

高雄榮民總醫院

上皮性卵巢癌、輸卵管癌、女性腹膜癌

診療指引

2022年 第一版 2022/01/25

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™ Ovarian Cancer, including Fallopian Tube Cancer and Primary Peritoneal Cancer (V.3 2021)

會議討論

上次會議：2021/01/19

本共識與上一版的差異

上一版	新版
<ol style="list-style-type: none">1. Homologous recombination deficiency (HRD) status。2. 流程二:前次手術分期不完整，懷疑無殘餘腫瘤，原分為「可能為Stage IA/IB」，以及「可能為Stage IC~IV」兩個組別做討論。Stage IA/IB後續作法為考慮完整分期手術，未提及化學治療。Stage IC~IV作法為完整分期手術或化學治療。(p.8)3. 流程四: 舊版無特別提及BRCA1/2 mutation及HR status。(p.10)4. 流程六:原無加註字眼。(p.12)5. 流程十:原無「Platinum-resistant」 and 「Platinum-sensitive」。(p.16)6. 化學藥物指引:原無Olaparib 健保適應症與Niraparib 健保適應症。(p.18)	<ol style="list-style-type: none">1. 將homologous recombination deficiency (HRD) status改為homologous recombination (HR) status。2. 流程二: 前次手術分期不完整，懷疑無殘餘腫瘤，修改分為「可能為Stage I」，和可能為「Stage II~IV」。其中stage I部分的治療增加考慮化學治療。Stage II~IV部分的治療改為接受6次化學治療，並考慮完整分期手術。(p.8)3. 流程四: 納入第一線化療有無合併bevacizumab、有無BRCA1/2 mutation、有無HR deficiency的考量來選擇第二~四期患者在首次治療後的維持療法。(p.10)4. 流程六: 加註「建議endometrioid carcinoma的所有患者都接受MSI/MMR檢查」。(p.12)5. 流程十: 加註「Platinum-resistant」 and 「Platinum-sensitive」。(p.16)6. 化學藥物指引:新增Olaparib 健保適應症與Niraparib 健保適應症。(p.18)

2014 FIGO Stage of Ovarian Cancer

卵巢癌之分期：上皮性卵巢癌，採用手術分期(surgical staging)，根據手術時的觀察及手術標本的組織病理檢查，來做分期的依據。病理報告需含有組織學類型、分化程度、卵巢以外的轉移與否及其轉移部位、淋巴結是否有轉移、卵巢有否向外生長的贅生物(exophytic vegetation)、以及腹水或腹腔腔灌洗(peritoneal lavage)之細胞學檢查結果。

第 I 期：癌症只限在卵巢(Tumor confined to ovaries)

第 IA 期：癌症局限在一側的卵巢；卵巢的表面完整，且表面處沒有癌病變，腹水中或腹腔沖洗液中無癌細胞 (Tumor limited to one ovary; capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings)。

第 IB 期：癌症局限在兩側的卵巢；卵巢的表面完整，且表面處沒有癌病變，腹水中或腹腔沖洗液中無癌細胞(Tumor limited to both ovaries; capsules intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings)。

第IC1期：癌症局限在一或兩側的卵巢，但手術中破裂 (Surgical spill)。

第IC2期：癌症局限在一或兩側的卵巢，但腫瘤術前已破裂或卵巢表面有腫瘤 (Capsule rupture before surgery or tumor on ovarian surface)。

第IC3期：癌症局限在一或兩側的卵巢，但腹水中或腹腔沖洗液中有癌細胞 (Malignant cells in the ascites or peritoneal washings)。

第 II 期：單側或兩側卵巢癌，並且有骨盆腔擴散(Tumor involves 1 or both ovaries with pelvic extension (below the pelvic brim) or primary peritoneal cancer)

第 IIA 期：擴散只限於子宮或輸卵管 (Extension and/or implants on uterus and/or Fallopian tubes)。

第 IIB 期：擴散至骨盆腔內的其他組織 (Extension to other pelvic intraperitoneal tissues)。

第 III 期：單側或兩側卵巢癌，有骨盆腔以外的腹膜轉移，或轉移到後腹腔的淋巴結 (Tumor involves 1 or both ovaries with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes)

第 IIIA 期：後腹腔淋巴結轉移和/或組織學的檢查證實有腹腔的轉移(Positive retroperitoneal lymph nodes and/or microscopic metastasis beyond the pelvis)

第 IIIA1期：只有後腹腔淋巴結轉移 (Positive retroperitoneal lymph nodes only)：

第 IIIA1(i) 期：轉移小於或等於10 mm (Metastasis \leq 10 mm)。

第 IIIA1(ii)期：轉移大於10 mm (Metastasis $>$ 10 mm)。

第 IIIA2期：組織學的檢查證實有腹腔的轉移和/或後腹腔淋巴結轉移(Microscopic, extrapelvic (above the brim) peritoneal involvement \pm positive retroperitoneal lymph nodes)。

第 IIIB 期：組織學檢查證實腹腔腹膜表面已經有了癌病變，但病變的最大徑並無超過兩公分者，和/或後腹腔淋巴結轉移(Macroscopic, extrapelvic, peritoneal metastasis \leq 2 cm \pm positive retroperitoneal lymph nodes)。

第 IIIC 期：腹腔轉移病灶的最大徑已超過兩公分，和/或後腹腔淋巴結轉移，包含肝臟或脾臟外膜侵襲(Macroscopic, extrapelvic, peritoneal metastasis $>$ 2 cm \pm positive retroperitoneal lymph nodes. Includes extension to capsule or liver/spleen)。

第 IV 期：遠端轉移超出腹膜(Distant metastasis excluding peritoneal metastasis)

第 IVA 期：肋膜積水有癌細胞 (Pleural effusion with positive cytology)。

第 IVB 期：肝臟或脾臟實質侵犯，轉移至腹外器官(包含腹股溝淋巴結與腹腔外淋巴結 (Hepatic and/or splenic parenchymal metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)。

通則

1. 對疑似惡性卵巢癌、輸卵管癌或腹膜癌患者，宜採腹部正中垂直開腹手術，此術式適用於第一次減癌手術(Primary cytoreduction)、期間減癌手術(Interval cytoreduction)與再次減癌手術(Secondary cytoreduction)。
2. 術中病理冰凍切片有助於決定手術方式與範圍。
3. 對特定的患者，可由婦癌醫師以微創手術進行分期或減癌手術；若無法進行完整減癌手術(Optimal cytoreduction)，則應改用腹部正中垂直開腹手術。
4. 對新診斷或復發之卵巢癌，可用微創手術評估適宜減癌手術的可行性；若評估後無法進行減癌手術，可考慮進行新輔助化學治療(Neoadjuvant chemotherapy)。

診斷

1. 大多數卵巢癌是根據病理切片做出診斷，病理切片可能來自於術前、術中、或術後的biopsy及手術檢體。
2. 若可能，在疑似早期卵巢癌患者上應盡量避免使用細針抽吸(FNA)作診斷，以避免腫瘤破裂或灑濺而讓惡性細胞進入腹腔。
3. 然而，若是一些患者不適合手術，如年紀大、腫瘤過大、共病過多，則可以考慮以FNA來做診斷方法。

手術紀錄

1. 手術紀錄宜記載下列要項：
 - a. 術前病灶範圍，包含骨盆腔、中腹部與上腹部。
 - b. 減癌手術後，上述範圍中殘餘腫瘤的數量。
 - c. 完全或不完全切除，若切除不完全，應註明主病灶的大小與位置、所有殘餘病灶的數量。

卵巢癌、輸卵管癌、女性腹膜癌 手術原則-2 (建議由婦癌醫師執行) (1-3)

1. 術前的腸道準備 (bowel preparation) 宜比照腸道手術之準備。
2. 宜用中央垂直開腹切口 (vertical incision) , 以獲取充分的手術視野 (exposure field) 。
3. 進入腹腔 , 即抽取腹水或經由腹腔灌洗 (peritoneal lavage) 取得腹膜腔細胞學檢查的標本(peritoneal cytologic examination) 。標本的採樣來自骨盆腔、左右兩側大腸側窩(right and left para-colic gutters)、及左右兩側橫膈膜下表面 (the under-surface of the right and left hemidiaphragms) 。
4. 盡可能完整地取出腫瘤(encapsulated mass) , 檢體需盡快送病理檢驗 , 並常規性送冷凍切片 (frozen section) 。
5. 全子宮及兩側卵巢輸卵管切除手術 (total hysterectomy, bilateral salpingo-oophorectomy) 。
6. 考慮儘量切除輸卵管漏斗部骨盆韌帶 (infundibulopelvic ligaments) 。
7. 粘黏處需切片送檢。評估所有的腸道表面 , 且所有的可疑處都要切片送檢。
8. 若無明顯的卵巢外擴散病灶 (extra-ovarian tumor spread) , 則需隨機腹膜取樣(random peritoneal biopsy) , 如子宮直腸陷窩(cul-de-sac)、骨盆腔側壁、膀胱漿膜(serosa)、兩側大腸側窩 (para-colic gutters)、橫膈膜下表面 (subdiaphragmatic surfaces)等。
9. 橫結腸下網膜切除手術 (infra-colic omentectomy) 。
10. 淋巴結評估 (lymph node assessment) : 要取主動脈旁淋巴結與骨盆淋巴結送病理檢查。主動脈旁的淋巴結 , 一般至少需取樣至 IMA (inferior mesenteric artery) , 但建議儘量能拿到 renal vein 之高度(漿液性(serous)卵巢癌 , 其淋巴結一開始的轉移位置往往高於 IMA 以上)。在所有的上皮性卵巢癌主動脈旁淋巴結轉移當中 , IMA 以上的高處乃是最常見的轉移部位。而在有主動脈旁淋巴結轉移的單側上皮性卵巢癌當中 , 11%有對側的主動脈旁淋巴結轉移 , 因此雙側的主動脈旁淋巴結皆宜考慮摘取。
11. 闌尾切除手術 (appendectomy) : 若是黏液性卵巢癌 , 則應施行闌尾切除手術。
12. 關於腹腔鏡埠管路徑 (trocar tracks) : 若在卵巢癌的診斷過程中曾使用腹腔鏡者 , 可考慮切除腹腔鏡埠管路徑。
13. 完整的手術記錄 : 需載明手術前之所有病變、所使用的手術方式、手術後殘餘腫瘤(residual tumor)的大小與位置。
14. 對於強烈想要保留生育能力者 , 若腫瘤分化良好或分化中等 (grade 1/2) 、且並不是亮細胞(clear cell)癌 , 以及手術時肉眼所見為單側卵巢病變 , 且無卵巢外可見病灶時 , 可以考慮保留子宮與對側的卵巢 , 但必須執行完整分期手術的其他項目 ; 另側卵巢在無 肉眼可見之病變 時 , 可以不必做楔狀切片(wedge biopsy) , 以免妨害生育能力。若為雙側卵巢癌 , 則子宮在檢查之後可保留 , 但雙側卵巢都應切除 ; 其餘步驟同完整的分期手術。保留子宮的患者 , 宜做子宮腔鏡(hysteroscopy) 及子宮內膜搔刮術 (curettage) 。
15. 對於卵巢以外的擴散病灶 , 應盡可能地做到最大程度的減積手術 (maximal cytoreduction) , 因為殘餘腫瘤的大小與預後有密切的關係。若標準手術無法達到適當的切除 (optimal resection ; 個別殘存腫瘤的最大直徑小於 1 公分) , 則宜考慮增加進一步手術(如部分腸道或臟器之切除)以達成此一目標。

高雄榮總婦癌團隊 上皮性卵巢癌、輸卵管癌、女性腹膜癌臨床治療指引

臨床表現

於腹部或骨盆腔檢查懷疑或觸診到骨盆腔腫塊及/或有腹水、及/或腹漲、及/或腹痛、骨盆腔疼痛、進食困難、一進食就飽、急尿或頻尿且沒有其他明顯惡性腫瘤的可能 (4-11)

1. 考慮完整家族史評估
2. 腹部及骨盆腔理學檢查
3. 如臨床懷疑為腸胃道轉移，則行消化系統評估(胃鏡與大腸鏡)
4. 婦產科超音波檢查*
5. 腹部或骨盆腔電腦斷層*
6. 必要時行胸部影像學檢查(X光*或電腦斷層)
7. CA-125 或其他腫瘤指數
8. 全血分析與完整生化檢查(含肝及腎功能)
9. 可考慮正子攝影
10. 可考慮進行遺傳檢驗與諮詢

(6, 12-14)

於前次手術或組織切片中發現

1. 考慮完整家族史評估
2. 婦產科超音波檢查*
3. 腹部或骨盆腔電腦斷層*
4. 胸部影像學檢查(X光*或電腦斷層)
5. CA-125 或其他腫瘤指數
6. 全血分析與完整生化檢查(含肝及腎功能)
7. 需要時請院內病理部門複閱
8. 可考慮正子攝影
9. 可考慮進行遺傳檢驗與諮詢

*與期別相關之主要檢查(必要項目)

評估檢查

初步治療 (建議由婦癌醫師執行) (18-20)

剖腹探查(腹式全子宮切除及雙側卵巢輸卵管切除及完整分期手術) (21-23)
或

(期別為 IA 或 IB，不論細胞分化如何，病患想保留生育能力，可行單或雙側卵巢輸卵管切除及完整分期手術) (24-29)
或

減癌手術(如期別為II、III、IV) (21-23)
或

先化學治療後再行減癌手術(如經細針抽取或切片證實之期別III或IV之巨大腫瘤不適合立即手術者) (15-17)
或

緩和醫療(對身體狀況不適合手術或化學治療者)

流程三

流程二

※ 臨床研究顯示此類癌症由婦癌醫師評估與手術者較非婦癌醫師評估與手術者有較高之存活率且併發症較少

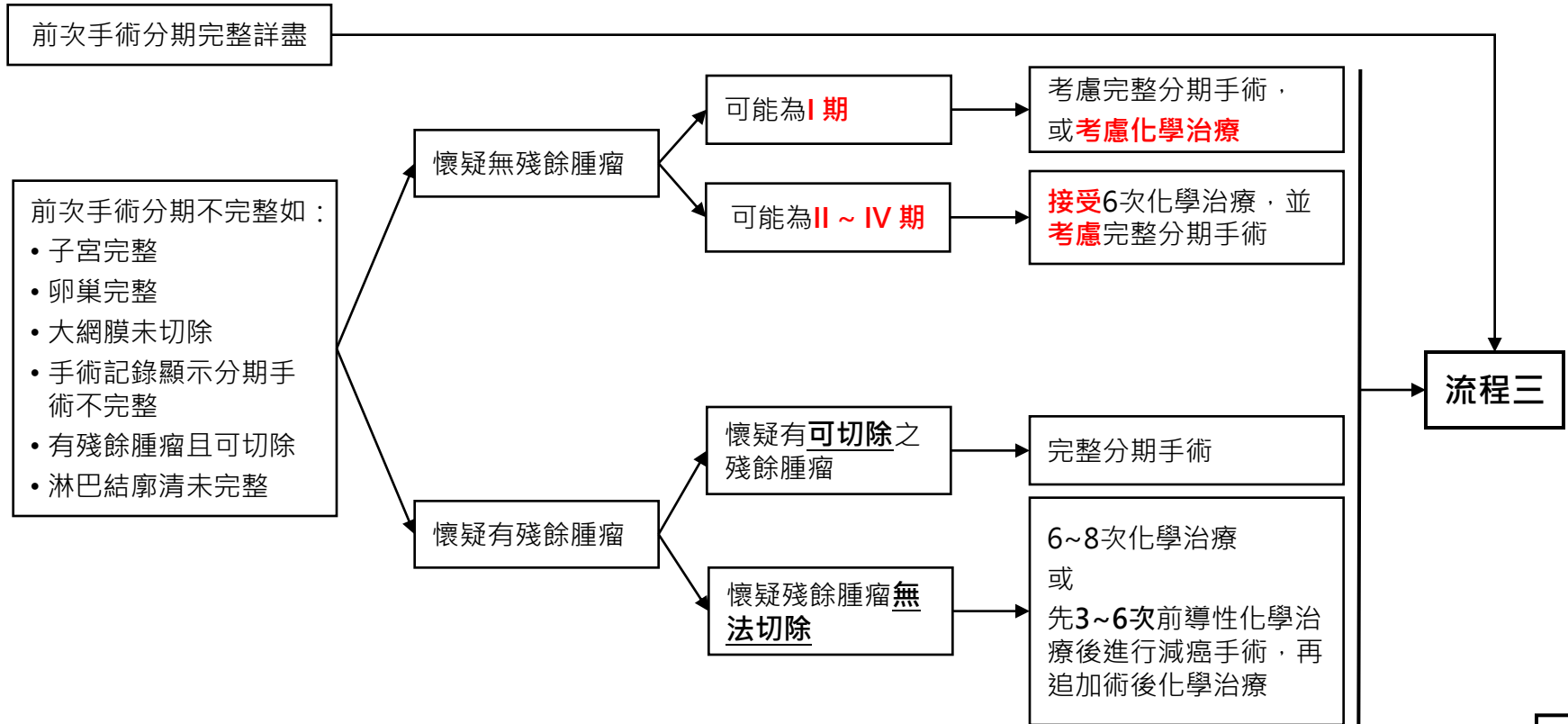
流程一

於前次手術後診斷

前次手術結果

評估檢查

初步治療 (建議由婦癌醫師執行)



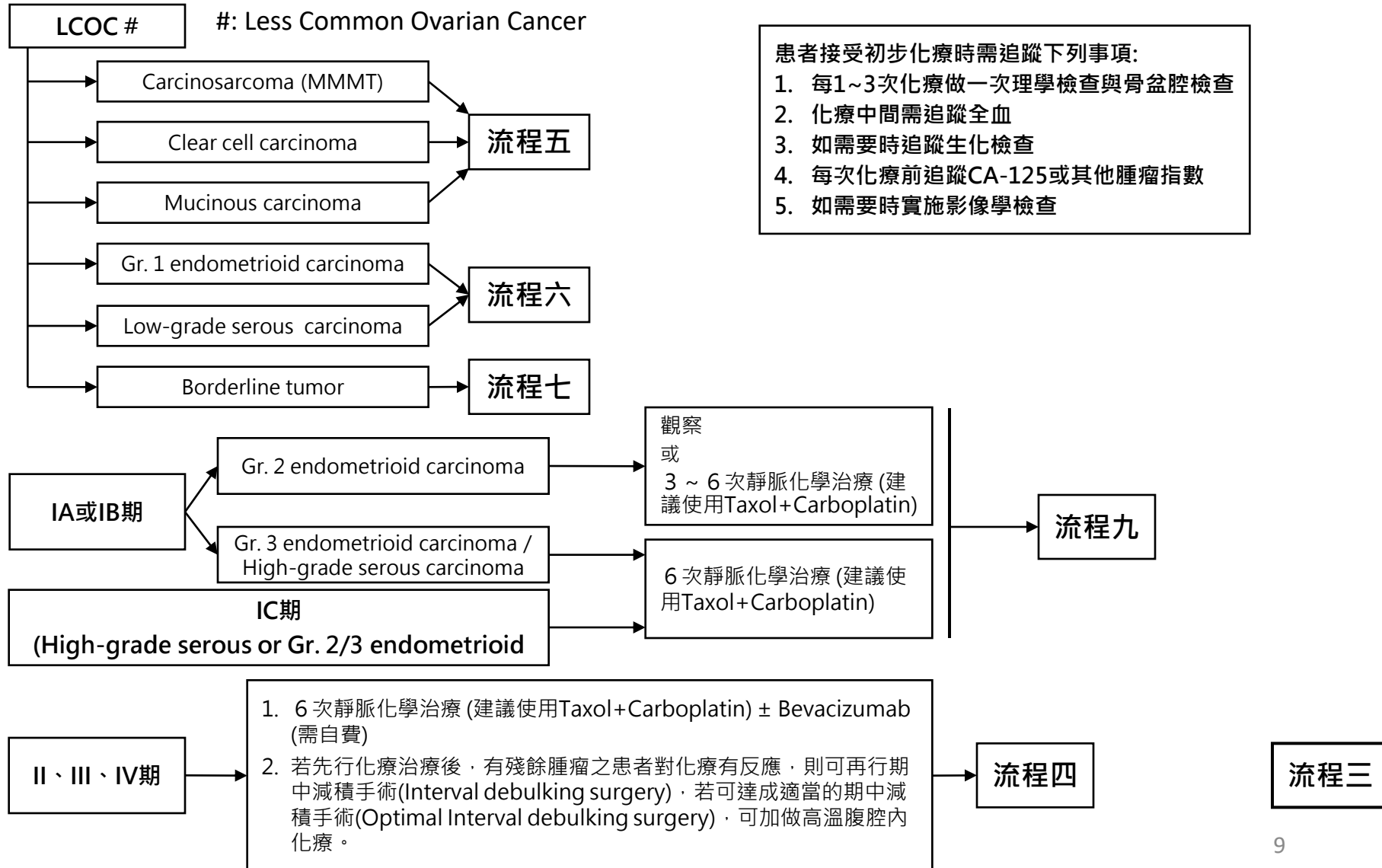
(30-33)

流程二

高雄榮總婦癌團隊 上皮性卵巢癌、輸卵管癌、女性腹膜癌臨床治療指引

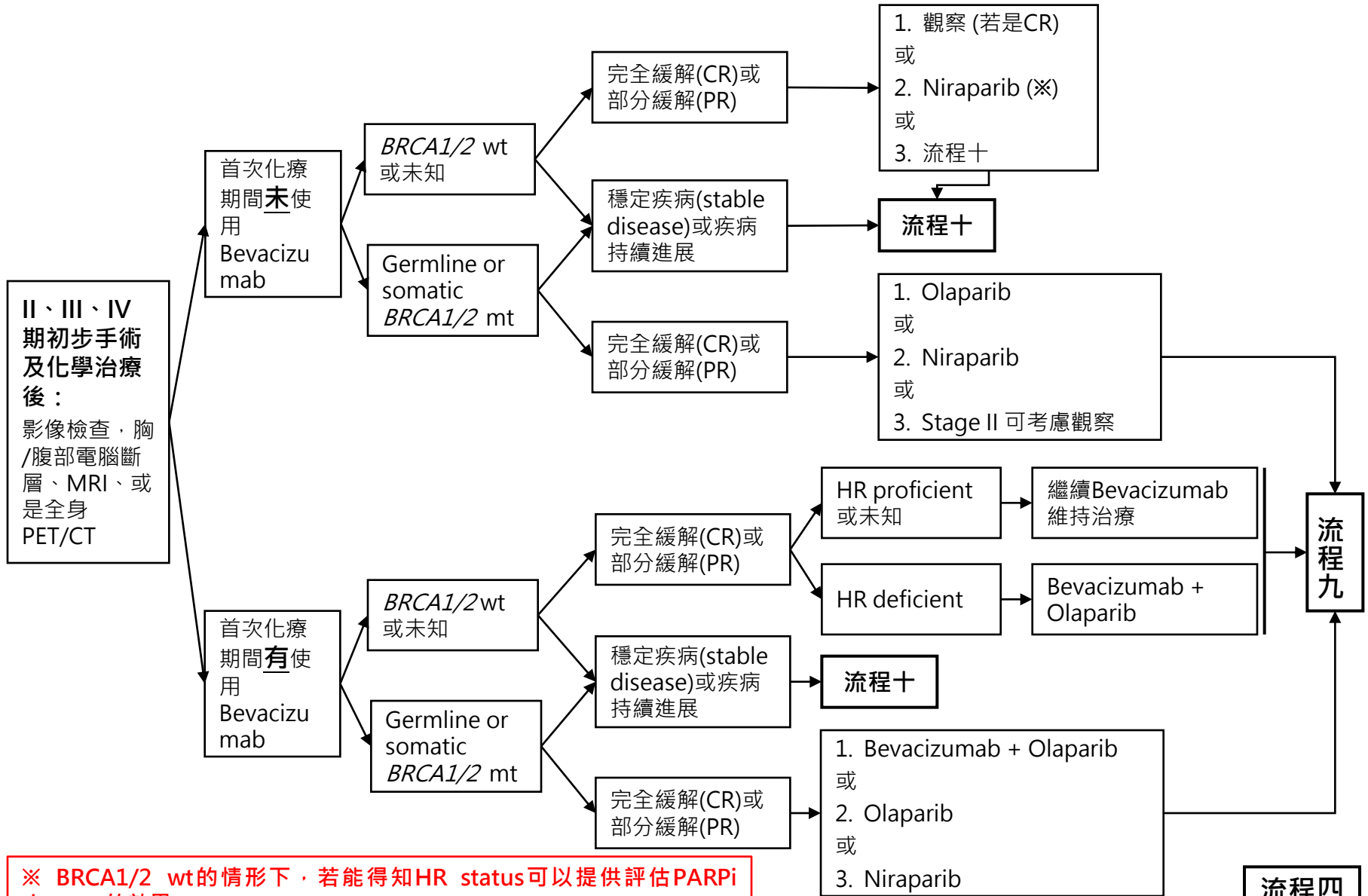
細胞型態 或 期別

初步輔助性化學治療



高雄榮總婦癌團隊 上皮性卵巢癌、輸卵管癌、女性腹膜癌臨床治療指引

維持治療



※ BRCA1/2 wt 的情形下，若能得知HR status 可以提供評估PARPi therapy 的效果。

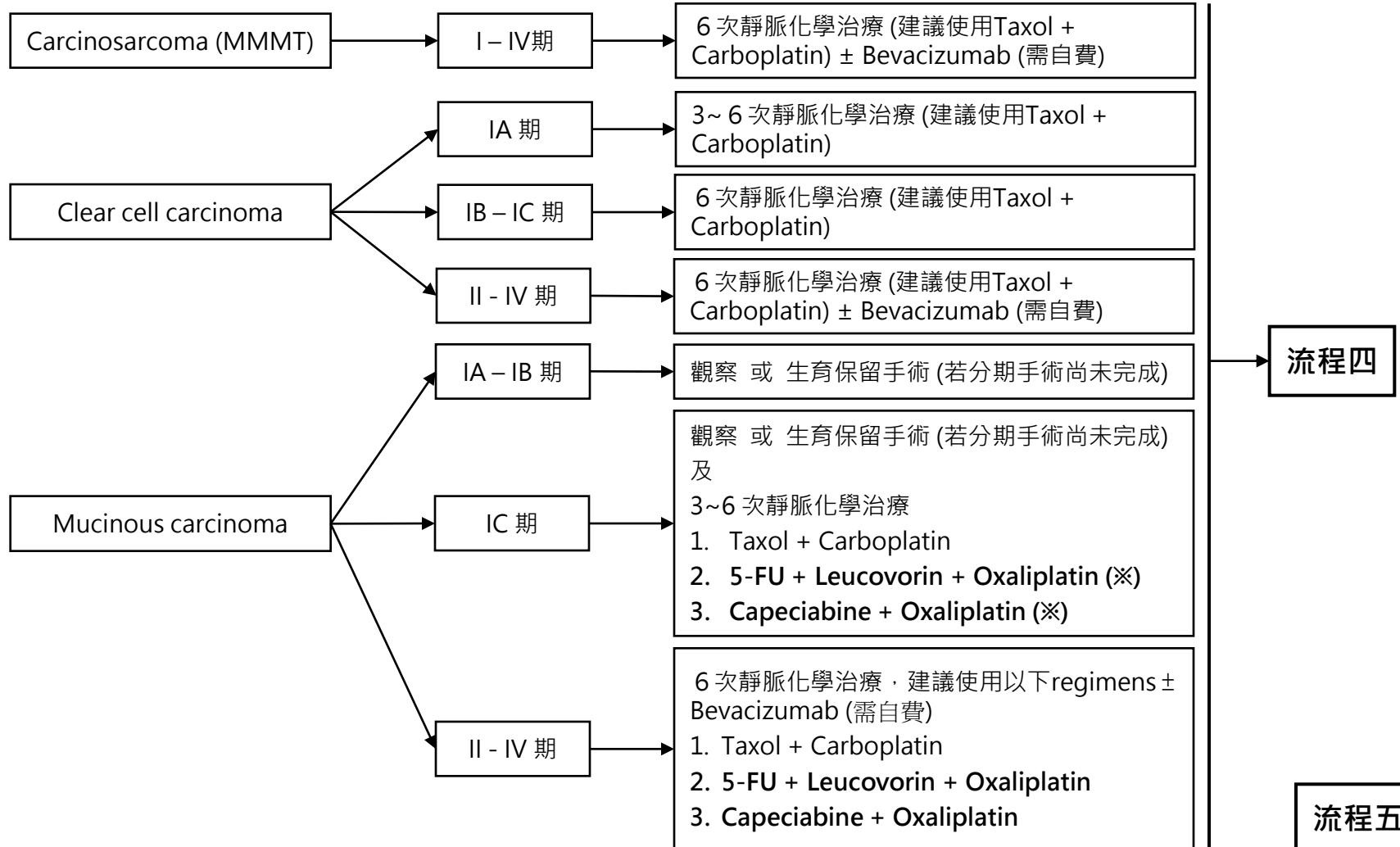
流程四

高雄榮總婦癌團隊 上皮性卵巢癌、輸卵管癌、女性腹膜癌臨床治療指引

細胞型態

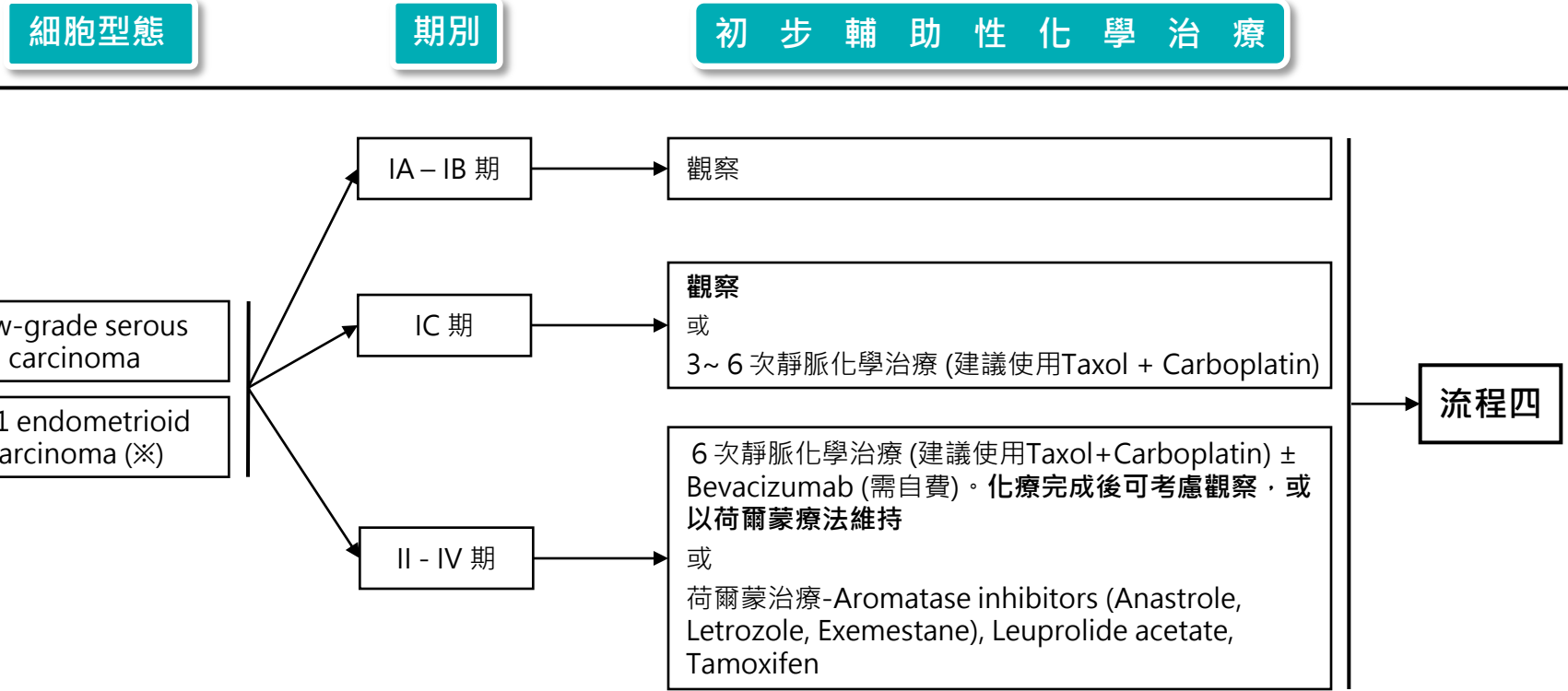
期別

初步輔助性化學治療



※ Mucinous carcinoma經第一線化療失敗或復發後, 可考慮更改為表列regimen

高雄榮總婦癌團隊 上皮性卵巢癌、輸卵管癌、女性腹膜癌臨床治療指引



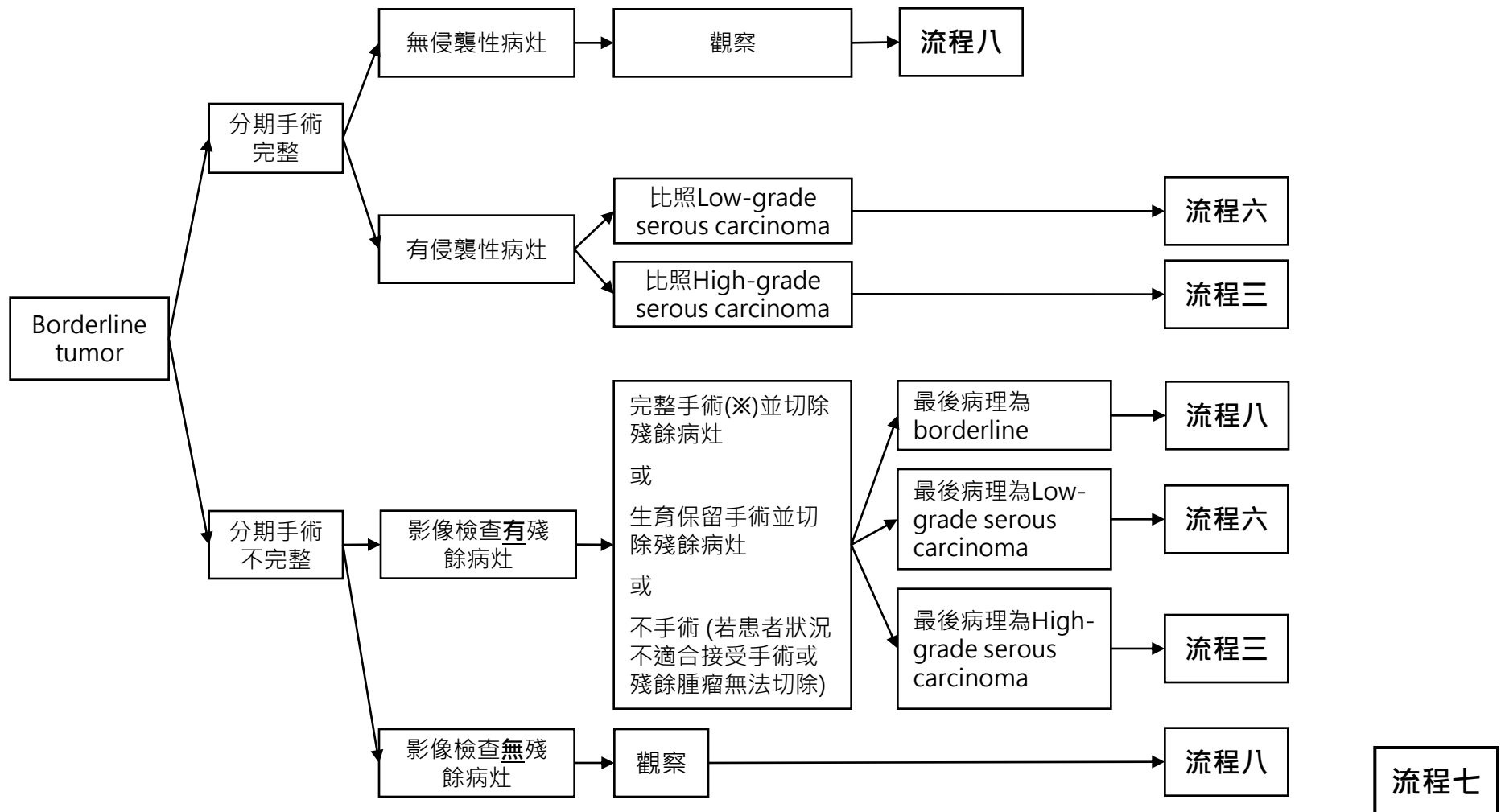
※ 建議endometrioid carcinoma的所有患者都接受MSI/MMR檢查

- 患者接受初步化療時需追蹤下列事項:
1. 每1~3次化療做一次理學檢查與骨盆腔檢查
 2. 化療中間需追蹤全血
 3. 如需要時追蹤生化檢查
 4. 每次化療前追蹤CA-125或其他腫瘤指數
 5. 如需要時實施影像學檢查

流程六

高雄榮總婦癌團隊 上皮性卵巢癌、輸卵管癌、女性腹膜癌臨床治療指引

初步輔助治療



※: 完整手術指病灶對側卵巢輸卵管切除及子宮切除，淋巴廓清術則依各病患狀況另作考慮

追蹤及監測

1. 每3~6個月追蹤一次持續五年，之後每年追蹤一次
2. CA-125或其他腫瘤指數若於治療前呈現異常，則於追蹤時檢查
3. 必要時行婦科超音波檢查
4. 必要時行全血分析及生化檢查
5. 理學檢查及骨盆腔檢查
6. 每年胸部X光檢查
7. 如臨床上有懷疑，可加做肺部、腹部或骨盆腔之電腦斷層、核磁共振掃描或正子攝影

臨床上發現復發

減癌或分期手術

無侵襲性病灶

觀察

仍然是
borderline
tumor的侵襲性病灶
或
Low-grade
carcinoma

比照Low-grade serous
carcinoma治療
流程六

侵襲性病灶
(High-grade
carcinoma)

比照上皮性卵巢癌治療
流程三

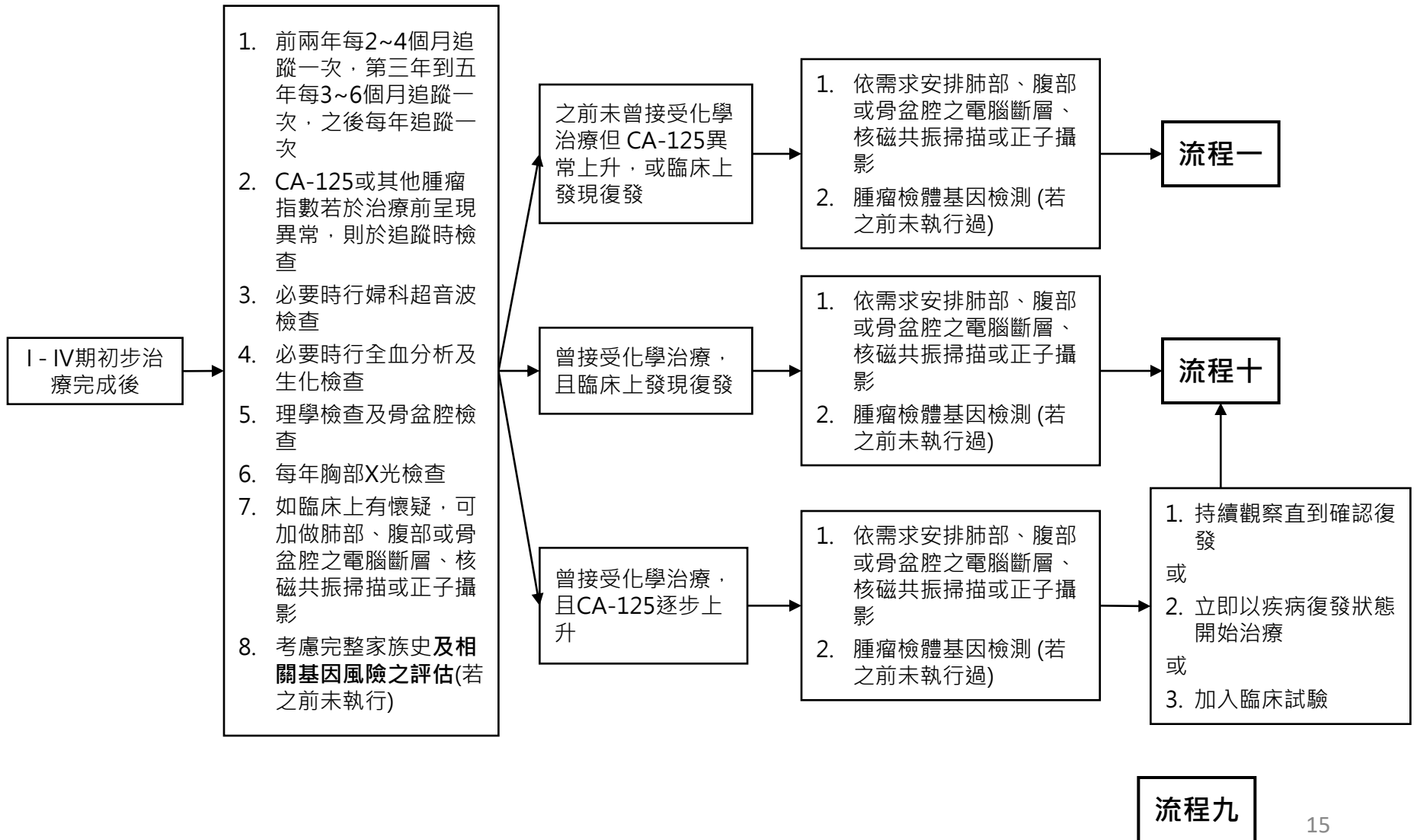
復發後治療

流程八

高雄榮總婦癌團隊 上皮性卵巢癌、輸卵管癌、女性腹膜癌臨床治療指引

追蹤

疾病復發



疾病狀態

持續性疾病或復發之治療

Platinum-resistant

初次化療後、於維持療法期間、
或於復發治療期間疾病持續進展

穩定(Stable disease)或持續性
(Persistent)疾病狀態

初次化療後完全緩解，但於完成
化療後六個月內復發

復發之治療
及/或
緩和治療
及/或
加入臨床試驗

Platinum-sensitive

初次化療後完全緩解，但於完成
化療後六個月後復發

影像學
及/或
臨床上復發

考慮再次減癌手術

1. 含鉑複方化療 (特別是首次復發)
及/或
2. 復發之治療 (其他化療處方)
或
3. Tumor directed R/T
或
4. 加入臨床試驗
及/或
5. 支持性療法

生化上復發
(CA-125上升但無影像
學證據)

1. 延遲治療直到確認復發
或
2. 立刻以含鉑之復發化療治療
或
3. 加入臨床試驗
及/或
4. 支持性療法

如經影像檢查後，發現部分(PR)或
完全緩解(CR)，考慮
Bevacizumab 或 PARP inhibitor
維持療法 (特別是具有BRCA
mutation的患者)，或是考慮觀察。

第一線化學治療與誘導輔助化學治療：

第一、二期：

1. Carboplatin (AUC=5) + Epirubicin 50 mg/m² + Cyclophosphamide 500 mg/m², every 21 days (58)
2. Taxol 175 mg/m² + Platinum (Carboplatin (AUC=5) or Cisplatin 50 mg/m²), every 21 days (有特殊狀況，如年齡大、ECOG PS差可先考慮單用Carboplatin) (34)
3. Paclitaxel 60mg/m² (Weekly D1, D8 & D15)+ Carboplatin (AUC=5) (3 Weekly),every 21 days (73)

第三、四期：(可視臨床需要加上Bevacizumab: 5~15 mg/kg)

1. Taxol 175 mg/m² + Platinum(Carboplatin (AUC=5) or Cisplatin 50 mg/m²), every 21 days (有特殊狀況，如年齡大、ECOG PS差可先考慮單用Carboplatin) (34-38)
2. Paclitaxel 60mg/m² (Weekly D1, D8 & D15)+ Carboplatin (AUC=5) (3 Weekly),every 21 days (73)

第二線或轉移化學治療：(可視臨床需要加上Bevacizumab: 5~15 mg/kg)

Platinum Sensitive：

1. Lipodoxorubicin 30 mg/m² + Carboplatin AUC=5, every 28 days (49)
2. Lipodoxorubicin 30 mg/m² + Gemcitabine 650 mg/m², D1& D8, every 21~28 days (57)
3. Gemcitabine 800~1200 mg/m² D1&D8 + Carboplatin AUC=5 D1, every 21 days (50)
4. Topotecan 0.75 mg/m² D1~D3 + Carboplatin AUC=5 D3, every 21 days (53-54)
5. Taxol 80 mg/m² + Carboplatin AUC=2 (Weekly D1, D8 & D15, every 21~28 days) (56)

Platinum Refractory or Resistant：

1. Lipodoxorubicin 40 mg/m² every 28 days (74)
2. Lipodoxorubicin 30 mg/m² + Gemcitabine 650 mg/m², D1& D8, every 21~28 days (57)
3. Topotecan 1.25 mg/m² D1~D5, every 21 days (51)
4. Topotecan 3~4 mg/m² D1, D8 & D15, every 28 days (51)
5. Taxol 80 mg/m² + Topotecan 1.75 mg/m² (Weekly D1, D8 & D15, every 21~28 days) (55)
6. Cyclophosphamide 100 mg, 1# qd. (75)

§ Mucinous carcinoma 於Stage IC第一線化療無效、Stage II~IV、或疾病復發時可考慮：

1. 5-FU + Leucovorin + Oxaliplatin (78, 79)
2. Capecitabine + Oxaliplatin (80)

復發後荷爾蒙治療：

Tamoxifen 10 mg, 1#, qd or bid. (52) Aromatase inhibitor, Leuprolide acetate, Megestrol acetate. (60-65)

維持治療

Bevacizumab 5~15 mg/kg (71-72)

Olaparib 300~600 mg/D (68-70)

Niraparib 300 mg/d(83-84)

Olaparib (300mg BID)+ bevacizumab (15mg/kg) (85)

腹腔內化學治療： Cisplatin 100 mg/m² (76, 77)

Olaparib 健保適應症

1. 晚期高度惡性上皮卵巢癌、輸卵管腫瘤或原發性腹膜癌，且具生殖細胞或體細胞BRCA1/2 (germline or somatic BRCA1/2) 致病性或疑似致病性突變，對第一線含鉑化療有反應 (完全反應或部分反應) 之成年病人作為維持治療。
2. 對先前含鉑藥物敏感且復發之高度惡性表皮卵巢、輸卵管腫瘤或原發性腹膜癌，在復發後對含鉑化療有反應 (完全反應或部分反應) 之成人病人，作為維持治療。

Niraparib 健保適應症

1. 晚期卵巢癌之第一線維持治療：用於對第一線含鉑化療有完全或部分反應的晚期表皮卵巢癌、輸卵管腫瘤或原發性腹膜癌成年病人之維持治療。
2. 復發性卵巢癌之維持治療：用於對含鉑化療有完全或部分反應的復發性表皮卵巢癌、輸卵管腫瘤或原發性腹膜癌成年病人之維持治療，病人須對復發前含鉑化療有敏感性。
3. 治療曾接受三種以上化療之晚期卵巢癌：用於治療先前曾接受三種以上化療療程的晚期卵巢癌、輸卵管腫瘤或原發性腹膜癌成年病人。腫瘤必須為同源重組缺陷 (Homologous Recombination Deficient, HRD)陽性，同源重組缺陷之定義如下：(1)具有致病性或疑似致病性 BRCA突變，或 (2)具基因體不穩定 (genomic instability)，且病人接受最近一次含鉑化療出現腫瘤反應後，至少六個月以上方產生疾病惡化。

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