



中山醫學大學附設醫院

子宮體癌診療指引

臨床指引參考台灣國家衛生研究院、與美國 NCCN 版本
再依據中山醫學大學附設醫院婦癌小組經驗作編修
婦癌醫療小組

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2021/11/24 Version 12.0
2020/11/04 Version 11.0
2019/12/11 Version 10.0
2018/10/24 Version 9.0
2017/11/22 Version 8.0
2016/12/07 Version 7.0
2015/11/24 Version 6.0
2014/12/17 Version 5.0
2014/01/08 Version 4.0
2012/12/13 Version 3.0
2011/11/24 Version 2.1
2011/02/21 Version 2.0
2010/07/12 Version 1.0

癌症委員會主任委員	癌症委員會執行長	癌症中心主任	團隊負責人



修訂內容

頁數	原文	修訂/新增																																												
1	本子宮體癌診斷及治療指引的內容有子宮內膜癌、子宮惡性肉瘤及妊娠組織瘤等，其內容除了依據已發表的實證醫學證據及專家意見外，並參考國家衛生研究院子宮內膜癌臨床指引、美國 National Comprehensive Cancer Network (NCCN) 的 Practice Guide-lines in endometrial Cancer 2022 Version1 版、FIGO Staging Classifications and Clinical Practice Guidelines in the Management of Gynecologic Cancer、MD Anderson cancer center 及中山醫學大學附設醫院子宮體癌治療經驗進行編修。	本子宮體癌診斷及治療指引的內容有子宮內膜癌、子宮惡性肉瘤及妊娠組織瘤等，其內容除了依據已發表的實證醫學證據及專家意見外，並參考國家衛生研究院子宮內膜癌臨床指引、美國 National Comprehensive Cancer Network (NCCN) 的 Practice Guide-lines in endometrial Cancer 2024 Version1 版、FIGO Staging Classifications and Clinical Practice Guidelines in the Management of Gynecologic Cancer、MD Anderson cancer center 及中山醫學大學附設醫院子宮體癌治療經驗進行編修。																																												
4	11. 病變完全緩解6個月，鼓勵病患受孕，孕前持續每3-6個月進行子宮內膜取樣檢查。暫無生育計畫者，於以雌激素維持治療及定期監測	11. 病變完全緩解6個月，鼓勵病患受孕，孕前持續每6-12個月進行子宮內膜取樣檢查。暫無生育計畫者，於以雌激素維持治療及定期監測																																												
5	新增	<p>第一型(Type I)及第二型(Type II)組織類型分組^{c1} 限定原發部位 癌症編碼=C54.0、C54.1、C54.3、C54.8、C54.9 扣除 2.6 原發部位=C54.2(myometrium)。^{c1}</p> <table border="1"> <thead> <tr> <th colspan="2">第一型(Type I)^{c1}</th> <th colspan="2">第二型(Type II)^{c1}</th> </tr> </thead> <tbody> <tr> <td>Endometrioid carcinoma^{c1}</td> <td>(M8380,8382-8383)^{c1}</td> <td>Serous carcinoma</td> <td>(M-8441, 8460-8461)^{c1}</td> </tr> <tr> <td></td> <td></td> <td>Clear cell carcinoma^{c1}</td> <td>(M-8310)^{c1}</td> </tr> <tr> <td>Mucinous adenocarcinoma^{c1}</td> <td>(M8480)^{c1}</td> <td>Small cell carcinoma^{c1}</td> <td>(M-8041, 8045)^{c1}</td> </tr> <tr> <td></td> <td></td> <td>Neuroendocrine carcinoma, NOS^{c1}</td> <td>(M-8246)^{c1}</td> </tr> <tr> <td>Adenosquamous carcinoma^{c1}</td> <td>(M-8560)^{c1}</td> <td>Large cell neuroendocrine carcinomas^{c1}</td> <td>(M-8013)^{c1}</td> </tr> <tr> <td></td> <td></td> <td>Undifferentiated/dedifferentiated carcinomas^{c1}</td> <td>(M-8020)^{c1}</td> </tr> <tr> <td>Endometrioid carcinoma with squamous differentiation^{c1}</td> <td>(M-8570)^{c1}</td> <td>Mixed cell adenocarcinoma^{c1}</td> <td>(M-8323)^{c1}</td> </tr> <tr> <td></td> <td></td> <td>Squamous cell carcinoma^{c1}</td> <td>(M-8070-8072, 8076)^{c1}</td> </tr> <tr> <td>Adenocarcinoma, NOS^{c1}</td> <td>(M-8140)^{c1}</td> <td>Adenocarcinoma with neuroendocrine differentiation^{c1}</td> <td>(M-8574)^{c1}</td> </tr> <tr> <td></td> <td></td> <td>Carcinosarcomas (malignant mixed Müllerian tumor)^{c1}</td> <td>(M-8950, 8980)^{c1}</td> </tr> </tbody> </table> <p>第二型 (type II) 子宮內膜癌病人應接受完整分期手術，包含Total hysterectomy, BSO, BPLND, PALND, omentectomy, washing cytology^{c1}</p>	第一型(Type I) ^{c1}		第二型(Type II) ^{c1}		Endometrioid carcinoma ^{c1}	(M8380,8382-8383) ^{c1}	Serous carcinoma	(M-8441, 8460-8461) ^{c1}			Clear cell carcinoma ^{c1}	(M-8310) ^{c1}	Mucinous adenocarcinoma ^{c1}	(M8480) ^{c1}	Small cell carcinoma ^{c1}	(M-8041, 8045) ^{c1}			Neuroendocrine carcinoma, NOS ^{c1}	(M-8246) ^{c1}	Adenosquamous carcinoma ^{c1}	(M-8560) ^{c1}	Large cell neuroendocrine carcinomas ^{c1}	(M-8013) ^{c1}			Undifferentiated/dedifferentiated carcinomas ^{c1}	(M-8020) ^{c1}	Endometrioid carcinoma with squamous differentiation ^{c1}	(M-8570) ^{c1}	Mixed cell adenocarcinoma ^{c1}	(M-8323) ^{c1}			Squamous cell carcinoma ^{c1}	(M-8070-8072, 8076) ^{c1}	Adenocarcinoma, NOS ^{c1}	(M-8140) ^{c1}	Adenocarcinoma with neuroendocrine differentiation ^{c1}	(M-8574) ^{c1}			Carcinosarcomas (malignant mixed Müllerian tumor) ^{c1}	(M-8950, 8980) ^{c1}
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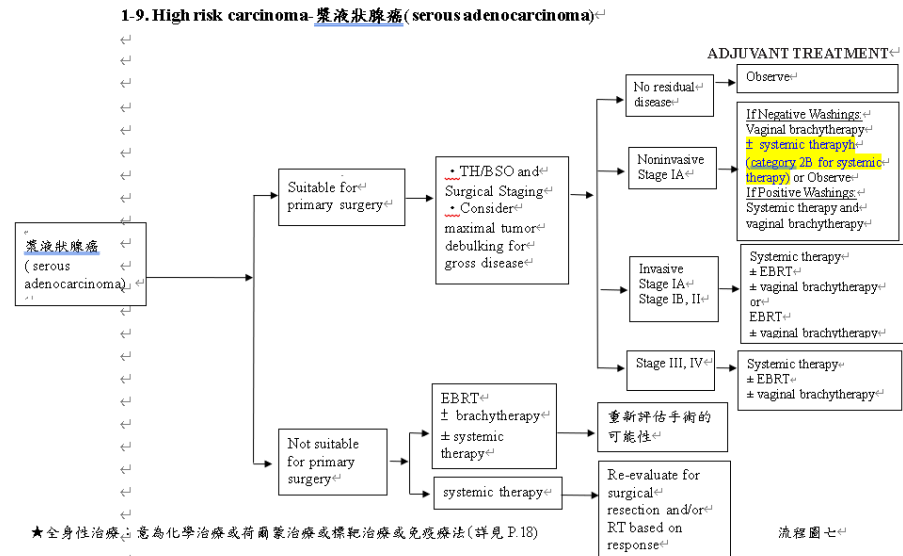


	<ul style="list-style-type: none"> • Undifferentiated uterine sarcoma (UUS) • Uterine leiomyosarcoma (uLMS) 	<ul style="list-style-type: none"> • High-grade ESS • Undifferentiated uterine sarcoma (UUS) • Uterine leiomyosarcoma (uLMS) • Other sarcoma
8	<p>【懷疑或巨觀下有子宮頸侵襲 FIGO Stage IIIA~IIIB】 可以手術 EBRT +brachytherapy TH/BSO and Surgical staging</p>	<p>【懷疑或巨觀下有子宮頸侵襲 FIGO Stage IIIA~IIIB】 可以手術 EBRT +brachytherapy TH/BSO and Surgical staging 4-12 weeks post RT</p>
8	<p>【懷疑或巨觀下有子宮頸侵襲 FIGO Stage IIIA~IIIB】 無法手術 EBRT +brachytherapy ± 全身性治療 Surgical resection,if rendered operable</p>	<p>【懷疑或巨觀下有子宮頸侵襲 FIGO Stage IIIA~IIIB】 無法手術 EBRT +brachytherapy ± 全身性治療 Surgical resection,if rendered operable 4-12 weeks post RT or Definitive RT if inoperable</p>
9	<p>【懷疑有子宮外病灶FIGO Stage IIIC~IVB】首次治療 (3) 無法手術 Abdominal/pelvic confined disease FIGO Stage IIIC~IVA EBRT ± brachytherapy ± systemic therapy 重新評估手術切除</p> <p>無法手術 Abdominal/pelvic confined disease FIGO Stage IIIC~IVA</p>	<p>【懷疑有子宮外病灶FIGO Stage IIIC~IVB】首次治療 (3) 無法手術 Abdominal/pelvic confined disease FIGO Stage IIIC~IVA EBRT ± brachytherapy ± systemic therapy 重新評估手術切除 4 - 12 weeks post RT</p> <p>無法手術 Abdominal/pelvic confined disease FIGO Stage IIIC~IVA Systemic therapy</p>

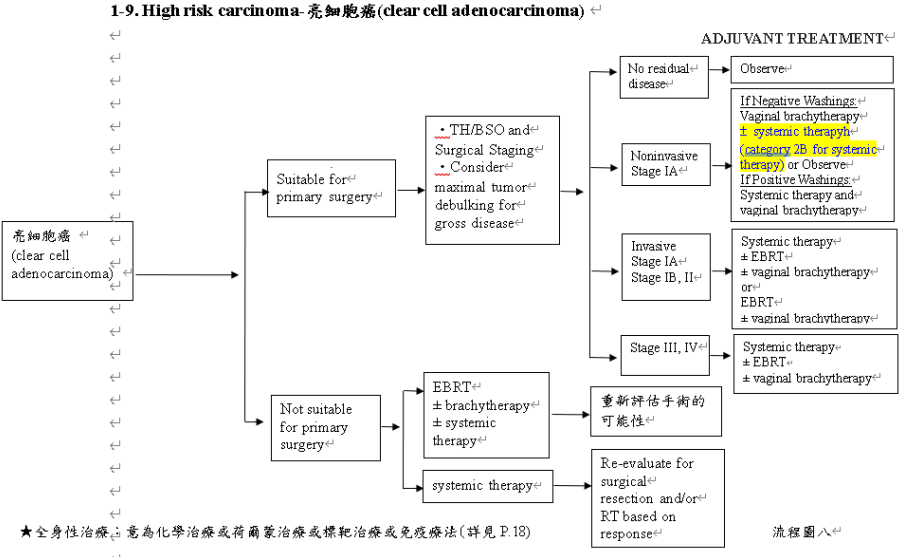
<p>11</p> <p>新增</p>	<p>1-7. 未接受完整手術分期之輔助治療</p> <p>不完全分期手術 (或意外發現) 僅子宮切除或 +/- 雙側/單側輸卵管卵巢切除</p>	<p>ADJUVANT TREATMENT</p> <p> * : risk-factors age ≥ 60 y, grade 2 or 3, depth of invasion to outer half, and LVSI * : 年齡小於45歲、Stage IA、G1者，卵巢可不切除 ★全身性治療：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見P18) </p> <p>流程圖五</p>
<p>12</p>	<p>1-8. 子宮內膜癌保留生育能力處置</p>	<p> 1. 育體激素 • Medroxyprogesterone • Levonorgestrel IUD (樂婷子宮內膜避孕系統) (preferred for fertility preservation) • Megestrol • Leupline 2. Weight management 3. and/or 降血糖藥物 • Glucophage </p> <p> 六個月後 無癌細胞 Encourage conception (with continued surveillance/endometrial sampling every 6-12 months and consider maintenance progestin based therapy if patient not actively trying to conceive) </p> <p> 六-十二個月後有癌細胞 TH/BSO with Staging after Childbearing complete or progression of disease on Endometrial sampling 見首次治療 1 Ovarian preservation may be considered in select premenopausal patients </p> <p>見首次治療 1 Ovarian preservation may be considered in select patients</p> <p>流程圖六</p>



13



14





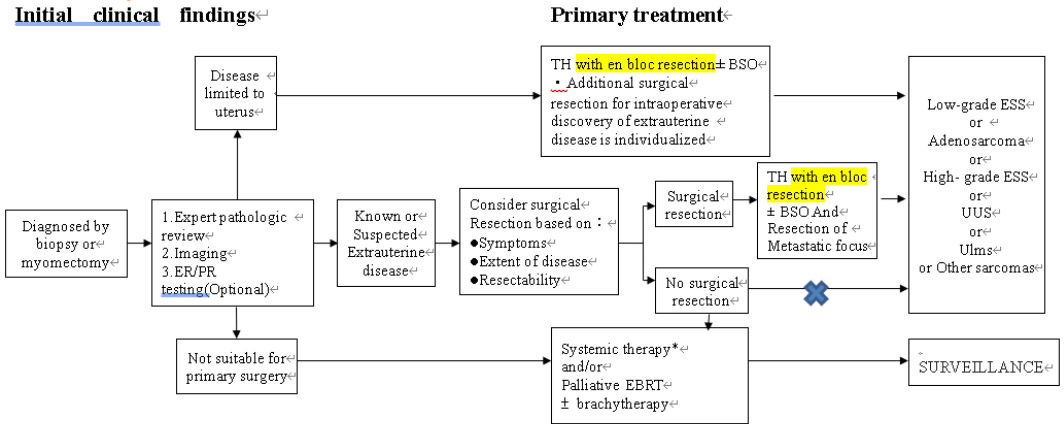
<p>16</p>		<p>1-9. High risk carcinoma - Carcinosarcoma[↵]</p> <p>★全身性治療[↵] 意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.18)</p> <p>流程圖[↵]</p>								
<p>18</p>	<p>Para-aortic or common iliac lymph node</p>	<p>刪除</p>								
<p>19</p>		<p>1-11. 子宮內膜癌之全身性治療[↵]</p> <table border="1"> <thead> <tr> <th data-bbox="1070 794 1518 817">Adjuvant Treatment When Used for Uterine Confined Disease</th> <th data-bbox="1518 794 1966 817">Primary or Adjuvant Therapy (Stage I-IV)[↵]</th> </tr> </thead> <tbody> <tr> <td data-bbox="1070 817 1518 1008"> <p>Chemoradiation Therapy[↵]</p> <p>Preferred Regimens[↵]</p> <ul style="list-style-type: none"> • Cisplatin plus RT followed by carboplatin/paclitaxel[↵] <p>Other Recommended Regimens[↵] (if cisplatin and carboplatin are unavailable)[↵]</p> <ul style="list-style-type: none"> • Capecitabine/mitomycin[↵] • Gemcitabine[↵] • Paclitaxel[↵] </td> <td data-bbox="1518 817 1966 1008"> <p>Systemic Therapy[↵]</p> <p>Preferred Regimens[↵]</p> <ul style="list-style-type: none"> • Carboplatin (or Cisplatin)/paclitaxel[↵] • Carboplatin/paclitaxel/pembrolizumab (for stage III-IV tumors, except for carcinosarcoma) (category 1)[↵] • Carboplatin/paclitaxel/dostarlimab-gzly (for stage III-IV tumors) (category 1)[↵] • Carboplatin/paclitaxel/trastuzumab (for stage III/IV HER2-positive uterine serous carcinoma)[↵] • Carboplatin/paclitaxel/trastuzumab (for stage III/IV HER2-positive carcinosarcoma)[↵] </td> </tr> <tr> <th data-bbox="1070 1040 1518 1062">RECURRENT DISEASE[↵]</th> <th data-bbox="1518 1040 1966 1062">RECURRENT DISEASE[↵]</th> </tr> <tr> <td data-bbox="1070 1062 1518 1401"> <p>First-Line Therapy for Recurrent Disease[↵]</p> <p>Preferred Regimens[↵]</p> <ul style="list-style-type: none"> • Carboplatin (or Cisplatin)/paclitaxel (category 1 for carcinosarcoma)[↵] • Carboplatin/paclitaxel/pembrolizumab (except for carcinosarcoma) (category 1)[↵] • Carboplatin/paclitaxel/dostarlimab-gzly (category 1)[↵] • Carboplatin (or Cisplatin)/paclitaxel/trastuzumab[↵] (for stage III/IV or recurrent HER2-positive uterine serous carcinoma and carcinosarcoma)[↵] <p>Other Recommended Regimens[↵]</p> <ul style="list-style-type: none"> • Carboplatin/docetaxel[↵] • Carboplatin/paclitaxel/bevacizumab[↵] <p>Useful in Certain Circumstances[↵]</p> </td> <td data-bbox="1518 1062 1966 1401"> <p>Second-Line or Subsequent Therapy[↵]</p> <p>Other Recommended Regimens[↵]</p> <ul style="list-style-type: none"> • Carboplatin/docetaxel[↵] • Cisplatin/doxorubicin[↵] • Cisplatin/doxorubicin/paclitaxel[↵] • Carboplatin/paclitaxel/bevacizumab[↵] • Cisplatin[↵] • Carboplatin[↵] • Doxorubicin[↵] • Liposomal doxorubicin[↵] • Paclitaxel[↵] • Albumin-bound paclitaxel[↵] • Topotecan[↵] • Bevacizumab[↵] • Temsirolimus[↵] • Cabozantinib[↵] • Docetaxel (category 2B)[↵] </td> </tr> </tbody> </table>	Adjuvant Treatment When Used for Uterine Confined Disease	Primary or Adjuvant Therapy (Stage I-IV) [↵]	<p>Chemoradiation Therapy[↵]</p> <p>Preferred Regimens[↵]</p> <ul style="list-style-type: none"> • Cisplatin plus RT followed by carboplatin/paclitaxel[↵] <p>Other Recommended Regimens[↵] (if cisplatin and carboplatin are unavailable)[↵]</p> <ul style="list-style-type: none"> • Capecitabine/mitomycin[↵] • Gemcitabine[↵] • Paclitaxel[↵] 	<p>Systemic Therapy[↵]</p> <p>Preferred Regimens[↵]</p> <ul style="list-style-type: none"> • Carboplatin (or Cisplatin)/paclitaxel[↵] • Carboplatin/paclitaxel/pembrolizumab (for stage III-IV tumors, except for carcinosarcoma) (category 1)[↵] • Carboplatin/paclitaxel/dostarlimab-gzly (for stage III-IV tumors) (category 1)[↵] • Carboplatin/paclitaxel/trastuzumab (for stage III/IV HER2-positive uterine serous carcinoma)[↵] • Carboplatin/paclitaxel/trastuzumab (for stage III/IV HER2-positive carcinosarcoma)[↵] 	RECURRENT DISEASE [↵]	RECURRENT DISEASE [↵]	<p>First-Line Therapy for Recurrent Disease[↵]</p> <p>Preferred Regimens[↵]</p> <ul style="list-style-type: none"> • Carboplatin (or Cisplatin)/paclitaxel (category 1 for carcinosarcoma)[↵] • Carboplatin/paclitaxel/pembrolizumab (except for carcinosarcoma) (category 1)[↵] • Carboplatin/paclitaxel/dostarlimab-gzly (category 1)[↵] • Carboplatin (or Cisplatin)/paclitaxel/trastuzumab[↵] (for stage III/IV or recurrent HER2-positive uterine serous carcinoma and carcinosarcoma)[↵] <p>Other Recommended Regimens[↵]</p> <ul style="list-style-type: none"> • Carboplatin/docetaxel[↵] • Carboplatin/paclitaxel/bevacizumab[↵] <p>Useful in Certain Circumstances[↵]</p>	<p>Second-Line or Subsequent Therapy[↵]</p> <p>Other Recommended Regimens[↵]</p> <ul style="list-style-type: none"> • Carboplatin/docetaxel[↵] • Cisplatin/doxorubicin[↵] • Cisplatin/doxorubicin/paclitaxel[↵] • Carboplatin/paclitaxel/bevacizumab[↵] • Cisplatin[↵] • Carboplatin[↵] • Doxorubicin[↵] • Liposomal doxorubicin[↵] • Paclitaxel[↵] • Albumin-bound paclitaxel[↵] • Topotecan[↵] • Bevacizumab[↵] • Temsirolimus[↵] • Cabozantinib[↵] • Docetaxel (category 2B)[↵]
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20		<p><i>(Biomarker-directed therapy: after prior platinum-based therapy⁴² including neoadjuvant and adjuvant)⁴²</i></p> <ul style="list-style-type: none"> • Lenvatinib/pembrolizumab (category 1) for MMR-proficient (pMMR) tumors /non-MSI-high (MSI-H)/non-MMR-deficient (dMMR) tumors⁴² • Pembrolizumab (for TMB-H/MSI-H/dMMR tumors)⁴² • Dostarlimab-gxly (for MSI-H/dMMR tumors)⁴² <p><i>Useful in Certain Circumstances (Biomarker-directed therapy)⁴²</i></p> <ul style="list-style-type: none"> • pMMR tumors⁴² Lenvatinib/pembrolizumab (category 1)⁴² • TMB-H tumors⁴² Pembrolizumab⁴² • MSI-H/dMMR tumors⁴² Pembrolizumab⁴² Dostarlimab-gxly⁴² • HER2-positive tumors (IHC 3+ or 2+)⁴² Fam-trastuzumab deruxetan⁴² • NTRK gene fusion-positive tumors⁴² Larotrectinib⁴² Entrectinib⁴² <p>HORMONE THERAPY for Recurrent or Metastatic Endometrial Carcinoma⁴²</p> <table border="1"> <thead> <tr> <th><i>Preferred Regimens⁴²</i></th> <th><i>Other Recommended Regimens⁴²</i></th> <th><i>Useful In Certain Circumstances⁴²</i></th> </tr> </thead> <tbody> <tr> <td> <ul style="list-style-type: none"> • Megestrol/tamoxifen (alternating)⁴² • Everolimus/letrozole (For endometrioid histology)⁴² Levonorgestrel intrauterine device(IUD)(For select fertility-sparing cases)⁴² </td> <td> <ul style="list-style-type: none"> • Medroxyprogesterone acetate/tamoxifen (alternating)⁴² • Progestational agents⁴² Medroxyprogesterone acetate 、Megestrol⁴² • Aromatase inhibitors⁴² • Tamoxifen⁴² • Fulvestrant⁴² </td> <td> <ul style="list-style-type: none"> N/A⁴² ER-positive tumors⁴² Letrozole/triciclib⁴² Letrozole/abemaciclib⁴² </td> </tr> </tbody> </table>	<i>Preferred Regimens⁴²</i>	<i>Other Recommended Regimens⁴²</i>	<i>Useful In Certain Circumstances⁴²</i>	<ul style="list-style-type: none"> • Megestrol/tamoxifen (alternating)⁴² • Everolimus/letrozole (For endometrioid histology)⁴² Levonorgestrel intrauterine device(IUD)(For select fertility-sparing cases)⁴² 	<ul style="list-style-type: none"> • Medroxyprogesterone acetate/tamoxifen (alternating)⁴² • Progestational agents⁴² Medroxyprogesterone acetate 、Megestrol⁴² • Aromatase inhibitors⁴² • Tamoxifen⁴² • Fulvestrant⁴² 	<ul style="list-style-type: none"> N/A⁴² ER-positive tumors⁴² Letrozole/triciclib⁴² Letrozole/abemaciclib⁴²
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21		<p>Hormonal Therapy for Uterine-Limited Disease Not Suitable for Primary Surgery or for Those Desiring Uterine Preservation for Fertility</p> <table border="1"> <thead> <tr> <th><i>Preferred Regimens</i></th> <th><i>Other Recommended Regimens</i></th> </tr> </thead> <tbody> <tr> <td>Levonorgestrel intrauterine device(IUD)</td> <td> <ul style="list-style-type: none"> • Progestational agents Medroxyprogesterone acetate 、 Megestrol </td> </tr> </tbody> </table>	<i>Preferred Regimens</i>	<i>Other Recommended Regimens</i>	Levonorgestrel intrauterine device(IUD)	<ul style="list-style-type: none"> • Progestational agents Medroxyprogesterone acetate 、 Megestrol 		
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30		<p>2-2.子宮急性肉瘤之臨床發現及處置⁴²</p>						



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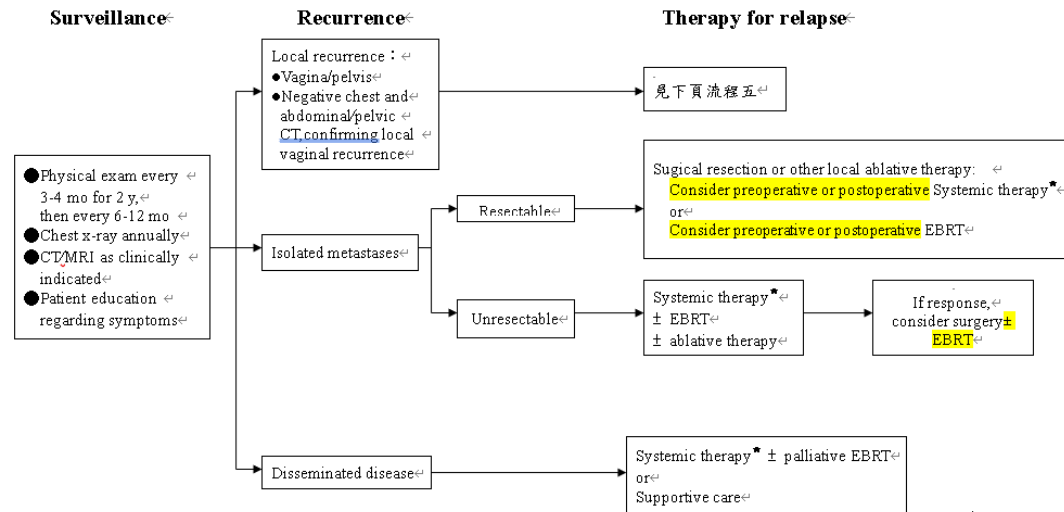


流程圖一

★Systemic therapy: 意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.32)

2-3. 子宮惡性肉瘤之復發處置

34



流程四

★Systemic therapy: 意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.32)



36		<p>2-4.子宮惡性肉瘤之全身性治療[↵]</p> <p style="text-align: center;">SYSTEMIC THERAPY FOR UTERINE SARCOMA[↵] (Clinical trials strongly recommended)[↵]</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; padding: 5px;">Systemic Therapy[↵]</td> <td style="width: 50%; padding: 5px;">HORMONE THERAPY[↵] (For Low-grade ESS or Hormone Receptor Positive (ER/PR) uLMS or Adenosarcoma Without SO)[↵]</td> </tr> <tr> <td style="padding: 5px;">First-Line Therapy[↵]</td> <td style="padding: 5px;"><i>Preferred Regimens:</i>[↵] ★ Aromatase inhibitors for low-grade ESS or adenosarcoma without SO[↵] ↵ <i>Other recommended regimens:</i>[↵] ★ Medroxyprogesterone acetate (category 2B for ER/PR positive uLMS)[↵] ★ Megestrol acetate (category 2B for ER/PR positive uLMS)[↵] ★ Aromatase inhibitors (for ER/PR positive uLMS)[↵] ★ GnRH analogs (category 2B for low-grade ESS and ER/PR positive uLMS-adenosarcoma without SO)[↵] ★ Fulvestrant[↵]</td> </tr> <tr> <td style="padding: 5px;"><i>Useful in Certain Circumstances</i>[↵] • Biomarker-directed therapy[↵] NTRK gene fusion-positive tumors[↵] ◊ Larotrectinib[↵] ◊ Entrectinib[↵] IMT with ALK translocation[↵] ◊ Crizotinib[↵] ◊ Ceritinib[↵] ◊ Brigatinib[↵] ◊ Lorlatinib[↵] ◊ Alectinib[↵] • PEComa[↵] Albumin-bound sirolimus[↵] ↵</td> <td style="padding: 5px;">Biomarker-Directed Systemic Therapy for Second-Line Treatment[↵] • Pembrolizumab for TMB-H tumors[↵] • Larotrectinib or entrectinib for NTRK gene fusion-positive tumors² (category 2B)[↵] • Consider PARP inhibitors for BRCA2-altered uLMS[↵] ■ Olaparib[↵] ■ Rucaparib[↵] ■ Niraparib[↵] ■ PEComa[↵] ◊ Sirolimus[↵] ◊ Everolimus[↵]</td> </tr> <tr> <td style="padding: 5px;">Second-Line or Subsequent Therapy[↵]</td> <td style="padding: 5px;"></td> </tr> </table>	Systemic Therapy [↵]	HORMONE THERAPY [↵] (For Low-grade ESS or Hormone Receptor Positive (ER/PR) uLMS or Adenosarcoma Without SO) [↵]	First-Line Therapy[↵]	<i>Preferred Regimens:</i> [↵] ★ Aromatase inhibitors for low-grade ESS or adenosarcoma without SO [↵] ↵ <i>Other recommended regimens:</i> [↵] ★ Medroxyprogesterone acetate (category 2B for ER/PR positive uLMS) [↵] ★ Megestrol acetate (category 2B for ER/PR positive uLMS) [↵] ★ Aromatase inhibitors (for ER/PR positive uLMS) [↵] ★ GnRH analogs (category 2B for low-grade ESS and ER/PR positive uLMS-adenosarcoma without SO) [↵] ★ Fulvestrant [↵]	<i>Useful in Certain Circumstances</i> [↵] • Biomarker-directed therapy [↵] NTRK gene fusion-positive tumors [↵] ◊ Larotrectinib [↵] ◊ Entrectinib [↵] IMT with ALK translocation [↵] ◊ Crizotinib [↵] ◊ Ceritinib [↵] ◊ Brigatinib [↵] ◊ Lorlatinib [↵] ◊ Alectinib [↵] • PEComa [↵] Albumin-bound sirolimus [↵] ↵	Biomarker-Directed Systemic Therapy for Second-Line Treatment [↵] • Pembrolizumab for TMB-H tumors [↵] • Larotrectinib or entrectinib for NTRK gene fusion-positive tumors ² (category 2B) [↵] • Consider PARP inhibitors for BRCA2-altered uLMS [↵] ■ Olaparib [↵] ■ Rucaparib [↵] ■ Niraparib [↵] ■ PEComa [↵] ◊ Sirolimus [↵] ◊ Everolimus [↵]	Second-Line or Subsequent Therapy[↵]	
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一、子宮內膜癌

1-1. 前言

共識手冊內所提之各種診治意見，為原則性之建議，希望能為癌症患者及其家屬提供一個正確的指引；但對臨床醫師之醫療行為無絕對之法律性約束力！由於醫藥科技持續在進步，每位患者的病情亦不盡相同；醫師應就病人之病情做個別的考量，病人和家屬亦應與醫師溝通討論，以決定最適當之診治方式。

台灣大部分子宮內膜癌發生在停經後之女性，其好發的年齡中位值是在52-54歲，大部分病人其年齡在45-59歲之間。雖然 60% 的病例發生在50歲之後，但仍有15%的病例出現在40歲之前。子宮內膜癌可以發生在生育年齡及其後的任何一個年齡層，但比較好發於更年期或停經後的婦女。70-80%的子宮內膜癌診斷時僅侷限在子宮。其早期症狀主要為停經後之陰道出血，病患會因此早期就醫，與其他女性生殖道惡性腫瘤比較，有較高的存活率。

子宮內膜癌的危險因子包括有糖尿病、高血壓、肥胖、未有生育之婦女、初經年齡早而停經年齡晚、使用更年期荷爾蒙治療未合併黃體素之婦女、遺傳及種族因素、乳癌病患使用抗癌藥物治療者。

本子宮體癌診斷及治療指引的內容有子宮內膜癌、子宮惡性肉瘤及妊娠組織瘤等，其內容除了依據已發表的實證醫學證據及專家意見外，並參考國家衛生研究院子宮內膜癌臨床指引、美國 National Comprehensive Cancer Network (NCCN) 的 Practice Guide-lines in endometrial Cancer 2024Version1版、FIGO Staging Classifications and Clinical Practice Guidelines in the Management of Gynecologic Cancer、MD Anderson cancer center及中山醫學大學附設醫院子宮體癌治療經驗進行編修。



1-2. 子宮內膜癌之分期 2023 FIGO 分期

Uterine Carcinomas and Carcinosarcoma

I	Confined to the uterine corpus and ovary 病灶只侷限在子宮體和卵巢
IA	Disease limited to the endometrium OR non-aggressive histological type, i.e. low- grade endometrioid, with invasion of less than half of myometrium with no or focal lymphovascular space involvement (LVSI) OR good prognosis disease 病灶只限在子宮內膜或屬非侵犯性組織類型：如低度 (grade 1 和2) 類子宮內膜癌，侵犯 < 1/2 肌肉層，沒有或僅局部淋巴血管侵犯、或屬良好預後的疾病
IA1	Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium 非侵犯性組織，只侷限在子宮內膜瘰肉內或子宮內膜中
IA2	Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI 非侵犯性組織，侵犯 < 1/2 肌肉層，沒有或僅局部淋巴血管侵犯
IA3	Low-grade endometrioid carcinomas limited to the uterus and ovary 低度類子宮內膜癌，侷限在子宮和卵巢中
IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI 非侵犯性組織，併侵犯 ≥ 1/2 肌肉層，沒有或僅局部淋巴血管侵犯
IC	Aggressive histological types limited to a polyp or confined to the endometrium 侵犯性組織，侷限在瘰肉內或子宮內膜層中
II	Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion 病灶侵犯至子宮頸基質內，或多量的淋巴血管侵犯，或侵犯性組織類型併肌肉層侵犯
IIA	Invasion of the cervical stroma of non-aggressive histological types 非侵犯性組織，侵犯至子宮頸基質內
IIB	Substantial LVSI of non-aggressive histological types 非侵犯性組織，多量的淋巴血管侵犯
IIC	Aggressive histological types with any myometrial involvement 侵犯性組織，併任何肌肉層侵犯
III	Local and/or regional spread of the tumor of any histological subtype 任何組織型病灶，有局部性擴散
IIIA	Invasion of uterine serosa, adnexa, or both by direct extension or metastasis 經擴散或轉移病灶侵犯至漿膜層、附屬器或二者
IIIA1	Spread to ovary or fallopian tube (except when meeting stage IA3 criteria) 擴散至卵巢和輸卵管 (不符合 Ia3 條件者)
IIIA2	Involvement of uterine subserosa or spread through the uterine serosa 擴散至子宮漿膜層下，或經子宮漿膜層擴散
IIIB	Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum 轉移或直接擴散至陰道、和/ 或至子宮旁組織、或骨盆腔腹膜
IIIB1	Metastasis or direct spread to the vagina and/or the parametria 轉移或直接擴散至陰道、和/ 或至子宮旁組織
IIIB2	Metastasis to the pelvic peritoneum 轉移至骨盆腔腹膜
IIIC	Metastasis to the pelvic or para-aortic lymph nodes or both 轉移至骨盆腔、主動脈旁淋巴結或二者



IIC1	Metastasis to the pelvic lymph nodes 轉移至骨盆腔淋巴結
IIC1i	Micrometastasis 顯微性轉移
IIC1ii	Macrometastasis 巨大轉移
IIC2	Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes 轉移至主動脈旁淋巴結，在腎血管下，有或沒有骨盆腔淋巴結轉移
IIC2i	Micrometastasis 顯微性轉移
IIC2ii	Macrometastasis 巨大轉移
IV	Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastasis 擴散至膀胱黏膜、和/或腸子黏膜、和/或遠端轉移
IVA	Invasion of the bladder mucosa and/or the intestinal/bowel mucosa 侵犯至膀胱的黏膜，和/或腸子黏膜
IVB	Abdominal peritoneal metastasis beyond the pelvis 腹腔腹膜轉移超過骨盆腔外
IVC	Distant metastasis, including metastasis to any extra- or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone 遠端轉移，包括任何腎血管上方的腹腔內、外淋巴結、肺、肝、腦或骨骼

AJCC Prognostic Stage Groups			
	T	N	M
Stage I	T1	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC1	T1-T3	N1/N1mi/N1a	M0
Stage IIIC2	T1-T3	N2/N2mi/N2a	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1



1-3. 子宮內膜腺癌保留生育功能：評估與方法
(特殊類型子宮內膜癌和肉瘤不能保留生育功能)

1. 子宮內膜腺癌，G1 級
2. MRI(首選)或陰道超陰波檢查確認病灶侷限於子宮內膜
3. 影像學檢查未發現可以轉移病灶
4. 無藥物治療或妊娠的禁忌症
5. 經充分諮詢了解保留生育功能並非子宮內膜癌的標準治療方式
6. 治療前諮詢生殖醫學
7. 有條件者可考慮遺傳諮詢或基因檢測
8. 可選擇 Medroxyprogesterone(400-600mg/D)、Levonorgestrel 和 Megestrol(160-320mg/D)藥物控制子宮內膜癌
9. 嚴密追蹤：每 3-6 個月 D&C 並採病理報告檢驗
10. 癌持續存在 6-12 個月，全子宮+雙附屬器官切除+手術分期
11. 病變完全緩解 6 個月，鼓勵病患受孕，孕前持續每 6-12 個月進行子宮內膜取樣檢查。暫無生育計畫者，於以雌激素維持治療及定期監測
12. 完成生育後或內膜取樣發現疾病進展，即行全子宮+雙附屬器官切除+手術分期



子宮內膜腺癌的手術原則

TH/BSO and lymph node assessment may be performed by any surgical route (eg, laparoscopic, robotic, vaginal, abdominal), although the standard in those with apparent uterine-confined disease is to perform the procedure via a minimally invasive approach.

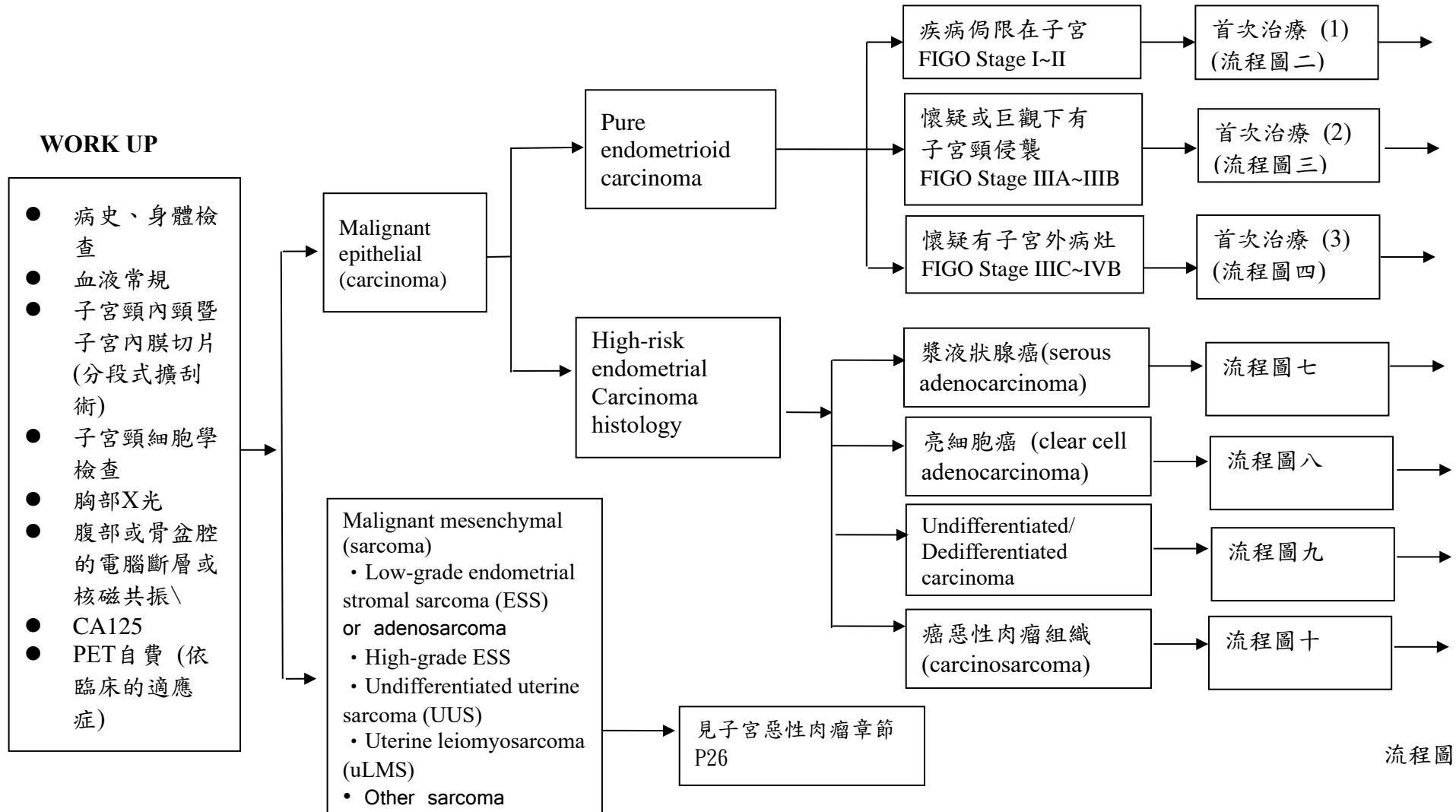
第一型(Type I)及第二型(TypeII)組織類型分組

限定原發部位 癌登編碼 =C54.0、C54.1、C54.3、C54.8、C54.9 扣除 2.6 原發部位=C54.2(myometrium)。

第一型(Type I)		第二型(TypeII)	
Endometrioid carcinoma	(M8380,8382-8383)	Serous carcinoma	(M-8441, 8460-8461)
		Clear cell carcinoma	(M-8310)
Mucinous adenocarcinoma	(M8480)	Small cell carcinoma	(M-8041, 8045)
		Neuroendocrine carcinoma, NOS	(M-8246)
Adenosquamous carcinoma	(M-8560)	Large cell neuroendocrine carcinomas	(M-8013)
		Undifferentiated/dedifferentiated carcinomas	(M-8020)
Endometrioid carcinoma with squamous differentiation	(M-8570)	Mixed cell adenocarcinoma	(M-8323)
		Squamous cell carcinoma	(M-8070-8072, 8076)
Adenocarcinoma, NOS	(M-8140)	Adenocarcinoma with neuroendocrine differentiation	(M-8574)
		Carcinosarcomas (malignant mixed Müllerian tumor)	(M-8950, 8980)

第二型 (type II) 子宮內膜癌病人應接受完整分期手術，包含Total hysterectomy, BSO, BPLND, PALND, omentectomy, washing cytology

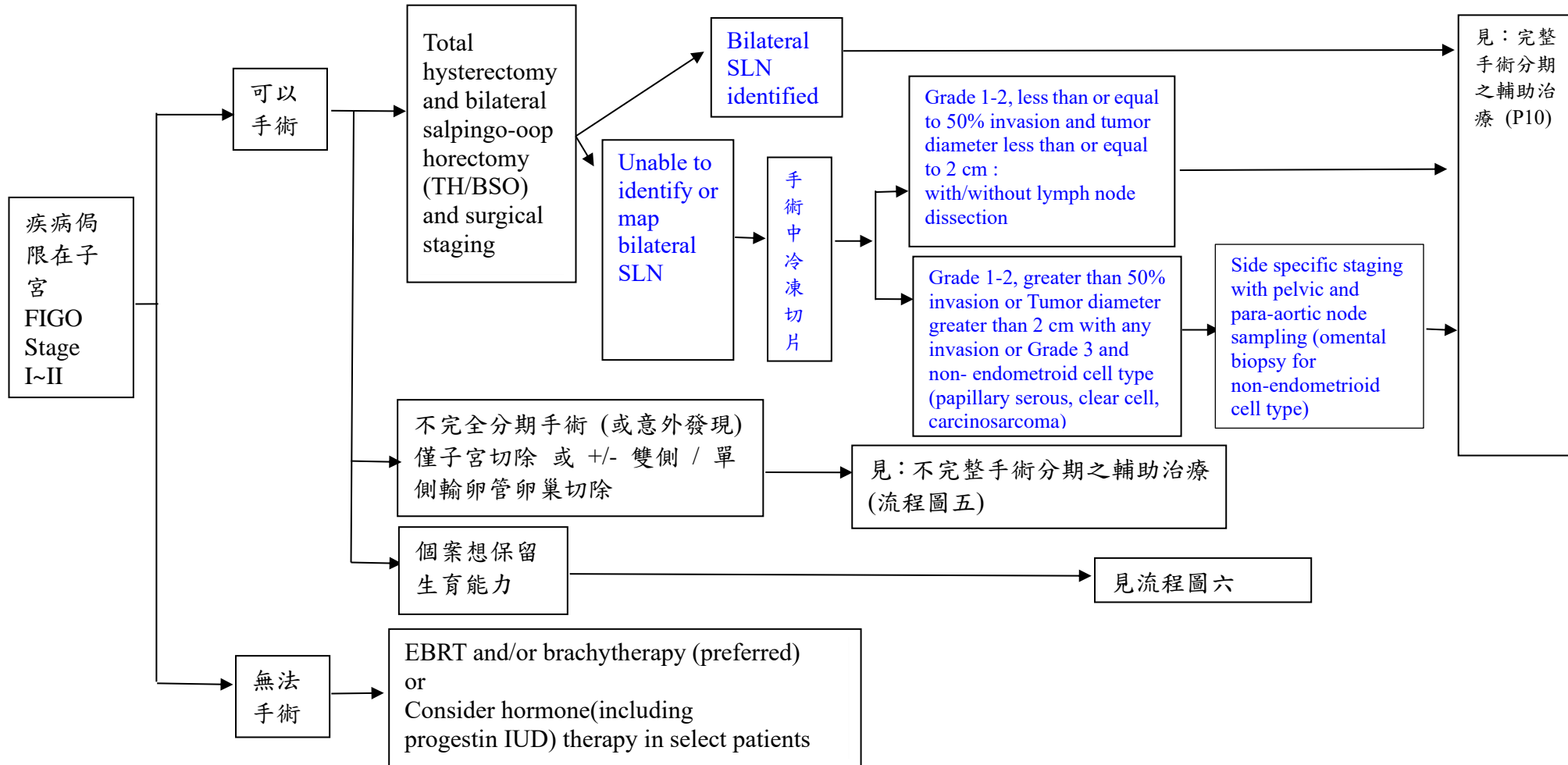
1-4.子宮內膜癌之診斷與評估



流程圖一

1-5. 子宮內膜癌之治療

【疾病侷限在子宮FIGO Stage I~II】首次治療 (1)

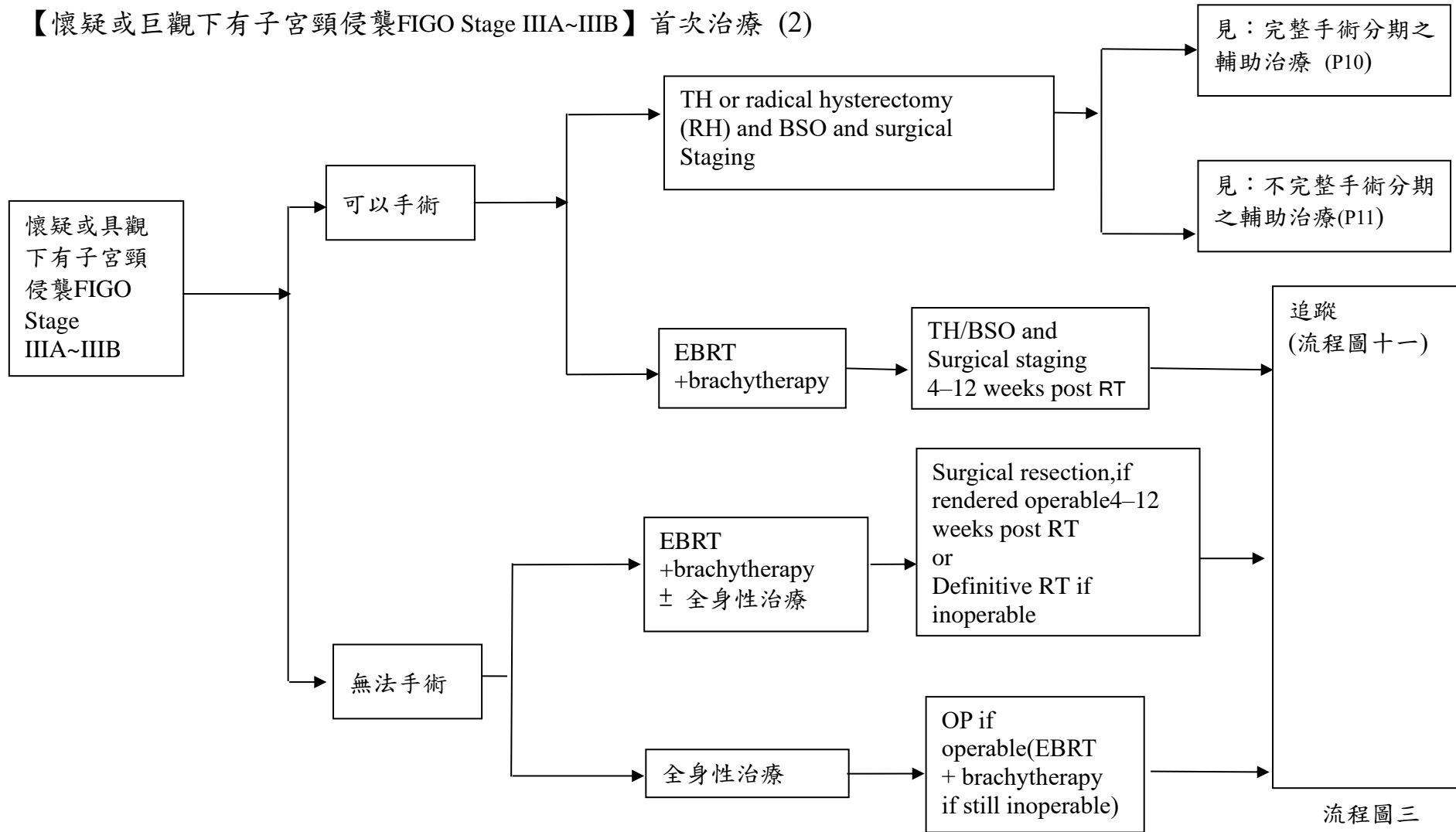


流程圖二



1-5. 子宮內膜癌之治療

【懷疑或巨觀下有子宮頸侵襲FIGO Stage IIIA~IIIB】首次治療 (2)



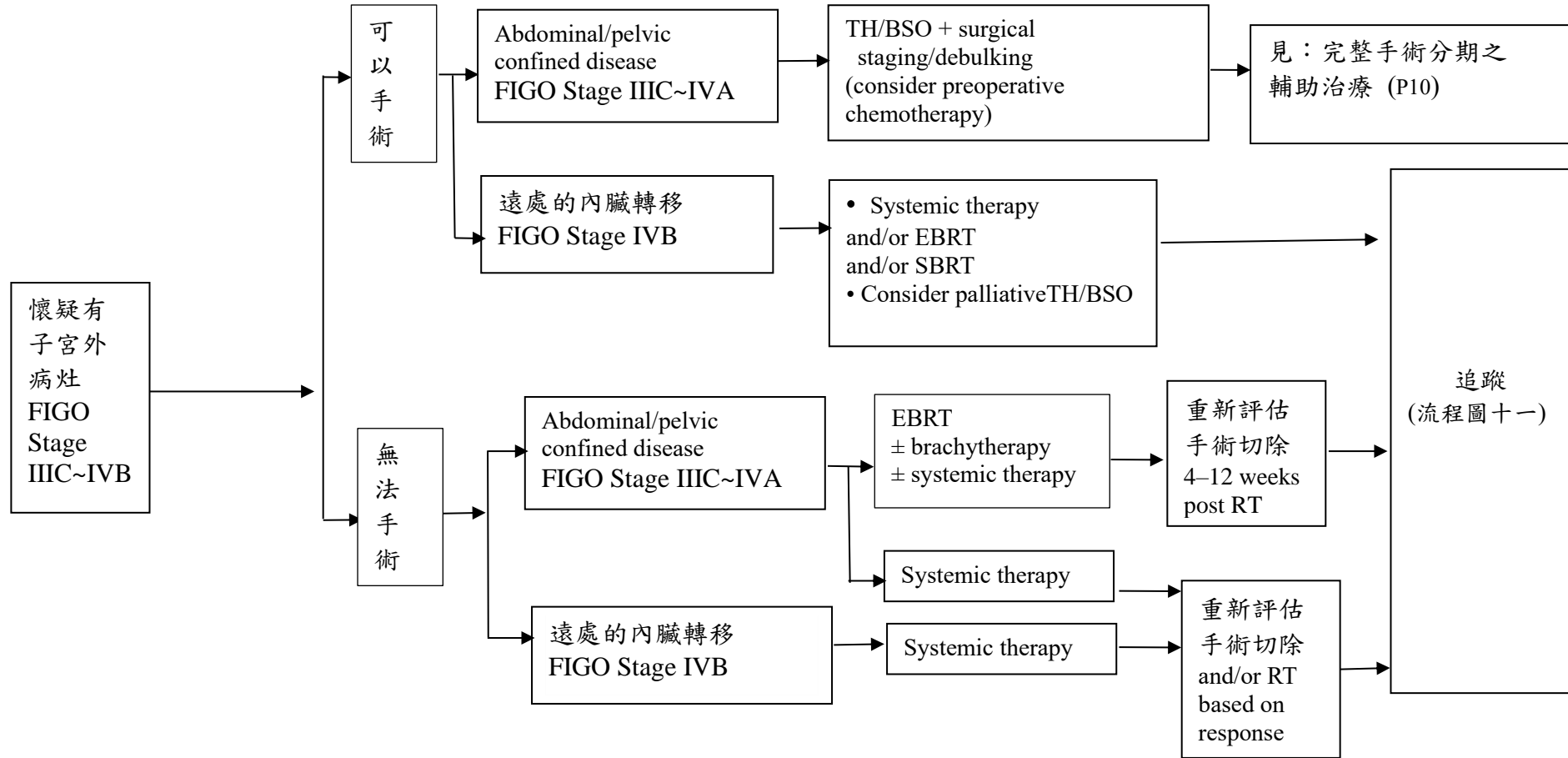
流程圖三

★全身性治療：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.18)



1-5. 子宮內膜癌之治療

【懷疑有子宮外病灶FIGO Stage IIIC~IVB】首次治療 (3)



流程圖四

★全身性治療：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.18)

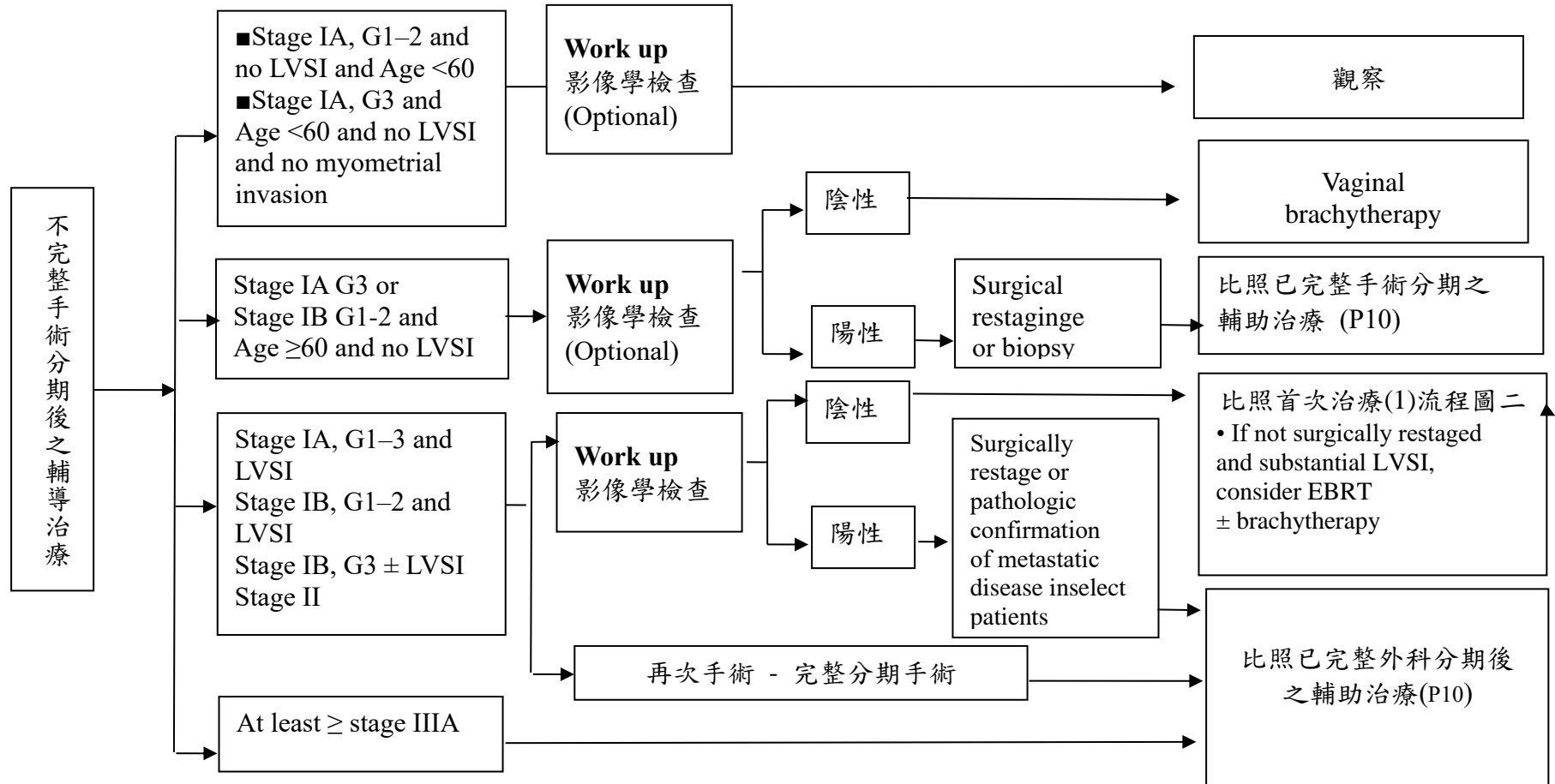
**1-6. 子宮內膜癌完整手術分期後之輔助治療**

FIGO Stage	Histologic Grade	Adjuvant Treatment
IA	G1, G2	Observation preferred or Consider vaginal brachytherapy if lymphovascular space invasion (LVSI) and/or age ≥ 60 y
	G3	Vaginal brachytherapy preferred or Consider observation if no myoinvasion or Consider EBRT if either age ≥ 70 y or LVSI (category 2B)
IB	G1	Vaginal brachytherapy preferred or Consider observation if age < 60 y and no LVSI
	G2	Vaginal brachytherapy preferred or Consider EBRT if ≥ 60 y and/or LVSI or Consider observation if age < 60 y and no LVSI
	G3	RT (EBRT and/or vaginal brachytherapy) \pm systemic therapy (category 2B for systemic therapy)
II	G1~G3	EBRT (preferred) and/or vaginal brachytherapy \pm systemic therapy (category 2B for systemic therapy)
III-IV		Systemic therapy \pm EBRT \pm vaginal brachytherapy

1-7. 未接受完整手術分期之輔助治療

不完全分期手術 (或意外發現) 僅子宮切除或+/- 雙側/單側輸卵管卵巢切除

ADJUVANT TREATMENT



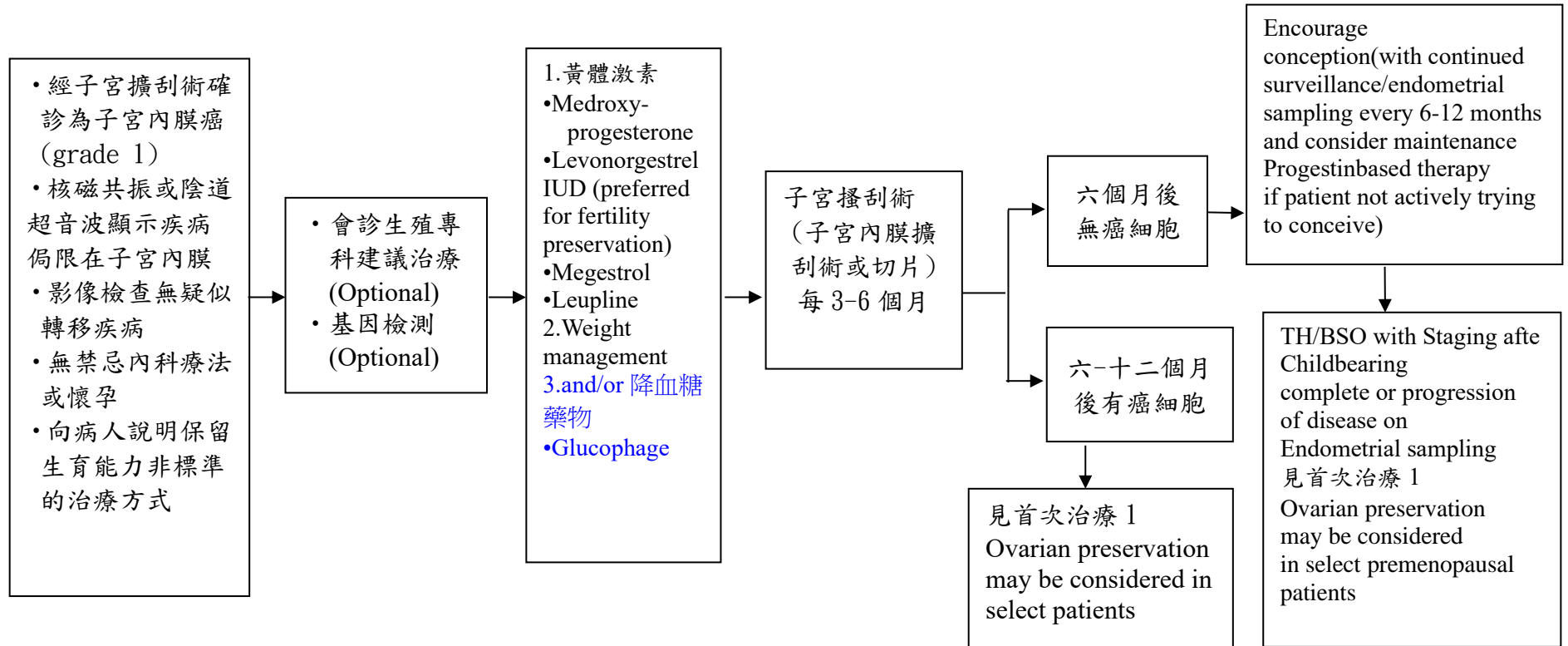
流程圖五

* : risk-factors age ≥60 y, grade 2 or 3, depth of invasion to outer half, and LVSI

* : 年齡小於45歲、Stage IA、G1者，卵巢可不切除

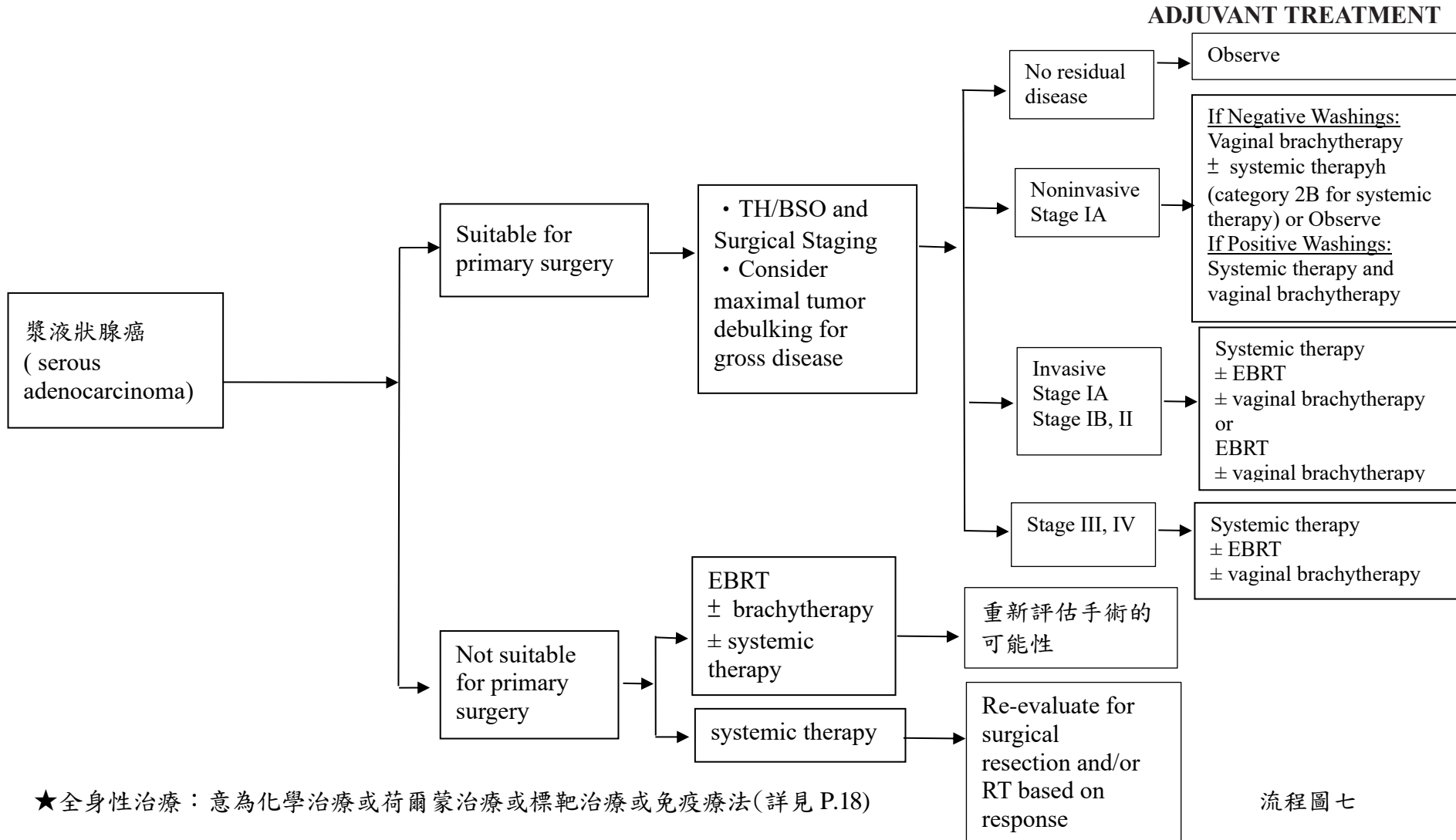
★全身性治療：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.18)

1-8.子宮內膜癌保留生育能力處置



流程圖六

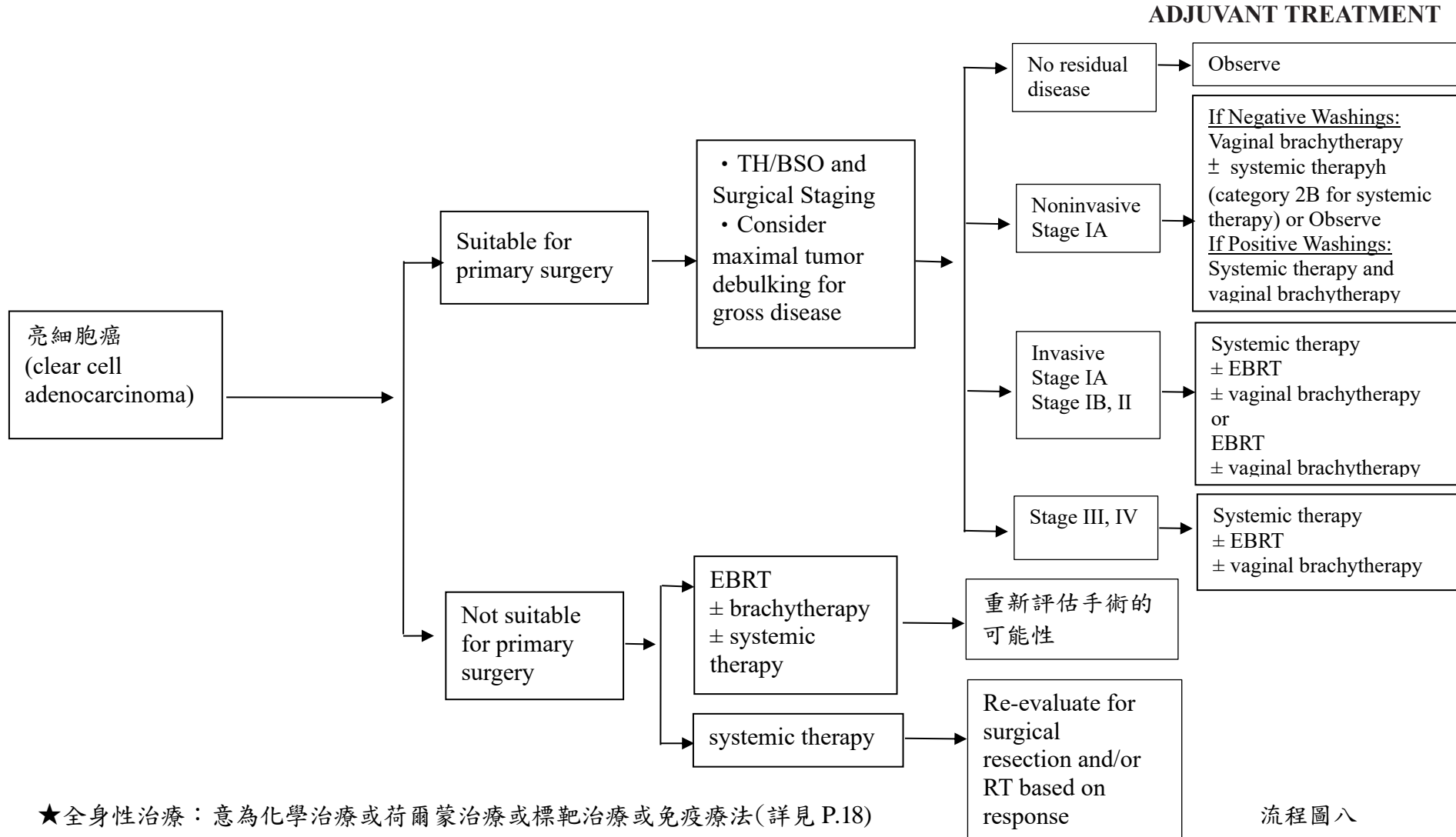
1-9. High risk carcinoma-漿液狀腺癌 (serous adenocarcinoma)



★全身性治療：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.18)

流程圖七

1-9. High risk carcinoma-亮細胞癌(clear cell adenocarcinoma)

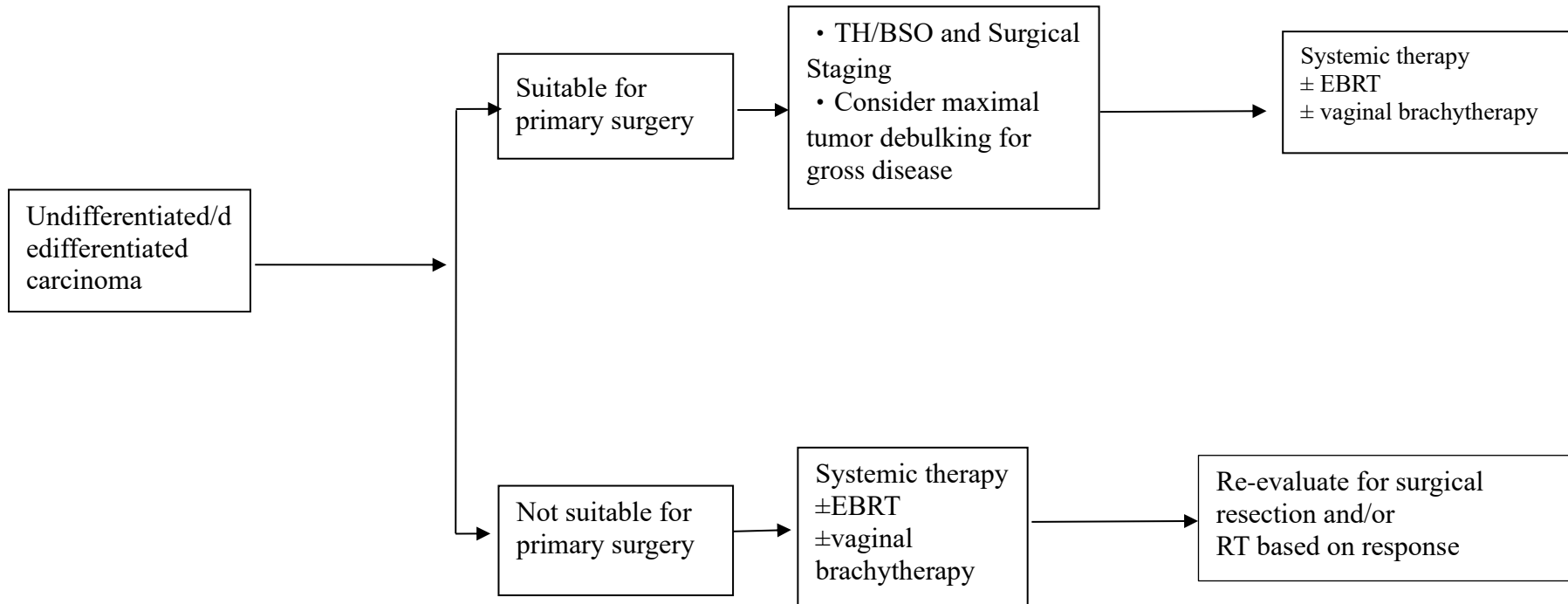


★全身性治療：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.18)

流程圖八

1-9. High risk carcinoma -Undifferentiated/dedifferentiated carcinoma

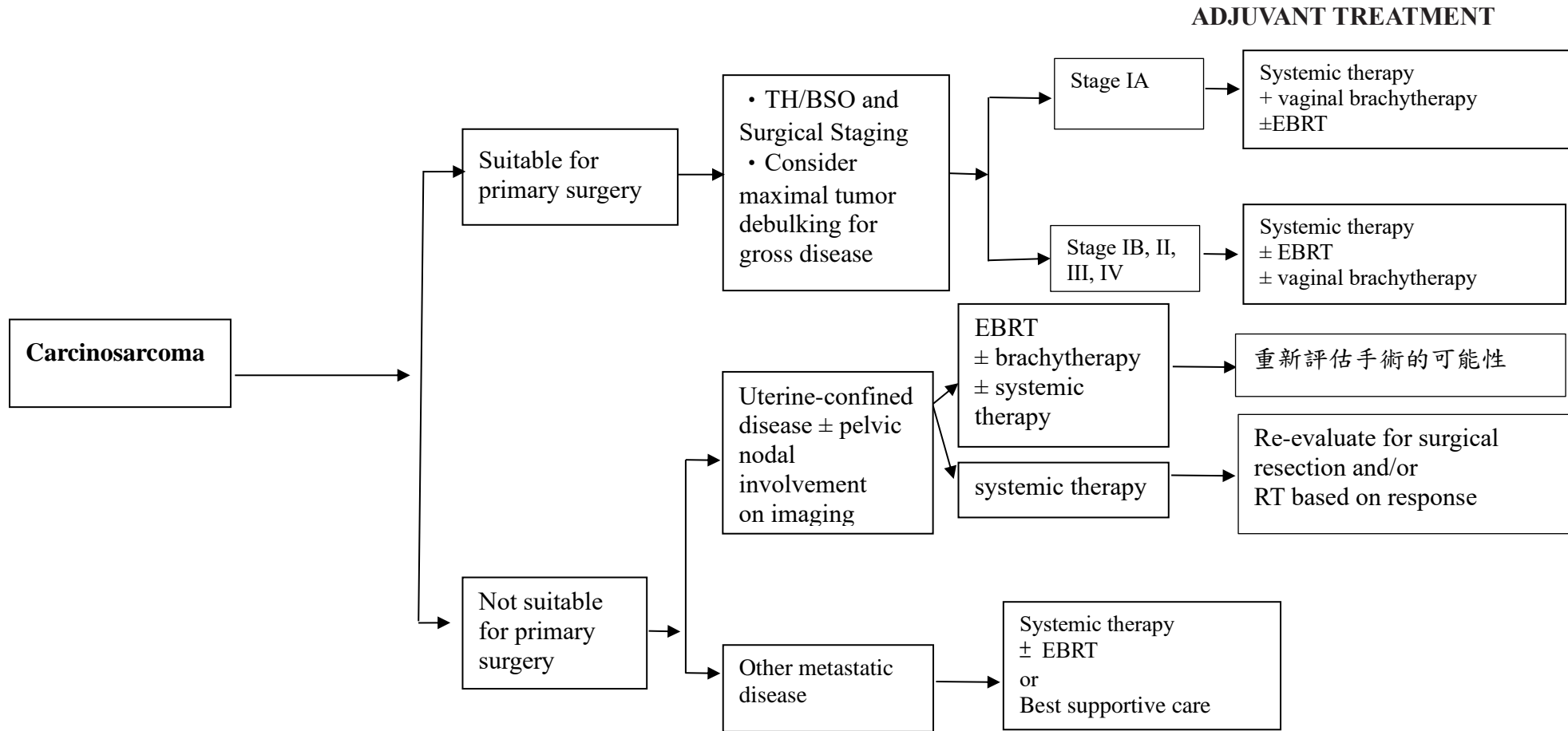
ADJUVANT TREATMENT



★全身性治療：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.18)

流程圖九

1-9. High risk carcinoma -Carcinosarcoma



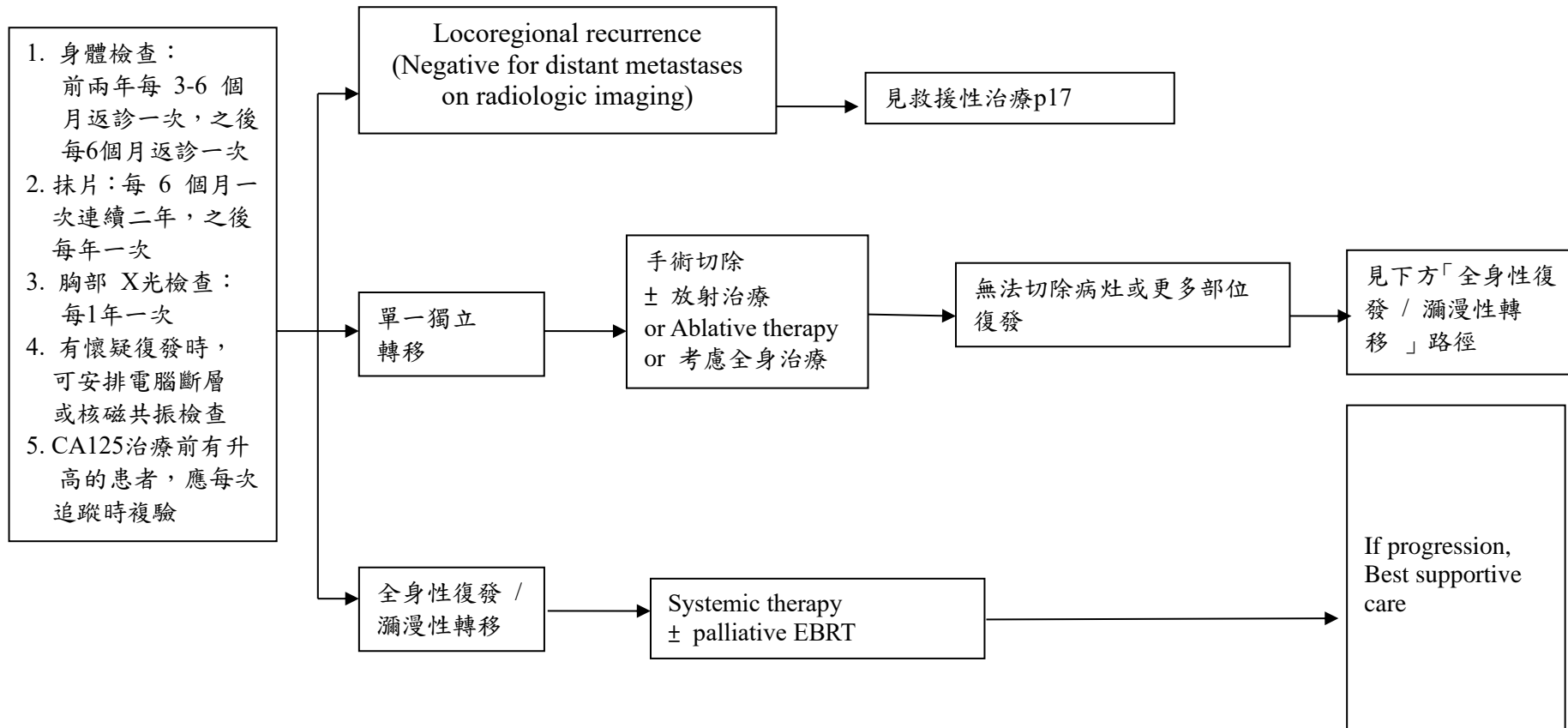
★全身性治療：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.18)

流程圖十

1-10. 接續治療，追蹤及復發處置

追蹤監測

復發轉移的臨床表徵 援救治療



★全身性治療：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.18)

流程圖十一

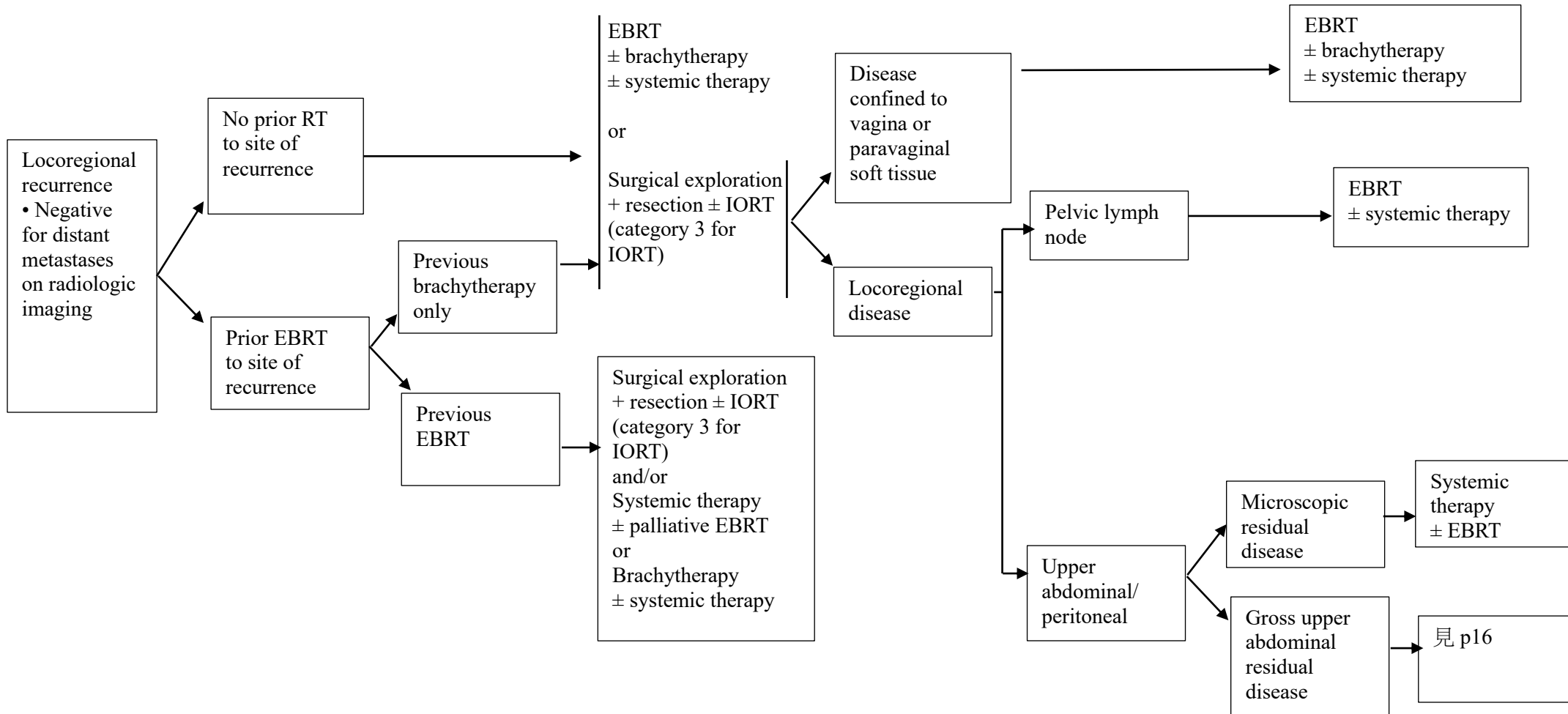


1-10. 接續治療，追蹤及復發處置(續)

CLINICAL PRESENTATION

THERAPY FOR RELAPSE

ADDITIONAL THERAPY





1-11. 子宮內膜癌之全身性治療

Primary or Adjuvant Therapy (Stage I–IV)	
Chemoradiation Therapy	Systemic Therapy
<u>Preferred Regimens</u> <ul style="list-style-type: none"> • Cisplatin plus RT followed by carboplatin/paclitaxel <u>Other Recommended Regimens</u> (if cisplatin and carboplatin are unavailable) <ul style="list-style-type: none"> • Capecitabine/mitomycin • Gemcitabine • Paclitaxel 	<u>Preferred Regimens</u> <ul style="list-style-type: none"> • Carboplatin(or Cisplatin)/paclitaxel • Carboplatin/paclitaxel/pembrolizumab (for stage III–IV tumors, except for carcinosarcoma) (category 1) • Carboplatin/paclitaxel/dostarlimab-gxly (for stage III–IV tumors) (category 1) • Carboplatin/paclitaxel/trastuzumab (for stage III/IV HER2-positive uterine serous carcinoma) • Carboplatin/paclitaxel/trastuzumab (for stage III/IV HER2-positive carcinosarcoma)

RECURRENT DISEASE	
First-Line Therapy for Recurrent Disease	Second-Line or Subsequent Therapy
<u>Preferred Regimens</u> <ul style="list-style-type: none"> • Carboplatin(or Cisplatin)/paclitaxel(category 1 for carcinosarcoma) • Carboplatin/paclitaxel/pembrolizumab(except for carcinosarcoma)(category 1) • Carboplatin/paclitaxel/dostarlimab-gxly (category 1) • Carboplatin(or Cisplatin)/paclitaxel/trastuzumab (for-HER2-positive uterine serous carcinoma and carcinosarcoma) <u>Other Recommended Regimens</u> <ul style="list-style-type: none"> • Carboplatin/docetaxel • Carboplatin/paclitaxel/bevacizumab <u>Useful in Certain Circumstances</u> (Biomarker-directed therapy: after prior platinum-based therapy including neoadjuvant and adjuvant)	<u>Other Recommended Regimens</u> <ul style="list-style-type: none"> • Cisplatin/doxorubicin • Cisplatin/doxorubicin/paclitaxel • Cisplatin • Carboplatin • Doxorubicin • Liposomal doxorubicin • Paclitaxel • Albumin-bound paclitaxel • Topotecan • Bevacizumab • Temsirolimus • Cabozantinib • Docetaxel(category 2B) • Ifosfamide (for carcinosarcoma) • Ifosfamide/paclitaxel (for carcinosarcoma)



<ul style="list-style-type: none"> • Lenvatinib/pembrolizumab (category 1) for MMR-proficient (pMMR) tumors • Pembrolizumab (for TMB-H/MSI-H/dMMR tumors) • Dostarlimab-gxly (for MSI-H/dMMR tumors) 	<ul style="list-style-type: none"> • Cisplatin/ifosfamide (for carcinosarcoma) <p><u><i>Useful in Certain Circumstances (Biomarker-directed therapy)</i></u></p> <ul style="list-style-type: none"> • pMMR tumors Lenvatinib/pembrolizumab (category 1) • TMB-H tumors Pembrolizumab • MSI-H/dMMR tumors Pembrolizumab Dostarlimab-gxly Avelumab Nivolumab • HER2-positive tumors (IHC 3+ or 2+) Fam-trastuzumab deruxetan • NTRK gene fusion-positive tumors Larotrectinib Entrectinib
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HORMONE THERAPY for Recurrent or Metastatic Endometrial Carcinoma		
<u><i>Preferred Regimens</i></u>	<u><i>Other Recommended Regimens</i></u>	<u><i>Useful In Certain Circumstances</i></u>
<ul style="list-style-type: none"> • Megestrol/tamoxifen (alternating) • Everolimus/letrozole 	<ul style="list-style-type: none"> • Medroxyprogesterone acetate/tamoxifen (alternating) • Progestational agents Medroxyprogesterone acetate 、 Megestrol • Aromatase inhibitors • Tamoxifen • Fulvestrant 	<ul style="list-style-type: none"> ER-positive tumors Letrozole/ribociclib Letrozole/abemaciclib



Hormonal Therapy for Uterine-Limited Disease Not Suitable for Primary Surgery or for Those Desiring Uterine Preservation for Fertility

Preferred Regimens

Levonorgestrel intrauterine device(IUD)

Other Recommended Regimens

•Progestational agents
Medroxyprogesterone acetate、Megestrol

Adjuvant chemotherapy

Paclitaxel+Cisplatin

Paclitaxel	(135/175)mg/m ² iv	d1
Cisplatin	75mg/m ² iv	d1
q3w x 6wks cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. *Gynecol Oncol* 2009;112:543-552.

Paclitaxel+Carboplatin

Paclitaxel	(135/175)mg/m ² iv	d1
Carboplatin	AUC (4-6) iv	d1
q3w x 6wks cycles		

Miller D, Filiaci V, Fleming G, et al. Randomized phase III noninferiority trial of first line chemotherapy for metastatic or recurrent endometrial carcinoma: a Gynecologic Oncology Group study [abstract]. *Gynecol Oncol* 2012;125:771.

Doxorubicin +Cisplatin

Doxorubicin	50mg/m ² iv	d1
Cisplatin	75mg/m ² iv	d1
q3w x 6 cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. *Gynecol Oncol* 2009;112:543-552.

Doxorubicin +Carboplatin

Doxorubicin	50mg/m ² iv	d1
Carboplatin	AUC (4-6) iv	d1

**q3w x 6 cycles**

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. *Gynecol Oncol* 2009;112:543-552.

Cisplatin+Ifosfamide

Cisplatin	50-100mg/m ² iv	d1
Ifosfamide	3-5g/m ² iv	d1

q3w x 6 cycles

Howard D. Homesley, Virginia Filiaci, Maurie Markman, et al. Phase III Trial of Ifosfamide With or Without Paclitaxel in Advanced Uterine Carcinosarcoma: A Gynecologic Oncology Group Study. *JCO* February 10, 2007 vol. 25 no. 5 526-531

Carboplatin+Ifosfamide

Carboplatin	AUC (4-6) iv	d1
Ifosfamide	3-5g/m ² iv	d1

q3w x 6 cycles

A. Pawinski¹, a, e, S. Tumolob, G. Hoeselc, A. Cervantesd, et al. Cyclophosphamide or ifosfamide in patients with advanced and/or recurrent endometrial carcinoma: a randomized phase II study of the EORTC Gynecological Cancer Cooperative Group. *European Journal of Obstetrics & Gynecology and Reproductive Biology* Volume 86, Issue 2, October 1999, Pages 179–183

Cisplatin + doxorubicin +paclitaxel (Taxol)

Doxorubicin 45mg/m ² IV + cisplatin 50mg/m ² iv	d1
Paclitaxel 160mg/m ² 3-hr iv	d2
Filgrastim 5mcg/kg SC.Repeat cycle every 3 weeks for max 7 cycles.	d3-12
Maximum BSA of 2.0 was used for calculations.	

1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.

2.Fleming, GF, Brunetto VL, Cella D, et al. Phase III trial of doxorubicin plus cisplatin with or without paclitaxel plus filgrastim in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. *J Clin Oncol*. 2004;22:2159 – 2166.

Ifosfamide (Ifex) + paclitaxel

Paclitaxel 135mg/m ² administered as a 3-hr iv	d1
Ifosfamide 1.6g/m ² /day iv (1.2g/m ² /day if patient received prior radiation).	d1-3
Repeat cycle every 3 weeks for 8 cycles.	

1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.



2.Homesley HD, Filiaci V, Markman M, et al. Phase III trial of ifosfamide with or without paclitaxel in advanced uterine carcinosarcoma:a Gynecologic Oncology Group study. J Clin Oncol.2007;25:526 – 531.

Bevacizumab (Avastin)+/-Chemotherapy

Bevacizumab	7.5- 15mg/kg iv	d1
Repeat cycle every 3 weeks		

1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.

2.Aghajanian C, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2011;29(16): 2259 – 2265.

Doxorubicin liposome

Doxorubicin liposome	(25-45)mg/ m ² iv	d1
q3w		

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Taxol+Lipo-dox

paclitaxel	135-175mg/m ² iv	d1
Doxorubicin liposome	(25-45)mg/ m ² iv	d1
q3w		

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Cisplatin+Lipo-dox

Cisplatin	75-100 mg/m ² iv	d1
Doxorubicin liposome	(25-45)mg/ m ² iv	d1
q3w		

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Carboplatin+Lipo-dox

Carboplatin	AUC (4-6) iv	d1
Doxorubicin liposome	(25-45)mg/ m ² iv	d1
q3w		



Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. *J Clin Oncol* 2010;28:3323-3329.

Hormonal therapy

Megestrol

Megestrol	40-160 mg /d
QD x 6months	

- 1.Fiorica JV, Brunetto VL, Hanjani P, et al. Phase II trial of alternating courses of megestrol acetate and tamoxifen in advanced endometrial carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol* 2004;92:10-14. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/14751131>.
- 2.Pandya KJ, Yeap BY, Weiner LM, et al. Megestrol and tamoxifen in patients with advanced endometrial cancer: an Eastern Cooperative Oncology Group Study (E4882). *Am J Clin Oncol* 2001;24:43-46.Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11232948>.

Medroxyprogesterone

Medroxyprogesterone	400-800 mg /d
QD x 6months	

- 1.Whitney CW, Brunetto VL, Zaino RJ, et al. Phase II study of medroxyprogesterone acetate plus tamoxifen in advanced endometrial carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol* 2004;92:4-9. Available at:<http://www.ncbi.nlm.nih.gov/pubmed/14751130>.
- 2.Thigpen JT, Brady MF, Alvarez RD, et al. Oral medroxyprogesterone acetate in the treatment of advanced or recurrent endometrial carcinoma: a dose-response study by the Gynecologic Oncology Group. *J Clin Oncol* 1999;17:1736-1744. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10561210>.

Levonorgestrel IUD

Levonorgestrel IUD	Intrauterine Devise x1
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Baker J, Obermair A, Gebiski V, Janda M. Efficacy of oral or intrauterine device-delivered progestin in patients with complex endometrial hyperplasia with atypia or early endometrial adenocarcinoma: a meta-analysis and systematic review of the literature. *Gynecol Oncol* 2012;125:263-270. Available at:<http://www.ncbi.nlm.nih.gov/pubmed/22196499>.

Leupline

Leupline	375mg IM
qm x 6months	

- 1.A.R. Jeyarajah, M.D.C.J. Gallagher, M.D., Ph.D.P.R. Blake, M.D,et al.Long-Term Follow-up of Gonadotrophin-Releasing Hormone Analog Treatment for Recurrent Endometrial Cancer. *Gynecologic Oncology Volume 63, Issue 1, October 1996, Pages 47 - 52*
2. Tirso Pérez-Medina, M.D.José Bajo, M.D.Gonzalo Folgueira, M.D.,et al.Atypical Endometrial Hyperplasia Treatment with Progestogens and Gonadotropin-Releasing Hormone Analogues: Long-Term Follow-up. *Gynecologic Oncology Volume 73, Issue 2, May 1999, Pages 299 - 304*



1-12. 子宮內膜癌之放射線治療

● Adjuvant treatment

- Whole pelvic irradiation: total 45-55Gy
- IVBT boost: HDR 4-6Gy x 2-3 Fractions
- IVBT alone: HDR 4-6 Gy x 6-8 Fractions
- Consider dose escalation to gross disease

IVBT : intravaginal brachytherapy

HDR(high dose rate)

● Definitive

- Whole pelvic irradiation: total 45-60Gy + HDR ICBT 4-6 Gy * 5-6 Fractions

ICBT : intracavitary brachytherapy

*Prefer 3D CRT , IMRT, or IGRT(optional)

*If gross disease in the lymph node(+) : Target dose for nodes can range from 54 to 66 Gy



二、 子宮惡性肉瘤

2-1.分期(Leiomyosarcoma and Endometrial Stromal Sarcoma)

TNM Categories	FIGO 分期	Primary Tumor
Tx		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to the uterus
T1a	IA	Tumor 5 cm or less in greatest dimension
T1b	IB	Tumor more than 5 cm
T2	II	Tumor extends beyond the uterus, within the pelvis
T2a	IIA	Tumor involves adnexa
T2b	IIB	Tumor involves other pelvic tissues
T3	III	Tumor infiltrates abdominal tissues
T3a	IIIA	One site
T3b	IIIB	More than one site
N1	IIIC	Regional lymph node metastasis
T4	IVA	Tumor invades bladder or rectum
M1	IVB	Distant metastasis(excluding adnexa, pelvic and abdominal tissue)



TNM Categories	FIGO 分期	Regional Lymph Nodes
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
N1	IIIC	Regional lymph node metastasis

TNM Categories	FIGO 分期	Distant Metastasis
M0		No distant metastasis
M1	IVB	Distant metastasis (excluding adnexa, pelvic, and abdominal tissues)

AJCC 8th	T	N	M
Stage I	T1	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC	T1-3	N1	M0
Stage IVA	T4	ANY	M0
Stage IVB	ANY	ANY	M1

**Uterine Sarcoma**

TNM Categories	FIGO 分期	Primary Tumor
Tx		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to the uterus
T1a	IA	Tumor limited to the endometrium/endocervix
T1b	IB	Tumor invades less than or equal to half myometrial invasion
T1c	IC	Tumor invades more than half myometrial invasion
T2	II	Tumor extends beyond the uterus, within the pelvis
T2a	IIA	Tumor involves adnexa
T2b	IIB	Tumor involves other pelvic tissues
T3	III	Tumor infiltrates abdominal tissues
T3a	IIIA	One site
T3b	IIIB	More than one site
N1	IIIC	Regional lymph node metastasis
T4	IVA	Tumor invades bladder or rectum
M1	IVB	Distant metastasis (excluding adnexa, pelvic, and abdominal tissues)

TNM Categories	FIGO 分期	Regional Lymph Nodes
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm



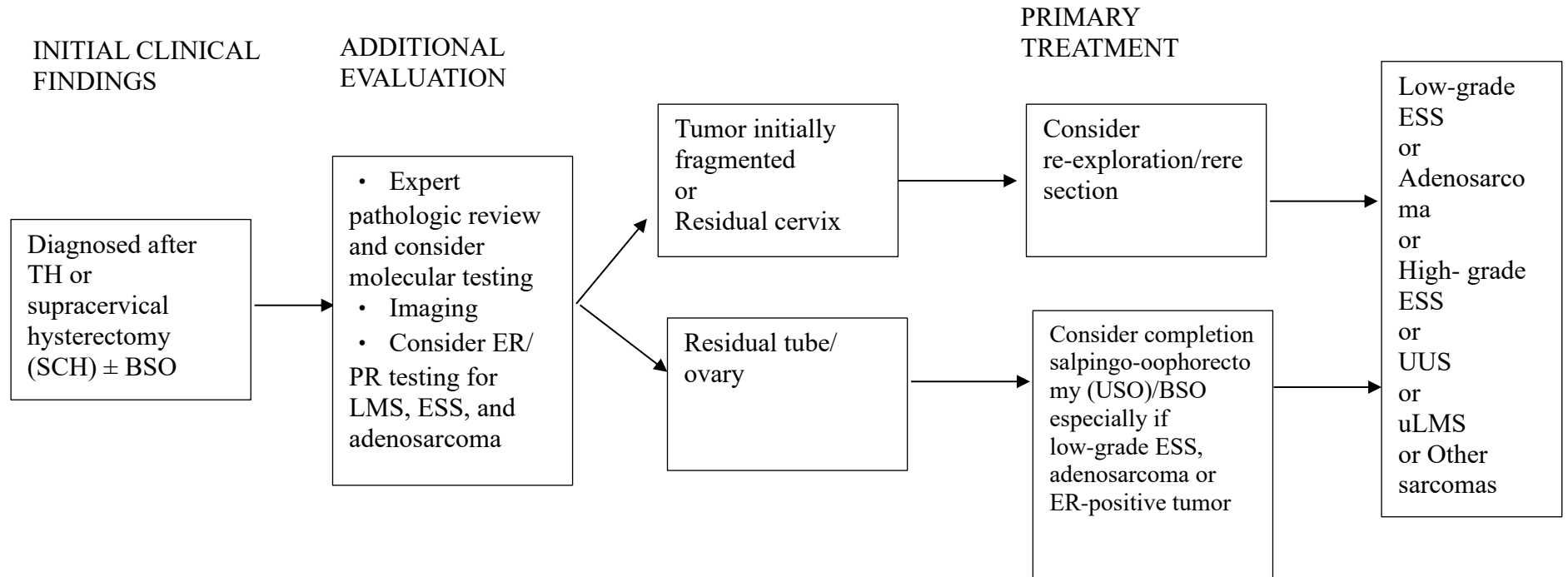
N1	IIIC	Regional lymph node metastasis
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TNM Categories	FIGO 分期	Distant Metastasis
M0		No distant metastasis
M1	IVB	Distant metastasis (excluding adnexa, pelvic, and abdominal tissues)

AJCC 8th	T	N	M
Stage I	T1	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage IC	T1c	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC	T1-3	N1	M0
Stage IVA	T4	ANY	M0
Stage IVB	ANY	ANY	M1



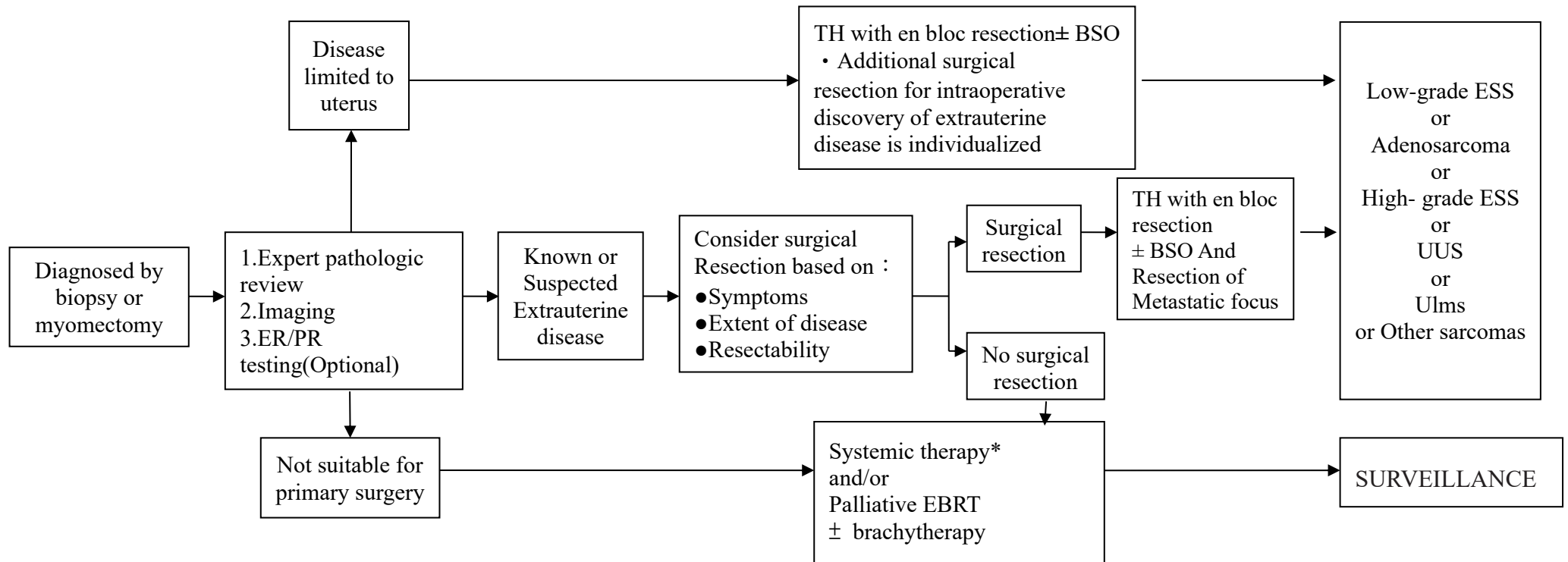
2-2.子宮惡性肉瘤之臨床發現及處置





Initial clinical findings

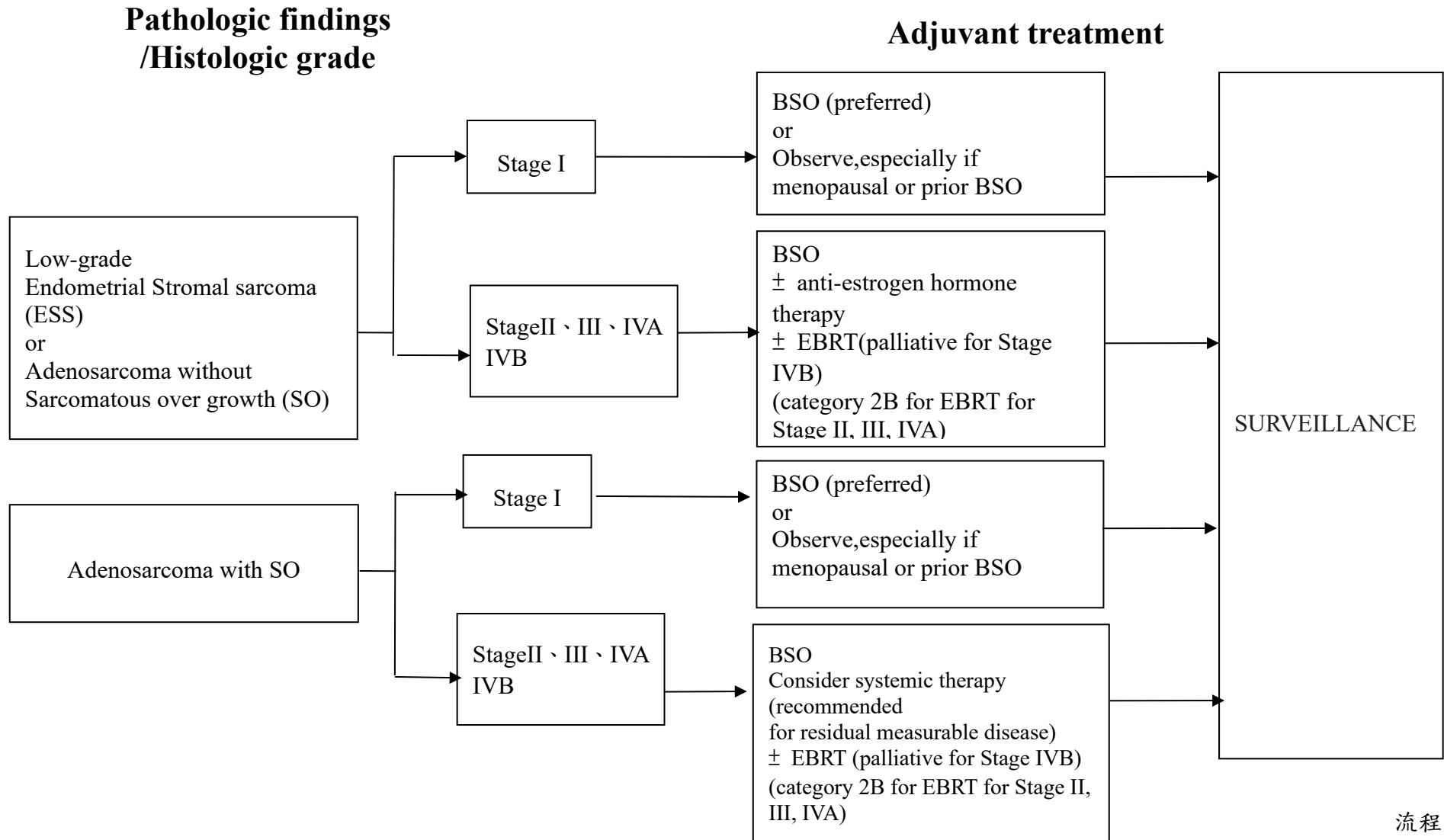
Primary treatment



流程圖一

★Systemic therapy：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.32)

2-2.子宮惡性肉瘤之臨床發現及處置



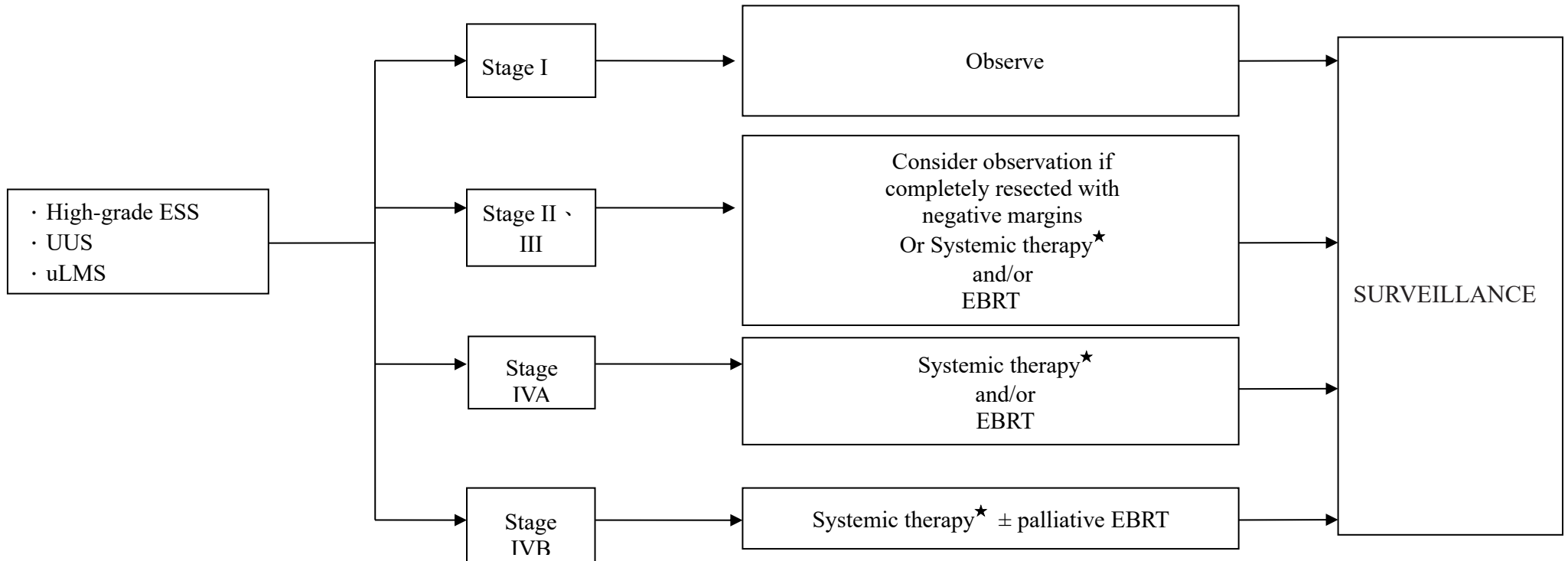
流程圖二



2-2.子宮惡性肉瘤之臨床發現及處置

Pathologic findings
/Histologic grade

Adjuvant treatment



流程圖三

★Systemic therapy：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.32)

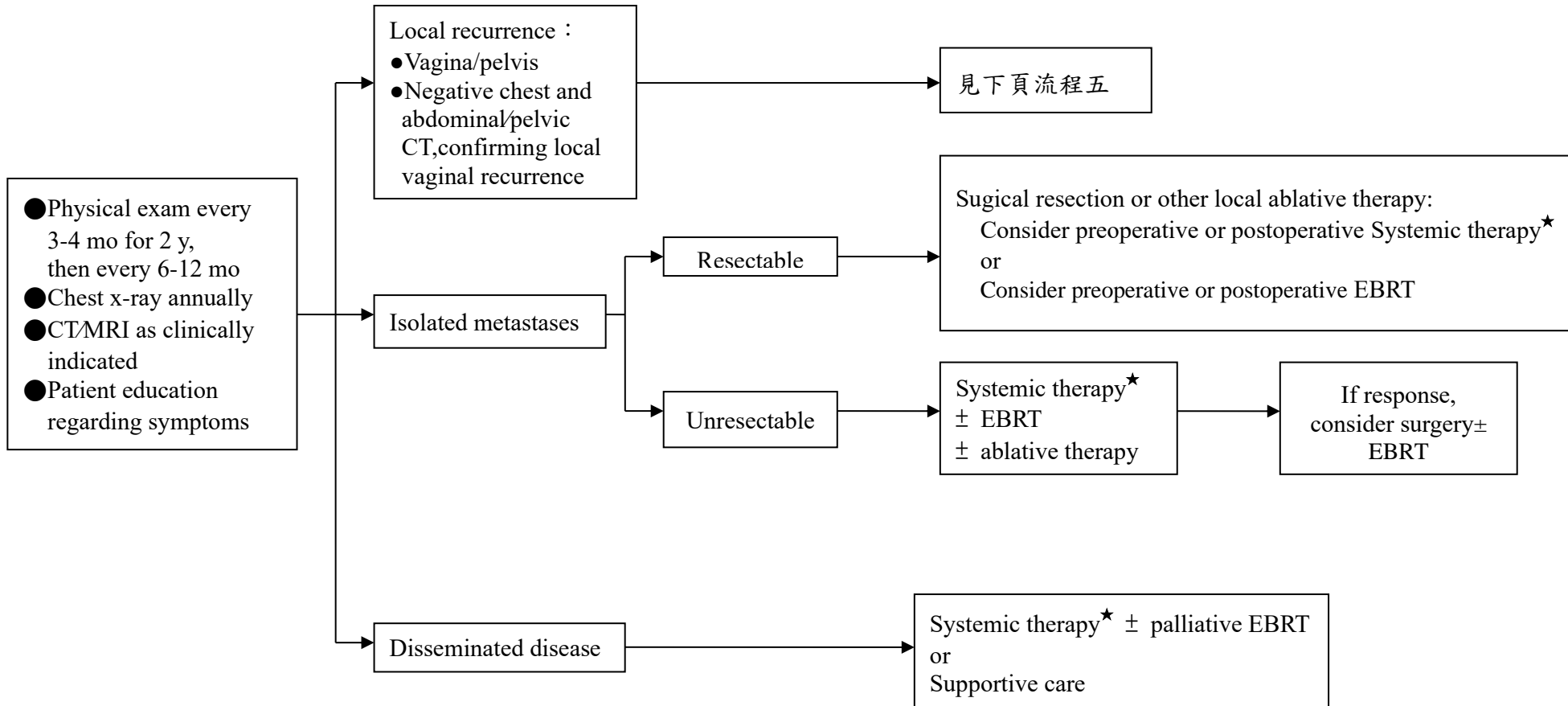


2-3.子宮惡性肉瘤之復發處置

Surveillance

Recurrence

Therapy for relapse



★Systemic therapy：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.32)

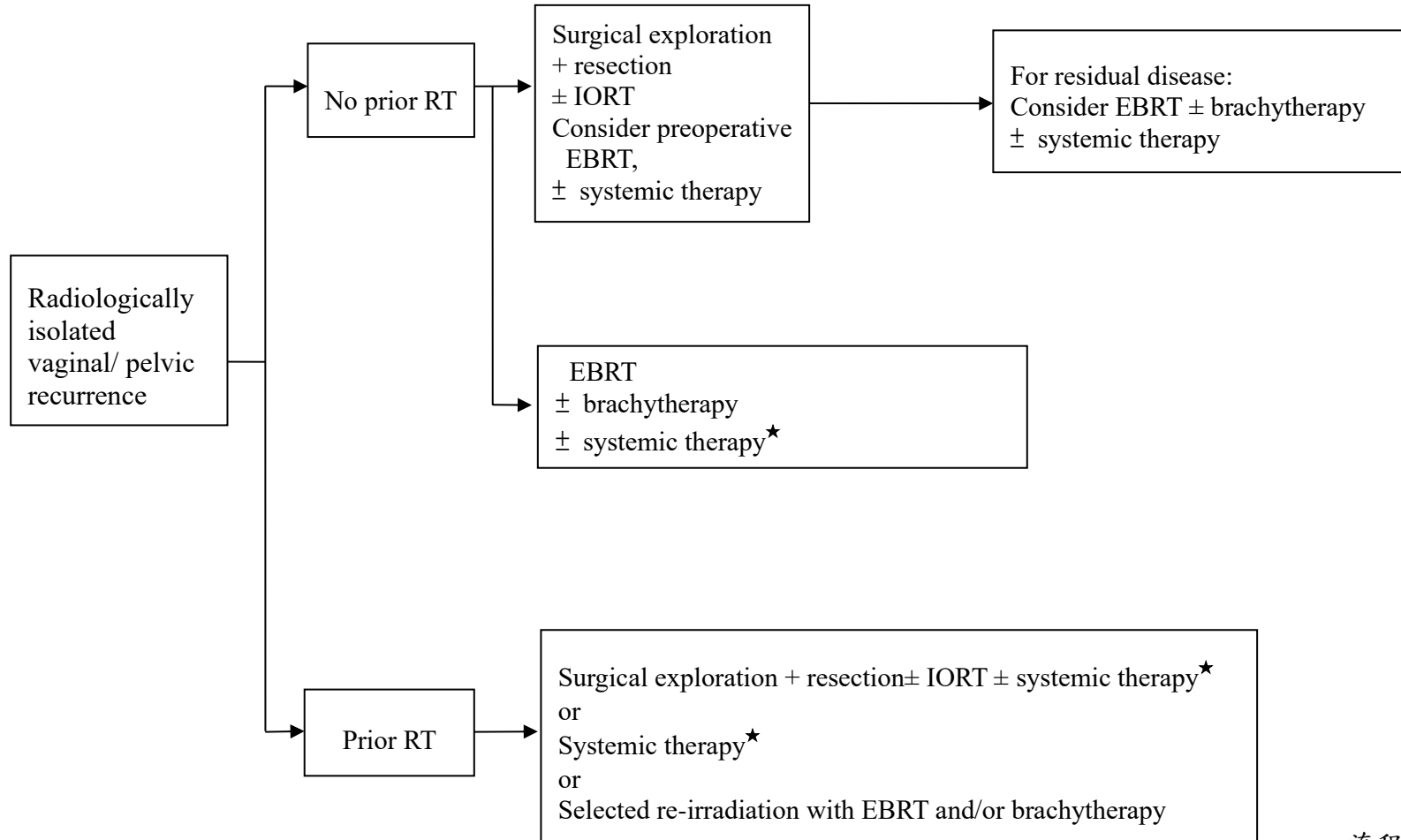
流程四



2-3. 子宮惡性肉瘤之復發處置

Recurrence

Therapy for relapse



流程圖五

★Systemic therapy：意為化學治療或荷爾蒙治療或標靶治療或免疫療法(詳見 P.32)



2-4.子宮惡性肉瘤之全身性治療

SYSTEMIC THERAPY FOR UTERINE SARCOMA
(Clinical trials strongly recommended)

Systemic Therapy	HORMONE THERAPY (For Low-grade ESS or Hormone Receptor Positive (ER/PR) uLMS or Adenosarcoma Without SO):
First-Line Therapy	<i>Preferred Regimens:</i> ★ Aromatase inhibitors for low-grade ESS or adenosarcoma without SO
<i>Preferred Regimens:</i> ★ Doxorubicin ★ Docetaxel/gemcitabine ★ Doxorubicin/trabectedin (for LMS) ¹ ★ Doxorubicin/ifosfamide ★ Doxorubicin/dacarbazine	<i>Other recommended regimens:</i> ★ Medroxyprogesterone acetate (category 2B for ER/PR positive uLMS) ★ Megestrol acetate (category 2B for ER/PR positive uLMS) ★ Aromatase inhibitors(for ER/PR positive uLMS) ★ GnRH analogs (category 2B for low-grade ESS and ER/PR positive uLMS) ★Fulvestrant
<i>Useful in Certain Circumstances</i> • Biomarker-directed therapy NTRK gene fusion-positive tumors ◇ Larotrectinib ◇ Entrectinib IMT with ALK translocation ◇ Crizotinib ◇ Ceritinib ◇ Brigatinib ◇ Lorlatinib ◇ Alectinib • PEComa Albumin-bound sirolimus	Biomarker-Directed Systemic Therapy for Second-Line Treatment • Pembrolizumab for TMB-H tumors •Consider PARP inhibitors for BRCA2-altered uLMS ■Olaparib ■Rucaparib ■Niraparib • PEComa ◇ Sirolimus ◇ Everolimus ◇ Temsirolimus
Second-Line or Subsequent Therapy	



Preferred Regimens

- Trabectedin

Other Recommended Regimens:

- ★ Gemcitabine/dacarbazine
- ★ Gemcitabine/vinorelbine
- ★ Dacarbazine
- ★ Gemcitabine
- ★ Epirubicin
- ★ Ifosfamide
- ★ Liposomal doxorubicin
- ★ Pazopanib(Votrient)
- ★ Temozolomide
- ★ Eribulin (category 2B)

*Adjuvant chemotherapy***Epirubicin+Cisplatin**

Epirubicin	60mg/m ²	iv	d1
Cisplatin	60mg/m ²	iv	d1
q3w x 6wks cycles			

Lissoni1, A. Gabriele1, G. Gorga2, et al. Cisplatin-, epirubicin- and aclitaxel-containing chemotherapy in uterine adenocarcinoma.*Ann Oncol* (1997) 8 (10): 969-972

Epirubicin+Carboplatin

Epirubicin	60mg/m ²	iv	d1
Carboplatin	AUC (4-6)	iv	d1
q3w x 6wks cycles			

F. Calero, E. Asins-Codoñer, J. Jimenoc, et al. Epirubicin in advanced endometrial adenocarcinoma: a phase II study of the grupo ginecologico Español para el tratamiento oncologico (GGETO).*European Journal of Cancer and Clinical Oncology*, Volume 27, Issue 7, July 1991, Pages 864–866

**Paclitaxel+Cisplatin**

Paclitaxel	(135/175)mg/m ² iv	d1
Cisplatin	75-100mg/m ² iv	d1
q3w x 6wks cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. *Gynecol Oncol* 2009;112:543-552.

Paclitaxel+Carboplatin

Paclitaxel	(135/175)mg/m ² iv	d1
Carboplatin	AUC (4-6) iv	d1
q3w x 6wks cycles		

Miller D, Filiaci V, Fleming G, et al. Randomized phase III noninferiority trial of first line chemotherapy for metastatic or recurrent endometrial carcinoma: a Gynecologic Oncology Group study [abstract]. *Gynecol Oncol* 2012;125:771.

Doxorubicin +Cisplatin

Doxorubicin	50mg/m ² iv	d1
Cisplatin	75-100mg/m ² iv	d1
q3w x 6 cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. *Gynecol Oncol* 2009;112:543-552.

Doxorubicin +Carboplatin

Doxorubicin	50mg/m ² iv	d1
Carboplatin	AUC (4-6) iv	d1
q3w x 6 cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. *Gynecol Oncol* 2009;112:543-552.

Cisplatin+Ifosfamide

Cisplatin	50-100mg/m ² iv	d1
Ifosfamide	3-5g/m ² iv	d1
q3w x 6 cycles		

Howard D. Homesley, Virginia Filiaci, Maurie Markman, et al. Phase III Trial of Ifosfamide With or Without Paclitaxel in Advanced Uterine

**carboplatin+Ifosfamide**

Carboplatin	AUC (4-6) iv	d1
Ifosfamide	3-5g/m ² iv	d1
q3w x 6 cycles		

A. Pawinski¹, a, e, S. Tumolob, G. Hoeselc, A. Cervantesd, et al. Cyclophosphamide or ifosfamide in patients with advanced and/or recurrent endometrial carcinoma: a randomized phase II study of the EORTC Gynecological Cancer Cooperative Group. European Journal of Obstetrics & Gynecology and Reproductive Biology Volume 86, Issue 2, October 1999, Pages 179–183

Doxorubicin (Adriamycin)

Doxorubicin 75mg/m ² iv bolus.	d1
Repeat cycle every 31 days OR 60mg/m ² –70mg/m ² iv typically dosed every 3 weeks.	

- 1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.
2. Sarcoma Meta-analysis Collaboration (SMAC). Cochrane Database Syst Rev. 2000;4:CD001419.

Gemcitabine (Gemzar) +docetaxel (Taxotere) +granulocyte-colony-stimulating factor (G-CSF)

Gemcitabine 900mg/m ² iv over 90 min(自費),	d1
Docetaxel 100mg/m ² iv over 60 min,	d8
G-CSF 150mcg/m ² SC(自費)	d9-15
OR Pegfilgrastim 6mg SC.	d9 or d10
Repeat cycle every 3 weeks until disease progression or toxicity occurs.	
NOTE: Patients with prior pelvic irradiation received Gemcitabine 675mg/m ² iv and Docetaxel 75mg/m ² iv	

- 1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.
- 2.Hensley ML, Blessing JA, Mannel R, Rose PG. Fixed-dose rate gemcitabine plus docetaxel as first-line therapy for metastatic uterine leiomyosarcoma: a Gynecologic Oncology Group phase II trial. Gynecol Oncol. 2008;109:329 – 34.

Gemcitabine

Gemcitabine 1,000mg/m ² iv. (自費)	d1,8,15
Repeat cycle every 4 weeks.	

- 1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.



2.Look KY, Sandler A, Blessing JA, Lucci JA 3rd, Rose PG; Gynecologic Oncology Group (GOG) Study. Phase II trial of gemcitabine as second-line chemotherapy of uterine leiomyosarcoma: a Gynecologic Oncology Group (GOG) Study. Gynecol Oncol. 2004;92:644 – 647.

Gemcitabine+Carboplatin

Gemcitabine	1,000mg/m ²	iv. (自費)	d1,8,15
Carboplatin	AUC(4-6)	iv	d1
Repeat cycle every 4 weeks.			

1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.

2.Look KY, Sandler A, Blessing JA, Lucci JA 3rd, Rose PG; Gynecologic Oncology Group (GOG) Study. Phase II trial of gemcitabine as second-line chemotherapy of uterine leiomyosarcoma: a Gynecologic Oncology Group (GOG) Study. Gynecol Oncol. 2004;92:644–647.

Doxorubicin liposome

Doxorubicin liposome	(25-45)mg/ m ²	iv	d1
q3w			

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Taxol+Lipo-dox

paclitaxel	135-175mg/m ²	iv	d1
Doxorubicin liposome	(25-45)mg/ m ²	iv	d1
q3w			

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Cisplatin+Lipo-dox

Cisplatin	75-100 mg/m ²	iv	d1
Doxorubicin liposome	(25-45)mg/ m ²	iv	d1
q3w			

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Carboplatin+Lipo-dox



Carboplatin	AUC (4-6)	iv	d1
Doxorubicin liposome	(25-45)mg/ m ²	iv	d1
q3w			

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. *J Clin Oncol* 2010;28:3323-3329.

Pazopanib(Votrient)

Pazopanib(Votrient)	800mg	po
QD		

Veli Sunar , Vakkas Korkmaz , Serkan Akin, et al.Efficacy of Pazopanib in patients with metastatic uterine sarcoma: A multi-institutional study.*JBUON* 2019; 24(6): 2327-2332

三、妊娠組織瘤

1. Definition

Complete hydatidiform mole. It arises from the fertilisation of an empty ovum lacking maternal genes. ¹ The sperm then duplicates, making a diploid number of chromosomes which are therefore entirely male in origin and thus no embryonic tissue is present. ¹ The overgrowth of the placenta is benign but can metastasise if left untreated. ^{2,3}

Partial hydatidiform moles differ in that the ovum retains its maternal genes, which results in a triploid chromosomal pattern after the addition of duplicated sperm to the normal ovum. ¹ In this case a foetus may be present but survival after 8 weeks is unlikely due to its abnormal genetic make-up. ²

Invasive moles occur as a result of local invasion of the myometrium by a complete or partial mole. ² In the spectrum of malignant potential they are intermediate between hydatidiform moles and choriocarcinomas. ⁴

Choriocarcinoma is a rare and overtly malignant condition both clinically and histologically. ² It occurs when chorionic cells become malignant and metastasise to other parts of the body. ² A choriocarcinoma can therefore arise subsequent to a molar pregnancy, or follow an otherwise normal pregnancy or miscarriage. ^{1,2}



PSTT are the least common form of GTD, comprising less than 2% of all cases.^{2,5} They arise from the non-villous trophoblast and are diploid in nature.² In contrast to the other GTDs, it is characterised by a late presentation (months to years) of symptoms caused by a prior pregnancy, miscarriage or hydatidiform mole.² The secretion of human Chorionic Gonadotrophin (hCG) is characteristic of all GTDs and is therefore used as part of their diagnosis, treatment and follow up.²

2. Treatment and follow-up:

2.1. Partial and complete mole

For complete and partial molar pregnancies suction evacuation (with dilation) is recommended.² An ultrasound scan should be performed prior to evacuation, to confirm the diagnosis, assess for the possible presence of a foetus and ensure absence of theca lutein cysts.^{2,4} Other preoperative evaluations include complete history, examination, measurement of baselines serum hCG level, chest x-ray, full blood count, coagulation profile and liver, renal and thyroid function tests.^{2,6} If excessive bleeding occurs after a complete evacuation, a single dose of oxytocin can be administered.²

Surveillance with serial serum hCG determinations commences within 48 hours following evacuation to obtain a baseline serum hCG level.² Thereafter this is performed weekly until the hCG level returns to normal.²

If the serum hCG level returns to normal within 8 weeks post-evacuation, monitoring of serum hCG levels can be stopped at 6 months.² However, if they do not monitoring stops 6 months after the first normal value following normalisation.^{2,4} After normalisation of the serum hCG levels, monitoring continues through urine hCG measurements monthly.^{2,4}

Following a molar evacuation, patients should avoid pregnancy until after the completion of the surveillance period.² Pregnancy naturally increases serum hCG levels, which could be perceived as abnormal and ultimately means that the hCG levels can no longer be used to monitor the patient.² Although, the oral contraceptive pill (and Hormone Replacement therapy) cannot be used until normal hCG values are obtained, thus other methods of contraception should be in place.^{2,7}

Complete mole frequently proceeds to invasive disease with 8-20% of patients requiring chemotherapy, whereas Partial mole rarely becomes malignant, with only 0.5% of patients requiring chemotherapy.^{2,3} A rise in the hCG level during surveillance can be used to detect this and patients should be treated with the appropriate



2.2. Indications for chemotherapy

The treatment of women with GTD is undertaken in conjunction with Charing Cross Hospital. Chemotherapy cycles are administered by them and therefore the assessment of whether or not a patient requires chemotherapy is decided using their guidelines ².

1. Brain, liver, GI mets or lung mets >2cm on CXR
2. Histological evidence of choriocarcinoma
3. Heavy PV bleeding or GI/intraperitoneal bleeding
4. Pulmonary, vulval or vaginal mets unless the hCG level is falling
5. Rising hCG in two consecutive serum samples
6. hCG > 20,000 IU/L more than 4 weeks after evacuation
7. hCG plateau in 3 consecutive serum samples
8. Raised hCG level 6 months after evacuation (even if falling)

Any one of these findings would be considered an indication for chemotherapy, however further assessments are carried out by Charing Cross Hospital.

2.3. FIGO Indications for chemotherapy treatment ^{2,7}

1. hCG plateau of 4 values +/- 10% over a 3 week period
2. hCG increase of >10% of three values over a 2 week period
3. Persistence of hCG for more than 6 months after molar evacuation.



4. Staging for chemotherapy

Human chorionic gonadotrophin (hCG) is a hormone that is predominantly produced by syncytiotrophoblast cells.^{1,2} The measurement of hCG allows for an estimation of the number of proliferating cells.² This forms the basis of disease risk assessment in patients with GTD, and allows for the monitoring of subsequent responses to treatment.²

There is now a revised 2000 FIGO prognostic score table^{2,7} which has parameters that allow clinicians to determine the risk category of individual patients.²

Scores	0	1	2	4
Age	<40	≥40	.	.
Antecedent pregnancy	Mole	Abortion	Term	.
Months from index pregnancy	<4	4-6	7-13	>13
Pre-Treatment hCG	<1,000	1,000-10,000	10,000-100,000	>100,000
Largest Tumour Size	.	3-5cm	≥5cm	.
Site of mets	Lung	Spleen, kidney	Gastro-Intestinal	Brain, Liver
Number of Mets	.	1-4	5-8	>8
Previous chemotherapy	.	.	Single agent	Two or more drug

According to FIGO 2002, if the patient scores between 0-6 they are considered to be in the low risk category and initial treatment will involve a single chemotherapeutic agent.^{2,8} However if their score is greater than 7, then the treatment regime will involve multi-agent combinations of chemotherapy.^{2,8}



5. Treatment

5.1. Low risk disease management

The standard treatment of low risk GTD is Methotrexate administered intra-muscularly, with oral Folinic Acid rescue.^{2,9} The first course of treatment is administered in hospital to minimise complications which may arise due to the rapid shrinkage of the tumour.² Cycles subsequent to this are administered at home.²

The treatment is generally well tolerated without major toxicity.² Common side effects include pleural inflammation, mucositis, and asymptomatic elevation of liver function tests.^{2,9} Alopecia, nausea and myelosuppression are possible but extremely rare.^{2,9}

To minimise the risk of development of CNS disease in patients with lung metastasis, CNS prophylaxis with intra-theal Methotrexate (12.5mg) is also added, and administered at 2 week intervals on 3 occasions.^{2,9}

Treatment is continued for 6 weeks after the normalisation of hCG levels.^{2,9} However, if patients have an inadequate response to Methotrexate therapy (as shown by an hCG plateau or rise), the treatment is switched to second line therapy using single agent Actinomycin D or EMA/CO combination chemotherapy (consisting of Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide and Vincristine), if the hCG level is above 300iu/L.^{2,9}

5.2. High risk disease management

EMA/CO chemotherapy has shown a cure rate of 86% for high risk patients.^{2,10} This intense treatment combines 5 chemotherapy agents delivered in 2 cycles one week apart (see appendix 8.2 for full details).^{2,10} This appears to be the most effective approach to this rapidly proliferating malignancy.² In patients with cerebral metastasis at the time of diagnosis of GTD (4%), treatment may also include surgical resection if the disease is superficial, and higher doses of chemotherapy may be implemented to enhance penetration into the CNS.^{2,11}

G-CSF (Granyocyte-Colony Stimulating Factor) support is frequently helpful as these drugs can be fairly myelosuppressive.^{2,11} Life threatening toxicity is rare and the majority of patients tolerate treatment without any major problems.²



Treatment is continued for 6 weeks after the normalisation of hCG levels, although the dose of Etoposide may be reduced after the hCG levels normalise to minimise the risk of developing secondary malignancies. If patients develop resistance to the EMA/CO treatment regime (17%), a change to a second line drug treatment is required. The general replacement is EP/EMA (consisting of Etoposide-Cisplatin and Etoposide-Methotrexate-Actinomycin D) which, combined with surgery to defined drug resistant areas of the uterus, produces a cure rate of 90% in this minority of patients.

5.3. Management of PSTT

Prognosis for these patients is dependent upon the time of presentation after the antecedent pregnancy, but data from Charing Cross hospital showed a 100% cure rate for those presenting within 4 years of the antecedent pregnancy (later presentation carries a poorer prognosis).^{2,12}

These tumours are characterised by resistance to the conventional chemotherapy used in the treatment of GTD, so a hysterectomy should be considered early in the course of treatment as a curative measure.^{2,4} For patients with disseminated disease, EP/EMA chemotherapy is recommended, which can be stopped 6-8 weeks after normalisation of the hCG levels.² Following this, hysterectomy is still also recommended.²



6. Follow-up

6.1. Post-chemotherapy follow up

Patients are reviewed 6 weeks after the completion of chemotherapy and the following inquiries should be undertaken, as stated by Charing Cross Hospital ²:

- Recheck the sites of original disease
- Doppler US of pelvis
- CXR or CT/MRI if abnormal at presentation
- Advise on the need for contraception for 12 months
- Advise re avoidance of excess sunlight exposure
- Outline the risk of relapse

All patients have routine hCG marker follow-up for life. ²

6.2. Post treatment hCG follow-up as stated by Charing Cross Hospital ²

Year 1	→ 2-weekly serum and urine hCG for 1 – 6 months 2 weekly urine hCG for 7-12 months
Year 2	→ 4 weekly urine hCG
Year 3	→ 8 weekly urine hCG
Year 4	→ 3-monthly urine hCG
Year 5	→ 4-monthly urine hCG
Year 6 – life	→ 6-monthly urine hCG

Note: hCG levels should also be taken 6 weeks after the delivery of any future pregnancy. ^{2\}

Women should be advised not to conceive until the hCG level has been normal for six months. (level C).

**GTD Chemotherapy Protocol 【Primary】****GTD-Low risk Methotrexate-FA**

MTX	1mg/kg IM	d 1,3,5,7
Folinic acid	0.1mg/kg IM	d 2,4,6,8
qow		

- 1.McNeish IA, Strickland S, Holden L, Rustin GJ, Foskett M, Seckl MJ, Newlands ES. Low-risk persistent gestational trophoblastic disease: outcome after initial treatment with low-dose methotrexate and folinic acid from 1992 to 2000. J Clin Oncol. 2002 Apr 1;20(7):1838-44
- 2.Newlands ES, Bagshawe KD, Begent RH, Rustin GJ, Holden L. Results with the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) regimen in high risk gestational trophoblastic tumours, 1979 to 1989. Br J Obstet Gynaecol. 1991 Jun;98(6):550-7.

GTD-Low risk Actinomycin-D

Actinomycin-D	1.25 mg/m2 iv	d1
q2w		

- Newlands ES, Bagshawe KD, Begent RH, Rustin GJ, Holden L. Results with the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) regimen in high risk gestational trophoblastic tumours, 1979 to 1989. Br J Obstet Gynaecol. 1991 Jun;98(6):550-7.

GTD-High EMA/CO

Etoposide	100 mg/m2	d1
Actinomycin-D	0.5 mg	d1
MTX	100mg/m2 iv push	d1
MTX	200mg/m2 iv 12hrs	d1
Etoposide	100 mg/m2	d2
Actinomycin-D	0.5 mg	d2
Folinic acid	15 mg P.O q12h*4	d2
Cyclophosphamide	60	d8

- Newlands ES, Bagshawe KD, Begent RH, Rustin GJ, Holden L. Results with the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) regimen in high risk gestational trophoblastic tumours, 1979 to 1989. Br J Obstet Gynaecol. 1991 Jun;98(6):550-7.

***GTD Chemotherapy Protocol 【Resistant】*****GTD-Resistant EMA/PE**

Etoposide	100 mg/m ²	d1
Actinomycin-D	0.5 mg	d1
MTX	100mg/m ² iv push	d1
MTX	200mg/m ² iv 12hrs	d1
Etoposide	100 mg/m ²	d2
Actinomycin-D	0.5 mg	d2
Folinic acid	15 mg P.O q12h*4	d2
Cisplatin	75~80 mg	d8

1. Newlands ES, Bagshawe KD, Begent RH, Rustin GJ, Holden L. Results with the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) regimen in high risk gestational trophoblastic tumours, 1979 to 1989. Br J Obstet Gynaecol. 1991 Jun;98(6):550-7.
2. Randall ME, Filiaci VL, Muss H, et al. Randomized phase III trial of whole-abdominal irradiation versus doxorubicin and cisplatin chemotherapy in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. J Clin Oncol 2006;24:36-44. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16330675>

四、緩和照護原則

若預期疾病難以治癒(如子宮體癌第四期或是子宮體癌復發的病人)，病人存活期大於6個月，緩和醫療的及早介入能減輕癌症病人及家屬在生理、社會、心理等問題，改善病人生活品質。許多民眾都會將緩和醫療與安寧照護畫上等號，其實它們還是有差異性，當癌病人接受緩和醫療服務時，也可同時併行癌症治療，但接受安寧醫療後，會由安寧醫療團隊接受後續照護，不再有癌症治療介入。(Thomas J et al.2012)

五、安寧照護原則

若預期疾病難以治癒時，病人存活期小於6個月便適合安寧療護(Pomeranz & Brustman, 2005; Waldrop & Rinfrette, 2009)。若藉由症狀、檢驗數據、及確切的腫瘤診斷，證實臨床上該惡性腫瘤已經廣泛侵犯、或進展快速；功能分數(Palliative Performance Scale)低於70%；拒絕進一步腫瘤治癒性治療，或者在治療之下仍持續惡化者，即可轉介安寧醫療團隊(彭等，2006)。

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七、子宮體癌各期治療完治定義

期別	治療方式	完治定義	備註
第 I 期	1.OP 2.RT	1.完成黃體激素(Megestrol、Medroxyprogesterone、Levonorgestrel IUD、Leupline)治療，每 3-6 個月子宮搔刮術(子宮內膜擴刮術或切片)，6 個月完治 or 2.完成手術 or 3.完成 EBRT and/or brachytherapy	
第 II 期	1.OP 2.RT ± C/T	1.完成手術 or 2.完成 EBRT +brachytherapy ± C/T	
第 III 期	1.OP 2.RT ± C/T 3.C/T + OP	1.完成手術 or 2.完成 EBRT +brachytherapy + C/T or 3.完成術前化療後再開刀	
第 IV 期	1.OP 2.CCRT 3.C/T + OP 4.Systemic therapy	1.接受手術或 C/T 3 次或 R/T 一個療程或荷爾蒙治療 3 個月完治 2.接受『安寧照護』	
High risk carcinoma 第 I~III 期	OP + Systemic therapy ± EBRT ± brachytherapy	完成手術+ Systemic therapy	漿液狀腺癌 (serous adenocarcinoma) 或亮細胞癌 (clear cell adenocarcinoma) 或未分化/去分化癌 (Undifferentiated/Dedifferentiated carcinoma) 或癌肉瘤 Carcinosarcoma