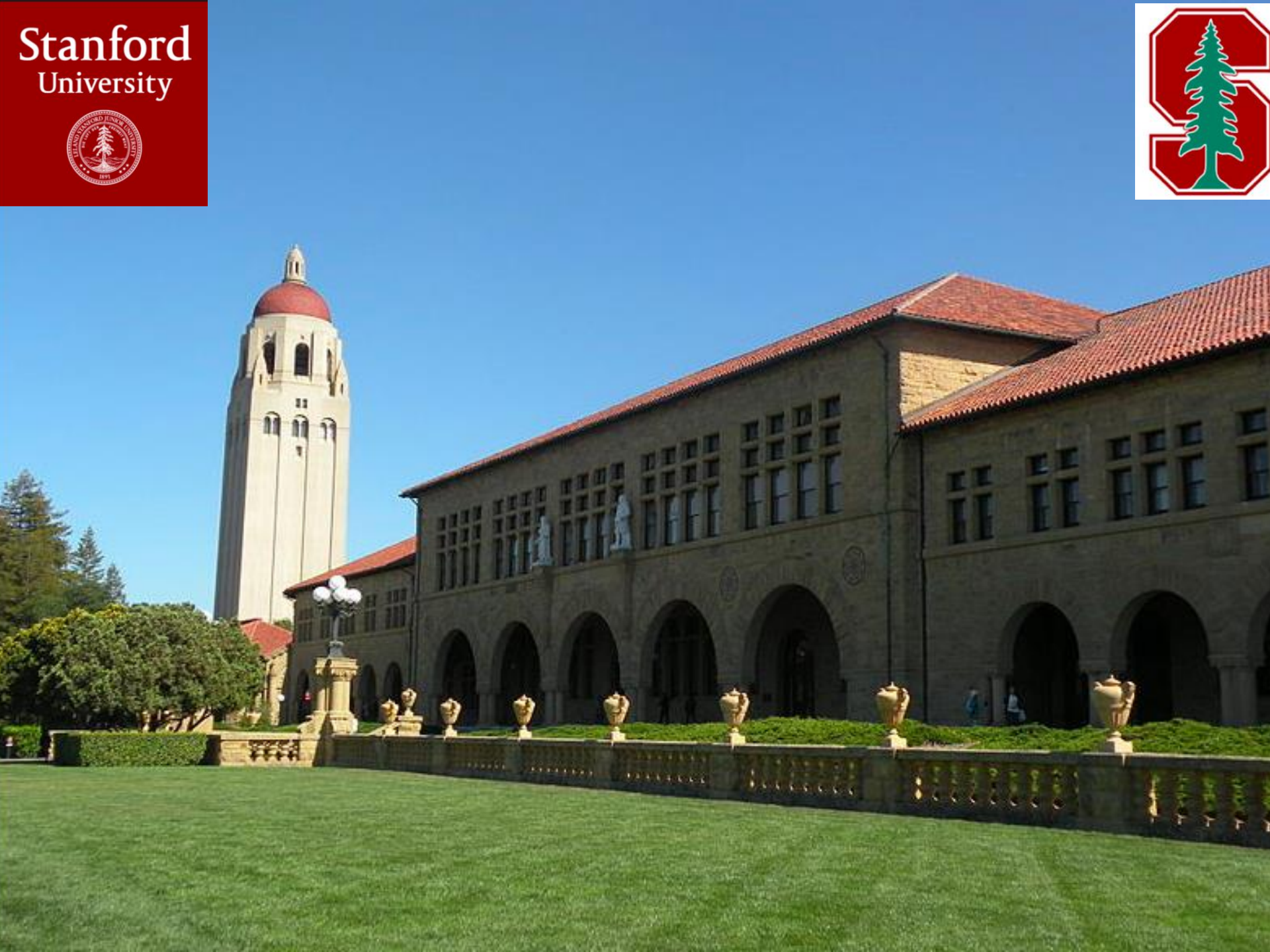
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Gynecologic Cancer InterGroup
Cervix Cancer Research Network

Cervical Cancer: 2018 FIGO Staging & ASCO Resource-stratified Guidelines

Jonathan S. Berek, MD, MMS

Laurie Kraus Lacob Professor
Stanford University School of Medicine
Director, Stanford Women's Cancer Center
Senior Advisor, Stanford Cancer Institute

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FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Stage I: The carcinoma is strictly confined to the cervix uteri (extension to the corpus would be disregarded)

IA Invasive carcinoma that can be diagnosed only by microscopy with measured deepest invasion < 5.0 mm

IA1 Measured stromal invasion < 3.0 mm

IA2 Measured stromal invasion ≥ 3.0 mm and < 5.0 mm

(The involvement of vascular/lymphatic spaces does not change the staging.)

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FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Stage I: The carcinoma is strictly confined to the cervix uteri (extension to the corpus would be disregarded)

IB	Invasive carcinoma with measured deepest invasion > 5.0 mm, limited to the cervix uteri
IB1	Invasive carcinoma ≥ 5.0 mm depth of invasion and < 2.0 cm in greatest dimension
IB2	Invasive carcinoma ≥ 2.0 cm and < 4.0 cm in greatest dimension
IB3	Invasive carcinoma ≥ 4.0 cm in greatest dimension

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Comment: Stage I cervical cancer is limited to the cervix. If there is only microscopic invasion less than 5.0 mm, it is assigned stage IA, further subdivided as stage IA1 and IA2 at a cut-off of 3.0 mm. The lateral extent of the lesion is no longer taken into consideration.

In stage IB, an additional cut-off at 2 cm has been introduced, based on oncological data from fertility-sparing operations including conization in stage IA and radical trachelectomy in early stage IB. Recurrence rates are significantly lower in patients whose primary stage I tumors are less than 2.0 cm compared with those who have tumors measuring 2.0-4.0 cm in their greatest dimension.

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Controversial issues: *Presence of vascular/lymph space invasion:* Lymphovascular space invasion does not change the stage.

Extension to the uterine corpus: Involvement of the uterine body does not change the stage.

Recommendations: The size and extent of the primary tumor can be assessed by clinical evaluation (pre- or intraoperative), imaging, and/or pathological measurement.

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Recommendations: Methods of imaging include ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), PET-CT, MRI-PET, etc. MRI has been shown to have the best sensitivity and specificity in assessing the size of the lesion. However, ultrasound has been shown to provide comparable information for staging in the hands of experienced operators.

In operated patients, the histopathological examination will provide information on size and extent of lesion.

The final stage is to be assigned after receiving all reports. The method of recording the size and assigning stage should be noted.

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Stage II Cervical carcinoma invades beyond the uterus, but not to the lower third of the vagina or to the pelvic wall

IIA Without parametrial invasion

- **IIA1** Invasive carcinoma < 4.0 cm in greatest dimension
- **IIA2** Invasive carcinoma ≥ 4.0 cm in greatest dimension

IIB With parametrial invasion

FIGO Staging of Carcinoma of the Cervix Uteri

Comment: In stage II, the tumor has extended beyond the uterus into the vagina and parametrium but not to the lower third of the vagina and not reaching the pelvic wall. In the sub-stages, the size of the lesion can be measured clinically, on imaging, or pathology, as in stage I.

Controversial issues: *Use of imaging for assessment of parametrial involvement:* The utility of imaging for evaluation of parametrium and upper vagina is less clear. MRI has been shown to perform better than CT scan for parametrial assessment. False negative as well as false positive results have been reported especially when there is infection or with larger tumor size and stretching of the upper vagina by the growth.

FIGO Staging of Carcinoma of the Cervix Uteri

Controversial issues: *Involvement of ovary:* Involvement of the ovary has been reported in <1% of cases of squamous cell carcinoma and in <5% of cases of nonsquamous cell carcinoma in early stage cervical cancer. Since it is often associated with the presence of other risk factors, there are limited data on its impact on survival as an independent risk factor. Presently, ovarian involvement does not change the stage.

Recommendations: Colposcopy may be used to assess the extent of vaginal involvement. Examination under anesthesia may be useful to improve the accuracy of clinical assessment where imaging facilities are lacking.
As in stage I, the method used to assess tumor size and extent should be recorded.

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Stage III 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

- IIIA Carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
- IIIB Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney
- IIIC Involvement of pelvic and/or paraaortic lymph nodes, irrespective of tumor size and extent (with r and p notations)
  - IIIC1 Pelvic lymph node metastasis only
  - IIIC2 Paraaortic lymph node metastasis

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PET-CT compared to CT for Detection of Lymph Node Metastasis in Cervical Cancer

Diagnostic Performance	PET-CT	CT	p-value
Abdomen			
Sensitivity	0.05 (CI,).44-0.56) 0.45-0.55	0.42 (CI, 0.36-0.48) 0.33-0.48	0.052
Specificity	0.85 (CI, 0.80-0.89) 0.75-0.90	0.89 (CI, 0.84-0.92) 0.832-0.95	0.210
Pelvis			
Sensitivity	0.83 (CI, 0.78 -0.87) 0.65-0.90	0.79 (CI, 0.73-0.83) 0.71-0.84	0.150
Specificity	0.63 (CI, 0.78-0.87) 0.54-0.73	0.62 (CI, 0.53-0.69) 0.38-0.73	0.830

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Comment: In stage III, the tumor has extended to the lower third of the vagina and/or reached the pelvic wall. Identification of hydronephrosis or a non-functioning kidney by any method assigns the case to stage IIIB regardless of other findings.

Similarly, the presence of pelvic or paraaortic lymph node metastases assigns the case to stage IIIC regardless of other findings, as they have poorer survival compared to those who do not have lymph node metastases. Pelvic and paraaortic lymph node involvement is allocated to stage IIIC1 and IIIC2, respectively

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Controversial issues in Stage III:

Presence of isolated tumor cells (ITCs) or micrometastases; Metastases in lymph nodes have been graded as ITCs (<0.2 mm), micrometastases (0.2-2.0 mm) or macrometastases (>2.0 mm). Presence of ITCs or micrometastases signifies low volume metastasis and their implication is not clear. The presence of micrometastases or isolated tumor cells may be recorded but their presence does not change the stage.

Differentiating metastases from infection: In many countries with a high cervical cancer burden there is also a high prevalence of infection with tuberculosis and human immunodeficiency virus (HIV). In these endemic areas, there is a possibility of nodes being enlarged without metastases. The assessment of metastatic lymph nodes versus infected lymph nodes does not have clear radiological criteria.

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Controversial issues in Stage III:

Sentinel lymph nodes: Sentinel lymph node dissection is commonly used in vulvar and endometrial cancer. In cervical cancer, good sensitivity and specificity has been reported with acceptable false negative rates. Appropriate facilities and expertise should be available to validate and follow the protocol for the sentinel lymph node approach, which also requires good backup of pathology for ultrastaging and immunohistochemistry. Following the protocol is essential for this procedure.

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Recommendations: Surgicopathological assessment of lymph node involvement requires advanced surgical skills, whether performed by conventional or MIS route. Since 85% of cases presently occur in low resource settings, the required professional skills and infrastructure facilities are presently not widely available. Pathological confirmation is the gold standard but imaging can be used to interpret disease extent.

The choice of imaging modality for nodal evaluation has not been fixed by FIGO. It depends upon the availability of the imaging modality and patients' affordability. Non-availability of an imaging modality should not be a reason for undue delay in initiation of treatment.

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Recommendations: FIGO does not define criteria to discriminate between malignancy and inflammation / infection on imaging, which is left to the discretion of the clinician. The clinician must opine on whether these look suspicious enough to upstage the case or not.

The best available technology should be used for assessment, and the lowest appropriate stage should be assigned, i.e., when in doubt assign the lower stage.

At the present time, lack of facilities universally is recognized and clinical assessment of staging with the use of other facilities as available is permissible. The method of assigning the stage is to be recorded and reported.

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Stage IV The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. [A bullous edema, as such, does not permit a case to be allotted to Stage IV].

IVA Spread to adjacent organs

IVB Spread to distant organs

FIGO Staging of Carcinoma of the Cervix Uteri (2018)

Comment: Stage IV remains unchanged.

Controversial issues: Loss of fat planes at imaging may suggest involvement of bladder and rectum but does not necessarily imply invasion by tumor.

Recommendations: Evaluation of the bladder and rectum by cystoscopy and proctosigmodoscopy, respectively, is recommended if the patient is symptomatic. Cystoscopy should be considered in cases with a barrel-shaped endocervical growth, extension of growth to the anterior vaginal wall. Histological confirmation should be done to assign the case to stage IV.

Treatment Capacity

Treatment	Setting			
	Basic	Limited	Enhanced	Maximal
Surgery	Simple (extrafascial) hysterectomy or more extensive hysterectomy can be performed* *Where medical facilities exist to take care of women who are at high risk for postoperative complications	**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 *Can be performed in some enhanced levels	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**

†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.

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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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Recommendations for Stage IB & IIA

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	If chemotherapy is available, NACT **followed by radical hysterectomy (see Note) plus PLND ± para-aortic LN sampling may be an option*** §	**Pelvic RT plus concurrent low-dose platinum-based chemotherapy plus brachytherapy**	Pelvic RT plus concurrent low-dose platinum-based chemotherapy plus brachytherapy
		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) OR **if no EBRT is available, then brachytherapy and concurrent low-dose platinum-based chemotherapy followed by radical hysterectomy (see Note)*** ***Recommended in setting where chemotherapy is not consistently available** †**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**	**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	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

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Recommendations for Stage IB & IIA

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IB2 and IIA		**Radical hysterectomy plus PLND ± para-aortic LN sampling**	Radical hysterectomy plus PLND ± para-aortic LND sampling‡ **and adjuvant RT or chemoRT if needed**	Radical hysterectomy plus PLND ± para-aortic LN sampling and adjuvant RT or chemoRT if needed **(plus RT ± concurrent low-dose platinum-based chemotherapy after hysterectomy if risk factors)**‡
Note	With risk factors on pathology specimen: adjuvant chemotherapy after hysterectomy	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**	With risk factors on pathology specimen: adjuvant RT ± concurrent low-dose platinum-based chemotherapy after hysterectomy	With risk factors on pathology specimen: adjuvant RT ± concurrent low-dose platinum-based chemotherapy after hysterectomy
Stage IIA1	See IB1	See IB1	See IB1	See IB1
IIA2	See IB2	See IB2	See IB2	See IB2

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Recommendations for Stage IIB & IIIA

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IIB and IIIA	NACT followed by extrafascial hysterectomy (modification as deemed necessary)	**ChemoRT or RT* followed by extrafascial or modified hysterectomy ± PLND† ± PANB** **NACT followed by extrafascial or modified hysterectomy ± PLND† § ± PANB***	**Pelvic RT plus** concurrent low-dose platinum-based chemotherapy **plus brachytherapy** **Adjuvant hysterectomy is an option only if residual disease after chemoRT**	Pelvic RT plus concurrent low-dose platinum-based chemotherapy plus brachytherapy Adjuvant hysterectomy is an option only if residual disease after chemoRT
	Extrafascial hysterectomy when chemotherapy is not consistently available	**Extrafascial or modified hysterectomy plus PLND ± para-aortic LN sampling‡ plus adjuvant therapy**		
	Palliative care			

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Recommendations for Stage IA, Stage IB and IIA Disease

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IA2 FS	Cone biopsy (if follow-up possible)	Cone biopsy (if follow-up possible)	Cone biopsy **plus PLND ± para-aortic LN sampling**‡	Cone biopsy plus pelvic LND ± para-aortic LN sampling‡
			Radical trachelectomy plus PLND	Radical trachelectomy plus pelvic LND
IA2 non-FS	Cone biopsy (if follow-up possible) or extrafascial hysterectomy (non-FS)	Cone biopsy **plus PLND ± para-aortic LN sampling**‡	Cone biopsy plus pelvic LND ± para-aortic LN sampling‡	See above
	Extrafascial hysterectomy	**Modified radical hysterectomy plus PLND ± para-aortic LN sampling** §	Modified radical hysterectomy plus PLND ± para-aortic LN sampling §	Modified radical hysterectomy plus PLND ± para-aortic LN sampling §
			OR pelvic RT and brachytherapy	OR pelvic RT and brachytherapy
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	radical trachelectomy plus pelvic LN sampling; **may offer SLN**

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Recommendations for Stage IA, Stage IB and IIA Disease

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IA1, LVSI negative, FS	1A1 (negative margins): cone biopsy* (with scalpel) Repeat cone biopsy or extrafascial hysterectomy for positive margins *This option in basic level only if follow-up is available	1A1 (negative margins): cone biopsy Repeat cone biopsy or extrafascial hysterectomy for positive margins	1A1 (negative margins): cone biopsy Repeat cone biopsy, or extrafascial hysterectomy for positive margins.	1A1 (negative margins): cone biopsy Repeat cone biopsy or extrafascial hysterectomy for positive margins
IA1, LVSI positive, FS	Cone biopsy in selected cases, if follow-up possible	Cone biopsy	Cone biopsy **plus PLND** (see Discussion regarding current evidence on FS sparing for women desiring fertility preservation)	Cone biopsy plus PLND
			OR **radical trachelectomy plus PLND**	OR radical trachelectomy plus PLND **(may offer ± SLN)**

Abbreviations: 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.
†For negative margins or operable tumor or positive margins for dysplasia or carcinoma.
‡For negative margins or inoperable tumor.
§ Margins for dysplasia or carcinoma.

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Recommendations for Stage IA, Stage IB and IIA Disease

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IA1, non-FS (no LVSI)	Cone biopsy (if follow-up possible) OR extrafascial hysterectomy,† then observe after initial cone biopsy, repeat cone, or extrafascial hysterectomy if margins are positive	Cone biopsy (if follow-up possible); observe (after cone biopsy)‡ OR extrafascial hysterectomy† (extrafascial hysterectomy OR modified radical **hysterectomy plus PLND** OR if positive margins repeat conization §)	Cone biopsy‡ OR extrafascial hysterectomy† (extrafascial hysterectomy OR modified radical hysterectomy plus pelvic LND OR if positive margins repeat conization §)	Cone biopsy‡ OR extrafascial hysterectomy† (extrafascial hysterectomy OR modified radical hysterectomy plus **pelvic LN sampling** if positive margins **[may offer ± SLN]** OR repeat conization §)
IA1, non-FS (with LVSI)	As above	Stage IA1 (with LVSI) and stage IA2: modified radical hysterectomy	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)**	Stage IA1 (with LVSI) and stage IA2: modified radical hysterectomy plus PLND ± para-aortic (**may offer ± SLN** OR pelvic irradiation plus brachytherapy [if patient is not eligible for surgery])

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Recommendations for Stage IA, Stage IB and IIA Disease

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
IB1, Non-FS	Extrafascial hysterectomy	**Radical hysterectomy plus PLND or radical hysterectomy (see Note) with adjuvant RT or RT with concurrent low-dose chemotherapy (concurrent chemoRT), if needed**	Radical hysterectomy plus PLND	Radical hysterectomy plus PLND; **may offer SLN**
	NACT if available, then extrafascial hysterectomy	**ChemoRT or RT followed by extrafascial or radical hysterectomy (see Note) ± PLND ± PANB*** 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*)** 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 *Selective lymphadenectomy or LN biopsy for suspicious lesions	**Pelvic RT plus brachytherapy plus concurrent low-dose platinum-based chemotherapy**	Pelvic RT plus brachytherapy plus concurrent low-dose platinum-based chemotherapy
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**		

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Recommendations for Stage IIB, III, IVA, IVB, and Recurrent Disease

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
Stage IIIB to IVA	Palliative care	**ChemoRT or RT* followed by extrafascial or radical hysterectomy (see Note) ± PLND § ± PANB** **NACT (followed by radical hysterectomy plus PLND § ± PANB may be an option]** and/or palliative care	**Pelvic RT plus brachytherapy plus** concurrent low-dose platinum-based chemotherapy **(in some cases extended-field RT)** AND/OR palliative care	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)
	NACT followed by extrafascial hysterectomy	**RT ± concurrent low-dose platinum-based chemotherapy (may offer systemic adjuvant chemotherapy)**	RT **+ brachytherapy ±** concurrent low-dose platinum-based chemotherapy (may offer systemic adjuvant chemotherapy)	RT + brachytherapy ± concurrent low-dose platinum-based chemotherapy (may offer systemic adjuvant chemotherapy)
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**		

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Recommendations for Stage IIB, III, IVA, IVB, and Recurrent Disease

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
Stage IVB	Palliative care and chemotherapy (if available)	Palliative care **and/or chemotherapy ± individualized RT** (palliative care may include palliative RT)	Chemotherapy ± individualized RT AND/OR palliative care	Chemotherapy **± bevacizumab** ± individualized RT AND/OR palliative care
Recurrent	Palliative care	**Depending on previous RT and either "no prior RT or failure outside of previously treated field", then may offer tumor-directed RT plus platinum-based chemotherapy**	**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	**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
	AND/OR central disease: chemotherapy		**Prior RT plus central disease: pelvic exenteration OR radical hysterectomy OR brachytherapy (latter two "in carefully selected patients with small (< 2 cm) lesions")**	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"
Note	This is best managed with exenteration (type of surgery that is not feasible to perform in low-resource setting)			

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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**

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Recommendations for Stage IIB, III, IVA, IVB, and Recurrent Disease

Type of Disease	Setting			
	Basic	Limited	Enhanced	Maximal
Recurrent		Prior RT plus noncentral disease: chemotherapy or best palliative care	**Prior RT plus noncentral disease: tumor-directed RT ± chemotherapy** or best palliative care	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
Note			Before palliative care alone, try options such as **RT boost, salvage surgery**, or chemotherapy	If recurrence after any of the above, then clinical trial OR chemotherapy OR best supportive care

Abbreviations: LN, lymph node; LND, lymph node dissection; NACT, neoadjuvant chemotherapy; PANB, para-aortic node biopsy; PLND, pelvic lymph node dissection; PLND, pelvic lymph node dissection; RT, radiotherapy.
*Recommended in setting where chemotherapy is not consistently available.
†When brachytherapy is not available, extrafascial hysterectomy is recommended only when there is persistent central pelvic disease and selective lymphadenectomy or LN biopsy for suspicious lesions.
‡Margins for dysplasia or carcinoma.
§ 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.

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