高雄榮民總醫院
子宮頸癌診療原則

2024年 第一版 2024/05/23

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 ™ Cervical Cancer (Version 3.2024 — May. 6, 2024)[1]
  - 婦癌研究委員會(2011)，子宮頸癌篩檢臨床指引與子宮頸癌臨床指引：國家衛生研究院[2-3]
  - 其他相關子宮頸癌臨床指引[4-10]

會議討論

上次會議：2023/06/14

本共識與上一版的差異

1.圖一：FIGO分期IA1治療方式選項。(p.9) 2.圖二：切片結果無後續建議處置方式。(p.10) 3.圖四：前導性化療後，考慮期間「全子宮切除」。(p.12) 4.圖七:救援性治療內容無近接治療選項。(p.15) 5.藥物指引:無列出新藥物。(p.15)	1.圖一：FIGO分期IA1增加「修正式根除性子宮切除手術+骨盆淋巴結摘除術（錐狀切片具邊緣侵犯）」、FIGO分期IB1/IB2或IIA1增加「±主動脈旁淋巴結取樣」。(p.9) 2.圖二：切片陽性後行「全身性化療±個人化放射線治療」，切片陰性後行「體外放射治療，同時合併化療及骨盆**併**主動脈旁淋巴結放射治療@+近接治療(brachytherapy)」。(p.10) 3.圖四：更改為「根除性全子宮切除」。(p.12) 4.圖七：增加救援性治療內容:「個人化體外放射線治療併化學治療±近接治療」。(p.15) 5.藥物指引:新增Enhertu(Fam-trastuzumab deruxtecan-nxki)及其reference。 (p.19、p.28)

2018 FIGO Staging

Box 1

Stage I:

The carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded).

- **IA** Invasive carcinoma that can be diagnosed only by microscopy with maximum depth of invasion ≤5 mm[a]
  - **IA1** Measured stromal invasion ≤3 mm in depth
  - **IA2** Measured stromal invasion >3 mm and ≤5 mm in depth
- **IB** Invasive carcinoma with measured deepest invasion >5 mm (greater than stage IA); lesion limited to the cervix uteri with size measured by maximum tumor diameter[b]
  - **IB1** Invasive carcinoma >5 mm depth of stromal invasion and ≤2 cm in greatest dimension
  - **IB2** Invasive carcinoma >2 cm and ≤4 cm in greatest dimension
  - **IB3** Invasive carcinoma >4 cm in greatest dimension

Stage II:

The cervical carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall

- **IIA** Involvement limited to the upper two-thirds of the vagina without parametrial invasion
  - **IIA1** Invasive carcinoma ≤4 cm in greatest dimension
  - **IIA2** Invasive carcinoma >4 cm in greatest dimension
- **IIB** With parametrial invasion but not up to the pelvic wall

Stage III:

The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes

- **IIIA** Carcinoma involves lower third of the vagina, with no extension to the pelvic wall
- **IIIB** Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)
- **IIIC** Involvement of pelvic and/or paraaortic lymph nodes **(including micrometastases)**[c], irrespective of tumor size and extent (with r and p notations).[d]
  - **IIIC1** Pelvic lymph node metastasis only
  - **IIIC2** Paraaortic lymph node metastasis

Stage IV:

The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to stage IV

- **IVA** Spread of the growth to adjacent organs
- **IVB** Spread to distant organs

- [a]Imaging and pathology can be used, when available, to supplement clinical findings with respect to tumor size and extent, in all stages. **Pathological findings supercede imaging and clinical findings.**
- [b]The involvement of vascular/lymphatic spaces should not change the staging. The lateral extent of the lesion is no longer considered.
- [c]Isolated tumor cells do not change the stage but their presence should be recorded
- [d]Adding notation of r (imaging) and p (pathology), to indicate the findings that are used to allocate the case to stage IIIC. For example, if imaging indicates pelvic lymph node metastasis, the stage allocation would be Stage IIIC1r; if confirmed by pathological findings, it would be Stage IIIC1p. The type of imaging modality or pathology technique used should always be documented. When in doubt, the lower staging should be assigned.

AJCC Cancer Staging System – Cervical Cancer Version 9

T Category	FIGO Stage	T Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded).
T1a	IA	Invasive carcinoma that can be diagnosed only by microscopy with maximum depth of invasion ≤5 mm
T1a1	IA1	Measured stromal invasion ≤3 mm in depth
T1a2	IA2	Measured stromal invasion >3 mm and ≤5 mm in depth
T1b	IB	Invasive carcinoma with measured deepest invasion >5 mm (greater than stage IA); lesion limited to the cervix uteri with size measured by maximum tumor diameter Note: The involvement of vascular/lymphatic spaces should not change the staging. The lateral extent of the lesion is no longer considered.
T1b1	IB1	Invasive carcinoma >5 mm depth of stromal invasion and ≤2 cm in greatest dimension
T1b2	IB2	Invasive carcinoma >2 cm and ≤4 cm in greatest dimension
T1b3	IB3	Invasive carcinoma >4 cm in greatest dimension
T2	II	Carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall
T2a	IIA	Involvement limited to the upper two-thirds of the vagina without parametrial invasion
T2a1	IIA1	Invasive carcinoma ≤4 cm in greatest dimension
T2a2	IIA2	Invasive carcinoma >4 cm in greatest dimension
T2b	IIB	With parametrial invasion but not up to the pelvic wall
T3	III	Carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney Note: The pelvic wall is defined as the muscle, fascia, neurovascular structures, and skeletal portions of the bony pelvis. Cases with no cancer-free space between the tumor and pelvic wall by rectal examination are FIGO III.
T3a	IIIA	Carcinoma involves lower third of the vagina, with no extension to the pelvic wall
T3b	IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney (unless known to be due to another cause)
T4	IVA	Carcinoma has involved (biopsy-proven) the mucosa of the bladder or rectum, or has spread to adjacent organs. (Bullous edema, as such, does not permit a case to be assigned to stage IVA.)

AJCC Cancer Staging System – Cervical Cancer Version 9

N Category	FIGO Stage	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) ≤0.2 mm, or single cells or clusters of cells ≤200 cells in a single lymph node cross section
N1	IIIC1	Regional lymph node metastasis to pelvic lymph nodes only
N1mi	IIIC1	Regional lymph node metastasis (>0.2 mm but ≤2.0 mm in diameter) to pelvic lymph nodes
N1a	IIIC1	Regional lymph node metastasis (>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 (>0.2 mm but ≤2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2a	IIIC2	Regional lymph node metastasis (>2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes

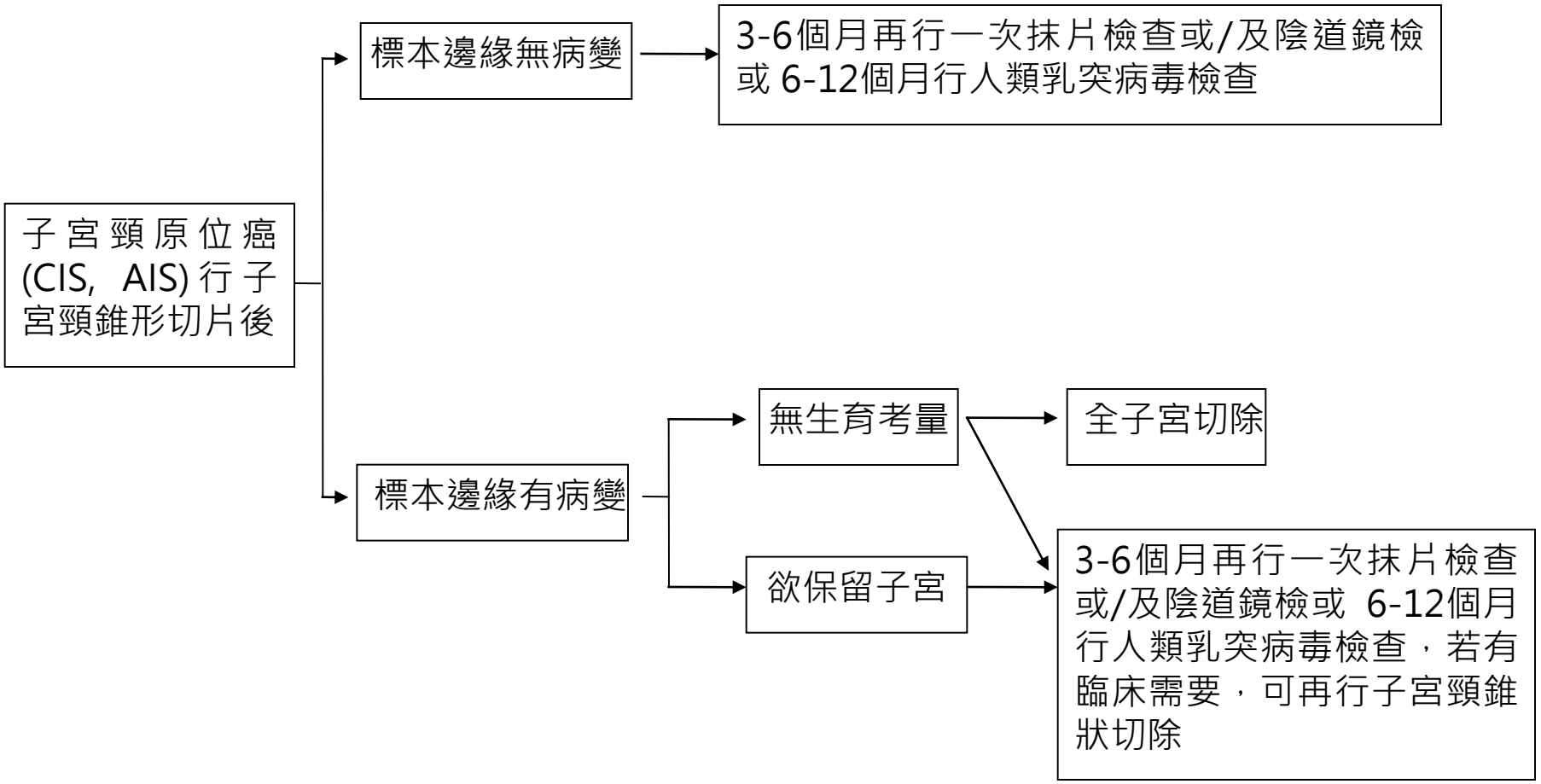
Note: Suffix (f) is added to the N category when metastasis is identified only by FNA or core biopsy. Suffix (sn) is added to the N category when metastasis is identified only by sentinel lymph node biopsy.

M Category	FIGO Stage	M Criteria
M0		No distant metastasis
cM1	IVB	Distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone) (excludes metastasis to pelvic or para-aortic lymph nodes, or vagina)
pM1	IVB	Microscopic confirmation of distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone) (excludes metastasis to pelvic or para-aortic lymph nodes, or vagina)

AJCC Cancer Staging System – Cervical Cancer Version 9

When T is…	And N is…	And M is…	Then the stage group is…
T1	N0	M0	I
T1a	N0	M0	IA
T1a1	N0	M0	IA1
T1a2	N0	M0	IA2
T1b	N0	M0	IB
T1b1	N0	M0	IB1
T1b2	N0	M0	IB2
T1b3	N0	M0	IB3
T2	N0	M0	II
T2a	N0	M0	IIA
T2a1	N0	M0	IIA1
T2a2	N0	M0	IIA2
T2b	N0	M0	IIB
T3	N0	M0	III
T3a	N0	M0	IIIA
T3b	N0	M0	IIIB
TX, T0, T1-3	N1	M0	IIIC1
TX, T0, T1-3	N2	M0	IIIC2
T4	Any N	M0	IVA
Any T	Any N	M1	IVB

原位癌行子宮頸錐狀切片



高雄榮總婦癌團隊　子宮頸癌臨床治療指引

子宮頸癌治療流程

治療前檢查：1.病史及理學檢查*；2.全血球計數；3.子宮頸切片之組織病理檢查；4.子宮頸錐狀手術+子宮頸管搔刮術(當子宮頸切片之組織病理檢查結果為微侵襲癌者)；5.胸部X光*；6.分期為IA者，可考慮骨盆核磁共振；分期高於IA者，安排腹部或骨盆電腦斷層*或核磁共振 *(52)；7.常規生化檢驗; 8. 血清腫瘤標記檢驗**(鱗狀細胞癌者:SCC、CEA；腺癌者:CEA、CA–125、CA-199)**

選擇性檢查：#分期為IB2或以上者，膀胱或直腸鏡檢；#葡萄糖正子攝影　　*與期別相關之主要檢查(必要項目)

輔助治療

FIGO分期 IA1

1. 筋膜外子宮切除（無生育考量或無錐形切片呈現切緣侵犯或無LVSI）若有LVSI可比照IA2處理
2. 修正式根除性子宮切除手術+骨盆淋巴結摘除術（錐狀切片具邊緣侵犯）
3. 欲保留生育能力或不適合手術者，於子宮頸錐狀手術後，密集追觀察 若有LVSI可比照IA2行根治性子宮頸切除術及骨盆淋巴結摘除術

FIGO分期 IA2

1. 較小範圍根治性子宮切除術及骨盆淋巴結摘除術，或併主動脈旁淋巴結取樣(選擇性，尚無定論)觀察 (14-15)
2. 近接治療(Brachytherapy)或併骨盆放射線治療@
3. 欲保留生育能力者可行根治性子宮頸切除術及骨盆淋巴結摘除術

FIGO分期 IB1/IB2或 IIA1

1. 根治性子宮切除術 * 及骨盆淋巴結摘除術，或合併主動脈旁淋巴結取樣
2. 骨盆放射線治療及近接治療(Brachytherapy)@
3. IB1,欲保留生育能力者可行根治性子宮頸切除術及骨盆淋巴結摘除術±主動脈旁淋巴結取樣

FIGO分期 IB3或IIA2

1. 骨盆放射線治療@及近接治療@同時合併含cisplatin之治療+/-子宮切除 (ATH or RH) (16-21, level Ib)
2. 根治性子宮切除術 * 及骨盆淋巴結摘除術，合併主動脈旁淋巴結取樣
3. 術前輔助性化學治療及根治性子宮切除術及骨盆淋巴結摘除術，合併主動脈旁淋巴結取樣(22-26,46)

FIGO分期 IVA

1. 骨盆腔臟器宛除術及骨盆淋巴結摘除術，合併主動脈旁淋巴結取樣
2. 骨盆放射線治療@及近接治療@同時合併含cisplatin之治療+/-骨盆腔臟器宛除術
3. 術前輔助性化學治療及骨盆腔臟器宛除術及骨盆淋巴結摘除術，合併主動脈旁淋巴結取樣(22-26,46)

手術標本組織病理檢查（註三）

- 無淋巴結轉移，無陰道切除邊緣侵襲，無子宮旁組織侵襲 或 血管淋巴侵犯者或腫瘤大小或基質侵犯不符合Sedlis criteria → 觀察
- 血管淋巴侵犯者或腫瘤大小或基質侵犯. (見Sedlis criteria 圖十) (50) → 放射線治療@ 註一
- 淋巴結轉移或陰道切除邊緣侵襲或子宮旁組織侵襲或任一項或以上） → 放射線治療@ 註一；化學治療# (38,44) 註二；同步化放療@ 註二
- 神經內分泌細胞癌 → 見圖四

*:含神經保留式根治性子宮切除術（nerve sparing radical hysterectomy）；#:請見表一；註一：病患年紀太大或合併多重內科疾病者；註二：年輕女性考慮避免性功能障礙者或接受過放射線治療者；@: 放射治療、近接治療或同步化放療請見放射腫瘤部治療指引　9

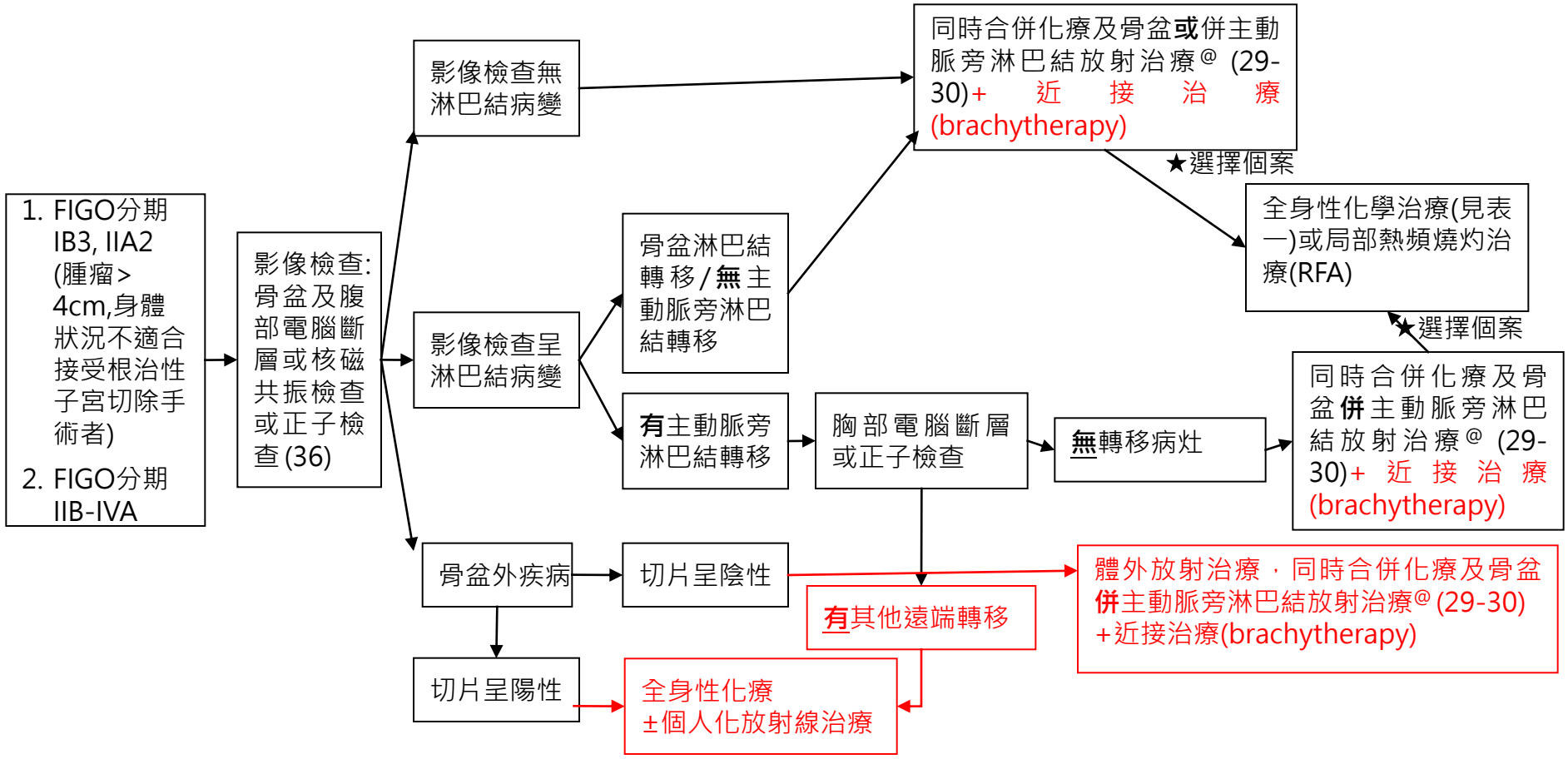
註三：於轉移性之疾病建議病理檢體做PD-L1以及MMR/MSI檢測

圖一

高雄榮總婦癌團隊　子宮頸癌臨床治療指引

FIGO分期IIB-IVA(局部晚期)子宮頸癌，或不適合施行根治性子宮切除手術之IB 、IIA治療流程

1. 放射治療包括體外放射治療及近接治療@
2. 同步化放療時使用含cisplatin 40 mg/m^2 /carboplatin 100 mg/m^2 or AUC=2 weekly x 6 courses （或配合放療療程）之化療或臨床試驗

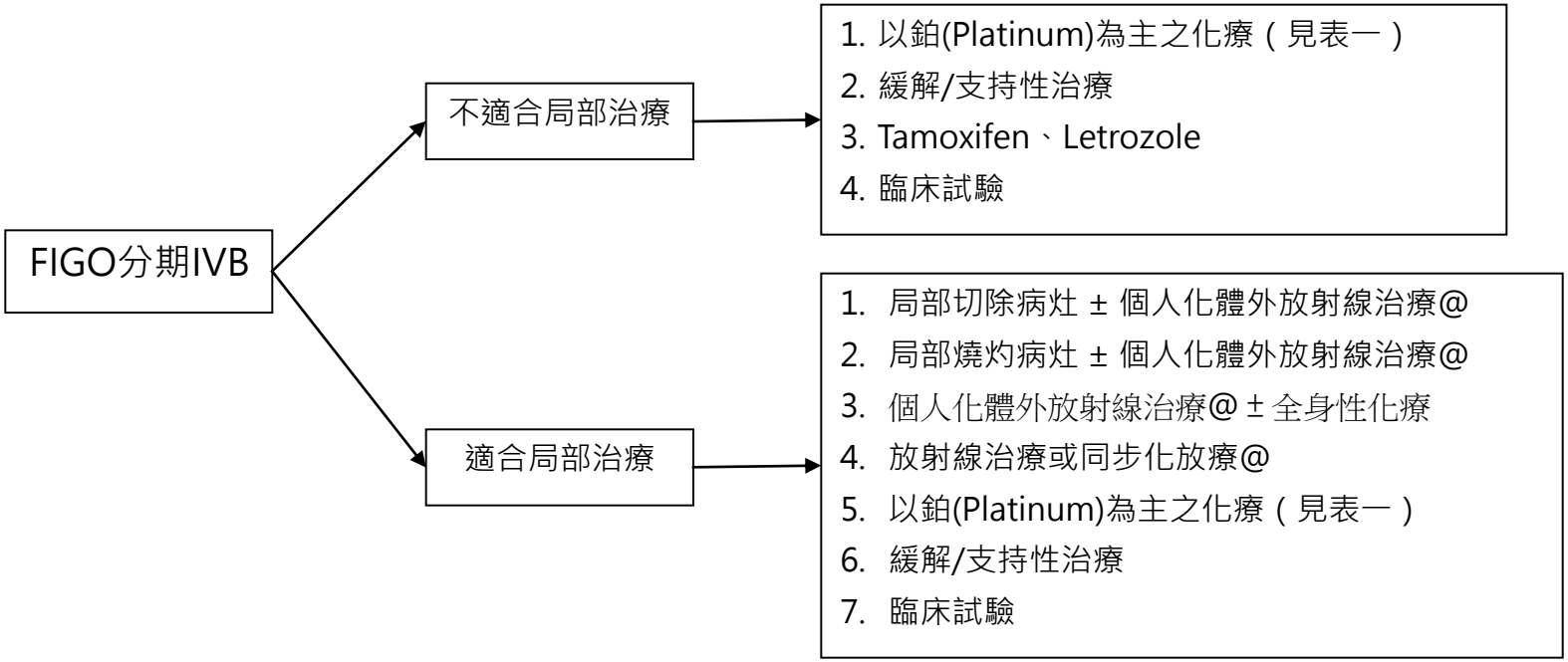


@: 放射治療或同步化放療及併主動脈旁淋巴結放射治療請見放射腫瘤部治療指引

★: 仍有residual tumor

圖二

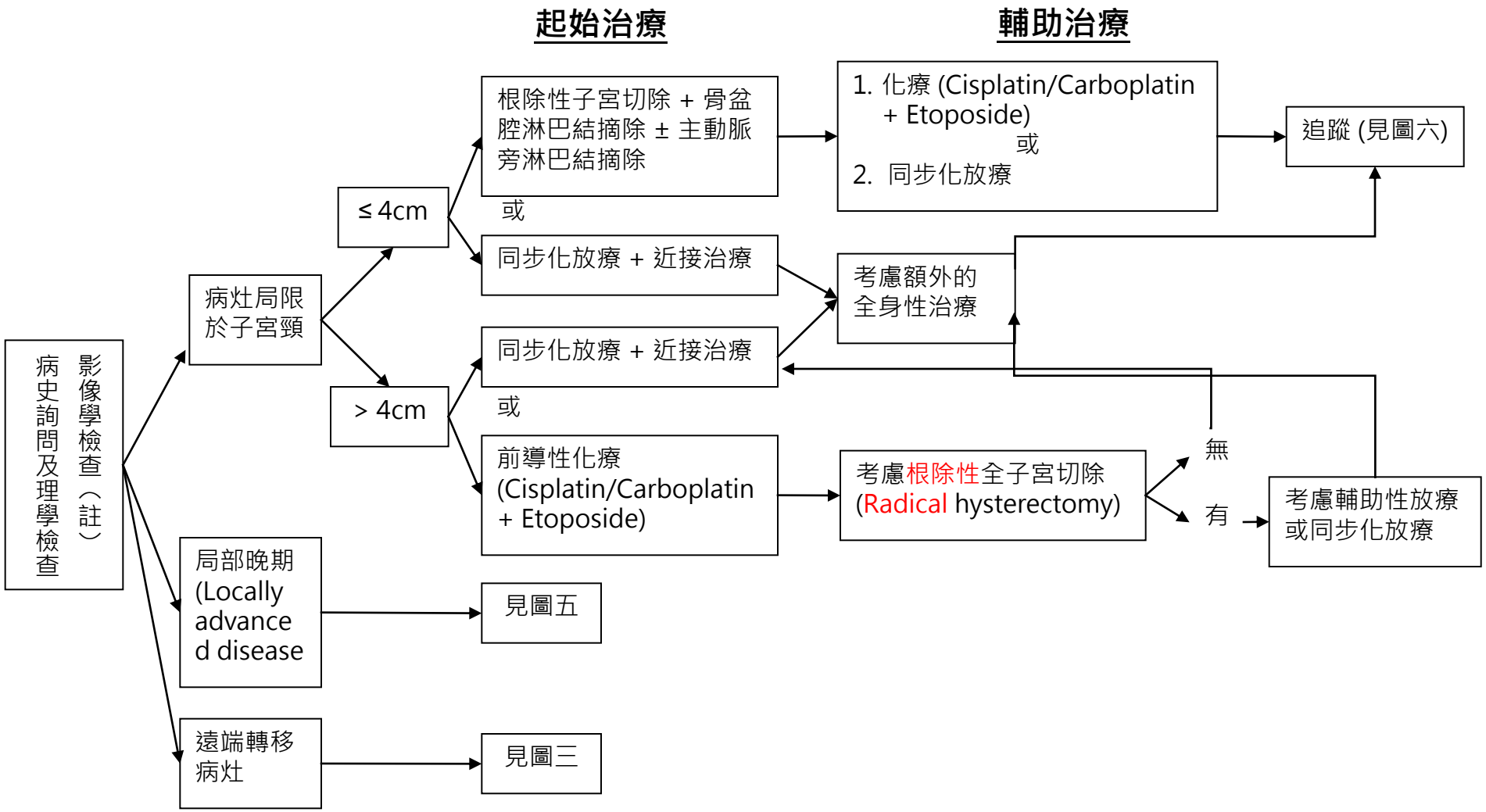
FIGO分期IVB或遠端轉移子宮頸癌治療流程



@：放射治療或同步化放療請見放射腫瘤部治療指引

圖三

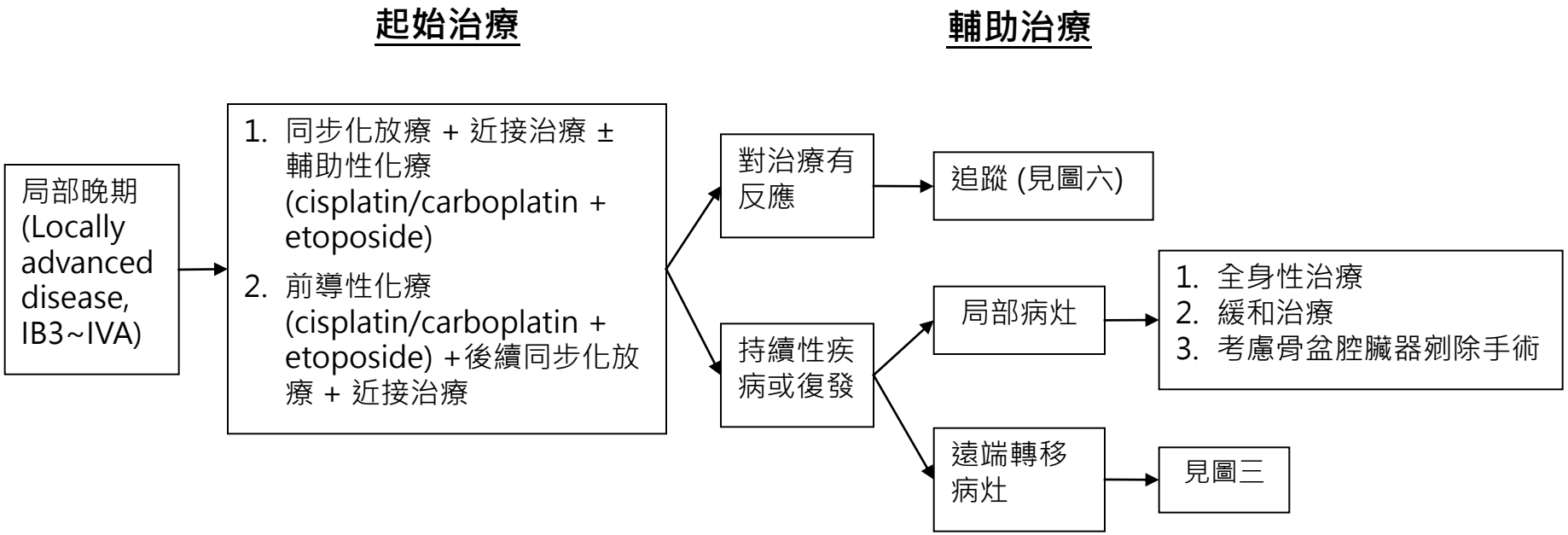
小細胞神經內分泌癌之治療流程



註：考慮加做 Neck/chest/abdomen/pelvis/groin PET/CT + brain MRI 或是 Chest/abdomen/pelvis CT + brain MRI
追蹤治療效果以及懷疑有復發時亦同

圖四

局部晚期(Locally advanced, IB3~IVA)小細胞神經內分泌癌之治療流程



圖五

子宮頸癌治療後追蹤及復發的處置

定期追蹤方法

1. 理學檢查
2. 抹片檢查：治療後兩年內每三個月一次，第三年每四~六個月一次, 第四至五年每六個月一次，以後每年一次
3. 腫瘤標記(鱗狀細胞癌者:SCC, CEA；腺癌者:CEA, CA–125, CA-199)
4. 全血(CBC)及腎功能(BUN、Cr)檢驗，有必要時可每六個月檢驗一次
5. 胸部X光檢查每年一次及電腦斷層檢查，有必要時可每年安排檢查一次

懷疑持續性
或
復發性疾病

進一步檢查

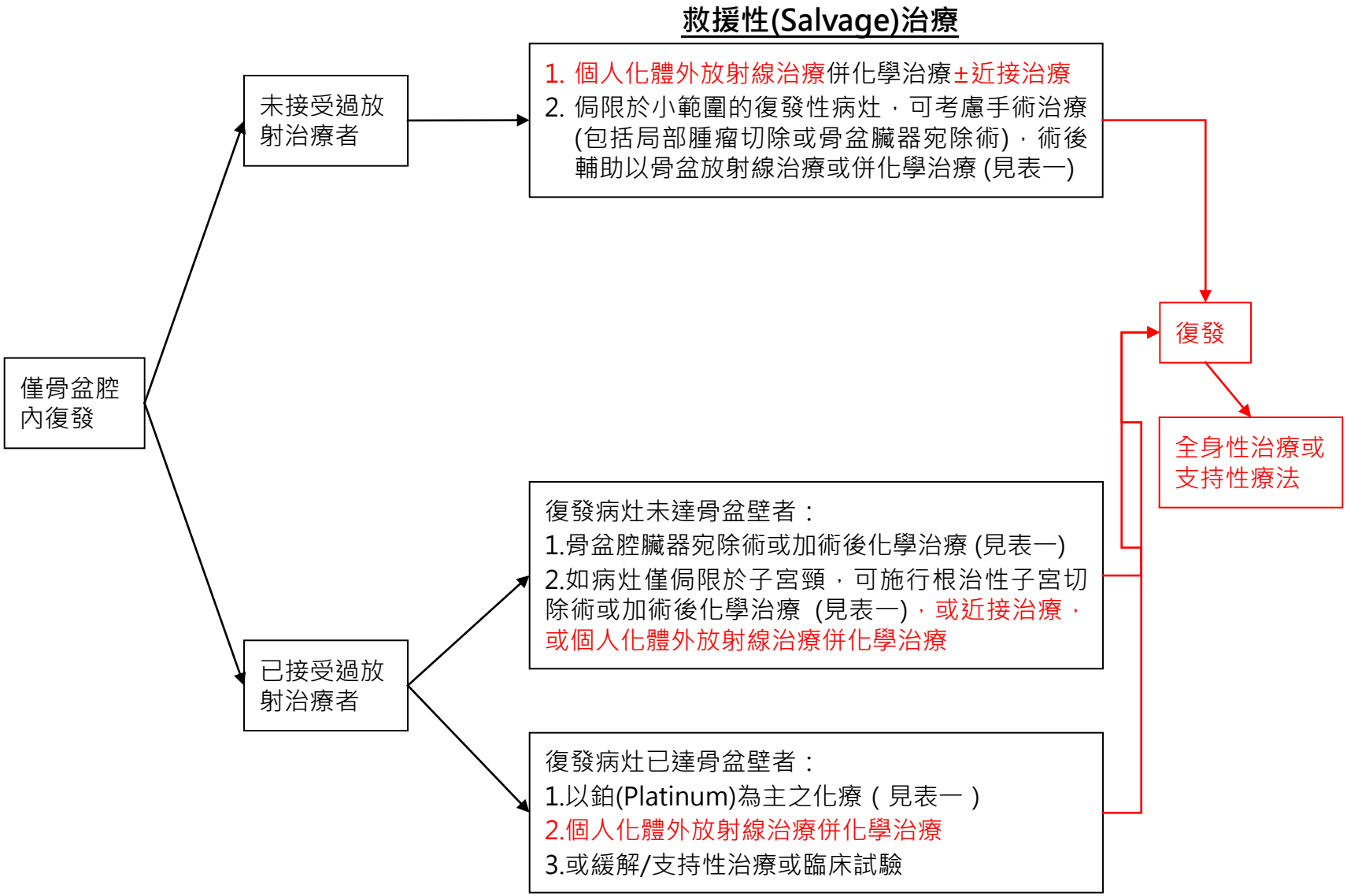
1. 骨盆及腹部電腦斷層檢查
2. 胸部X光檢查(若為陰性，仍高度懷疑胸部轉移則考慮胸部電腦斷層檢查)
3. 若有病灶，技術可行下，考慮直接切片或超音波或電腦斷層導引下切片
4. 安排正子掃描 (31-35)
5. 有必要時可以施行手術探查
6. 建議病理檢體做PD-L1以及MMR/MSI之檢驗
7. 考慮廣泛型癌症基因檢測(comprehensive genomic profiling, CGP)
8. 若無法取得病理組織，考慮檢測血漿循環腫瘤DNA（plasma ctDNA）之廣泛型癌症基因檢測 (CGP)

僅骨盆腔內復發 → 見圖七

骨盆腔外復發 → 見圖八

圖六

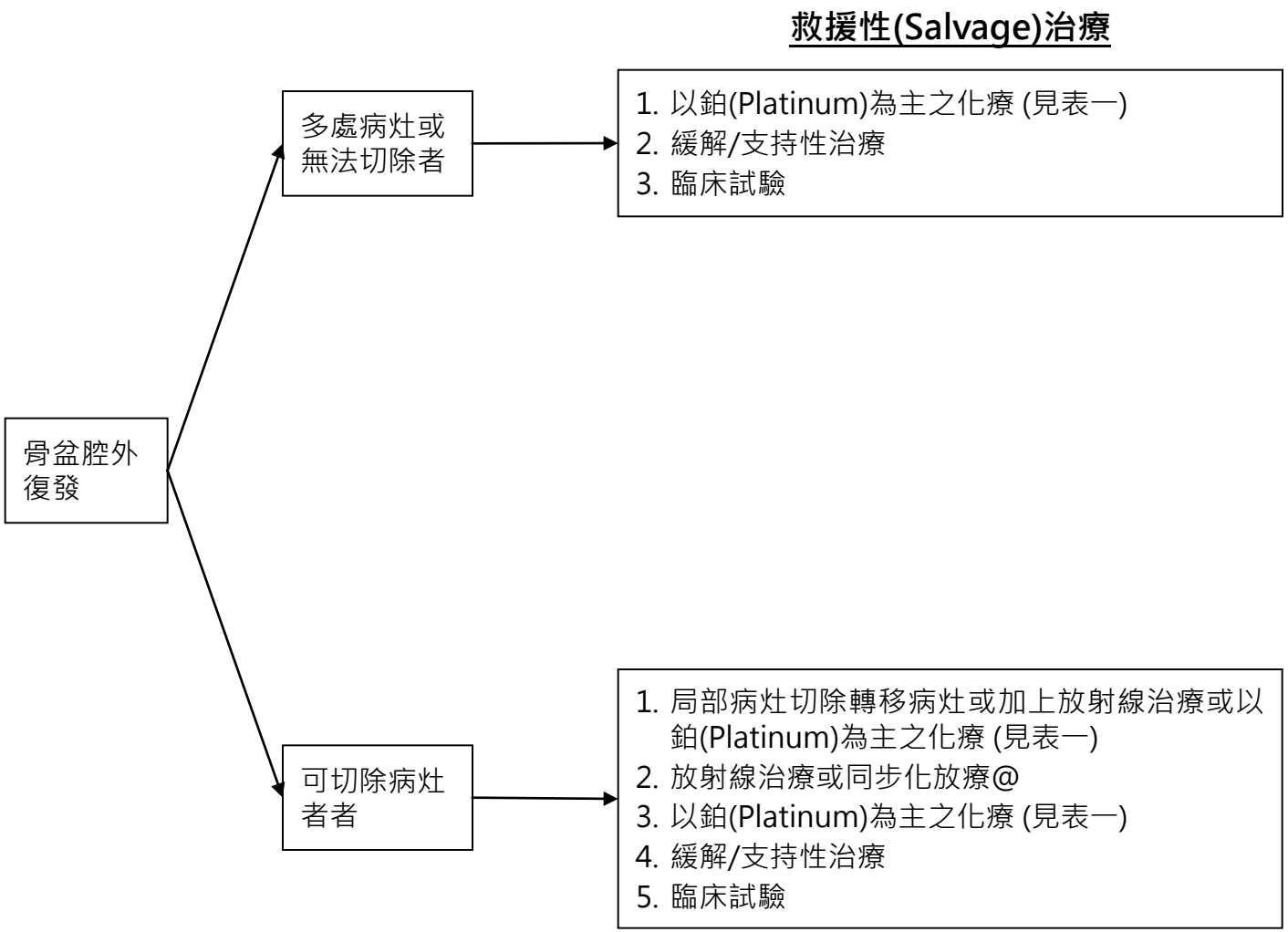
子宮頸癌治療後追蹤及復發的處置



@：放射治療或同步化放療請見放射腫瘤部治療指引

圖七

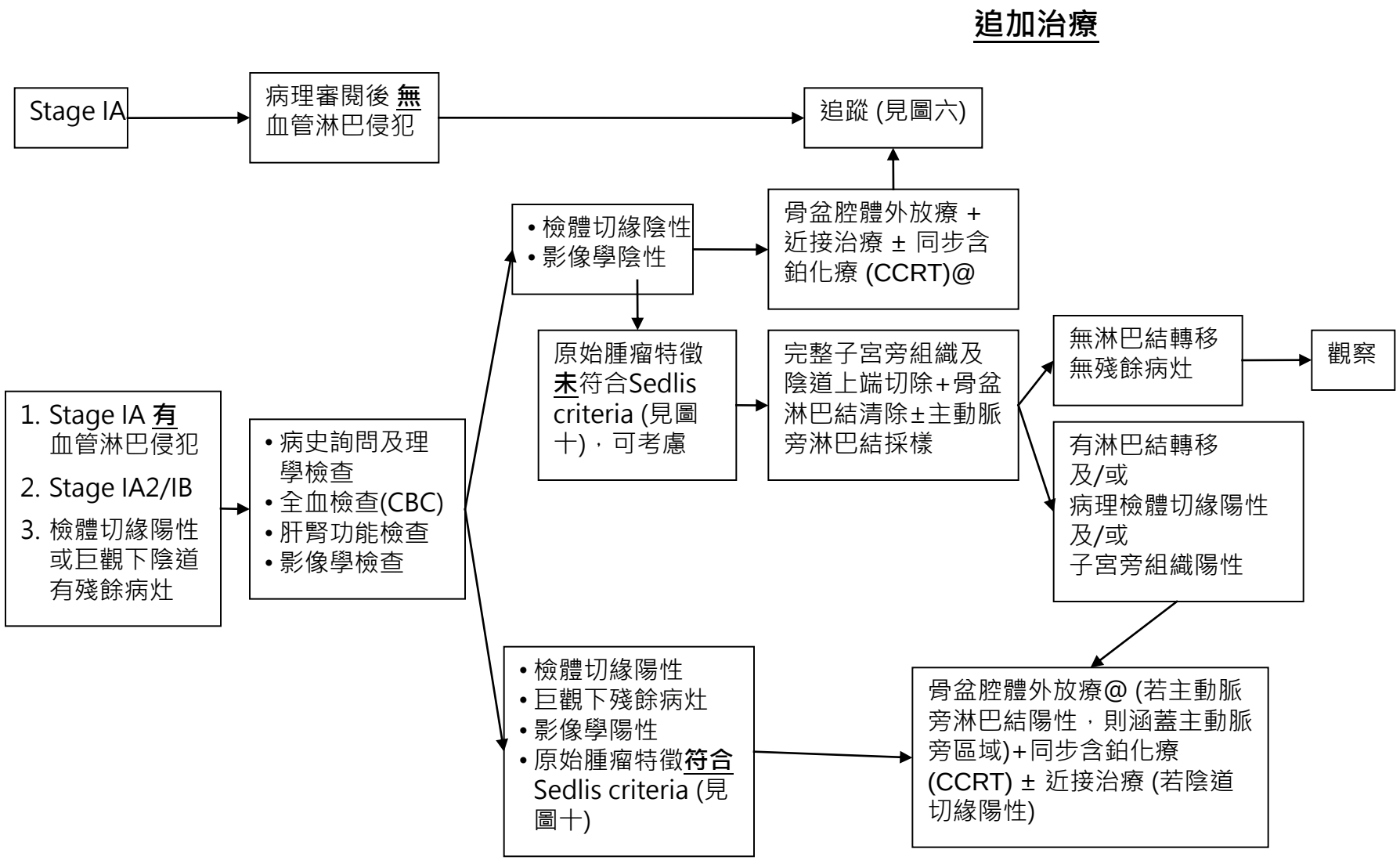
子宮頸癌治療後追蹤及復發的處置



@：放射治療或同步化放療請見放射腫瘤部治療指引

圖八

單純子宮全切除後意外發現侵襲性癌症



@: 放射治療或同步化放療請見放射腫瘤部治療指引

圖九

SEDLIS CRITERIA FOR EXTERNAL PELVIC RADIATION AFTER RADICAL HYSTERECTOMY IN NODE-NEGATIVE, MARGIN-NEGATIVE, PARAMETRIA-NEGATIVE CASES[1,2,3,4]

LVSI	Stromal Invasion	Tumor Size (cm) (Determined by clinical palpation)
+	Deep 1/3	Any
+	Middle 1/3	≥2
+	Superficial 1/3	≥5
-	Middle or Deep 1/3	≥4

LVSI: Lymphovascular space invasion

圖十

高雄榮總婦癌團隊　子宮頸癌臨床治療指引 - 化學治療或同步化學與放射治療（表一）

術前新輔助化學治療：以 platinum-based 為原則，可使用以下的選擇

1. **IP (Ifosfamide 4 gm/m² + cisplatin 50mg/m² or carboplatin AUC=5 every 21 days x 3~6 cycles)**(48,49)
2. **Irinotecan 60mg/m² + cisplatin 50mg/m² or carboplatin AUC=5 every 28 days x 3~6 cycles (optional)**(43,47)
3. **(IB2-IIB) Weekly Taxol + Carboplatin(AUC=2) (D1,D8,D15)x 9 cycles**(58)

手術後輔助化學治療：以 platinum-based 為原則，可使用以下的選擇

1. **IP (Ifosfamide 4 gm/m² + cisplatin 50mg/m² or carboplatin AUC=5 every 21 days x 6 cycles)** (38,45,49)

神經內分泌癌手術後輔助化學治療或化放療以 platinum-based 為原則可使用以下的選擇

1. **Etoposide + Platinum (Etoposide 100mg/m² + Cisplatin 50mg/m² or Carboplatin AUC =5, every 21 days x 4~6 cycles**

第IV期B，持續性疾病 (persistent disease)復發或轉移性疾病 (recurrent/metastatic disease)之全身性化學治療或免疫療法為原則，可使用以下的選擇

1. **Topotecan 0.75mg/m² x 3 days + cisplatin 50mg/m² or carboplatin AUC=5 every 21 days x 6 cycles**(GOG 179, level Ib) (42) ± Bevacizumab 7.5~15 mg/kg
2. **IP (ifosfamide 4gm/m² + cisplatin 50mg/m² or carboplatin AUC=5 every 21 days x 6 cycles)**(GOG 110, level Ib)
3. **Paclitaxel 175mg/m² + cisplatin 50mg/m² or carboplatin AUC=5 every 21 days x 6 cycles)(optional)**(GOG 169, GOG 204, level Ib) (51) ± Bevacizumab 7.5~15 mg/kg (GOG 240) (55)

4.Pembrolizumab + Paclitaxel 175mg/m² + cisplatin 50mg/m² or carboplatin AUC=5 every 21 days x 6 cycles)(optional) ± Bevacizumab 7.5~15 mg/kg for PD-L1 (+) tumors (Keynote-826) (65)

5.Irinotecan/platinum (Irinotecan 60mg/m² + cisplatin 50mg/m² or carboplatin AUC=5 every 28 days x 6 cycles) (optional) (43,47)

6.Paclitaxel 175mg/m² (D1)+ topotecan 0.75mg/m² (D1-3) ± Bevacizumab 7.5~15 mg/kg(D1) every 21~28 days (63)

7.Tamoxifen 10mg QD (61,62)

8.Keytruda(Pembrolizumab) for PD-L1(+) or MSI-H/dMMR tumors ((59, 60, 64 (KEYNOTE-028,158))

9.Nivolumab for PD-L1 (+) tumors (66)

10.Irinotecan 125mg/ m² (D1, D8, D15, D22 then rest for D29 and D36, every 6 weeks)

11.Clinical trials

12.Enhertu 5.4mg/kg Q21D for HER2 positive tumors (IHC 3+ or 2+) (68)

同步化放療時使用含cisplatin 40 mg/m² /carboplatin 100 mg/m² or AUC=2 weekly x6 cycles 之化療或臨床試驗藥物(29)

1. CCRT – Cisplatin (40mg/m2)
2. CCRT – Carboplatin (100mg/m2) or AUC =2
3. CCRT – Weekly cisplatin (40mg/m2) + gemcitabine (120mg/m2)
4. P (Carboplatin, AUC =5) C (Cyclophosphamide, 500mg/m2) + VP-16 (100mg/m2) 【CCR <60ml/min】
5. P (Cisplatin, 50mg/m2) C + VP-16 (100mg/m2) 【CCR >60ml/min】
6. **1st Line**: I (Ifosfamide) + Mesna (4gm/m2)) + P (Carboplatin, AUC =5) 【CCR <60ml/min】
7. **1st Line**: IP (Cisplatin, 50mg/m2) 【CCR>60ml/min】
8. **2nd Line**: Taxol (175 mg/m2, palself)(D1) + Topotecan (0.75mg/m2)(D1-3)
9. **2nd Line:** Irinotecan (Payself) (60mg/m2) + Carboplatin (AUC =5) (D1)
10. **2nd Line:** Irinotecan (Payself) (60mg/m2) + Cisplatin (50mg/m2) (D1)
11. **2nd Line:** Irinotecan (Payself) (60mg/m2) (D8 or D15)

12. **2nd Line**: Taxol (Payself) (175mg/m2) + Carboplatin (AUC =5) 【CCR<60ml/min】
13. **2nd Line**: Taxol (Payself) (175mg/m2) + Cisplatin (50mg/m2) 【CCR>60ml/min】
14. **2nd Line**: Topotecan (0.75mg/m2) + Carboplatin (AUC=5) 【CCR <60ml/min】
15. **2nd Line**: Topotecan (0.75mg/m2) + Cisplatin (50mg/m2) 【CCR >60ml/min】
16. Weekly Taxol (80mg/m2) + Cisplatin (20mg/m2) (D1 or D8 or D15)
17. Weekly Taxol (80mg/m2) + Carboplatin (AUC =2) (D1 or D8 or D15)
18. Avastin (Payself) (7.5~15mg/kg)
19. Tamoxifen 10mg QD
20. Pembrolizumab (Keytruda)
21. Nivolumab
22. Irinotecan 125mg/ m^2 (D1, D8, D15, D22 then rest for D29 and D36, every 6 weeks)
23. Enhertu 5.4mg/kg Q21D for HER2 positive tumors (IHC 3+ or 2+)

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