

屏東榮民總醫院

子宮內膜癌

診療指引

2024年03月06日

婦癌醫療團隊擬訂

注意事項

這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

修訂指引

- 本共識依下列參考資料修改版本
 - NCCN Clinical Practical Guidelines in Oncology, Uterine Neoplasms (**Version 1. 2024**)
 - 子宮內膜癌臨床指引：國家衛生研究院
 - 婦癌研究委員會

會議討論

本次會議：20240306

新版

1. 更新Endometrial cancer 2023 FIGO stage。
2. 流程十二(P.21)及流程十五(P.24) · Endometrial serous carcinoma 及carcinosarcoma · 若為advanced stage或已有遠端轉移 · 建議檢測HER2 gene。
3. 根據NRG-GY018 and RUBY trial · pembrolizumab以及dostarlimab兩種immune-checkpoint inhibitor作為在Stage III/IV患者接受第一線C/T的配方 · 或是疾病復發後的配方 · 皆有生存優勢 · 故列入化療處方選擇。(p.25、26)

Primary Tumor (T)		
T	FIGO	T Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor confined to the corpus uteri, including endocervical glandular involvement
T1a	IA	Tumor limited to the endometrium or invading less than half the myometrium
T1b	IB	Tumor invading one half or more of the myometrium
T2	II	Tumor invading the stromal connective tissue of the cervix but not extending beyond the uterus. Does NOT include endocervical glandular involvement.
T3	III	Tumor involving serosa, adnexa, vagina, or parametrium
T3a	IIIA	Tumor involving the serosa and/or adnexa (direct extension or metastasis)
T3b	IIIB	Vaginal involvement (direct extension or metastasis) or parametrial involvement
T4	IVA	Tumor invading the bladder mucosa 及/或 bowel mucosa (bullous edema is not sufficient to classify a tumor as T4)

Regional Lymph Node (N)		
N	FIGO	N Criteria
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	IIIC1	Regional lymph nodes metastasis to pelvic lymph nodes
N1mi	IIIC1	Regional lymph node metastasis (greater than 0.2 mm but not greater than 2.0 mm in diameter) to pelvic lymph nodes
N1a	IIIC1	Regional lymph node metastasis (greater than 2.0 mm in diameter) to pelvic lymph nodes
N2	IIIC2	Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2mi	IIIC2	Regional lymph node metastasis (greater than 0.2 mm but not greater than 2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2a	IIIC2	Regional lymph node metastasis (greater than 2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes

Distant Metastasis (M)		
M	FIGO	M Criteria
M0		No distant metastasis
M1	IVB	Distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone). (It excludes metastasis to pelvic or para-aortic lymph nodes, vagina, uterine serosa, or adnexa).

2023 Endometrial cancer FIGO Stage

Stage I (Confined to the uterus and ovary)					
IA	<ul style="list-style-type: none"> - 侷限在 EM - 或是 non-aggressive histology type 侵犯 < 1/2 myometrium w/o or only focal LVSI - 或 good prognosis disease 	IA1	Non-aggressive histology, 僅存在 EM polyp 內, 或是侷限在內膜		
		IA2	Non-aggressive histology, < 1/2 myometrium w/o or only focal LVSI		
		IA3	Low-grade endometrioid carcinoma, 侷限在子宮及卵巢(單側)		
		IAm ^{POLEmut}	POLEmut EC, confined to uterus or with cervical extension, regardless of degree of LVSI or histology type		
IB	Non-aggressive histology, ≥1/2 myometrium w/o or only focal LVSI				
IC	Aggressive histology, 僅存在 EM polyp 內, 或是侷限在內膜				
Stage II (To cervix stroma w/o 子宮外侵犯 · 或 with substantial LVSI · 或 aggressive histology with myometrial invasion)					
IIA	Cervical stroma (+), non-aggressive histology				
IIB	Non-aggressive histology, but with substantial LVSI				
IIC	Aggressive histology with any myometrial involvement				
IIC _{mp53abn}	p53abn EC confined to uterus with any myometrial invasion with or w/o cervical invasion, regardless of degree of LVSI or histology type				
Stage III (Local and/or regional spreading)					
IIIA	To serosa and/or adnexa by direct extension or metastasis	IIIA1	To ovary or fallopian tube (除非符合 IA3)		
		IIIA2	Uterine subserosa or spread through uterine serosa		
IIIB	Vaginal and/or to parametrium or pelvic peritoneum	IIIB1	Vagina and/or parametrium		
		IIIB2	Pelvic peritoneum		
IIIC	To pelvic and/or para-aortic LN	IIIC1	To pelvic LN	IIIC1i	Micrometastasis
				IIIC1ii	Macrometastasis
		IIIC2	To para-aortic LN up to renal vessels	IIIC2i	Micrometastasis
				IIIC2ii	Macrometastasis
Stage IV (Invasion of bladder or bowel mucosa, and/or distant metastasis)					
IVA	mucosa of bladder and/or bowel				
IVB	abdominal peritoneum metastasis beyond pelvis				
IVC	distant meta (extra- or intra-abdominal LN above renal vessels, lung, liver, brain, or bone)				

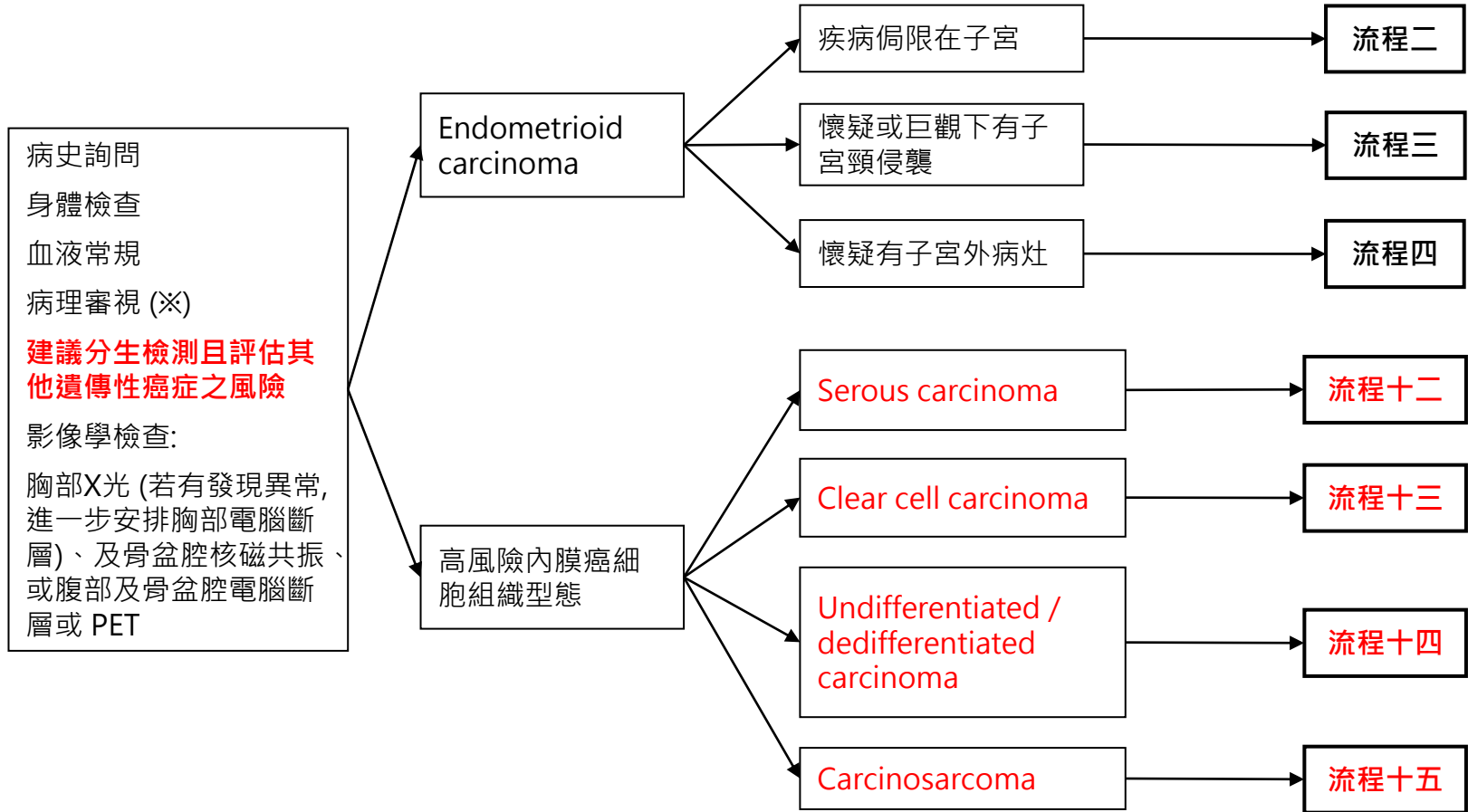
2023 Endometrial cancer FIGO Stage

- ◆ Low-grade EEC 侵犯內膜及卵巢(IA3) · 必須要和 stag IIIA1 最區分 · 若符合下列 criteria 則被視為具有 good prognosis · 不需要 adjuvant Tx
 - Myometrial invasion < 50%
 - No extensive or substantial LVSI
 - No additional metastasis
 - Ovarian tumor is UNILATERAL without capsule invasion or rupture.
- ◆ Extensive / Substantial LVSI: ≥ 5 vessels involved
- ◆ Aggressive histology: High-grade EEC (Gr.3), serous, clear cell, undifferentiated, mesonephric-like, mixed, GI-type mucinous endometrial carcinoma, carcinosarcoma
- ◆ Non-aggressive histology: low-grade EEC (Gr.1 and Gr.2)
- ◆ High-grade EEC 是一個在預後、臨床表現、以及分生分類多樣性表現的疾病。如果沒有 molecular profiling · high-grade EEC 很難被分類 risk group。
- ◆ 若是患者有接受分生檢驗，則應該將檢驗結果紀錄在分期當中, e.g. Stage III_{mPOLE} or Stage IV_{m_{p53}abn}

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

初步評估

初步臨床發現



※: 建議在D&C的檢體，或是在最後手術切除的子宮檢體上常規進行MMR protein / MSI 染色檢測

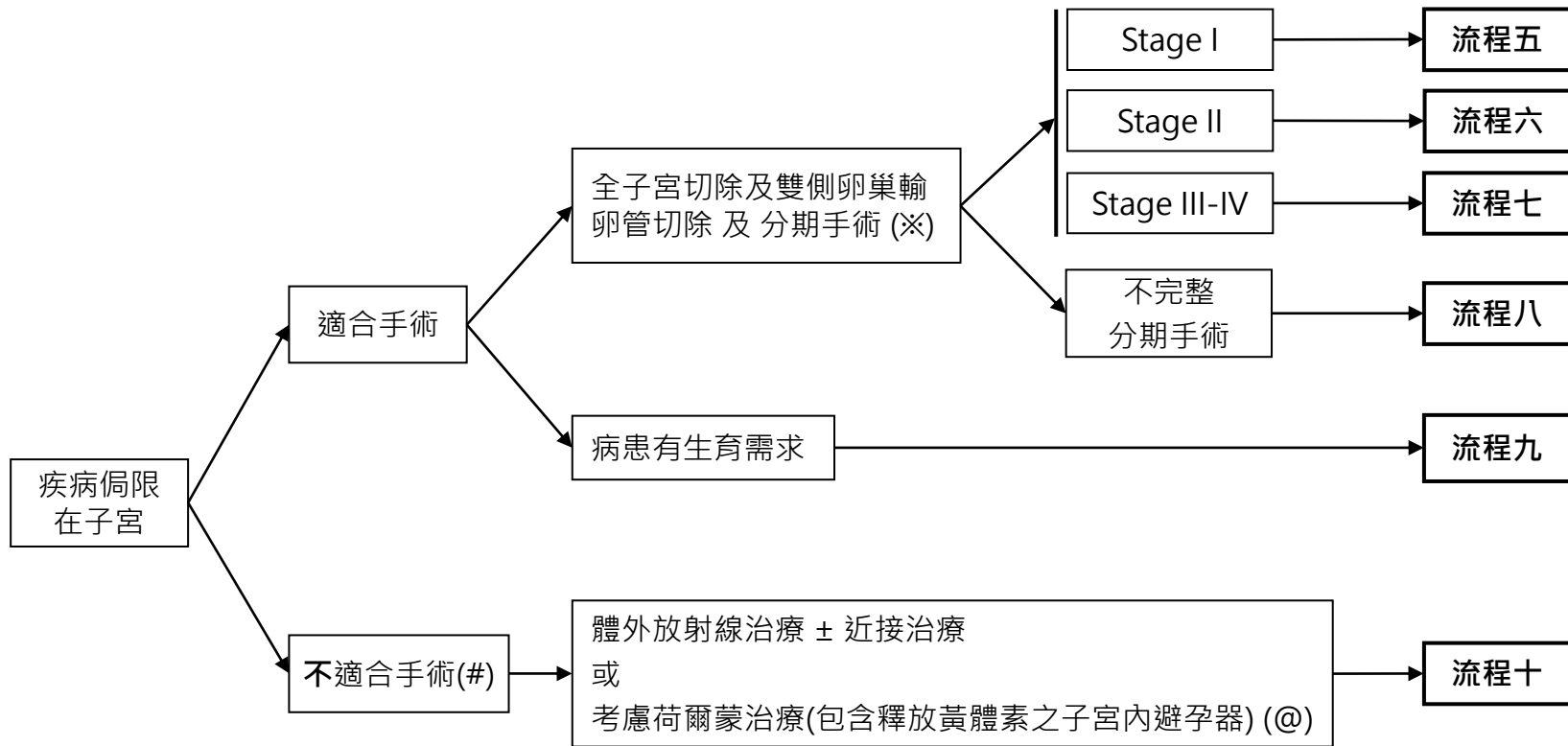
流程一

屏東榮總婦癌團隊 子宮內膜癌臨床治療指引

初步臨床發現

術後病理分期

術後輔助治療



※: 若執刀醫師及病患病況許可，建議微創手術

#: 患者拒絕手術或是因本身其他共病不適合手術

@: 多用於low-grade endometrioid carcinoma, 且患者的腫瘤體積小或是病灶生長緩慢

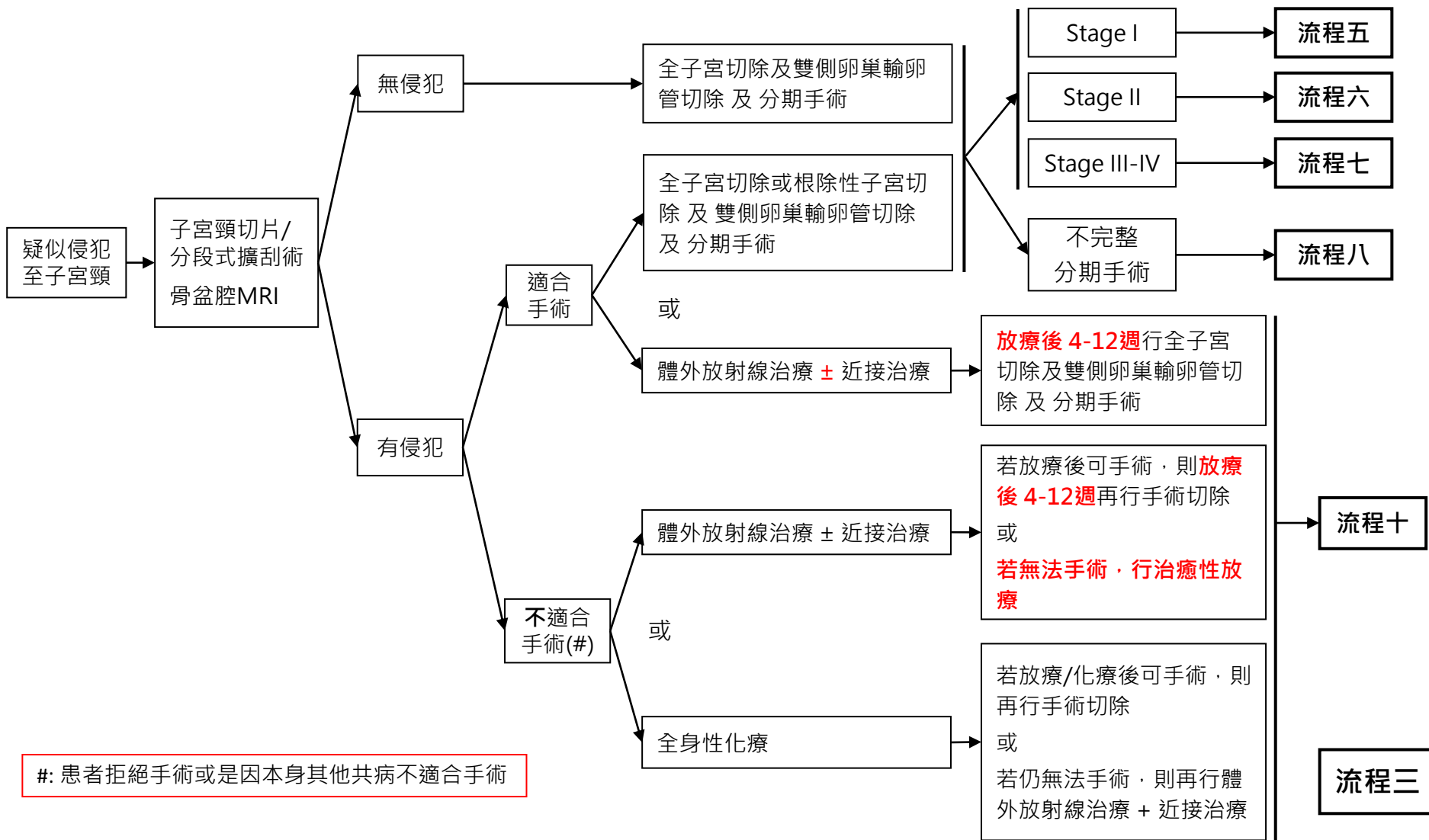
流程二

屏東榮總婦癌團隊 子宮內膜癌臨床治療指引

初步臨床發現

術後病理分期

術後輔助治療



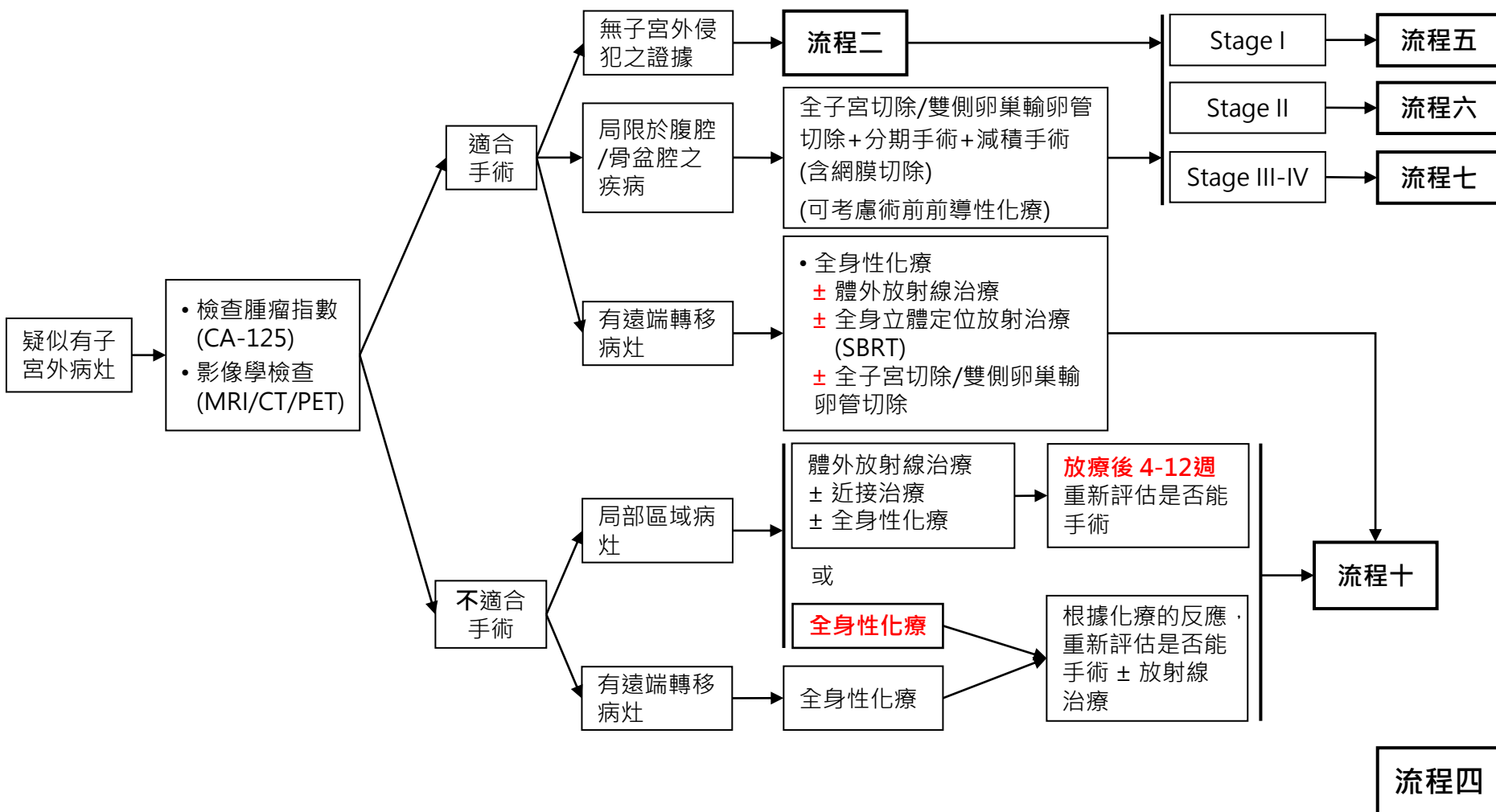
#: 患者拒絕手術或是因本身其他共病不適合手術

屏東榮總婦癌團隊 子宮內膜癌臨床治療指引

初步臨床發現

初步治療

術後輔助治療



Endometrioid carcinoma, FIGO stage I 分期手術術後輔助治療

FIGO stage	Histologic grade	輔助治療
IA	Gr. 1 / Gr. 2	觀察 (建議) 或 考慮陰道近接治療 · 若LVSI (+) 及/或 age \geq 60 y/o (※)
	Gr.3	陰道近接治療(建議) 或 觀察 (若無子宮侵犯) 或 若 \geq 70歲或LVSI(+), 考慮體外放射治療
IB	Gr.1	陰道近接治療(建議) 或 考慮觀察 · 若 $<$ 60歲且LVSI(-)
	Gr.2	陰道近接治療(建議) 或 考慮體外放射線治療 · 若 $>$ 60歲及/或LVSI(+) 或 考慮觀察 · 若 $<$ 60歲且LVSI(-)
	Gr.3	放射治療 (體外放射治療 \pm 近接治療) \pm 全身性化療

※: 若同時LVSI(+)且年紀 \geq 60歲則強烈建議陰道近接治療

流程五

Endometrioid carcinoma, FIGO stage II 分期手術術後輔助治療

FIGO stage	Histologic grade	輔助治療
II	Gr. 1 – Gr. 3	體外放射線治療 (建議) 及/或 陰道近接治療 (※) ± 全身性化療

※: 若Gr.1/2, myometrium invasion \leq 1/2, LVSI (-), and 子宮頸顯微侵犯 (microscopic invasion) 可考慮做近接治療

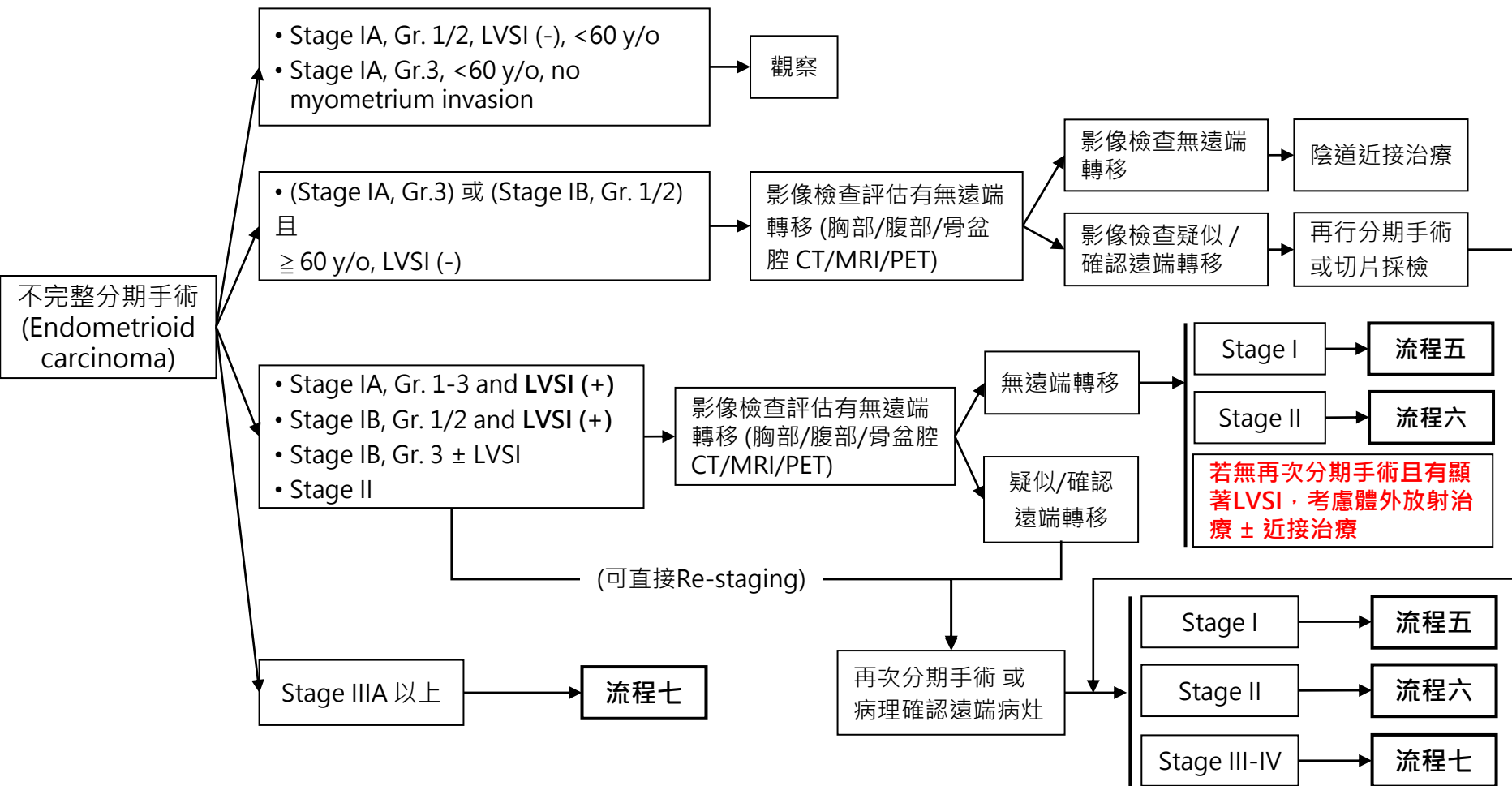
Endometrioid carcinoma, FIGO stage III-IV 分期手術術後輔助治療

FIGO stage	輔助治療
III-IV	全身性化療 ± 體外放射線治療 ± 陰道近接治療 (※)

※: 若為stage IIIB and IIIC則傾向合併放射治療 (EBRT and brachytherapy)

流程七

不完整分期手術後輔助治療 (Endometrioid carcinoma)

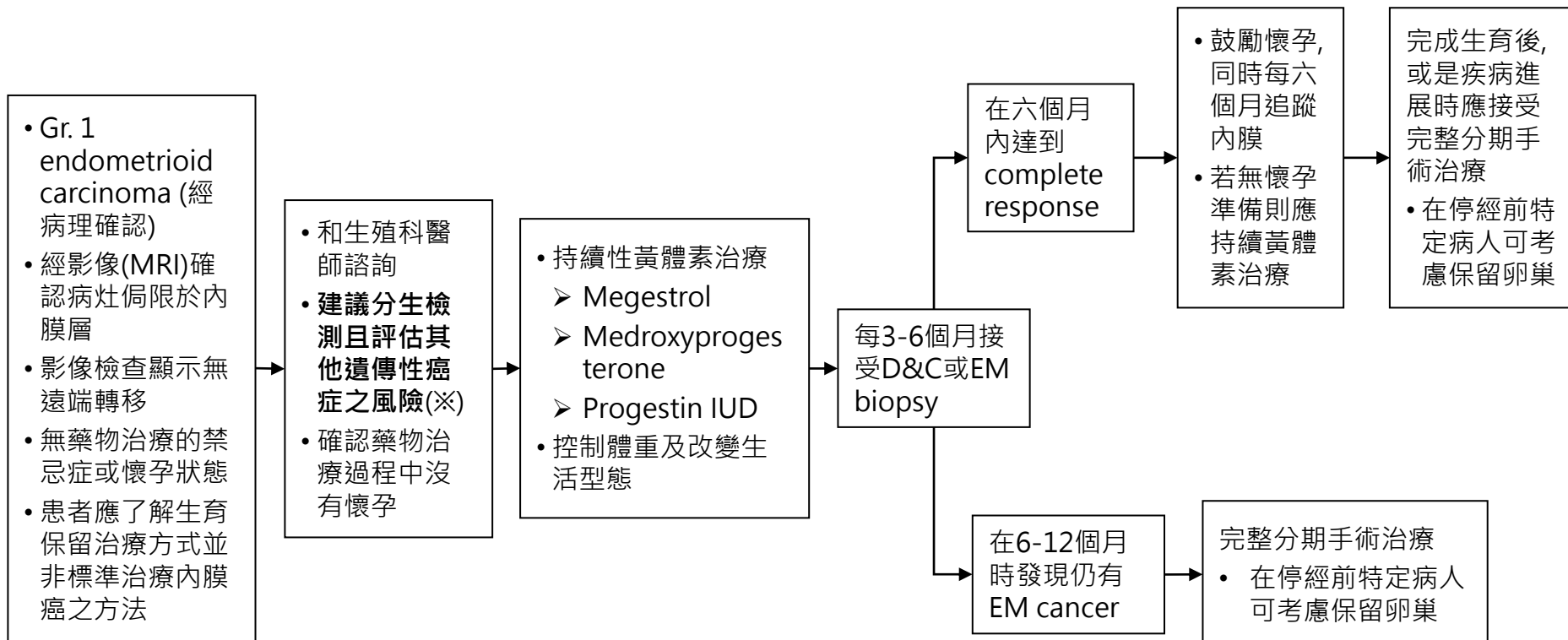


生育保留治療方式

必須滿足以下條件

初始治療

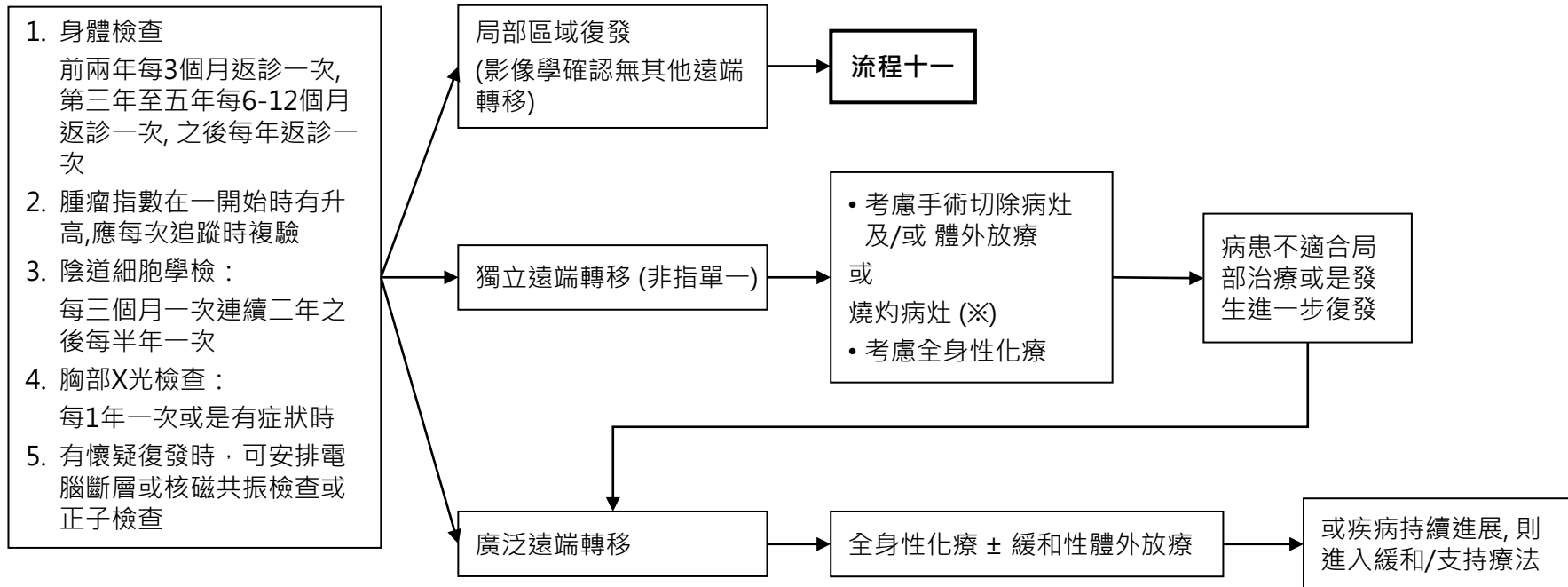
復發後治療



追蹤及監測

臨床表現

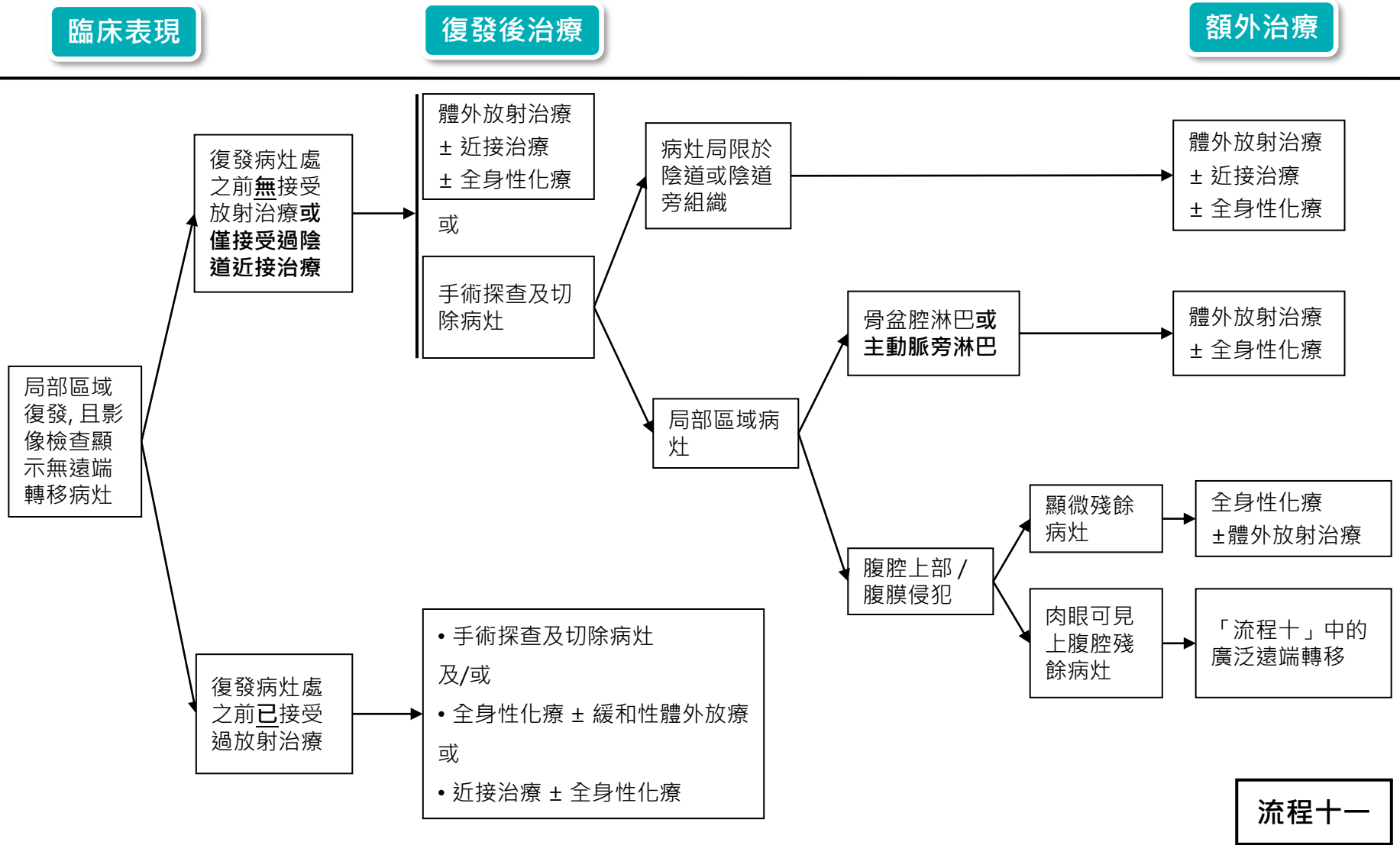
復發後治療



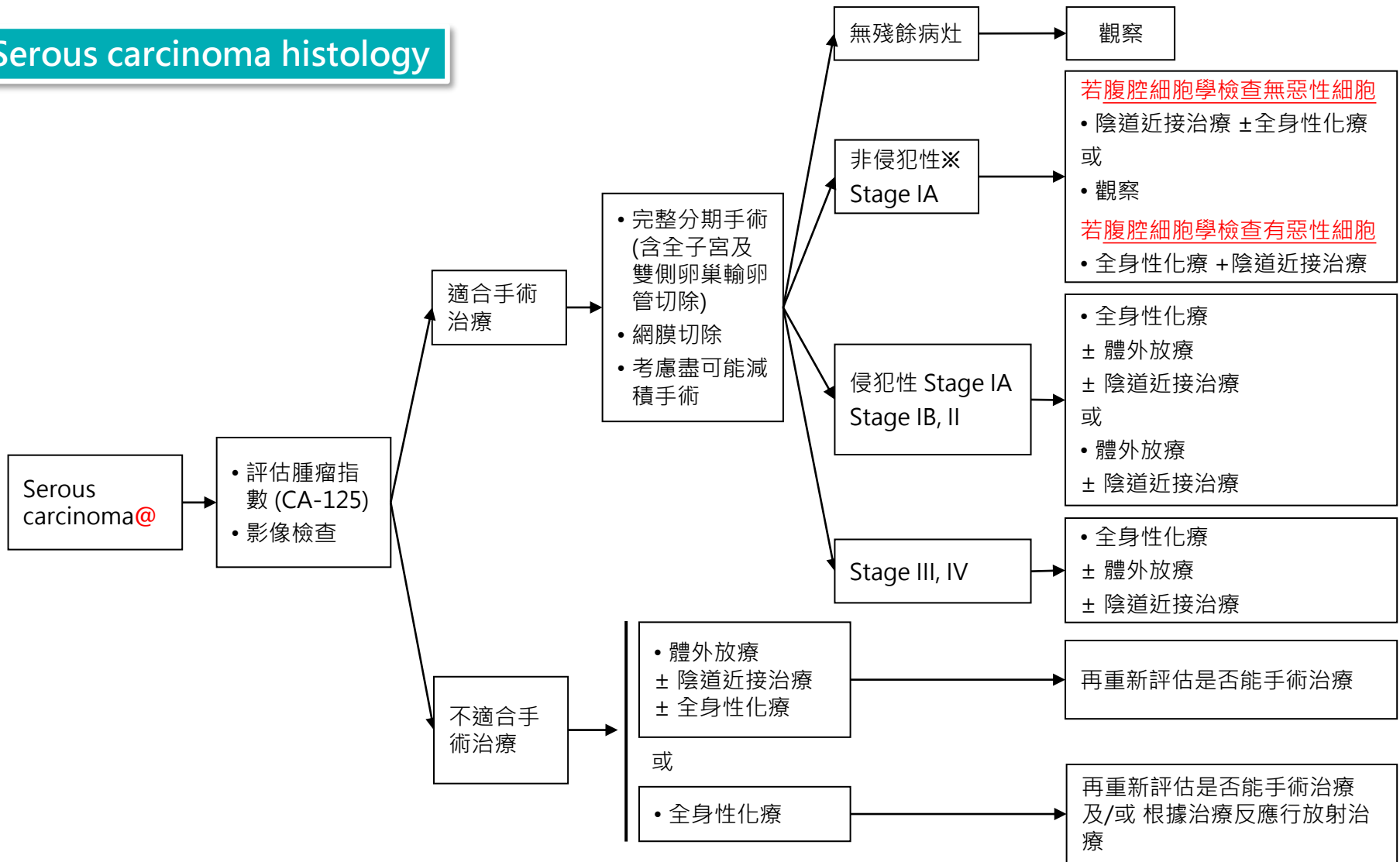
※: 若遠端轉移病灶數為 1-5 個且原始病灶部位已獲得控制時可考慮遠端病灶燒灼術

流程十

局部區域復發治療方式

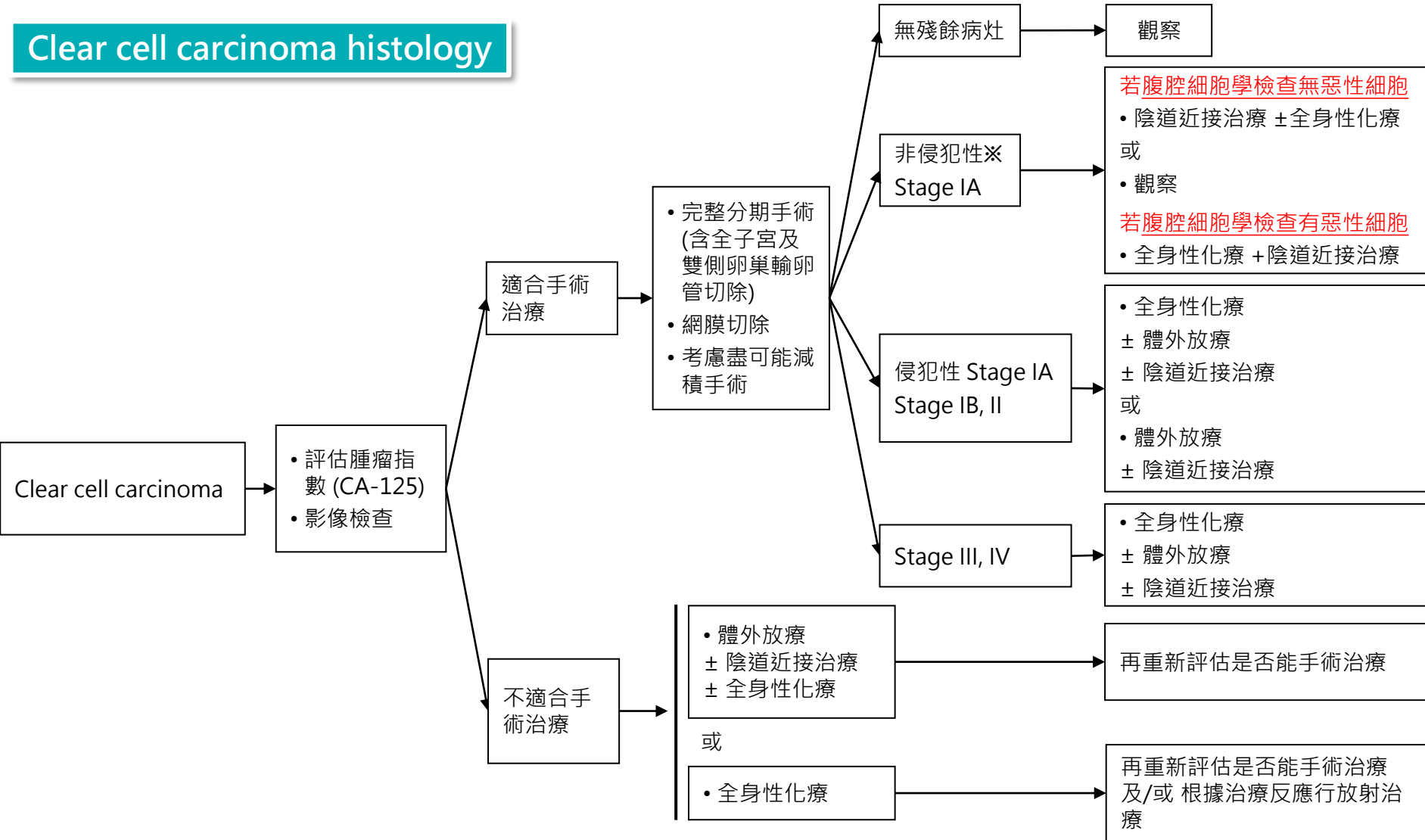


Serous carcinoma histology



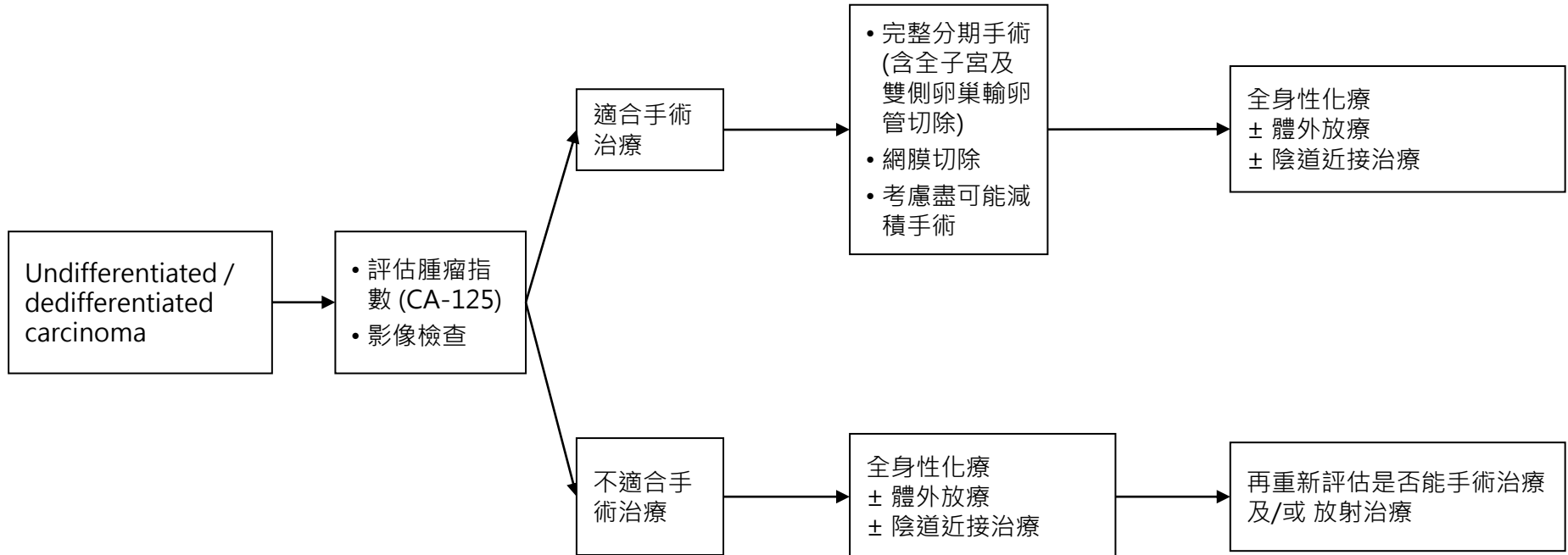
@ Advanced stage或已有遠端轉移之疾病建議
檢測HER2 gene
※ noninvasive stage IA: 沒有肌肉層的侵犯

Clear cell carcinoma histology

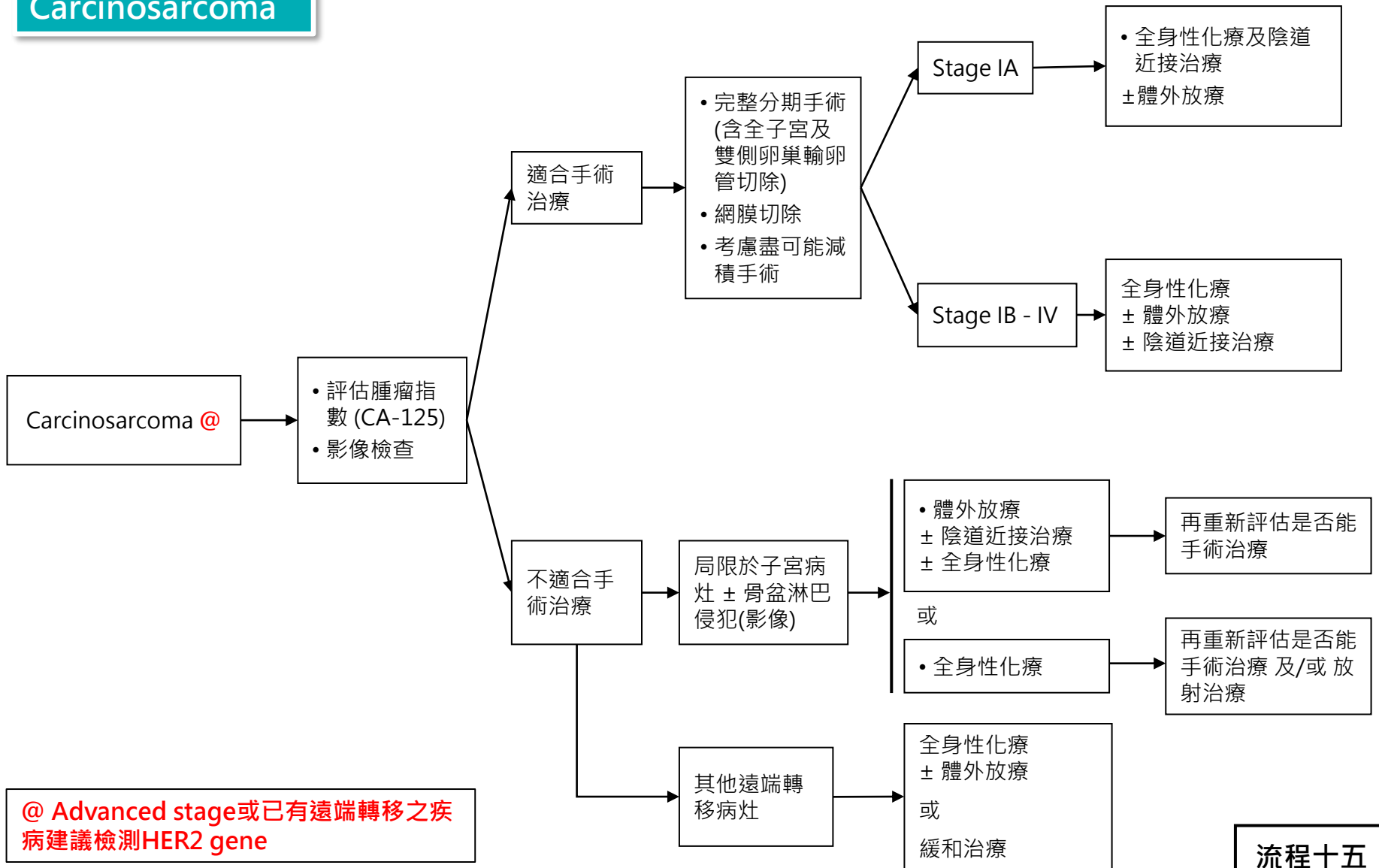


※ noninvasive stage IA: 沒有肌肉層的侵犯

Undifferentiated / Dedifferentiated carcinoma



Carcinosarcoma



Primary or Adjuvant 可選用配方 (Stage I ~ IV)

Taxol (payself) (175 mg/m²) + Cisplatin (50 mg/m²) if CCr > 60ml/min
Taxol (payself) (175 mg/m²) + Carboplatin (AUC=5) if CCr < 60ml/min

Taxol (payself) + Carboplatin + Pembrolizumab (Stage III/IV, **except for carcinosarcoma**) (Ref.43)
Taxol (payself) + Carboplatin + Dostarlimab (Stage III/IV) (Ref.44)

針對stage III/IV or 復發的serous carcinoma or carcinosarcoma with **HER2 positive**
Carboplatin (AUC=5) + Paclitaxel (175 mg/m²)+ Trastuzumab (38)
Trastuzumab: (8mg/kg in 1st cycle, then 6mg/kg since 2nd cycle)

子宮內膜癌 化療藥物指引

針對 復發/轉移 疾病時可選用配方

Taxol (payself) (175 mg/m²) + Cisplatin (50 mg/m²) if CCr > 60ml/min
 Taxol (payself) (175 mg/m²) + Carboplatin (AUC=5) if CCr < 60ml/min
 Taxol (payself) + Carboplatin + **Pembrolizumab** (Stage III/IV, **except for carcinosarcoma**)
 Taxol (payself) + Carboplatin + **Dostarlimab** (Stage III/IV)
 針對stage III/IV or 復發的**serous** carcinoma or carcinosarcoma with **HER2 positive**
 Carboplatin (AUC=5) + Paclitaxel (175 mg/m²) + Trastuzumab (8mg/kg in 1st cycle, then 6mg/kg since 2nd cycle) (38)

復發後第一線
選擇配方

針對接受過至少一線含鉑金類化療後復發，且有 (MSI-H / MMR proteins deficiency) 的病患
 Pembrolizumab (Keytruda) (200mg), Every 21 days (35, 39, 40)
 Dostarlimab

針對接受過至少一線含鉑金類化療後復發，且沒有 (MSI-H / MMR proteins deficiency) 的病患
 Lenvatinib(20mg orally QD) + Pembrolizumab (Keytruda) (200mg), Every 21 days (42)

PEI (Epirubicin 為optional) (8)
 Epirubicin (50mg/m²) + Cisplatin(50mg/m²) + Ifosfamide+mesna (4gm/m²) if CCr > 60ml/min
 Epirubicin (50mg/m²) + Carboplatin(AUC=5) + Ifosfamide+mesna (4gm/m²) if CCr < 60ml/min

Topotecan(0.75mg/m²) + Cisplatin (50mg/m²), if CCr > 60ml/min (30,31)
 Topotecan(0.75mg/m²) + Carboplatin (AUC=5), if CCr < 60ml/min

Lipodoxorubicin (payself) (30 mg/m²) + Cisplatin(50mg/m²), if CCr > 60ml/min (32,33)
 Lipodoxorubicin (payself) (30 mg/m²) + Carboplatin(AUC=5), if CCr > 60ml/min (32,33)

Lipodoxorubicin (payself) (40 mg/m²), every 28 days (32, 33)

Weekly topotecan (4mg/m²) (34)
 Topotecan alone (1mg/m²) on D1-D5, every 21 days (Ref Walder S. et al., 2003)

Taxol (payself) (175 mg/m²) + Carboplatin (AUC=5) + Avastin (5-15mg/kg) (36, 37)

Avastin (payself) (5~15mg/kg) (29)

復發後第二線
選擇配方

子宮內膜癌 荷爾蒙藥物指引

可選用配方
Megestrol 160 mg/QD
Medroxyprogesterone acetate (Farlutal) 500mg 1# QD (27)
Levonorgestrel IUD (For fertility sparing)
Letrozole 2.5mg 1# QD (28)
Tamoxifen 10mg 1# BID (26)
針對復發或是遠端轉移的endometrioid carcinoma Everolimus 10mg QD + Letrozole 2.5mg QD (41)

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