高 雄 榮 民 總 醫 院
子宮頸癌診療原則

2020年 第一版 2020/12/08

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 (V.1 2021)[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：2019/10/24

本共識與上一版的差異

上一版	新版
1. 小細胞神經內分泌癌與其他細胞型別並無分開制定治療流程。 2. 針對小細胞神經內分泌癌的現有線上化療處方為 Etoposide+ cyclophosphamide+ cisplatin/carboplatin 3. FIGO stage IB3 & IIA2 治療流程中(圖一)的『根除性子宮切除及骨盆腔淋巴結摘除術』治療選項原為第一順位。	1. 將小細胞神經內分泌癌的治療流程獨立出來，其中包含在前導性化療後可考慮interval hysterectomy。(圖四、五) (p.12, 13) 2. 新增針對小細胞神經內分泌癌的化療處方 (Cisplatin/Carboplatin + Etoposide) (p.17)。 3. FIGO stage IB3 & IIA2 治療流程中(圖一)的『根除性子宮切除及骨盆腔淋巴結摘除術』治療選項，改為第二順位 (p.9)。 4. 參考NCCN guideline將stage IVB之治療方式稍作修改 (p.11)。 5. 更正FIGO stage IA1~2、IB1~3、IIA1~2內各界定範圍的等號放置位置(p.4)。 6. 更新AJCC stage 至 “9th Version” (p.5,6,7)

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

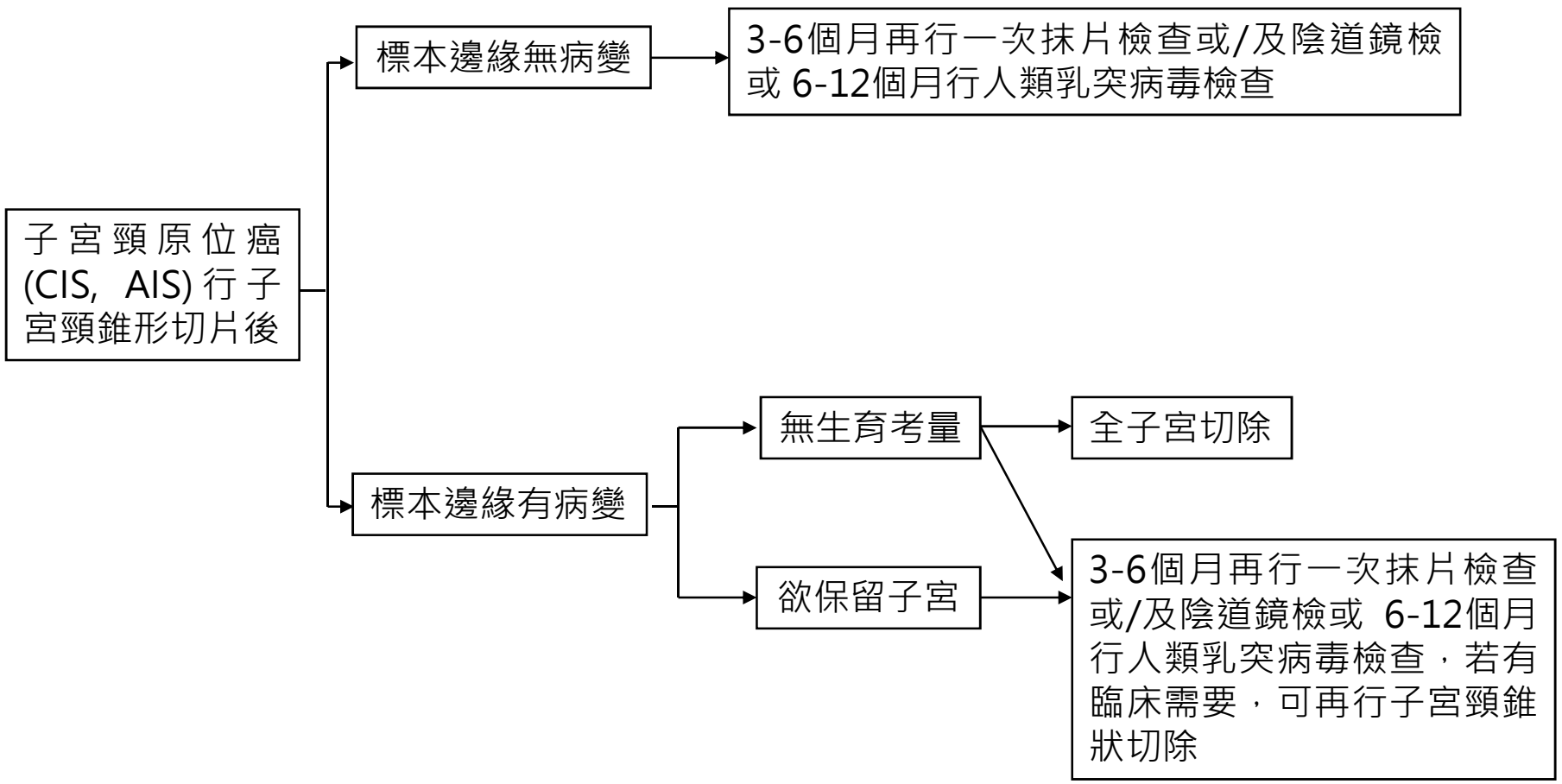
Note: Suffix (f) is added to the N category when metastasis is identified only by FNA or core biopsy. Suffix (sn) is added to the N category when metastasis is identified only by sentinel lymph node biopsy.

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

高雄榮總婦癌團隊　子宮頸原位癌臨床治療指引

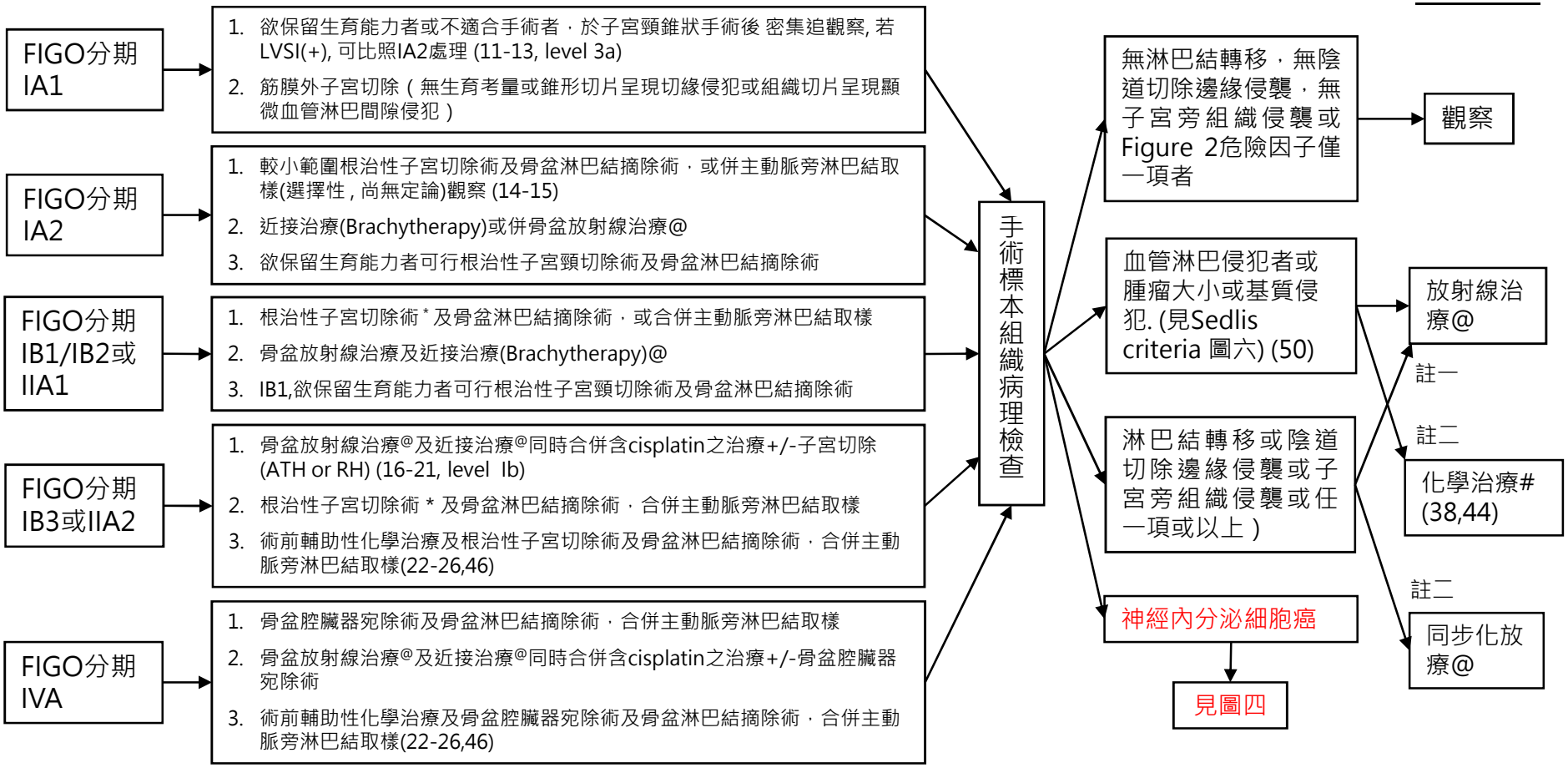


高雄榮總婦癌團隊　子宮頸癌臨床治療指引

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)



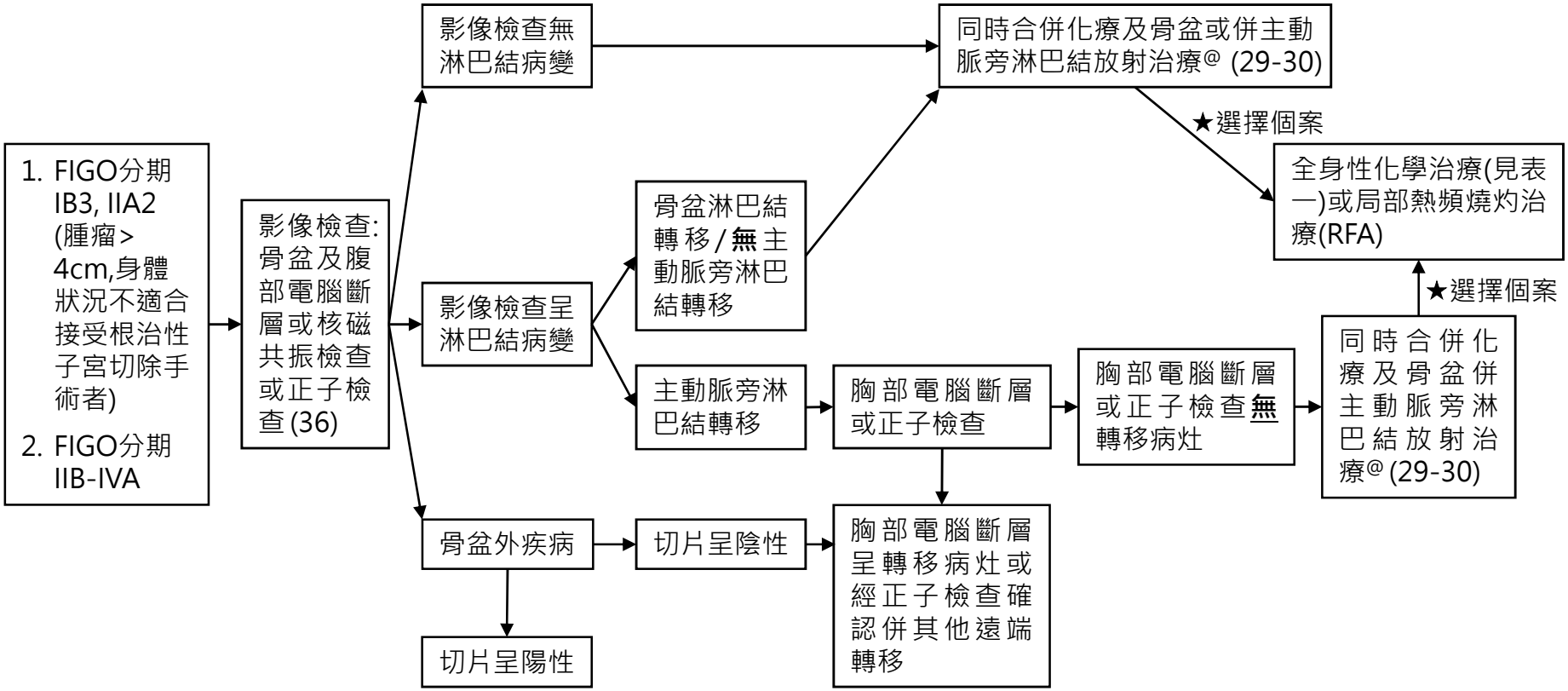
圖一

*: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

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

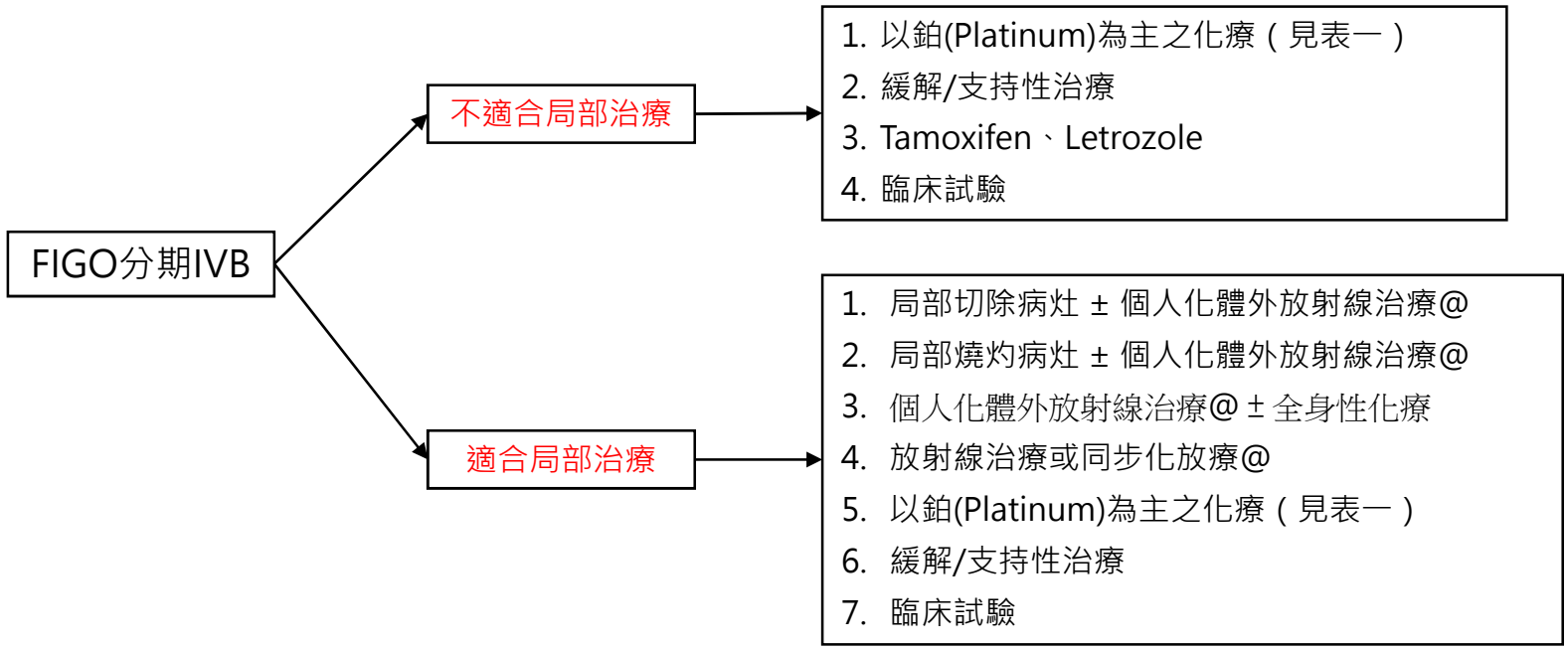


@: 放射治療或同步化放療及併主動脈旁淋巴結放射治療請見放射腫瘤部治療指引

★: 仍有residual tumor

圖二

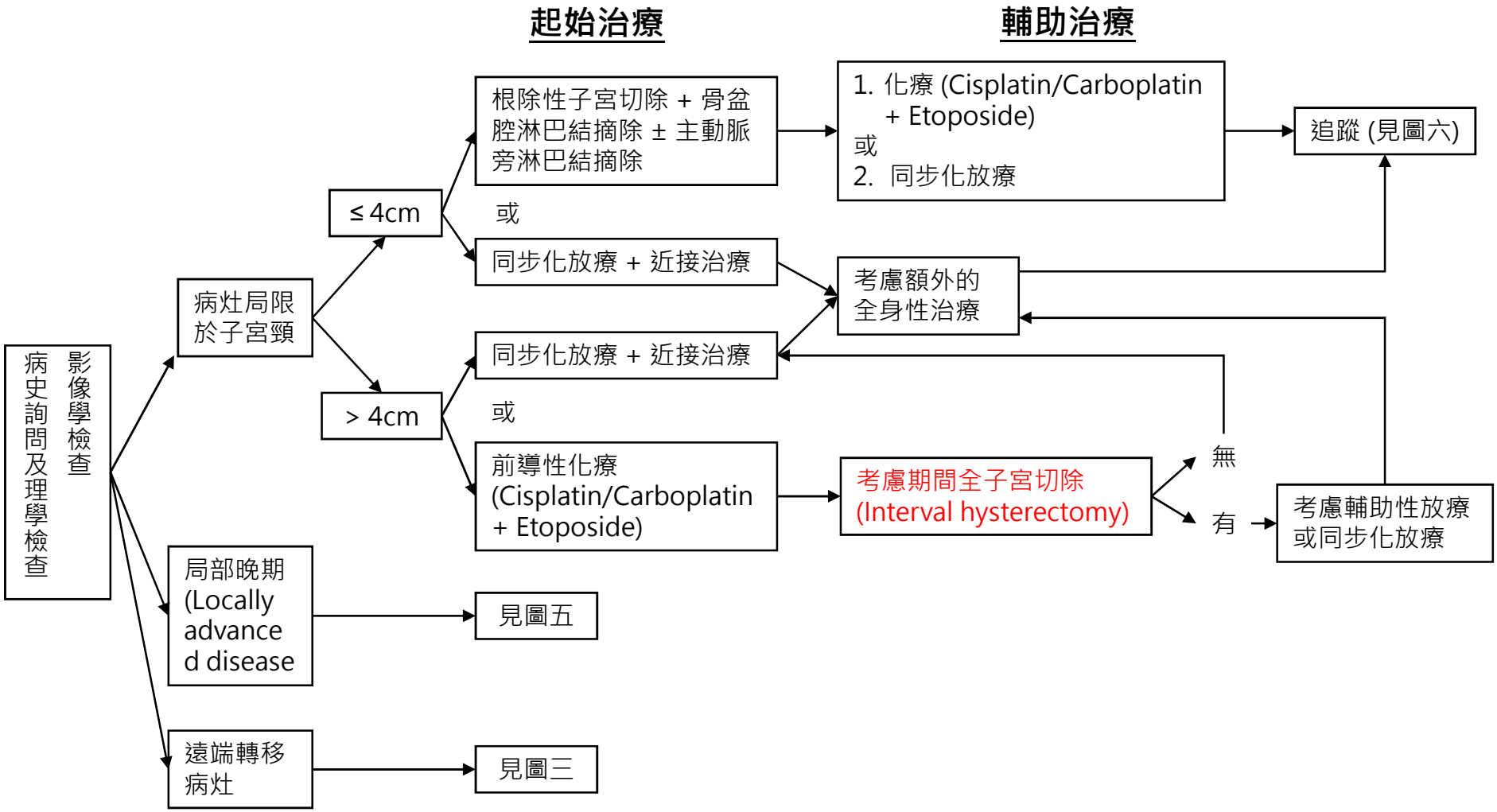
FIGO分期IVB或遠端轉移子宮頸癌治療流程



@：放射治療或同步化放療請見放射腫瘤部治療指引

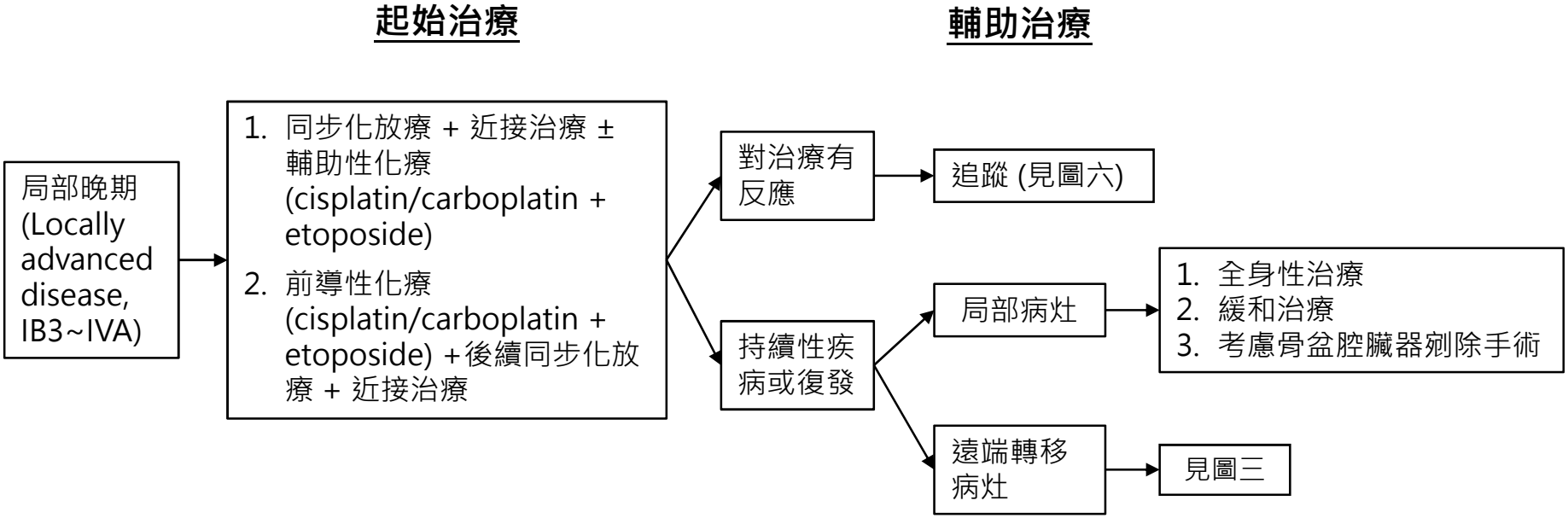
圖三

小細胞神經內分泌癌之治療流程



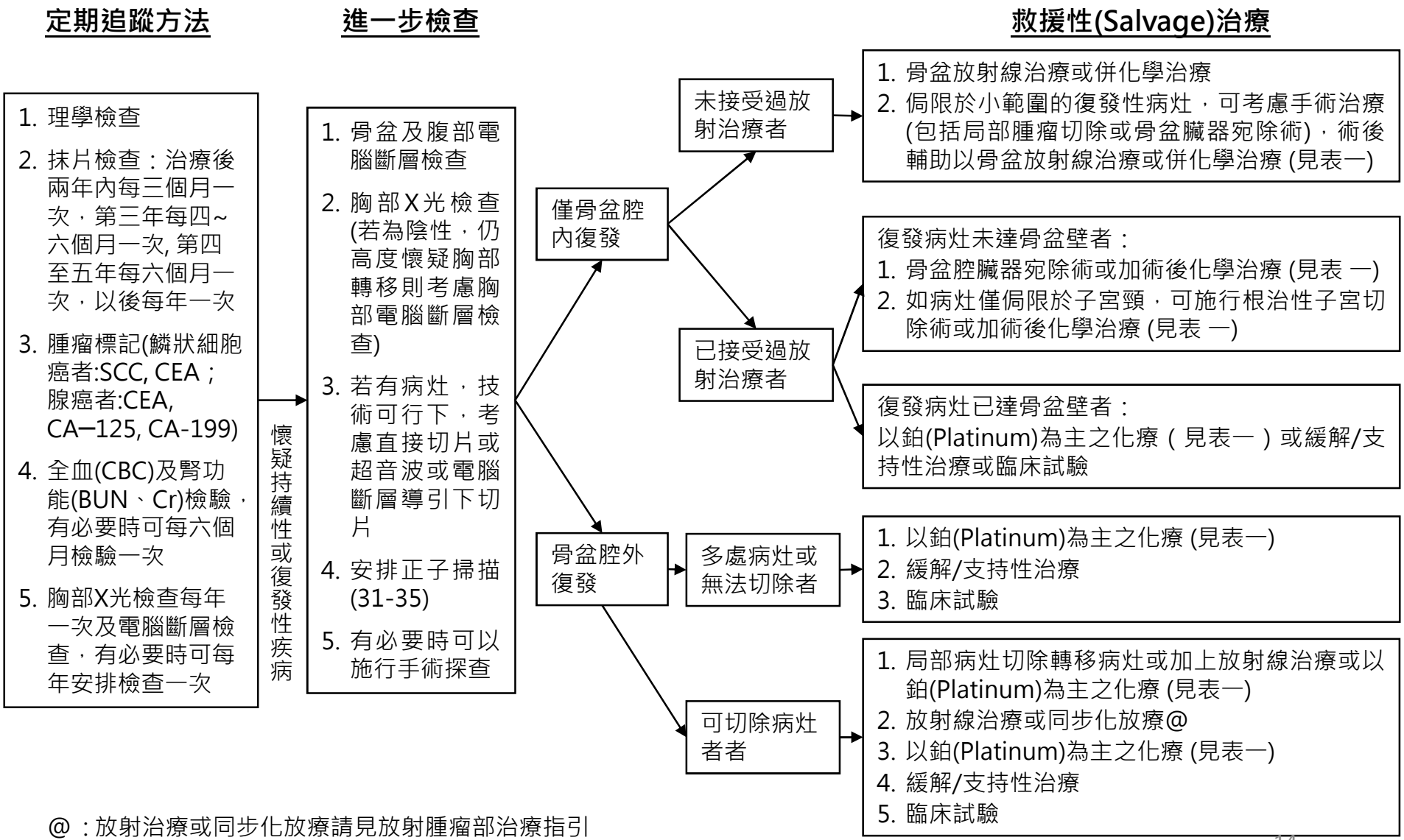
圖四

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



圖五

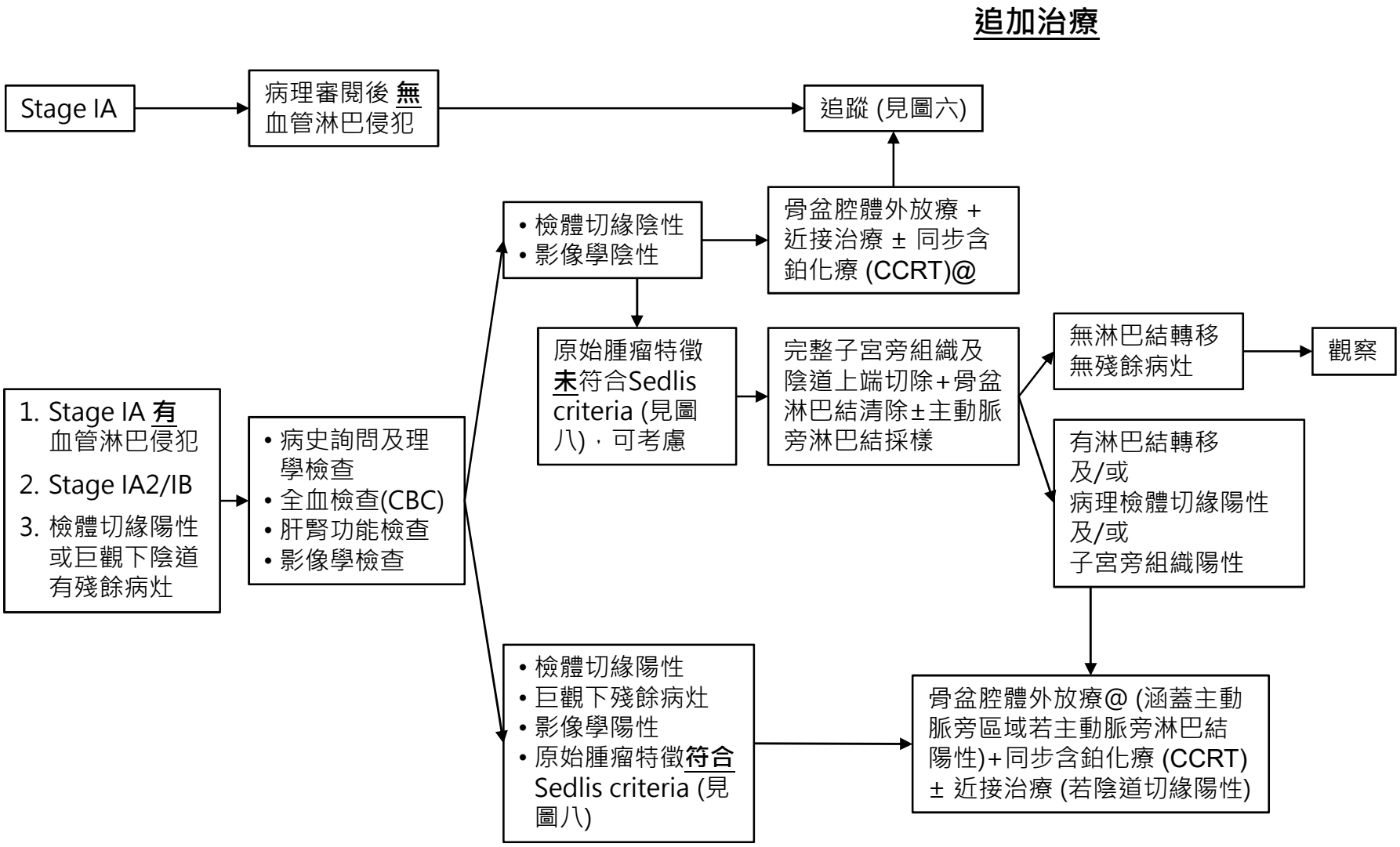
子宮頸癌治療後追蹤及復發的處置



@：放射治療或同步化放療請見放射腫瘤部治療指引

圖六

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

圖七

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

圖八

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

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)
4. **Clinical trials**

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)
2. **Clinical trials**

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. **Irinotecan/platinum (Irinotecan 60mg/m2+cisplatin 50mg/m2 or carboplatin AUC=5 every 28 days x 6 cycles) (optional)** (43,47)
5. **Paclitaxel 175mg/m2(D1)+ topotecan 0.75mg/m2(D1-3) ±Bevacizumab 7.5~15 mg/kg(D1) every 21~28 days** (63)
6. **Tamoxifen 10mg QD** (61,62)
7. **Keytruda(Pembrolizumab) for PD-L1(+) or MSI-H/dMMR tumor** ((59, 60, 64 (KEYNOTE-028,158))
8. **Clinical trials**

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

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

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)

   2nd Line: Irinotecan (Payself) (60mg/m2) + Cisplatin (50mg/m2) (D1)

   2nd Line: Irinotecan (Payself) (60mg/m2) (D8 or D15)

10. **2nd Line**: Taxol (Payself) (175mg/m2) + Carboplatin (AUC =5)
    【CCR<60ml/min】
11. **2nd Line**: Taxol (Payself) (175mg/m2) + Cisplatin (50mg/m2)
    【CCR>60ml/min】
12. **2nd Line**: Topotecan (0.75mg/m2) + Carboplatin (AUC=5) 【CCR <60ml/min】
13. **2nd Line**: Topotecan (0.75mg/m2) + Cisplatin (50mg/m2) 【CCR >60ml/min】
14. Weekly Taxol (80mg/m2) + Cisplatin (20mg/m2) (D1 or D8 or D15)
15. Weekly Taxol (80mg/m2) + Carboplatin (AUC =2) (D1 or D8 or D15)
16. Avastin (Payself) (7.5~15mg/kg)
17. Tamoxifen 10mg QD
18. Pembrolizumab (Keytruda)

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