Endometrial Cancer

Version 1.2013

本共識依下列參考資料修改版本：

NCCN Clinical Practice Guidelines in Oncology- Cervical cancer V.1.2013

2009年Revised FIGO staging for carcinoma of the Vulva, Cervix, and Endometrium

國家衛生研究院之『子宮體癌臨床指引』

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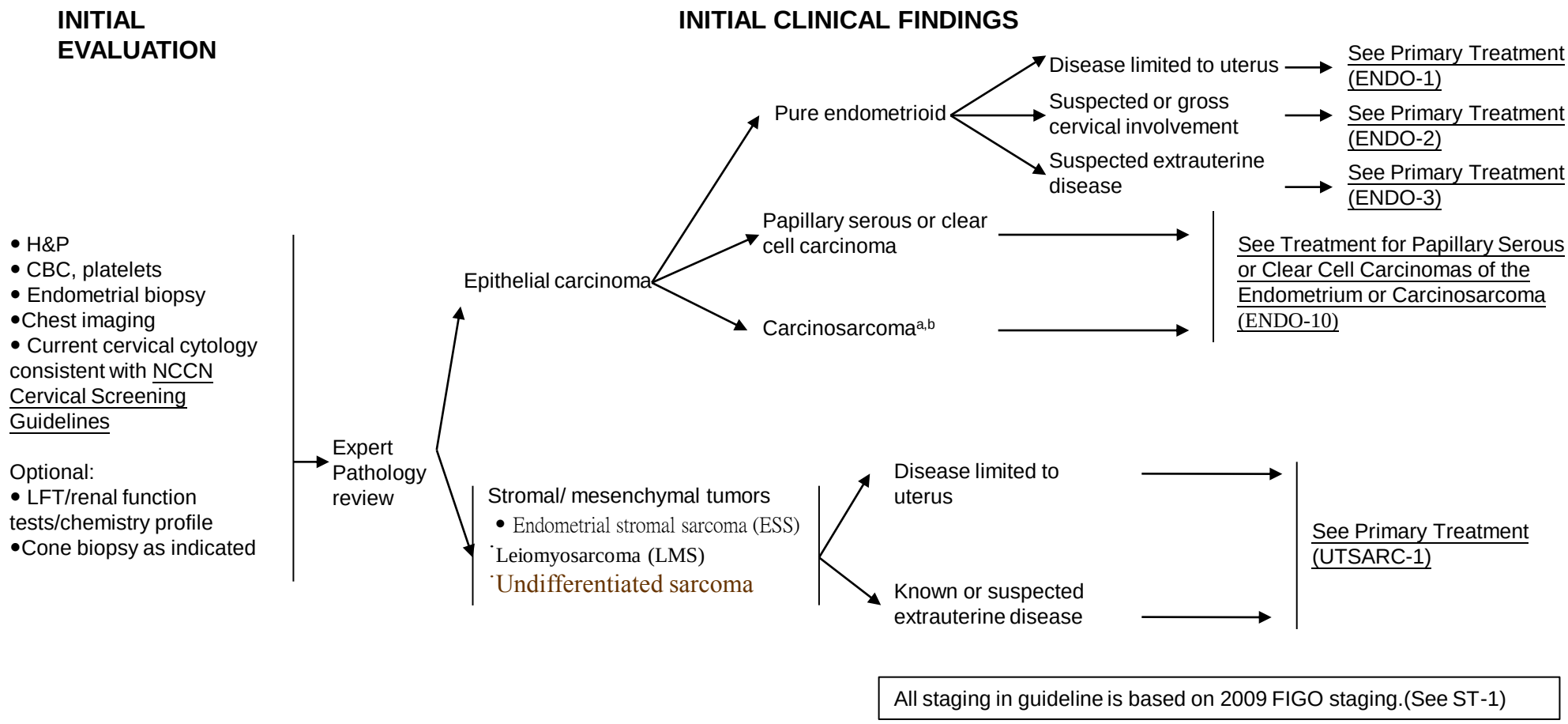
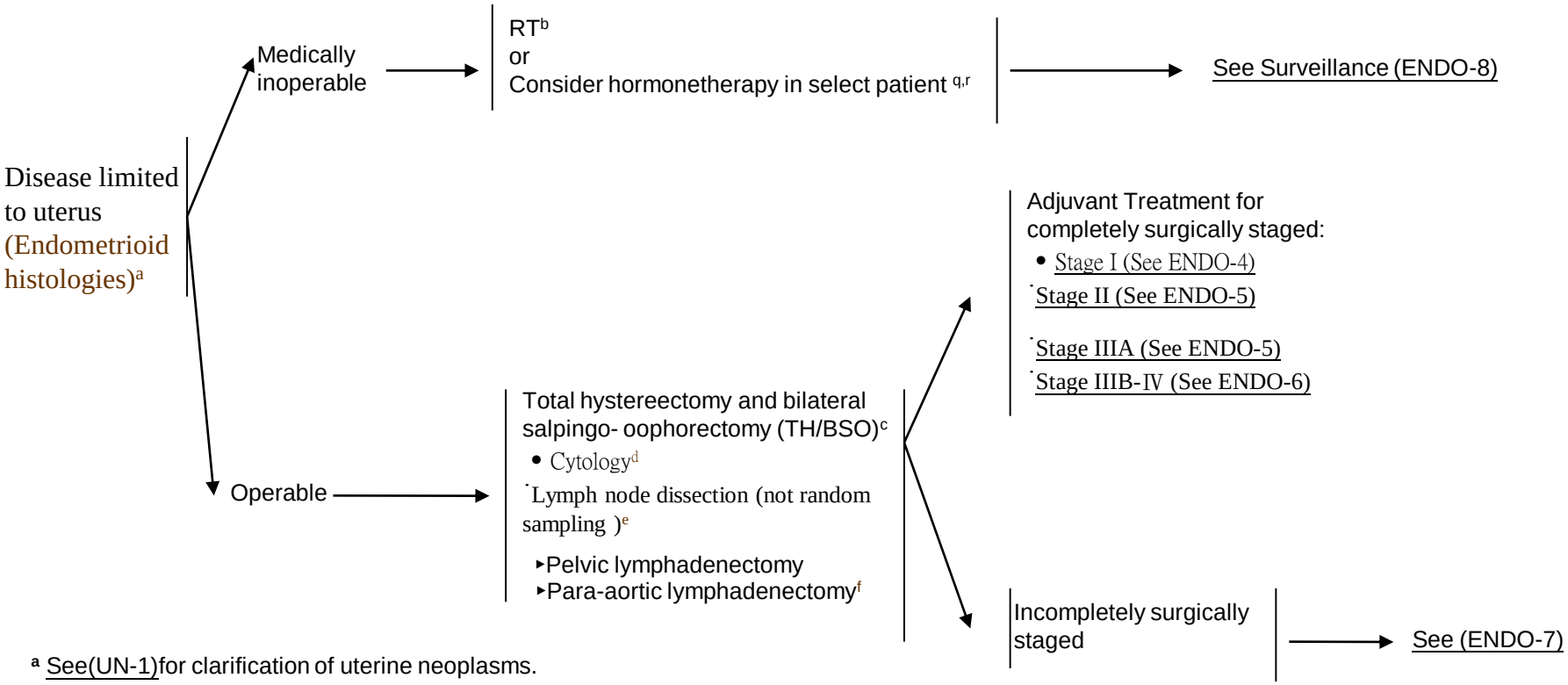


[a] Staged aggressive,should be treated as a high-grade endometrial cancer.

[b] Also known as malignant mixed mesodermal tumor or malignant mixed Mullerian tumor and including those with either homologous or heterologous stromal elements..

INITIAL CLINICAL FINDINGS **PRIMARY TREATMENT**



[a] See(UN-1)for clarification of uterine neoplasms.

[b] See Principles of Radiation Therapy (UN-A).

[c] See Hysterectomy (ENDO-A).

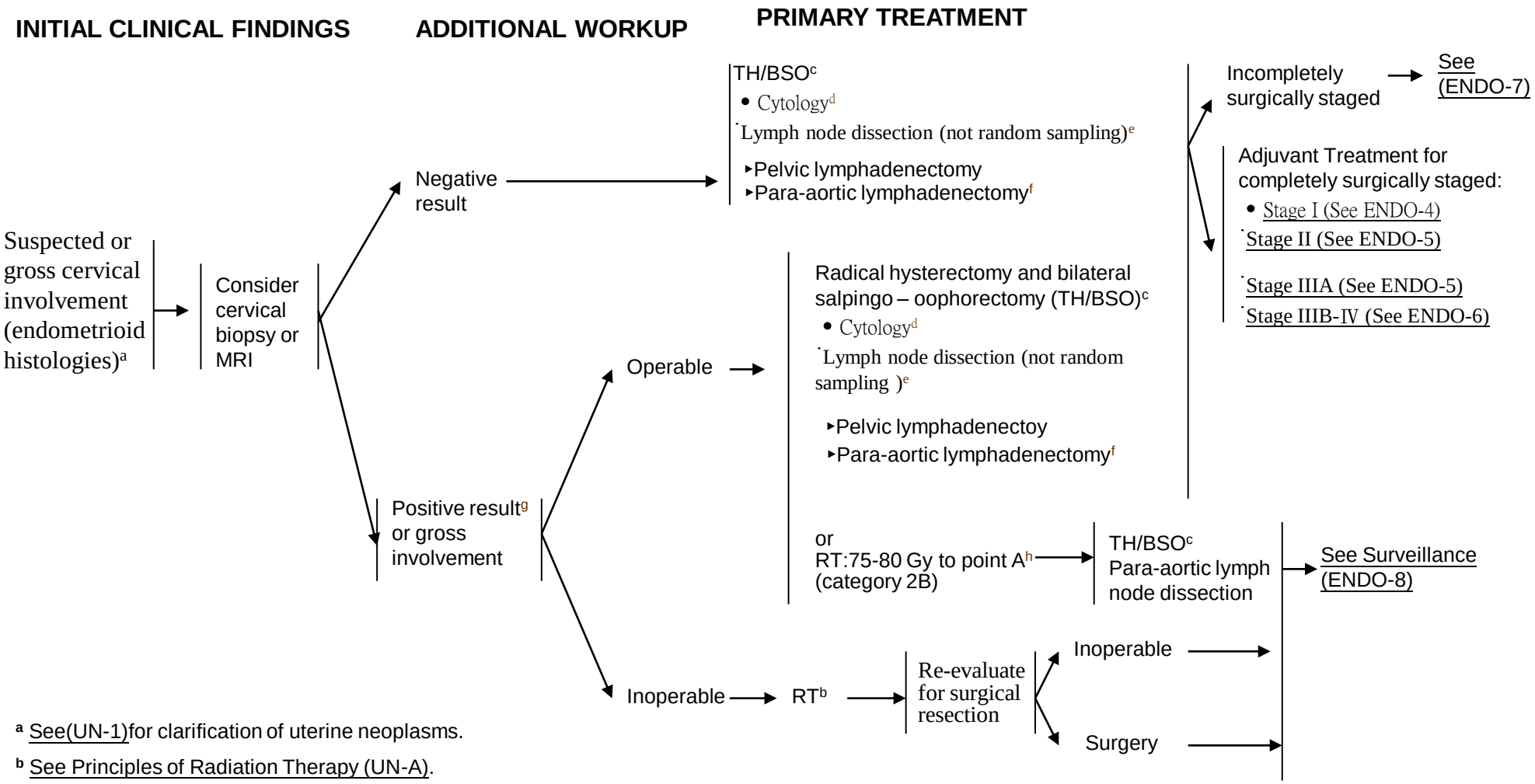
[d]Althought peritoneal cytology by itself does not affect 2009 FIGO staging, cytology results should still be obtained and recorded.

[e] American College of Obstetricians and Gynecologists practice bulletin, clinical management guidelines for obstetrician-gynecologists, number 65,August 2005:management of endomerial cancer. Obstet Gynecol 2005 Aug;106;413-425.

[h] See Discussion for routine lymphadenectomy.

[f]A complete para-aortic lymphadenectomy would includes nodes up to the renal vessel.

[r] Some patients may not be candidates for lymph node dissection.



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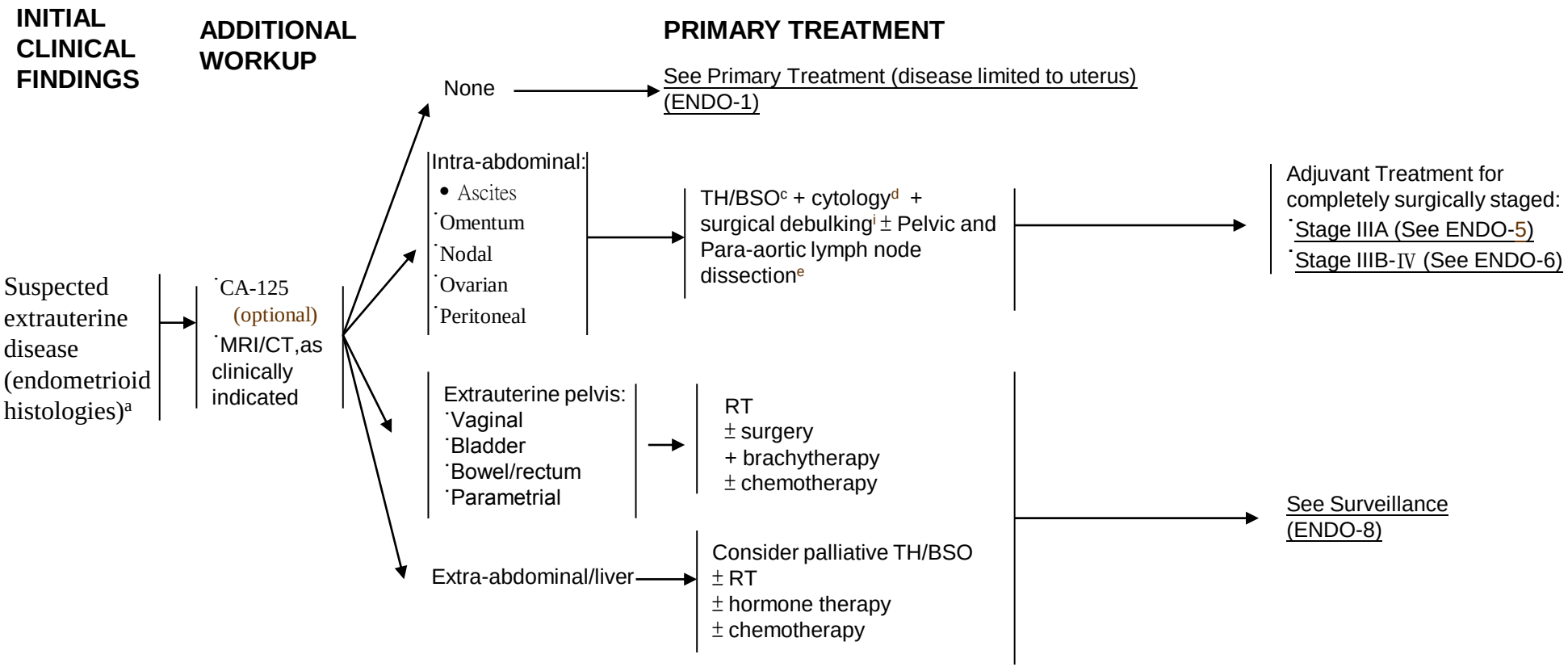
[f] A complete para-aortic lymphadenectomy would includes nodes up to the renal vessel.

[h] Based on summation of conventional external-beam fractionation and low-dose-rate brachytherapy equivalent.



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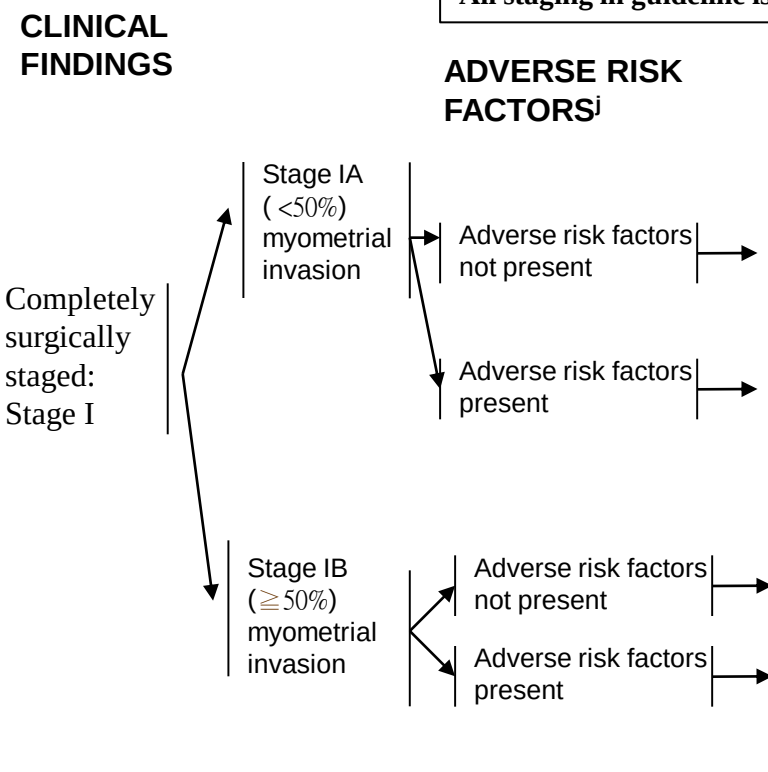
[e] American College of Obstetricians and Gynecologists practice bulletin, clinical management guidelines for obstetrician-gynecologists, number 65,August 2005:management of endometrial cancer. Obstet Gynecol 2005 Aug;106;413-425.

[i] The surgical goal is to have no measurable residual disease.

All staging in guideline is based on updated 2009 FIGO staging. (See ST-1)



HISTOLOGIC GRADE/ADJUVANT TREATMENT[b,k]

	G1	G2	G3
Stage IA (<50%) myometrial invasion	Observe	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy
Stage IA (<50%) myometrial invasion	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy ± Pelvic RT (category 2B for pelvic RT)	Observe or Vaginal brachytherapy ± Pelvic RT
Stage IB (≧50%) myometrial invasion	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy	Observe or Vaginal brachytherapy ± Pelvic RT
Stage IB (≧50%) myometrial invasion	Observe or Vaginal brachytherapy ± Pelvic RT	Observe or Vaginal brachytherapy ± Pelvic RT	Observe or Vaginal brachytherapy ± Pelvic RT ± chemotherapy[l,m] (category 2B for chemotherapy)

[b] See Principles of Radiation Therapy (UN-A).

[j] Potential adverse risk factors include the following; Age≧60 y/o, positive lymphovascular invasion, tumor size ≧2 cm, lower uterine (cervical/ gandular) involvement.

[k] Adjuvant therapy determinations are made on the basis of risk factors.

[l] The role of adjuvant chemotherapy in invasive high-grade uterine confined disease is the subject of current studies (Creutzberg,CL Clinical Trial: Chemotherapy and Radiation Therapy Compared With Radiation Therapy Alone in Treating Patienta With High-Risk Stage I, Stage II, or Stage III Endometrial cancer; Clinical trial summary from the National Cancer Institute's PDQ® database.Study ID Numbers:CDR0000521447;CKTO-2006-04;ISRCTN14387080;CKTO-PORTEC-3;EU-20664--http://clinicaltrials.gov/ct/show/NCT00411138;jsessionid=2309E60C1051E921B4E2614F2BE708A4?order=9.Hogberg T, Rosenberg P, Kristensen G,et al.A randomized phase-III study on adjuvant treatment with radiation (RT)± chemotherapy (CT) in early-stage high-risk endometrial cancer(NSGO-EC-9501/EORTC55991)[abstract].J Clin Oncol 2007;25:5503).

[m] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

See Surveillance(ENDO-6)
第ENDO-4頁

All staging in guideline is based on updated 2009 FIGO staging. (See ST-1)

CLINICAL FINDINGS | **HISTOLOGIC GRADE/ADJUVANT TREATMENT[b,k,m]**

Completely surgically staged: Stage II[n] →

G1	G2	G3
Vaginal brachytherapy ± Pelvic RT	Pelvic RT +Vaginal brachytherapy	Pelvic RT +Vaginal brachytherapy ± chemotherapy[l,m] (category 2B for chemotherapy)

Completely surgically staged: Stage ⅢA →

G1	G2	G3
Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or Pelvic RT ± Vaginal brachytherapy	Chemotherapy ± RT or RT ± chemotherapy or Pelvic RT ± Vaginal brachytherapy	Chemotherapy ± RT or RT ± chemotherapy or Pelvic RT ± Vaginal brachytherapy

[b] See Principles of Radiation Therapy (UN-A).

[k] Adjuvant therapy determinations are made on the basis of risk factors.

[l]The role of adjuvant chemotherapy in invasive high-grade uterine confined disease is the subject of current studies (Creutzberg, CL Clinical Trial: Chemotherapy and Radiation Therapy Compared With Radiation Therapy Alone in Treating Patient With High-Risk Stage I, Stage II,or Stage III Endometrial cancer; Clinical trial summary from the National Cancer Institute's PDQ® database. Study ID Numbers:CDR0000521447;CKTO-2006-04;ISRCTN14387080;CKTO-PORTEC-3;EU-20664--http://clinicaltrials.gov/ct/show/NCT00411138;jsessionid=2309E60C1051E921B4E2614F2BE708A4?order=9.Hogberg T, Rosenberg P, Kristensen G,et al.A randomized phase-III study on adjuvant treatment with radiation (RT)± chemotherapy (CT) in early-stage high-risk endometrial cancer(NSGO-EC-9501/EORTC55991)[abstract].J Clin Oncol 2007;25:5503).

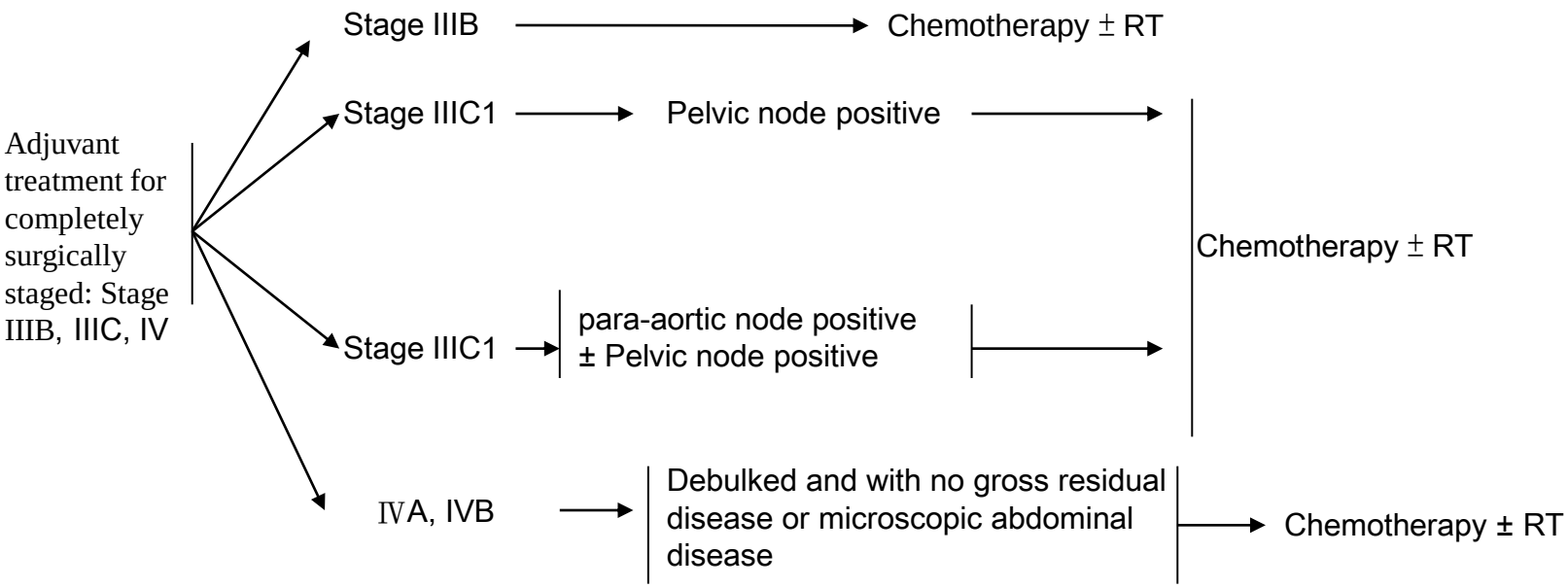
[m] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

See Surveillance(ENDO-8)
第ENDO-5頁

All staging in guideline is based on updated 2009 FIGO staging. (See ST-1)

CLINICAL FINDINGS

ADJUVANT TREATMENT [b,k,m]



[b] See Principles of Radiation Therapy (UN-A).

[i] The surgical goal is to have no measurable residual disease.

[k] Adjuvant therapy determinations are made on the basis of risk factors.

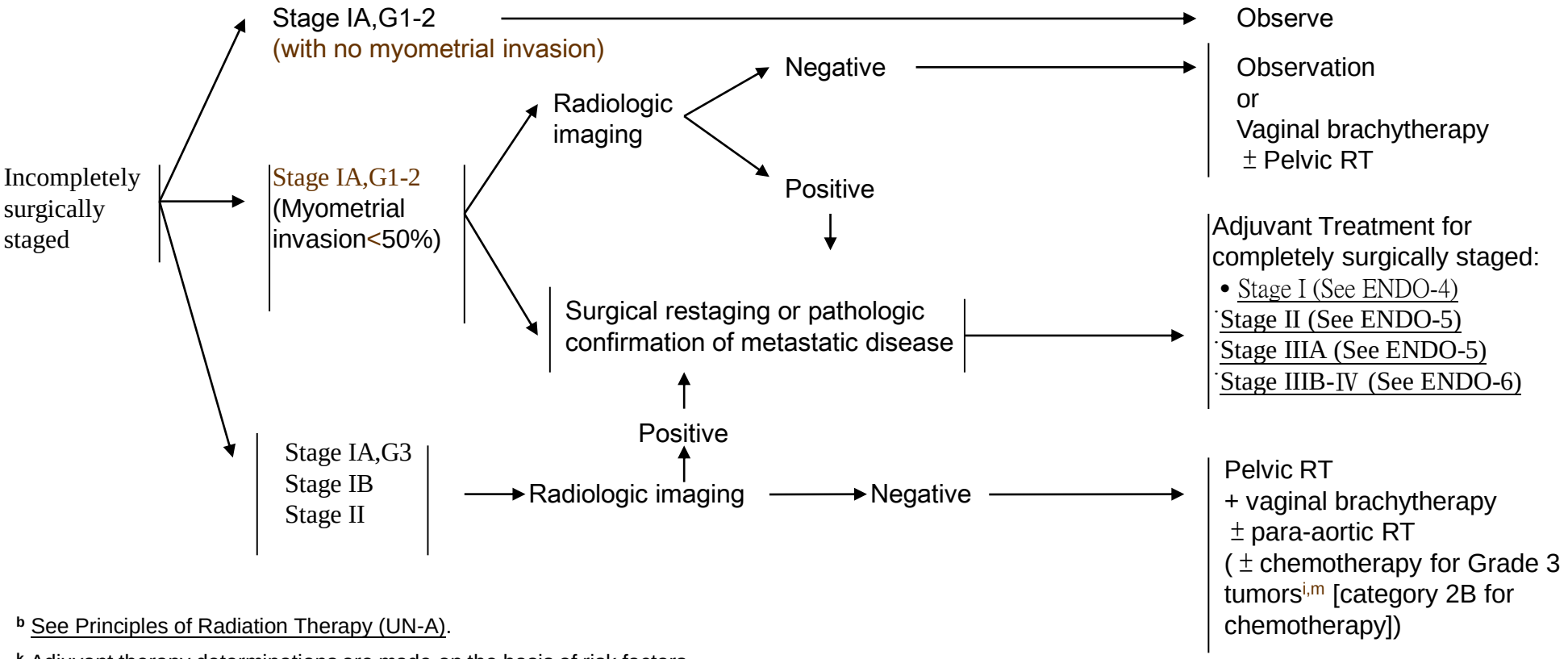
[m] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

See Surveillance(ENDO-8)
第ENDO-6頁

CLINICAL INTRAUTERINE FINDINGS

All staging in guideline is based on updated 2009 FIGO staging. (See ST-1)

ADJUVANT TREATMENT [b,k]



[b] See Principles of Radiation Therapy (UN-A).

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[m] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

See Surveillance(ENDO-8)
第ENDO-7頁

SURVEILLANCE

- Physical exam every 3-6 mo for 2y, then 6 mo or annually
- Vaginal cytology (category 3)
- Patient education regarding symptoms
- CA-125 (optional)
- Chest x-ray annually (category 2B)
- CT/MRI as clinically indicated

CLINICAL PRESENTATION

TREATMENT FOR RELAPSE

Local/ regional recurrence
- Negative distant metastases on radiologic imaging

→ Stage Therapy For Relapsy (ENDO-9)

Isolated metastases → Consider resection ± RT[b] → Unresectable or further recurrence → Treat as disseminated metastases (See below)

Disseminated metastases

Asymptomatic or Low grade → Hormonal therapy [m] → If progression, chemotherapy [m]

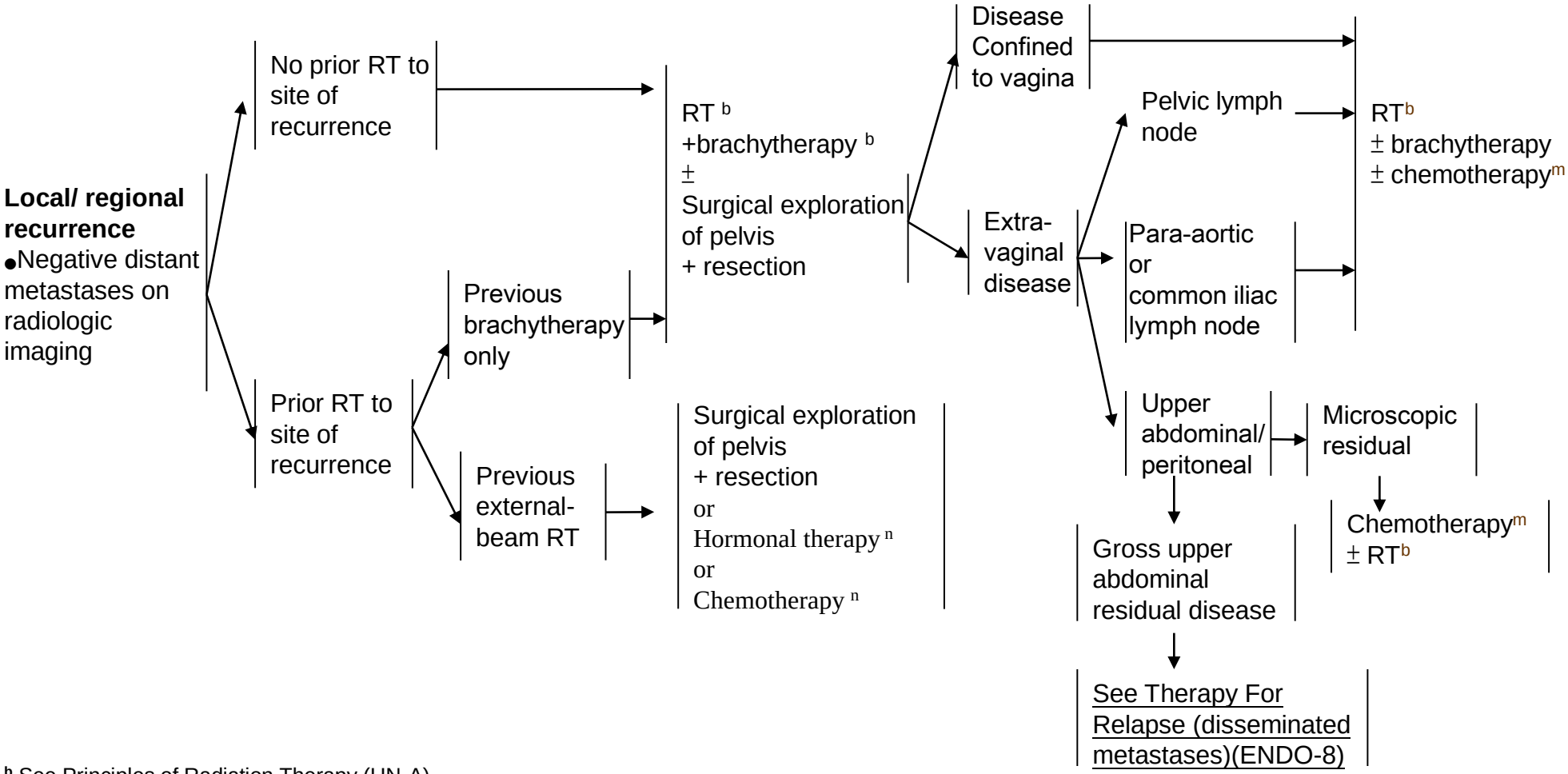
Symptomatic or Grade 2,3 Or Large volume → Chemotherapy [m] ± palliative RT[b]

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

[b] See Principles of Radiation Therapy (UN-A).

[m] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

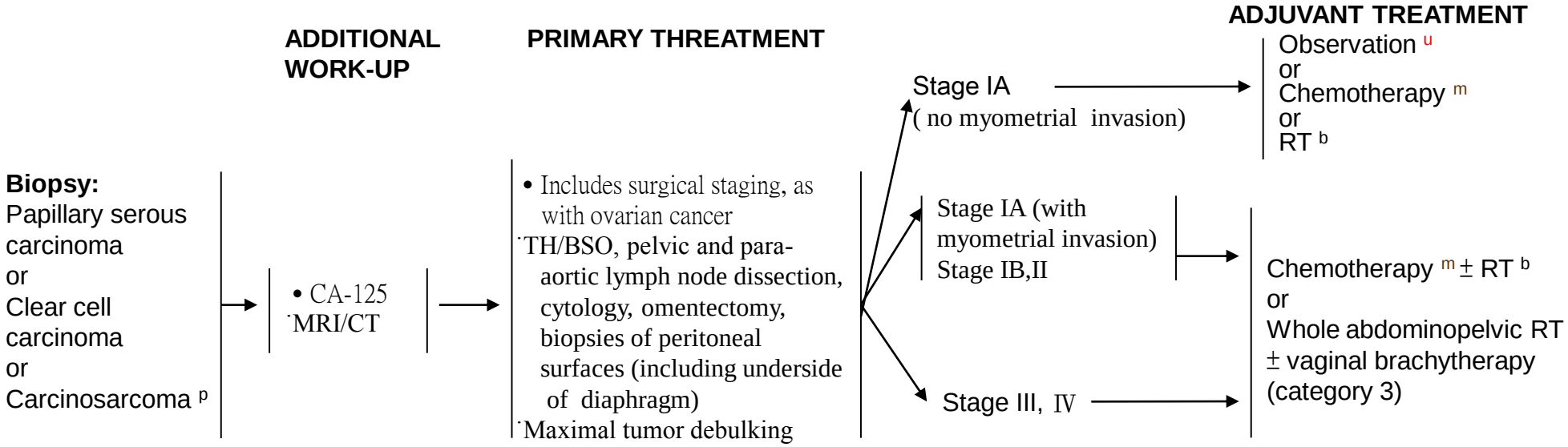
CLINICAL PRESENTATION | **TREATMENT FOR RELAPSE** | **ADDITIONAL TREATMENT**



[b] See Principles of Radiation Therapy (UN-A).

[m] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

PAPILLARY SEROUS OR CLEAR CELL CARCINOMA OF THE ENDOMETRIUM OR CARCINOSARCOMA [p]



See Surveillance(ENDO-8)
第ENDO-10頁

[b] See Principles of Radiation Therapy(UN-A).

[m] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

[p] Also known as malignant mixed mesodermal tumor or malignant mixed Müllerian tumor. Most carcinosarcomas are treated the same as poorly differentiated adenocarcinomas.

[u] Observation only for select patients with no residual disease in the hysterectomy specimen.

HYSTERECTOMY

TH/BSO: Total hysterectomy + bilateral salpingo-oophorectomy
RH: Radical hysterectomy

Pathology assessment to include:

- **Nodes**
  - Level of nodal involvement (pelvic, common iliac, para-aortic)

- **Peritoneal cytology**

- **Uterus**
  - Ratio of depth of myometrial/ stromal invasion to myometrial thickness
  - Cervical stromal or glandular involvement
  - Tumor size
  - Tumor location (fundus vs lower uterine segment/ cervix)
  - Histologic subtype with grade
  - Lymphovascular space invasion
  - Consider mismatch repair analysis to identify genetic problems

- **Fallopian tube/ ovares**

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believe that the best management of any cancer patient is in a clinical trial. Paticipation in clinical trials is especially encouraged.

SYSTEMIC THERAPY FOR RECURRENT, METASTATIC OR HIGH-RISK DISEASE (STRONGLY ENCOURAGE PARTICIPATION IN CLINICAL TRIALS)

HORMONAL THERAPY [1]

- Aromatase inhibitors
- Progestational agents
- Tamoxifen

CHEMOTHERAPY REGIMENS [2]

(Multi-agent chemotherapy regiments preferred, if tolerated)

- Cisplatin/ doxorubicin (category 1)
- Cisplatin/ doxorubicin/ paclitaxel (cash)(category 1)
- Ifosfamide plus paclitaxel (cash)(category 1 for carcinosarcoma)
- Carboplatin / paclitaxel (cash)
- Cisplatin
- Carboplatin
- Doxorubicin
- Paclitaxel (cash)
- Cisplatin/ ifosfamide (for carcinosarcoma)
- Ifosfamide

[1] Hormonal therapy is for endometrioid histologies only (ie, not for papillary serous carcinoma, clear cell carcinoma, or carcinosarcoma).

[2] Chemotherapy regiments are for endometrioid histoloies, papillary serous carcinoma, or clear cell carcinoma. A few of the agents can also be used for carcinosarcoma, as indicated.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believe that the best management of any cancer patient is in a clinical trial. Paticipation in clinical trials is especially encouraged.

PRINCIPLES OF RADIATION THERAPY

- Pelvic radiotherapy should target the gross disease (if present), the lower common iliacs, external iliacs, internal iliacs, parametrium, upper vagina, and presacral lymph nodes (in patients with cervical invilvement). Extended-field radiotherapy should include the pelvic volume and also target the entire common iliac chain and para-aortic lymph node region. The upper border of the extended field depends on the clinical situation but should at least be to the level of the renal vessels. External-beam doses for microscopic disease should be 45-50 Gy. Multiple conformal fields based on CT-treatment planning should be utilized.

- Brachytherapy doses for definitive therapy are individualized based on the clinical situation. For preoperative therapy in patients with gross stage IIB disease, in general, a total dose of 75-80 Gy low-dose rate equivalent to the tumor volume is recommended. For vaginal brachytherapy, the dose should be prescribed to the vaginal surface or at a depth of 0.5 cm from the vaginal surface; the dose depends on the use of EBRT.
  - The target for vaginal brachytherapy after hysterectomy should be limited to the upper vagina.
  - For high-dose rate brachytherapy, when used as a boost to EBRT, dose of 5-6 Gy × 2 fractions prescribed to the vaginal mucosa are commonly used.
  - For high-dose of 0.5 cm from the vaginal brachytherapy alone, commonly used regimens include 7 Gy × 3 prescribed at a depth of 0.5 cm from the vaginal surface or 6 Gy × 5 fractions prescribed to the vaginal surface.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believe that the best management of any cancer patient is in a clinical trial. Paticipation in clinical trials is especially encouraged.

Staging

Table 1
International Federation of Gynecology and Obstetrics (FIGO) and Tumor-Node-Metastases (TNM) Surgical Staging Systems for Endometrial Cancer*

FIGO Stage	Surgical-Pathologic Findings	TNM Categories
		Primary Tumor (T)
	Primary tumor cannot be assessed	TX
	No evidence of primary tumor	T0
0	Carcinoma in situ (preinvasive carcinoma)	Tis
I	Tumor confined to the corpus uteri	T1
IA	Tumor limited to endometrium	T1a
IB	Tumor invades one half or less of the myometrium	T1b
IC	Tumor invades more than one half of the myometrium	T1c
II	Tumor invades cervix but dose not extend beyound uterus	T2
IIA	Endocervical glandular involvement only	T2a
IIB	Cervical stromal invasion	T2b
III	Local and/or regional spread as specified in IIIA,B,C	T3 and/or N1
IIIA	Tumor involves serosa and/or adnexa (direct extension or metastasis) and/or cancer cells in ascites or peritoneal washings	T3a
IIIB	Vaginal involvement (direct extension or metastasis)	T3b
IIIC	Metastasis to pelvic and/or para-aortic lymph nodes	T3c
IVA	Tumor invades bladder mucosa and/or bowl mucosa (the presence of bullous edema is not sufficient to classify tumor T4)	T4
IVB	Distant metastasis (excluding metastasis to vagina, pelvic serosa, or adnexa; including metastasis to intra-abdominal lymph nodes other than para-aortic and/or inquinal lymph node)	M1

Regional Lymph Nodes (N)
- Nx Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis

Distant metastasis (M)
- Mx Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis

*Reprinted form: Benedet JL, Bender H, Jones H 3rd, et al. FIGO staging classifications and clinical practice guidelines in the management of gynecologic centers. FIGO Committee on Gynecologic Oncology. Int J Gynaecol Obstet 2000;70:209-262. Copyright2000, with permission from International Federation of Gynecology and Obstetrics .

update

NCCN最新乳癌最新指引是2013 V.1，之前本院參考版本是2012 V.2，有將修改處用紅色標記出來。

【UN-1頁】之「INITIAL EVALUATION」有修改一項目『Fourth bullet: “Chest x-ray” changed to “Chest imaging”』。

【UN-1頁】之Second column: “Pathology review” changed to “Expert pathology review”。

【ENDO-2頁】，改成Inoperable pathway; After “RT”:The following recommendations were added, “Re-evaluate for surgical resection”.Operable patients would then have surgery followed by surveillance; inoperable patients would undergo surveillance.。

【ENDO-8頁】 Surveillance改成; Second bullet: The recommendation “Vaginal cytology every 6 mo for 2 y; then annually (category 2B)” changed to “Vaginal cytology (category)。

【ENDO-10頁】，Papillary Serous or Clear Cell Carcinoma of the Endometrium or Carcinosarcoma改成

- Fourth column; Third row: “(adequately debulked)” was removed from Stage III, IV. The “Stage III, IV (inadequately debulked)” pathway was removed.
- Adjuvant treatment for Stage IA (no myometrial invasion): A new footnote “u” was added to Observe that states, “Observation only for select patients with no residual disease in the hysterectomy specimen”。