高雄榮民總醫院

子宮內膜癌

診療指引

2024年 第一版 2024/01/25

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

上次會議：2023/02/14

本共識與上一版的差異

上一版	新版
1. 分期採用2017 FIGO staging (p.4-7) 2. 流程一：建議在D&C的檢體，或是在最後手術切除的子宮檢體上進行MMR ．．．(p.8) 3. 流程二：若執刀醫師及病患病況許可，建議微創手術(p.9) 4. 流程三：「疑似侵犯至子宮頸」字眼修改。(p.10) 5. 流程七：輔助治療-全身性化療(p.14) 6. 流程八：考慮影像評估有無「遠端轉移」字眼修改(p.15) 7. 流程九：字眼修正（原為基因檢測、藥物治療過程中沒有懷孕）(p.16) 8. 化療藥物指引：Taxol+platinum欄位，新增備註(p.23)	1. 新增2023 FIGO staging, 及molecular classification (p.4-7) 2. 流程一：建議在D&C的檢體，或是在最後手術切除的子宮檢體上進行MMR……後續新增「p53 / POLE 分子檢測，尤其細胞型態為endometrioid carcinoma grade 3者」。(p.12) 3. 流程二：若執刀醫師及病患病況許可，建議微創手術……後續新增「特定細胞型態（例如：serous, carcinosarcoma…），建議加上網膜切除」。(p.13) 4. 流程三：修改為「懷疑或巨觀下有子宮頸侵襲」，並放療後手術，新增「放療後4-12週」備註 (p.14) 5. 流程七：新增±免疫治療(p.18) 6. 流程八：考慮影像評估有無「殘存病灶」，後續流程新增處置方法 7. 流程九：字眼修正（分子檢測、非懷孕狀態）(p.20) 8. 流程十-十五：新增±免疫治療(p.21-26) 9. 化療藥物指引：Taxol+platinum欄位，新增「針對stage III/IV，除卻carcinosarcoma，建議再加上Pembrolizumab 」(p.27)

高雄榮總婦產部 子宮內膜癌臨床治療指引
2023 FIGO staging of cancer of the endometrium

Stage	Description
Stage I	Confined to the uterine corpus and ovary[c]
IA	Disease limited to the endometrium OR non-aggressive histological type, i.e. low-grade endometroid, with invasion of less than half of myometrium with no or focal lymphovascular space involvement (LVSI) OR good prognosis disease
	IA1 Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium
	IA2 Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI
	IA3 Low-grade endometrioid carcinomas limited to the uterus and ovary[c]
IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI[d]
IC	Aggressive histological types[e] limited to a polyp or confined to the endometrium
Stage II	Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion
IIA	Invasion of the cervical stroma of non-aggressive histological types
IIB	Substantial LVSI[d] of non-aggressive histological types
IIC	Aggressive histological types[e] with any myometrial involvement

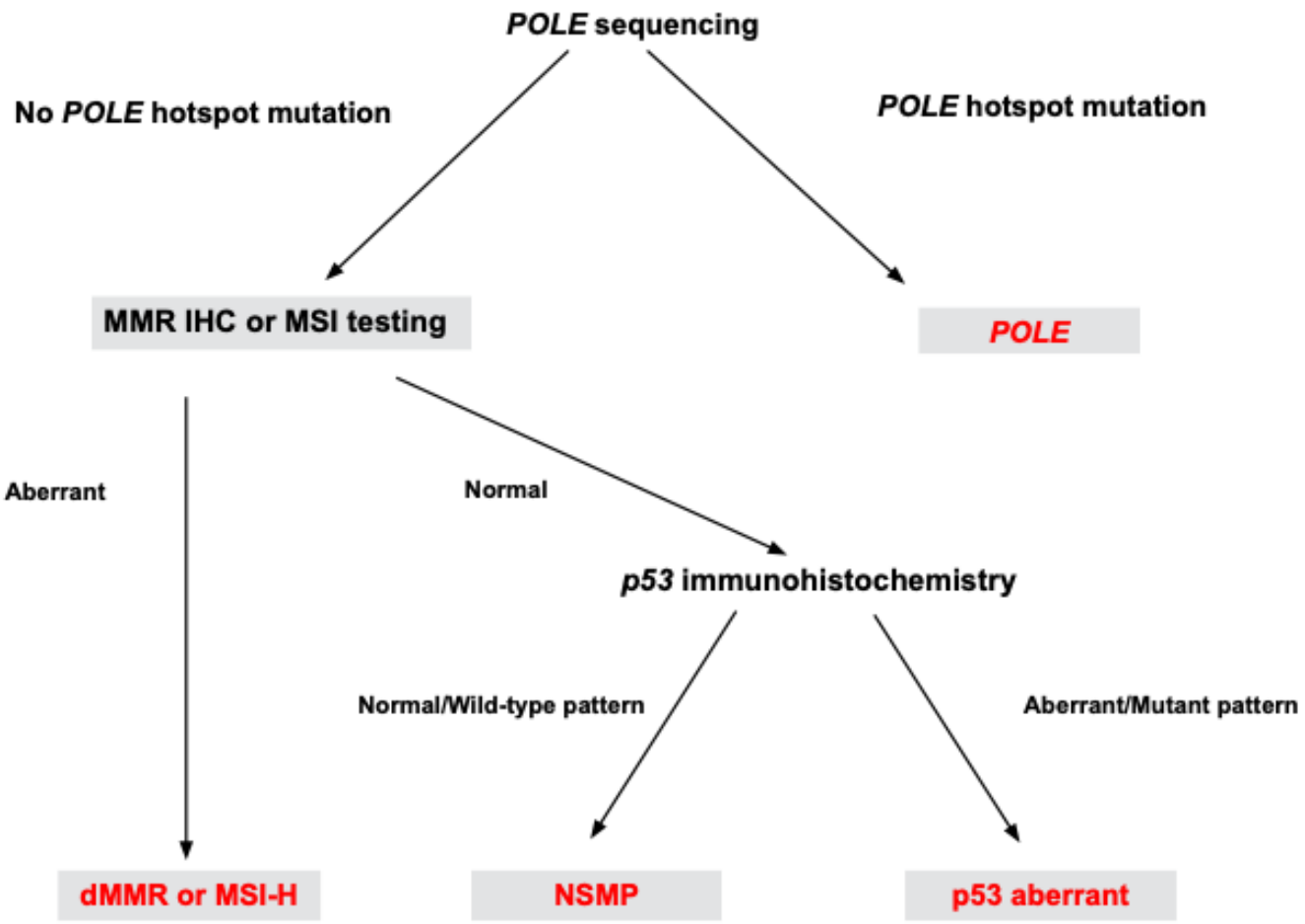
※ Non-aggressive histological type: Endometrioid carcinoma (ECC) grade 1/2
其餘皆為aggressive histological type

高雄榮總婦產部 子宮內膜癌臨床治療指引
2023 FIGO staging of cancer of the endometrium

Stage III	Local and/or regional spread of the tumor of any histological subtype
IIIA	Invasion of uterine serosa, adnexa, or both by direct extension or metastasis
	IIIA1 Spread to ovary or fallopian tube (except when meeting stage IA3 criteria)[c] IIIA2 Involvement of uterine subserosa or spread through the uterine serosa
IIIB	Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum
	IIIB1 Metastasis or direct spread to the vagina and/or the parametria IIIB2 Metastasis to the pelvic peritoneum
IIIC	Metastasis to the pelvic or para-aortic lymph nodes or both[f]
	IIIC1 Metastasis to the pelvic lymph nodes IIIC1i Micrometastasis IIIC1ii Macrometastasis IIIC2 Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes IIIC2i Micrometastasis IIIC2ii Macrometastasis
Stage IV	Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastasis
IVA	Invasion of the bladder mucosa and/or the intestinal/bowel mucosa
IVB	Abdominal peritoneal metastasis beyond the pelvis
IVC	Distant metastasis, including metastasis to any extra- or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone

高雄榮總婦產部 子宮內膜癌臨床治療指引
2023 FIGO staging of cancer of the endometrium – molecular subtype

※建議在D&C的檢體，或是在最後手術切除的子宮檢體上進行MMR / p53 / POLE 分子檢測



高雄榮總婦產部 子宮內膜癌臨床治療指引
2023 FIGO staging of cancer of the endometrium – molecular subtype

※建議在D&C的檢體，或是在最後手術切除的子宮檢體上進行MMR / p53 / POLE 分子檢測

Prognosis	Molecular subtype
Good	*POLE* mutation (*POLEmut*)
Intermediate	MMR deficiency (MMRd) microsatellite instability and no specific molecular profile (NSMP)
Poor	p53 abnormal (p53abn)

※分期為stage I/II， molecular subtype若為*POLEmut*或 p53abn，根據下表修改FIGO stage

Stage designation	Molecular findings in patients with early endometrial cancer (Stages I and II after surgical staging)
Stage $IAm_{POLEmut}$	*POLEmut* endometrial carcinoma, confined to the uterine corpus or with cervical extension, regardless of the degree of LVSI or histological type
Stage $IICm_{p53abn}$	p53abn endometrial carcinoma confined to the uterine corpus with any myometrial invasion, with or without cervical invasion, and regardless of the degree of LVSI or histological type

※分期為stage IIIIV，不根據molecular subtype修改分期

高雄榮總婦產部 子宮內膜癌臨床治療指引
2017 FIGO and TNM staging (AJCC 8th)

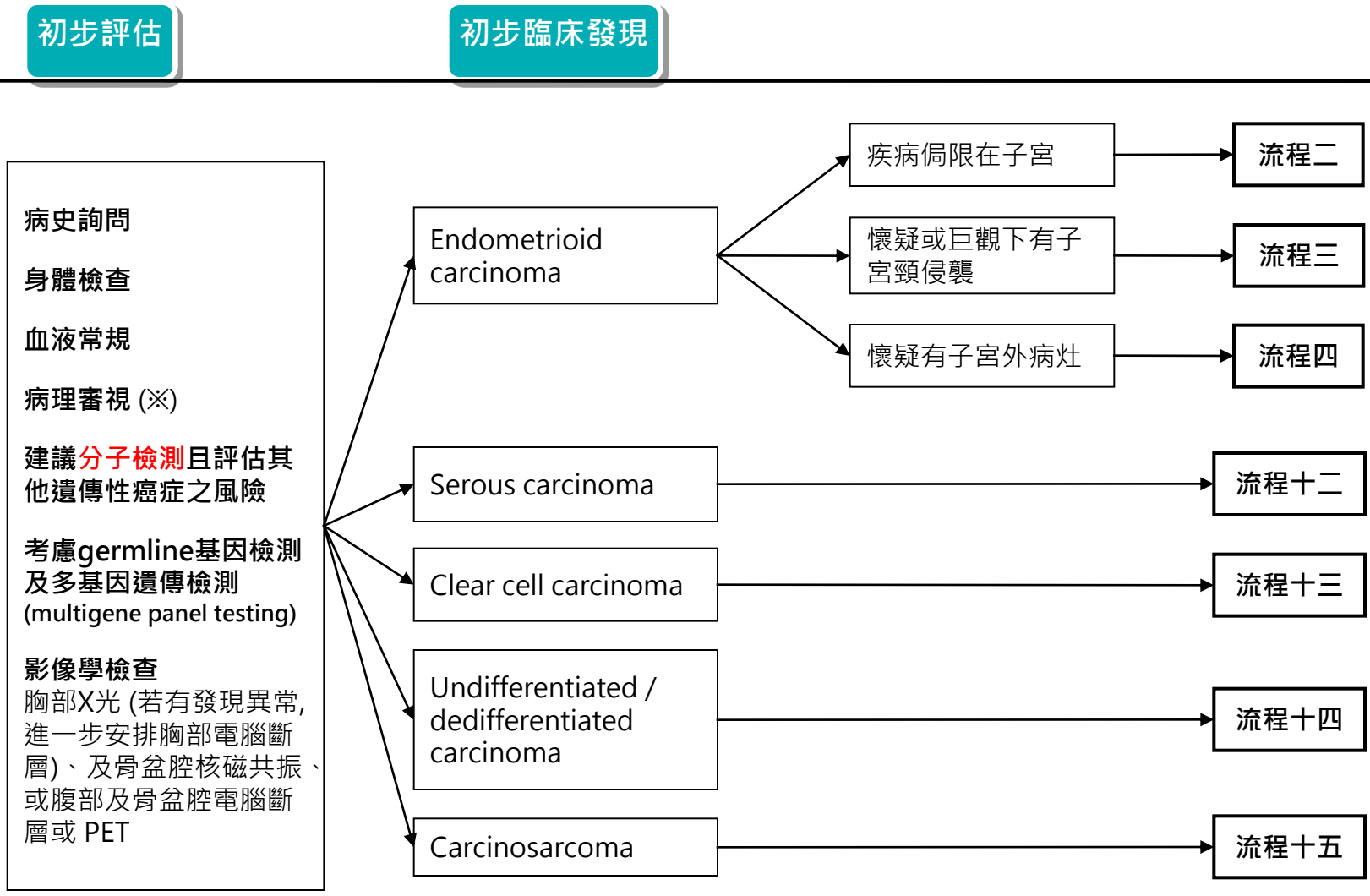
Primary Tumor (T)		
T	**FIGO**	**T Criteria**
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor confined to the corpus uteri, including endocervical glandular involvement
T1a	IA	Tumor limited to the endometrium or invading less than half the myometrium
T1b	IB	Tumor invading 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 pelvie 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).

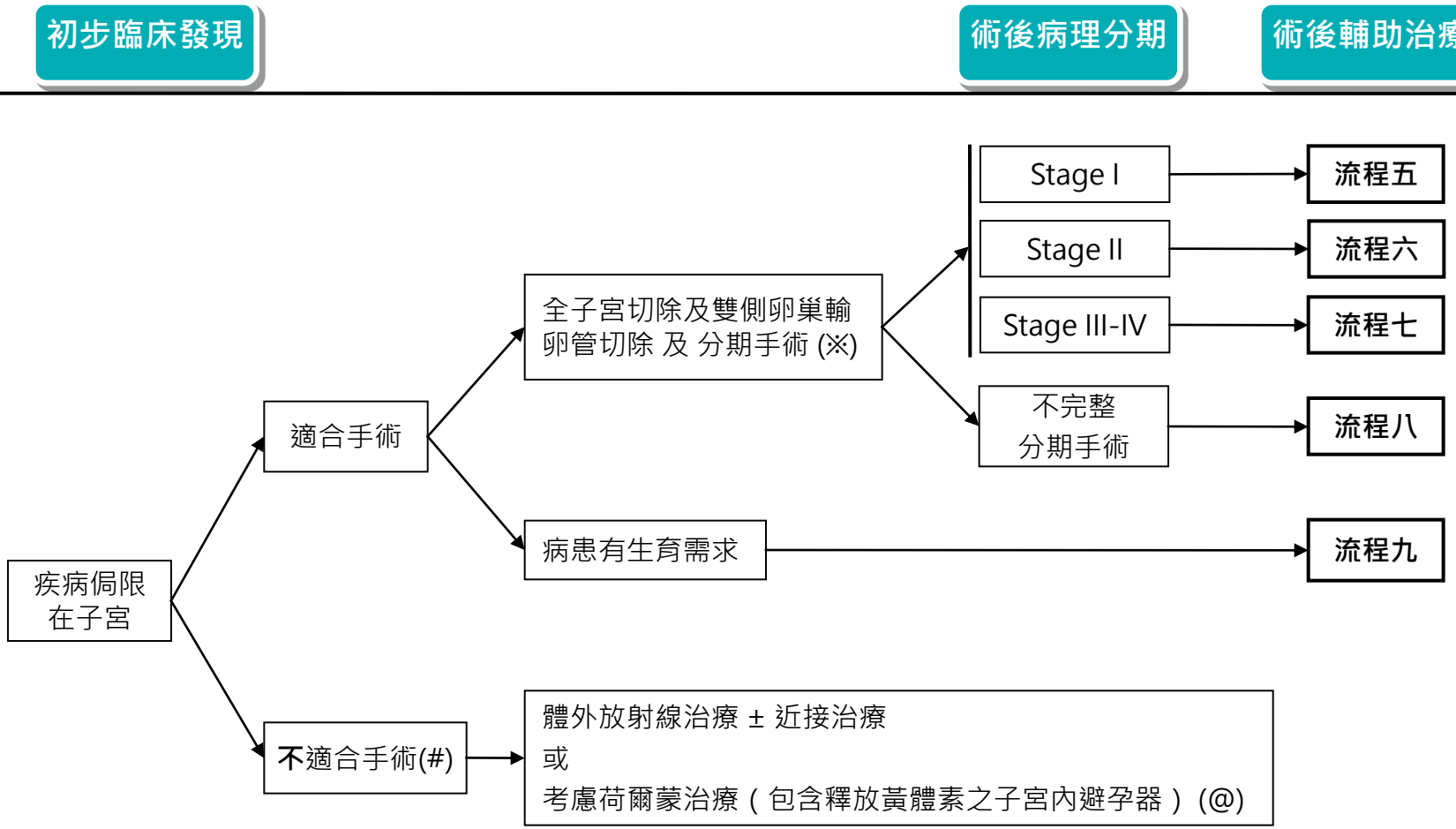
STAGE GROUPS			
T	**N**	**M**	**stage**
T1	N0	M0	I
T1a	N0	M0	IA
T1b	N0	M0	IB
T2	N0	M0	II
T3	N0	M0	III
T3a	N0	M0	IIIA
T3b	N0	M0	IIIB
T1-T3	N1/N1mi/N1a	M0	IIIC1
T1-T3	N2/N2mi/N2a	M0	IIIC2
T4	Any N	M0	IVA
Any T	Any N	M1	IVB

高雄榮總婦癌團隊　子宮內膜癌臨床治療指引



※ 建議在D&C的檢體，或是在最後手術切除的子宮檢體上進行MMR / p53 / POLE 分子檢測，尤其細胞型態為 endometrioid carcinoma grade 3者。

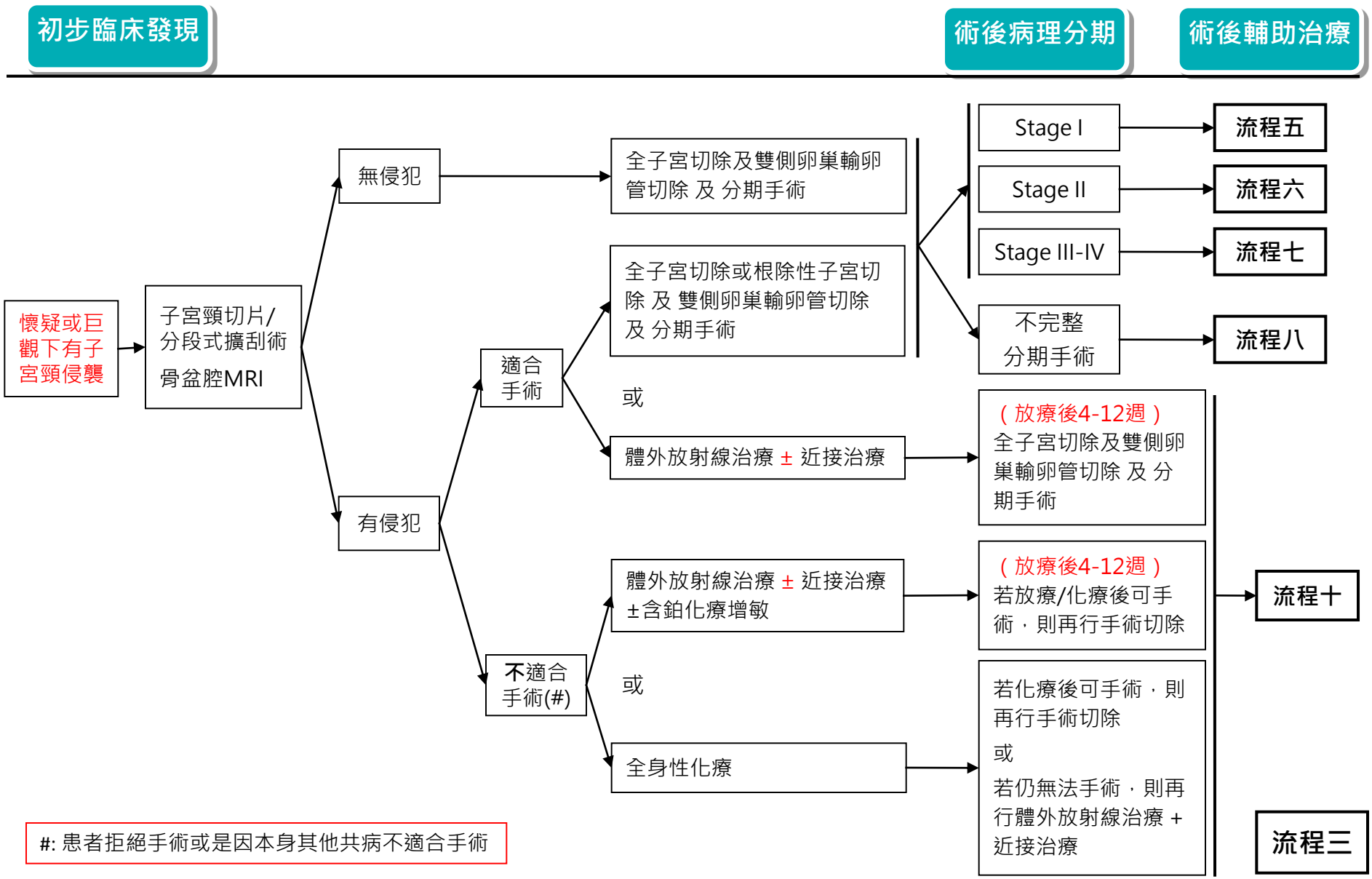
高雄榮總婦癌團隊　子宮內膜癌臨床治療指引



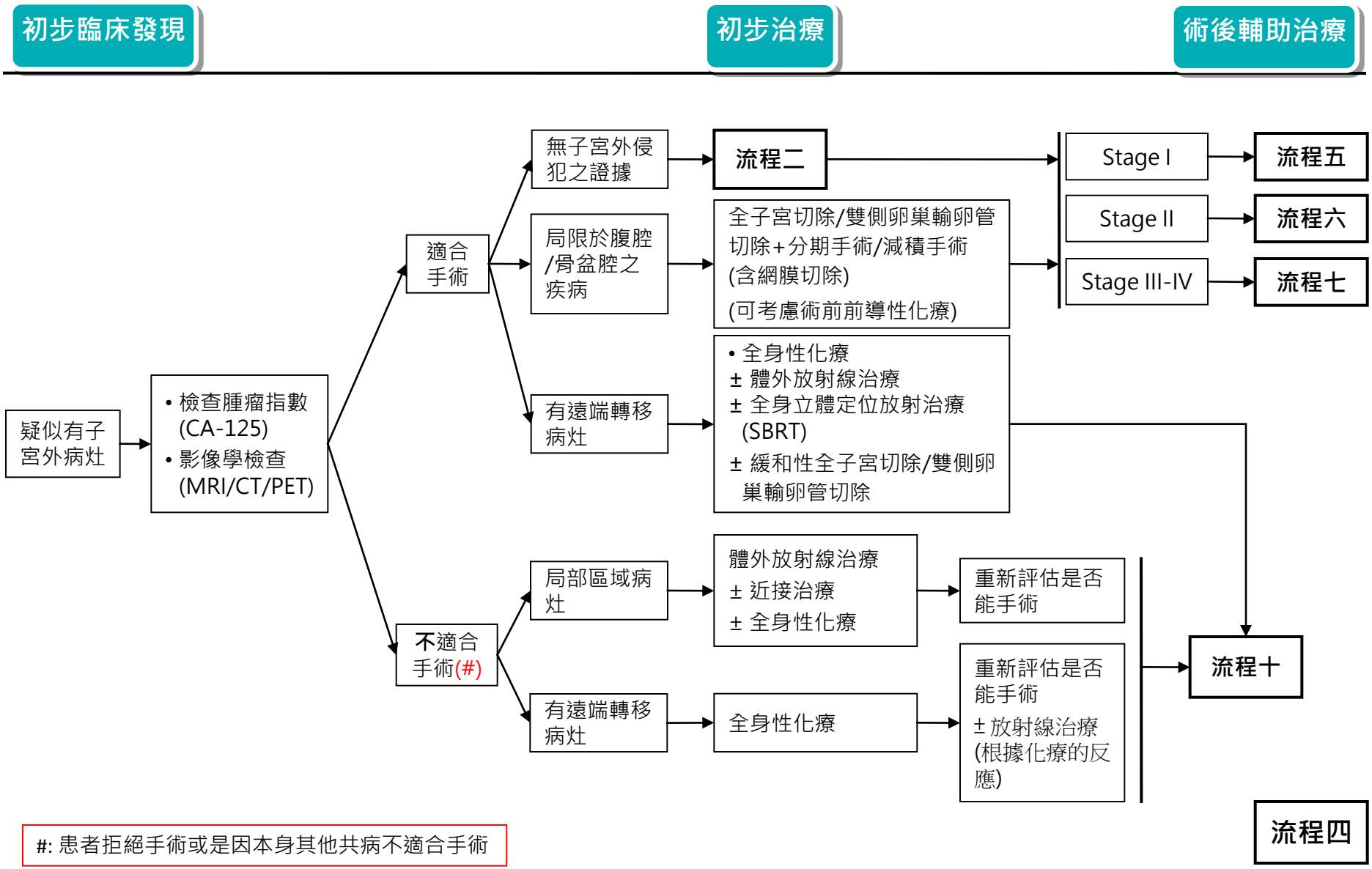
※: 若執刀醫師及病患病況許可，建議微創手術；特定細胞型態（例如：serous, carcinosarcoma…），建議加上網膜切除
#: 患者拒絕手術或是因本身其他共病不適合手術
@: 多用於low-grade endometrioid carcinoma, 且患者的腫瘤體積小或是病灶生長緩慢

流程二

高雄榮總婦癌團隊　子宮內膜癌臨床治療指引



高雄榮總婦癌團隊　子宮內膜癌臨床治療指引



#: 患者拒絕手術或是因本身其他共病不適合手術

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 ≧ 60 y/o (※)
	Gr.3	陰道近接治療(建議) 或 觀察 (若無子宮侵犯) 或 若≧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 ± 近接治療) ± 全身性化療

※: 若同時LVSI(+)且年紀≧60歲則強烈建議陰道近接治療

流程五

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 ≦ 1/2, LVSI (-), and 子宮頸顯微侵犯 (microscopic invasion) 可考慮做近接治療

流程六

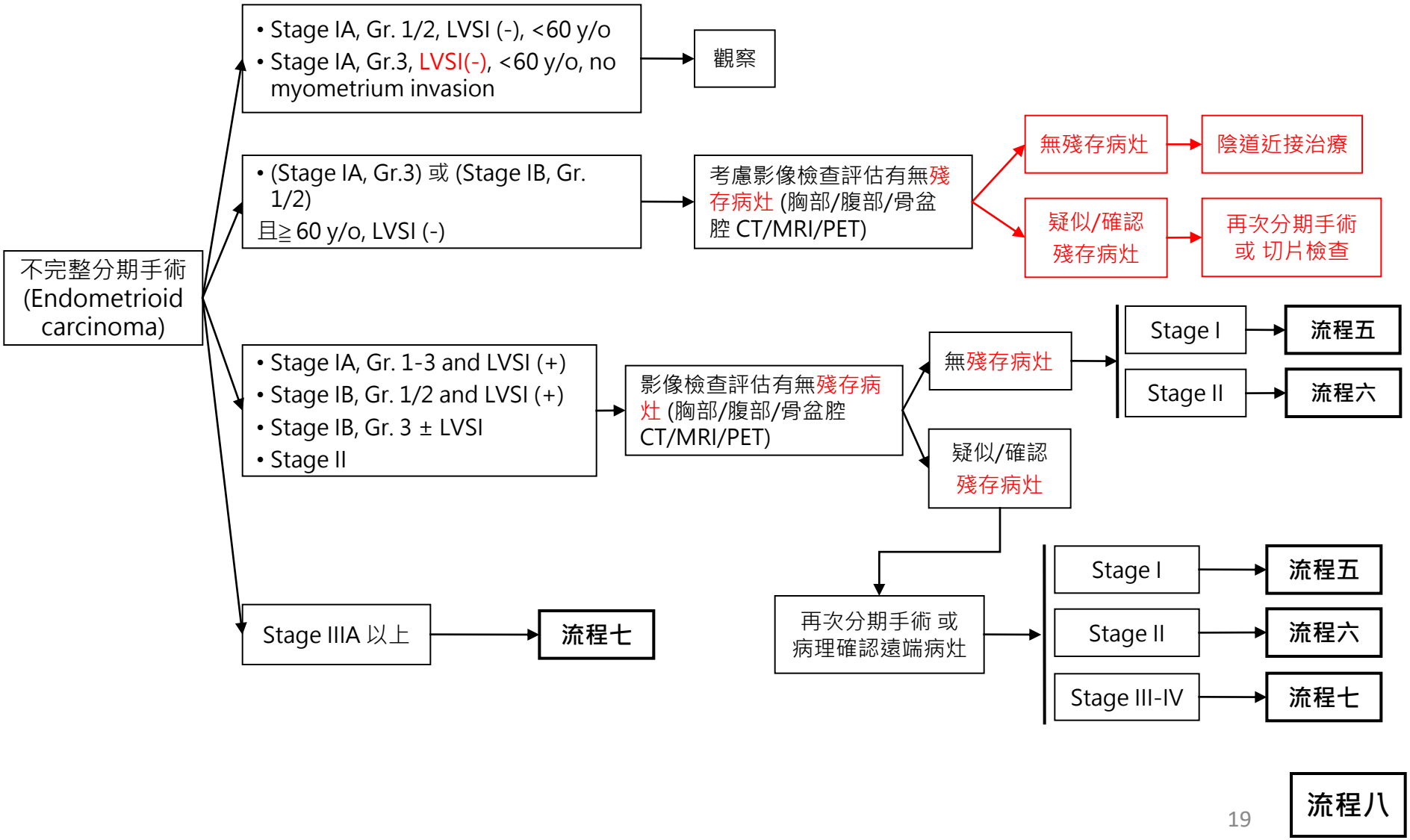
FIGO stage III-IV 分期手術術後輔助治療

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

※: 若為stage IIIB-IIIC則可考慮合併治療

流程七

不完整分期手術後輔助治療 (Endometrioid carcinoma)



高雄榮總婦癌團隊　子宮內膜癌臨床治療指引

生育保留治療方式

必須滿足以下條件

- Gr. 1 endometrioid carcinoma (經病理確認)
- 經影像(MRI)確認病灶侷限於內膜層
- 影像檢查顯示無遠端轉移
- 無藥物治療的禁忌症或懷孕狀態
- 患者應了解生育保留治療方式並非標準治療子宮內膜癌之方法

初始治療

- 和生殖科醫師諮詢
- 建議分子檢測且評估其他遺傳性癌症之風險(※)
- 確認非懷孕狀態

- 持續性黃體素治療
  - Megestrol
  - Medroxyprogesterone
  - Progestin IUD
- 控制體重及改變生活型態

每3-6個月接受D&C或EM biopsy

復發後治療

在6個月內達到complete response

- 鼓勵懷孕, 同時每6-12個月追蹤內膜
- 若無懷孕準備則應持續黃體素治療

完成生育後, 或是疾病進展時應接受完整分期手術治療

•在停經前特定病人可考慮保留卵巢

在6-12個月時發現仍有EM cancer

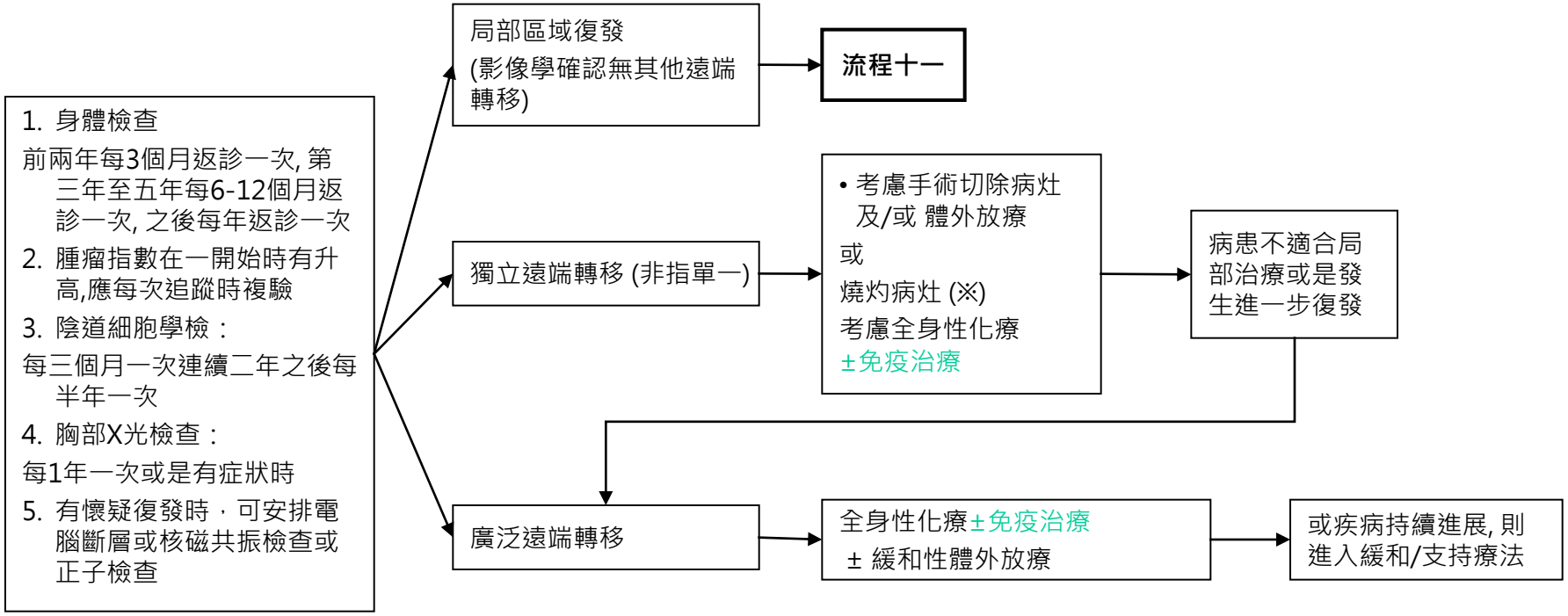
完整分期手術治療

•在停經前特定病人可考慮保留卵巢

流程九

高雄榮總婦癌團隊　子宮內膜癌臨床治療指引

追蹤及監測　臨床表現　復發後治療

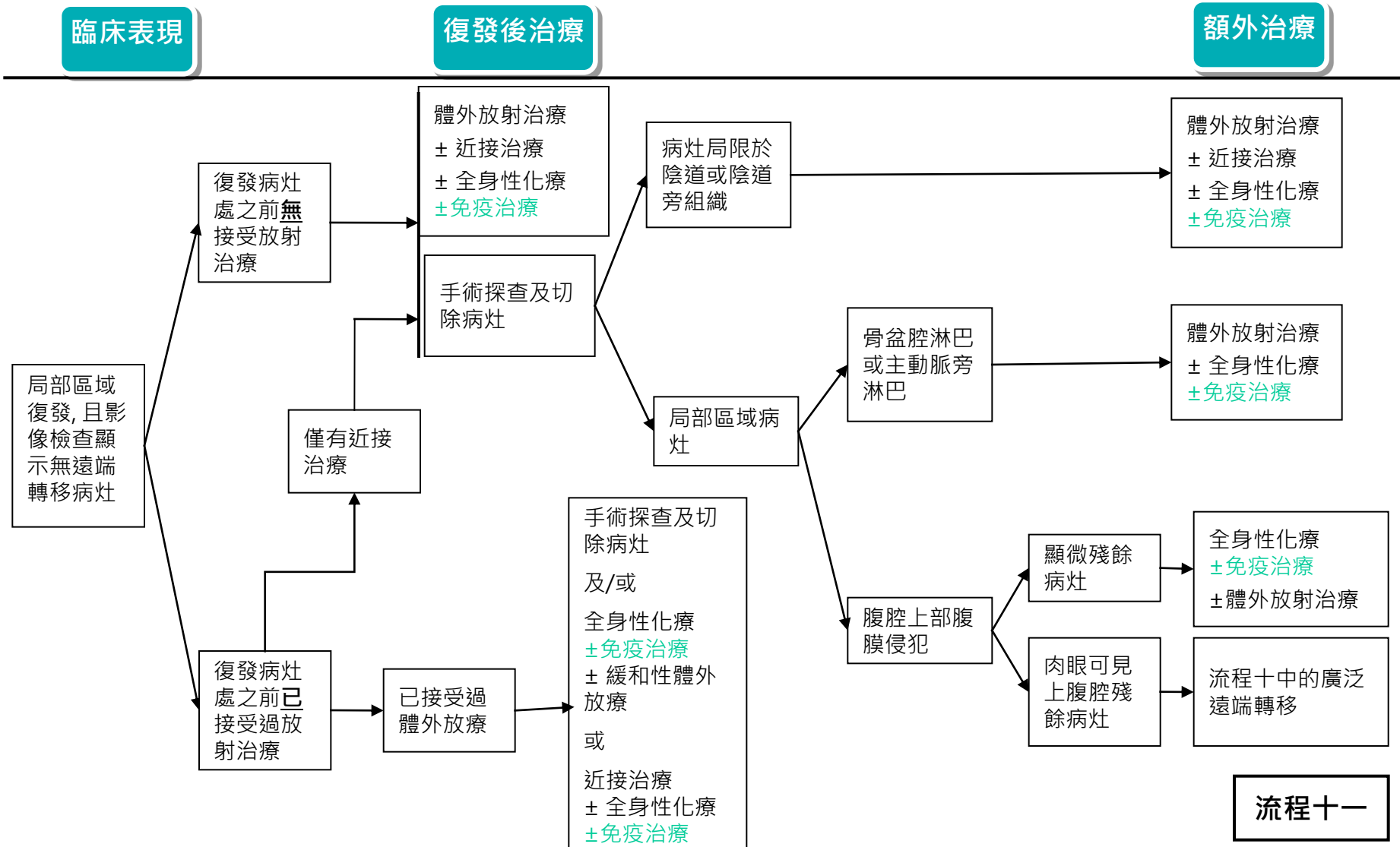


※: 若遠端轉移病灶數為 1-5 個且原始病灶部位已獲得控制時可考慮遠端病灶燒灼術

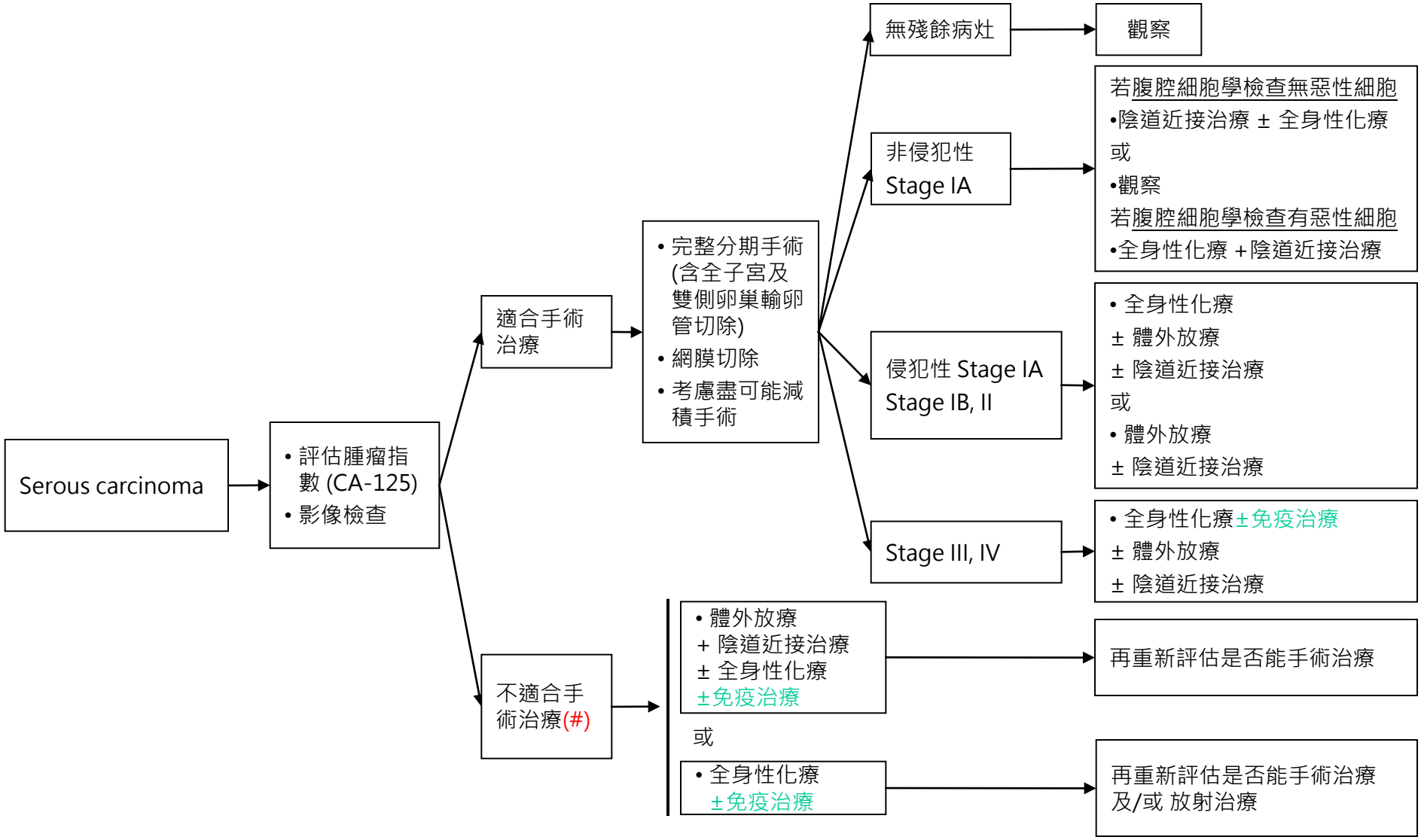
流程十

高雄榮總婦癌團隊　子宮內膜癌臨床治療指引

局部區域復發治療方式



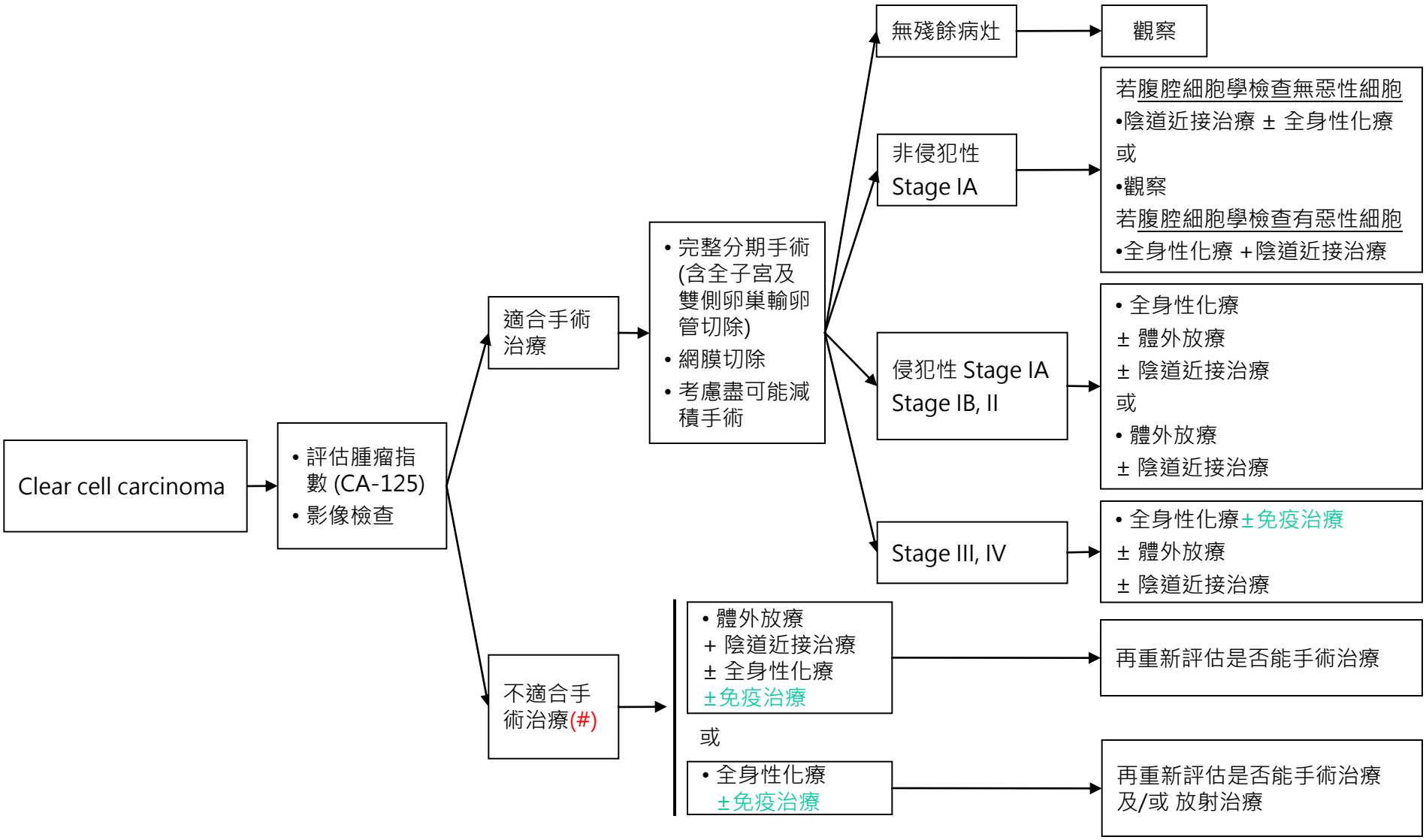
高雄榮總婦癌團隊　子宮內膜癌臨床治療指引



#: 患者拒絕手術或是因本身其他共病不適合手術

流程十二

高雄榮總婦癌團隊　子宮內膜癌臨床治療指引



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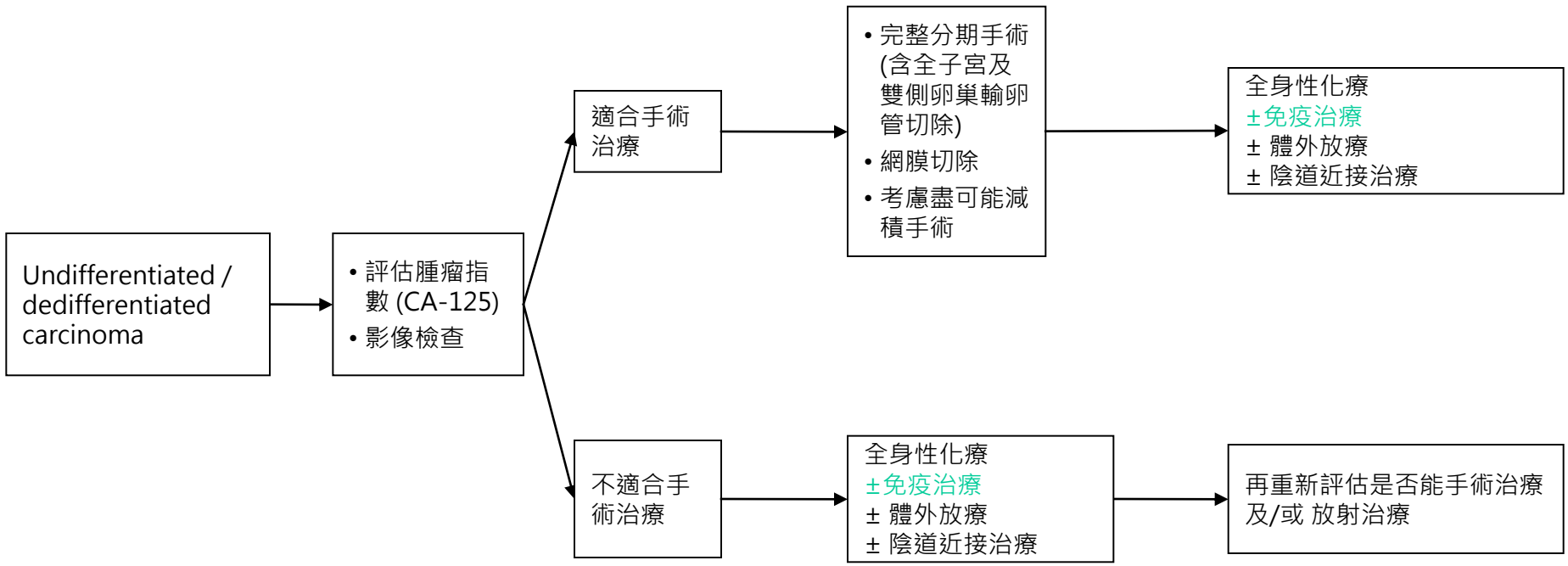
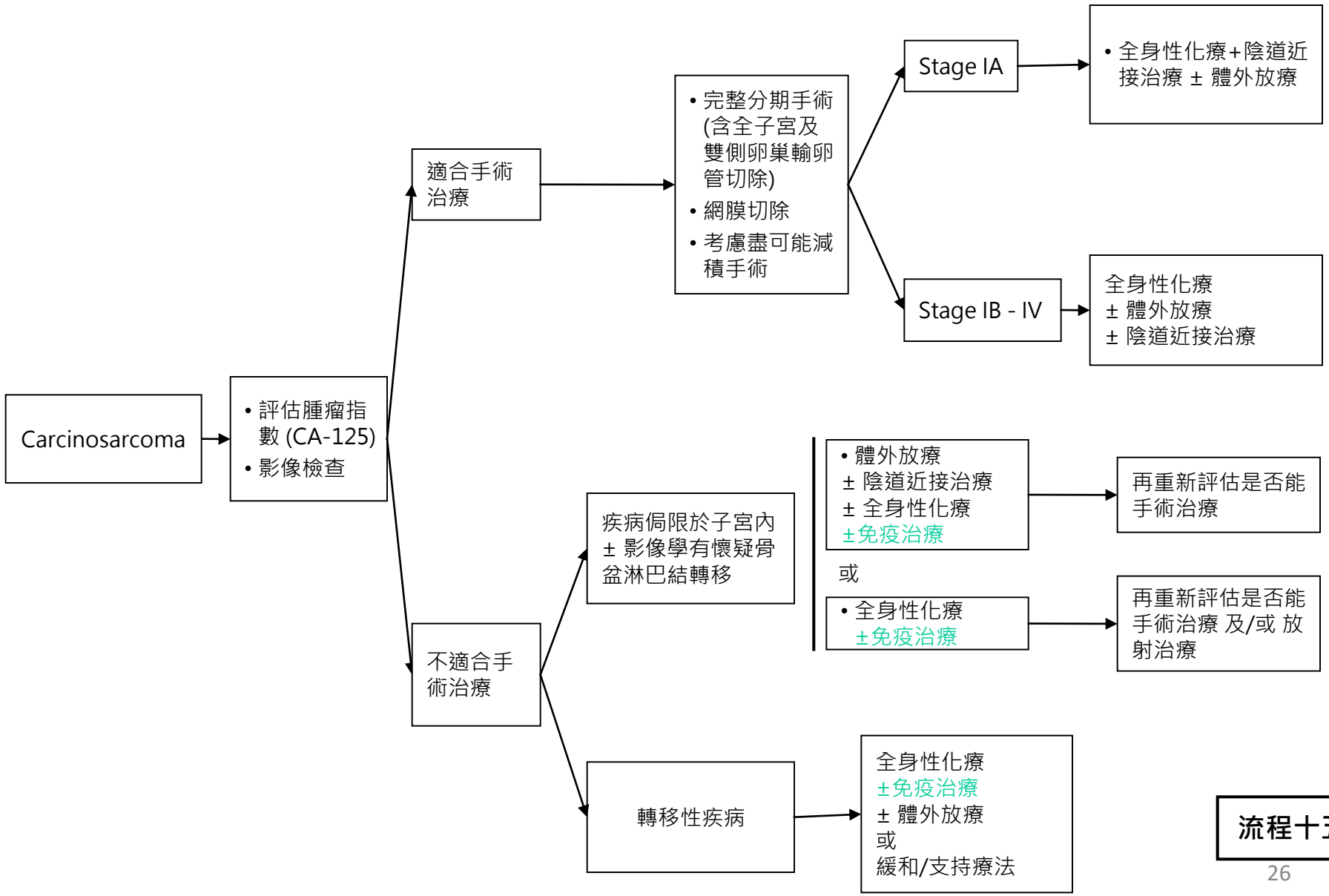
流程十三

高雄榮總婦癌團隊　子宮內膜癌臨床治療指引



流程十四

高雄榮總婦癌團隊　子宮內膜癌臨床治療指引



流程十五

子宮內膜癌 化療藥物指引

全身性治療（Systemic Therapy）
Taxol (payself) (175 mg/m^2) + Cisplatin (50 mg/m2) if CCr > 60ml/min (43) Taxol (payself) (175 mg/m^2) + Carboplatin (AUC=5) if CCr < 60ml/min (43) (針對stage III/IV，除卻carcinosarcoma，建議再加上Pembrolizumab）(44)
PEI (Epirubicine 為optional) (8) Epirubicine (50mg/m^2) +Cisplatin(50mg/m^2) + Ifosfamide+mesna (4gm/m^2) if CCr > 60ml/min Epirubicine (50mg/m^2) + Carboplatin(AUC=5) + Ifosfamide+mesna (4gm/m^2) if CCr < 60ml/min
Topotecan(0.75mg/m^2) + Cisplatin (50mg/m^2), if CCr > 60ml/min (30,31) Topotecan(0.75mg/m^2) + Carboplatin (AUC=5), if CCr < 60ml/min
Lipodoxorubicin (payself) (30 mg/m^2) + Cisplatin(50mg/m^2), if CCr > 60ml/min (32,33) Lipodoxorubicin (payself) (30 mg/m^2) + 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)
針對stage III/IV or 復發的serous carcinoma 或是 carcinosarcoma with HER2 positive Carboplatin (AUC=5) + Paclitaxel (175 mg/m2)+ Trastuzumab (8mg/kg in 1st cycle, then 6mg/kg since 2nd cycle) (38)
針對有 (MSI-H / MMR proteins deficiency) 的病患 Pembrolizumab (Keytruda) (200mg), Every 21 days (35, 39, 40)
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)

子宮內膜癌 荷爾蒙藥物指引

可選用配方
Medroxyprogesterone acetate (Farlutal) 500mg 1# QD (27)
Megestrol 160 mg/QD
Levonorgestrel IUD (生育保留或是特定臨床情境考量)
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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