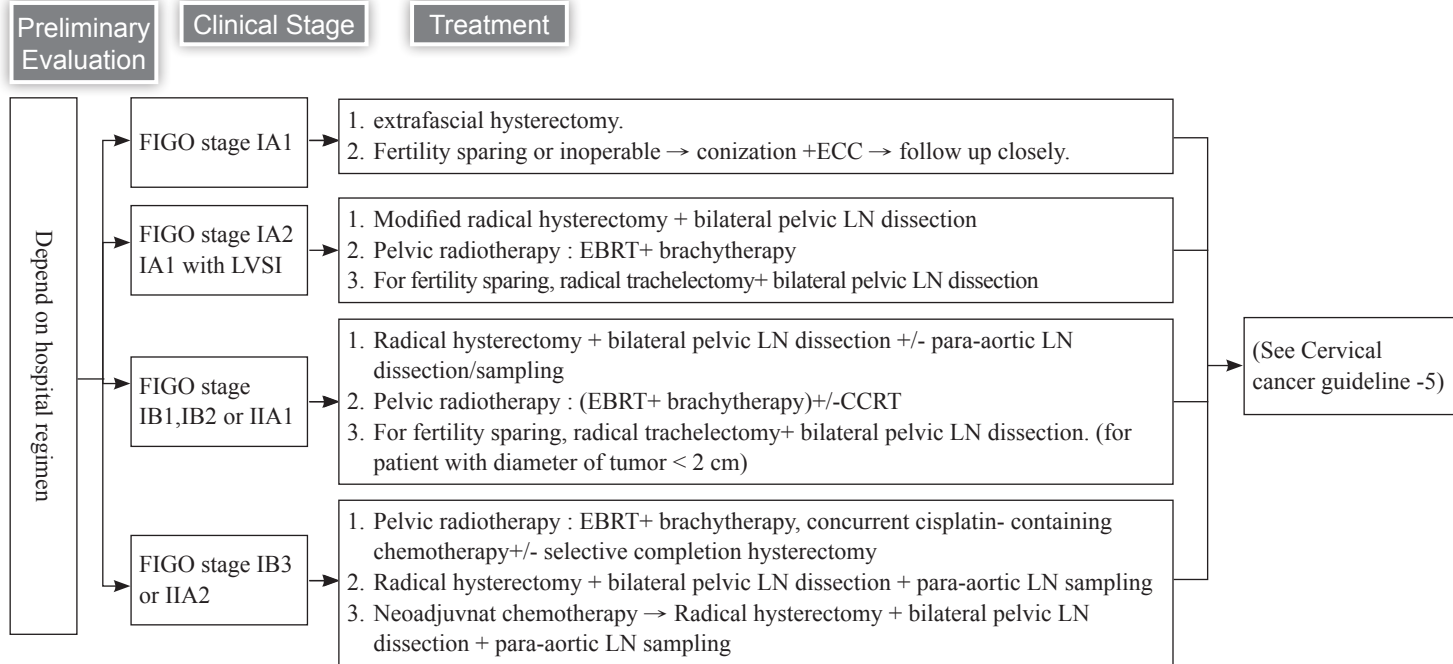


The background features a light gray gradient with several overlapping geometric shapes. A large, light gray diamond is centered, with a smaller, darker gray diamond to its left. A white diamond is also present, overlapping the light gray one. In the corners, there are faint, semi-transparent circles. The text is centered within the white diamond.

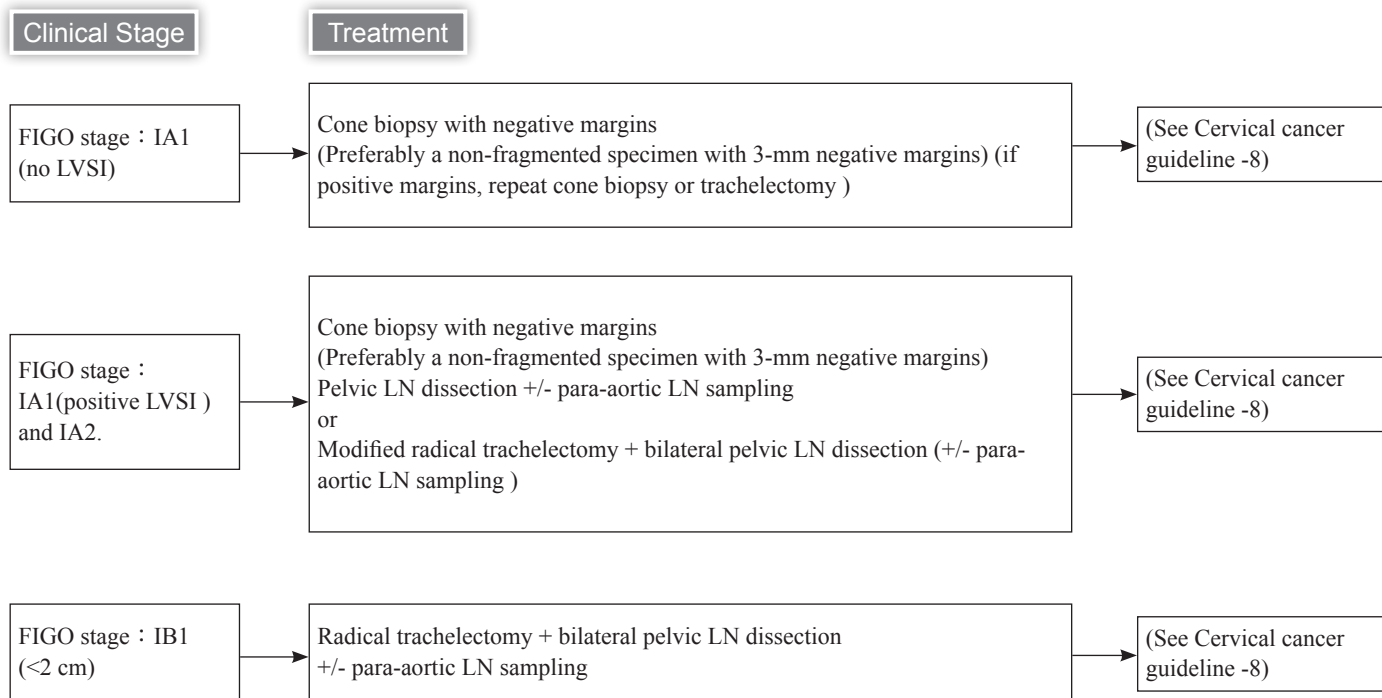
# **Gynecologic Cancers**

# 《 Cervical cancer guideline-1 》

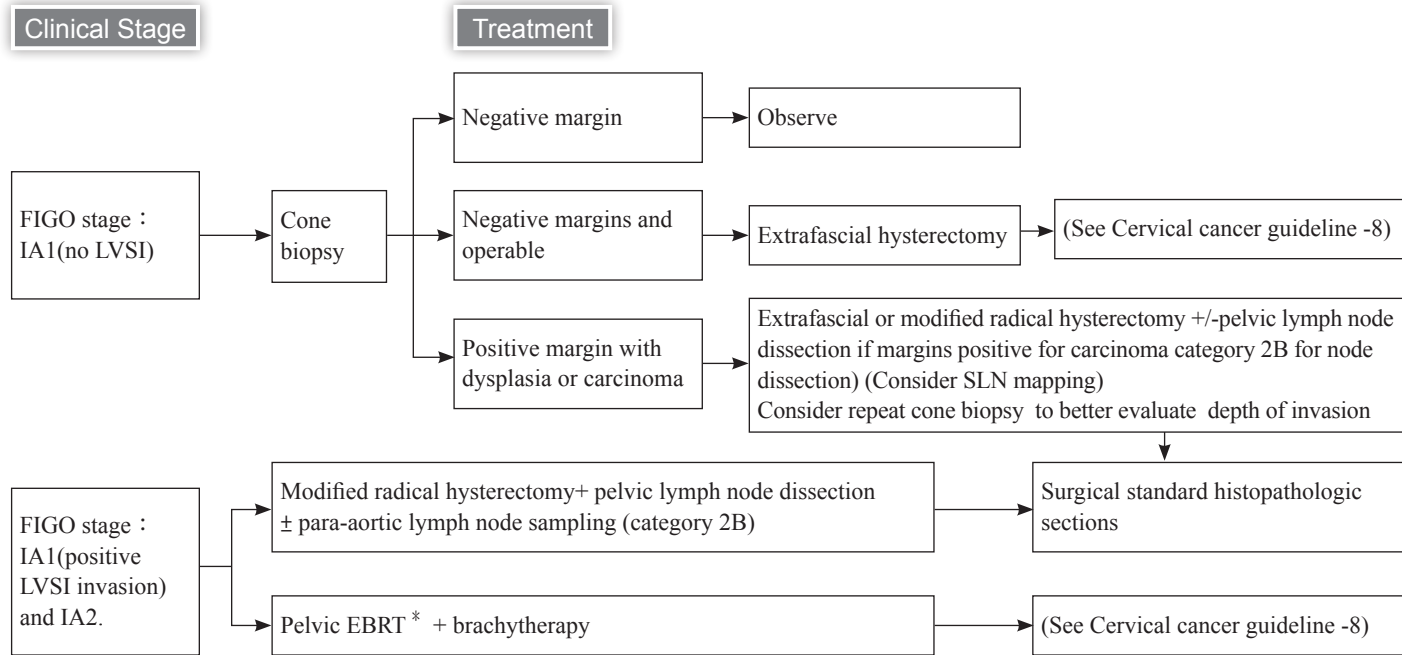


Note: Cervical cancer is diagnosed as adenocarcinoma or squamous cell carcinoma , Because of the high degree of malignancy and poor prognosis, if surgery is suitable, the tumor should be removed as much as possible after imaging evaluation. Postoperative radiotherapy or simultaneous chemoradiation or systemic therapy will be given depending on the situation

## 《 Cervical cancer guideline-2 (Fertility considerations) 》



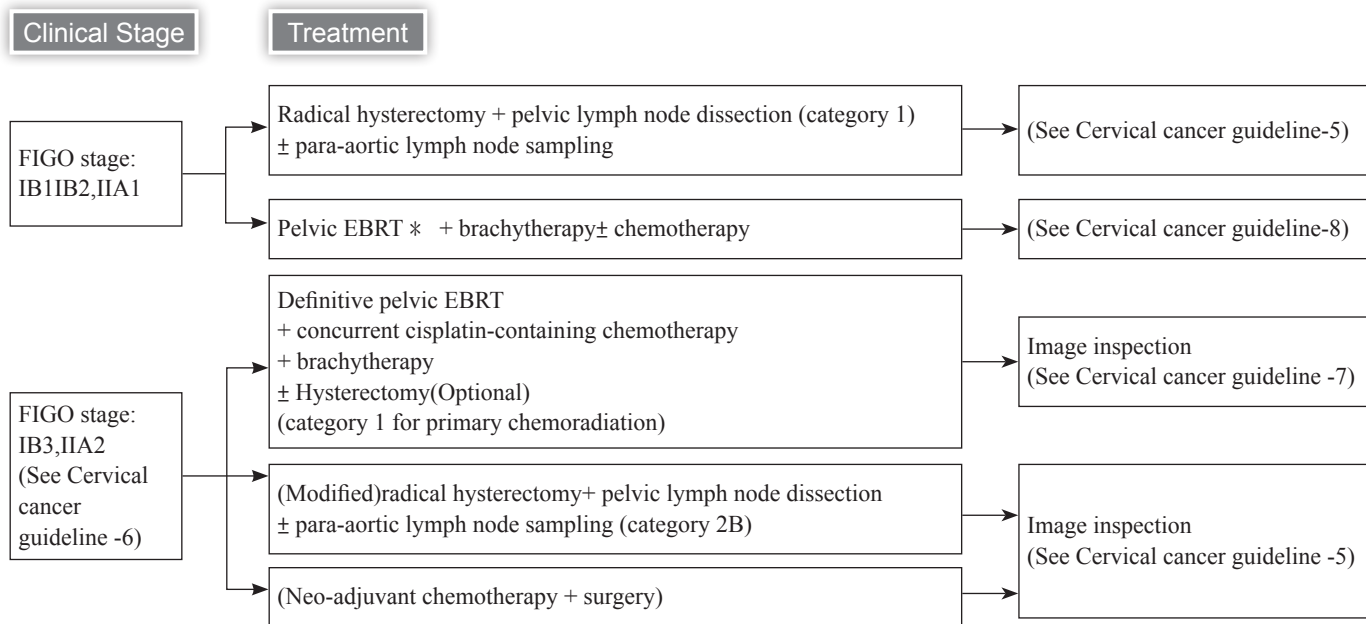
## 《 Cervical cancer guideline -3 (No Fertility considerations) 》



Note : New bullets added - Select patients with Stage IA2-IB1 disease based on cone biopsy and who meet all the conservative surgery criteria listed below, may be treated with conization or simple hysterectomy with bilateral pelvic lymphadenectomy or sentinel node mapping:

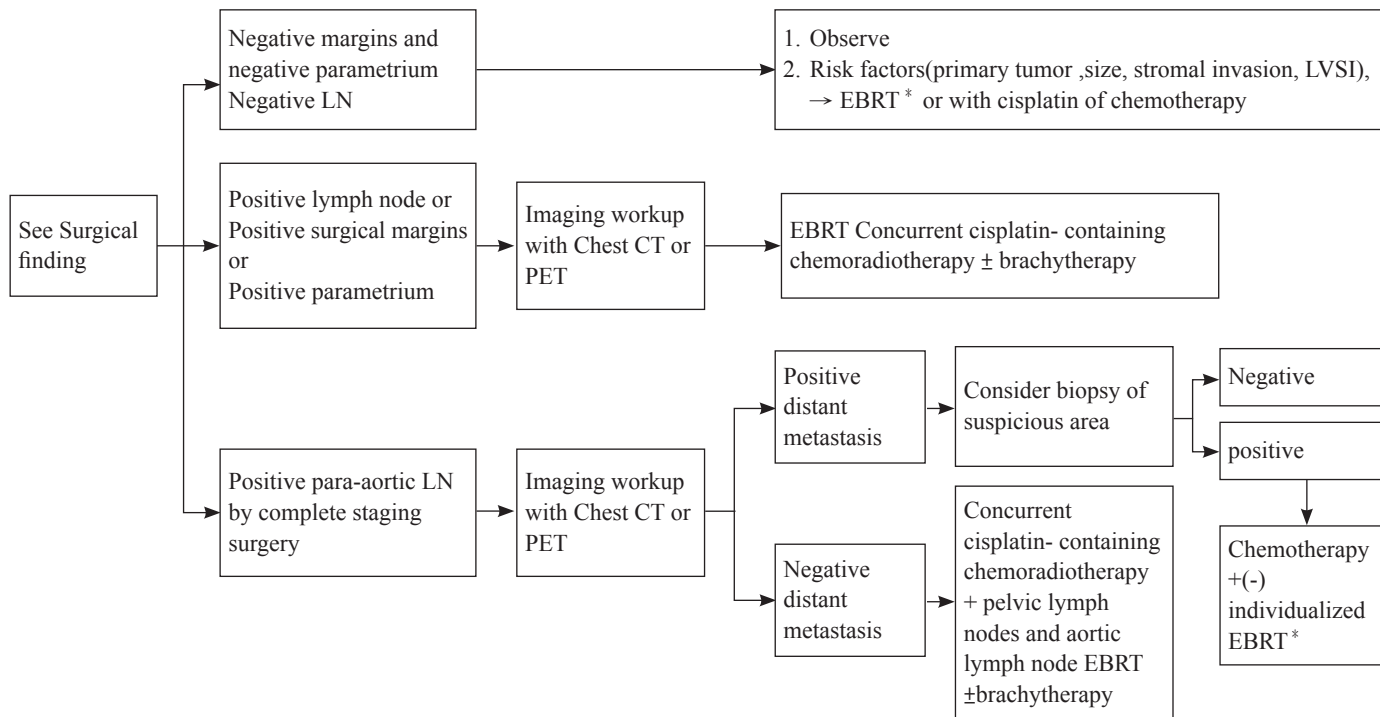
- 1.No LVSI
- 2.Negative cone margins
- 3.Squamous cell (any grade) or usual type adenocarcinoma (grade 1 or 2 only)
- 4.Tumor size ≤ 2 cm
- 5.Depth of invasion ≤ 10 mm
6. Negative imaging for metastatic disease

## 《 Cervical cancer guideline -4 (No Fertility considerations) 》



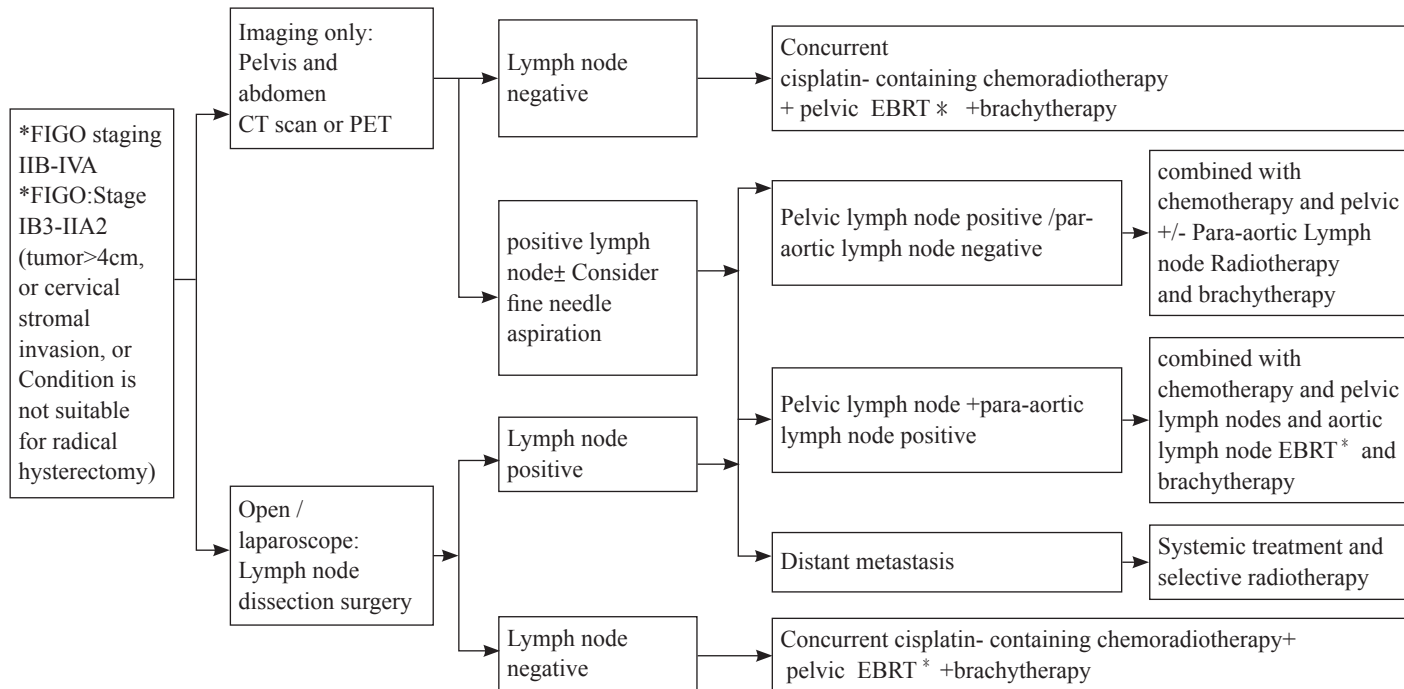
Note: Cervical cancer is diagnosed as adenocarcinoma or squamous cell carcinoma , Because of the high degree of malignancy and poor prognosis, if surgery is suitable, the tumor should be removed as much as possible after imaging evaluation. Postoperative radiotherapy or simultaneous chemoradiation or systemic therapy will be given depending on the situation

## 《 Cervical cancer guideline -5 》



## 《 Cervical cancer guideline-6 》

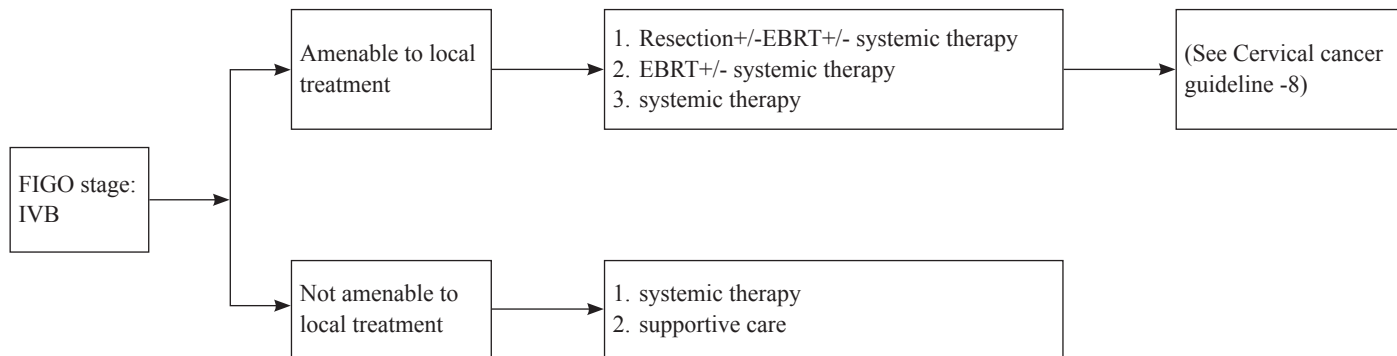
- ◆ radiation therapy, including in vitro radiotherapy and adjuvant therapy
- ◆ squamous cell carcinoma with cisplatin containing chemotherapy; non-squamous cell carcinoma can be used different from cisplatin chemotherapy drugs



## 《 Cervical cancer guideline-7 》

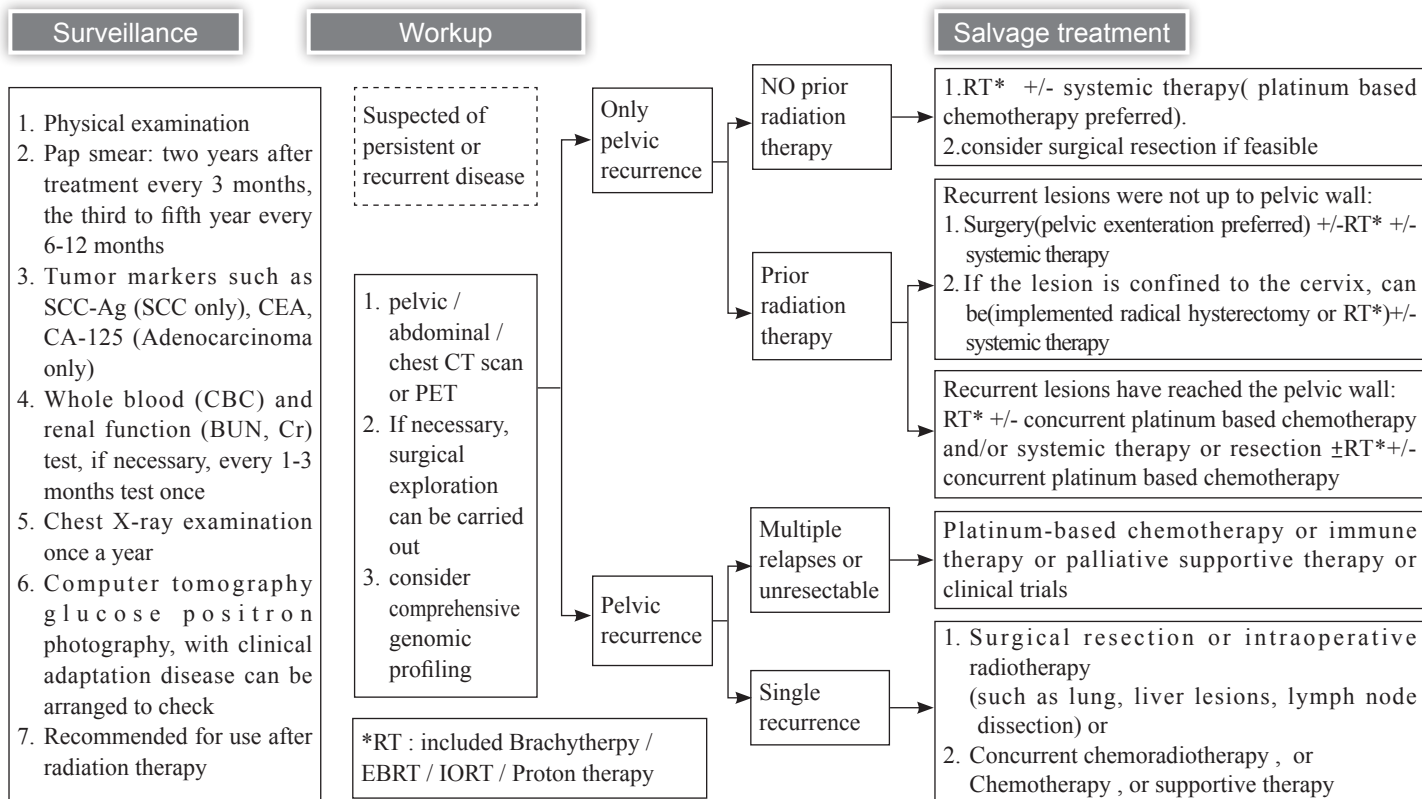
Clinical stage

Treatment





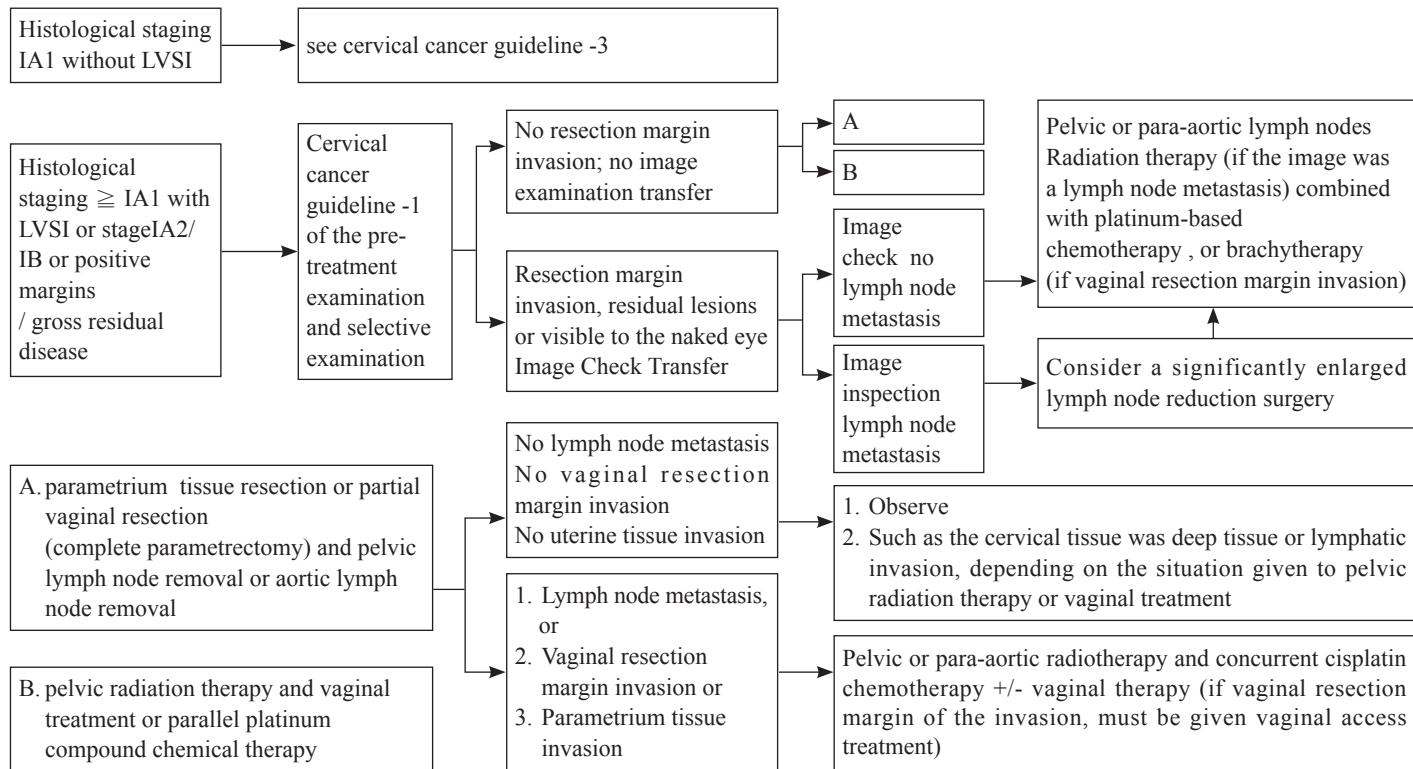
## 《 Cervical cancer guideline-8 》



SYSTEMIC THERAPY FOR CERVICAL CANCER<sup>a</sup>

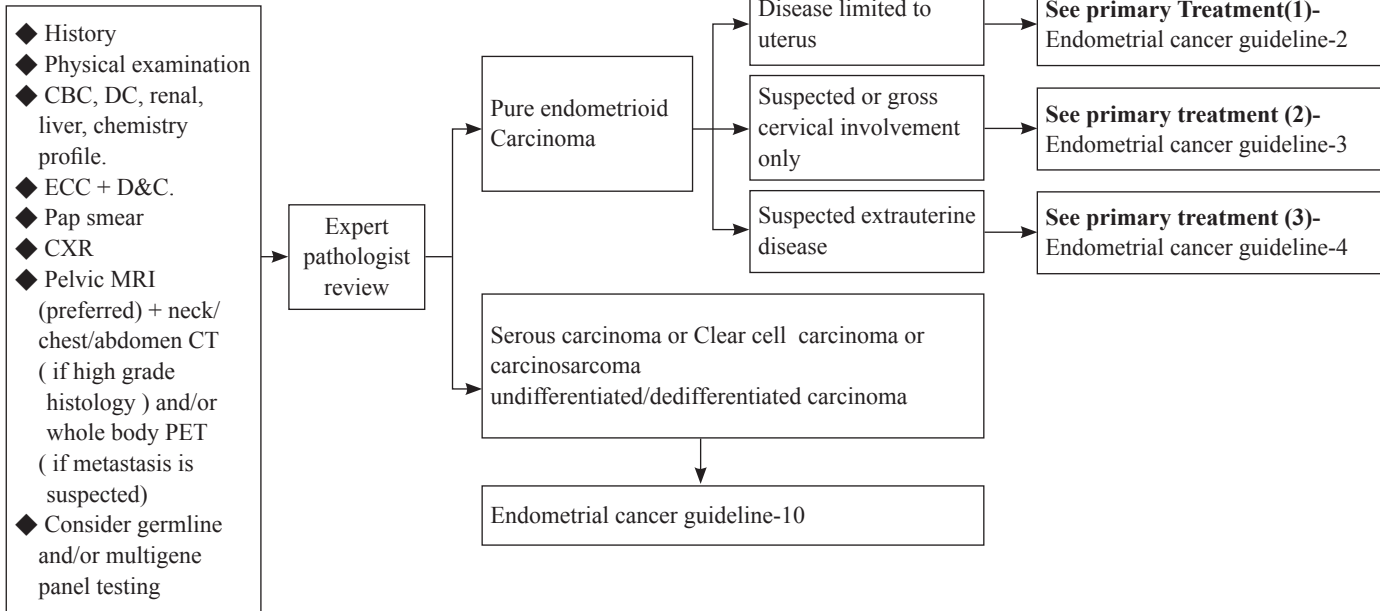
Squamous Cell Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma		
Chemoradiation <sup>b</sup>	Recurrent or Metastatic Disease	
	First-line Therapy <sup>b,d</sup>	Second-line or Subsequent Therapy <sup>i</sup>
<p><b>Preferred Regimens</b></p> <ul style="list-style-type: none"> <li>• Cisplatin</li> <li>• Carboplatin if patient is cisplatin intolerant</li> </ul> <p><b>Other Recommended Regimens<sup>c</sup></b>  <b>(if cisplatin and carboplatin are unavailable)</b></p> <ul style="list-style-type: none"> <li>• Capecitabine/mitomycin<sup>1</sup></li> <li>• Gemcitabine<sup>2</sup></li> <li>• Paclitaxel<sup>3,4</sup></li> </ul>	<p><b>Preferred Regimens</b></p> <ul style="list-style-type: none"> <li>• PD-L1–positive tumors           <ul style="list-style-type: none"> <li>▶ Pembrolizumab + cisplatin/paclitaxel ± bevacizumab (category 1)<sup>e,f,g,h,5</sup></li> <li>▶ Pembrolizumab + carboplatin/paclitaxel ± bevacizumab (category 1)<sup>e,f,g,h,5</sup></li> </ul> </li> <li>• Cisplatin/paclitaxel/bevacizumab<sup>e,h,6</sup> (category 1)</li> <li>• Carboplatin/paclitaxel/bevacizumab<sup>e,h</sup></li> </ul> <p><b>Other Recommended Regimens</b></p> <ul style="list-style-type: none"> <li>• Cisplatin/paclitaxel (category 1)<sup>7,8</sup></li> <li>• Carboplatin/paclitaxel<sup>9,10</sup> (category 1 for patients who have received prior cisplatin therapy)</li> <li>• Topotecan/paclitaxel/bevacizumab<sup>e,h,6,11</sup> (category 1)</li> <li>• Topotecan/paclitaxel<sup>11</sup></li> <li>• Cisplatin/topotecan<sup>11</sup></li> <li>• Cisplatin<sup>8</sup></li> <li>• Carboplatin<sup>12,13</sup></li> </ul>	<p><b>Preferred Regimens</b></p> <ul style="list-style-type: none"> <li>• Pembrolizumab for TMB-H tumors<sup>f,j</sup> or PD-L1–positive<sup>9</sup> or MSI-H/dMMR tumors<sup>f,14</sup></li> <li>• Tisotumab vedotin-tftv<sup>15</sup></li> <li>• Cemiplimab<sup>f,16</sup></li> </ul> <p><b>Other Recommended Regimens</b></p> <ul style="list-style-type: none"> <li>• Bevacizumab<sup>9</sup></li> <li>• Paclitaxel<sup>13,17</sup></li> <li>• Albumin-bound paclitaxel</li> <li>• Docetaxel</li> <li>• Fluorouracil</li> <li>• Gemcitabine</li> <li>• Pemetrexed</li> <li>• Topotecan</li> <li>• Vinorelbine</li> <li>• Irinotecan</li> </ul> <p><b>Useful in Certain Circumstances</b></p> <ul style="list-style-type: none"> <li>• PD-L1–positive tumors           <ul style="list-style-type: none"> <li>▶ Nivolumab<sup>f,9,18</sup></li> </ul> </li> <li>• HER2-positive tumors (IHC 3+ or 2+)           <ul style="list-style-type: none"> <li>▶ Fam-trastuzumab deruxtecan-nxki<sup>19</sup></li> </ul> </li> <li>• RET gene fusion-positive tumors           <ul style="list-style-type: none"> <li>▶ Selpercatinib</li> </ul> </li> <li>• <i>NTRK</i> gene fusion-positive tumors           <ul style="list-style-type: none"> <li>▶ Larotrectinib</li> <li>▶ Entrectinib</li> </ul> </li> </ul>

## 《 Cervical cancer guideline-9(Invasive cancer found only after hysterectomy) 》



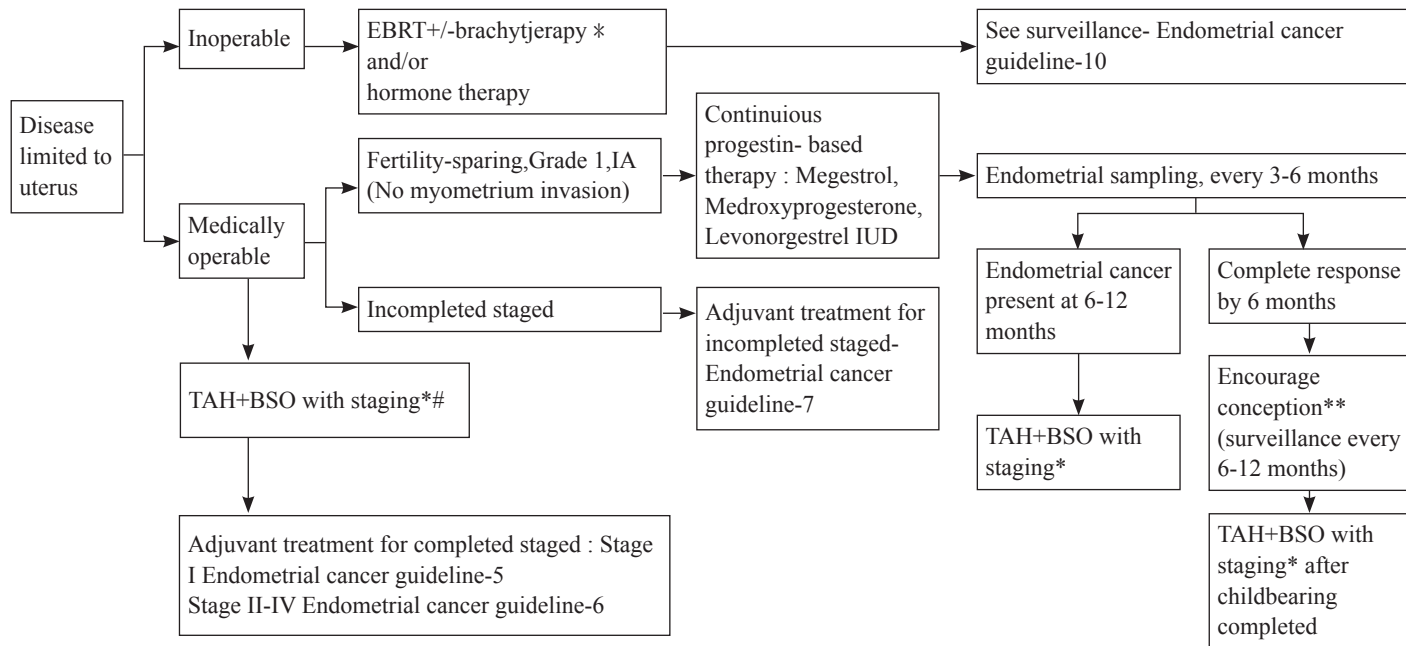
## 《 Endometrial cancer guideline -1 》

### Preliminary evaluation



## 《 Endometrial cancer guideline -2 》

### Primary treatment (1)



\* TAH+ BSO with completed staging : total hysterectomy , bilateral salpingo-oophorectomy 、 pelvic LN +/- para-aortic LN dissection 、 washing /ascites cytology.

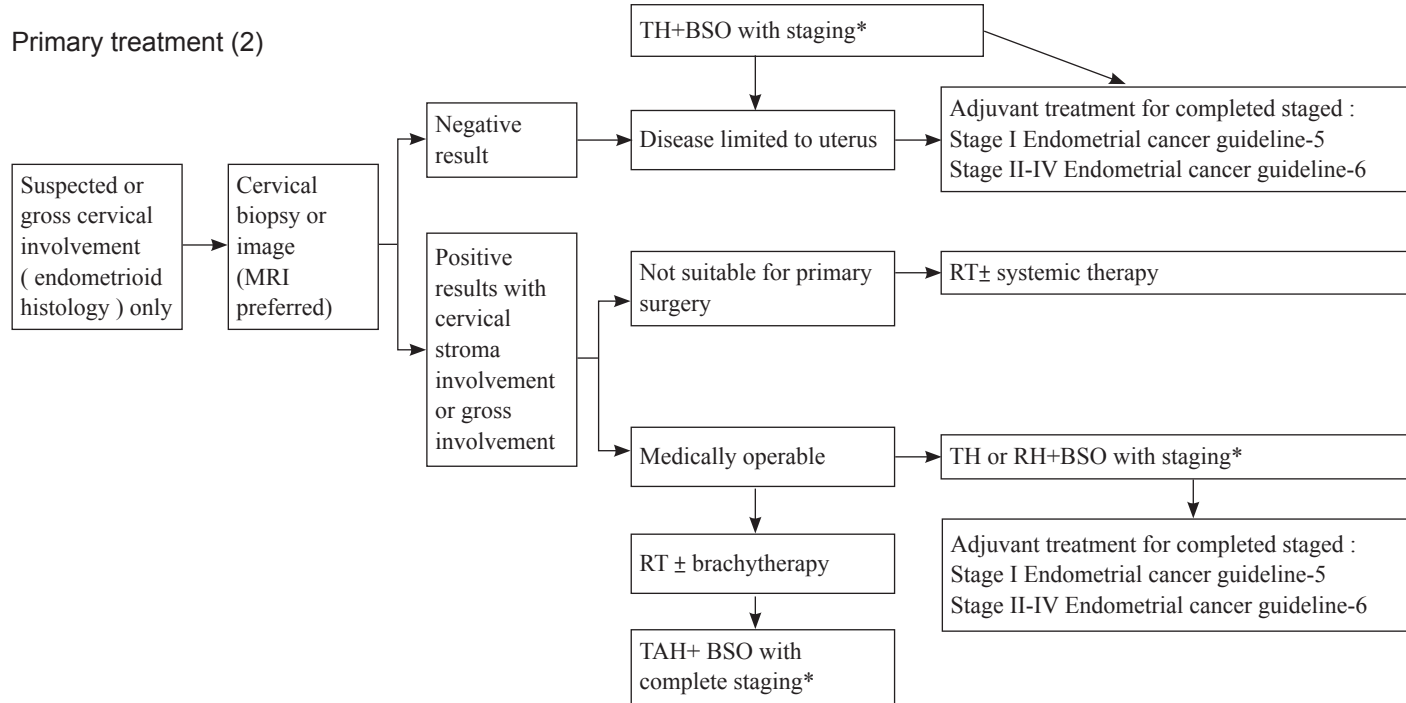
\* EBRT(External Beam Radiation Therapy)

# Ovarian preservation maybe safe in select premenopausal women with early stage endometrial cancer. Salpingectomy is Preferred.

\*\* Endometrial sampling every 6month and progestin-based therapy are recommended if patient is not in the active process of trying to conceive.

## 《 Endometrial cancer guideline-3 》

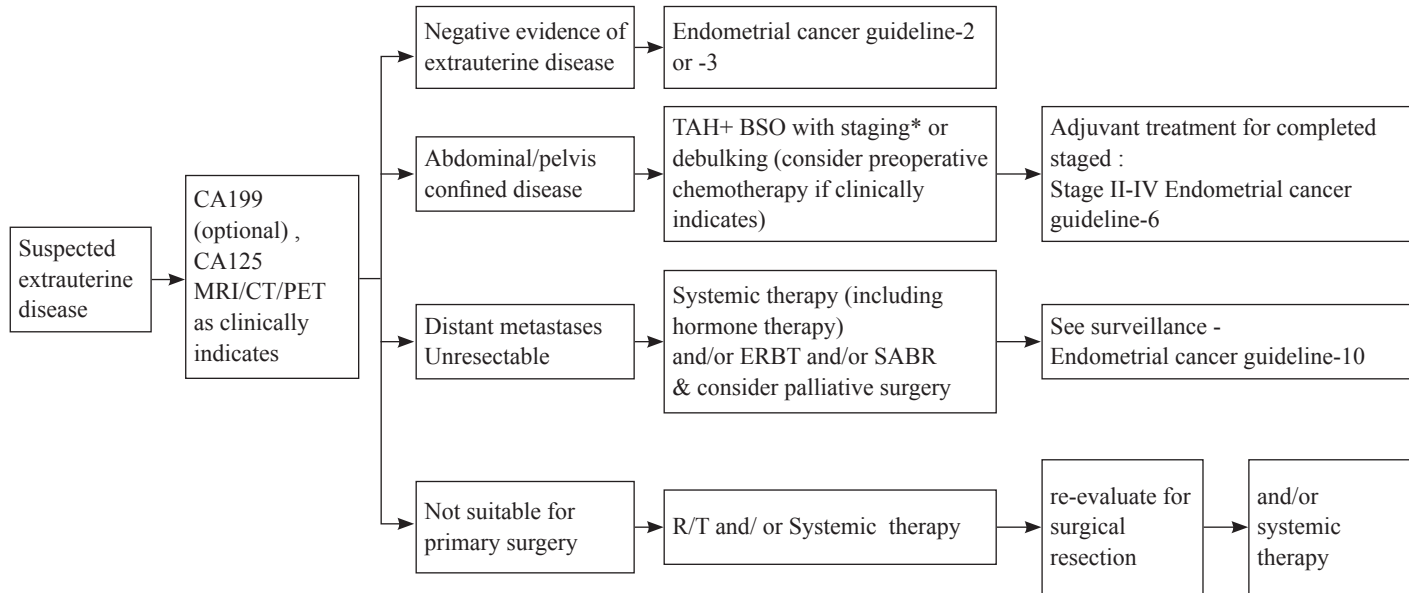
### Primary treatment (2)



\* TAH+BSO with staging : total hysterectomy , bilateral salpingo-oophorectomy 、 pelvic LN +/- para-aortic LN dissection 、 washing /ascites cytology.

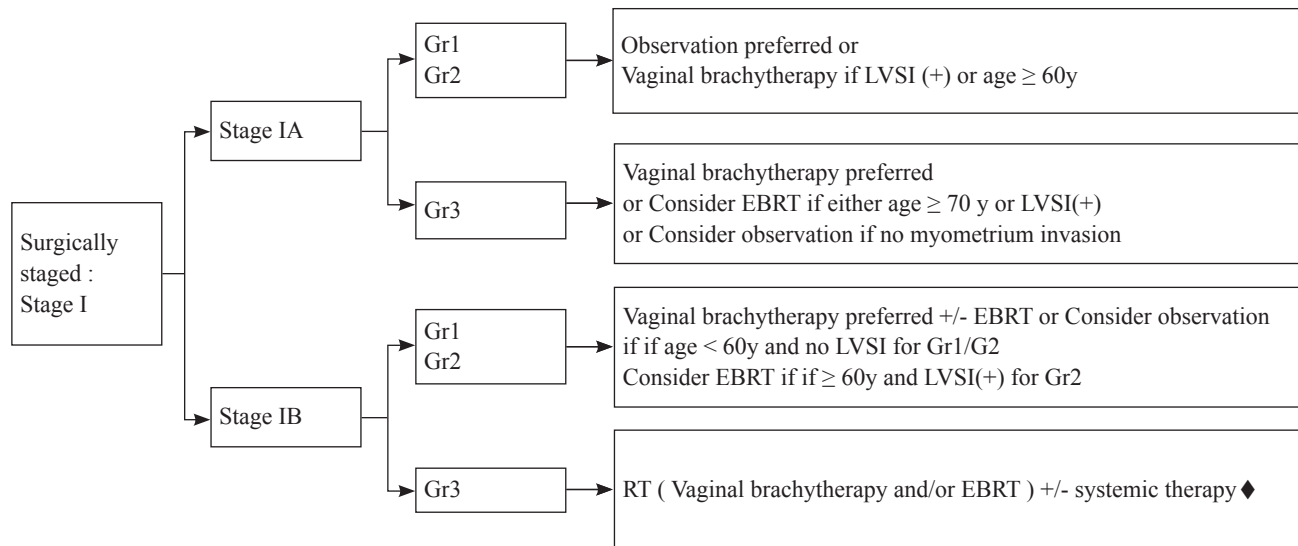
## 《 Endometrial cancer guideline-4 》

### Primary treatment (3)



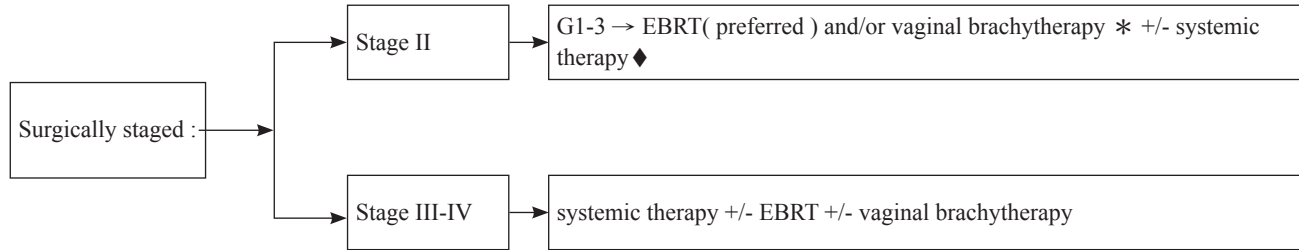
\* TAH+BSO with staging : total hysterectomy , bilateral salpingo-oophorectomy 、 pelvic LN +/- para-aortic LN dissection 、 washing /ascites cytology.

## 《 Endometrial cancer guideline-5 》





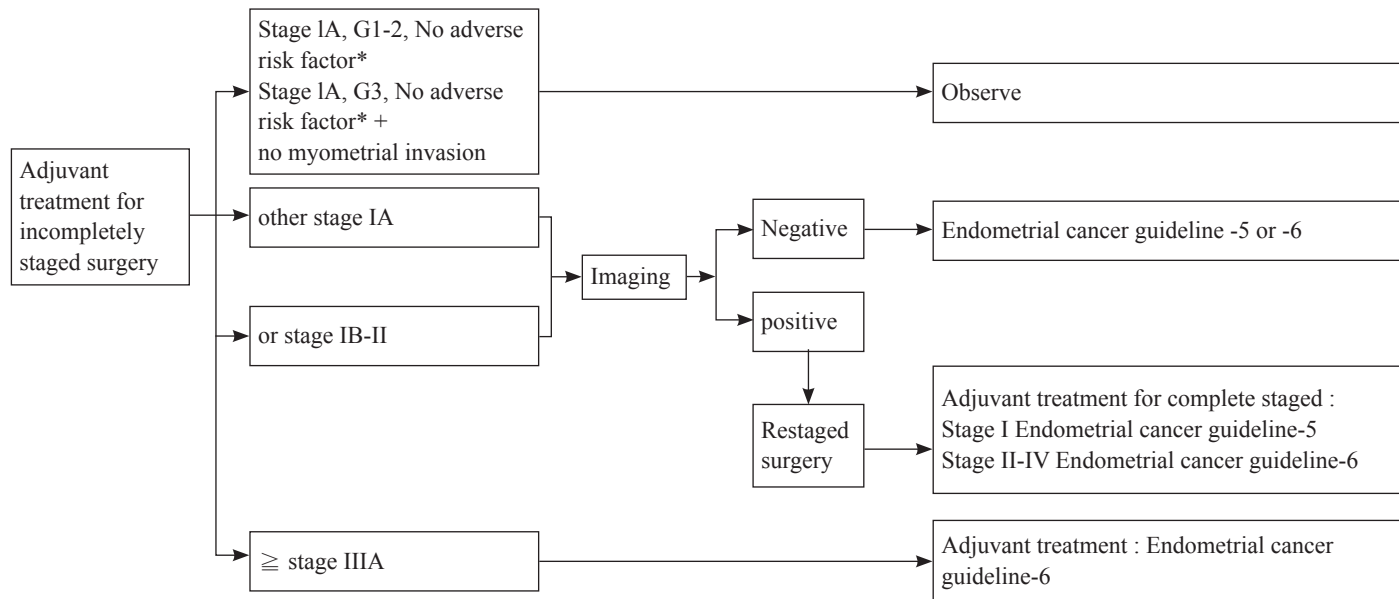
## 《 Endometrial cancer guideline-6 》



- 
- \* vaginal brachytherapy is also an option for G1/G2 + < 50% myometrium invasion + LVSI (-) + microscopic cervical invasion stage II disease.
  - ◆ risk of recurrence is higher with older age (especially > 60y), extensive LVSI, and deeper myoinvasion (>50%) °

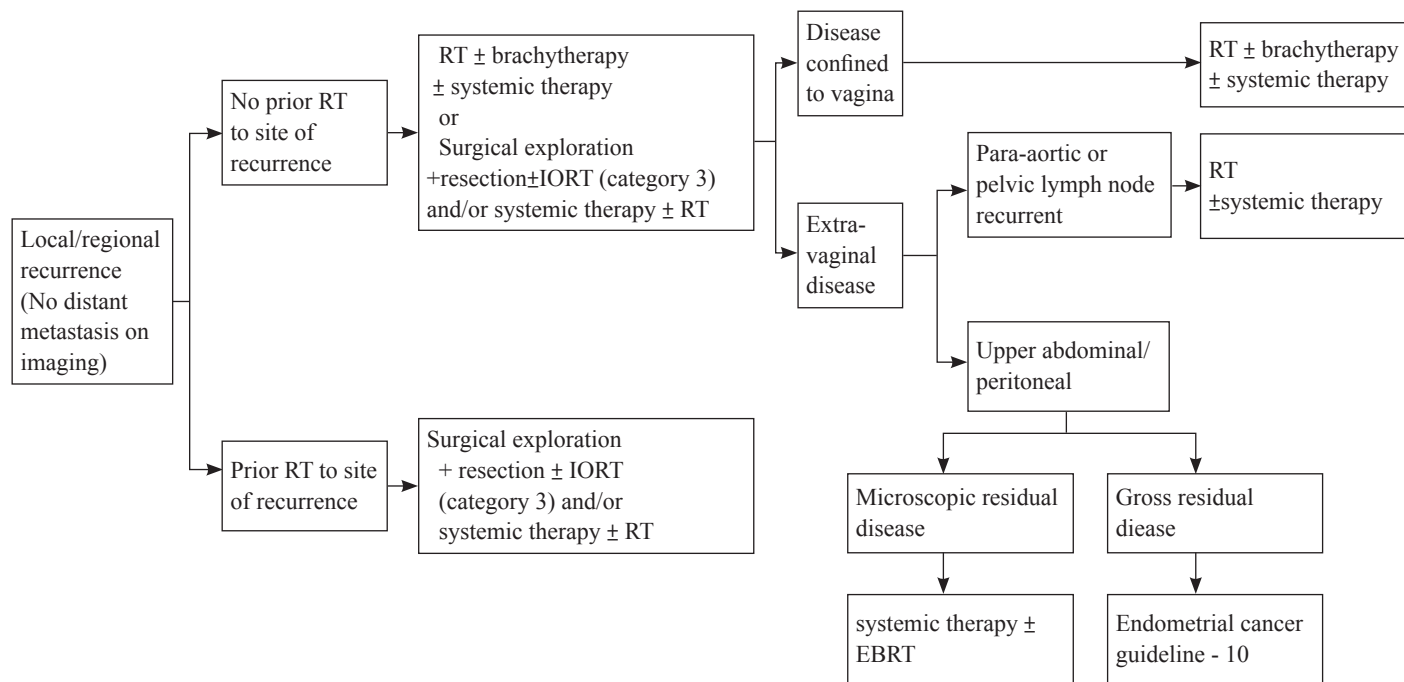
## 《 Endometrial cancer guideline-7 》

Incomplete staged surgery (or found accidentally) : TAH only or +/- bilateral /Unilateral salpingectomy.

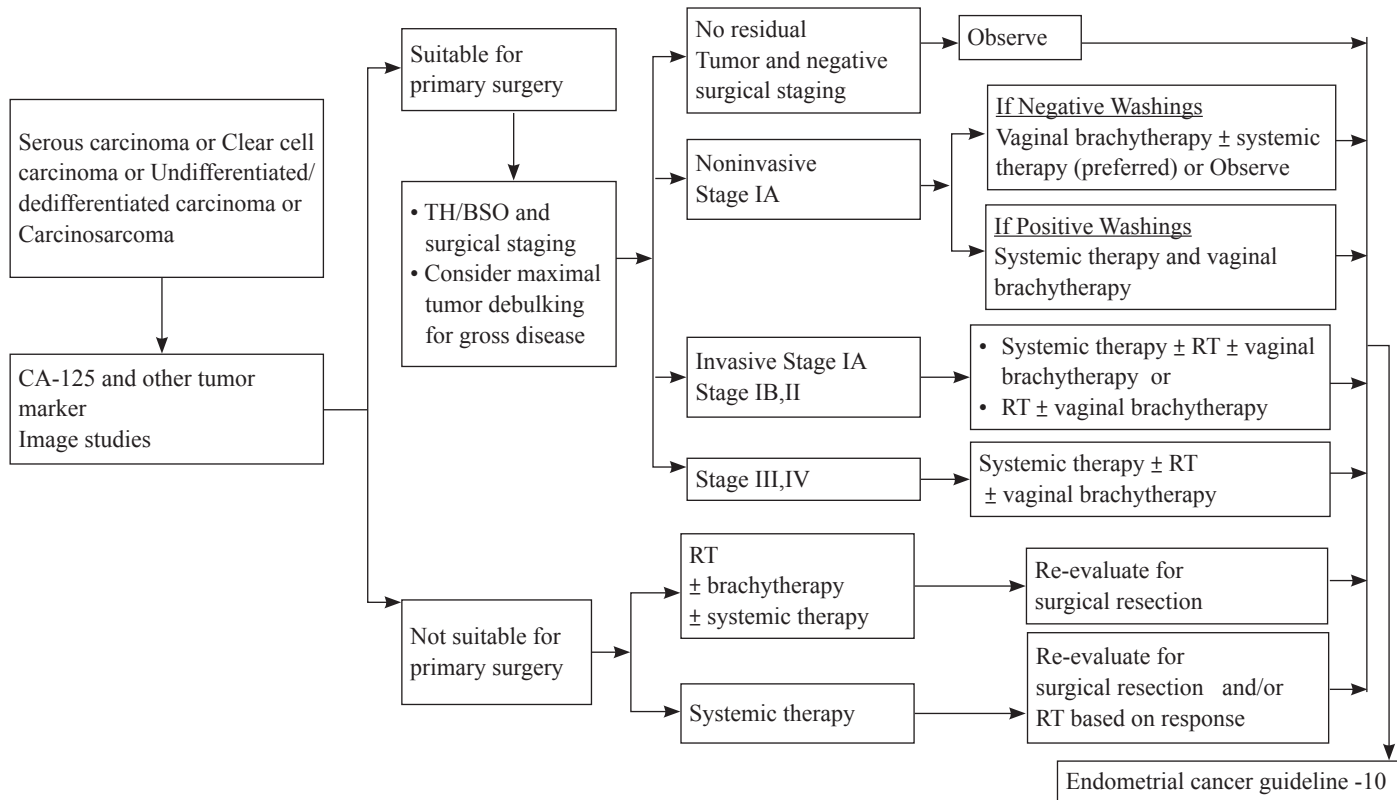


\* : Adverse risk factors including : age > 60, LVSI(+), tumor size  $\geq$  2cm

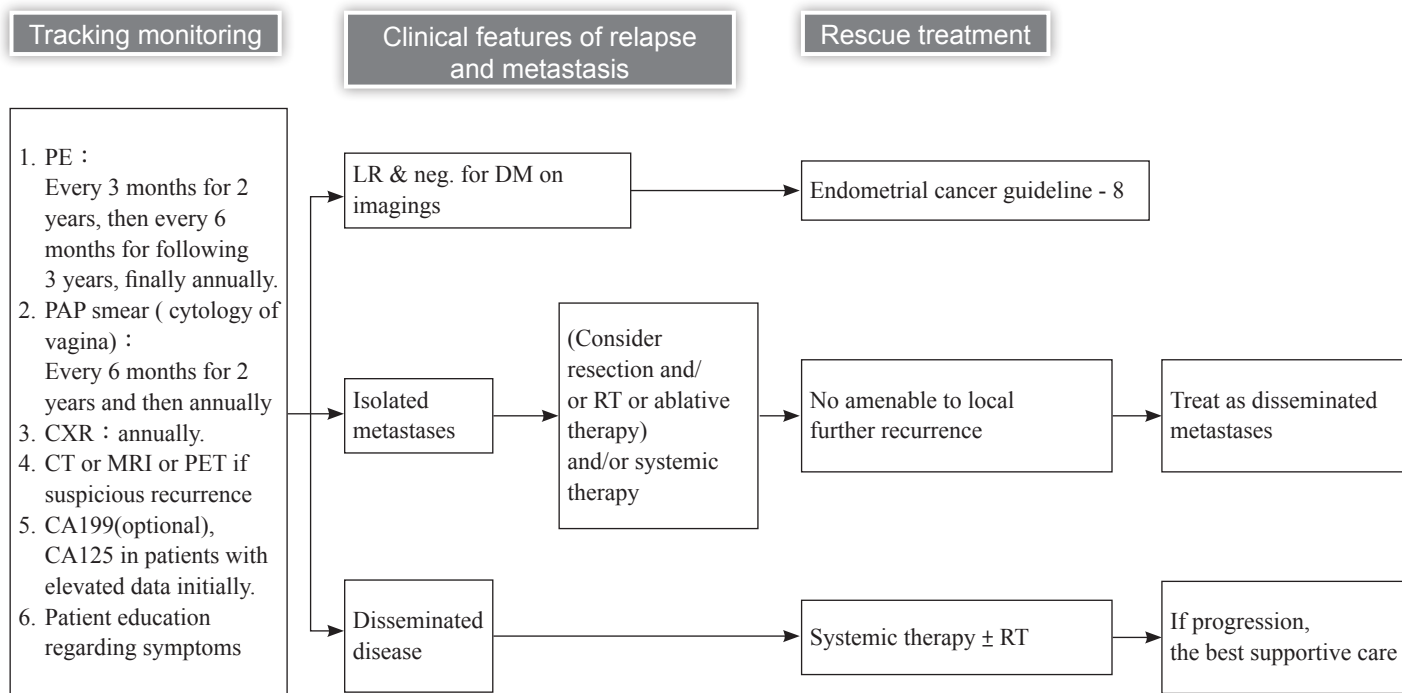
## 《 Endometrial cancer guideline-8 》



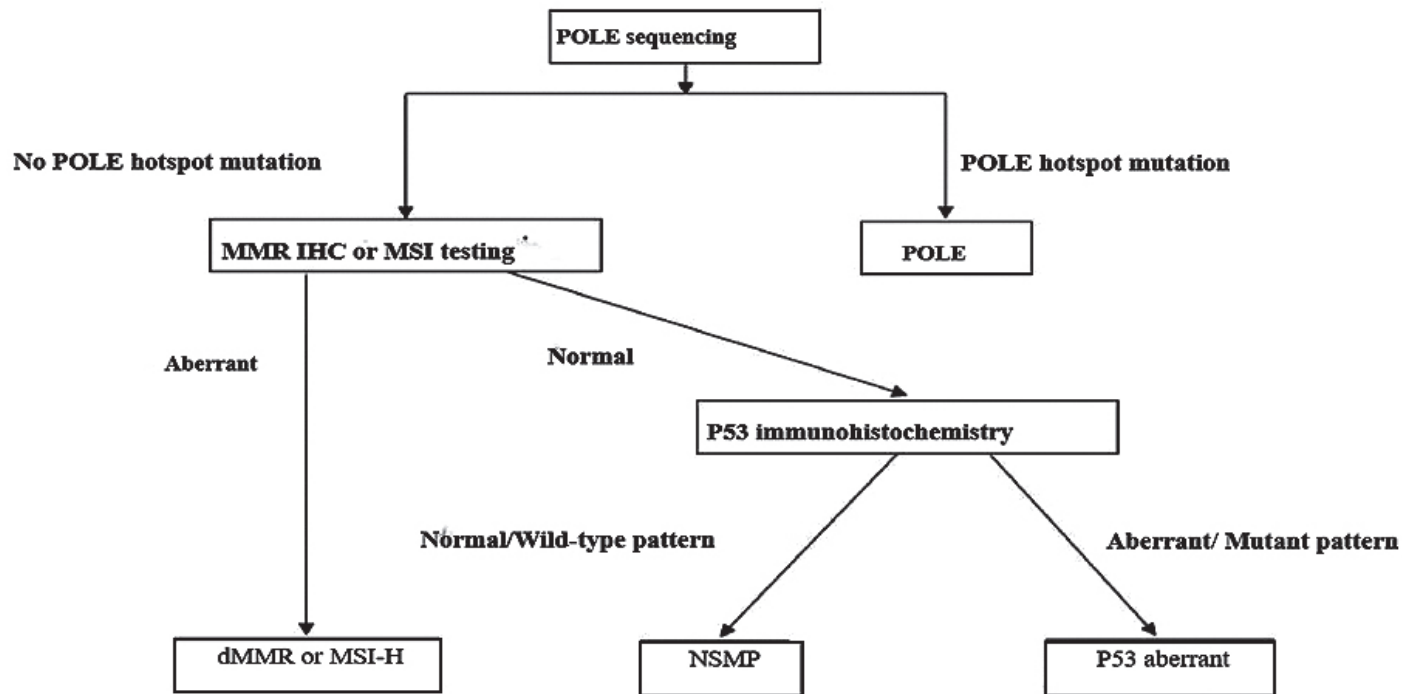
# 《 Endometrial cancer guideline-9 》



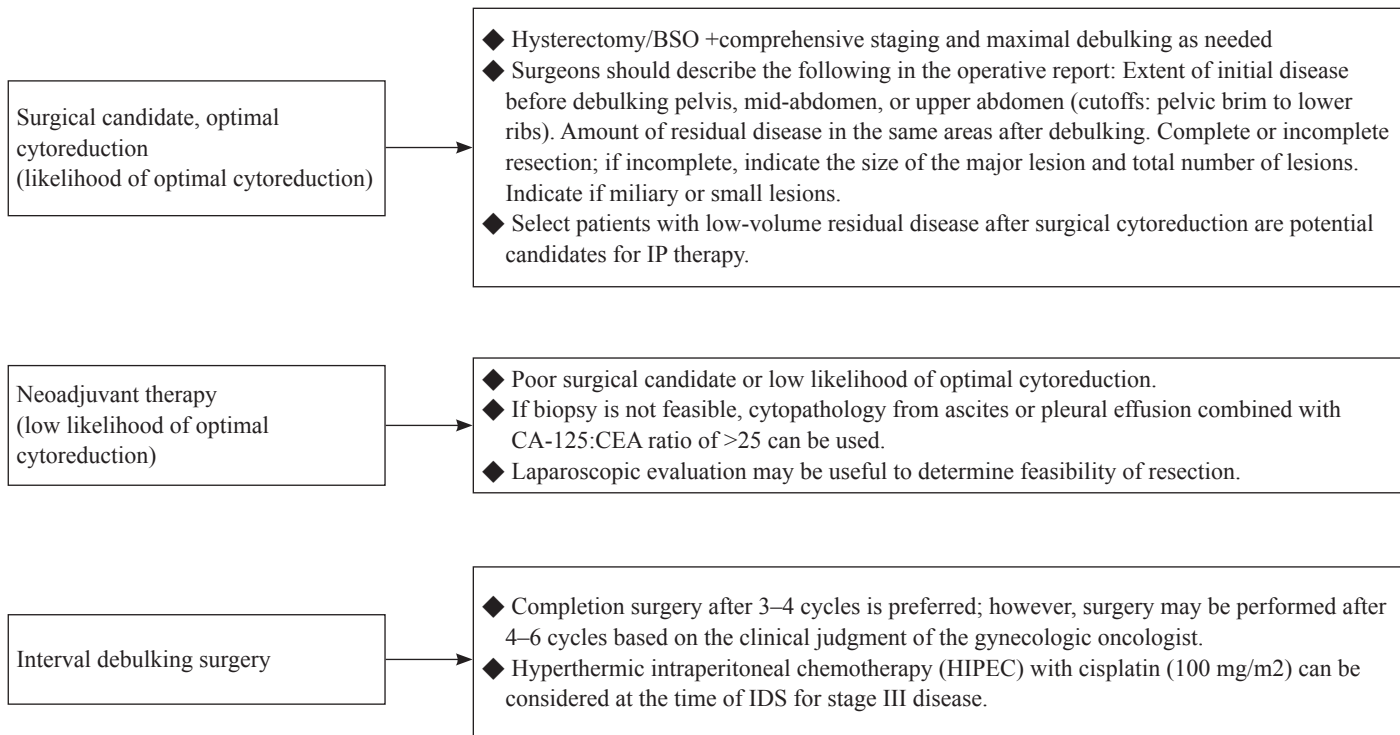
## 《 Endometrial cancer guideline-10 》



《 附件 -1 》



## Ovarian Cancer Guideline-1 : Surgery



## Pre-Operative Survey

- ◆ Ultrasonography
- ◆ Obtain family history
- ◆ Imaging as clinically indicated (eg, ultrasound and/or chest/abdominal/pelvic CT/MRI as clinically indicated, chest CT as clinically indicated, PET/CT as clinically indicated, and/or ultrasound)
- ◆ CBC, chemistry profile with LFTs
- ◆ CA-125 or other tumor markers as clinically indicated
- ◆ Gastrointestinal evaluation as clinically indicated
- ◆ Reproductive endocrinology and infertility (REI) evaluation as clinically indicated

## standard staging surgery

- ◆ An open laparotomy including a vertical midline abdominal incision should be used in most patients with a suspected malignant ovarian/fallopian tube/primary peritoneal neoplasm in whom a surgical staging procedure, a primary debulking procedure, an interval debulking
- ◆ Surgeons should describe the following in the operative report: Extent of initial disease before debulking pelvis, mid-abdomen, or upper abdomen (cutoffs: pelvic brim to lower ribs). Amount of residual disease in the same areas after debulking. Complete or incomplete resection; if incomplete, indicate the size of the major lesion and total number of lesions. Indicate if miliary or small lesions.
- ◆ In general, every effort should be made during a primary cytoreduction procedure to achieve maximum cytoreduction of all pelvic disease and to evaluate for occult disease in the upper abdomen or retroperitoneum.
- ◆ BSO and hysterectomy should be performed with every effort to keep an encapsulated mass intact during removal.
- ◆ For selected patients desiring to preserve fertility, USO or BSO with uterine preservation may be considered. Uterine preservation allows for potential future assisted reproductive approaches.

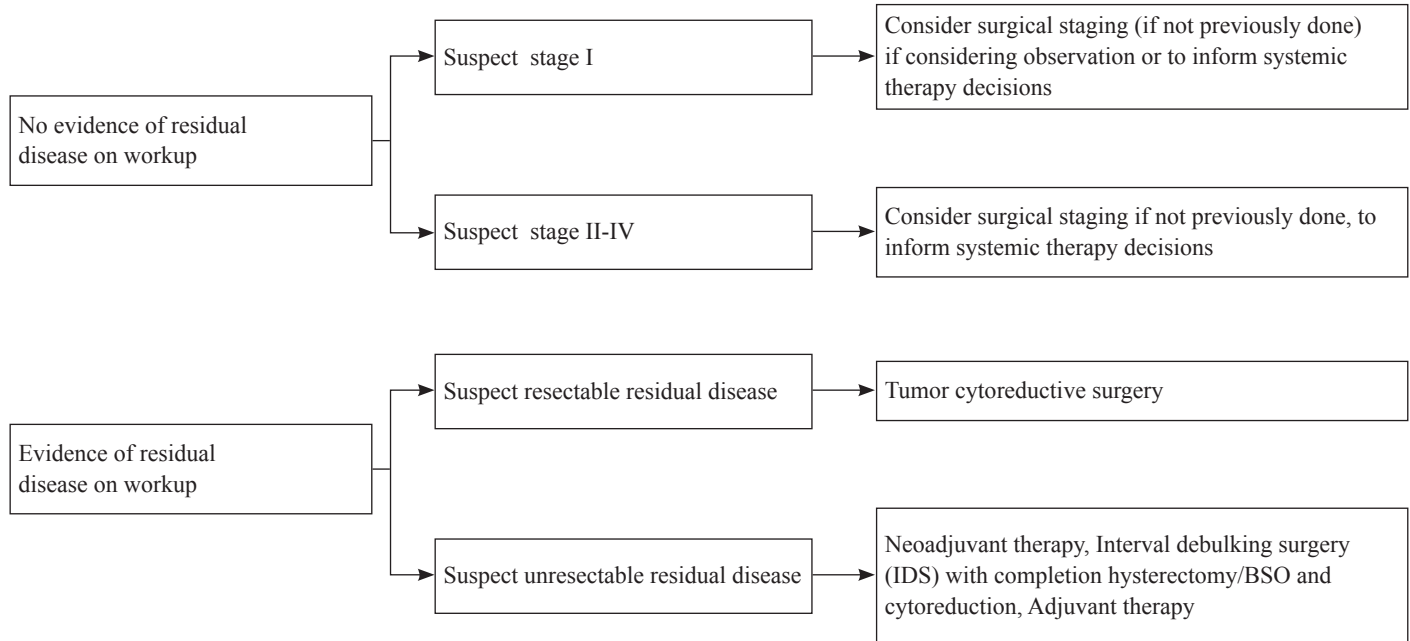


- ◆ Omentectomy should be performed.
- ◆ Para-aortic lymph node dissection should be performed by stripping the nodal tissue from the vena cava and the aorta bilaterally to at least the level of the inferior mesenteric artery and preferably to the level of the renal vessels.
- ◆ The preferred method of dissecting pelvic lymph nodes is bilateral removal of lymph nodes overlying and anterolateral to the common iliac vessel, overlying and medial to the external iliac vessel, overlying and medial to the hypogastric vessels, and from the obturator fossa at a minimum anterior to the obturator nerve.
- ◆ In general, every effort should be made during a primary cytoreduction procedure to achieve maximum cytoreduction of all abdominal, pelvic, and retroperitoneal disease. Residual disease <1 cm defines optimal cytoreduction; however, maximal effort should be made to remove all gross disease since this offers superior survival outcomes.
- ◆ Aspiration of ascites (if present) should be performed for peritoneal cytologic examinations. All involved omentum should be removed.
- ◆ Suspicious and/or enlarged nodes, identified on preoperative imaging or during surgical exploration, should be resected, if possible. Resection of clinically negative nodes is not required.
- ◆ Procedures that may be considered for optimal surgical cytoreduction (in all stages) include bowel resection and/or appendectomy, stripping of the diaphragm or other peritoneal surfaces, splenectomy, partial cystectomy and/or ureteroneocystostomy, partial hepatectomy, partial gastrectomy, cholecystectomy, and/or distal pancreatectomy.
- ◆ Select patients with low-volume residual disease after surgical cytoreduction for invasive epithelial ovarian or peritoneal cancer are potential candidates for IP therapy. In these patients, consideration should be given to placement of IP catheter with initial surgery.
- ◆ For select patients, a minimally invasive surgical approach may be employed by an experienced surgeon to manage early-stage disease. Laparoscopy may be useful to evaluate whether optimal cytoreduction can be achieved in patients with newly diagnosed advanced stage or recurrent disease. Minimally invasive techniques can be used for select patients for interval debulking procedures. Patients who are unable to be optimally debulked using minimally invasive techniques should be converted to an open procedure.

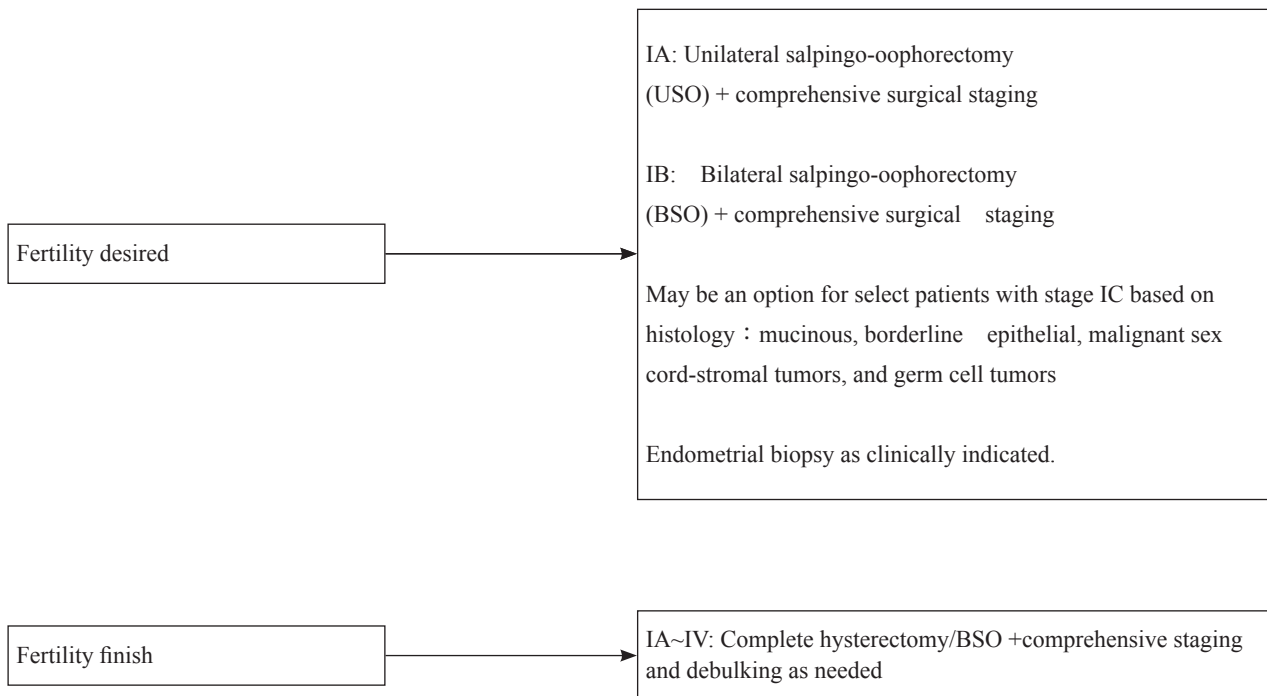
## Secondary cytoreduction

- ◆ A secondary cytoreduction procedure can be considered in patients with recurrent ovarian cancer who develop a recurrence more than 6 months since completion of initial chemotherapy, have a good performance status, have no ascites, and have an isolated focus or limited foci of disease amenable to complete resection. In addition to preoperative imaging, laparoscopy may be used to determine if complete resection can be achieved. Secondary cytoreduction can be performed with either open or minimally invasive approaches. Consider using validated scoring methods to assess suitability for secondary cytoreduction.

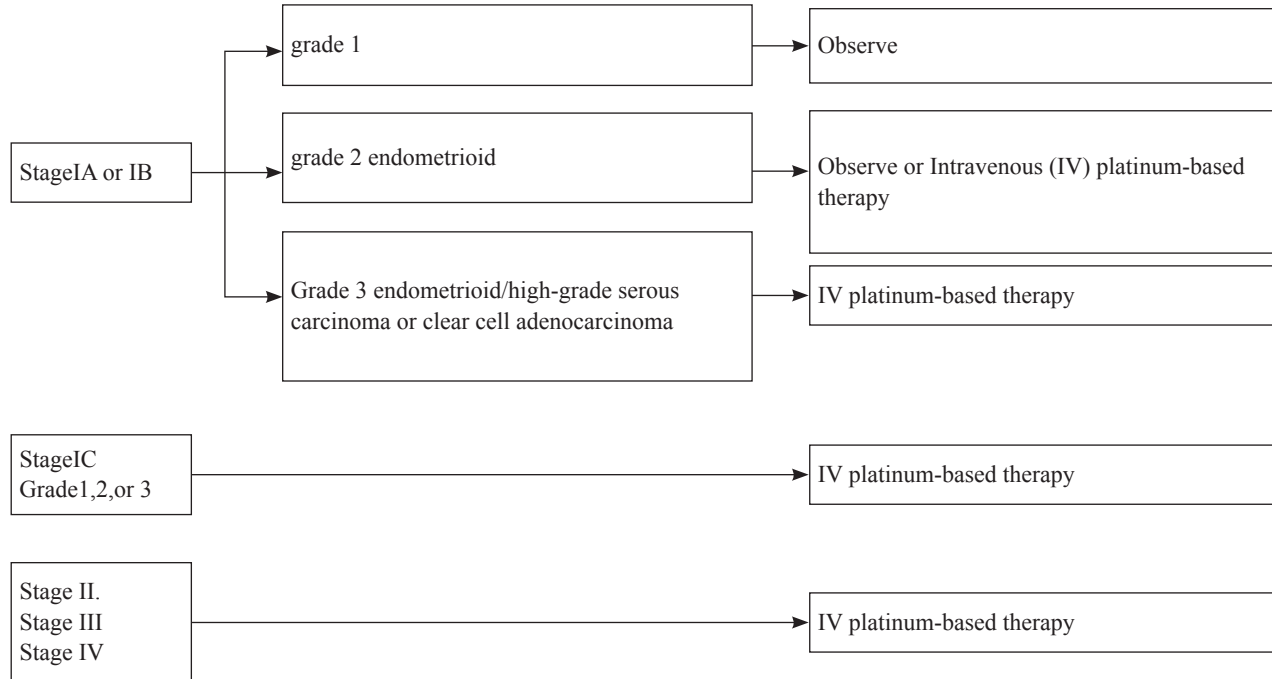
## Ovarian Cancer Guideline-2: Diagnosis by previous surgery



## Ovarian Cancer Guideline-3: Surgery in fertility preservation



## Ovarian Cancer Guideline-4: Adjuvant therapy



## Ovarian Cancer Guideline-5: Post Treatment

### ◆ Post Primary Treatment

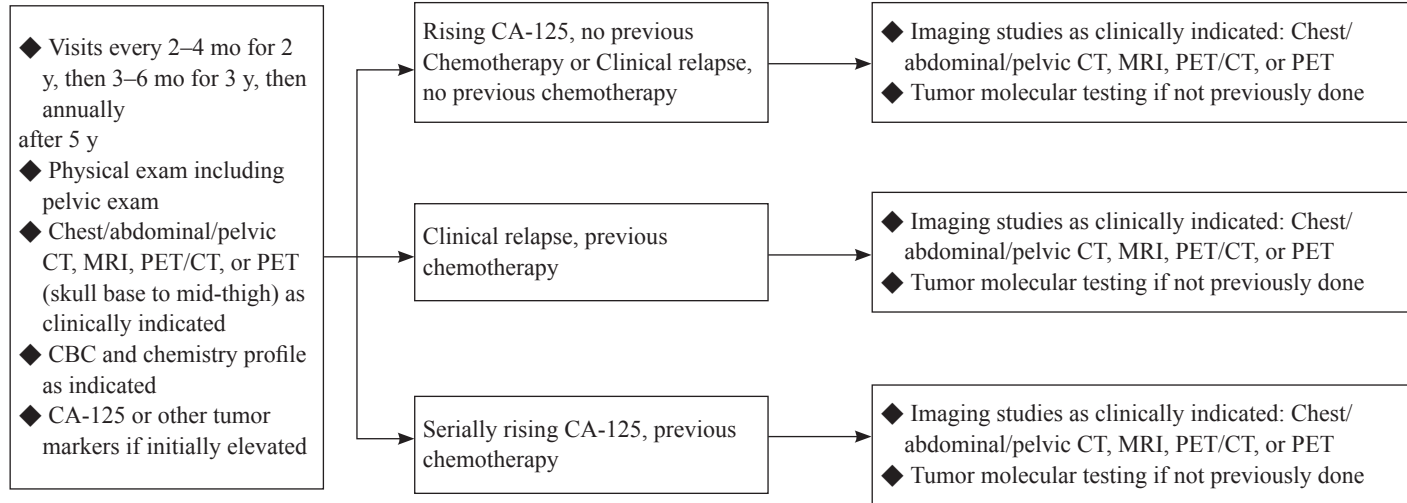
Certain patients with newly diagnosed stage II–IV disease (high grade serous, grade 2/3 endometrioid, or BRCA1/2-mutated clear cell carcinoma or carcinosarcoma) may benefit from maintenance therapy with PARPi if CR or PR is achieved after primary treatment with surgery and platinum-based first-line therapy. Data are limited for use of maintenance PARPi post primary treatment in patients with stage II disease and for those with LCOs.

### ◆ Post Recurrence Treatment

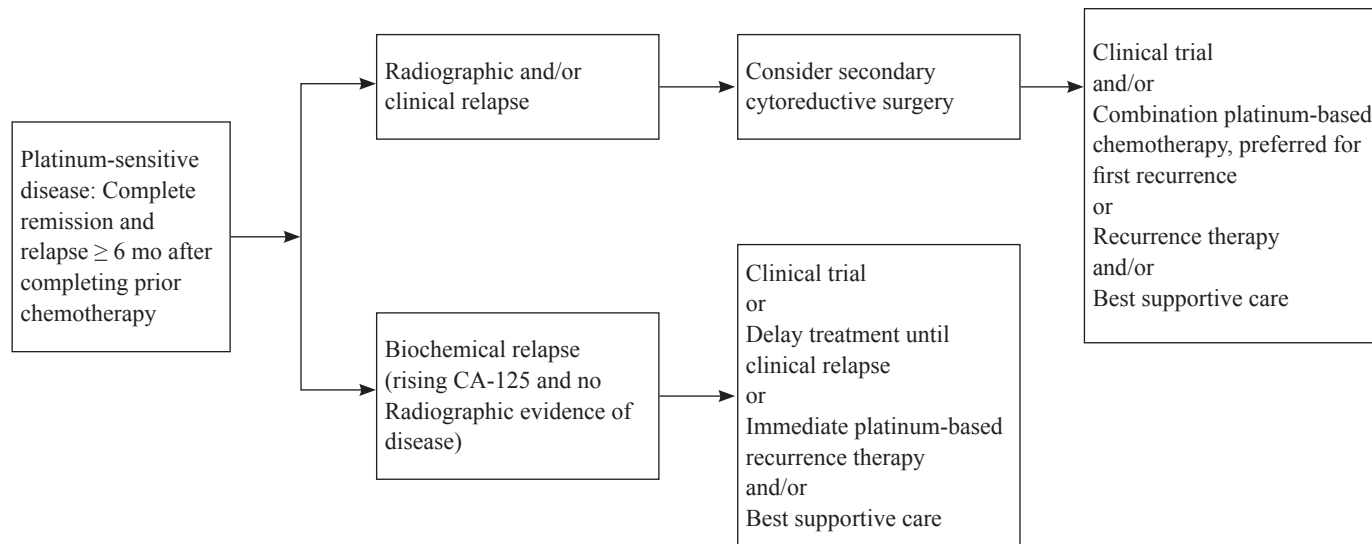
Certain patients with recurrent disease may benefit from maintenance therapy with PARPi after recurrence therapy, if in CR or PR after platinum-based recurrence therapy, and if no prior progression on a PARPi.

Regimen	Setting	Dose	Duration
Olaparib+ Bevacizumab	Maintenance post primary chemotherapy + bevacizumab	Olaparib 300mg PO twice daily Bevacizumab 15mg/kg IV every 21 days	Olaparib: Until disease progression or unacceptable toxicity or up to 2 years Bevacizumab: Until disease progression or unacceptable toxicity or up to 15 months
Niraparib + bevacizumab	Maintenance post primary chemotherapy + bevacizumab	Niraparib: 300 mg PO once daily (or 200 mg once daily for patients with a baseline body weight of <77 kg, and/or a platelet count of <150,000/mm <sup>3</sup> ) Bevacizumab: 15 mg/kg IV every 21 days	Niraparib: Until disease progression or unacceptable toxicity or up to 3 years Bevacizumab: Until disease progression or unacceptable toxicity or up to 15 months
Niraparib monotherapy	Maintenance post recurrence chemotherapy	200–300mg PO once daily (or 200 mg once daily for patients with a baseline body weight of <77 kg, and/or a platelet count of <150,000/mm <sup>3</sup> ; after 2 to 3 months, in the absence of hematologic toxicity, may consider escalation to 300 mg once daily)	Until disease progression or unacceptable toxicity or up to 36 months
Olaparib monotherapy	Maintenance post recurrence chemotherapy	200–300mg PO once daily	Until disease progression or unacceptable toxicity
	Maintenance post primary chemotherapy	300mg PO twice daily	Until disease progression or unacceptable toxicity
	Maintenance post recurrence chemotherapy	300mg PO twice daily	Until disease progression or unacceptable toxicity or CR(NED) in 2 years

## Ovarian Cancer Guideline-6: Follow up after treatment

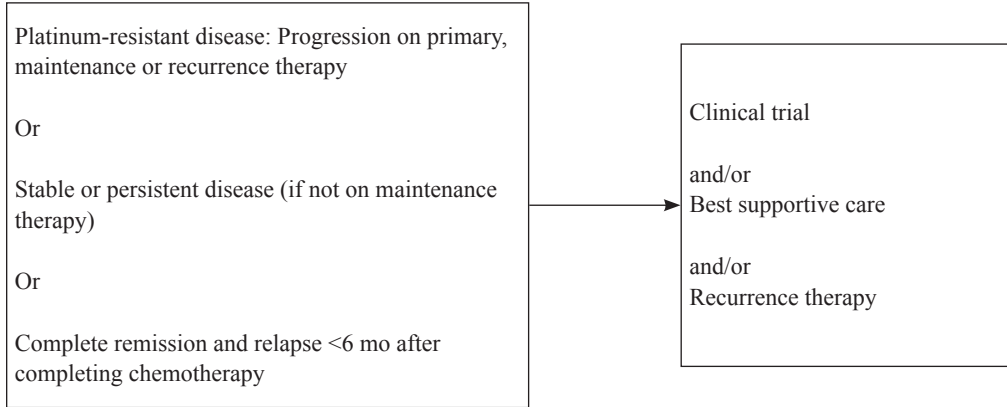


## Ovarian Cancer Guideline-7: Platinum-sensitive

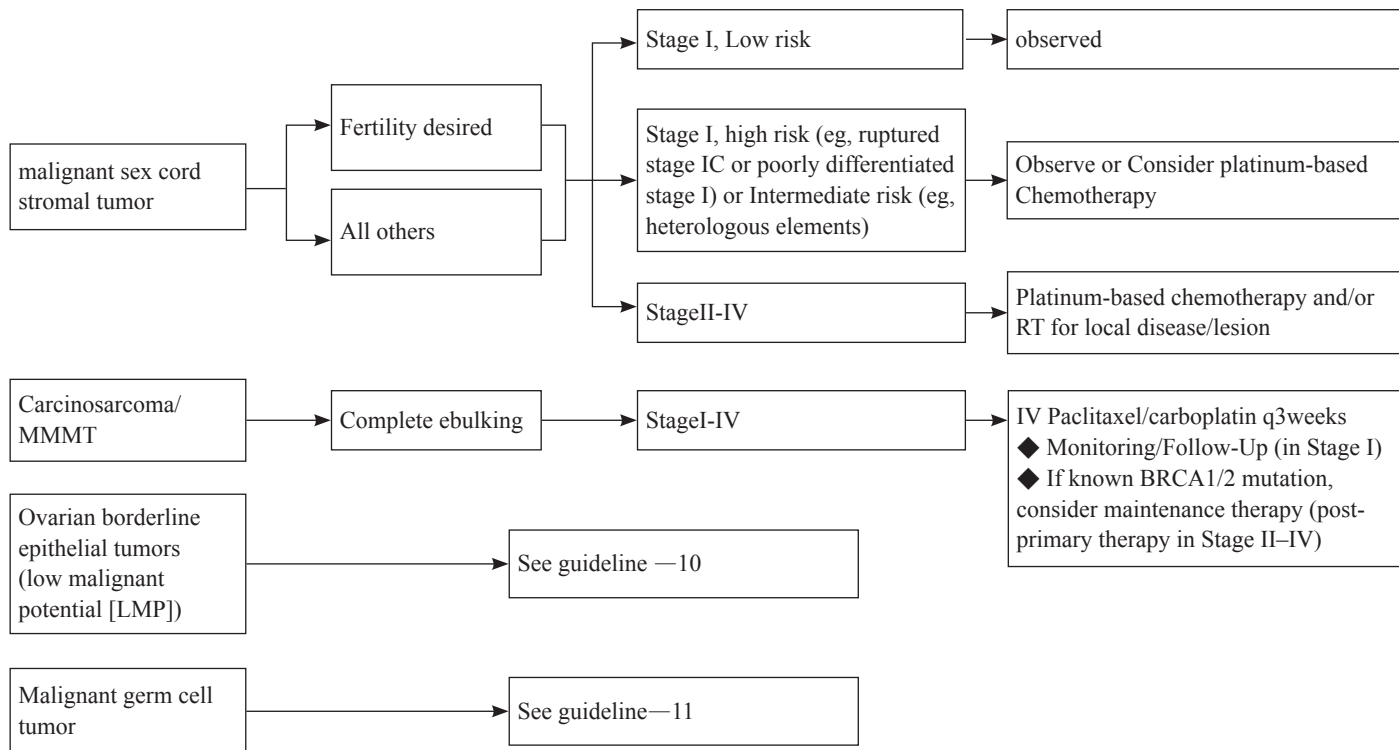




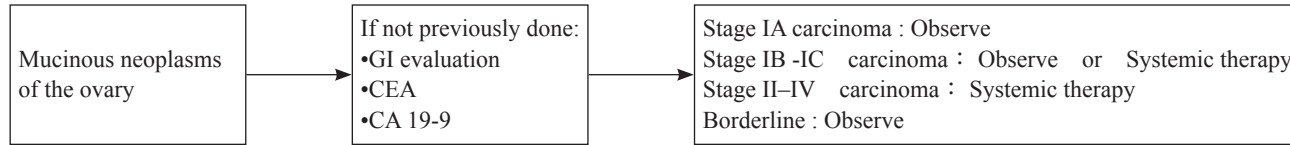
## Ovarian Cancer Guideline-8: Platinum-resistant



## Ovarian Cancer Guideline-9: Less common histology

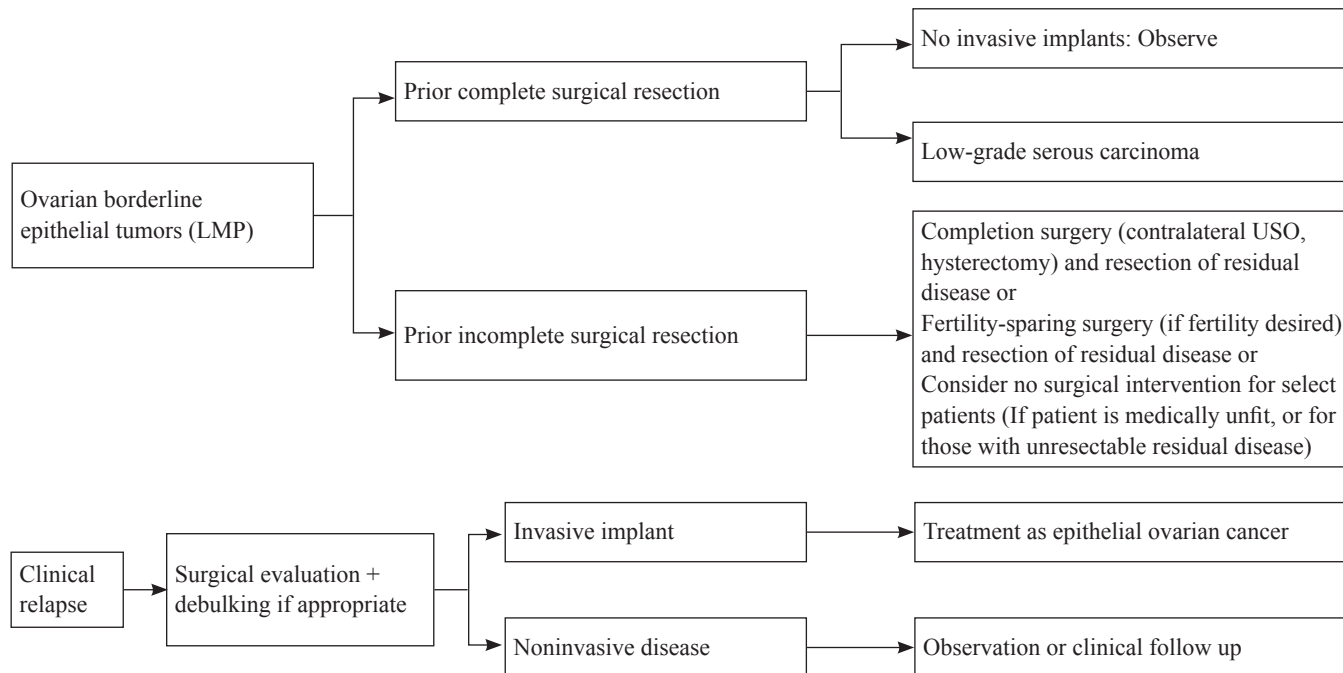


- ◆ Mucinous tumors: Primary invasive mucinous tumors of the ovary are uncommon. Thus, the upper and lower GI tract should be carefully evaluated to rule out an occult GI primary with ovarian metastases, and an appendectomy need only be performed in patients with a suspected or confirmed mucinous ovarian neoplasm if it appears to be abnormal. A normal appendix does not require surgical resection in this setting. If mucinous histology is confirmed by intraoperative frozen section analysis and there are no suspicious lymph nodes, consider omitting lymphadenectomy.

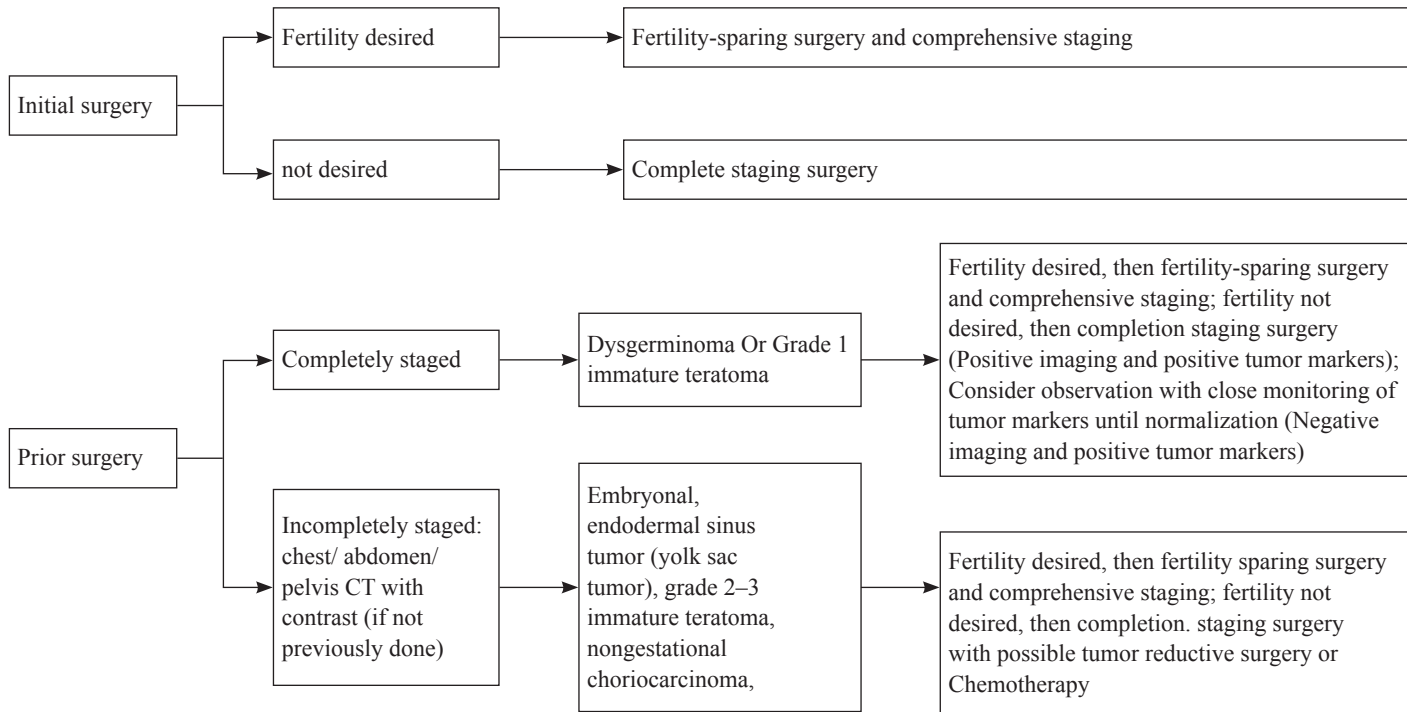


- ◆ Ovarian borderline epithelial (LMP) tumors: Although data show upstaging with lymphadenectomy, other data show that lymphadenectomy does not affect overall survival. However, omentectomy and multiple biopsies of peritoneum (the most common sites of peritoneal implants) may upstage patients in approximately 30% of cases and may affect prognosis.

## Ovarian Cancer Guideline-10: Borderline tumors (low malignant potential, LMP)



## Ovarian Cancer Guideline-11: Malignant germ cell tumors



### ◆ Fertility-sparing surgery:

Fertility-sparing surgery with USO (preserving the uterus and contralateral ovary) or BSO (preserving the uterus) can be considered for patients with apparent early-stage disease and/or low-risk tumors (early-stage invasive epithelial tumors, LMP lesions, malignant germ cell tumors, mucinous, or malignant sex cord-stromal tumors) who wish to preserve fertility. Refer to reproductive endocrinologist for evaluation and consultation as clinically indicated. Comprehensive surgical staging should still be performed to rule out occult higher stage disease but may be omitted in pediatric, adolescent, and young adult patients with clinically apparent early-stage malignant germ cell tumors based on the pediatric surgical literature.

### ◆ Risk-Reducing Salpingo Oophorectomy (RRSO) Protocol:

The RRSO protocol is recommended for patients at risk for HBOC and is described in detail in the algorithm. RRSO can also result in early diagnosis of gynecologic cancer. Occult ovarian, fallopian tube, and primary peritoneal cancer is sometimes found by RRSO (in 3.5%–4.6% of patients with BRCA1/2 mutations), and in some cases only detected by pathologic examination of specimens. This emphasizes the need for well-tested protocols that include careful pathologic review of the ovaries and tubes.

- Perform minimally invasive laparoscopic surgery.
- Survey upper abdomen, bowel surfaces, omentum, appendix (if present), and pelvic organs.
- Biopsy any abnormal peritoneal findings.
- Obtain pelvic washing for cytology (50 cc normal saline instilled and aspirated immediately).
- Perform total BSO, removing 2 cm of proximal ovarian vasculature/IP ligament, all tube up to the cornua, and all peritoneum surrounding the ovaries and tubes, especially peritoneum underlying areas of adhesion between tube and/or ovary and the pelvic sidewall.
- Engage in minimal instrument handling of the tubes and ovaries to avoid traumatic exfoliation of cells.
- Both ovaries and tubes should be placed in an endobag for retrieval from the pelvis.

◆ **Risk-Reducing Surgery for High-Risk Patients:**

In women at high risk (with either BRCA1 or BRCA2 mutations), risk-reducing bilateral salpingo-oophorectomy (BSO) is associated with a reduced risk for breast, ovarian, fallopian tube, and primary peritoneal cancers. Prospective studies have shown that among patients at high risk due to BRCA1 or BRCA2 mutation, occult ovarian, fallopian tube, or primary peritoneal cancer is found in up to 5% of patients undergoing risk-reducing salpingo-oophorectomy (RRSO), enabling them to be diagnosed at an earlier and possibly more treatable stage. However, there is a residual risk for primary peritoneal cancer after risk-reducing BSO in these women at high risk for ovarian cancer.

## Reference:

1. NCCN Clinical Practice in Oncology: Ovarian cancer Version 3, 2024, uterine neoplasms Version 3, 2024, cervical cancer version 4, 2024.



# Principle of Radiation Therapy for Cervical cancer

## A. Treatment field

1. Cervical tumor
2. Vaginal stump and high risk area for recurrence
3. Pelvic LAPs
4. Pelvis LN area for high risk of metastasis
5. Abdominal paraaortic LAPs
6. Abdominal paraaortic LN area for high risk of metastasis

## B. Dose and fractionation

External beam radiotherapy

1. Total dose: For definitive radiotherapy, EBRT alone for early stage needs over EQD2 80Gy, EBRT alone for locally advanced stage needs over EQD2 85Gy or EBRT is 45~50.4Gy and then with brachytherapy; for lymphadenopathy, total dose could be 55-65 Gy. For adjuvant radiotherapy, EBRT is 45~50.4Gy and then boost 5~10 Gy to bulky parametrial/pelvic side wall disease until 55~60Gy according to risk factor or combining brachytherapy; for lymphadenopathy, total dose could be 55-70 Gy.
2. Dose per fraction: 1.8~2.0Gy

Brachytherapy

1. For definitive radiotherapy, besides EBRT, intra-cavitary brachytherapy was implicated by remote after-loading brachytherapy with HDR, Ir-192. Prescription would be 4-6Gy per fractions, total 4-6 fractions with 2-3 fractions per week.
2. For adjuvant radiotherapy, besides EBRT, for closer distance from vaginal cuff or residual vaginal lesion, intra-vaginal brachytherapy was implicated by remote after-loading brachytherapy with HDR, Ir-192. Prescription would be 4-6Gy per fractions, total 2-4 fractions with 2-3 fractions per week.

## C. Treatment :

Tumor-directed radiotherapy may adopt 3D-CRT or IMRT, including VAMT or Tomotherapy, along with IGRT. Dose

prescription may consider SIB or sequential boost as higher dose for higher risk area.

#### **D. Reference :**

1. NCCN clinical practice guidelines in oncology-Cervical cancer. 2024, version 4.
2. Kim JY, Kim JY, Kim JH, et al: Curative chemoradiotherapy in patients with stage IVB cervical cancer presenting with paraortic and left supraclavicular lymph node metastases. *Int J Radiat Oncol Biol Phys* 84:741-7, 2012
3. Wu SY, Huang EY, Chanchien CC, et al. Prognostic factors associated with radiotherapy for cervical cancer with computed tomography-detected para-aortic lymph node metastasis. *Journal of radiation research* 2014; 55(1): 129-38.
4. QUANTEC Bentzen SM, Constine LS, Deasy JO, et al. Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC): an introduction to the scientific issues. *International journal of radiation oncology, biology, physics* 2010; 76(3 Suppl): S3-9.

# Principle of Radiation Therapy for Endometrial cancer

## A. Treatment field

1. Vaginal stump and nearby mucosal area after operation
2. Residual tumor (papillary serous cell, clear cell and sarcomatoid cancer) after operation
3. High risk area for LN metastasis in pelvis

## B. Dose and fractionation

External beam radiotherapy

1. Total dose: 45-50.4 Gy
2. Boost for residual tumor: 10-16 Gy
3. Dose per fraction: 1.8-2.0 Gy

Intravaginal brachytherapy

1. Post EBRT boost: 4-6 Gy \* 2-4 Fx. to vaginal mucosa
2. Brachytherapy alone: 6 Gy \* 5 Fx. to vaginal mucosa or 7 Gy \* 3 Fx. or 5.5 Gy \* 4 Fx. to 5 mm below the vaginal surface

## C. Treatment :

Tumor-directed radiotherapy may adopt 3D-CRT or IMRT, including VAMT or Tomotherapy, along with IGRT. Dose prescription may consider SIB or sequential boost as higher dose for higher risk area.

## D. Reference :

1. NCCN clinical practice guidelines in oncology for uterine neoplasms, 2024 version 3.
2. 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; 56:419-427.3. 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.
3. 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.

4. 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.
5. Murphy KT, Rotmensch J, Yamada SD, Mundt AJ. Outcome and patterns of failure in pathologic stages I-IV clear-cell carcinoma of the endometrium: implications for adjuvant radiation therapy. *Int J Radiat Oncol Biol Phys* 2003; 55 ( 5 ) :1272-1276.