高雄榮民總醫院癌症診療指引

上皮性卵巢癌、輸卵管癌、女性腹膜癌

高雄榮總 2015年第1版
修定時間 2015年9月29日

婦癌醫療團隊制定

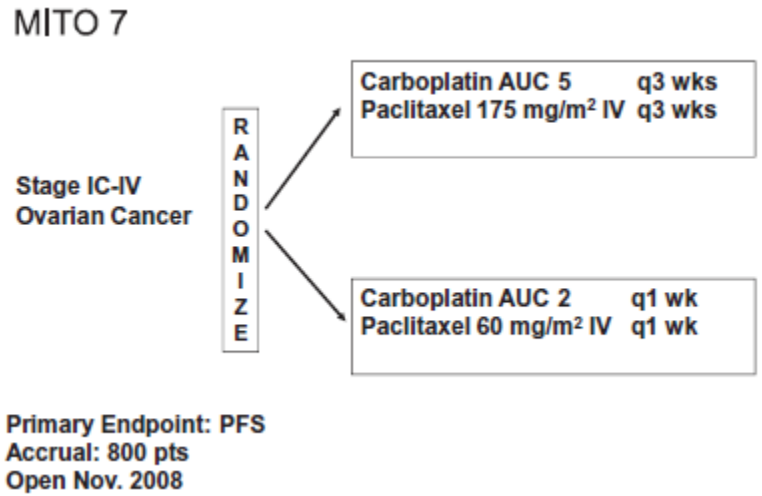
注意事項：這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如妳是一個癌症病人，直接引用這個診療指引並不恰當，只有妳的醫師與妳才能共同決定給屬於妳最恰當的治療。

修訂指引

- 本共識依下列參考資料修改版本
  - NCCN Clinical Practical Guidelines in Oncology (NCCN Guidelines) **Ovarian Cancer**, including Fallopian Tube Cancer and Primary Peritoneal Cancer, Version 2.2015
  - 前次會議時間: 2014年9月30日

與上一版的差異

1. 流程1：檢查需包含genetic risk evaluation, 例如: BRCA mutation.
2. 在第一線化學治療的部分加上: Paclitaxel 60mg/m^2 IV over 1 hour followed by carboplatin AUC 2 IV over 30 minutes. Weekly for 18 weeks. **(category 1),**尤其對於老年人或身體不好(ECOG lower than 2)的患者。



3. 復發後疾病荷爾蒙治療的部分多加上）Aromatase inhibitor, Leuprolide acetate, Megestrol acetate.

卵巢癌的分期

卵巢癌之分期：上皮性卵巢癌，採取手術分期(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)、以及腹水或腹膜腔灌洗(peritoneal lavage)之細胞學檢查結果。

第 I 期：癌症只限在卵巢(Tumor limited to ovaries(one or both))：

- 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 IC 期：不管是 IA 或 IB，一側或兩側卵巢且卵巢表面已經有了癌病變、或者卵巢腫瘤已經破裂、或者腹水或腹腔沖洗液中檢出癌細胞(Tumor limited to one or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites or peritoneal washings)。【手術中造成之卵巢破裂並不改變原有癌症期別】

第 II 期：單側或兩側卵巢癌，並且有骨盆腔擴散(Tumor involves one or both ovaries with pelvic extension and/or implants)：

- 第 IIA 期：擴散只限於子宮或輸卵管，腹水中或腹腔沖洗液中無癌細胞(Extension and/or implants on uterus and/or tube(s). No malignant cells in ascites or peritoneal washings)。
- 第 IIB 期：擴散至骨盆腔內的其他組織，腹水中或腹腔沖洗液中無癌細胞(Extension to and/or implants on other pelvic tissues. No malignant cells in ascites or peritoneal washings)。
- 第 IIC 期：不管是 IIA 或 IIB，但是卵巢的表面已經有了癌病變；或卵巢腫瘤已經破裂；或腹水或腹腔沖洗液檢出癌細胞(Pelvic extension and/or implants (T2a or T2b) with malignant cells in ascites or peritoneal washings)。

第 III 期：單側或兩側卵巢癌，有骨盆腔以外的腹膜轉移，或轉移到後腹腔或鼠蹊部的淋巴結。表淺的肝臟轉移視為第三期。癌症雖仍局限在骨盆內，但是組織學的檢查，已證實有小腸或大網膜的轉移(Tumor involves one or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis. Superficial liver metastasis equals stage III. Tumor is limited to the true pelvis but with histologically verified malignant extension to small bowel or omentum)：

- 第 IIIA 期：肉眼看起來癌病變只局限在骨盆腔內，而且沒有淋巴的轉移。但是組織學的檢查已證實有腹腔腹膜的轉移(Microscopic peritoneal metastasis beyond pelvis (no macroscopic tumor), Nodes negative)。
- 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。淋巴結沒有轉移(Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension, Nodes negative)。
- 第 IIIC 期：腹腔轉移病灶的最大徑已超過兩公分，或者有後腹腔或鼠蹊淋巴結的轉移(Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or positive retroperitoneal or inguinal nodes)。

第 IV 期：單側或兩側卵巢癌，有遠端轉移(Ovarian cancer is growth involving one or both ovaries with distant metastasis)。如果有胸膜積水，必須細胞學檢查陽性呈現才能算是第四期。肝臟實質部的轉移算是第四期(If pleural effusion is present, there must be positive cytologic test results to allot a case to stage IV. Parenchymal liver metastasis equals stage IV)。

卵巢癌、輸卵管癌、女性腹膜癌 初次手術之基本原則 (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。

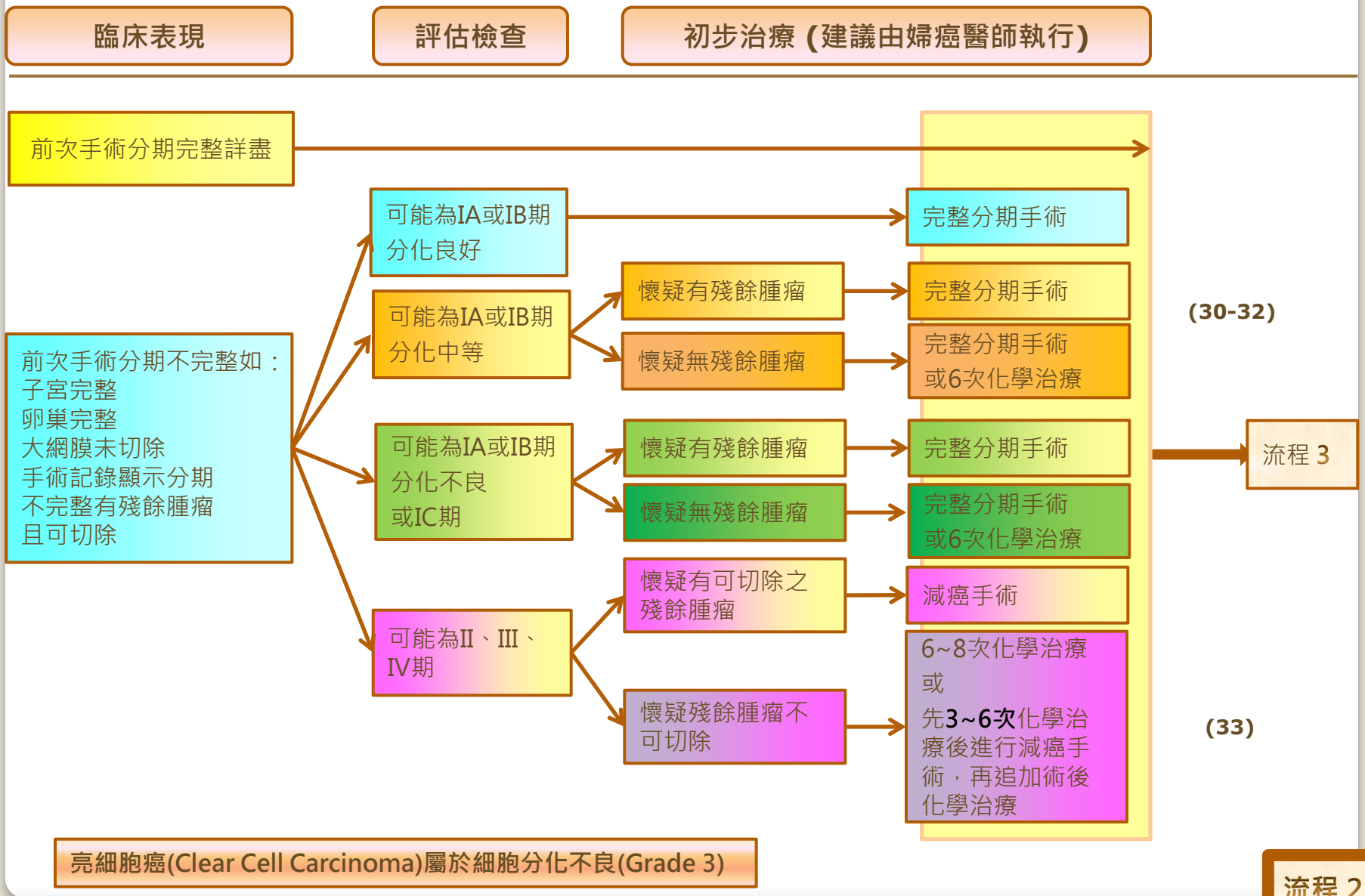
上皮性卵巢癌、輸卵管癌、女性腹膜癌

臨床表現	評估檢查	初步治療 (建議由婦癌醫師執行) (18-20)
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. 胸部影像學檢查(X光或電腦斷層) 7. CA-125 或其他腫瘤指數(含HE4) 8. 全血分析 9. 肝及腎功能檢查 10. 可考慮正子攝影 11. 可考慮基因風險評估檢查 (6, 12-14)	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) 或 (21-23) (期別為 IA 或 IC，不論細胞分化如何，病患想保留生育能力，可行單側卵巢輸卵管切除及完整分期手術) 或 (24-29) 減癌手術(如期別為II、III、IV) 或 (21-23) 先化學治療後再行減癌手術 (如經細針抽吸、切片證實之期別III或IV之巨大腫瘤不適合立即手術者) 或 (15-17) 緩和醫療(對身體狀況不適合手術與化學治療者) → 流程 3
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 7. 肝及腎功能檢查 8. 需要時請院內病理部門複閱 9. 可考慮正子攝影	→ 流程3

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 1

上皮性卵巢癌、輸卵管癌、女性腹膜癌



流程 2

上皮性卵巢癌、輸卵管癌、女性腹膜癌

評估檢查

初步輔助性化學治療

- IA或IB期
  - 分化良好 → 觀察
  - 分化中等 → 觀察 或 3~6 次靜脈化學治療(建議使用 Taxol+Carboplain)
  - 分化不良 (含亮細胞癌) → 3~6 次靜脈化學治療 (建議使用 Taxol+Carboplain) (亮細胞癌建議用 6 次化學治療) → 流程 5
- IC期 → 3~6 次靜脈化學治療 (建議使用 Taxol+Carboplain) (亮細胞癌建議用 6 次化學治療)
- II、III、IV期 → 化學治療
  - 6~8 次靜脈化學治療(建議使用含Taxol及Carboplain之配方)
  - 或
  - 考慮腹腔內化學治療(於 II 或 III 期且手術後殘餘腫瘤<1公分)

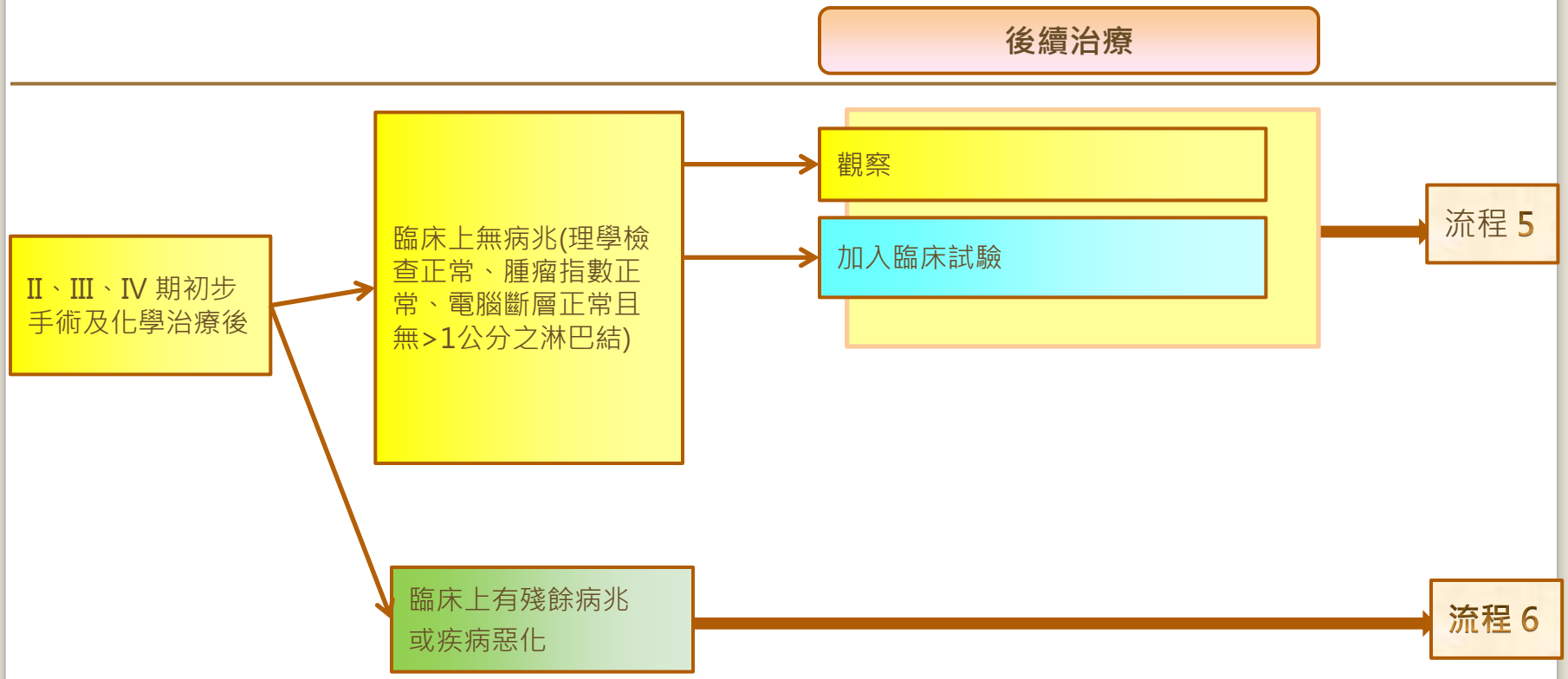
  若先行化學治療且殘餘腫瘤對化療有反應而可再次切除者，則進行完整分期手術 → 流程 4

患者接受初步化療時需追蹤下列事項:

1. 每2化學療程做一次骨盆腔檢查
2. 化療中間需追蹤全血
3. 如需要時監測生化檢查
4. 每次化療前監測CA-125或其他腫瘤指數
5. 如需要時實施影像學檢查

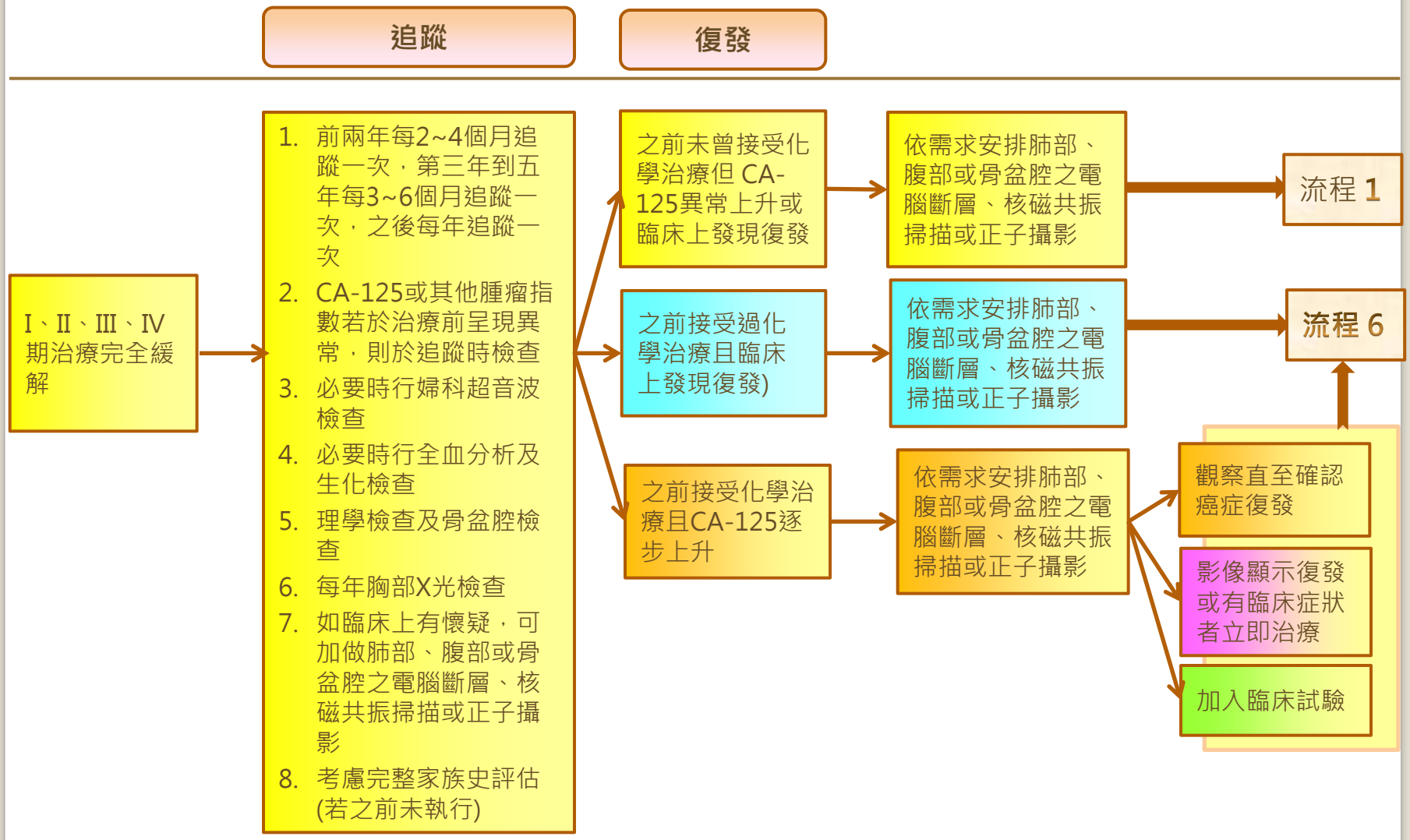
流程 3

上皮性卵巢癌、輸卵管癌、女性腹膜癌



流程 4

上皮性卵巢癌、輸卵管癌、女性腹膜癌 (39-40)



流程 5

上皮性卵巢癌、輸卵管癌、女性腹膜癌 (41-43)

疾病狀態	持續性疾病或復發之治療
初次化療後惡化(progression)、穩定(stable)或持續性(persistent)疾病狀態	臨床試驗 或 支持療法 或 復發治療(註)
初次化療後完全緩解但於停藥後 6 個月內復發或II, III, IV 期治療後只有部分緩解(partial response)	臨床試驗 或 復發治療(註)
初次化療後完全緩解但於停藥後6個月後復發	影像學及/或臨床上復發：含白金類藥物之複方化學治療(尤其是第一次復發時) 或 復發治療(註(含RFA)) 或 Tumor directed RT (44-48) 或 臨床試驗 影像學及/或臨床上復發：考慮再次腫瘤減積手術：含白金類藥物之複方化學治療(尤其是第一次復發時) 或 復發治療(註(含RFA)) 或 Tumor directed RT (44-48) 或 臨床試驗
初次化療後完全緩解但於停藥後6個月後復發	生化上復發(CA-125上升但無影像學的變化)：延遲治療直至臨床上復發 或 臨床試驗

註：當病患接受過連續兩種不同配方之化學治療後病況仍無改善時，再予以治療可能毫無幫助，建議進入臨床試驗

流程 6

上皮性卵巢癌、輸卵管癌、女性腹膜癌　化療藥物用藥指引

第一線化學治療：

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 + Carboplatin AUC=5, every 21 days (34)
3. For stage II patient, Paclitaxel 60mg/m2 IV over 1 hour followed by carboplatin AUC 2 IV over 30 minutes. Weekly for 18 weeks. (category 1), esp. for elderly patients and those with poor performance status. (59)

第三、四期：

1. Taxol 175 mg/m2 + Carboplatin AUC=5, every 21 days (+Avastin: 5~15 mg/kg) (34-38)
2. Paclitaxel 60mg/m2 IV over 1 hour followed by carboplatin AUC 2 IV over 30 minutes. Weekly for 18 weeks. (category 1), esp. for elderly patients and those with poor performance status. (59)

第二線化學治療：(可視臨床需要加上Avastin: 5~15 mg/kg)

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

第三線化學治療：(可視臨床需要加上Avastin: 5~15 mg/kg)

1. Taxol 80 mg/m2 + Carboplatin AUC=2 (Weekly D1, D8 & D15, every 21~28 days) (56)
2. Topotecan 1.25 mg/m2 D1~D5, every 21 days (51)
3. Topotecan 3~4 mg/m2 D1, D8 & D15, every 28 days (51)
4. Taxol 80 mg/m2 + Topotecan 1.75 mg/m2 (Weekly D1, D8 & D15, every 21~28 days) (55)
5. Lipodoxorubicin 30 mg/m2 + Gemcitabine 650 mg/m2, D1& D8, every 21~28 days (57)
6. Cyclophosphamide 100 mg, 1# qd.

復發後荷爾蒙治療：

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

復發後標靶治療：

Avastin (Bevacizumab).

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