

Uterine Cancers

Version 1.2003

Continue

NCCN Endometrial Cancer and Uterine Sarcoma Panel Members

* Nelson Teng, MD, PhD/Chair
Stanford Hospital and Clinics

Nadeem Abu-Rustum, MD
Memorial Sloan-Kettering Cancer
Center

Michael A. Bookman, MD
Fox Chase Cancer Center

Susana Campos, MD
Dana-Farber/Partners CancerCare

Kathleen R. Cho, MD
University of Michigan Comprehensive
Cancer Center

Larry Copeland, MD
Arthur G. James Cancer Hospital &
Richard J. Solove Research Institute
at The Ohio State University

Patricia Eifel, MD
The University of Texas M. D.
Anderson Cancer Center

*Writing Committee Member

James Fiorica, MD
H. Lee Moffitt Cancer Center & Research
Institute at the University of South Florida

Benjamin E. Greer, MD
Fred Hutchinson Cancer Research
Center/Seattle Cancer Care Alliance

Daniel S. Kapp, MD, PhD
Stanford Hospital and Clinics

John Kavanagh, MD
The University of Texas M. D. Anderson
Cancer Center

Wui-Jin Koh, MD
Fred Hutchinson Cancer Research
Center/Seattle Cancer Care Alliance

Michael Kuettel, MD, PhD, MBA
Roswell Park Cancer Center

Paul Lin, MD
City of Hope Cancer Center

John R. Lurain, MD
Robert H. Lurie Comprehensive Cancer
Center of Northwestern University

Kelly Molpus, MD
UNMC Eppley Cancer Center at The
Nebraska Medical Center

Subir Nag, MD
Arthur G. James Cancer Hospital &
Richard J. Solove Research Institute at
The Ohio State University

Edward E. Partridge, MD
University of Alabama at Birmingham
Comprehensive Cancer Center

C. Bethan Powell, MD
UCSF Comprehensive Cancer Center

R. Kevin Reynolds, MD
University of Michigan Comprehensive
Cancer Center

William Small, Jr., MD
Robert H. Lurie Comprehensive Cancer
Center of Northwestern University

John Soper, MD
Duke Comprehensive Cancer Center

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

To find clinical trials online at NCCN member institutions, [click here:
nccn.org/clinical_trials/physician.html](#)

NCCN Categories of Consensus: All recommendations are Category 2A unless otherwise specified.

See [NCCN Categories of Consensus](#)

These guidelines are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no representations nor warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way. These guidelines are copyrighted by National Comprehensive Cancer Network. All rights reserved. These guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN. ©2004.

INITIAL
EVALUATION

- H&P
- CBC, platelets
- Endometrial biopsy
- Chest x-ray
- Current cervical pathology/PAP smear consistent with [NCCN Cervical Screening Guidelines](#)

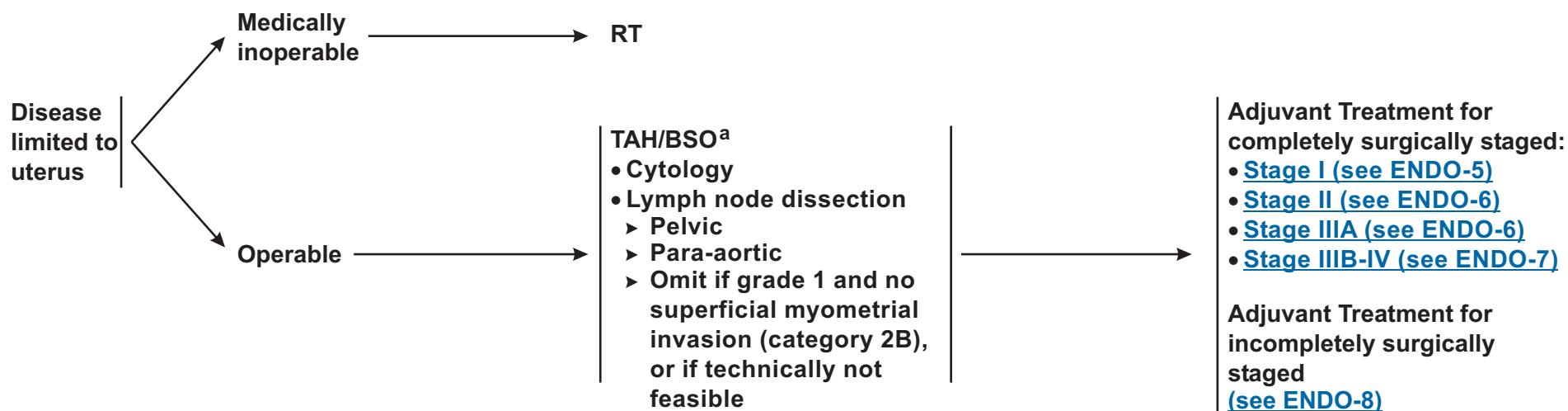
Optional:

- LFT/renal function tests/chemistry profile

INITIAL CLINICAL
FINDINGSPathology
reviewOther
endometrial
cancer
histologiesPapillary
serous or
clear cell
carcinomaDisease
limited to
uterusSuspected
or gross
cervical
involvementSuspected
extrauterine
disease[Primary Treatment
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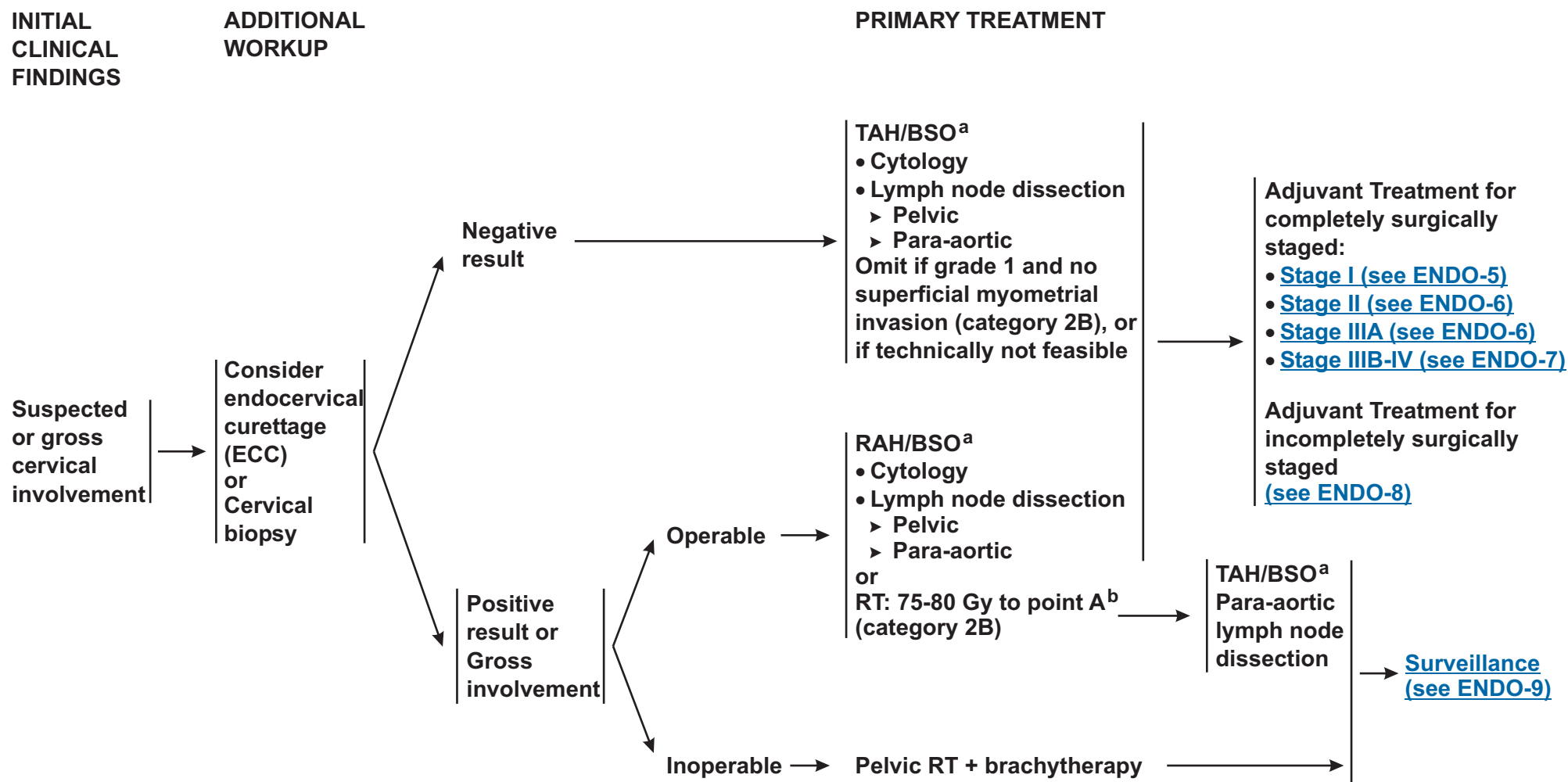
INITIAL CLINICAL
FINDINGSPRIMARY
TREATMENT

[Surveillance](#)
([see ENDO-9](#))

^a[See Hysterectomy \(ENDO-A\).](#)

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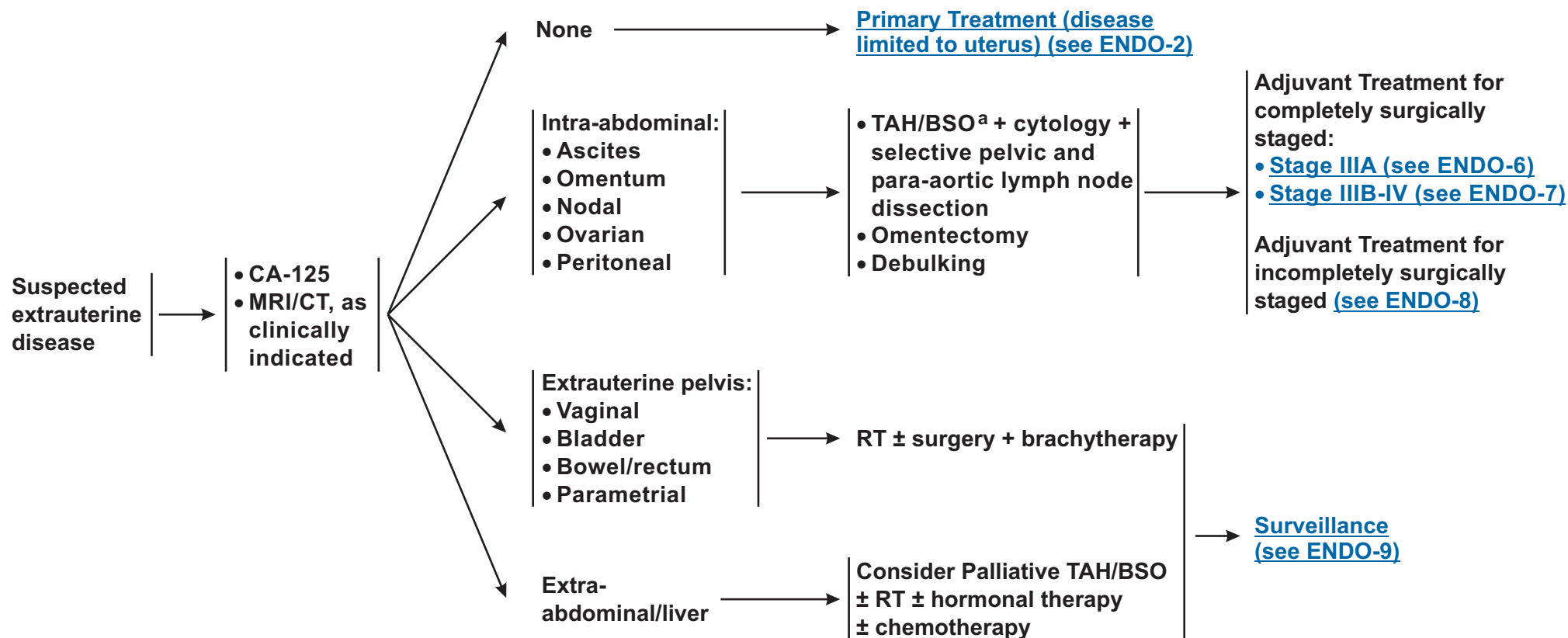
^a[See Hysterectomy \(ENDO-A\).](#)^bBased on summation of conventional external-beam fractionation and low-dose-rate brachytherapy equivalent.

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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.

INITIAL
CLINICAL
FINDINGSADDITIONAL
WORKUP

PRIMARY TREATMENT

^a[See Hysterectomy \(ENDO-A\).](#)**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.

CLINICAL FINDINGS

ADVERSE RISK
FACTORS^cHISTOLOGIC GRADE/ADJUVANT TREATMENT^{d,e}

G1

G2

G3

Adjuvant treatment for completely surgically staged: Stage I	Stage IA	Adverse risk factors not present	→	Observe	Observe	Observe or Vaginal brachytherapy
		Adverse risk factors present	→	Observe	Observe	Pelvic RT and/or vaginal brachytherapy (category 2B) ^f
	Stage IB (< 50%)	Adverse risk factors not present	→	Observe	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy
		Adverse risk factors present	→	Observe or Vaginal brachytherapy	Pelvic RT and/or vaginal brachytherapy (category 2B) ^f	Pelvic RT and/or vaginal brachytherapy (category 2B) ^f
	Stage IC	Adverse risk factors not present	→	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy	Pelvic RT and/or vaginal brachytherapy (category 2B) ^f
		Adverse risk factors present	→	Pelvic RT and/or vaginal brachytherapy (category 2B) ^f	Pelvic RT and/or vaginal brachytherapy (category 2B) ^f	Pelvic RT and/or vaginal brachytherapy (category 2B) ^f

^cAdverse risk factors include the following: advanced age, lymphovascular invasion, tumor size, depth of invasion, involvement of outer third of uterus.^dAdjuvant therapy determinations are made on the basis of pathologic findings.^eAdjuvant pelvic RT: 45-50 Gy.^fSome institutions will not consider pelvic RT for completely staged, stage I disease.[Surveillance](#)
(see ENDO-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.

CLINICAL FINDINGS

HISTOLOGIC GRADE/ADJUVANT TREATMENT^{d,e}

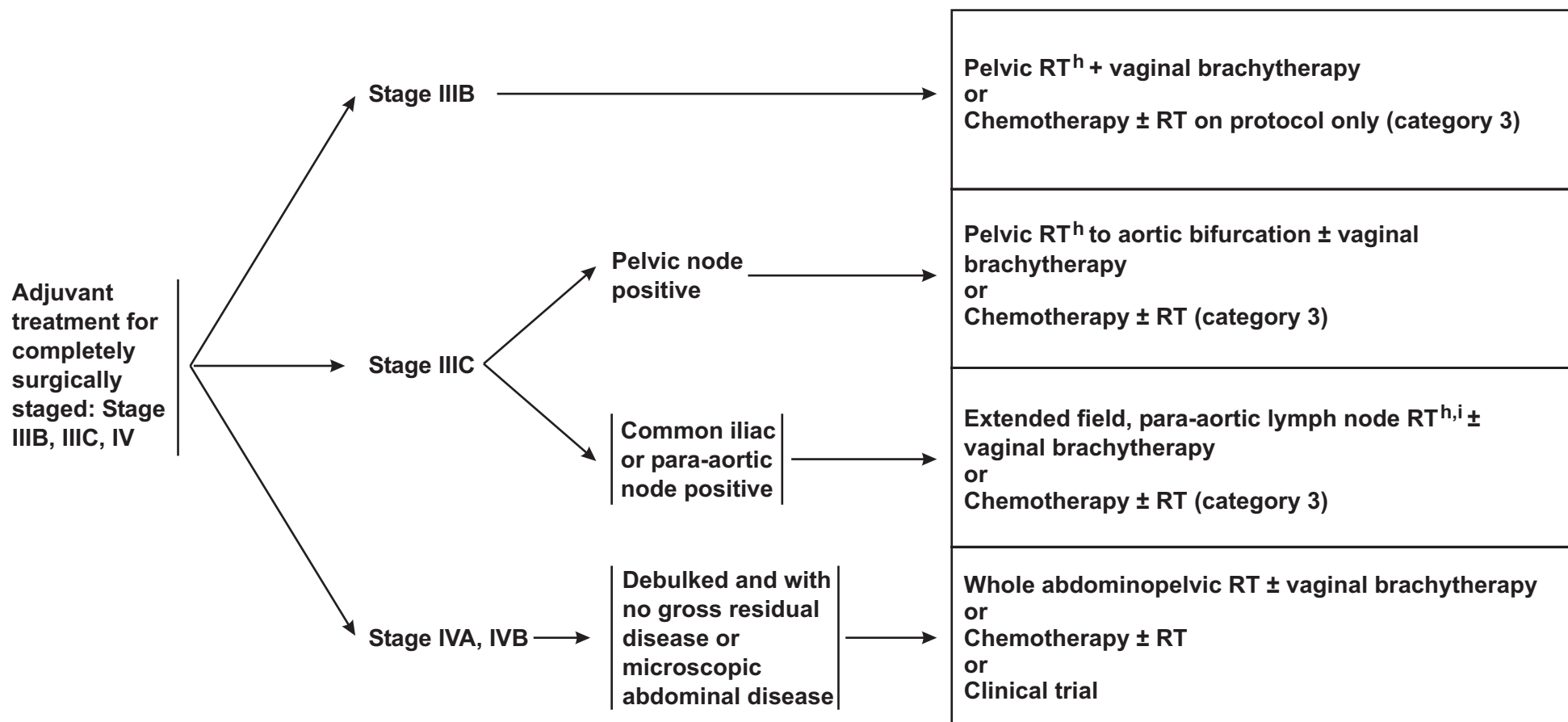
		G1	G2	G3
Adjuvant treatment for completely surgically staged: Stage II	Stage IIA	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy or Pelvic RT ± vaginal brachytherapy	Vaginal brachytherapy ± pelvic RT
	Myometrial invasion < 50%			
Adjuvant treatment for completely surgically staged: Stage IIIA	Myometrial invasion > 50%	Vaginal brachytherapy ± pelvic RT	Vaginal brachytherapy ± pelvic RT	Pelvic RT + vaginal brachytherapy
	Stage IIB ^g	Pelvic RT + vaginal brachytherapy	Pelvic RT + vaginal brachytherapy	Pelvic RT + vaginal brachytherapy
Adjuvant treatment for completely surgically staged: Stage IIIA	Positive cytology only, noninvasive tumor confined to fundus	Observe	Observe	Observe or Vaginal brachytherapy or Pelvic RT ± vaginal brachytherapy
	All other IIIA	Pelvic RT ± vaginal brachytherapy or Whole abdominopelvic RT (category 2B) ± vaginal brachytherapy or Chemotherapy ± RT (category 3)	Pelvic RT ± vaginal brachytherapy or Whole abdominopelvic RT ± vaginal brachytherapy or Chemotherapy ± RT (category 3)	Pelvic RT ± vaginal brachytherapy or Whole abdominopelvic RT ± vaginal brachytherapy or Chemotherapy ± RT (category 3)

^dAdjuvant therapy determinations are made on the basis of pathologic findings.^eAdjuvant pelvic RT: 45-50 Gy.^gObservation or vaginal brachytherapy is an option for patients with Stage IIB disease who are postprimary radical hysterectomy, with negative surgical margins and no evidence of extrauterine disease.[Surveillance](#)
(see ENDO-9)

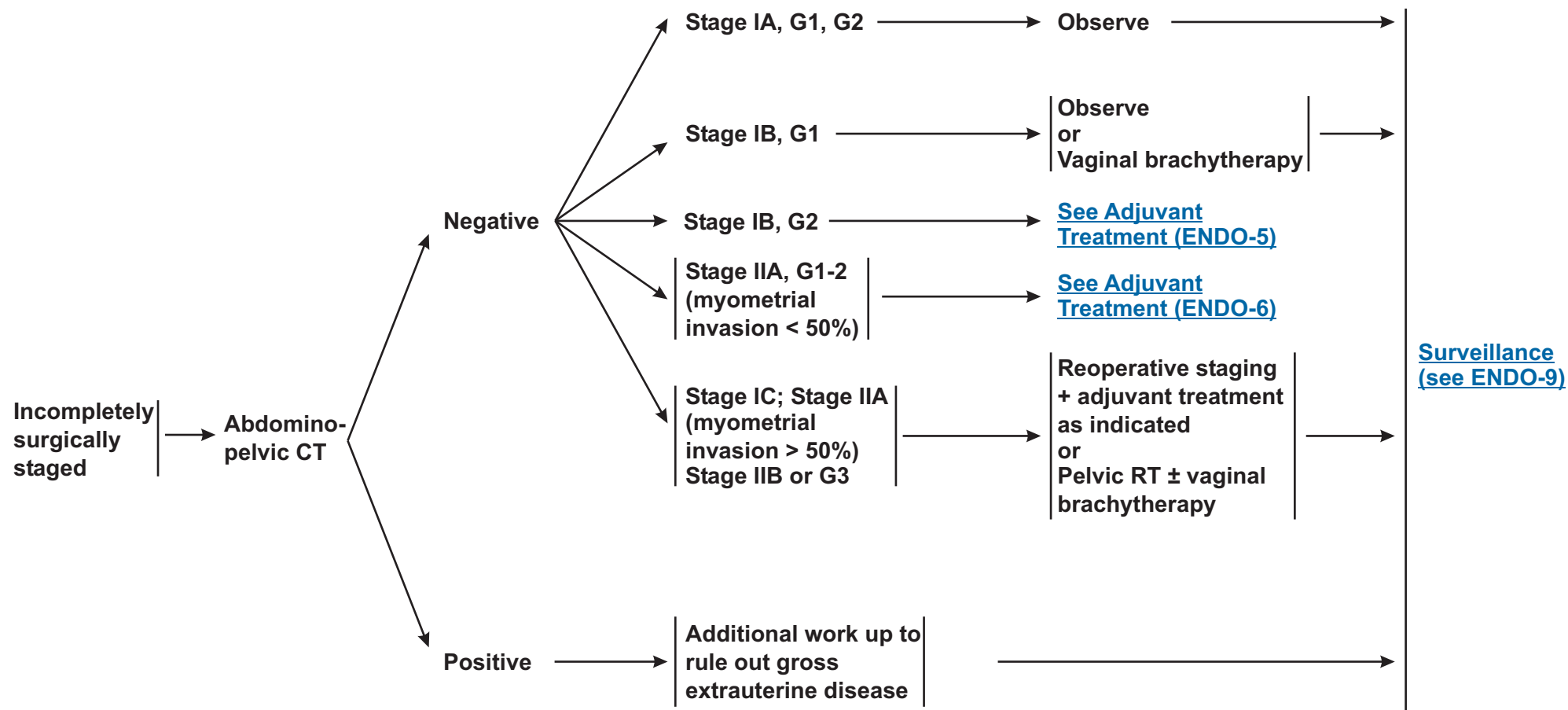
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CLINICAL FINDINGS

HISTOLOGIC GRADE/ADJUVANT TREATMENT^d
G1, G2, G3^dAdjuvant therapy determinations are made on the basis of pathologic findings.^hOptional whole abdominopelvic RT for adnexa involvement and/or positive cytology.ⁱRT to para-aortic nodes: 45-50 Gy.[Surveillance](#)
(see ENDO-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.

CLINICAL FINDINGS

ADJUVANT TREATMENT^d

^dAdjuvant therapy determinations are made on the basis of pathologic findings.

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SURVEILLANCE

- Physical exam every 3-6 mo for 2 y, then 6 mo or annually
- CA-125 if initially elevated, then at each visit
- Chest x-ray annually (category 2B)
- Vaginal cytology every 6 mo for 2 y, then annually
- If low risk, surgery alone:
 - Consider immediate hormone replacement therapy^j
 - If adjuvant treatment, wait 6-12 mo, then hormone replacement therapy
- Patient education regarding symptoms

CLINICAL PRESENTATION

Local recurrence

- Vagina
- Negative chest x-ray
- Negative chest, abdominal CT

Isolated metastases

Disseminated metastases

Resectable

Unresectable

Asymptomatic or Low grade

Symptomatic or Grade 2, 3 or Large volume

SALVAGE THERAPY

[Salvage Therapy \(see ENDO-10\)](#)

Consider resection ± RT

Recurrence

Treat as disseminated metastases (See below)

Treat as disseminated metastases (See below)

Hormonal therapy^k

If progression, chemotherapy^k

If progression, Best supportive care
(See [NCCN Palliative Care Guidelines](#))
or
Clinical trial

Chemotherapy and/or RT for symptom relief

If 2 chemotherapy regimens fail: Best supportive care
(See [NCCN Palliative Care Guidelines](#))
or
Clinical trial

^jHormone replacement therapy following treatment for endometrial cancer should be limited to clinical trial participation because of the limited literature documentation regarding its safety.

^k[For hormonal therapy and chemotherapy regimens, see Salvage Therapy \(ENDO-B\)](#)

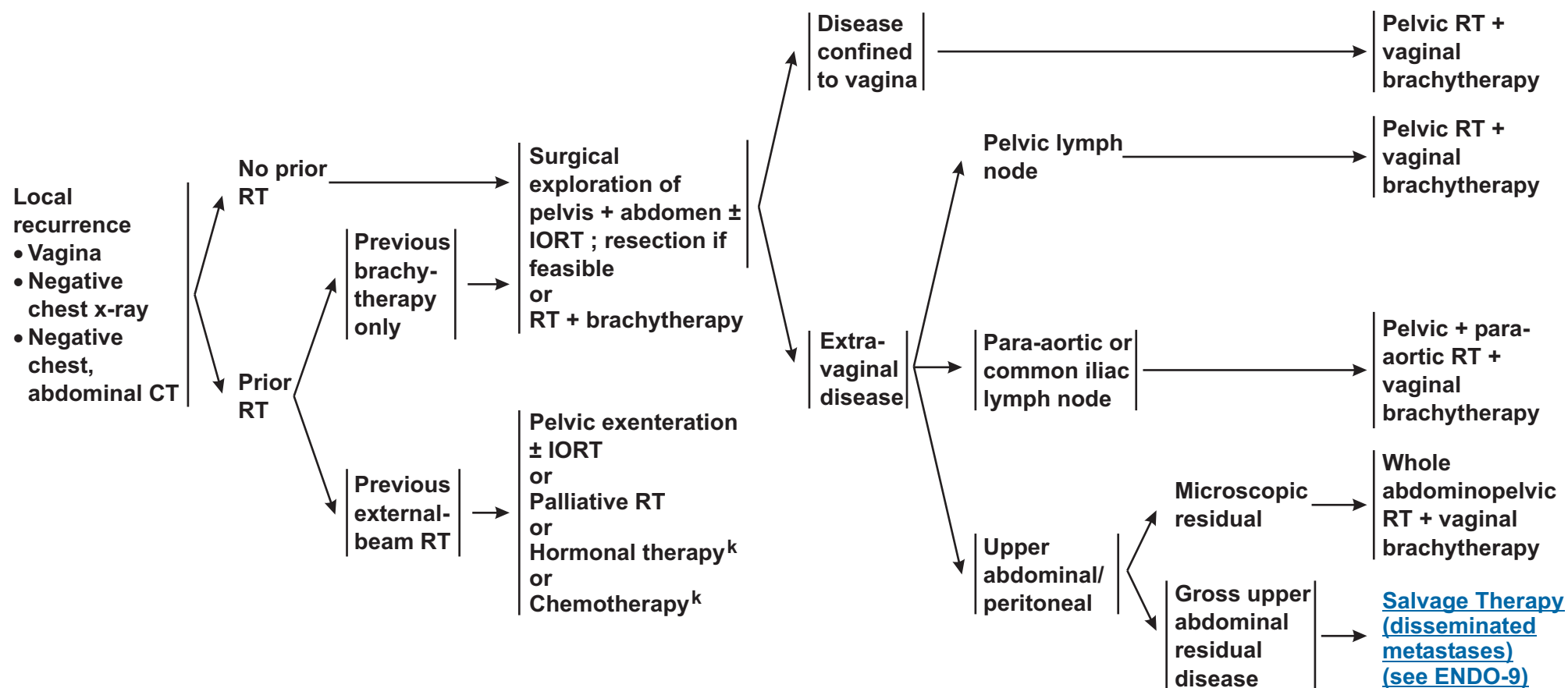
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CLINICAL PRESENTATION

SALVAGE THERAPY

ADDITIONAL
THERAPY^k[For hormonal therapy and chemotherapy regimens, see Salvage Therapy \(ENDO-B\)](#)

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

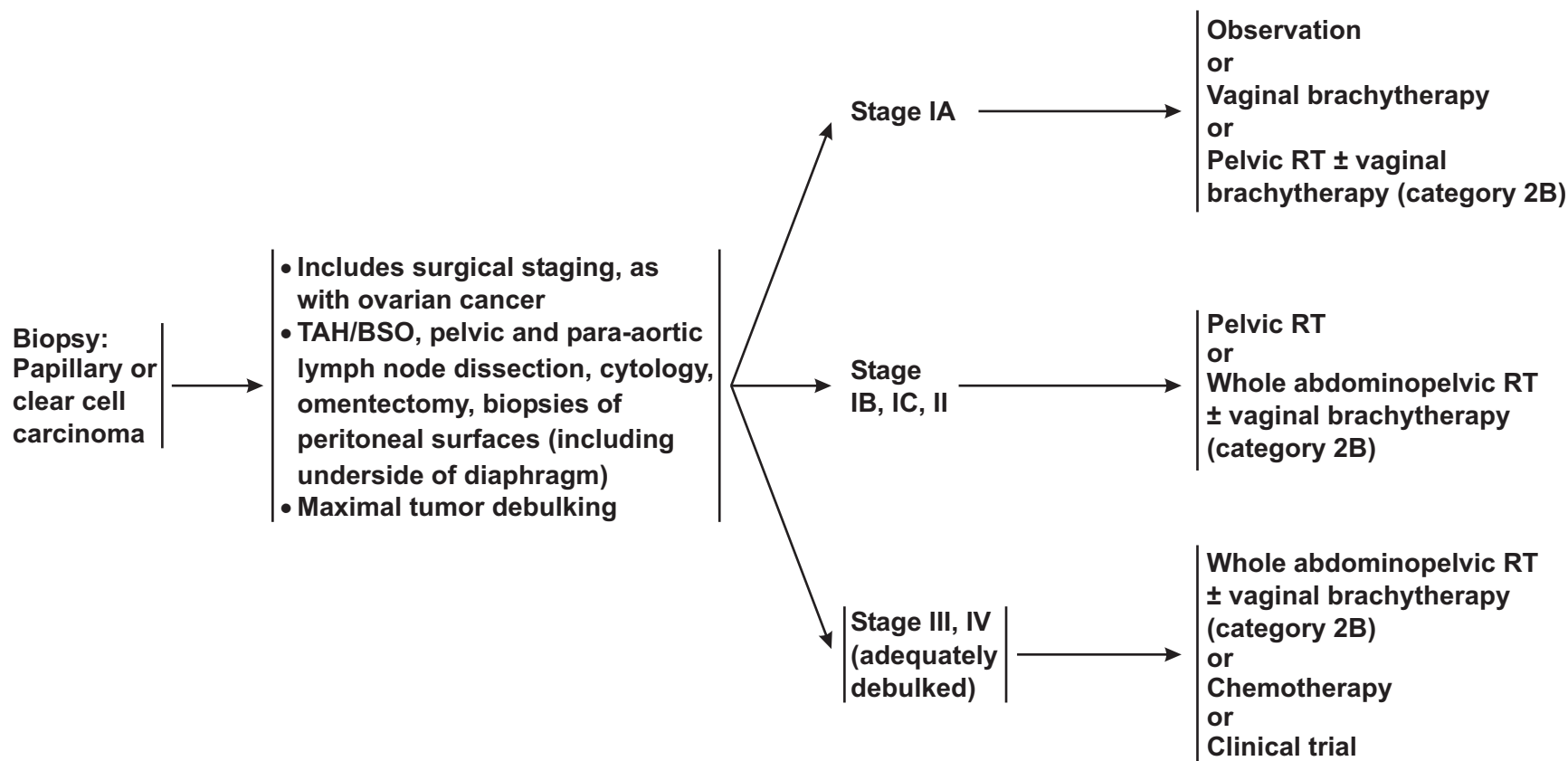
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PAPILLARY SEROUS OR CLEAR CELL CARCINOMA OF THE ENDOMETRIUM

PRIMARY TREATMENT

ADJUVANT TREATMENT



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HYSTERECTOMY

**TAH/BSO: Total abdominal hysterectomy +
bilateral salpingo-oophorectomy**

RAH: Radical abdominal hysterectomy

**1. Laparoscopy-assisted vaginal hysterectomy
should be performed in the context of a clinical
trial**

2. Operative assessment to include:

- **Depth of myometrial invasion**
- **Tumor size**
- **Tumor location (fundus vs lower uterine
segment/cervix)**
- **Frozen section as indicated**

[Back to Initial Evaluation
\(ENDO-1\)](#)

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SALVAGE THERAPY**HORMONAL THERAPY**

- Progestational agents
- Tamoxifen

CHEMOTHERAPY REGIMENS

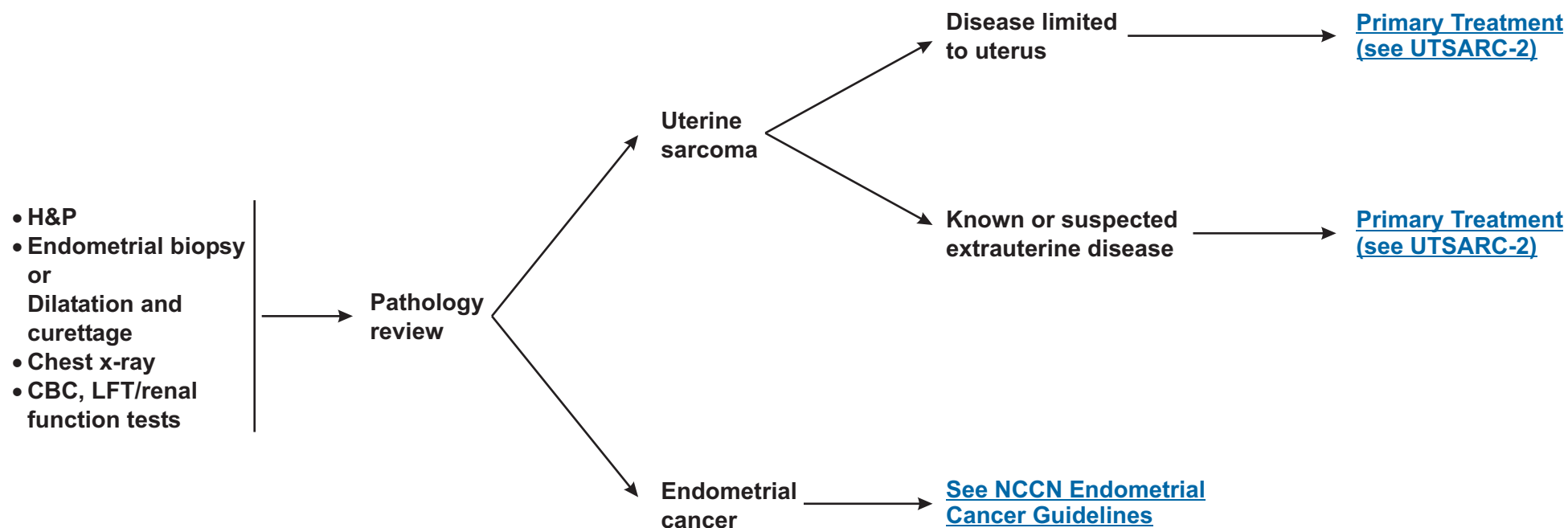
- Doxorubicin
- Cisplatin
- Cisplatin/doxorubicin ± cyclophosphamide
- Carboplatin
- Paclitaxel
- Strongly encourage clinical trials

[Back to Salvage Therapy \(ENDO-9\)](#)

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INITIAL EVALUATION

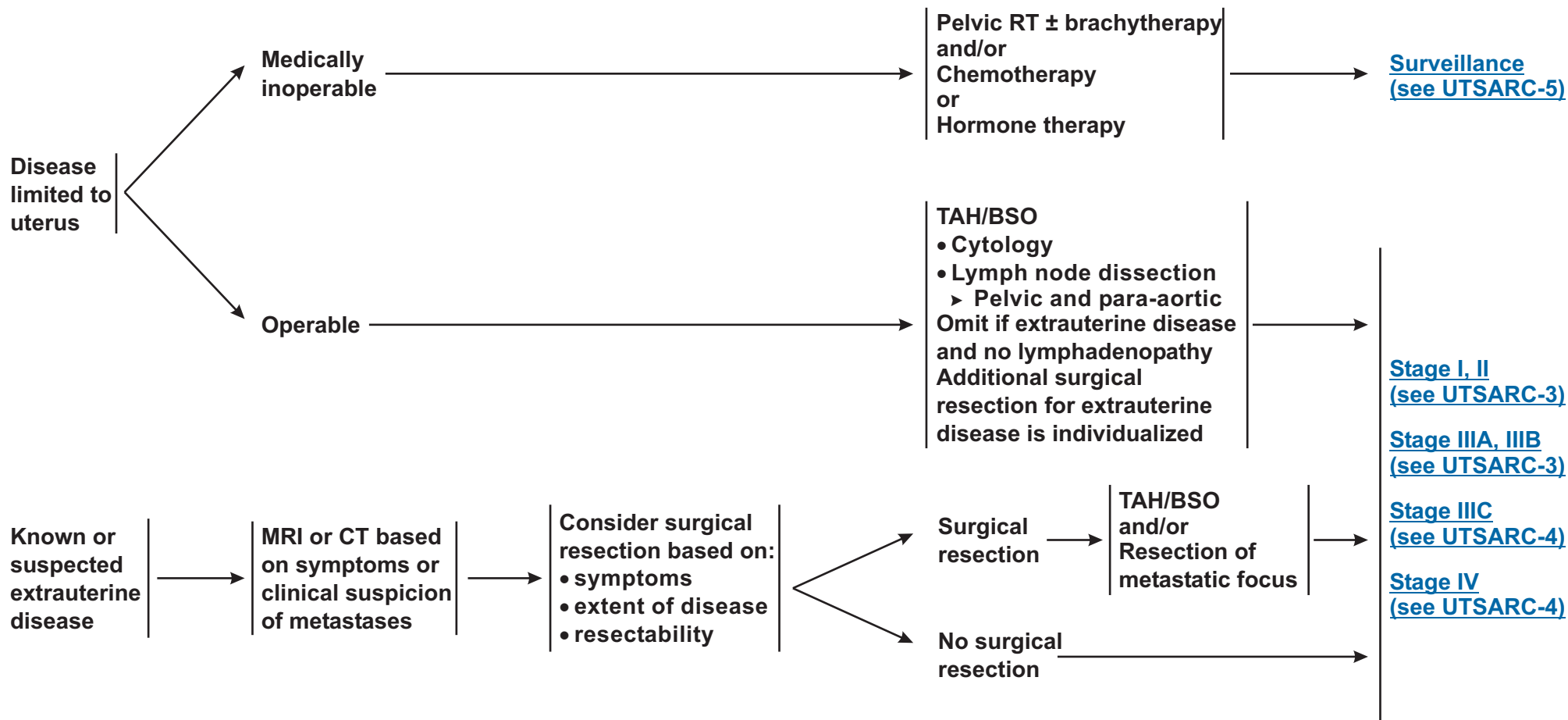
INITIAL CLINICAL
FINDINGS

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INITIAL CLINICAL FINDINGS

PRIMARY TREATMENT

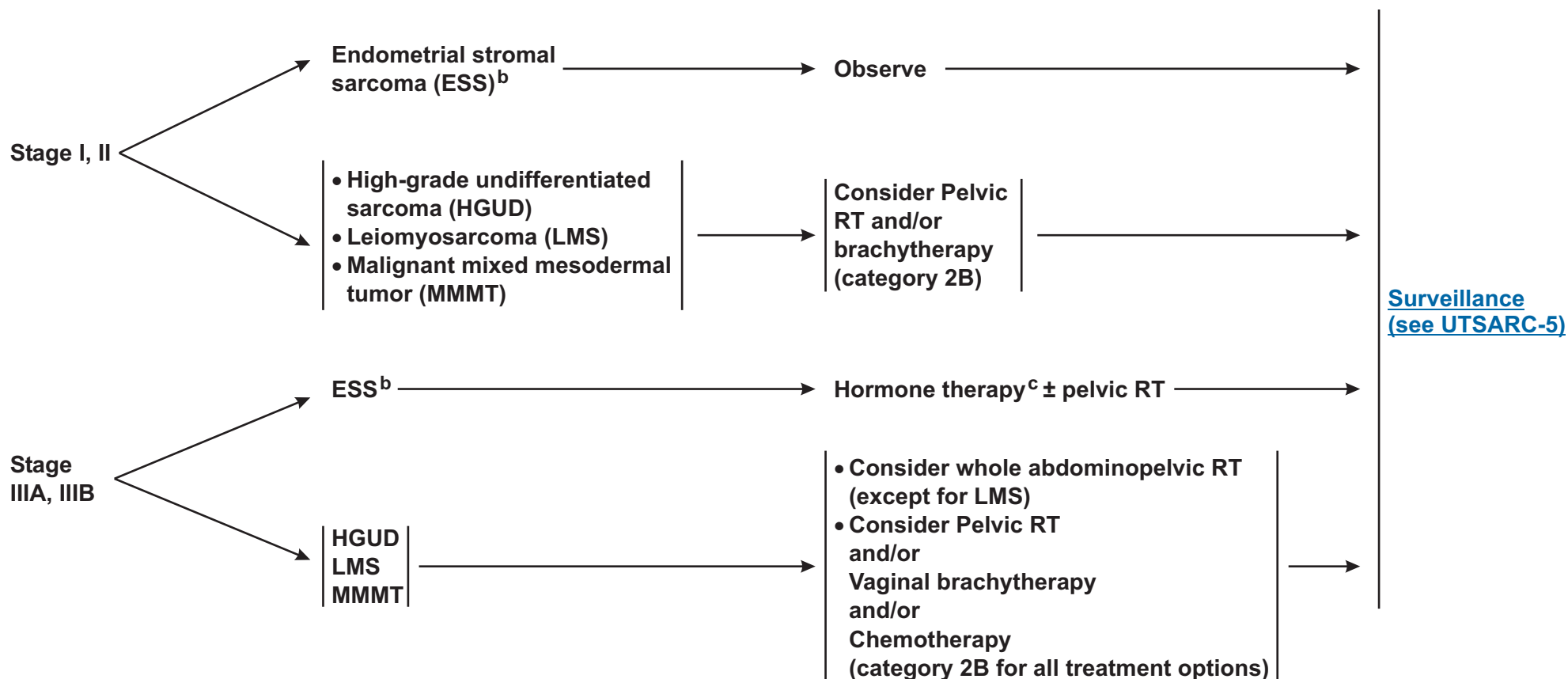


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**PATHOLOGIC FINDINGS/
HISTOLOGIC GRADE^a**

ADJUVANT TREATMENT



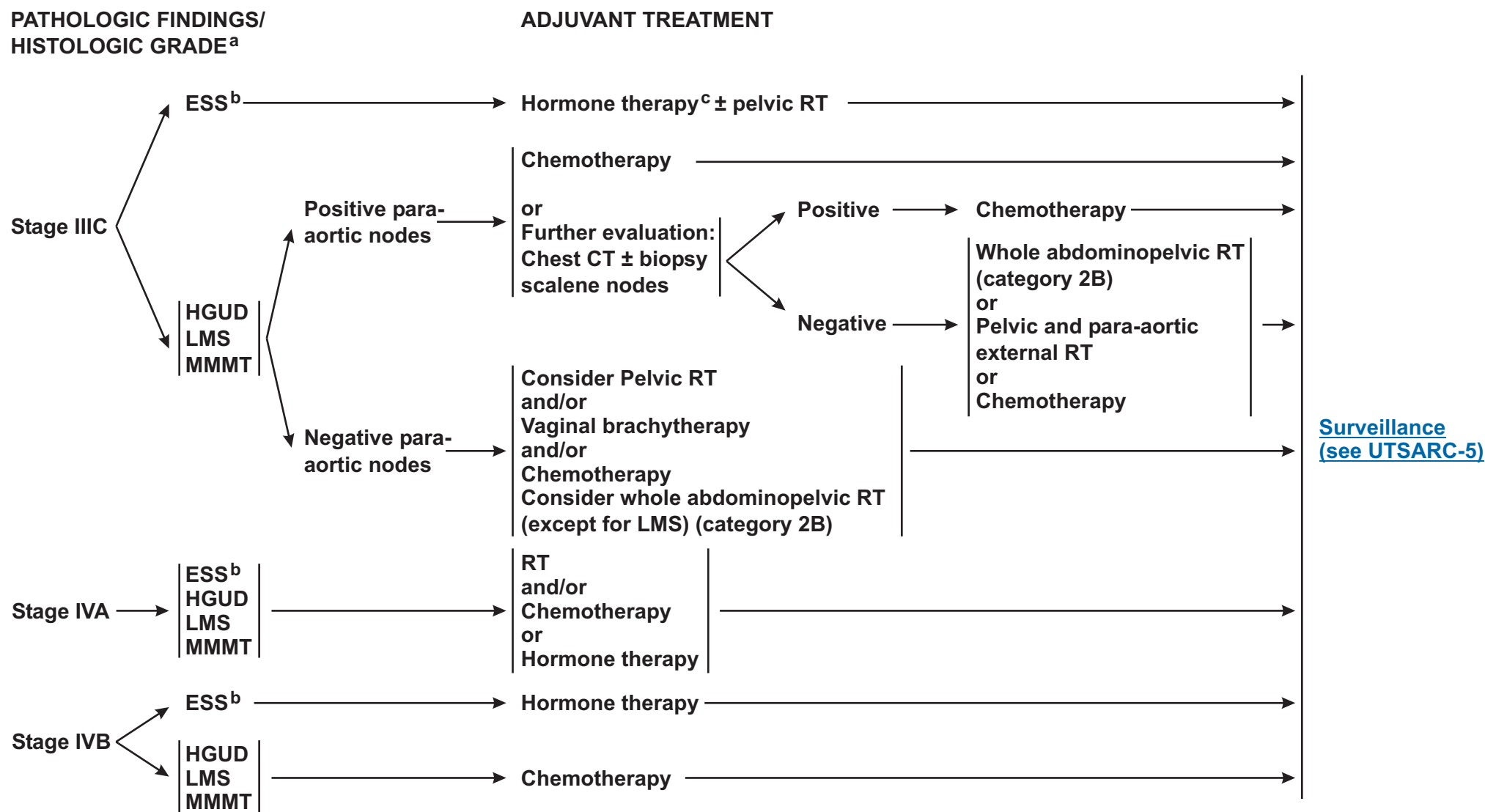
^aSee [Uterine Sarcoma Classification \(UTSARC-A\)](#).

^bBy definition, ESS is a low-grade sarcoma.

^cFor hormone therapy and chemotherapy regimens, see [Salvage Therapy \(UTSARC-B\)](#).

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^aSee [Uterine Sarcoma Classification \(UTSARC-A\)](#).

^bBy definition, ESS is a low-grade sarcoma.

^cFor hormone therapy and chemotherapy regimens, see [Salvage Therapy \(UTSARC-B\)](#).

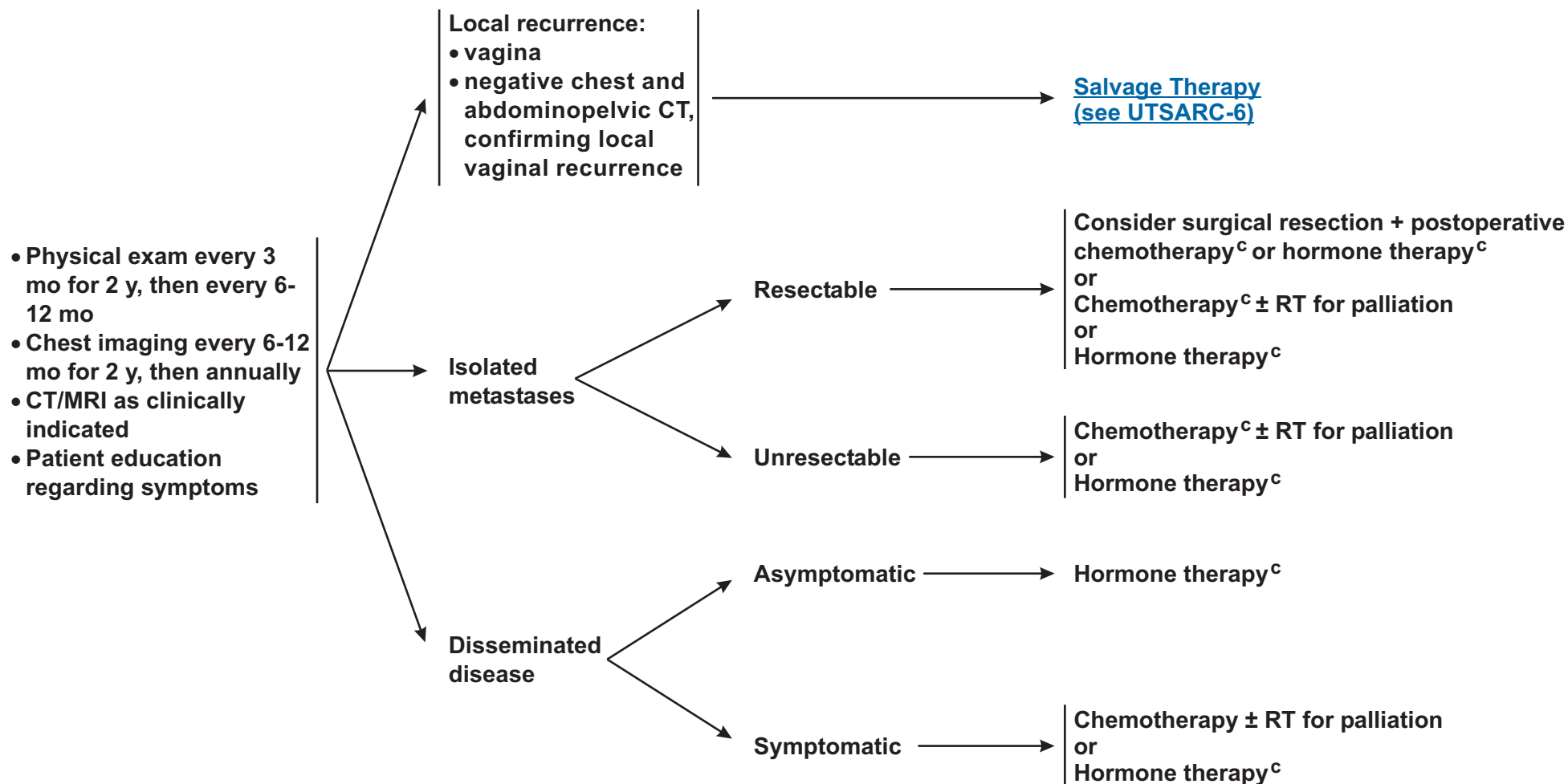
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SURVEILLANCE

RECURRENCE

SALVAGE THERAPY



^cFor hormone therapy and chemotherapy regimens, see Salvage Therapy (UTSARC-B).

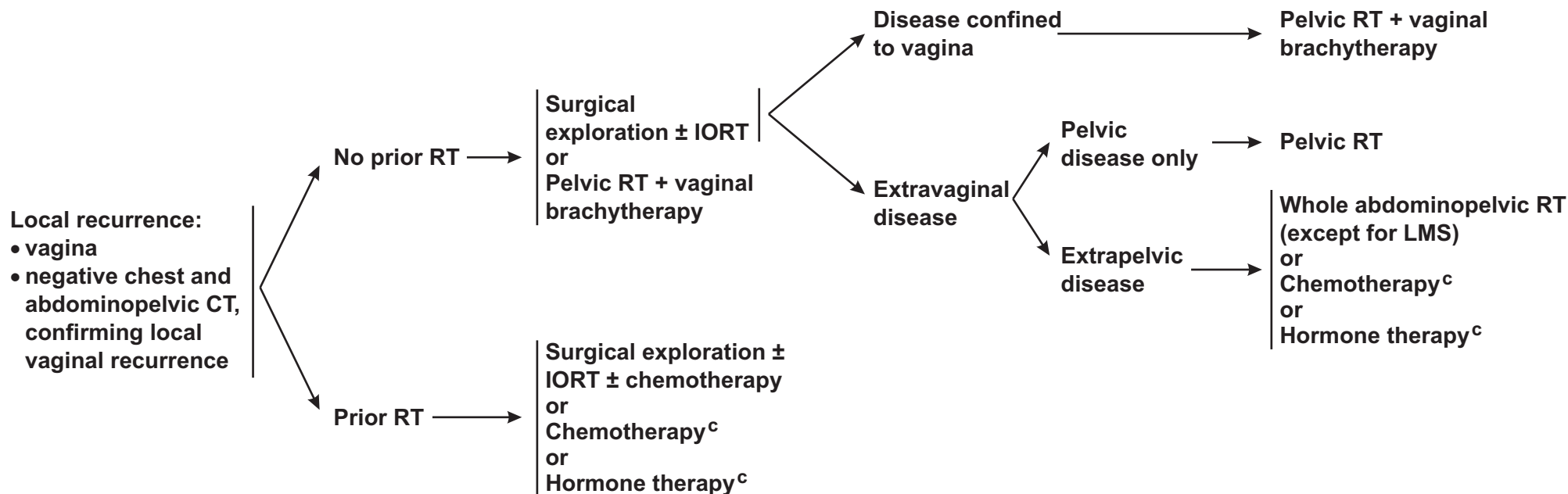
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RECURRENCE

SALVAGE THERAPY



^c[For hormone therapy and chemotherapy regimens, see Salvage Therapy \(UTSARC-B\).](#)

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UTERINE SARCOMA CLASSIFICATION

Pure Uterine Sarcoma:

- Endometrial stromal sarcoma^d
- Undifferentiated sarcoma (high-grade endometrial stromal sarcoma)^e or pure heterologous sarcoma^f
- Leiomyosarcoma^g

Mixed Epithelial-Nonepithelial Malignant Tumors:

- Malignant mixed mesodermal tumor^h
- Adenosarcomaⁱ

^dEndometrial stromal sarcomas displaying morphologic features of proliferative phase endometrial stroma and showing any mitotic index.

^eHigh-grade stromas showing pleomorphism or anaplasia greater than that seen in proliferative phase endometrial stroma or completely lacking recognizable stromal differentiation; mitotic index almost always > 10 mf/10 hpf.

^fRare group of tumors including malignant fibrous histiocytoma, rhabdomyosarcoma, angiosarcoma, liposarcoma, chondrosarcoma, osteosarcoma, alveolar soft-part sarcoma, and other sarcomas with morphology comparable to extrauterine counterparts.

^gExcludes smooth muscle tumors of uncertain malignant potential, epithelioid smooth muscle tumors, benign metastasizing leiomyomas, intravenous leiomyomatosis, diffuse leiomyomatosis; management in individual cases may be modified based on clinicopathologic prognostic factors, such as size (< or > 5 cm), mitotic activity (< or > 10 mf/10 hpf), age (< or > 50 years), and presence or absence of vascular invasion.

^hAlso known as carcinosarcomas or malignant mixed Müllerian tumors and including those with either homologous or heterologous stromal elements.

ⁱRare tumors for which management is individualized based on pathologic prognostic factors such as grade of sarcomatous component, presence or absence of stromal overgrowth.

[Back to Histologic Findings \(UTSARC-3\)](#)

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SALVAGE THERAPY**CHEMOTHERAPY REGIMENS**

The following agents can be used as single agents
or in combination, as clinically appropriate:

- Ifosfamide (most active single agent for MMMT)
- Doxorubicin (most active single agent for LMS)
- Single-agent cisplatin, paclitaxel, docetaxel, epirubicin and DTIC have activity in other soft tissue sarcomas, and could also be considered.

HORMONE THERAPY

- Megestrol acetate
- Medroxyprogesterone acetate
- Tamoxifen
- GnRH analogs

Clinical trials strongly recommended

[Back to Recurrence
\(UTSARC-5\)](#)

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Staging

Table 1**FIGO^a Staging for Endometrial Cancer: 1988**

Stage IA	G1, G2, G3	Tumor limited to endometrium
Stage IB	G1, G2, G3	Invasion to less than one half of the myometrium
Stage IC	G1, G2, G3	Invasion to more than one half of the myometrium
Stage IIA	G1, G2, G3	Endocervical glandular involvement only
Stage IIB	G1, G2, G3	Cervical stromal invasion
Stage IIIA	G1, G2, G3	Tumor invades serosa and/or adnexa, and/or positive peritoneal cytology
Stage IIIB	G1, G2, G3	Vaginal metastases
Stage IIIC	G1, G2, G3	Metastases to pelvic and/or paraaortic lymph nodes
Stage IVA	G2, G3	Tumor invasion of bladder and/or bowel mucosa
Stage IVB		Distant metastases including intra-abdominal and/or inguinal lymph nodes

Histopathology - Degree of Differentiation

Cases of carcinoma of the corpus should be classified (or graded) according to the degree of histologic differentiation, as follows:
G1 = 5% or less of a nonsquamous or nonmorular solid growth pattern

G2 = 6% to 50% of a nonsquamous or nonmorular solid growth pattern

G3 = more than 50% of a nonsquamous or nonmorular solid growth pattern

Notes on Pathologic Grading:

1. Notable nuclear atypia, inappropriate for the architectural grade, raises the grade of a grade 1 or grade 2 tumor by 1.
2. In serous adenocarcinomas, clear-cell adenocarcinomas, and squamous cell carcinomas, nuclear grading takes precedence.
3. Adenocarcinomas with squamous differentiation are graded according to the nuclear grade of the glandular component.

Rules Related to Staging:

1. Because corpus cancer is now staged surgically, procedures previously used for determination of stages are no longer applicable, such as the findings from fractional dilation and curettage to differentiate between stage I and II.
2. It is appreciated that there may be a small number of patients with corpus cancer who will be treated primarily with radiation therapy. If that is the case, the clinical staging adopted by FIGO in 1971 should still apply, but designation of that staging system would be noted.
3. Ideally, width of the myometrium should be measured along with the width of tumor invasion.

^aFederation Internationale de Gynecologie et d'Obstetrique
Reprinted from the International Journal of Gynecology and Obstetrics, Vol 28, Cancer Committee to the General Assembly of FIGO, Annual Report on the Results of Treatment in Gynecological Cancer, pp. 189-190, 1989, with permission from Elsevier Science.

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

Adenocarcinoma of the endometrium is the most common malignancy of the female genital tract in the United States. It is estimated that 40,100 new cases will be diagnosed in 2003, with 6,800 deaths resulting from the disease (Jemal et al, 2003).

In approximately 75% of patients with adenocarcinoma of the endometrium, the invasive neoplasm is confined to the uterus at diagnosis. Because of early symptoms of irregular vaginal bleeding in this predominantly postmenopausal patient population, the often localized nature of the disease, and the generally high survival rate, many physicians have the attitude that adenocarcinoma of the endometrium is a relatively benign disease. A critical evaluation of

survival data, however, indicates that this belief is inaccurate. Although the estimated incidence of endometrial cancer in the United States has remained relatively constant over the past decade, the estimated number of deaths from this disease has more than doubled from 2,900 in 1987 to 6,300 in 1998 (Podratz et al, 1998).

The reasons underlying this increase in deaths are probably multifactorial, but they indicate the need for a critical reassessment of the guidelines for managing endometrial cancer. It is imperative that physicians identify high-risk patients and tailor treatment appropriately to provide the best opportunity for long-term survival.

Diagnosis and Workup

Most patients (90%) with endometrial carcinoma have abnormal vaginal bleeding, most commonly in the postmenopausal period. Initial preoperative evaluation for early-stage endometrial cancer should include a history and physical exam, chest x-ray, a complete blood count, and platelet count. Diagnosis can usually be made by an office endometrial biopsy. If cervical involvement is suspected, endocervical curettage or cervical biopsy should be performed.

Given the typical age group at risk for endometrial carcinoma and the presence of comorbid illnesses, it is prudent in selected patients to also include assessments of serum electrolytes, blood urea nitrogen, serum creatinine, serum glucose, and renal and liver function.

Other ancillary tests, such as cystoscopy, sigmoidoscopy, ultrasound, computed tomography, and magnetic resonance imaging should be reserved for evaluating extrauterine disease as indicated by clinical symptoms, physical findings, or abnormal laboratory findings. In patients with extrauterine disease or papillary

serous or clear cell histology, a serum CA 125 assay can be helpful in monitoring clinical response (Duk et al, 1986).

The histologic information from the endometrial biopsy (with or without endocervical curettage) should be sufficient for planning definitive treatment. Office endometrial biopsies have a false-negative rate of about 10%. Thus, a negative endometrial biopsy in a symptomatic patient must be followed by a fractional curettage under anesthesia. Hysteroscopy may be helpful in evaluating the endometrium for lesions, such as a polyp, if the patient has persistent or recurrent undiagnosed bleeding (Gimpelson and Rappold, 1998).

Endometrial Cancer Staging

The FIGO (International Federation of Gynecology and Obstetrics) system is most commonly used for staging. The original 1970 criteria for staging endometrial cancer incorporated only information gained from presurgical evaluation, including physical examination and diagnostic fractional dilation and curettage. A significant number of patients at that time were not treated with primary surgery because of obesity or various other medical problems. Thus, this staging system should only be used if the patient is not a surgical candidate.

Over the past 20 years, several studies in the literature demonstrated that clinical staging was inaccurate and did not reflect actual disease extent in 15% to 20% of patients (Boronow et al, 1984; Cowles et al, 1985; Creasman et al, 1987). This reported understaging and, more importantly, the ability to identify multiple prognostic factors with a full pathologic review made possible with surgical staging, motivated a change in the staging classification. Therefore, in 1988 the Cancer Committee of FIGO modified its

staging system (Cancer Committee to the General Assembly of FIGO, 1989) to emphasize complete surgicopathologic assessment of data, such as histologic grade, myometrial invasion, and the extent and location of extrauterine spread, including retroperitoneal lymph node metastases (See [Staging](#)).

Primary Treatment

A pathology review will provide clinical findings of various endometrial cancer histologies, or papillary serous or clear cell carcinoma. These guidelines divide endometrial cancer into three categories for delineating treatment: 1) disease limited to the uterus, 2) suspected or gross cervical involvement, and 3) suspected extrauterine disease.

Disease Limited to the Uterus

The majority of patients with endometrial cancer have stage I disease at presentation. If medically operable, the surgical procedure for the staging of a patient with endometrial cancer clinically confined to the fundal portion of the uterus includes peritoneal lavage for cytology, total abdominal hysterectomy/bilateral salpingo-oophorectomy (TAH/BSO), and dissection of pelvic and para-aortic lymph nodes via an abdominal approach. During surgery, the abdominal organs including the diaphragm, liver, omentum, and pelvic and bowel peritoneal surfaces should be carefully inspected and palpated. The pathologic information obtained provides an optimal basis for the decision and design of adjuvant therapy. For medically inoperable patients, exclusive radiation therapy has been demonstrated as a well-tolerated and effective treatment (Fishman et al, 1996).

Whether or not pelvic and aortic lymphadenectomy should be

required for all patients with disease confined to the uterus is a controversial issue. Factors that need to be considered are the need for the operating surgeon to be familiar with gynecological cancer surgery, the required extent of lymphadenectomy, the contention of some physicians that low-grade and noninvasive endometrial cancers do not justify routine lymphadenectomy, and the reality that some patients, such as those who are obese, are not technically suitable for nodal dissection.

The incidence of pelvic and aortic node metastasis is related to the grade of tumor and the depth of myometrial invasion and the presence of vascular space invasion. Based upon retrospective analysis of patients who have undergone full surgicopathologic correlation, it is suggested that patients with grade 1 tumors and invasion of less than one-third of the myometrium may be spared the risks associated with lymph node dissection, whereas nodal dissection is recommended for all patients with grade 2 to 3 tumors, deep myometrial invasion, cervical involvement, or suspect nodes at surgery.

Other intraoperative and postoperative considerations must be factored into the decision to perform lymphadenectomy. Studies show that in 15% to 20% of cases, the preoperative grade, as assessed by endometrial biopsy or curettage, is upgraded on final fixed pathologic evaluation of the hysterectomy specimen (Daniel and Peters, 1988). As the grade of the tumor increases, the accuracy of intraoperative evaluation of myometrial invasion by gross examination of fresh tissue decreases. In one study, the depth of invasion was accurately determined by gross examinations in 87.3% of grade 1 lesions, 64.9% of grade 2 lesions, and 30.8% of grade 3 lesions (Goff and Rice, 1990). A further indication for complete surgical staging is suggested in a recent report

demonstrating statistically improved survival in patients with complete node dissection versus no node dissection or limited node sampling, even after adjusting for other clinicopathologic variables (Kilgore et al, 1995).

Suspected or Gross Cervical Involvement

Patients with suspected or gross cervical involvement should be further evaluated with endocervical curettage (ECC) or cervical biopsy. If negative result, patients are treated as disease limited to uterus as mentioned above. For operable patients with cervical involvement, radical abdominal hysterectomy with bilateral salpingo-oophorectomy (RAH/BSO) and dissection of pelvic and para-aortic lymph nodes are recommended. Alternatively, the patient may undergo radiation therapy (RT) (75-80 Gy to point A) followed by TAH/BSO with para-aortic lymph node dissection. However, there was no consensus among the NCCN panel members on the radiation therapy, therefore it was considered Category 2B. For medically inoperable patients, pelvic RT with brachytherapy can provide long-term local control and cancer-specific survival rates approaching those of surgical treatment (Fishman et al, 1996).

Suspected Extrauterine Disease

If extrauterine disease is suspected, laboratory test of CA 125 level or imaging study such as MRI or CT should be considered if clinically indicated. Patients with negative results are treated following the guidelines for disease limited to uterus. Intra-abdominal disease, such as ascites, omental, nodal, ovarian, or peritoneal involvement, warrant surgical intervention using TAH/BSO with cytology and selective pelvic and para-aortic lymph node dissection, omentectomy, or debulking. Patients with extrauterine pelvic disease such as vaginal, bladder, bowel/rectal, or parametrial involvement are treated with RT and brachytherapy with

or without surgery. For extra-abdominal disease such as liver involvement, palliative TAH/BSO with or without RT, hormonal, or chemotherapy is recommended.

Adjuvant Therapy

Given the lack of definitive data regarding the effectiveness of adjuvant therapy in patients with uterine-confined disease the guidelines represent an evolving process. The basic concept underlying the recommendations is the trend toward selection of more aggressive adjuvant therapy for patients as tumor grade and myometrial and/or cervical invasion advances. Other pathologic factors that may influence the decision regarding adjuvant therapy in surgical stage I and stage II endometrial cancer include patient age, lymphovascular space invasion, tumor volume, and involvement of the lower uterine segment.

There is a consensus that patients with documented extrauterine disease are at increased risk for recurrence and need adjuvant therapy. The optimal form of adjuvant therapy has yet to be determined. Treatment is often tailored to the surgically defined extent of disease. A point of historical controversy has been whether positive peritoneal cytology (stage IIIA) is an independent prognostic factor, after adjustment for other known risk factors (Morrow et al, 1991; Kadar et al, 1992). At present, there is general agreement that in the absence of other adverse pathologic features (high-grade tumors, deep myometrial invasion, papillary serous or clear cell histologies, or documented extrauterine disease), a positive peritoneal cytology may be a clinically inconsequential finding.

Completely Surgically Staged Patients

The imprecision of preoperative and intraoperative assessment of

grade and myometrial invasion and the potential therapeutic benefit of lymph node dissection make the concept of intraoperative decision-based lymph node dissection difficult to apply prospectively with accuracy. Therefore, complete surgical staging to gather full pathologic and prognostic data on which base decisions regarding adjuvant treatment should be advocated for all patients who do not have medical or technical contraindications to lymph node dissection. The exception would be those with grade 1 noninvasive disease. Ideally, the grade and lack of invasive disease in such patients should be confirmed by frozen section.

Recently, laparoscopic pelvic and para-aortic lymphadenectomy in association with laparoscopically assisted vaginal hysterectomy has been proposed as an alternative surgical approach; however, the panel recommends that this approach be used only in the context of a clinical trial and patients should be followed over a long term to compare their outcomes with those of traditional laparotomy. Trials evaluating this new potentially less invasive method are underway (Childers et al, 1993).

Adequate surgical staging provides important information to assist in selection of adjuvant therapy for endometrial tumors. Patients with completely surgically staged stage I endometrial cancer are stratified by adverse risk factors such as advanced age, lymphovascular invasion, tumor size, depth of invasion and involvement of lower uterine segment. All the stage IA, G1-3 patients should be observed. However, vaginal brachytherapy is also recommended for stage IA, G3 disease if no adverse risk factors present; or otherwise, pelvic RT and/or vaginal brachytherapy (Category 2B) are needed. Stage IB patients without adverse risk factors can be observed, or treated with vaginal brachytherapy (G2-3). If adverse factors present, stage IB, G1

patients should be observed or undergo vaginal brachytherapy. However, stage IB, G2-3 tumors need pelvic RT and/or vaginal brachytherapy (Category 2B). For stage IC patients with adverse risk factors, pelvic RT and/or vaginal brachytherapy is recommended (Category 2B), regardless of their histologic grade. Otherwise, if no adverse risk factors present, observation or vaginal brachytherapy is needed for G1-2 patients, pelvic RT and/or vaginal brachytherapy (Category 2B) for G3 patients.

Based upon a prospective evaluation of surgicopathologic patterns of spread in endometrial cancer by the Gynecologic Oncology Group (GOG) and others, it is now recognized that much of the adverse prognosis associated with intrauterine risk factors is mediated through nodal involvement. The incidence of pelvic nodal metastases is 5% or less for grade 1 and 2 tumors with inner one-third myometrial invasion. For patients with outer third infiltration, nodal disease was found in 19% of grade 2 cancers and 34% of grade 3 cancers (Creasman et al, 1987). Given the wider acceptance of formal surgicopathologic evaluation and the adoption of the 1988 FIGO staging classification (see [Staging](#)), clinical stage I and stage II patients with adverse intrauterine features who were once deemed at risk for nodal metastases are now upstaged to stage III and stage IV when extrauterine disease is documented. The implications of this “stage migration” should be considered when evaluating historical data.

Significant controversy centers on appropriate adjuvant therapy in patients with surgical stage I and stage II endometrial cancer, regardless of intrauterine features, for whom extrauterine disease has been clearly ruled out. In a large prospective study, the GOG reported that the 5-year survival rate for surgical stage I patients with no adverse risk factors other than grade and myometrial

invasion (i.e., without extrauterine disease, isthmus/cervical involvement, or lymphovascular space invasion) was 92.7% (Morrow et al, 1991). The practice of surgical staging has led to a decrease in the use of adjuvant therapy for stage I endometrial carcinoma (Gretz et al, 1996).

The benefit of external irradiation in pathologic stage I endometrial carcinoma with unfavorable prognostic factors was demonstrated by a prospective clinical study. Kucera and colleagues reported on a large series of 605 patients with stage I endometrial carcinoma initially treated with TAH/BSO. Patients with low-grade and superficially invasive disease received vaginal brachytherapy only, whereas those with higher-grade disease and deeper myometrial infiltration underwent vaginal and external-beam radiation. The five-year survival results showed that patients with poor prognostic factors who received external-beam radiation and vaginal brachytherapy did as well as the patients with a good prognosis who were treated with vaginal radiation alone. This suggested that external radiation was able to compensate for the expected poorer outcome in patients with unfavorable risk factors (Kucera et al, 1990).

For stage IIA patients with myometrial invasion less than 50%, observation or vaginal brachytherapy are recommended for G1-2 disease. Pelvic RT with or without vaginal brachytherapy is another treatment option for G2 tumors. Patients with G3 tumors are managed by vaginal brachytherapy with or without pelvic RT. Patients with deeper myometrial (greater than 50%) are treated with vaginal brachytherapy with or without pelvic RT (G1-2). G3 disease is managed by pelvic RT and vaginal brachytherapy, which is also the recommended treatment option for stage IIB patients.

To assess the role of adjuvant radiation in surgically staged

endometrial cancer patients without extrauterine disease, the GOG completed a multicenter trial that randomized patients with stage IB, stage IC, and occult stage II disease (any grade) to pelvic radiotherapy versus observation alone following primary surgery. Initial analysis of the study showed a significant decrease in overall recurrences and an improvement in the 2-year progression-free interval favoring the radiated cohort, but overall survival was not statistically different between the two groups (Roberts et al, 1998). Patterns of failure analysis in the GOG trial revealed an intriguing finding: the majority of initial pelvic recurrences in the observation group were limited to the vagina. This finding has prompted some clinicians to ask if vaginal brachytherapy is sufficient adjuvant treatment for patients with tumors that are histologically confined to the uterus, despite the existence of other intrauterine risk features (Chadha et al, 1999). The GOG randomized trial has also been criticized for including patients with a broad range of relapse risk, including many who are often considered to have excellent prognoses, hence diluting the possibility of detecting a benefit to adjuvant therapy.

Patients with extrauterine disease confined to the lymph nodes or the adnexa may be adequately treated with pelvic or extended-field RT (Greven et al, 1993). Noninvasive stage IIIA tumors confined to fundus, or those with only positive cytology should be observed. G3 tumors can also be managed with vaginal brachytherapy, or pelvic RT with or without vaginal brachytherapy. All other stage IIIA tumors are treated with pelvic RT with or without vaginal brachytherapy, whole abdominopelvic RT (Category 2B for G1) with or without vaginal brachytherapy. There was a major disagreement on the recommendation of chemotherapy with or without RT and it was considered Category 3 (pending the final results of the GOG trial).

Despite of the histologic grade, patients with stage IIIB are treated with pelvic RT with vaginal brachytherapy, or chemotherapy with or without RT (Category 3). In the cases with adnexa involvement and/or positive cytology, optional whole abdominopelvic RT should be considered. Patients with stage IIIC disease metastasized to pelvic nodes are managed with pelvic RT to aortic bifurcation with or without vaginal brachytherapy, and with or without para-aortic radiation. For stage IIIC tumor with common iliac or para-aortic node metastasis, extended field, para-aortic lymph node RT with or without vaginal brachytherapy is recommended. Although chemotherapy with or without RT could be another treatment option for stage IIIC patients, it received major disagreement among NCCN panel members and is considered as Category 3. Following tumor debulking, stage IVA or IVB tumor with no gross residual disease or microscopic abdominal disease should be managed with whole abdominopelvic RT with or without vaginal brachytherapy, chemotherapy with or without RT, or be enrolled in a pertinent clinical trial.

For patients deemed at risk of peritoneal failure, whole abdominal RT in carefully selected cases appears to provide therapeutic benefit (Gibbons et al, 1991; Greer and Hamberger, 1983). A randomized phase III GOG trial seeks to elucidate optimal adjuvant therapy for endometrial cancer with extrauterine disease. In this trial, patients with stage III and intra-abdominal stage IV disease with minimal residual disease are randomized to whole abdominopelvic RT (WAI) versus seven cycles of combined doxorubicin (60 mg/m²) and cisplatin (50 mg/m²) treatment, with an additional cycle of cisplatin (AP). Results of this study revealed that AP chemotherapy improved progression-free survival and overall survival when compared with WAI. Still, recurrences were frequent, predominantly in the pelvis and abdomen in both arms.

Approximately 55% of patients with advanced endometrial carcinoma recurred (Randall et al 2003). An ongoing GOG trial investigating combination chemotherapy with more limited radiation fields is underway.

Incompletely Surgically Staged Patients

For incompletely surgically staged patients, abdominopelvic CT is required. Positive CT findings necessitate additional work-up to rule out gross extrauterine disease. Patients with negative CT results should proceed to adjuvant treatment. It is recommended that stage IA, G1-2 tumors be observed, and stage IB, G1 tumors be observed or treated with vaginal brachytherapy. Patients with more aggressive tumors such as stage IC, stage IIA with myometrial invasion 50%, stage IIB, or G3 tumors are managed with reoperative staging followed by adjuvant treatment as indicated, or undergo pelvic RT with or without vaginal brachytherapy. Otherwise, treatment for stage IB, G2, or stage IIA, G1-2 tumors with myometrial invasion 50% follow the same guidelines as explained for completely surgically staged patients.

The potential benefit of selective adjuvant pelvic radiation in nonsurgically staged patients with high-risk intrauterine features was echoed in a clinical report on 384 patients (Carey et al, 1995). An early prospective phase III study of stage I endometrial cancer (without lymph node sampling) randomized patients to vaginal brachytherapy alone or in combination with external irradiation (40 Gy with central shielding after 20 Gy). Although there was no overall 5-year survival benefit from the addition of external-beam RT, there was some improvement in pelvic control (Aalders et al, 1980).

Hormone Replacement Therapy for Endometrial Cancers

Hypoestrogenism is associated with hot flashes, mood lability,

vaginal dryness, pelvic soft tissue atrophy, osteoporosis, and an increased risk of cardiovascular disease. Estrogen replacement therapy in postmenopausal women has been shown to reduce or reverse these signs and symptoms. Because endometrial adenocarcinoma has historically been considered an estrogen-linked malignancy (Smith et al, 1975; Ziel and Finkle, 1975), women who have been successfully treated for this cancer have usually been denied estrogen replacement therapy for fear of inducing a higher relapse rate. However, estrogen replacement therapy for such patients remains controversial. A higher relapse rate in endometrial cancer patients who receive estrogen replacement therapy following hysterectomy has never been proven. Indeed, several retrospective trials of estrogen replacement following treatment of early-stage endometrial cancer have shown no increase in tumor recurrence or cancer-related deaths (Creasman et al, 1986; Lee et al, 1990; Chapman et al, 1996). However, estrogen replacement trials in postmenopausal females without a history of malignancy have demonstrated a significant increased risk of breast cancer.

Panel members agree that estrogen replacement therapy is a reasonable option for patients who are at low risk for tumor recurrence, but initiating such therapy should be individualized and discussed in detail with the patient. If adjuvant treatment is carried out, there should be a 6 to 12 month wait before initiation of hormonal replacement therapy and participation in clinical trials is strongly encouraged. Recently developed selective estrogen-receptor modulators (SERMs) may prove to be attractive options in hormone replacement therapy. For example, the SERM raloxifene does not exhibit a stimulatory effect on uterine or breast tissue but retains beneficial activity on bone and lipid metabolism. Unfortunately, raloxifene does not reduce vasomotor instability.

Long-term comparisons between conjugated estrogens and SERMs for hormone replacement therapy are needed.

Postoperative Surveillance

The panel recommends a postoperative surveillance protocol for endometrial cancer consisting of a clinic visit with a physical examination every 3 to 6 months for 2 years, then at 6 month to 1 year intervals. If CA 125 is elevated initially it should be repeated at each surveillance visit. Chest x-ray should be monitored annually (Category 2B) and vaginal cytology should be performed every 6 months for 2 years, then annually. These recommendations recognize that the value of intensive surveillance has not been demonstrated in this disease, and ancillary testing is therefore not recommended (Podczaski et al, 1992; Shumsky et al, 1994; Berchuck et al, 1995; Reddoch et al, 1995). A 1992 survey confirmed that, with some variations, these follow-up guidelines were widely practiced (Barnhill et al, 1992).

A recent review of the literature for routine intensive postoperative surveillance in patients with clinical stage I and stage II endometrial cancer showed approximately a 15% recurrence rate (Greer et al, 1997). Fifty-eight percent of the patients had symptomatic recurrences. For most patients, disease recurred within 3 years of initial treatment.

All patients should receive verbal and written information regarding the symptoms of recurrent disease. Patients with bleeding (vaginal, bladder, or rectal), decreased appetite, weight loss, pain (in the pelvis, abdomen, hip, or back), cough, shortness of breath, and swelling (in the abdomen or legs) should seek prompt evaluation and not delay until the next scheduled appointment.

In the absence of recurrence, post-treatment surveillance provides psychosocial reassurance and improves the quality of life for patients and their families. Health maintenance has been incorporated into the follow-up schedule and should include blood pressure determination, breast examination, mammography as clinically indicated, stool guaiac test, immunizations, and an opportunity to evaluate other health problems that often coexist in patients with endometrial cancer. Given the lack of prospective studies regarding the optimal frequency of post-therapy follow-up, it was the panel's opinion that the guidelines given in the algorithm represented a reasonable surveillance scheme.

Treatment of Relapsed or Metastatic Disease

Patients with recurrences confined to the pelvis following surgical therapy should be evaluated for surgical extirpation and/or RT. Vaginal recurrences treated with RT have reported survival rates of 40%, with a significantly worse results if there is pelvic extension or pelvic lymph node involvement (Poulsen and Roberts, 1988). Patients with recurrences confined to the pelvis following RT are unusual. The management of such patients is still controversial.

For patients previously treated with external-beam RT, recommended salvage therapy includes pelvic exenteration with or without IORT (intraoperative radiotherapy), palliative radiotherapy, hormonal therapy, or chemotherapy. Radical surgery, such as pelvic exenteration, has been performed with reported survival rates approximating 20% (Barakat et al, 1999). For patients without prior RT to the site of recurrence, or with previous brachytherapy only, surgical exploration of pelvis and abdomen should be performed with or without IORT. If feasible, surgical resection should be

considered. In addition, RT with brachytherapy is considered another treatment option. For the recurrence confined to vagina, or with pelvic lymph node invasion, additional therapy such as pelvic RT with vaginal brachytherapy is needed. Para-aortic or common iliac lymph node invasion is treated with pelvic and para-aortic RT with vaginal brachytherapy. For recurrences with upper abdominal or peritoneal invasion, microscopic residual needs whole abdominopelvic RT with vaginal brachytherapy. However, gross upper abdominal residual needs more aggressive salvage treatment as outlined for disseminated metastases. Resectable isolated metastases can be treated with surgical resection with or without RT. Further recurrences or unresectable isolated metastases are treated as disseminated metastases.

The management of systemic disease is usually palliative. The principles of therapy include the amelioration of symptomatic metastatic sites with RT, appropriate use of consultants in pain management, and the involvement of support organizations, such as hospice care. The hormonal therapy of metastatic disease involves mainly the use of progestational agents. No particular drug, dose, or schedule has been found to be superior. The main predictors of response in the treatment of metastatic disease are well-differentiated tumors, a long disease-free interval, and the location and extent of extrapelvic (particularly pulmonary) metastases.

For asymptomatic or low grade disseminated metastases, hormonal therapy with progestational agents has good response for estrogen and progesterone receptor positive patients (Kauppila, 1989). Tamoxifen has a 20% response rate in those who do not respond to standard progesterone therapy (Quinn et al, 1989). Other hormonal modalities have not been well studied, and adjuvant therapy with hormonal agents in the treatment of endometrial cancer remains

unproved (Quinn, 1999). If disease progression is observed following hormonal therapy, cytotoxic chemotherapy should be considered. However, clinical trials or best supportive care (see [NCCN Palliative Care Guidelines](#)) are appropriate for patients with disseminated metastatic recurrence and poor response to hormonal and chemotherapy.

For symptomatic, G2-3, or large volume disseminated metastases, salvage therapy, such as chemotherapy and/or RT, is recommended to relieve symptoms. If two chemotherapy regimens fail, patients should receive best supportive care or be enrolled in an appropriate clinical trial.

Chemotherapy for Advanced and Recurrent Disease

Chemotherapy in endometrial cancer has been extensively studied. Single-agent therapy usually includes cisplatin, carboplatin, doxorubicin, and paclitaxel. Responses with these agents in advanced disease have ranged from 21% to 36%. Single-agent therapy has not been proven to improve quality of life or prolong survival.

Combination chemotherapy regimens have also been studied extensively. Response rates generally have improved with the combinations of doxorubicin and cisplatin/carboplatin, with or without concomitant cyclophosphamide. The response rates have ranged from 31% to 81%, but with relatively short durations. The median survival for patients in such trials remains approximately 1 year (Muss, 1994; Reddy et al, 1996). The combination of cisplatin and paclitaxel is undergoing study.

Combination chemotherapy regimens in endometrial cancer should be undertaken judiciously with careful attention to toxicity as, again, there is no demonstrated improvement in quality of life and survival

of patients. Biologic and molecular therapies have no proven role at this time in the treatment of recurrent or metastatic endometrial carcinoma.

Papillary Serous and Clear Cell Carcinomas

Uterine papillary serous and clear cell carcinomas ([ENDO-11](#)) are considered more aggressive histologies, with a higher incidence of extrauterine disease at presentation (Goff et al, 1994; Hendrickson et al, 1994). Patterns of failure mimic those of ovarian cancer. Surgical staging for these tumor subtypes should follow the procedures performed for ovarian cancer, which include detailed

examination of the entire abdominopelvic cavity and retroperitoneal spaces and appropriate biopsies, with maximal tumor debulking as indicated. Adjuvant therapy is highly individualized (Grice et al, 1998). Adjuvant therapy choices for stage IA include observation, vaginal brachytherapy, or pelvic RT with or without vaginal brachytherapy (Category 2B). For stages IB, IC, and II, pelvic RT, or whole abdominopelvic RT with or without vaginal brachytherapy (Category 2B) is recommended. Patients with stage III or adequately debulked stage IV disease are treated with whole abdominopelvic RT with or without vaginal brachytherapy, or chemotherapy, or participation in a clinical trial.

References

Aalders J, Abeler V, Kolstad P et al. Postoperative external irradiation and prognostic parameters in stage I endometrial carcinoma. Clinical and histopathologic study of 540 patients. *Obstet Gynecol* 1980;56:419-427.

Barakat RR, Goldman NA, Patel DA et al. Pelvic exenteration for recurrent endometrial cancer. *Gynecol Oncol* 1999;75(1):99-102.

Barnhill D, O'Connor D, Farley J et al. Clinical surveillance of gynecologic cancer patients. *Gynecol Oncol* 1992;46:275-280.

Berchuck A, Anspach C, Evans AC et al. Postsurgical surveillance of patients with FIGO stage I/II endometrial adenocarcinoma. *Gynecol Oncol* 1995;59:20-22.

Boronow RC, Morrow CP, Creasman WT et al. Surgical staging in endometrial cancer: Clinical-pathologic findings of a prospective study. *Obstet Gynecol* 1984;63:825-832.

Cancer Committee to the General Assembly of FIGO. Annual report on the results of treatment in gynecologic cancer. *Int J Gynaecol Obstet* 1989;28:189-190.

Carey MS, O'Connell GJ, Johanson CR et al. Good outcome associated with a standardized treatment protocol using selective postoperative radiation in patients with clinical stage I adenocarcinoma of the endometrium. *Gynecol Oncol* 57: 1995;138-144.

Chadha M, Nanavati PJ, Liu P et al. Patterns of failure in endometrial carcinoma stage IB, grade 3 and IC patients treated with postoperative vaginal vault brachy-therapy. *Gynecol Oncol* 1999;75:103-107.

Chapman JA, DiSaia PJ, Osann K et al. Estrogen replacement in surgical stage I and II endometrial cancer survivors. *Am J Obstet Gynecol* 1996;175:1195-1200.

Childers JM, Brzechffa PR, Hatch KD et al. Laparoscopically assisted surgical staging (LASS) of endometrial cancer. *Gynecol Oncol* 1993;71:612-614.

Cowles TA, Magrina JF, Masterson BJ et al. Comparison of clinical and surgical-staging in patients with endometrial carcinoma. *Obstet Gynecol* 1985;66:413-416.

Creasman WT, Henderson D, Hinshaw W et al. Estrogen replacement therapy in the patient treated for endometrial cancer. *Obstet Gynecol* 1986;67:326-330.

Creasman WT, Morrow CP, Bundy BN et al. Surgical pathologic spread patterns of endometrial cancer: A Gynecologic Oncology Group study. *Cancer* 1987;60:2035-2041.

Daniel AG, Peters WA III. Accuracy of office and operating room curettage in the grading of endometrial carcinoma. *Gynecol Oncol* 1988;71:612-614.

Duk JM, Aalders JG, Fleuren GJ et al. CA 125: A useful marker in endometrial carcinoma. *Am J Obstet Gynecol* 1986;155:1097-1102.

Fishman DA, Roberts KB, Chambers JT et al. Radiation therapy as exclusive treatment for medically inoperable patients with stage I and II endometrioid carcinoma of the endometrium. *Gynecol Oncol* 1996;61:189-196.

Gibbons S, Martinez A, Schray M et al. Adjuvant whole abdominopelvic irradiation for high-risk endometrial carcinoma. *Int J Radiat Oncol Biol Phys* 1991;21:1019-1025.

Gimpelson RJ, Rappold HO. A comparative study between panoramic hysterectomy with directed biopsies and dilatation and curettage: A review of 276 cases. *Am J Obstet Gynecol* 1998;158:489-492.

Goff BA, Kato D, Schmidt RA et al. Uterine papillary serous carcinoma: Patterns of metastatic spread. *Gynecol Oncol* 1994;53:264-268.

Goff BA, Rice LW. Assessment of depth of myometrial invasion in endometrial adenocarcinoma. *Gynecol Oncol* 1990;38:46-48.

Greer BE, Goff BA, Koh W-J. Endometrial carcinoma. In: Johnson FE, Virgo KS, eds. *Cancer Patient Follow-up*. St. Louis: Mosby 1997:357-377.

Greer BE, Hamberger AD. Treatment of intraperitoneal metastatic adenocarcinoma of the endometrium by the whole-abdomen moving-strip technique and pelvic boost irradiation. *Gynecol Oncol* 1983;16:365-373.

Gretz HF III, Economos K, Husain A et al. The practice of surgical staging and its impact on adjuvant treatment recommendations in patients with stage I endometrial carcinoma. *Gynecol Oncol* 1996;61:409-415.

Greven KM, Lanciano RM, Corn B et al. Pathologic stage III endometrial carcinoma: prognostic factors and patterns of recurrence. *Cancer* 1993;71:3697-3702.

Grice J, Ek M, Greer BE et al. Uterine papillary serous carcinoma (UPSC): Evaluation of long-term survival in 36 surgically staged patients. *Gynecol Oncol* 1998;69:69-73.

Hendrickson MR, Longacre TA, Kempson RL. Uterine papillary

serous carcinoma revisited. *Gynecol Oncol* 1994;54:261-263.

Jemal A, Murray T, Samuels A et al. *Cancer Statistics, 2003*. *CA Cancer J Clin* 2003;53:5-26.

Kadar N, Homesley HD, Malfetano JH. Positive peritoneal cytology is an adverse factor in endometrial carcinoma only if there is other evidence of extrauterine disease. *Gynecol Oncol* 1992;46:145-149.

Kaupila A. Oestrogen and progestin receptors as prognostic indicators in endometrial cancer. A review of the literature. *Acta Oncol* 1989;28:561-566.

Kilgore LC, Partridge EE, Alvarez RD et al. Adenocarcinoma of the endometrium: Survival comparisons of patients with and without pelvic node sampling. *Gynecol Oncol* 1995;56:29-33.

Kucera H, Vavra N, Weghapt K. Benefit of external irradiation in pathologic stage I endometrial carcinoma: A prospective clinical trial of 605 patients who received postoperative vaginal irradiation and additional pelvic irradiation in the presence of unfavorable prognostic factors. *Gynecol Oncol* 1990;38:99-104.

Lee RB, Burke TW, Parke RC. Estrogen replacement therapy following treatment for stage I endometrial carcinoma. *Gynecol Oncol* 1990;36:189-191.

Morrow CP, Bundy BN, Kurman RJ et al. Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: A Gynecologic Oncology Group study. *Gynecol Oncol* 1991;40:55-65.

Muss HB. Chemotherapy of metastatic endometrial cancer. *Semin Oncol* 1994;21(1):107-113.

Podczaski E, Kaminski P, Gurski K et al. Detection and patterns of treatment failure in 300 consecutive cases of “early” endometrial cancer after primary surgery. *Gynecol Oncol* 1992;47:323-327.

Podratz KC, Mariani A, Webb MJ. Editorial: Staging and therapeutic value of lymphadenectomy in endometrial cancer. *Gynecol Oncol* 1998;70:163-164.

Poulsen MG, Roberts SJ. The salvage of recurrent endometrial carcinoma in the vagina and pelvis. *Int J Radiat Oncol Biol Phys* 1988;15:809-813.

Quinn MA. Hormonal treatment of endometrial cancer. *Hematol Oncol Clin North Am* 1999;13:163-187.

Quinn MA, Campbell JJ. Tamoxifen therapy in advanced/recurrent endometrial carcinoma. *Gynecol Oncol* 1989;32:1-3.

Randall ME, Brunetto G, Muss H et al. Whole abdominal radiotherapy versus combination doxorubicin-cisplatin chemotherapy in advanced endometrial carcinoma: A randomized phase III trial of the Gynecologic Oncology Group. *Proc Am Soc Clin Oncol* 2003;22:2 (abstr 3).

Reddoch JM, Burke TW, Morris M et al. Surveillance for recurrent endometrial carcinoma: Development of a follow-up scheme. *Gynecol Oncol* 1995;59:221-225.

Reddy SP, Kudelka AP, Gonzalez de Leon C et al. Tumors of the uterine corpus. In Pazdur R, ed *Medical Oncology: A Comprehensive Review*. Huntington, New York: PRR 1996: 407-416.

Roberts JA, Brunetto VL, Keys HM et al. A phase III randomized study of surgery vs. surgery plus adjunctive radiation therapy in intermediate risk endometrial adenocarcinoma (GOG no. 99). (Abstract presented at the 29th annual meeting of the Society of Gynecologic Oncologists, Orlando, Florida, Feb 1998). *Gynecol Oncol* 1998;68(1):135.

Shumsky AG, Stuart GC, Brasher PM et al. An evaluation of routine follow-up of patients treated for endometrial carcinoma. *Gynecol Oncol* 1994;55:229-233.

Smith DC, Prentice R, Thompson DJ et al. Association of exogenous estrogen and endometrial cancer. *N Engl J Med* 1975;293:1164-1167.

Ziel HK, Finkle WD. Increased incidence of endometrial carcinoma among users of conjugated estrogens. *N Engl J Med* 1975;293:1167-1170.