

National Comprehensive
Cancer Network[®]

Cervical Cancer

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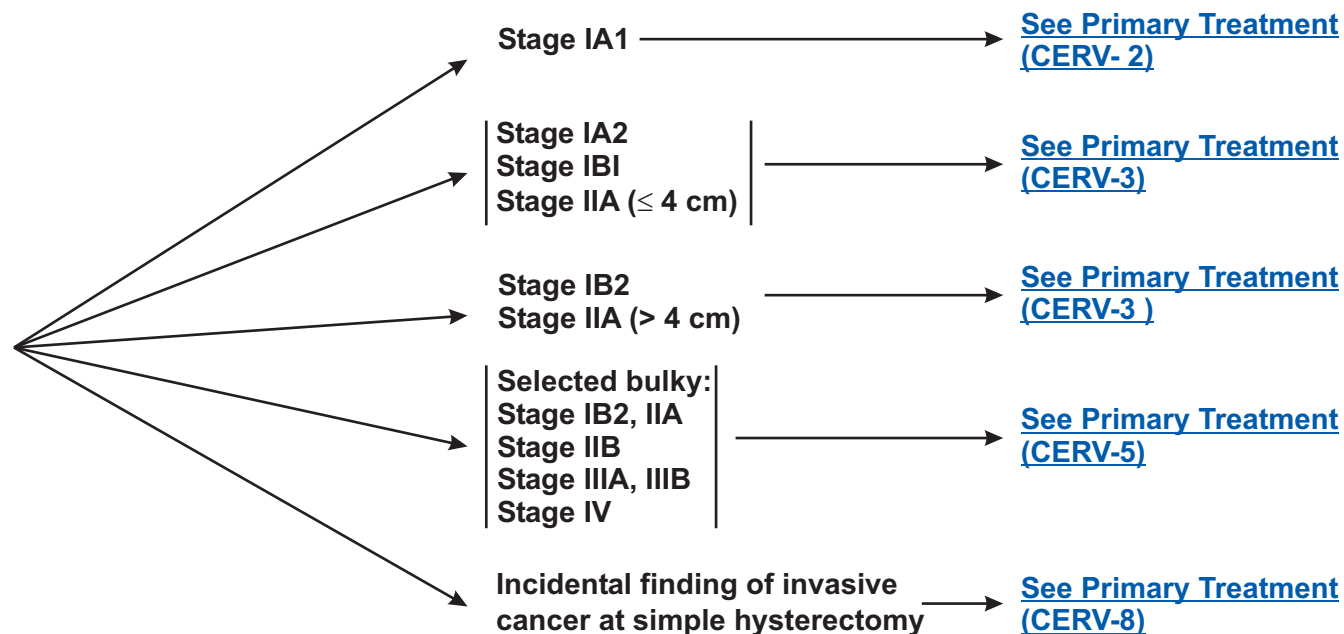
NCCN Categories of Consensus: All recommendations are Category 2A unless otherwise specified.
See [NCCN Categories of Consensus](#)

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WORK-UP

- H&P
 - CBC, platelets
 - Cervical biopsy, pathologic review
 - Cone biopsy as indicated
 - Chest x-ray, IVP, or CT/MRI (optional for $\leq$ stage IB1)
- Optional:
- Lymphangiography
 - EUA^a cystoscopy/proctoscopy for $\geq$ stage IB2
 - LFT^b/renal function studies

CLINICAL STAGE



^aEUA = examine under anesthesia.

^bLFT = liver function tests.

Note: All recommendations are category 2A unless otherwise indicated.

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CERV-1

CLINICAL STAGE

PRIMARY TREATMENT

Stage IA1



Extrafascial hysterectomy
or
Observe if patient desires fertility or if inoperable
(only if cone biopsy has negative margins)

[See Surveillance
\(CERV-9\)](#)

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CERV-2

CLINICAL STAGE

PRIMARY TREATMENT

Stage IA2

Radical hysterectomy + pelvic lymph node dissection
± para-aortic lymph node sampling (category 2B)
or
Brachytherapy ± pelvic RT (point A dose: 75-80 Gy^c)

Stage IB1
and stage IIA
(≤ 4 cm)

Radical hysterectomy + pelvic lymph node dissection
+ sample para-aortic nodes (category 1)
or
Pelvic RT + brachytherapy (point A dose: 80-85 Gy^c)

Stage IB2 and
stage IIA (> 4 cm)

Radical hysterectomy + pelvic lymph node dissection
+ para-aortic lymph node sampling with or without
neoadjuvant chemotherapy (category 3)
or
Pelvic RT + concurrent cisplatin-containing
chemotherapy + brachytherapy
(Point A dose ≥ 85 Gy^c or Point A dose 75-80 Gy^c
+ adjuvant hysterectomy [category 2B])

[See Surgical Findings
\(CERV-4\)](#)

^cThese doses are recommended for most patients based on summation of conventional external-beam fractionation and low-dose rate (40-60 cGy/h) brachytherapy equivalents. Modify treatment based on normal tissue tolerance.

[See Surveillance
\(CERV-9\)](#)

Note: All recommendations are category 2A unless otherwise indicated.

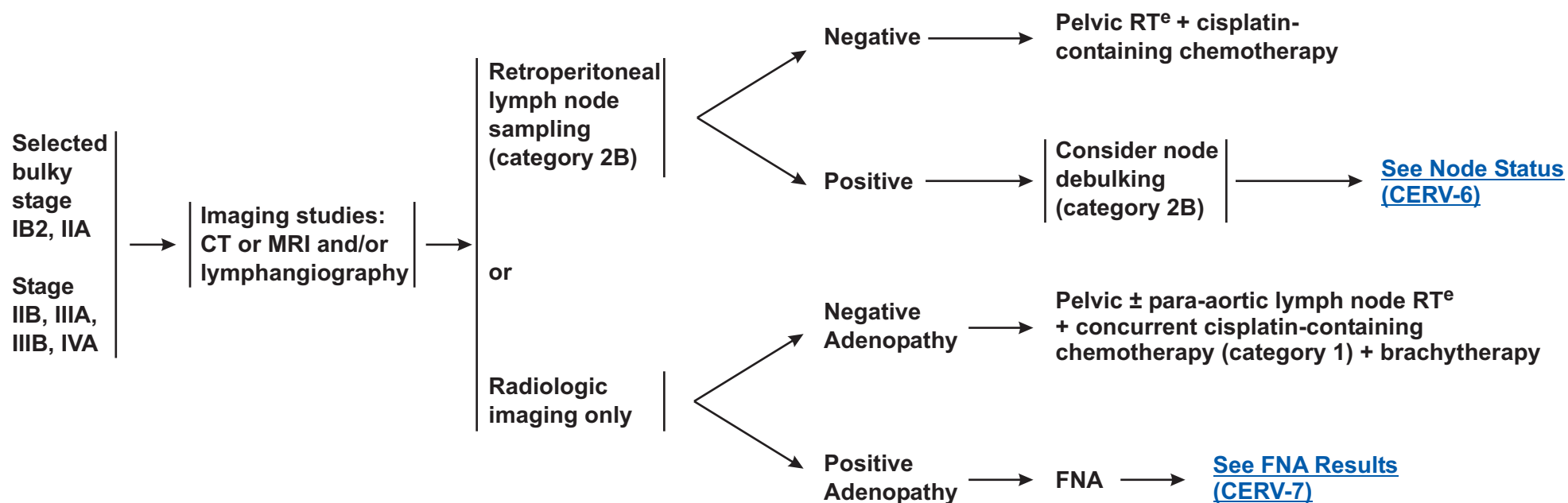
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

CERV-3

**STAGE IA2, IB1 AND IIA (≤ 4 cm)
SURGICAL FINDINGS****ADJUVANT TREATMENT****Negative
nodes****Observe**
Optional pelvic RT ± vaginal brachytherapy if
deep stromal invasion or lymph vascular space invasion**Positive nodes
or
Positive vaginal margin^d
or
Positive parametrium****Pelvic RT + concurrent cisplatin-containing**
chemotherapy (category 1) ± vaginal brachytherapy
(vaginal brachytherapy indicated if positive
vaginal margin)^dInvasive cancer at surgical margin.[See Surveillance
\(CERV-9\)](#)**Note: All recommendations are category 2A unless otherwise indicated.****Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.****CERV-4**

CLINICAL STAGE

PRIMARY TREATMENT



^eAll RT on this page should be RT + brachytherapy (total point A dose ≥ 85 Gy).

[See Surveillance \(CERV-9\)](#)

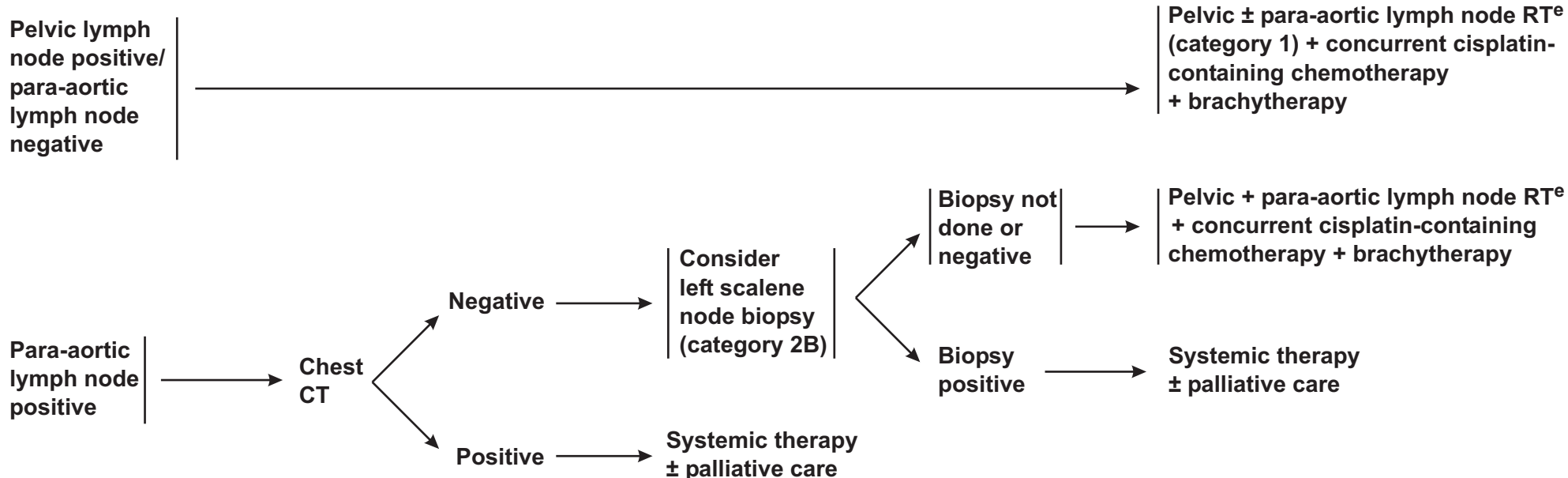
Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

CERV-5

**SELECTED BULKY
STAGE IB2, IIA, IIB, IIIA, IIIB, IV
NODE STATUS**

PRIMARY TREATMENT



^eAll RT on this page should be RT + brachytherapy (total point A dose ≥ 85 Gy).

[See Surveillance
\(CERV-9\)](#)

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

CERV-6

**SELECTED BULKY
STAGE IB2, IIA, IIB, IIIA, IIIB, IV
FNA RESULTS****PRIMARY TREATMENT**FNA
negative

Pelvic ± para-aortic lymph node RT^e
+ concurrent cisplatin-containing
chemotherapy (category 1) + brachytherapy
or
[Retroperitoneal lymph node
sampling \(See CERV-5\)](#)

FNA
positive
or FNA
not done

Pelvic node

Pelvic ± para-aortic lymph node RT^e
+ concurrent cisplatin-containing
chemotherapy + brachytherapy
or
[Retroperitoneal lymph node
sampling \(See CERV-5\)](#)

Para-aortic
lymph nodeChest
CT

Negative

Consider
left scalene
node biopsy

Biopsy not
done or
negative

Consider
retroperitoneal
node debulking
(category 2B)

Pelvic + para-aortic
lymph node RT^e
+ concurrent
cisplatin-containing
chemotherapy
+ brachytherapy

Biopsy
positive

Systemic therapy
± palliative care

Positive

Systemic therapy
± palliative care

^eAll RT on this page should be RT + brachytherapy (total point A dose ≥ 85 Gy).

[See Surveillance
\(CERV-9\)](#)

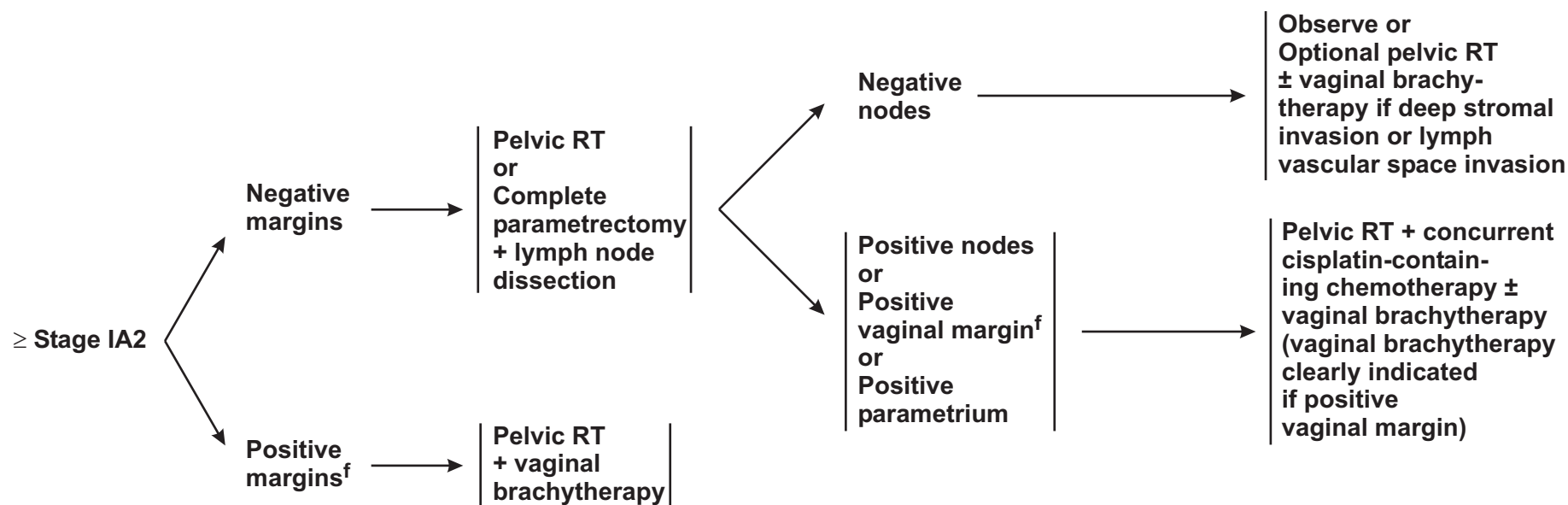
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Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

CERV-7

INCIDENTAL FINDING
OF INVASIVE CANCER
AT SIMPLE HYSTERECTOMY

PRIMARY TREATMENT



^fInvasive cancer at surgical margin.

[See Surveillance \(CERV-9\)](#)

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

CERV-8

SURVEILLANCE

WORK-UP

- Interval H&P
- Pap test + visit every 3 mo for 1 yr, every 4 mo for 1 yr, every 6 mo for 3 yr, then annually
- Chest x-ray annually (category 2B)
- CBC, BUN, creatinine every 6 mo (optional)
- CT for advanced stage annually (optional)

Persistent
or recurrent
disease

- Pelvic/abdominal CT
- Chest x-ray (if negative, consider chest CT)
- Surgical exploration in selected cases

[See Salvage Therapy
\(pelvic recurrence\)
\(CERV-10\)](#)

[See Salvage Therapy
\(extrapelvic recurrence\)
\(CERV-11\)](#)

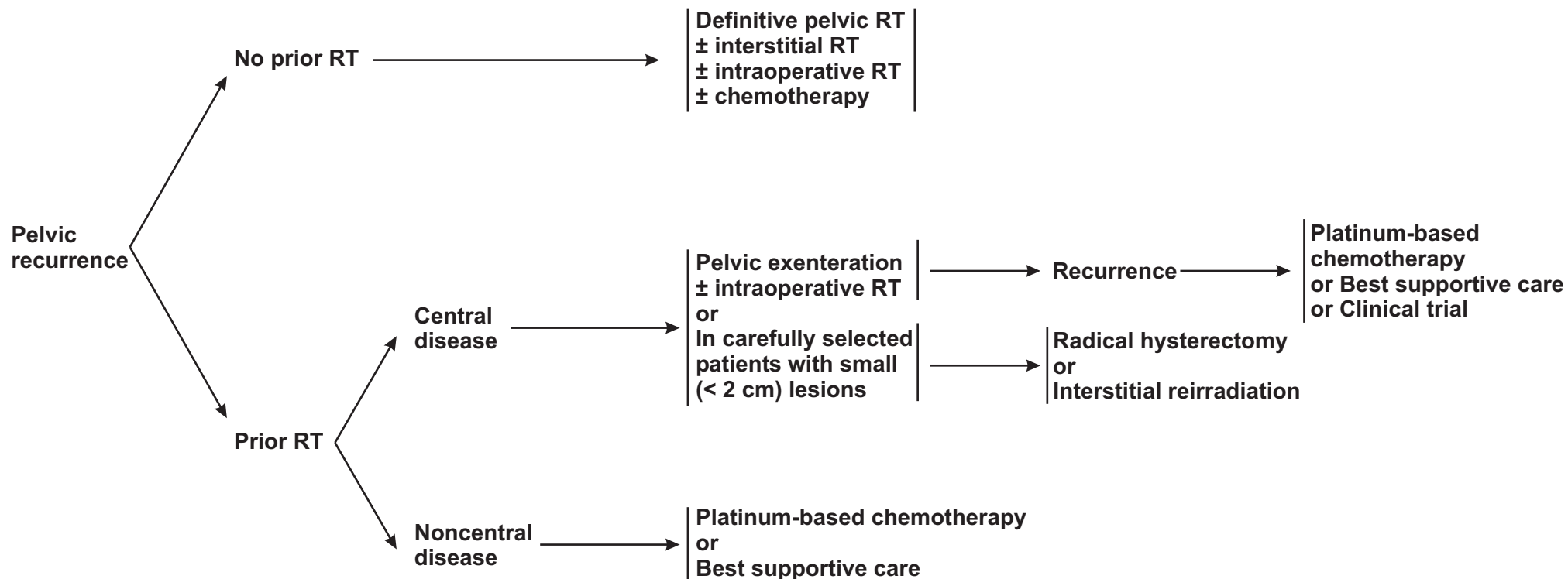
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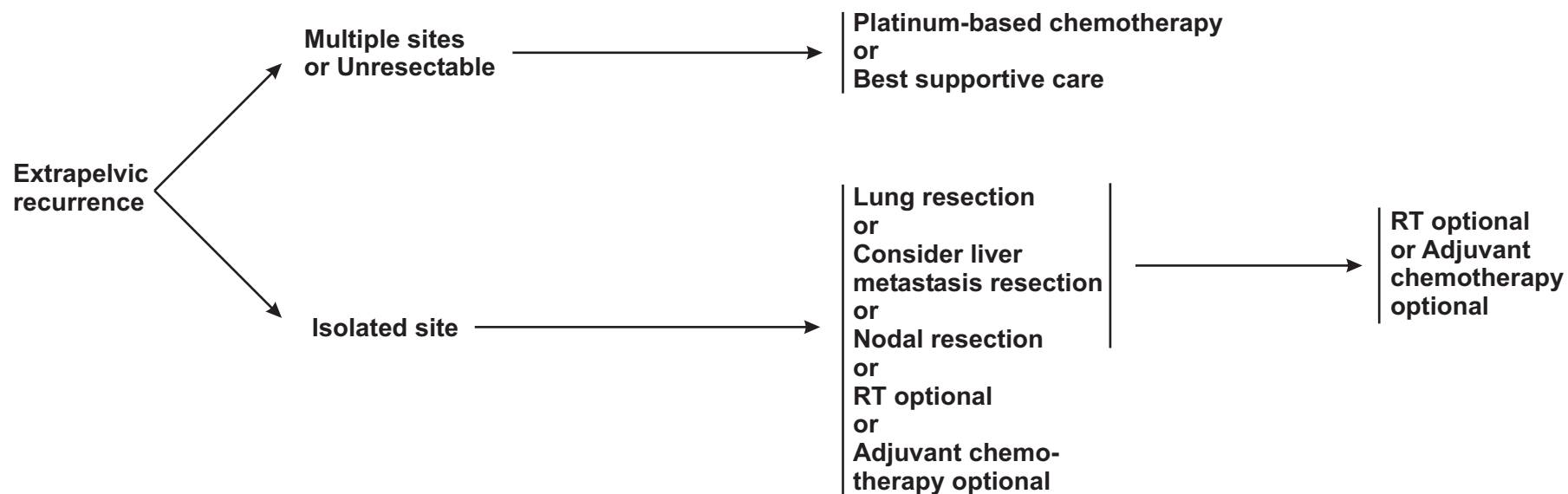
CERV-9

SALVAGE THERAPY

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CERV-10

SALVAGE THERAPY



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Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

CERV-11

Staging

Table 1	
Carcinoma of the Uterine Cervix: FIGO^a Nomenclature (Montreal, 1994)	
Stage 0	Carcinoma in situ, cervical intraepithelial neoplasia grade III.
Stage I	The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded).
IA	Invasive carcinoma that can be diagnosed only by microscopy. All macroscopically visible lesions – even with superficial invasion – are allotted to stage IB carcinomas. Invasion is limited to a measured stromal invasion with a maximal depth of 5.0 mm and a horizontal extension no wider than 7.0 mm. (Depth of invasion should be no greater than 5.0 mm taken from the base of the epithelium of the original tissuesuperficial or glandular. The involvement of vascular spaces – venous or lymphatic – should not change the stage designation.)
IA1	Measured stromal invasion no greater than 3.0 mm in depth and extension no wider than 7.0 mm.
IA2	Measured stromal invasion greater than 3.0 mm and no greater than 5.0 mm with an extension no wider than 7.0 mm.
IB	Clinically visible lesions limited to the cervix uteri or preclinical cancers greater than stage IA.
IB1	Clinically visible lesions no greater than 4.0 cm.
IB2	Clinically visible lesions greater than 4.0 cm.
Stage II	Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina.
IIA	No obvious parametrial involvement.
IIB	Obvious parametrial involvement.
Stage III	The carcinoma has extended to the pelvic wall. On rectal examination, there is no cancer-free space between the tumor and the pelvic wall. The tumor involves the lower third of the vagina. All cases with hydronephrosis or nonfunctioning kidney are included, unless they are due to other causes.
IIIA	Tumor involves lower third of the vagina, with no extension to the pelvic wall.
IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney.
Stage IV	The carcinoma has extended beyond the true pelvis, or has involved the mucosa of the bladder or rectum (biopsy-proven). (A bullous edema, as such, does not permit a case to be designated as stage IV.)
IVA	Spread to adjacent organs.
IVB	Spread to distant organs.

^a International Federation of Gynecology and Obstetrics

Manuscript

NCCN Categories of Consensus

Category 1: There is uniform NCCN consensus, based on high-level evidence, that the recommendation is appropriate.

Category 2A: There is uniform NCCN consensus, based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 2B: There is nonuniform NCCN consensus (but no major disagreement), based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 3: There is major NCCN disagreement that the recommendation is appropriate.

All recommendations are category 2A unless otherwise noted.

Overview

Cervical cancer is more of a problem in developing countries than in the United States. In this country, an estimated 12,900 new cases will be diagnosed in the year 2001, and 4,400 deaths will result from the disease (Greenlee et al, 2001). Cervical cancer is a major world health problem for women. The global yearly incidence of cervical cancer is 371,000, and the annual death rate is 190,000. It is the third most common cancer in women worldwide (Parkin et al, 1999). Most cases (78%) occur in developing countries, where cervical cancer is the second most frequent cause of cancer death.

The substantial decline in mortality, most significantly in developing countries, is thought to be a result of effective screening. Human papillomavirus (HPV) is considered the most important factor contributing to the development of cervical cancer. There appears to

be a relationship between the incidence of cervical cancer and the prevalence of HPV in the population.

The prevalence of HPV in countries with a high incidence of cervical cancer is about 10% to 20%, whereas in low-incidence countries it is 5% to 10% (Parkin et al, 1999). Other epidemiological risk factors associated with cervical cancer are a history of smoking, parity, contraceptive use, early age of onset of coitus, number of sexual partners, and history of sexually transmitted disease.

By definition, the practice guidelines cannot incorporate all possible clinical variations and are not intended to replace good clinical judgment or individualization of patients. There were “many exceptions to the rule” discussed among the members of the Endometrial/Cervical Carcinoma Practice Guidelines Panel during the process of developing these guidelines. A 5% rule (omitting clinical scenarios that comprise less than 5% of all cases) was used to eliminate uncommon clinical occurrences or conditions from cluttering the schema.

Diagnosis and Work-up

This guideline confines itself to squamous cell carcinoma and adenocarcinoma of the cervix. Neuroendocrine small cell tumors, glassy-cell carcinomas, and other histologic types are not within the scope of this guideline.

Early cervical carcinoma is often associated with a watery vaginal discharge and postcoital bleeding or intermittent spotting. These early symptoms frequently go unrecognized by the patient. Because of the accessibility of the uterine cervix to the physician, Pap smears and cervical biopsies can usually result in an accurate diagnosis (see NCCN Practice Guidelines for Cervical Cancer Screening).

Cone biopsy is recommended if the cervical biopsy is inadequate to define invasiveness or if accurate assessment of microinvasive disease is required.

There is debate as to the value of a noninvasive work-up, such as intravenous pyelography (IVP) or lymphangiography, versus computed tomography (CT) or magnetic resonance imaging (MRI). The appropriate stage for performing cystoscopy and/or proctoscopy examination under anesthesia is also a subject of disagreement.

The majority of the panel members agreed that, except for selected bulky stage IB, these procedures should be reserved for stages IB2 or higher. There was some debate regarding the need for laboratory tests, such as liver and renal function tests, and HIV screening. Although these tests are informative, they are not considered necessary for patients during their work-up.

Staging

The use of noninvasive radiographic imaging for cervical cancer staging is also a controversial issue. The International Federation of Gynecology and Obstetrics (FIGO) system limits the imaging methodology to chest x-ray, IVP, and barium enema. The staging of carcinoma of the cervix remains largely a clinical evaluation. The guidelines panel adopted the 1994 FIGO definitions and staging system ([Staging](#)).

Historically, FIGO has made numerous definition changes, mostly in the area of microinvasive carcinoma of the cervix. Currently, the FIGO definition of stage IA is limited to invasive cancer that can be identified only microscopically on pathology. Stage IA1 cancer includes invasive cancer with a measured invasion of the stroma of up to 3.0 mm. Stage IA2 includes invasion of the stroma greater

than 3.0 mm but not more than 5.0 mm. Both stages IA1 and IA2 require a horizontal spread no wider than 7.0 mm.

It is important to note that lymphatic vascular space involvement (LVSI) would not alter the FIGO classification. FIGO did not exclude vascular space involvement because of the difficulty of reproducing LVSI among pathologists. Some panel members felt that the presence of LVSI should exclude the lesion from the treatment schema for stage IA1. Since a provision of extrafascial hysterectomy is available as an option, this guideline did not specifically discuss LVSI in staging considerations.

The use of lymphangiography, MRI, and/or CT scans may aid in treatment planning but is not accepted for staging purposes. In addition, FIGO has always maintained that staging is intended for comparison purposes only and not as a guide for therapy. As a result, although the panel uses the FIGO definitions as the stratification system for this guideline, the findings on imaging studies, such as CT and MRI, are used to substratify treatment options.

Currently, the FIGO surgical procedures for staging are limited to colposcopy, biopsy, conization of the cervix, cystoscopy, and proctosigmoidoscopy. Laparoscopy, hysteroscopy, and retroperitoneal exploration are not accepted. There was considerable discussion among representatives of the different institutions serving on the guideline panel about the inclusion of laparoscopy as part of the guideline in both staging and treatment. The consensus is that while laparoscopic staging, lymphadenectomies, and radical hysterectomies can be performed satisfactorily and are used routinely in selected patients in several member institutions, the techniques are not uniformly used and remain investigational (Chi, 1999).

Primary Treatment

The primary treatment of early-stage cervical cancer following careful clinical evaluation and staging remains either surgery or radiation therapy. The treatment schema is stratified using the FIGO staging system ([Staging](#)). There is general agreement among the representatives of the participating institutions based on the results of five randomized clinical trials that radiation therapy and concurrent cisplatin-based chemotherapy should be the treatment of choice for stage IIB, IIIA, IIIB, and IVA disease (see below). Surgery is reserved for lower-stage disease and smaller lesions.

There was significant discussion about the optimal treatment of bulky stage IB2 and IIA disease. Although FIGO separates IB1 from IB2 tumors at a dividing point of greater than 4.0 cm, some members of the panel felt that, for treatment decisions, 6.0 cm should be the dividing point. The role of retroperitoneal lymph node sampling, which was employed in some but not all of the studies investigating the treatment of this subset of patients, remains unresolved and makes comparisons between studies all the more difficult.

A recent randomized Italian study compared radiation therapy alone versus radical hysterectomy and lymph node dissection (Landoni et al, 1997). This study employed adjuvant radiation therapy after surgery for women with surgical stage pT2b (which corresponds to FIGO stage IIB) or more extensive disease, 3 mm or more of safe cervical stroma, and cut-through or positive nodes. Identical outcomes were noted for patients treated with radiation versus surgery, with or without postoperative radiation, but higher complication rates were noted for the combined modality approach. This study has been criticized by surgeons for its broad use of postoperative radiation therapy in the surgery arm and the high complication rate.

The Gynecological Oncology Group (GOG) Study 71 compared radiation therapy alone with radiation therapy (with the dose to point A reduced to 75 Gy) followed by a simple hysterectomy. The preliminary results of this investigation demonstrated an improvement in disease-free survival for the patients who underwent hysterectomy, but the final results are pending.

Radiation Therapy Oncology Group (RTOG) Trial 79-20 compared pelvic versus pelvic and para-aortic nodal radiation in patients with stage IB or stage IIA disease who had tumors measuring at least 4 cm in diameter, or patients who had stage IIB disease. The para-aortic nodal status was either unknown or negative, based upon radiological studies on these patients. The 10-year survival rate for the pelvic plus para-aortic treatment arm was 55%, compared with 44% for the pelvic radiation alone treatment arm ($p = .02$) (Rotman et al, 1995).

A neoadjuvant chemotherapy trial comparing chemotherapy followed by radical hysterectomy and lymph node dissection versus radical hysterectomy and lymph node dissection is currently in progress (GOG-141).

Use of Radiation Therapy

In developing guideline recommendations for radiation therapy, the panel elected to include dosage as a reference in the schema, but realized that, in order to be complete, other aspects of radiation therapy techniques would be necessary. These dosages should not be interpreted as stand-alone recommendations; other considerations of radiation therapy techniques and clinical judgment are paramount.

The external-beam doses represent the range of doses employing conventionally fractionated regimens of treatments. The

brachytherapy doses are used for low-dose-rate applications (40 to 60 cGy/h), with doses to point A added to the external-beam doses to permit treatments to be compared. These doses may be modified for individual patients to provide adequate tumor coverage and to take into account normal tissue tolerances.

Considerable refinement in external-beam radiation therapy and brachytherapy techniques, as well as a better understanding of the influence of overall treatment time on outcome, has occurred over the past decade. Optimum staging of patients to precisely delineate the primary tumor volume and draining lymph nodes, including abdominopelvic radiological studies (CT or MRI scans), should be considered in patients with bulky or advanced-stage tumors.

Planning Treatment Fields

The use of three-dimensional treatment planning for both the external-beam radiation therapy fields and the brachytherapy placements may assist in customized shaping of dose distributions to ensure adequate tumor coverage in all dimensions and minimal normal tissue exposure. The anterior field margins should include, where indicated, possible extensions of the tumor into the body of the uterus. The posterior field margins should include tumor extension into the uterosacral ligament and presacral lymph nodes. Lateral field margins need to adequately include the pelvic lymph nodes.

For lesions in the lower third of the vagina, the inguinal lymph nodes need to be treated. The use of extended-field radiation to treat occult or macroscopic para-aortic lymph node disease needs to be carefully planned to ensure adequate dose (45 Gy for microscopic disease) without exceeding bowel, spinal cord, or renal tolerances. Intracavitary or interstitial brachytherapy techniques have proven to

be a vital component of treatment of invasive cervical tumors. This is particularly true for more advanced stages of disease.

Initial radiation treatment of 40 Gy to the whole pelvis is often necessary to obtain tumor shrinkage to permit optimal intracavitary placements. With low-dose-rate intracavitary systems, total doses from brachytherapy and external-beam radiation to point A of at least 80 Gy are currently recommended for small tumors, with doses of at least 85 Gy recommended for larger tumors.

Minimizing Tissue Damage

Adjustments need to be made to minimize radiation doses to normal surrounding tissues (eg, bladder, rectum, and sigmoid colon). Coned-down shaped boost fields should be employed to involved pelvic lymph nodes and areas of parametrial extension. These regions should be treated with total doses of 60 to 65 Gy. Individualized central blocking techniques should be used to shield from the intracavitary placements those portions of the small bowel, rectum, and bladder that had been included in the high-dose regions. Similar considerations apply to high-dose-rate intracavitary systems, where a wide range of treatment regimens has been employed (generally using between three and six fractions, with doses usually between 5 and 10 Gy per fraction). Dose modifications need to be considered for patients who will undergo hysterectomy or for postoperative treatment.

Several, but not all, retrospective analyses have suggested an adverse effect of prolonged treatment duration on outcome. Extending the overall treatment beyond 6 to 8 weeks can result in approximately a 0.5% to 1% diminution in pelvic control and cause-specific survival for each extra day of overall treatment time. Even though prospective randomized trials confirming these findings are lacking, it would be

prudent to attempt to complete the entire radiation therapy course in a timely fashion (eg, less than 8 weeks) and avoid, whenever possible, delays or splits in the radiation treatment.

Concurrent Chemoradiation

As this practice guideline was developed, five additional randomized trials have matured that demonstrated the statistically significant benefit of concurrent cisplatin-containing chemotherapy regimens with radiation in the treatment of advanced cervical cancers ([Table 2](#)).

Intergroup Trial INT-0107 (SWOG-8797) investigated the value of postoperative pelvic radiation therapy with or without 5-fluorouracil (5-FU) and cisplatin for the treatment of stage IA2, IB, and IIA cervical cancer with positive lymph nodes, and/or positive margins, and/or microscopic parametrial involvement at the time of surgery (Peters et al, 1999a). The 4-year progression-free survival was significantly improved with the use of radiation plus chemotherapy, compared with radiation therapy alone (81% vs. 63%, respectively; $p = .01$). The relative risk of death was reduced by 50% for the group receiving adjuvant 5-FU and cisplatin in conjunction with radiation.

GOG Trial 123 studied the use of cisplatin as an adjunct to radiation therapy in patients who subsequently underwent extrafascial hysterectomies. The study included patients with bulky stage IB tumors that were ≥ 4 cm or more in diameter or barrel-shaped in configuration. The 3-year survival rates were 83% for the radiation plus cisplatin plus hysterectomy group, compared with 74% for the radiation plus hysterectomy group. The addition of cisplatin resulted in a relative risk of death of 0.54 (Keys et al, 1999).

GOG Trial 120 investigated the use of standard pelvic radiation with one of three concurrent chemotherapy regimens: cisplatin alone, hydroxyurea alone, or cisplatin plus 5-FU plus hydroxyurea in patients with stage IIB, III, or IVA cancer and negative para-aortic lymph nodes. The 3-year survival rate in both cisplatin-containing treatment arms was 65%, compared with 47% for the pelvic radiation plus hydroxyurea treatment group. The relative risk of death was 0.61 for pelvic radiation plus cisplatin, and 0.58 for cisplatin plus 5-FU plus hydroxyurea plus pelvic radiation, compared with patients treated with pelvic radiation plus hydroxyurea alone (Rose et al, 1999).

RTOG Trial 9001 compared pelvic plus para-aortic radiation to pelvic radiation plus 5-FU plus cisplatin treatment in patients with stage IIB through stage IVA cervical cancer and in patients with stage IB or stage IIA disease with tumors ≥ 5 cm or larger or with metastases to the pelvic lymph nodes. The 5-year survival rate for the cisplatin treatment arm was 73%, compared with 58% for patients treated with pelvic plus para-aortic radiation ($p = .004$). The addition of chemotherapy resulted in a relative risk of death of 0.59 (Morris et al, 1999).

The final study, which demonstrated a significant benefit for the concurrent use of cisplatin-based chemotherapy, was GOG Trial 85 (Whitney et al, 1999). Patients enrolled in this study had stage IIB through stage IVA cervical cancer with surgically staged negative para-aortic lymph nodes. These patients were randomized between pelvic radiation with concurrent hydroxyurea or pelvic radiation with cisplatin plus 5-FU. A statistically significant improvement in the 3-year survival rate was noted for the cisplatin-containing regimen (67% vs. 57%), resulting in a relative risk of death of 0.74.

These five trials have demonstrated that the use of concurrent cisplatin-based chemoradiation therapy results in a decreased risk of death of 30% to 50%. Although the determination of the optimum chemotherapy to be used with concurrent radiation will require further investigation, it appears that cisplatin-containing regimens or cisplatin alone should now be considered as part of the standard treatment regimen in patients with locally advanced cervical cancer.

Adjuvant Treatment After Radical Hysterectomy

As previously noted, Intergroup Trial 0107 showed a statistically significant benefit of adjuvant pelvic radiation with 5-FU and cisplatin in the treatment of stage IA2, IB, and IIA patients who had positive lymph nodes, positive margins, or microscopic parametrial involvement found at surgery (Peters et al, 1999a). In addition, adjuvant pelvic radiation therapy alone versus no further therapy was tested in a randomized trial (GOG 92) of selected patients with stage IB carcinoma of the cervix after hysterectomy and pelvic lymphadenectomy (Sedis et al, 1999). Patients were eligible for this trial following radical hysterectomy and pelvic lymphadenectomy if they had at least two of the following risk factors: (1) greater than one-third stromal invasion; (2) capillary lymphatic space involvement; or (3) large cervical tumor diameters.

Patients with positive lymph nodes or involved surgical margins were excluded. There was a statistically significant diminution in recurrence in the radiation therapy arm compared with the no additional treatment arm (15% vs. 28%). Life-table analysis indicated a statistically significant (47%) reduction in risk of recurrence (relative risk = 0.53; $p = .008$) in the radiation therapy group. At 2 years, the recurrence-free rates were 88% for the radiation therapy group versus 79% for the no further treatment group.

Surveillance

Because there is no definitive study or uniform agreement on the best methodology for posttreatment surveillance for cervical cancer, the practice guidelines panel combined the practice patterns of member institutions and issued consensus recommendations. Many of the tests remain optional, such as semiannual complete blood counts, blood urea nitrogen, and serum creatinine determinations, chest x-rays, and annual CT scans for advanced-stage patients.

Salvage Therapy

Patients with a localized recurrence of cervical cancer following surgery should be evaluated for salvage radiotherapy. Salvage rates of approximately 40% have been reported in such situations (Thomas et al, 1993). Patients with local pelvic recurrences following radiation therapy should be evaluated for pelvic exenteration, with or without intraoperative radiotherapy, (or, in carefully selected patients with small lesions, radical hysterectomy or interstitial reirradiation). Operative mortality is generally 5% or lower, with survival rates between 20% and 60%. Concomitant measures with such radical procedures include adequate rehabilitation programs dealing with the psychosocial and psychosexual consequences of the operation (Averette et al, 1984; Morley, 1984) and reconstructive procedures. Patients with isolated pulmonary, liver, or nodal recurrences may benefit from surgical resection. Patients with incidental findings of invasive cancer as a result of a simple hysterectomy may benefit from radiation therapy and vaginal brachytherapy.

The palliation of pelvic recurrences in heavily irradiated sites that are not amenable to local pain control technique or surgical resection is an unresolved clinical issue. Such sites are generally not responsive to chemotherapy. It remains a clinical challenge as to

how to adequately palliate the complications of pain and fistulae from such recurrences.

Occasionally, patients may benefit from radiotherapy to localized recurrences of disease. Generally, these areas would be supraclavicular, bone metastases, or painful periaortic nodal recurrences. Chemotherapy has a limited role in prolonging survival or improving quality of life. Clearly, pain relief of a transient nature may be achieved in responders to chemotherapy. The efficacy of combination therapy versus single-agent therapy in the treatment of metastatic disease has not been proven.

Cisplatin is generally considered to be the most active drug. Response rates are approximately 20% to 30%, with an occasional complete response. Carboplatin has also been reported to have a 19% response rate. Other drugs with reported positive response rates include ifosfamide, epirubicin, and vindesine. The use of combination chemotherapy in patients who have had primary treatment with surgery or radiotherapy is associated in some studies with a higher response rate. Durations of response are usually 3 to 6 months, and median survival remains around 1 year. Palliation with single-agent cisplatin or carboplatin is a reasonable approach in patients with recurrent disease not amenable to surgical or

radiotherapeutic approaches. Biologic molecular and vaccine therapies have no established role at the present time (Vermorken, 1993; Lopez et al, 1996).

Patients with refractory systemic cancer warrant a comprehensive coordinated approach involving hospice care, pain consultants, and emotional/spiritual support, suited to the individual situation.

Incidental Cervical Cancer

A clinical scenario requiring oncologic management is the finding of invasive cervical carcinoma following simple hysterectomy. No definitive data exists regarding the appropriate follow-up treatment of these patients. The panel felt that a reasonable treatment schema for patients with tumors that were stage 1A2 or higher was based on the status of the margins. If margins were positive, pelvic RT plus brachytherapy would be recommended.

If margins are negative, options include pelvic RT or a complete parametrectomy with a lymph node dissection. If disease is found in the lymph nodes, parametrium, or vaginal margin, RT with cisplatin chemotherapy is recommended. If no residual disease is found, observation or RT may be employed.

Table 2:**Estimates of the Relative Risk of Death in Five Clinical Trials of Concurrent Chemotherapy and Radiotherapy.**

Study	FIGO Stage*	Treatment	
		Control Group	Comparison Group
Keys et al.	IB2	Radiotherapy	Radiotherapy plus weekly cisplatin Radiotherapy plus cisplatin, fluorouracil, and hydroxyurea
Rose et al.	IIB-IVA	Radiotherapy plus Hydroxyurea	
Morris et al.	IB2-IVA	Extended-field radiotherapy	Radiotherapy plus cisplatin and fluorouracil
Whitney et al.	IIB-IVA	Radiotherapy plus hydroxyurea	Radiotherapy plus cisplatin and fluorouracil
Peters et al.	IB or IIA (selected postoperatively)	Radiotherapy	Radiotherapy plus cisplatin and fluorouracil

*FIGO denotes the International Federation of Gynecology and Obstetrics

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