# 高 雄 榮 民 總 醫 院
# 子宮惡性肉瘤診療指引

2017年05月16日 第一版

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 Sarcoma Cancer (V.2. 2017)
  - 婦癌研究委員會，子宮惡性肉瘤癌篩檢臨床指引 (2011)：國家衛生研究院
  - 其他相關子宮惡性肉瘤臨床指引

# 會議討論

上次會議：2016/05/03

## 本共識與上一版的差異

| 上一版 | 新版 |
| --- | --- |
| 1. 流程圖四及流程圖五:局部復發僅陰道及胸部x光正常及電腦斷層腹部及骨盆腔檢查，僅局部陰道復發的治療，在之前從未接受放射線治療的狀況下，治療選項在手術切除治療僅有外科手術切除 ±手術中行病灶放射線治療，而在接受過放射線治療的狀況下，放射線治療選項僅有針對腫瘤直接放射治療。(p.9,10)<br><br>2. 流程圖四:多處轉移復發狀況下，在其他肉癌治療方式為化學治療 ±緩解放射線治療或支持療法。(p.9) | 1. 流程圖四及流程圖五:局部復發增加骨盆腔復發的治療，在之前從未接受放射線治療的狀況下，治療選項增加考慮術前體外放射線治療，而在接受過放射線治療的狀況下，治療選項增加±陰道近接治療。(p.9,10)<br><br>2. 流程圖四:多處轉移復發狀況下，在子宮內膜基質惡性肉癌治療方式更改與僅單獨一處轉移復發下之不可切除狀況下的治療方式相同(化學治療 ±緩和放射線治療(之後若可切除病灶，可考慮手術)或其他局部熱頻燒灼治療(RFA: Radiofrequency Ablation)或荷爾蒙治療(此僅對子宮內膜基質惡性肉瘤)或緩解放射線治療。(p.9) |

**分期**

## CORPUS UTERI SARCOMA STAGING FORM

*(Carcinosarcomas should be staged as carcinomas)*

| Clinical<br>*Extent of disease before any treatment* | Stage Category Definitions | | Pathologic<br>*Extent of disease through completion of definitive surgery* |
|---|---|---|---|
| ☐ y clinical – staging completed after neoadjuvant therapy but before subsequent surgery | **Tumor Size:** _____ | **Laterality:** ☐ left ☐ right ☐ bilateral | ☐ y pathologic – staging completed after neoadjuvant therapy and subsequent surgery |

| TNM Category | FIGO Stage | Primary Tumor (T) | TNM Category | FIGO Stage |
|---|---|---|---|---|
| | | **Leiomyosarcoma, Endometrial Stromal Sarcoma** | | |
| ☐ TX | | Primary tumor cannot be assessed | ☐ TX | |
| ☐ T0 | | No evidence of primary tumor | ☐ T0 | |
| ☐ T1 | I | Tumor limited to the uterus | ☐ T1 | I |
| ☐ T1a | IA | Tumor 5 cm or less in greatest dimens | ☐ T1a | IA |
| ☐ T1b | IB | Tumor more than 5 cm | ☐ T1b | IB |
| ☐ T2 | II | Tumor extends beyond the uterus, within the pelvis | ☐ T2 | II |
| ☐ T2a | IIA | Tumor involves adnexa | ☐ T2a | IIA |
| ☐ T2b | IIB | Tumor involves other pelvic tissues | ☐ T2b | IIB |
| ☐ T3 | III* | Tumor infiltrates abdominal tissues | ☐ T3 | III* |
| ☐ T3a | IIIA | One site | ☐ T3a | IIIA |
| ☐ T3b | IIIB | More than one site | ☐ T3b | IIIB |
| ☐ T4 | IVA | Tumor invades bladder or rectum | ☐ T4 | IVA |
| | | **Adenosarcoma** | | |
| ☐ TX | | Primary tumor cannot be assessed | ☐ TX | |
| ☐ T0 | | No evidence of primary tumor | ☐ T0 | |
| ☐ T1 | I | Tumor limited to the uterus | ☐ T1 | I |
| ☐ T1a | IA | Tumor limited to the endometrium/endocervix | ☐ T1a | IA |
| ☐ T1b | IB | Tumor invades to less than half of the myometrium | ☐ T1b | IB |
| ☐ T1c | IC | Tumor invades more than half of the myometrium | ☐ T1c | IC |
| ☐ T2 | II | Tumor extends beyond the uterus, within the pelvis | ☐ T2 | II |
| ☐ T2a | IIA | Tumor involves adnexa | ☐ T2a | IIA |
| ☐ T2b | IIB | Tumor involves other pelvic tissues | ☐ T2b | IIB |
| ☐ T3 | III* | Tumor involves abdominal tissues | ☐ T3 | III* |
| ☐ T3a | IIIA | One site | ☐ T3a | IIIA |
| ☐ T3b | IIIB | More than one site | ☐ T3b | IIIB |
| ☐ T4 | IVA | Tumor invades bladder or rectum | ☐ T4 | IVA |

Note: Simultaneous tumors of the uterine corpus and ovary/pelvis in association with ovarian/pelvic endometriosis should be classified as independent primary tumors.

* In this stage, lesions must infiltrate abdominal tissues and not just protrude into the abdominal cavity.

| TNM Category | FIGO Stage | Regional Lymph Nodes (N) | TNM Category | FIGO Stage |
|---|---|---|---|---|
| ☐ NX | | Regional lymph nodes cannot be assessed | ☐ NX | |
| ☐ N0 | | No regional lymph node metastasis | ☐ N0 | |
| ☐ N1 | IIIC | Regional lymph node metastasis | ☐ N1 | IIIC |

| TNM Category | FIGO Stage | Distant Metastasis (M) | TNM Category | FIGO Stage |
|---|---|---|---|---|
| ☐ M0 | | No distant metastasis (no pathologic M0; use clinical M to complete stage group) | | |
| ☐ M1 | IVB | Distant metastasis (excluding adexa, pelvic, and abdominal tissue) | ☐ M1 | IVB |

# 高雄榮總婦癌團隊子宮惡性肉瘤臨床診療指引

**分期**

## CORPUS UTERI SARCOMA STAGING FORM

*(Carcinosarcomas should be staged as carcinomas)*

**Anatomic Stage · Prognostic Groups**

| | Clinical | | | | Pathologic | | | |
|---|---|---|---|---|---|---|---|---|
| | **GROUP** | **T** | **N** | **M** | **GROUP** | **T** | **N** | **M** |
| ☐ | I | T1 | N0 | M0 | I | T1 | N0 | M0 |
| ☐ | IA* | T1a | N0 | M0 | IA* | T1a | N0 | M0 |
| ☐ | IB* | T1b | N0 | M0 | IB* | T1b | N0 | M0 |
| ☐ | IC** | T1c | N0 | M0 | IC** | T1c | N0 | M0 |
| ☐ | II | T2 | N0 | M0 | II | T2 | N0 | M0 |
| ☐ | IIIA | T3a | N0 | M0 | IIIA | T3a | N0 | M0 |
| ☐ | IIIB | T3b | N0 | M0 | IIIB | T3b | N0 | M0 |
| ☐ | IIIC | T1-3 | N1 | M0 | IIIC | T1-3 | N1 | M0 |
| ☐ | IVA | T4 | Any N | M0 | IVA | T4 | Any N | M0 |
| ☐ | IVB | Any T | Any N | M1 | IVB | Any T | Any N | M1 |
| ☐ | Stage unknown | | | | Stage unknown | | | |

* Note: Stages IA and IB differ from those applied for leiomyosarcoma and endometrial stromal sarcoma.
** Note: Stage IC does not apply for leiomyosarcoma and endometrial stromal sarcoma.

### Prognostic Factors (Site-Specific Factors)

**Required For Staging:** None
**Clinically Significant:**
FIGO Stage: _____
Peritoneal cytology results: _____
Pelvic nodal dissection with number of nodes positive/examined: _____
Para-aortic nodal dissection with number of nodes positive/examined: _____
Percentage of non-endometrioid cell type in mixed histology tumors: _____
Omentectomy performed: _____

**Histologic Grade (G)** (also known as overall grade)

| | **Grading system** | | **Grade** |
|---|---|---|---|
| ☐ | 2 grade system | ☐ | Grade I or 1 |
| ☐ | 3 grade system | ☐ | Grade II or 2 |
| ☐ | 4 grade system | ☐ | Grade III or 3 |
| ☐ | No 2, 3, or 4 grade system is available | ☐ | Grade IV or 4 |

Endometrioid adenocarcinomas should be graded according to the degree of differentiation of the **adenocarcinoma** as follows:
☐ G1 5% **or** less of a non-squamous or non-morular solid growth pattern
☐ G2 6% **to** 50% of a non-squamous or non-morular solid growth pattern
☐ G3 **More** than 50% of a non-squamous or non-morular solid growth pattern

**Notes on Pathologic Grading**
1. **Notable** nuclear atypia, inappropriate for the architectural grade, raises the grade by one.
2. **Serous**, clear cell, and mixed mesodermal tumors are Grade 3.

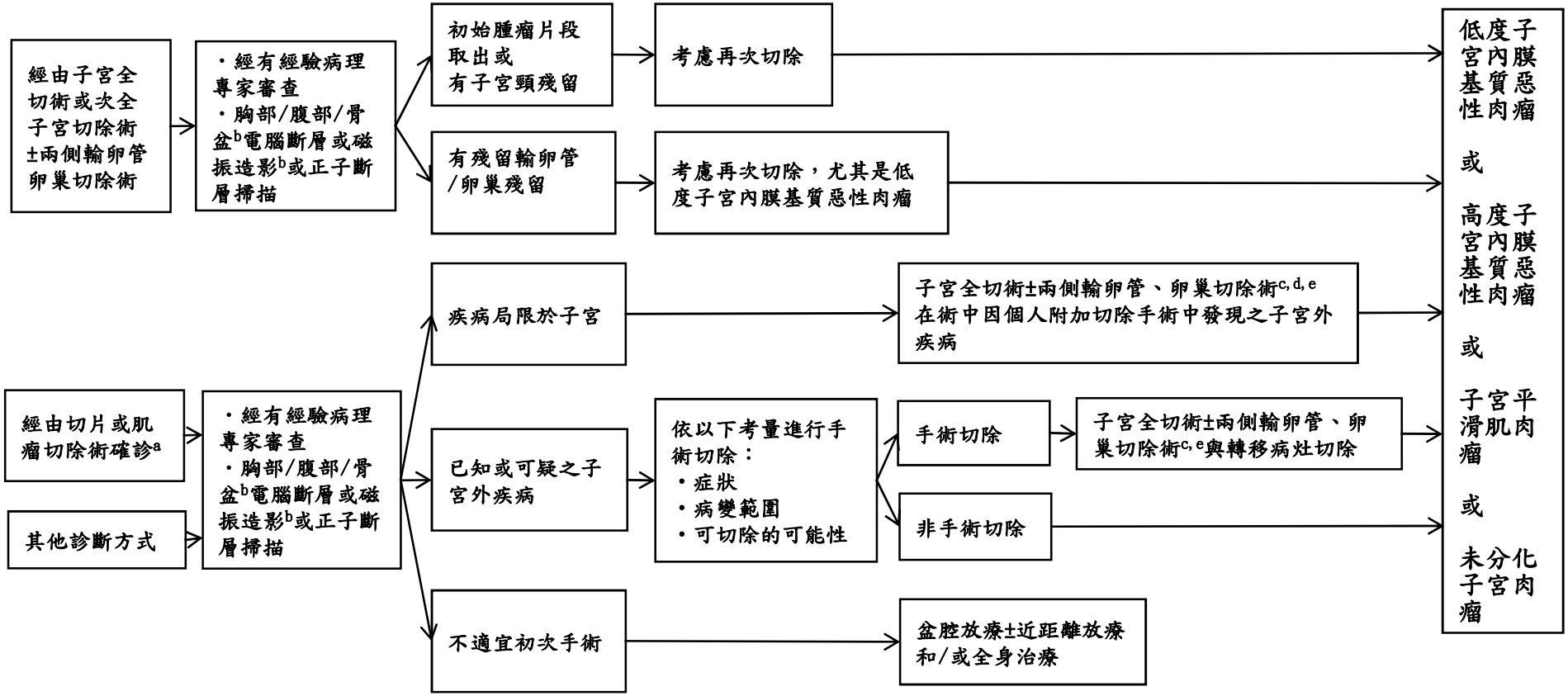
**Additional Descriptors**
**Lymphatic Vessel Invasion (L) and Venous Invasion (V)** have been combined into Lymph-Vascular Invasion (LVI) for collection by cancer registrars. The College of American Pathologists' (CAP) Checklist should be used as the primary source. Other sources may be used in the absence of a Checklist. Priority is given to positive results.
☐ Lymph-Vascular Invasion Not Present (absent)/Not Identified
☐ Lymph-Vascular Invasion Present/Identified
☐ Not Applicable
☐ Unknown/Indeterminate

**Residual Tumor (R)**
The absence or presence of residual tumor after treatment. In some cases treated with surgery and/or with neoadjuvant therapy there will be residual tumor at the primary site after treatment because of incomplete resection or local and regional disease that extends beyond the limit of ability of resection.
☐ RX Presence of residual tumor cannot be assessed
☐ R0 No residual tumor
☐ R1 Microscopic residual tumor
☐ R2 Macroscopic residual tumor

### General Notes:

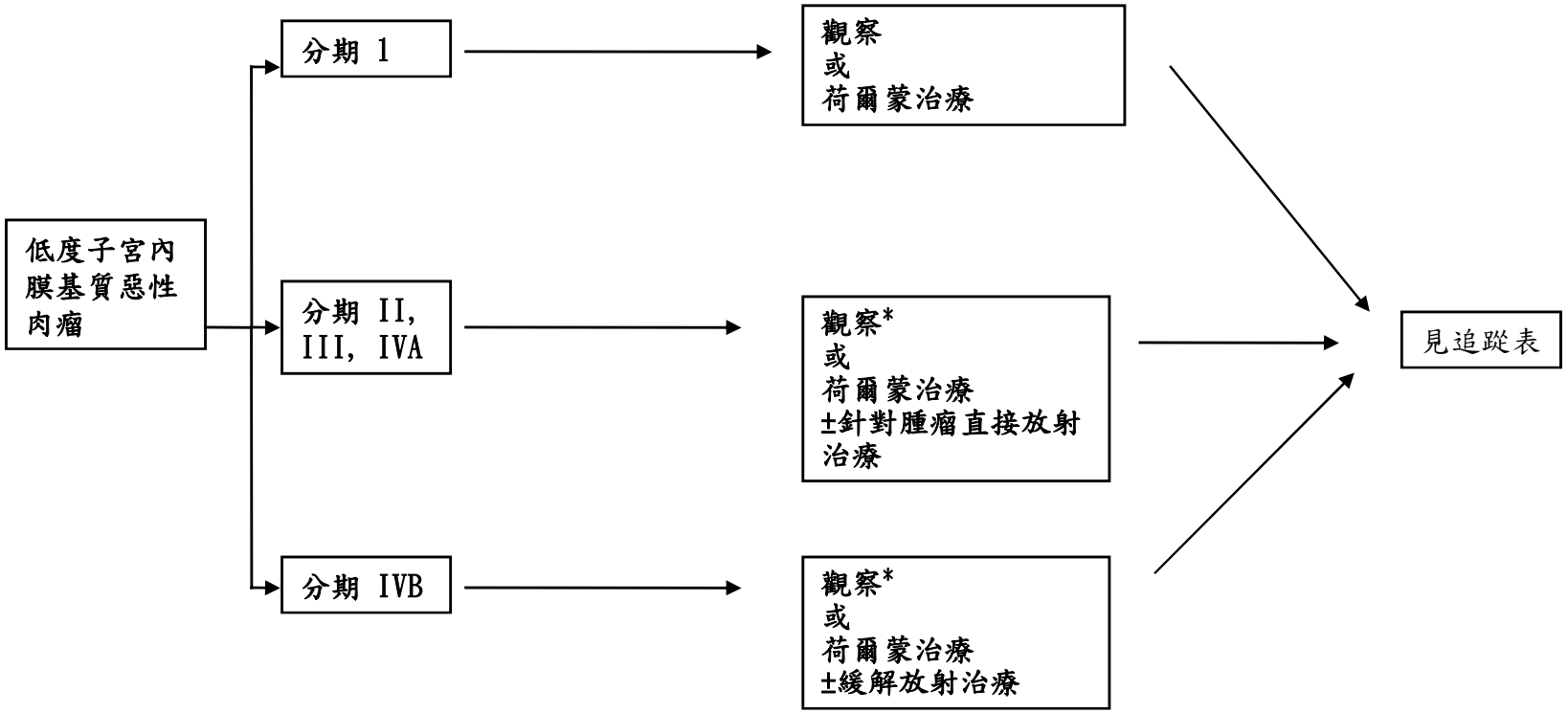
For identification of special cases of TNM or pTNM classifications, the "m" suffix and "y," "r," and "a" prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.
**m suffix** indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.
**y prefix** indicates those cases in which classification is performed during or following initial multimodality therapy. The cTNM or pTNM category is identified by a "y" prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The "y" categorization is not an estimate of tumor prior to multimodality therapy.
**r prefix** indicates a recurrent tumor when staged after a disease-free interval, and is identified by the "r" prefix: rTNM.
**a prefix** designates the stage determined at autopsy: aTNM.
**surgical margins** is data field recorded by registrars describing the surgical margins of the resected primary site specimen as determined only by the pathology report.
**neoadjuvant treatment** is radiation therapy or systemic therapy (consisting of chemotherapy, hormone therapy, or immunotherapy) administered prior to a definitive surgical procedure. If the surgical procedure is not performed, the administered therapy no longer meets the definition of neoadjuvant therapy.

初步臨床發現　額外檢查　　初級處理



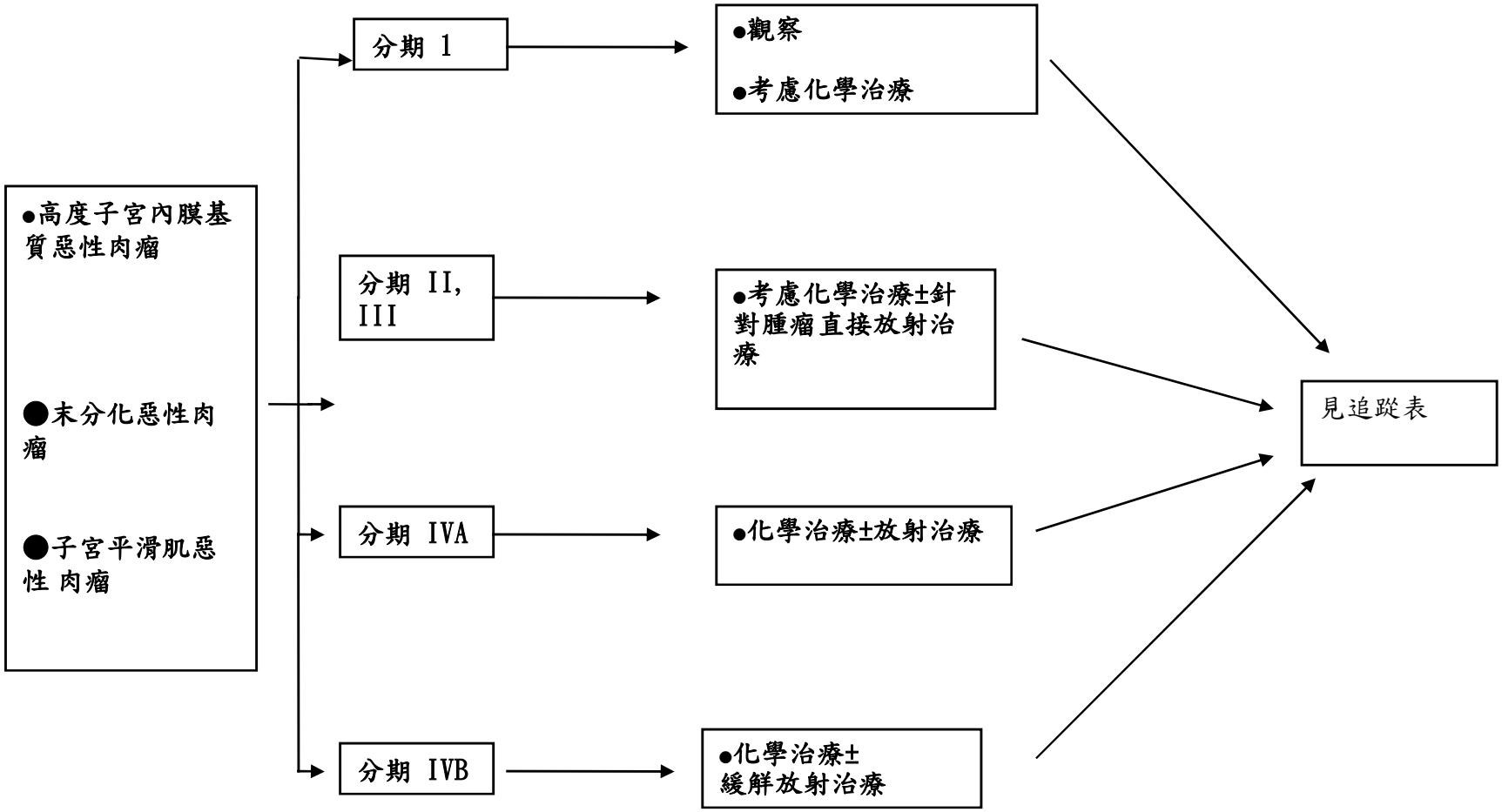

a. 術前影像學和切片可能有助於確定子宮肉瘤，雖然切片靈敏度小於子宮內膜癌。如果有基質惡性肉瘤的嫌疑，腫瘤片段取出應該避免。
b. 除非有禁忌，電腦斷層或磁振造影的對比要遵循準則。胸部斷層是不需要對比劑。
c. 卵巢摘除會因病人是否為已進入更年期而考慮。
d. 對於經TH/ BSO或切片標本後發現子宮肉瘤：建議依個人狀態進行影像及額外的手術切除
e. 子宮肉瘤應該整塊移除以獲取最佳結果；取出時應避免分碎組織

流程圖一



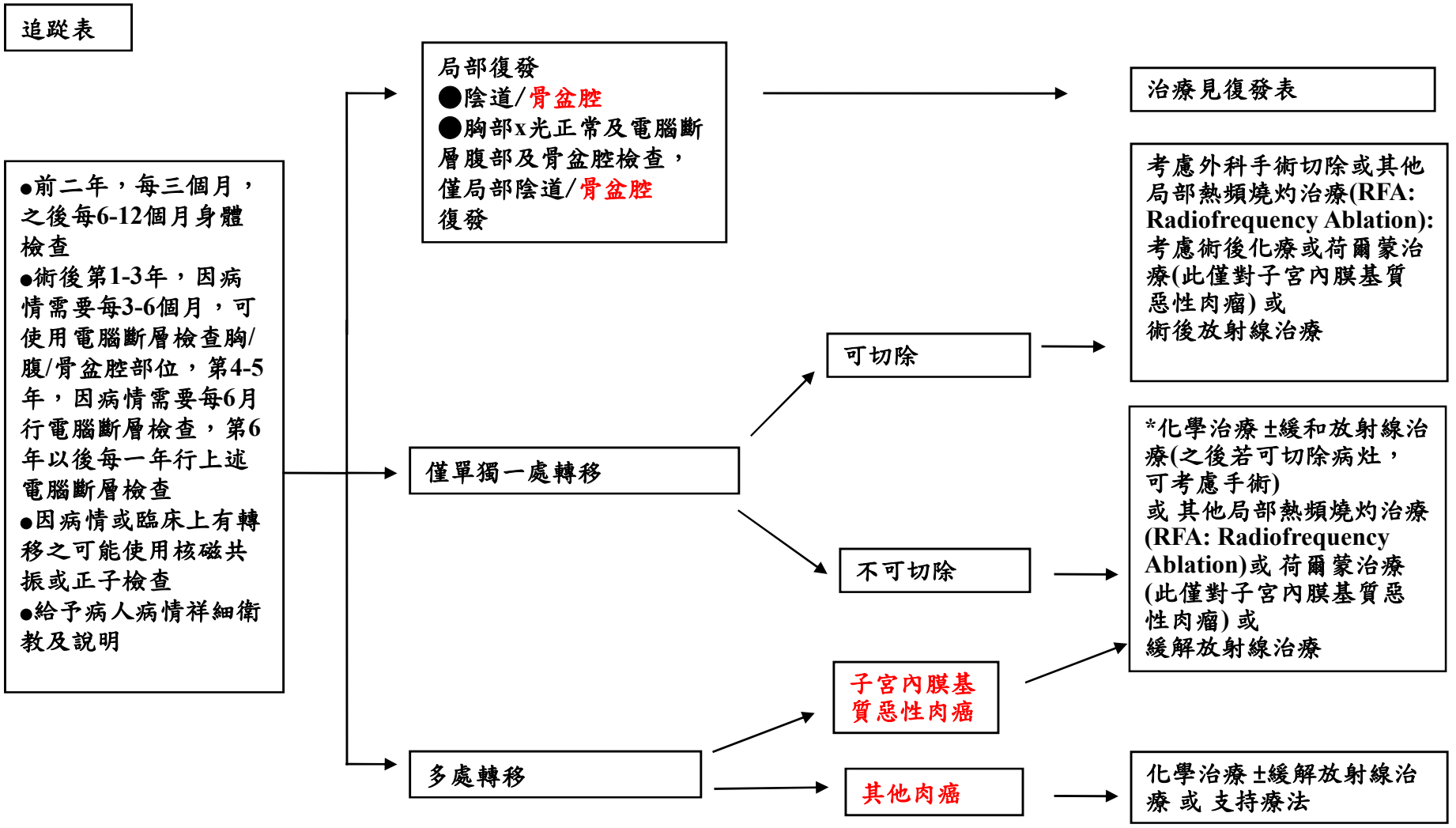

*若手術時已將病灶完全切除。

流程圖二


●高度子宮內膜基質惡性肉瘤
●末分化惡性肉瘤
●子宮平滑肌惡性 肉瘤
分期 1
分期 II, III
分期 IVA
分期 IVB
●觀察
●考慮化學治療
●考慮化學治療±針對腫瘤直接放射治療
●化學治療±放射治療
●化學治療± 緩解放射治療
見追蹤表

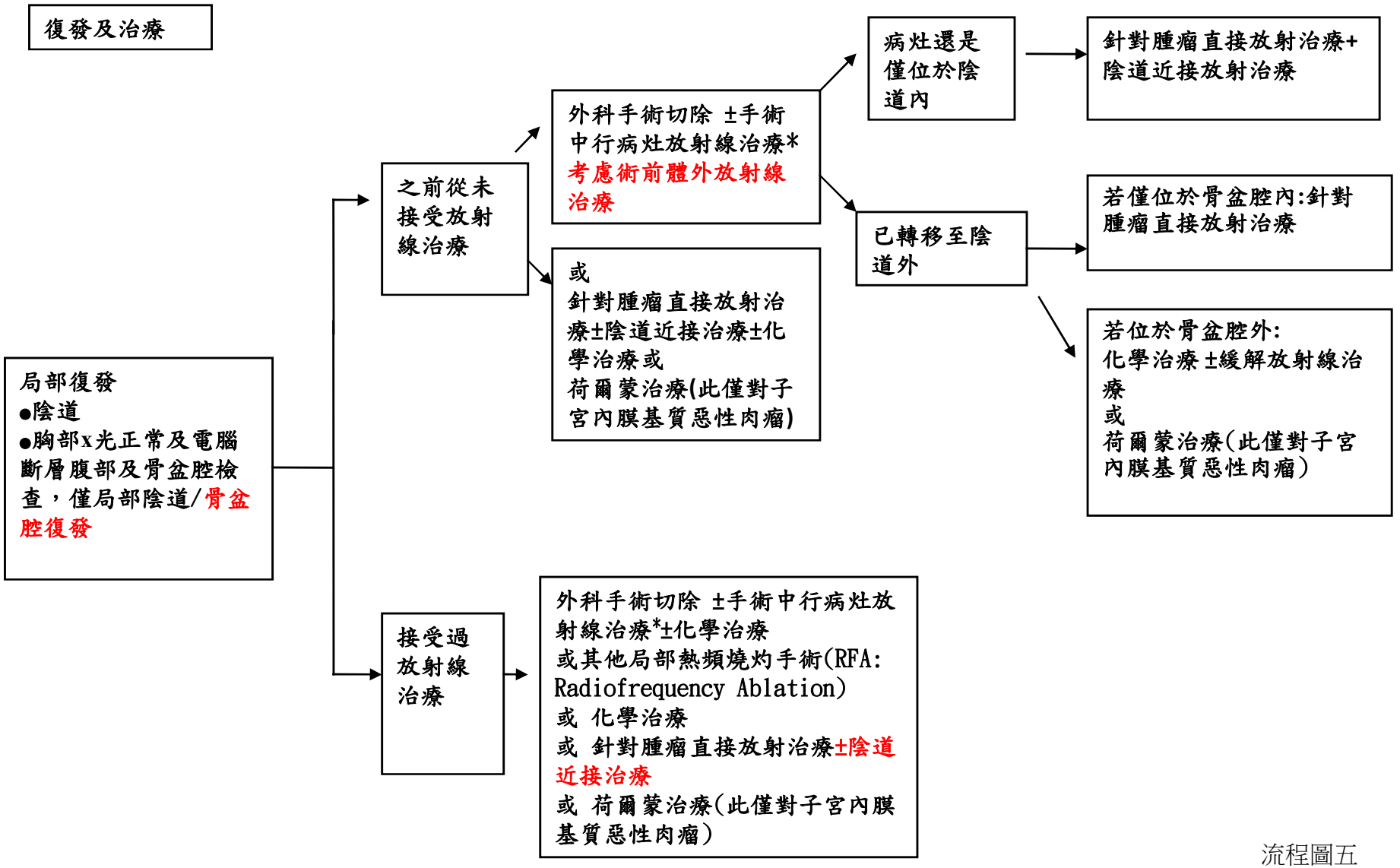
流程圖三

# 高雄榮總婦癌團隊子宮惡性肉瘤臨床診療指引




流程圖四

# 高雄榮總婦癌團隊子宮惡性肉瘤臨床診療指引




流程圖五

*手術中行病灶放射線治療目前在本科未有此項服務。

# 高雄榮總婦癌團隊子宮惡性肉瘤臨床診療指引

- 子宮惡性肉瘤之化學治療及荷爾蒙治療

**SYSTEMIC THERAPY FOR UTERINE SARCOMA[1]**
**(Clinical trials strongly recommended)**

**Combination regimens:**
- Docetaxel/gemcitabine (preferred for leiomyosarcoma)
- Doxorubicin/ifosfamide
- Doxorubicin/dacarbazine
- Gemcitabine/dacarbazine
- Gemcitabine/vinorelbine

**Single-agent options:**
- Dacarbazine
- Doxorubicin
- Epirubicin
- Eribulin
- Gemcitabine
- Ifosfamide
- Liposomal doxorubicin
- Pazopanib
- Temozolomide
- Trabectedin[3]
- Vinorelbine (category 2B)
- Docetaxel (category 3)

**HORMONE THERAPY**
**(For Low-grade ESS or Hormone Receptor Positive (ER/PR) uLMS[2]):**
- Medroxyprogesterone acetate (category 2B for ER/PR positive uLMS)
- Megestrol acetate (category 2B for ER/PR positive uLMS)
- Aromatase inhibitors
- GnRH analogs (category 2B for low-grade ESS and ER/PR positive uLMS)

# 子宮肉癌分類

**UTERINE SARCOMA CLASSIFICATION[1]**

- **Low-grade endometrial stromal sarcoma (ESS)[2]**
- **High-grade ESS[3]**
- **Undifferentiated uterine sarcoma (UUS)[4]**
- **Uterine leiomyosarcoma (uLMS)[5]**

**Other Rare Uterine Mesenchymal Sarcoma Subtypes:**
**(see the NCCN Guidelines for Soft Tissue Sarcoma)**

- **Adenosarcomas**
- **PEComas**
- **Rhabdomyosarcoma**

| Adjuvant /or Salvage 化學治療 | | |
|---|---|---|
| protocol | 劑量 | 時程 |
| DTIC<br>(Decarbazine,<br>Epirubicin, Platinum,<br>Ifosfamide) | Dacarbazine 200mg qd x 5 days<br>Epirubicin 50mg/$m^2$ st<br>Carboplatin AUC x5mg st, CCR＜60<br>（Cisplatin 50mg/$m^2$ st, CCR≧60）<br>Ifosfamide 4mg/$m^2$ st | Q3W x 6 cycles |
| Gemcitabine+Docetaxel | D1/D8 Gemcitabine 675-900 mg/$m^2$<br>D8 Docetaxel 75-100 mg/$m^2$ | Q4W x 6 cycles |
| Paclitaxel+Cisplatin | Paclitaxel 175 mg/$m^2$<br>Cisplatin 50 mg/$m^2$ | Q3W x 6 cycles |
| Paclitaxel+Carboplatin | Paclitaxel 175 mg/$m^2$<br>Carboplatin AUC( 5MG) | Q3W x 6 cycles |

321. Trope CG, Abeler VM, Kristensen GB. Diagnosis and treatment of sarcoma of the uterus. A review. Acta Oncol 2012;51:694-705. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22793037.

322. Amant F, Coosemans A, Debiec-Rychter M, et al. Clinical management of uterine sarcomas. Lancet Oncol 2009;10:1188-1198. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19959075.

323. Novetsky AP, Powell MA. Management of sarcomas of the uterus. Curr Opin Oncol 2013;25:546-552. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23942299.

324. Lax SF. Molecular genetic changes in epithelial, stromal and mixed neoplasms of the endometrium. Pathology 2007;39:46-54. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17365822.

325. Huang HY, Ladanyi M, Soslow RA. Molecular detection of JAZF1-JJAZ1 gene fusion in endometrial stromal neoplasms with classic and variant histology: evidence for genetic heterogeneity. Am J Surg Pathol 2004;28:224-232. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15043312.

326. Leath CA, 3rd, Huh WK, Hyde J, Jr., et al. A multi-institutional review of outcomes of endometrial stromal sarcoma. Gynecol Oncol 2007;105:630-634. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17320937.

327. Koontz JI, Soreng AL, Nucci M, et al. Frequent fusion of the JAZF1 and JJAZ1 genes in endometrial stromal tumors. Proc Natl Acad Sci U S A 2001;98:6348-6353. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11371647.

328. Lee CH, Marino-Enriquez A, Ou W, et al. The clinicopathologic features of YWHAE-FAM22 endometrial stromal sarcomas: a histologically high-grade and clinically aggressive tumor. Am J Surg Pathol 2012;36:641-653. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22456610.

329. Sciallis AP, Bedroske PP, Schoolmeester JK, et al. High-grade endometrial stromal sarcomas: a clinicopathologic study of a group of tumors with heterogenous morphologic and genetic features. Am J Surg Pathol 2014;38:1161-1172. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25133706.

330. Kurman RJ, Carcangiu ML, Herrington CS, Young RH. WHO Classification of Tumours of Female Reproductive Organs. Fourth Edition. Vol. 6: World Health Organization; 2014.

331. Zivanovic O, Leitao MM, Iasonos A, et al. Stage-specific outcomes of patients with uterine leiomyosarcoma: a comparison of the international Federation of gynecology and obstetrics and american joint committee on cancer staging systems. J Clin Oncol 2009;27:2066-2072. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19255317.

332. Prat J. FIGO staging for uterine sarcomas. Int J Gynaecol Obstet 2009;104:177-178. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19135669.

333. Rauh-Hain JA, del Carmen MG. Endometrial stromal sarcoma: a systematic review. Obstet Gynecol 2013;122:676-683. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23921879.

334. Group EESNW. Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2012;23 Suppl 7:vii92-99. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22997462.

335. Barney B, Tward JD, Skidmore T, Gaffney DK. Does radiotherapy or lymphadenectomy improve survival in endometrial stromal sarcoma? Int J Gynecol Cancer 2009;19:1232-1238. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19823060.

336. Shah JP, Bryant CS, Kumar S, et al. Lymphadenectomy and ovarian preservation in low-grade endometrial stromal sarcoma. Obstet Gynecol 2008;112:1102-1108. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18978112.

337. Signorelli M, Fruscio R, Dell'Anna T, et al. Lymphadenectomy in uterine low-grade endometrial stromal sarcoma: an analysis of 19 cases and a literature review. Int J Gynecol Cancer 2010;20:1363-1366. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21051978.

338. Reichardt P. The treatment of uterine sarcomas. Ann Oncol 2012;23 Suppl 10:x151-157. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22987952.

339. Thanopoulou E, Judson I. Hormonal therapy in gynecological sarcomas. Expert Rev Anticancer Ther 2012;12:885-894. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22845404.

340. Pink D, Lindner T, Mrozek A, et al. Harm or benefit of hormonal treatment in metastatic low-grade endometrial stromal sarcoma: single center experience with 10 cases and review of the literature. Gynecol Oncol 2006;101:464-469. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16368128.

341. Reich O, Regauer S. Estrogen replacement therapy and tamoxifen are contraindicated in patients with endometrial stromal sarcoma. Gynecol Oncol 2006;102:413-414; author reply 414. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16712906.

342. Mansi JL, Ramachandra S, Wiltshaw E, Fisher C. Endometrial stromal sarcomas. Gynecol Oncol 1990;36:113-118. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2295442.

343. Berchuck A, Rubin SC, Hoskins WJ, et al. Treatment of endometrial stromal tumors. Gynecol Oncol 1990;36:60-65. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2295453.

344. Weitmann HD, Knocke TH, Kucera H, Pötter R. Radiation therapy in the treatment of endometrial stromal sarcoma. Int J Radiat Oncol Biol Phys 2001;49:739-748. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11172957.

345. Brenner DJ, Hall EJ. Computed tomography--an increasing source of radiation exposure. N Engl J Med 2007;357:2277-2284. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18046031.

346. Sampath S, Schultheiss TE, Ryu JK, Wong JY. The role of adjuvant radiation in uterine sarcomas. Int J Radiat Oncol Biol Phys 2010;76:728-734. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19700247.

347. Mahdavi A, Monk BJ, Ragazzo J, et al. Pelvic radiation improves local control after hysterectomy for uterine leiomyosarcoma: a 20-year experience. Int J Gynecol Cancer 2009;19:1080-1084. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19820372.

348. Giuntoli RL, 2nd, Metzinger DS, DiMarco CS, et al. Retrospective review of 208 patients with leiomyosarcoma of the uterus: prognostic indicators, surgical management, and adjuvant therapy. Gynecol Oncol 2003;89:460-469. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12798712.

349. Dusenbery KE, Potish RA, Judson P. Limitations of adjuvant radiotherapy for uterine sarcomas spread beyond the uterus. Gynecol Oncol 2004;94:191-196. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15262141.

350. Ricci S, Giuntoli RL, 2nd, Eisenhauer E, et al. Does adjuvant chemotherapy improve survival for women with early-stage uterine leiomyosarcoma? Gynecol Oncol 2013;131:629-633. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24016408.

351. Hensley ML, Wathen JK, Maki RG, et al. Adjuvant therapy for high-grade, uterus-limited leiomyosarcoma: results of a phase 2 trial (SARC 005). Cancer 2013;119:1555-1561. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23335221.

352. Maki RG, Wathen JK, Patel SR, et al. Randomized phase II study of gemcitabine and docetaxel compared with gemcitabine alone in patients with metastatic soft tissue sarcomas: results of sarcoma