Taipei Veterans General Hospital Practice Guidelines for Gynecologic Cancer

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目錄

前言

95年癌症委員會與本院癌症治療專家，共同參與討論制定癌症治療準則，於95年5月制定本院子宮頸癌治療準則，婦癌多專科醫療團隊以國家衛生研究院婦癌診療指引及NCCN Guideline治療準則為基準，於96年10月始召開本院第一次子宮頸癌團隊會議，腫瘤個案管理師並於96年10月針對新診斷子宮頸癌個案開始收案，為服務更多婦癌病患，於98年1月開始進行子宮內膜癌個案收案(不含惡性肉瘤，99年開始MMMT併入子宮內膜癌收案)，99年1月開始，針對卵巢癌個案收案(限上皮性卵巢癌，於100年1月開始進行非上皮性卵巢癌收案)，101年1月開始將腹膜癌及輸卵管癌列入卵巢癌診療指引，102年10月開始新增外陰、陰道癌、絨毛膜疾病/絨毛膜腫瘤子宮體肉瘤診療指引並開始收案，為服務全院全癌個案，103年01月開始針對以上婦科癌症外之其他婦癌列入收案，團隊成員經多次會議修訂本院婦癌診療共識，並至少每年修訂診療指引一次，據以公告週知以供查閱。

前言

備註：各癌收案時間

- 96年10月-子宮頸癌
- 98年01月-子宮內膜癌(不含惡性肉瘤，MMMT於99年1月併入子宮內膜癌收案)
- 99年01月-上皮性卵巢癌(不含非上皮性卵巢癌)
- 100年1月-非上皮性卵巢癌
- 101年1月-腹膜癌及輸卵管
- 102年10月-外陰、陰道、絨毛膜腫瘤及子宮體肉瘤
- 103年01月-其他婦癌

新診斷、新復發個案收案定義：含class 1~3病人

- class 1：本院診斷，於**本院接受全部或部分首次治療療程**，含拒絕治療決定不治療
- class 2：外院診斷，於**本院接受全部或部分首次治療療程**，含拒絕治療決定不治療
- class 3：外院診斷，於外院接受全部首次治療療程，**首次復發**至本院求治

Cervical Cancer

分期	診療指引	全身性藥物	持續或復發性疾病	追蹤	核心指標

分期 (FIGO 2018)

FIGO	Criteria
I	The Carcinoma is strictly confined to the crervix(extension to the uterine corpus should be disregarded)
IA	Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion <5mm[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[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
II	The 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 involvement
IIA1	Invasive carcinoma ≤4 cm in greatest dimension
IIA2	Invasive carcinoma >4 cm in greatest dimension
IIB	With parametrial involvement but not up to the pelvic wall
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 para-aortic lymph nodes[c]
IIIA	The carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney (unless known to be due to another cause)
IIIC	Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent (with r and p notations)[c]
IIIC1	Pelvic lymph node metastasis only
IIIC2	Para-aortic lymph node metastasis
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 to adjacent pelvic organs
IVB	Spread to distant organs

When in doubt, the lower staging should be assigned

[a]Imaging and pathology can be used, where available, to supplement clinical findings with respect to tumor size and extent, in all stages.

[b]The involvement of vascular/lymphatic spaces does not change the staging. The lateral extent of the lesion is no longer considered.

[c]Adding notation of r (imaging) and p (pathology) to indicate the findings that are used to allocate the case to Stage IIIC. Example: if imaging indicates pelvic lymph node metastasis, the stage allocation should be Stage IIIC1r, and if confirmed by pathologic findings, it wound be Stage IIIC1p. The type of imaging modality or pathology technique used should always be documented.

Cervical Cancer

TNM	FIGO	Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Cervical carcinoma confined to the uterus (extension to corpus should be disregarded)
-T1a	IA	Invasive carcinoma diagnosed only by microscopy. Stromal invasion with a maximum depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less. Vascular space involvement, venous or lymphatic, dose not affect classification.
--T1a1	IA1	Measured stromal invasion of 3.0 mm or less in depth
--T1a2	IA2	Measured stromal invasion of more than 3.0 mm and not more than 5.0 mm
-T1b	IB	Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a/IA2. Includes all macroscopically visible lesions, even those with superficial invasion.
--T1b1	IB1	Clinically visible lesion 4.0 cm or less in greatest dimension
--T1b2	IB2	Clinically visible lesion more than 4.0 cm in greatest dimension
T1b3	IB3	Invasive carcinoma >4 cm in greatest dimension
T2	II	Cervical carcinoma invading beyond the uterus but not to the pelvic wall or to lower third of the vagina
-T2a	IIA	Tumor without parametrial invasion
--T2a1	IIA1	Clinically visible lesion 4.0cm or less in greatest dimension
--T2a2	IIA2	Clinically visible lesion more than 4.0cm in greatest dimension
-T2b	IIB	Tumor with parametrial invasion
T3	III	Tumor extending to the pelvic sidewall* and/or involving the lower third of the vagina and/or causing hydronephrosis or nonfunctioning kidney
-T3a	IIIA	Tumor involving the lower third of the vagina but not extending to the pelvic wall
-T3b	IIIB	Tumor extending to the pelvic wall and/or causing hydronephrosis or nonfunctioning kidney
T4	IVA	Tumor invading the mucosa of the bladder or rectum and/or extending beyond the true pelvis (bullous edema is not sufficient to classify a tumor as T4)
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
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 greatest dimension) to pelvic lymph nodes
N1a	IIIC1	Regional lymph node metastasis (>2.0 mm in greatest dimension) 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 greatest dimension) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2a	IIIC2	Regional lymph node metastasis (>2.0 mm in greatest dimension) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
M0		No distant metastasis
cM1	IVB	Distant metastasis (including peritoneal spread or involvement of the supraclavicular, mediastinal, or distant lymph nodes; lung; liver; or bone)

子宮頸癌診療指引

術前準備

- Blood analysis
- Pathology proved
- Tumor marker
- IVP/CT/MRI/PET-CT
- Cystoscopy/Colonoscopy if clinically indicated

Cervical Cancer

子宮頸癌診療指引

FIGO Early Stage (IA to IIA, selective IIB)

Stage	Treatment Plan	
IA1	no LVSI	• cold knife with negative margin (if fertility preservation is desired) or extrafascial total hysterectomy (No PLND)
	with LVSI	• Radical trachelectomy or cold knife conization with negative margins (if fertility preservation is desired) + PLND • modified radical hysterectomy + PLND • Pelvic R/T+ brachytherapy
IA2	• Modified radical hysterectomy + PLND ± PALNS • Radical hysterectomy + PLND ± PALNS • Pelvic R/T+Brachytherapy (total point A dose: 75-80 Gy) • Radical trachelectomy + PLND ± PALNS (if fertility preservation is desired)	
IB1 IB2 IIA1	• Radical hysterectomy + PLND ± PALNS • Pelvic R/T (Point A 80-85 Gy) + brachytherapy ± concurrent platinum- containing chemotherapy • Radical trachelectomy (tumor ≦ 2 cm, stage IB1 only) + PLND ± PALNS (if fertility preservation is desired)	
IB3 IIA2 Selective IIB	• Radical hysterectomy + PLND ± PALNS • Neoadjuvant chemotherapy + Radical hysterectomy + PLND ± PALNS • CCRT + brachytherapy (Point A ≧80-85 Gy, platinum-containing C/T)	

- BSO considered if: age > 50 y/o, adenocarcinoma, and poorly differentiated carcinoma.
- Treatment guideline for other cell types (adenosarcoma、clear cell、MMMT、sarcoma) will be planned after evaluation and discussion by the gynecology oncology committee.
- Ovarian transposition during RH if adjuvant radiotherapy considered (No oophorectomy).
- Laparoscopic or robotic surgery is acceptable for stage IA1, IA2, IB1 and IIA1(<2cm). Given recently presented findings of significantly poorer survival outcomes with laparoscopic/robotic approach compared to the open approach in a randomized trial of women with early-stage cervical cancer, women should be carefully counseled about the short-term versus long-term outcomes and oncologic risks of the different surgical approaches.
- FIGO期別IB2或以上的子宮頸癌病人，骨盆腔淋巴結摘除宜≧12顆
- Point A dose is referred to the summation of external beam radiotherapy and brachytherapy (low dose rate equivalent) dose.

子宮頸癌診療指引

FIGO Advanced Stage (by imaging results: stage IIBr, IIIr, IVAr, IVBr)	
Stage	Treatment Plan
IIBr	• CCRT + brachytherapy (Point A ≧80-85 Gy, platinum-containing C/T) • Radical hysterectomy + PLND + PALNS
IIIAr IIIBr IIICr	• CCRT + brachytherapy (Point A ≧80-85 Gy, platinum-containing C/T) ± consolidation chemotherapy • Radical hysterectomy + PLND + PALNS • Surgical staging of nodal status (laparotomy, extraperitoneal or laparoscopic lymph node sampling)
IVAr	• CCRT + brachytherapy (Point A ≧80-85 Gy, platinum-containing C/T) ± consolidation chemotherapy
IVBr	• Systemic therapy ± radiotherapy (biopsy confirmation as clinically indicated)

子宮頸癌診療指引

FIGO早期不能手術患者	
Step 1	Lymph Node Assessment • Image Study (CT, MRI or PET/CT) ± FNA
Step 2	**Lymph Node (-)** • CCRT (platinum-containing chemotherapy) + brachytherapy
	Lymph Node (+) **Pelvic LN (+), para-aortic LN (-)** • CCRT (Platinum-containing chemotherapy) + brachytherapy ± Para-aortic boost (Point A ≧85Gy for large or ≧ 80Gy for small volume tumor) **Pelvic LN (+), para-aortic LN (+)** • CCRT (Platinum-containing chemotherapy) + brachytherapy + Para-aortic boost (Point A ≧85Gy for large or ≧ 80Gy for small volume tumor)

子宮頸癌診療指引

Prognostic Risk Factors	
High Risk	• LN (+) • Parametrial involvement (+) • Surgical margin (+)
Intermediate Risk	• Bulky tumor size (≥ 4 cm) • LVSI (+) • DSI (+)
Others	• Age • Diploidy • Differentiation • Histological type (Adenocarcinoma)

Cervical Cancer

子宮頸癌診療指引›輔助治療

手術後的輔助治療				
LN	Parametrium	Margin	Intermediate risk factor	Management
(−)	(−)	(−)	LVSI (−) DSI (−) Bulky size(−)	• Observation
			LVSI (+) and/or DSI (+) and/or Bulky size (+)	• Radiotherapy ± concurrent platinum-containing chemotherapy or • Observation (only 1 risk factor)
	(−)	(+)		• CCRT ± vaginal brachytherapy
	(+)	(−)		• CCRT ± vaginal brachytherapy
		(+)		
(+)				• CCRT ± vaginal brachytherapy or • Systemic therapy ± radiotherapy

備註

- For adenocarcinoma, adjuvant systemic treatment may be considered in stage IB; IB2 with intermediate risk → CCRT for primary treatment followed by systemic chemotherapy
- If vaginal cut end (+) → additional radiotherapy required
- 子宮頸癌患者以放射治療或合併化學及放射治療為首次治療者，宜於診斷後30天(含) 內開始，於接受治療63天(含)內完成
- FIGO期別第I~IVA期子宮頸癌治療結束180天(含)內宜接受抹片追蹤
- Definition of Deep stroma invasion [DSI (+)] : DSI > 20 mm or >50%

子宮頸癌診療指引

Fertility Sparing Surgery

- Radical trachelectomy or conization (margin free)
- Treatment should be individualized; criteria are as follow:
  - Young age
  - Cell type: Squamous cell carcinoma
  - Post conization: DSI ≤ 10mm/LVSI (−)/Tumor size ≤ 20 mm
- Pelvic LN: (−) by image study
- 當病患強烈要求保留生育能力，經過詳細分析及病患了解相關之風險，病患可密切配合及追蹤

子宮頸癌診療指引

子宮切除後意外發現為癌症者			
Stroma Invasion	Surgical Margin	LN status (Image study)	Management
Depth < 3 mm with LVSI (-)	NA		• Observation
Depth < 3mm with LVSI (+) or Depth ≧ 3mm	(−)	(−)	• Re-operation* or • Pelvic R/T + brachytherapy or • CCRT
		(+)	• LND + CCRT or • CCRT or • Re-operation*
	(+)	(−)	• CCRT ± vaginal brachytherapy or • Radiotherapy or • Re-operation*
		(+)	• LND + CCRT or • CCRT or • Re-operation*

* Re-operation includes the following:
- Radical parametrectomy + Upper vaginectomy + PLND ± PALNS
- Image study consistent with the following:
  - No parametrial invasion
  - No pelvic side-wall invasion
  - No rectal or bladder invasion

子宮頸癌診療指引

Small cell neuroendocrine tumors of the cervix (NECC)		
Disease status		Treatment Plan
Disease confined to cervix	Tumor ≤4 cm	• Radical hysterectomy + PLND ± PALNS → chemotherapy or CCRT • CCRT+ brachytherapy ± additional systemic therapy
	Tumor >4 cm	• CCRT+ brachytherapy ± additional systemic therapy • Neoadjuvant chemotherapy + interval hysterectomy ± CCRT or radiotherapy • Neoadjuvant chemotherapy + CCRT + brachythearpy
Locally advanced disease (IIA-IVA)		• CCRT+ brachytherapy ± chemotherapy • Neoadjuvant chemotherapy + CCRT + brachytherapy
Metastatic disease (IVB)		• Systemic therapy ± radiotherapy

全身性藥物處方建議

子宮頸癌化療處方適應症

- Adjuvant chemotherapy for postoperative lymph node metastasis
- Neoadjuvant chemotherapy for bulky tumor
  - Followed by surgery
  - Followed by radiotherapy
- Concurrent chemoradiotherapy
  - Early bulky tumor followed by surgery
  - Postoperative with parametrial involvement and lymph node metastasis
  - Local advanced cancer
- Consolidation chemotherapy after concurrent chemoradiotherapy for advanced cancer
- If distant metastasis or recurrence → Systemic chemotherapy ± Palliative Radiotherapy
- Palliative chemotherapy for distant, recurrent, or metastatic cancer

全身性藥物處方建議

Neoadjuvant Chemotherapy (先輔助化療)

Regimens	Dosage	Route	Day	Interval
1. Cisplatin only RH performed on 3rd day after completing chemotherapy				
Cisplatin	40 mg/m^2 (at least 25 mg/m^2)	IVD 1 hr	Day 1	QW
2. Paclitaxel + Cisplatin, Q10D, x3 cycles RH performed within 3 weeks after completing chemotherapy				
Paclitaxel Cisplatin	60 mg/m^2 60 mg/m^2	IVD 1.5 hr IVD 1 hr	Day 1 Day 1	Q10D

CCRT (同步化學放射治療)

Regimens	Dosage	Route	Day	Interval
1. **Cisplatin** Only, QW (preferred regimen)				
Cisplatin	40 mg/m^2	IVD 1 hr	Day 1	QW
2. **Carboplatin**, if patient is cisplatin intolerant				
Carboplatin	AUC 2	IVD 1 hr	Day 1	QW

全身性藥物處方建議

Radiation therapy + chemotherapy (合併化學放射治療)

Regimens	Dosage	Route	Day	Interval
1. **Cisplatin + Paclitaxel**				
Paclitaxel Cisplatin	175 mg/m^2 50 mg/m^2	IVD 3 hr IVD 1 hr	Day 1 Day 1	Q3W
2. **Cisplatin + Gemcitabine**				
Gemcitabine Cisplatin	1000 mg/m^2 50 mg/ m^2	IVD 30 mins IVD 1hr	D1, D8 D1	Q3W
3. **Cisplatin + docetaxel**				
Cisplatin Docetaxel	30 mg/m2 30 mg/m2	IVD 1 hr IVD 1 hr	Day 1 Day 1	QW
4. **Cisplatin + 5FU**				
5-FU Cisplatin	1000 mg/m2 50 mg/m^2	IVD for 24 hr IVD 1hr	D1-D5	Q3W
5. **POB**: Not recommended, do not provide superior results, but treatment toxicities could increase. Bleomycin 累積劑量不可＞150mg				
Cisplatin Vincristine Bleomycin	50 mg/m^2 1 mg/m^2 15 mg	IVD 1 hr IVD 15-30 mins IVD 15 mins	Day 1-3	

全身性藥物處方建議

Consolidation Chemotherapy Regimen: (鞏固化療)

Regimens	Dosage	Route	Day	Interval
1. **Ifosfamide + Cisplatin**, x6 cycles				
Ifosphamide Cisplatin or Ifosphamide Cisplatin	5 g/m^2 50 mg/m^2 or 1 g/m^2 50 mg/m^2	IVD 24 hrs IVD 1 hr or IVD 24 hrs IVD 1 hr	Day 1 Day 1 or Day 1-3 Day 1	Q3W
2. **Paclitaxel + Cisplatin**, x6 cycles				
Paclitaxel Cisplatin	175 mg/m2 50 mg/m2	IVD 3 hrs IVD 1 hr	Day 1 Day 1	Q3W
3. **Topotecan + Platinum**, x6 cycles Cisplatin考量毒性，臨床建議用於第一天、Carboplatin考量毒性，臨床建議用於第三天。				
Topotecan Cisplatin or Carboplatin (CCr<60)	0.75 mg/m^2 50 mg/m^2 AUC 5	IVD 30 mins IVD 1hr	Day 1-3 Day 1 Day 3	Q3W
4. **Gemcitabine + Cisplatin**, x6 cycles				
Gemcitabine Cisplatin	1000 mg/m^2 50 mg/m^2	IVD 30 mins IVD 1 hr	Day 1, 8 Day 1	Q3W
5. **Topotecan + Cisplatin**, x6 cycles				
Topotecan Cisplatin	2 or 2.5 mg/m^2 40 mg/m^2	IVD IVD 1 hr	Day 1, 8, 15 Day 1, 8, 15	Q3W

Cervical Cancer

全身性藥物處方建議

Disseminated or Recurrent Disease Chemotherapy Regimen: Commonly used Regimen for Squamous Cell Carcinoma

Regimens	Dosage	Route	Day	Interval
1. **Paclitaxel + Cisplatin, QW**				
Paclitaxel Cisplatin	175 mg/m^2 50 mg/m^2	IVD 3 hrs IVD 1 hr	Day 1 Day 1	QW2
2. **Paclitaxel + Cisplatin ± Bevacizumab, Q3W** 備註: Bevacizumab可和化療同天施打(GOG240)				
Paclitaxel Cisplatin Bevacizumab	175 or 135 mg/m^2 50 mg/m^2 7.5-15 mg/kg	IVD 3 hrs IVD 1 hr IVD	Day 1 Day 1	Q3W
3. **Topotecan + Cisplatin, Q3W**				
Topotecan Cisplatin	0.75 mg/m^2 50 mg/m^2	IVD 30 mins IVD 1 hr	Day 1-3 Day 1	Q3W
4. **Topotecan + Cisplatin, QW**				
Topotecan Cisplatin	2 or 2.5 mg/m^2 40 mg/m^2	IVD IVD 1 hr	Day 1, 8, 15 Day 1	QW
5. **Topotecan+ Paclitaxel ± Bevacizumab, Q3W**				
Paclitaxel Topotecan Bevacizumab	175 mg/m^2 0.75 mg/m^2 7.5- 15 mg/kg	IVD 3 hrs IVD 30 min IVD	Day 1 Day 1-3	Q3W
6. **Topotecan + Paclitaxel**, Q3W				
Topotecan Paclitaxel	0.75 mg/m^2 1 75 mg/m^2	IVD 30 mins IVD 3 hr	Day 1-3 Day 1	Q3W

Regimens	Dosage	Route	Day	Interval
7. **Ifosfamide + Cisplatin, Q3W**				
Ifosfamide Cisplatin	5 g/m^2 50 mg/m^2	IVD 24 hrs IVD 1 hr	Day 1 Day 1	Q3W
8. **Gemcitabine + Cisplatin, Q3W**				
Gemcitabine Cisplatin	1000 mg/m^2 50 mg/m^2	IVD 30 mins IVD 1 hr	Day 1, 8 Day 1	Q3W
9. **Epirubicin + Ifosfamide + Cisplatin, Q3W**				
Epirubicin Ifosfamide Cisplatin	50 mg/m^2 1 g/m^2 50 mg/m2	IVD IVD 24 hrs IVD 1 hr	Day 1 Day 1-3 Day 1	Q3W
10. **Paclitaxel + Ifosfamide + Cisplatin, Q3W x6 cycles**				
Paclitaxel Ifosfamide Cisplatin	175 mg/m^2 1 g/m^2 50 mg/m^2	IVD 3 hrs IVD 24 hrs IVD 1 hr	Day 1 Day 1-3 Day 1	Q3W
11. **Irinotecan+ Cisplatin**				
Irinotecan Cisplatin	60 mg/m^2 60 mg/m^2	IVD IVD 1 hr	Day 1, 8, 15 Day 1	
12. **Pembrolizumab** (for PD-L1 positive or MSI-H/dMMR tumors, TMB-H tumors) for second-line therapy				
Pembrolizumab	200mg	IVD 30 mins	Day 1	Q3W

全身性藥物處方建議

Commonly used Regimen for Non-squamous Cell Carcinoma

Regimens	Dosage	Route	Day	Interval
1. Paclitaxel + Cisplatin, Q3W				
Paclitaxel Cisplatin	175 mg/m^2 75 mg/m^2	IVD 3 hrs IVD 1 hr	Day 1 Day 1	Q3W
2. Paclitaxel Only, Q3W Dose escalation to 200 mg/m2 or de-escalation to 110 mg/m2 depending on toxicity				
Paclitaxel	175 mg/m^2 135 mg/m^2 if prior RT	IVD 3 hrs IVD 3 hrs	Day 1 Day 1	Q3W
3. Cisplatin + Etoposide, Q4W				
Cisplatin Etoposide	100mg/m2 100mg/m2	IVD 2hrs IVD 1hr	Day 1 Day 1-3	Q4W
4. Etoposide Only (every 28 days) Dose escalation to 60mg/m2/day depending on toxicity				
Etoposide	50 mg/m^2/day 40 mg/m^2/day if prior RT	PO PO	Day 1-21 Day 1-21	Q4W
5. **EIP** Regimen (for neuroendocrine cell type), Q3-4W, x6 cycles				
Etoposide Ifosfamide Cisplatin	100 mg/m^2 1500 mg/m^2 50 mg/m^2	IVD 1 hr IVD 1 hr IVD 1 hr	Day 1-3 Day 1-3 Day 1	Q3-4W

備註：
Cisplatin 為子宮頸癌治療化學治療首選藥物，若(CCr < 60)，Carboplatin可做為替代藥物取代 。
婦癌個案注射Cisplatin若因CCR ≤ 60，weekly Cisplatin 40 mg/m^2，可改為Carboplatin AUC 2；若非weekly用法，如Cisplatin Q3W使用，則為 75 mg/m2改為Carboplatin AUC 5。

持續性或復發性疾病

考慮因素：

- Site of recurrence or metastases
  - Pelvic: Central, Side wall, Combined
  - Extrapelvic: Intra-abdominal organs, distant lymph nodes, distant disseminated metastasis
- Prior therapy
  - Surgery → Radiotherapy
  - Radiotherapy → Surgery
- Possible routes or mechanisms of spread
- Status of patient's performance
- Palliative or Curative treatment

持續性或復發性疾病

Cervical Cancer with Central Recurrence (中央復發)

Prior Surgery

- Surgical intervention if no contraindication
- Radiotherapy if surgical intervention not possible

Prior Radiotherapy

- Surgical intervention if no contraindication
- Radiotherapy indicated if recurrence outside of previously treated field
- Palliative radiotherapy
- Palliative chemotherapy

Surgical Intervention

If previous surgery is only total abdominal hysterectomy:

- Radical parametrectomy + PLND + PALNS

If previous surgery is radical hysterectomy + PLND + PALNS

- Exenteration can be considered (Total/Anterior/Posterior) ± IORT
- Exenterative surgery should NOT be used as a palliative treatment, except in the presence of malignant fistulas in the pelvis.

➢ Final intraoperative assessment: The final decision to proceed with exenteration will not be made until the abdomen has been opened and assessment of the pelvic side-wall and posterior abdominal wall has been made, utilizing frozen section where necessary.

持續性或復發性疾病

Contraindication of exenterative surgery

Absolute contraindication

- Metastases to extrapelvic LN
- Metastases to abdominal viscera
- Metastases to lung or bone

Relative contraindication

- Obesity
- Pelvic side-wall spread (direct extension or nodal metastases)
- Triad:
    1. Unilateral uropathy, non-functional kidney, or ureteric obstruction
    2. Unilateral leg edema
    3. Sciatic leg pain

持續性或復發性疾病

Cervical Cancer with Pelvic Side Wall Recurrence (側壁復發)

Prior Surgery

Radiotherapy recommended

Prior Radiotherapy

Surgical intervention if no contraindication

- LEER procedure: laterally extended endopelvic resection
- CORT procedure: combined operative and radio-therapeutic treatment for close or positive margins

Indication:

-Histological confirmed, unifocal pelvic side-wall recurrence
-Free from tumor dissemination
-Tumor limited to a maximal diameter of < 5 cm
-Medical condition compatible with major surgery
-Willingness to accept urinary or fecal diversion
-Radiotherapy ± chemotherapy indicated if recurrence outside of previously treated field
-Palliative radiotherapy
-Palliative chemotherapy

持續性或復發性疾病

Cervical Cancer with Central and Pelvic Side Wall Recurrence (中央及側壁復發)

Prior Surgery

Radiotherapy recommended

Prior Radiotherapy

Radiotherapy indicated if recurrence outside of previously treated field
Palliative radiotherapy
Palliative chemotherapy

Only Distant LN Metastasis (including para-aortic LN)**(只有遠處淋巴結轉移[包括腹主動脈旁淋巴結])**

Radiotherapy recommended
Chemotherapy recommended
CCRT recommended

Intra-abdominal Organ Metastasis (腹內臟器轉移)

Chemotherapy recommended
Palliative surgery only for intestinal obstruction

Dissemination (遠處轉移)

Multiple sites or unresectable → Chemotherapy recommended
Resectable → Surgery → R/T ± chemotherapy or Chemotherapy ± R

Cervical Cancer

追蹤

Follow up interval

- Every 3 months for 2 years
- Every 4 months for 3rd-4th year
- Every 6 months for 5th year
- Every 6-12 months for more than 5 years
- Based on patient's risk of disease recurrence

Examination in OPD

- Pelvic examination
- Pap smear (cytology)
- Image (chest-X-ray, CT, MRI, PET/CT) as indicated based on symptoms or examination findings suspicious for recurrence
- Lab assessment (CBC/DC, BUN/Creatinine) as indicated based on symptoms or examination findings suspicious for recurrence

Patient education regarding symptoms of potential recurrence, lifestyle, obesity, exercise, smoking cessation and nutrition counseling

子宮頸癌核心測量指標

指標類型	測量指標	分子	分母
前趨病灶-1	病理確診為第三級上皮內贅瘤(CIN 3)/子宮頸原位癌(CIS)病人，以子宮頸錐狀手術為完整治療的比率。	分母中，個案以子宮頸錐狀手術為完整治療的人數。(定義係指癌登手冊申報原發部位手術方式為≥20且≤29)。	病理確診為第三級上皮內贅瘤(CIN 3)/子宮頸原位癌(CIS)的人數。
子宮頸癌-1	以手術為首次治療的FIGO期別IA2或以上期別的子宮頸癌病人，其骨盆腔淋巴結摘除≥12顆的比率。	分母中，骨盆腔淋巴結摘除≥12顆的人數。	所有接受手術為首次治療的FIGO期別 IA2或以上子宮頸癌的人數。
子宮頸癌-2	子宮頸癌患者以放射或合併化學及放射治療為首次治療者，放射治療於63天(含)內完成的比率。	分母中，放射治療於63天(含)內完成的人數。	子宮頸癌患者以放射或合併化學及放射治療為首次治療的人數。
子宮頸癌-3	子宮頸癌患者以放射或合併化學及放射治療為首次治療者，其治療包含近接放射治療的比率。(排除子宮頸癌FIGO期別IVB期別的個案)	分母中，其治療包含近接放射治療的人數。	子宮頸癌患者以放射或合併化學及放射治療為首次治療的人數。(排除子宮頸癌FIGO期別IVB期別的個案。)
備註：基準3.2 治療計畫書上應呈現以「病人為中心」之完整治療模式，且須於主要治療前即完成**子宮頸癌個案須於術前定版治療計畫書**			

Endometrial Cancer

分期	診療指引	全身性藥物 賀爾蒙	持續或 復發性疾病	追蹤	品質指標

分期 (Carcinoma & Carcinosarcoma)

TNM	FIGO	Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor confined to the corpus uteri, including endocervical glandular involvement
-T1a	IA	Tumor limited to the endometrium or invading less than half the myometrium
-T1b	IB	Tumor invading one half or more of the myometrium
T2	II	Tumor invading the stromal connective tissue of the cervix but not extending beyond the uterus. Does NOT include endocervical glandular involvement.
T3	III	Tumor involving serosa, adnexa, vagina, or parametrium
-T3a	IIIA	Tumor involving the serosa and/or adnexa (direct extension or metastasis)
-T3b	IIIB	Vaginal involvement (direct extension or metastasis) or parametrial involvement
T4	IVA	Tumor invading the bladder mucosa and/or bowel mucosa (bullous edema is not sufficient to classify a tumor as T4)
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
N1	IIIC1	Regional lymph node metastasis to pelvic lymph nodes
-N1mi	IIIC1	Regional lymph node metastasis (greater than 0.2 mm but not greater than 2.0 mm in diameter) to pelvic lymph nodes
-N1a	IIIC1	Regional lymph node metastasis (greater than 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 (greater than 0.2 mm but not greater than 2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
-N2a	IIIC2	Regional lymph node metastasis (greater than 2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
M0		No distant metastasis
M1	IVB	Distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone). (It excludes metastasis to pelvic or para-aortic lymph nodes, vagina, uterine serosa, or adnexa)

子宮內膜癌診療指引

Initial evaluation

- Blood analysis- CBC/ chemistry profile (including tumor marker)
- Ultrasound / Doppler /Chest X-ray/ CT (Pelvic /Abdominal /Chest) / Pelvic MRI / Whole body PET-CT
- Pathology proved (endometrial D&C or biopsy)
- Genetic testing (依個人狀況選擇):
  Age <50 years old
  Family history of endometrial cancer, colorectal cancer, Lynch syndrome

Histologic Type

- Type I: Pure endometrioid type
- Type II: Non-endometrioid type (clear cell, serous, carcinosarcoma, undifferentiated/dedifferentiated)

Endometrial Cancer

子宮內膜癌診療指引

Endometrial Carcinoma, histological type	
Malignant epithelial carcinoma	Pure endometrioid carcinoma Serous Adenocarcinoma Clear cell carcinoma

Endometrial Carcinoma, Grading	
Cases of carcinoma of the corpus should be grouped with regard to the degree of differentiation of the adenocarcinoma as follows:	
G1	5 percent or less of a non-squamous or non-morular solid growth pattern
G2	6 percent to 50 percent of a non-squamous or non-morular solid growth pattern
G3	More than 50 percent of a non-squamous or non-morular solid growth pattern

Endometrial Carcinoma, type 1 vs. type 2		
	Type 1	Type 2
Histology	Endometrioid carcinoma	Serous carcinoma, clear cell carcinoma Mixed type MMMT (carcinosarcoma)
Typical patient	Peri-menopausal or early postmenopausal women	Elderly, atrophic endometrium
	Background of endometrial hyperplasia	
	Low-grade	High-grade
	Estrogen-dependent	Non-estrogen dependent
	May show a focal or diffuse papillary pattern	A glandular variant shows little or no papillary formation but has high-grade cytology
Estrogen receptor	Usually positive; high-grade cases may be negative	Negative
Molecular genetic changes	PTEN or KRAS gene mutation microsatellite instability	P53 or HER2 or E-cadherin mutation

子宮內膜癌診療指引›主要治療

Suitable for Primary Surgery		
Type I	Stage I	Total hysterectomy + BSO + Peritoneal cytology + BPLND ± PALNS
	Stage II	Total hysterectomy + BSO + Peritoneal cytology + BPLND + PALNS
		Radical hysterectomy + BSO + Peritoneal cytology + BPLND + PALNS
	Stage III	Total hysterectomy + BSO + Peritoneal cytology + BPLND + PALNS / Debulking (surgical goal : no measurable residual tumor) [consider preoperative chemotherapy]
	Stage IVA	Anterior and posterior pelvic exenteration (include Total hysterectomy + BSO + Peritoneal cytology + BPLND + PALNS)
	Stage IVB	Systemic therapy and/or Radiotherapy
		Palliative surgery
Type II	Any stage	Total hysterectomy + BSO + Peritoneal cytology + BPLND + PALNS + Omentectomy
		Maximal tumor debulking for gross disease

子宮內膜癌診療指引›主要治療

Not Suitable for Primary Surgery		
Type I	Stage I	Radiotherapy
		Consider systemic therapy in select patients
	Stage II	Radiotherapy ± systemic therapy→ Surgical resection (if rendered operable)
		Systemic therapy → Surgical resection (if rendered operable) or Radiotherapy (if still inoperable)
	Stage III/IV	Radiotherapy ± systemic therapy→ Re-evaluate for surgical resection
		Systemic therapy→ Re-evaluate for surgical resection and/or Radiotherapy based on response
Type II	Any stage	Radiotherapy ± systemic therapy→ Re-evaluate for surgical resection
		Systemic therapy→ Re-evaluate for surgical resection and/or Radiotherapy based on response

子宮內膜癌診療指引›主要治療

備註：

- Although cytology does not affect FIGO staging, it should still be obtained because positive cytology is an adverse factor.
- Sentinel lymph node dissection may be considered in early stage.
- BPLND includes external iliac, internal iliac, obturator, common iliac LN.
- PALNS dissected from infra-mesenteric and intrarenal region.
- Ovarian preservation may be safe in selected premenopausal women with early-stage endometrioid cancer, normal-appearing ovaries, and no family history of breast cancer, ovarian cancer or Lynch syndrome. Salpingectomy is recommended.

子宮內膜癌診療指引›主要治療

備註：

- Universal testing of endometrial carcinomas for MMR proteins/MSI (initial biopsy or D&C or the final hysterectomy specimen) is recommended.
- HER2 testing is recommended for possible treatment of advanced stage , serous type.
- Molecular analysis of endometrial carcinoma has identified four clinically significant molecular subgroups with differing clinical prognoses:

  POLE mutations, MSI-H, copy number low, and copy number high.

子宮內膜癌診療指引›輔助治療

Risk group	Description	Adjuvant therapy
Low	Stage I endometrioid, grade 1-2, <50% MI, LVSI (-) or focal	Observation or Vaginal brachytherapy
Intermediate	Stage I endometrioid, grade 1-2, ≧50% MI, LVSI(-) or focal	Vaginal brachytherapy or Observation
	Stage I endometrioid, grade 3, <50% MI, LVSI(-) or focal	
	Stage I non-endometrioid without MI	
High-intermediate	Stage I endometrioid, LVSI(+) , regardless of grade and MI status	EBRT and/or Vaginal brachytherapy
	Stage I endometrioid, grade 3, ≧50% MI, regardless of LVSI status	EBRT ± Vaginal brachytherapy ± Systemic therapy Systemic therapy ± Vaginal brachytherapy
	Stage II endometrioid*	EBRT ± Vaginal brachytherapy ± Systemic therapy
High	Stage III-IVA endometrioid, no residual disease	Systemic therapy ± EBRT ± Vaginal brachytherapy Concurrent radio-chemotherapy + adjuvant systemic therapy Systemic therapy
	Stage I-IVA non-endometrioid with MI, no residual disease	
Advanced	Stage III –IVA endometrioid, residual disease	Systemic therapy ± EBRT ± Vaginal brachytherapy
Metastatic	Stage IVB endometrioid	

1. Cytology(+) preferred adjuvant treatment, if low risk, no adjuvant treatment may be considered.
2. If clinical assessment the possibility high risk distant metastasis with positive cytology & LVSI, adjuvant systemic therapy may be considered.
3. *If stage II patient received radical hysterectomy, they can be treated as stage I
   - Observation or vaginal brachytherapy being option in cases had radical hysterectomy with negative surgical margin and without extra-uterine disease
   - Adjuvant pelvic radiotherapy (RT): 40-50 Gy to CTV
   - Upper vaginal tumor bed as vaginal cut end + parametrium + pelvic lymph nodes

Endometrial Cancer

全身性藥物處方建議

Single Agent Regimen

Regimens	Dosage	Route	Day	Interval
Carboplatin, x6 cycles	AUC 5以上	IVD 1 hr	Day 1	Q3W
Cisplatin, x6 cycles	50-75 mg/m^2	IVD 1 hr	Day 1	Q3W
Doxorubicin, x6 cycles	40-60 mg/m^2	IVD 20 mins - 1 hr	Day 1	Q3W
Ifosphamide, x6 cycles	1500 mg/m^2	IVD 1~2 hrs	Day 1-3	Q3W
Paclitaxel, x6 cycles	175 mg/m^2	IVD 3 hrs	Day 1	Q3W
Topotecan, x6 cycles	4 mg	IVD 1 hrs	Day 1, 8, 15	Q4W
*__Docetaxel__, x6 cycles	100 mg/m^2	IVD 1 hrs	Day 1	Q3W
Bevacizumab, x6 cycles	7.5-15 mg/kg	IVD 30-90 mins	Day 1	Q3W
Temsirolimus	25mg	IVD 30 mins	Day 1, 8, 15	Q4W
#**Pembrolizumab**	200mg	IVD 30 mins	Day 1	Q3W

*may be considered for patients in whom paclitaxel is contraindicated
for MSI-H/dMMR tumors/TMB-H tumors

Endometrial Cancer

全身性藥物處方建議

Combination Agent Regimen (組合藥劑處方)

Regimens	Dosage	Route	Day	Interval
1. Paclitaxel + Carboplatin, x6 cycles				
Paclitaxel Carboplatin	175 mg/m^2 AUC 4-7.5	IVD 3 hrs IVD 1 hr	Day 1 Day 1	Q3W
2. Paclitaxel + Cisplatin, x6 cycles				
Paclitaxel Cisplatin	175 mg/m^2 50 mg/m^2	IVD 3 hrs IVD 1 hr	Day 1 Day 1	Q3W
3. Paclitaxel (weekly) + Carboplatin, x6 cycles				
Paclitaxel Carboplatin	80 mg/m^2 AUC 4-7.5	IVD 1 hrs IVD 1 hr	Day 1, 8, 15 Day 1	Q3W
4. Paclitaxel (weekly) + Cisplatin, x6 cycles				
Paclitaxel Cisplatin	80 mg/m^2 50 mg/m^2	IVD 1 hrs IVD 1 hr	Day 1, 8, 15 Day 1	Q3W
5. Paclitaxel + Carboplatin + Trastuzumab, x6 cycles or disease progression, Only for advanced (stage III/IV) and recurrent serous carcinomas that are HER-2 positive				
Paclitaxel Carboplatin Trastuzumab	175 mg/m^2 AUC 4-7.5 6-8 mg/kg	IVD 3 hrs IVD 1 hr IVD 90 mins	Day 1 Day 1 Day 1	Q3W

Regimens	Dosage	Route	Day	Interval
6. Paclitaxel + Cisplatin + Trastuzumab, x6 cycles or disease progression only for advanced (stage III/IV) and recurrent **serous** carcinomas that are **HER-2** positive				
Paclitaxel Cisplatin Trastuzumab	175 mg/m^2 50 mg/m^2 6-8 mg/kg	IVD 3 hrs IVD 1 hr IVD 90 mins	Day 1 Day 1 Day 1	Q3W
7. Doxorubicin + Cisplatin, x8 cycles				
Doxorubicin Cisplatin	60 mg/m^2 50 mg/m^2	IVD 1 hr IVD 1 hr	Day 1 Day 1	Q3W
8. Paclitaxel + Carboplatin (both weekly), x18 cycles				
Paclitaxel Carboplatin	60 mg/m^2 AUC 2	IVD 1 hr IVD 1 hr	Day 1 Day 1	QW
9. Paclitaxel + Carboplatin (both weekly), x18 cycles				
Paclitaxel Carboplatin	60 mg/m^2 AUC 2	IVD 1 hr IVD 1 hr	Day 1 Day 1	QW
10. Docetaxel + Carboplatin, x6 cycles (may be considered for patients in whom paclitaxel is contraindicated)				
Docetaxel Carboplatin	60 mg/m^2 AUC 4-7.5	IVD 1 hr IVD 1 hr	Day 1 Day 1	Q3W

Endometrial Cancer

全身性藥物處方建議

Combination Agent Regimen (組合藥劑處方)

Regimens	Dosage	Route	Day	Interval
11. Docetaxel + Cisplatin, x6 cycles (may be considered for patients in whom paclitaxel is contraindicated)				
Docetaxel Cisplatin	60 mg/m^2 50 mg/m^2	IVD 1 hr IVD 1 hr	Day 1 Day 1	Q3W
12. Paclitaxel + Carboplatin + Bevacizumab, x6 cycles or disease progression				
Paclitaxel Carboplatin Bevacizumab	175 mg/m^2 AUC 4-7.5 7.5-15 mg/kg	IVD 3 hrs IVD 1 hr IVD 30-90 mins	Day 1 Day 1 Day 1	Q3W
13. Ifosfamide + Paclitaxel or Cisplatin, x8 cycles (for carcinosarcoma)				
Ifosfamide Paclitaxel, or Cisplatin	1.0 mg/m^2 135 mg/m^2 50 mg/m^2	IVD 24 hrs IVD 3 hr IVD 1 hr	Day 1-3 Day 1 Day 1	Q3W
14. CAP: Cyclophosphamide + Doxorubicin + Cisplatin, x6 cycles				
Cyclophosphamide Doxorubicin Cisplatin	600 mg/m^2 45 mg/m^2 50 mg/m^2	IVD >30 mins IVD 1-2 hrs IVD 1 hr	Day 1 Day 1 Day 1	Q4W
15. TAP: Paclitaxel + Doxorubicin + Cisplatin + GCSF, x7 cycles				
Paclitaxel Doxorubicin Cisplatin	160 mg/m^2 45 mg/m^2 50 mg/m^2	IVD 3 hrs IVD > 30 mins IVD 1 hr	Day 1 Day 1 Day 1	Q3W

Regimens	Dosage	Route	Day	Interval
16. Lenvatinib + Pembrolizumab *(high grade tumor without high MSI)*				
Lenvatinib Pembrolizumab	20mg 200mg	PO IVD 30 mins	Day 1-21 Day 1	Q3W

Endometrial Cancer

賀爾蒙處方建議

Regimens	Dosage	Route	Day	Interval
MPA (Provera)	200mg	PO	Daily	QD
Megestrol	160mg	PO	Daily	QD
Anastrozole (Arimidex)	1mg	PO	Daily	At least 28 days
Tamoxifen	20mg	PO	Daily	BID
Fulvestrant	500mg	IM	Day 1	QM

註：Hormone therapy is only for endometrioid histologic type

子宮內膜癌診療指引›不完整分期手術後意外發現

Incomplete staging →image survey		
Low risk	After hysterectomy with bilateral salpingo-oophorectomy	Observation (negative finding)
	After hysterectomy only	Observation (negative finding) or Complete surgical staging
Intermediate risk	Negative image finding	Vaginal brachytherapy
		Complete surgical staging
High-Intermediate to High risk	Negative image finding	Complete surgical staging
		Adjuvant treatment
	Suspicious/positive image finding	Complete surgical staging
		Pathological confirmation of metastatic lesion

Endometrial Cancer

早期保守治療

Fertility sparing option

Patient criteria

- A well-differentiated, grade 1, endometrioid endometrial carcinoma (by D&.C) confirmed by expert pathology review
- Disease limited to the endometrium (by MRI)
- No extrauterine involvement (no synchronous ovarian tumor or metastasis, no suspicious retroperitoneal nodes) by imaging
- Strong desire for fertility sparing
- No contraindication for medical treatment or pregnancy
- Patients should undergo counseling that fertility-sparing option is NOT standard of care for the treatment of endometrial carcinoma
- Patients should be supervised in close cooperation with specialist gynecological oncology.

Medical treatment (high-dose progestin)

- Medroxyprogesterone acetate: 200-600mg/day for 6 months
- Megestrol acetate: 160-320mg/day
- Levonorgestrel IUD with or without gonadotropin-releasing hormone (GnRH) analogues

Follow-up

Endometrial sampling/biopsy every 3-6 months (D&C or biopsy)

- Complete response for 6 months
  - Encourage conception
  - After childbearing or disease progression: hysterectomy + BSO + BPLND + PALNS
- Endometrial cancer at 6-12 months
  - hysterectomy + BSO + BPLND + PALNS

	Biopsy (−)	Biopsy (+)
D&C every 3 months (maximum up to 12 months)	Encourage pregnancy or Intermittent biopsy	Surgical intervention

Endometrial Cancer

持續或復發性疾病

Local or Regional Recurrence (no distant metastasis)				
No prior RT		• EBRT ± vaginal brachytherapy ± systemic therapy or Surgical exploration (debulking)#		
Prior RT	Previous brachytherapy	• EBRT ± brachytherapy ± systemic therapy or • Surgical exploration (debulking surgery) then:		
		Confined to vagina		• EBRT ± vaginal brachytherapy ± systemic therapy
		Extra-vagina	Pelvic LN (+)	• EBRT± systemic therapy
			Para-aortic LN or common iliac LN	• EBRT± systemic therapy
			Upper abdomen or peritoneum	• Systemic therapy ± EBRT
	Previous EBRT	• Surgical exploration (debulking) and/or Systemic therapy ± palliative EBRT • Brachytherapy ± Systemic therapy		

持續或復發性疾病

Metastatic Lesion		
Isolated metastasis	Resectable lesion	• Resection and/or EBRT
	Un-resectable lesion	• Ablative therapy
		• Systemic therapy
Disseminated metastases	• Systemic therapy ± palliative EBRT	

備註：

- HER2 testing is recommended for possible treatment of recurrent serous endometrial carcinoma.

追蹤

1st-3rd year

- Physical examination & Pap smear every 3-6 months
- Tumor marker F/U every 3-6 months (if initially elevated)
- CXR every 6-12 months

4-5th year

- Tumor marker every 6 months (if initially elevated)
- Pap smear annually.
- CXR annually

Arrange MRI or CT scan if recurrence suspected.

子宮內膜癌品質指標

指標類型	測量指標	分子	分母
診斷-1	子宮內膜確診病人，治療前有任何影像(包含超音波、CT、MR)紀錄的比率。	分母中，治療前一個月內有接受任何影像(包含超音波、CT、MRI)檢查的人數。	所有確診為子宮內膜的人數。
診斷-2	子宮內膜確診病人，治療前有病理組織的確認。	分母中，首次治療前有病理組織的人數。	所有確診為子宮內膜的人數。
治療-1	子宮內膜癌確診病人，在手術時檢測cytology的比率。	分母中，在手術時有檢測cytology。	所有確診為子宮內膜癌行手術治療的人數。
治療-2	子宮內膜癌確診病人，在手術治療時，type 1手術中發現子宮以外有病灶時及type 2 病人行完整分期手術的比率。	分母中，行完整分期手術(行omentectomy)的比率	所有確診為子宮內膜type 1的第3、4期，或任何期別病理為type 2人數。
治療-3	FIGO期別 I~II 子宮內膜癌，術後放射治療於手術後八週內開始	分母中，FIGO期別 I~II 子宮內膜癌，接受術後單獨放射治療或同步放化療，且於八週內開始之人數	FIGO期別 I~II 子宮內膜癌，接受術後單獨放射治療或同步放化療之人數
追蹤-1	子宮內膜癌確診病人，手術治療結束後180天(含)內已接受內診追蹤的比率。	分母中，首次手術結束後180天(含)內已接受抹片追蹤的人數。	子宮內膜癌於本院接受治療的人數。

備註：基準3.2 治療計畫書上應呈現以「病人為中心」之完整治療模式，且須於主要治療前即完成子宮內膜癌個案須於**術前定版治療計畫書**

Sarcoma

分期 LMS or ESS Adenosarcoma	診療指引	化療處方 賀爾蒙處方	持續或 復發性疾病	追蹤

Leiomyosarcoma or Endometrial Stromal Sarcoma

TNM	FIGO	Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to the uterus
-T1a	IA	Tumor 5 cm or less in greatest dimension
-T1b	IB	Tumor more than 5 cm
T2	II	Tumor extends beyond the uterus, within the pelvis
-T2a	IIA	Tumor involves adnexa
-T2b	IIB	Tumor involves other pelvic tissues
T3	III	Tumor infiltrates abdominal tissues
-T3a	IIIA	One site
-T3b	IIIB	More than one site
T4	IVA	Tumor invades bladder or rectum
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
N1	IIIC	Regional lymph node metastasis
M0		No distant metastasis
M1	IVB	Distant metastasis (excluding adnexa, pelvic, and abdominal tissues)

Adenosarcoma

TNM	FIGO	Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to the uterus
-T1a	IA	Tumor limited to the endometrium/endocervix
-T1b	IB	Tumor invades to less than half of the myometrium
-T1c	IC	Tumor invades one half or more of the myometrium
T2	II	Tumor extends beyond the uterus, within the pelvis
-T2a	IIA	Tumor involves adnexa
-T2b	IIB	Tumor involves other pelvic tissues
T3	III	Tumor infiltrates abdominal tissues
-T3a	IIIA	One site
-T3b	IIIB	More than one site
T4	IVA	Tumor invades bladder or rectum
NX		Regional lymph nodes cannot be assessed*
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
N1	IIIC	Regional lymph node metastasis
M0		No distant metastasis
M1	IVB	Distant metastasis (excluding adnexa, pelvic, and abdominal tissues)

子宮肉癌診療指引›術前準備

- Blood analysis (CBC, liver function test, renal function test, chemistry profile)
- Tumor marker
- Ultrasound / Doppler
- Chest/abdomen/pelvic CT or abdominal/pelvic MRI and chest CT or Neck/chest/abdomen/pelvis/groin PET/CT
- Consider preoperative endometrial biopsy

(如果術前懷疑為惡性肉瘤，術中避免使用 morcellator)

子宮肉癌診療指引›主要治療

若術前或術中確定診斷 Staging surgery (分期手術)

Stage I

- Peritoneal cytology + Hysterectomy (Level 1) ± BSO* ± (BPLND + PALNS)**

  * Favor BSO if ER/PR positive

  ** Lymphadenectomy is controversial. Lymph node metastases are uncommon in high-grade uterine sarcomas.

Stage II-IV (as ovarian cancer staging surgery)

- Peritoneal cytology + Hysterectomy (Level 1) + BSO + BPLND + PALNS + omentectomy + debulking surgery

Inoperable condition (不能手術情況)

- Systemic therapy and/or Palliative EBRT ± brachytherapy

子宮肉癌診療指引›輔助治療

Post-operation Treatment			
Stage	Low grade ESS	Adenosarcoma	High grade ESS, Undifferentiated sarcoma or Leiomyosarcoma
I	BSO or Observe if menopause	Observe	Observe
II	BSO ± anti-estrogen hormone therapy ± EBRT*	Systemic therapy and/or EBRT or Observe**	Systemic therapy and/or EBRT or Observe**
III	BSO ± anti-estrogen hormone therapy ± EBRT*	Systemic therapy and/or EBRT or Observe**	Systemic therapy and/or EBRT or Observe**
IVA	BSO ± anti-estrogen hormone therapy ± EBRT*	Systemic therapy and/or EBRT	Systemic therapy and/or EBRT
IVB	BSO ± anti-estrogen hormone therapy ± palliative EBRT	Systemic therapy ± palliative EBRT	Systemic therapy ± palliative EBRT

*未達共識
** In select, completely resected cases with no evidence of disease on postoperative imaging

子宮肉癌診療指引›手術後意外發現

Complete image study→

- If final pathology is low-grade ESS or ER/PR positive tumor
  - Myomectomy or hysterectomy or with residual cervix/tube/ovary → complete staging
  - Hysterectomy + BSO → no need further operation
- If others histology type
  - Myomectomy or supracervical hysterectomy only → complete staging
  - Hysterectomy only → no need further operation
- If known or suspected extra-uterine disease → resection of metastatic focus

全身性藥物處方建議
(Clinical trials strongly recommended)

Single Agent Regimen (單一藥劑處方)

Regimens	Dosage	Route	Day	Interval
Doxorubicin, x6 cycles **(Preferred regimen)**	60 mg/m^2	IVD 1 hr	Day 1	Q3W
Gemcitabine, x6 cycles	1000 mg/m^2	IVD 1 hr	Day 1, 8, 15	Q4W
Epirubicin, x6 cycles	75 mg/m2	IVD	Day 1	Q3W
Ifosfamide, x6 cycles	1500 mg/m^2	IVD 1-2 hrs	Day 1-3	Q4W
Dacarbazine (DTIC), x6 cycles	850 mg/m^2	IVD 1 hr	Day 1	Q3W
Liposomal doxorubicin, x6 cycles	40-50 mg/m^2	IVD 20-60 mins	Day 1	Q4W
Pazopanib*	400-800 mg/day	PO	Day 1	QD, till PD or intolerance
Temozolomide*	80 mg/day	PO	Day 1	QD, till PD or intolerance
Trabectedin**	1.2 mg/m^2	IVD 24 hrs	Day 1	Q3W, till PD or intolerance
Eribulin* (未達共識)	1.4 mg/m^2	IVD	Day 1 , 8	Q3W
Docetaxel, x6 cycles (未達共識)	100 mg/m^2	IVD 1 hr	Day 1	Q3W
Cisplatin, x6 cycles (未達共識)	50 mg/m^2	IVD 1 hr	Day 1	Q3W
Paclitaxel, x6 cycles (Only for angiosarcoma)	175 mg/m^2	IVD 3 hrs	Day 1	Q3W

* In recurrent or metastatic disease which progressed on prior chemotherapy
** Leiomyosarcoma with prior anthracyline-containing regimen treatment

Sarcoma

全身性藥物處方建議

(Clinical trials strongly recommended)

Combination Agent Regimen (組合藥劑處方)

Regimens	Dosage	Route	Day	Interval
Gemcitabine + Docetaxel, x6 cycles				
Gemcitabine Docetaxel	800 mg/m^2 60 mg/m^2	IVD 1 hr IVD 1 hr	Day 1, 8 Day 8	Q3W
Doxorubicin + ifosfamide, x6 cycles				
Doxorubicin Ifosphamide	40-50 mg/m^2 5 g/m^2	IVD 3 hrs IVD 1 hr	Day 1 Day 1	Q3W
Doxorubicin + Dacarbazine (DTIC)				
Doxorubicin Dacarbazine	15 mg/m^2 (60 mg/m^2) 187.5mg/m^2	IVD 24 hrs (IVD) IVD 24 hrs	Day 1-4 Day 1-4	Q3W, until reaching lifetime cumulative dose
Gemcitabine + Dacarbazine (DTIC)				
Gemcitabine Dacarbazine	1800 mg/m^2 500 mg/m^2	IVD 10mg/m2/minute IVD 1 hr	Day 1 Day 1	Q2W, till PD or intolerance
Gemcitabine + Vinorelbine				
Gemcitabine Vinorelbine	800 mg/m^2 25 mg/m^2	IVD 10mg/m2/minute IVD 5-10 mins	Day 1, 8 Day 1, 8	Q3W, till PD or intolerance

全身性藥物處方建議

(Clinical trials strongly recommended)

Biomarker-Directed Systemic Therapy for Second-Line Treatment

Regimens	Dosage	Route	Day	Interval
Pembrolizumab (TMB-H tumors)*	200 mg or 400 mg	IVD 30 mins	Day 1	Q3-6W till PD or intolerance or up to 24months
Larotrectinib or **Entrectinib** (NTRK gene fusion-positive tumors) **	Larotrectinib 100mg BID Entrectinib 600mg QD	PO	Day 1	BID, till PD or intolerance QD, till PD or intolerance

* TMB-H: tumor mutational burden-high [≥10 mut/Mb], in unresectable or metastatic tumors which progressed on prior chemotherapy and have no satisfactory alternative treatment options
** In recurrent or metastatic disease which progressed on prior chemotherapy (category 2B)

Sarcoma

賀爾蒙處方建議

Anti-estrogen hormone therapy (low-grade ESS or ER/PR(+) leiomyosarcoma*)

Regimens	Dosage	Route	Day	Interval
Aromatase inhibitor **(Preferred Regimens)**				
Letrozole Anastrozole	2.5 mg/day 1.0 mg/day	PO		
Progestins **				
Medroxyprogesterone acetate or Megestrol acetate	200-600 mg/day 80-160 mg/day	PO PO		
Oestrogen receptor (ER) antagonist				
Fulvestrant	500 mg	IM	Day1	Q2W X3, then Q4W
GnRH analogs				
Leuprolide acetate (未達共識)	3.75 mg	IM	Day1	Q4W

* Preferably with small tumor volume or an indolent growth pace
** 於ER/PR-positive leiomyosarcoma 仍未達共識

持續性或復發性疾病

Local recurrence: vagina/pelvis	No prior RT	• Surgery ± IORT**, Consider preoperative EBRT ± systemic therapy* For residual disease: Consider EBRT ± brachytherapy ± systemic therapy* or • EBRT ± brachytherapy ± systemic therapy*
	Prior RT	• Surgery ± IORT** ± systemic therapy* or • Systemic therapy* or • Selected re-irradiation with EBRT and/or brachytherapy
Isolated metastases	Resectable	• Surgical resection or other local ablative therapy -Consider postoperative systemic therapy* -Consider postoperative EBRT
	Unresectable	• Systemic therapy* → If response, considered surgery and/or • Local therapy (EBRT or local ablative therapy)

Disseminated disease → Systemic therapy* ± palliative EBRT or Supportive care

*For low-grade ESS, the first choice of systemic therapy is anti-estrogen hormone therapy
**未達共識

追蹤

- History and physical exam: every 3 months for 2-3 years, then every 6-12 months.
- CT imaging (chest/abdomen/pelvis): every 3-6 months for 3 years, then every 6-12 months for next 2 years, consider every 1-2 years imaging thereafter up to an additional 5 years.
- Optional abdominal/pelvic MRI and chest CT can be considered.
- Consider neck/chest/abdomen/pelvis/groin PET/CT if metastasis is suspected in select patients.

Ovary, Fallopian Tube and Peritoneal Carcinoma

分期	診療指引 卵巢腫瘤 邊緣性卵巢腫瘤	全身性藥物 上皮細胞 生殖細胞 性線間質細胞 賀爾蒙處方	持續或 復發性疾病	追蹤	核心指標

Ovary, Fallopian Tube and Peritoneal Carcinoma

分期

TNM	FIGO	Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to ovaries (one or both) or fallopian tube(s)
-T1a	IA	Tumor limited to one ovary (capsule intact) or fallopian tube surface; no malignant cells in ascites or peritoneal washings
-T1b	IB	Tumor limited to one or both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings
-T1c	IC	Tumor limited to one or both ovaries or fallopian tube, with any of the following:
--T1c1	IC1	Surgical spill
--T1c2	IC2	Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface
--T1c3	IC3	Malignant cells in ascites or peritoneal washings
T2	II	Tumor involves one or both ovaries or fallopian tubes with pelvic extension below pelvic brim or primary peritoneal cancer
-T2a	IIA	Extension and/or implants on the uterus and/or fallopian tubes(s) and/or ovaries
-T2b	IIB	Extension to and/or implants on other pelvic tissues
T3	III	Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with microscopically confirmed peritoneal metastasis outside the pelvis and/or metastasis to the retroperitoneal (pelvic and/or para-aortic) lymph nodes
-T3a	IIIA2	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
-T3b	IIIB	Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension with or without metastasis to the retroperitoneal lymph nodes
-T3c	IIIC	Macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ)
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
N1	IIIA1	Positive retroperitoneal lymph nodes only (histologically confirmed)
-N1a	IIIA1i	Metastasis up to 10 mm in greatest dimension
-N1b	IIIA1ii	Metastasis more than 10 mm in greatest dimension
M0		No distant metastasis
M1	IV	Distant metastasis, including pleural effusion with positive cytology; liver or splenic parenchymal metastasis; metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); and transmural involvement of intestine
-M1a	IVA	Pleural effusion with positive cytology
-M1b	IVB	Liver or splenic parenchymal metastases; metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); transmural involvement of intestine

上皮性卵巢癌診療指引

(Include fallopian tube cancer and primary peritoneal cancer from 2012.01.01)

Primary Treatment

- Initial surgical cytoreduction followed by systemic therapy
- Neoadjuvant chemotherapy + interval cytoreductive surgery + adjuvant systemic therapy

Salvage Therapy

- Secondary cytoreductive surgery+/- HIPEC
- Systemic therapy
- Radiotherapy for local control
- Tumor-directed ablation treatment (ex. RFA, cryotherapy, microwave, and so on)
- 2nd look surgical reassessment

Palliative Therapy

- Palliative systemic therapy
- Palliative radiotherapy
- Palliative surgery
- Hospice care

*Stage IVB with malignant pleural effusion → consider pleurodesis

上皮性卵巢癌診療指引

術前準備

- Chest X-ray, EKG, CBC/DC , Chemistry profile with liver and renal function tests
- Ultrasound and / or abdominal CT;
- MRI, PET/CT scan, if clinically indicated
- CA-125 or other tumor markers as clinically indicated
- Upper/Lower GI endoscopy if clinically indicated
- Breast image survey if clinically indicated
- Institutional pathology review (if diagnosis by previous surgery or tissue biopsy)
- Genetic consultation (if high risk for gene-predisposing)

上皮性卵巢癌診療指引

建議之減積手術

Complete staging surgery

- Peritoneal cytology + Hysterectomy + BSO + BPLND + PALNS + (Appendectomy) + Infracolic omentectomy + Sub-diaphragm smear + Liver surface smear

Primary Debulking surgery

- Complete staging surgery + dissection of all removable tumors
- Residual disease <1cm defines optimal cytoreduction, however, maximal effort should be made to remove all gross disease since this offers superior survival outcomes

Interval debulking surgery

- Neoadjuvant chemotherapy x 3-4 cycles +Interval debulking (± HIPEC) + systemic therapy x 3-6 cycles

Conservative staging surgery*

- Peritoneal cytology + Unilateral (or bilateral) salpingo-oophorectomy + ipsilateral (or bilateral) PLND + PALNS + (Appendectomy) + Infra-colic omentectomy + Sub-diaphragm smear + Liver surface smear

*Only for Early stage (IA & IB) and Grade I, and for selected patients with grade II or stage IC diseases

*且強烈要求保留生育能力的患者

上皮性卵巢癌診療指引

完整或保守的分期手術治療策略		
Stage	Management	
Stage IA or IB	Grade 1	Observation
	Grade 2	Observation or Intravenous chemotherapy for 3-6 cycles
	Grade 3	Intravenous chemotherapy for 6 cycles
Stage Ic	Intravenous chemotherapy for 4-6 cycles	
Stage II, III, IV	Intravenous platinum-based chemotherapy+/- bevacizumab for a total of 6-9 cycles or Intraperitoneal chemotherapy [if Optimally debulked (< 1 cm)] Consider maintenance therapy with bevacizumab and/or PARPi after primary treatment	

上皮性卵巢癌診療指引

不完整分期手術後意外發現		
Suspicion		Management**
Stage IA or IB Grade 1		Surgical staging procedure
Stage IA or Stage IB Grade 2 or 3 Stage IC	Clinically residual Tumor (−)	Chemotherapy for 6 cycles or Surgical staging procedure
	Clinically residual Tumor (+)	Surgical staging procedure
Stage II, III, IV	Resectable residual tumor	Debulking surgery
	Unresectable residual tumor	Chemotherapy for a total of 6-9 cycles or Neoadjuvant chemotherapy for 3 cycles followed by interval debulking procedure and postoperative chemotherapy

*The reassessment includes institutional pathology review, CBC with chemical profiles, CXR, CA-125 (± other markers), image studies such as ultrasound, CT scan or MRI as clinically indicated. It is recommended that a patient was evaluated by a gynecologic oncologist prior to initiating further management.
**Arrange treatment plan as recommended by guideline after complete staging surgery and determining final disease stage (see above)

全身性藥物處方建議

Primary or Adjuvant systemic Regimens for Stage I			
Histology	Preferred regimen	Other recommended Regimen	Useful in certain circumstances
• High-grade serous • Endometrioid (Grade 2/3) • Clear cell carcinoma • Carcinosarcoma	• Paclitaxel+ carboplatin	• Carboplatin+ liposomal doxorubicin • Docetaxel+ carboplatin • **Cyclophosphamide + platinum**	• Carboplatin (if elderly [age >70] and/or for those with comorbidities) For carcinosarcoma: • Carboplatin/ifosfamide • Cisplatin/ifosfamide • Paclitaxel/ifosfamide (category 2B)
• Mucinous Carcinoma (stage IC)	• Paclitaxel+ carboplatin • 5FU+leucovorin+oxaliplatin • Capecitabine+ oxaliplatin	• Carboplatin+ liposomal doxorubicin • Docetaxel+ carboplatin	• Carboplatin (if elderly [age >70] and/or for those with comorbidities)
• Low-Grade Serous (stage IC) • Grade I Endometrioid (stage IC)	• Paclitaxel+ carboplatin • Hormone therapy(Aromatase inhibitor)	• Carboplatin+ liposomal doxorubicin • Docetaxel+ carboplatin • Carboplatin/Cisplatin+ cyclophophamade • Hormone therapy(GnRHa, tamoxifen)	• Carboplatin (if elderly [age >70] and/or for those with comorbidities)

全身性藥物處方建議

Primary or Adjuvant systemic Regimens for Stage II-IV			
Histology	Preferred regimen	Other recommended Regimen	Useful in certain circumstances
• High-grade serous • Endometrioid (Grade 2/3) • Clear cell carcinoma • Carcinosarcoma	• Paclitaxel+ carboplatin • Paclitaxel+ carboplatin+ bevacizumab + maintenance bevacizumab	• Paclitaxel(weekly)+ carboplatin(weekly) • Docetaxel+ carboplatin • Carboplatin+ liposomal doxorubicin • Paclitaxel(weekly)+ carboplatin(Q3W) • Paclitaxel+ carboplatin+ bevacizumab • **Cyclophosphamide + platinum**	• IP/IV paclitaxel+ cisplatin • Carboplatin (if elderly [age >70] and/or for those with comorbidities) For carcinosarcoma: • Carboplatin/ifosfamide • Cisplatin/ifosfamide • Paclitaxel/ifosfamide (category 2B)
• Mucinous Carcinoma	• Paclitaxel+ carboplatin • Paclitaxel+ carboplatin+ bevacizumab + maintenance bevacizumab • 5FU+leucovorin+oxaliplatin± bevacizumab • Capecitabine+ oxaliplatin± bevacizumab	• Paclitaxel(weekly)+ carboplatin(weekly) • Docetaxel+ carboplatin • Carboplatin+ liposomal doxorubicin • Paclitaxel(weekly)+ carboplatin(Q3W) • Paclitaxel+ carboplatin+ bevacizumab	Carboplatin (if elderly [age >70] and/or for those with comorbidities)
• Low-Grade Serous • Grade I Endometrioid	• Paclitaxel+ carboplatin • Paclitaxel+ carboplatin+ bevacizumab + maintenance bevacizumab	• Paclitaxel(weekly)+ carboplatin(weekly) • Docetaxel+ carboplatin • Carboplatin+ liposomal doxorubicin • Paclitaxel(weekly)+ carboplatin(Q3W) • Paclitaxel+ carboplatin+ bevacizumab • carboplatin/cisplatin+ cyclophosphamide • Hormone therapy	Carboplatin (if elderly [age >70] and/or for those with comorbidities)

全身性藥物處方建議

Primary or Adjuvant systemic Regimens

Regimens	Dosage	Route	Day	Interval
1. Paclitaxel + Carboplatin or Cisplatin, x6 cycles (Stage III, IV)				
Paclitaxel Carboplatin, or Cisplatin	175 mg/m^2 AUC 5-7.5 75 mg/m^2	IVD 3 hrs IVD 1 hr IVD 1 hr	Day 1 Day 1 Day 1	Q3W
2. **Paclitaxel + Carboplatin +Bevacizumab**, x6 cycles, **+Maintenance Bevacizumab**(自費), 2-18 cycles				
Paclitaxel Carboplatin Bevacizumab	175 mg/m^2 AUC 5-6 7.5-15 mg/kg	IVD 3 hrs IVD 1 hr IVD 30-90 mins	Day 1 Day 1 Day 1 (from C2)	Q3W Q3W Q3W (from C2)
3. **Paclitaxel + Carboplatin or Cisplatin**, x6 cycles, **+Maintenance Paclitaxel**(自費)(for clinical complete responders Individualized QM x 12 courses)				
Paclitaxel Carboplatin Paclitaxel	175 mg/m^2 AUC 5-6 135 mg/m^2	IVD 3 hrs IVD 1 hr IVD 3 hrs	Day 1 Day 1 Day 1 (maintain)	Q3W Q3W Q4W (maintain)
4. Paclitaxel (weekly) + Carboplatin, Q3W				
Paclitaxel Carboplatin	80 mg/m^2 AUC 5-6	IVD 1 hr IVD 1-2 hrs	Day 1, 8, 15 Day 1	Q3W
5. Pegylated Liposomal Doxorubicin + Platinum				
Pegylated Liposomal Doxorubicin Carboplatin or Cisplatin	30-40 mg/m^2 AUC 5 30-50 mg/m^2	IVD 90 min IVD 1 hr	Day 1 Day 1	Q4W

Regimens	Dosage	Route	Day	Interval
6. Cyclophosphamide + Cisplatin, x6 cycles (stage I, II)				
Cyclophosphamide Cisplatin	750 mg/m^2 75 mg/m^2	IVD 2 hrs IVD 1 hr	Day 1 Day 1	Q3W
7. Cyclophosphamide + Carboplatin, x6 cycles				
Cyclophosphamide Carboplatin	750 mg/m^2 AUC 5-7.5	IVD 2 hrs IVD 1 hr	Day 1 Day 1	Q3W
8. Paclitaxel (over 24 hrs) + Cisplatin, x6 cycles				
Paclitaxel Cisplatin	135 mg/m^2 75 mg/m^2	IVD 24 hrs IVD 1 hr	Day 1 Day 1	Q3W
9. Gemcitabine + Paclitaxel, x4–6 cycles (需團隊共識討論)				
Gemcitabine Paclitaxel	1000 mg/m^2 175 mg/m^2	IVD 1 hr IVD 3 hrs	Day 1, 8 Day 8	Q3W Q3W, x4 cycles
10. Topotecan + Carboplatin (需團隊共識討論)				
Topotecan Carboplatin	0.75 mg/m^2/day AUC 2.5	IVD 1 hr	Day 1-3 Day 3	Q4W

全身性藥物處方建議

Primary or Adjuvant systemic Regimens

Regimens	Dosage	Route	Day	Interval
11. **5-FU/leucovorin/oxaliplatin ± bevacizumab** (only in mucinous carcinoma)				
12. **Paclitaxel (weekly)+ carboplatin**				
Paclitaxel Carboplatin	60-75 mg/m^2 AUC 5-6	IVD 1 hr IVD 30 mins	Day 1,8,15 Day 1	QW Q3W
13. **Docetaxel+ carboplatin**				
Docetaxel carboplatin	60-75 mg/m^2 AUC 5-6	IVD	Day1	Q3W

腹內化療處方建議

Primary or Adjuvant Chemotherapy Regimens

Regimens	Dosage	Route	Day	Interval
1. Intraperitoneal Paclitaxel + Cisplatin, x6 cycles				
Paclitaxel Cisplatin or Carboplatin	175 mg/m^2 100 mg/m^2 AUC 5	IVD 3 hrs IP 1 hr IP 1 hr	Day 1	Q3W
2. Intraperitoneal Paclitaxel + Cisplatin + Paclitaxel, x6 cycles				
Paclitaxel Cisplatin or Carboplatin Paclitaxel	135 mg/m^2 75-100 mg/m^2 (Cisplatin) or AUC 5 (carboplatin) 60 mg/m^2	IVD 24 hrs IP 1 hr IP 1 hr	Day 1 Day 1 Day 8	Q3W

賀爾蒙處方建議

Primary or Adjuvant systemic Regimens for Stage II-IV

Regimens	Dosage	Route	Day	Interval
Aromatase inhibitor				
Anastrozole(Arimidex) Letrozole(Femara) Exemestane(Aromasin)	1mg 2.5mg 25	PO PO PO	Day 1 Day 1 Day 1	QD QD QD
Leuprolide				
Leuprolide acetate -Leuplin -Leuplin Depot 1M -Leuplin Depot 3M	 1mg 3.75mg 11.25mg	 SC SC SC	 Day 1 Day 1 Day 1	 QD Q4W Q12W
Antiestrogen: useful in low grade serous/grade I endometrioid epithelial ovarian carcinomas				
Tamoxifen (Nolvadex) Fulvestrant (Faslodex)	20-40mg 500mg	PO IM	Day 1 Day 1	QD Q2W X3, then Q4W

全身性藥物處方建議

Recurrent or persistent disease after primary treatment: if platinum sensitive

Preferred regimen	Other recommended Regimen	Useful in certain circumstances
Chemotherapy	**Chemotherapy**	**Chemotherapy**
• Platinum + paclitaxel ± bevacizumab • Platinum + liposomal doxorubicin± bevacizumab • Platinum + gemcitabine ± bevacizumab	• Carboplatin + docetaxel • Carboplatin + paclitaxel(weekly) • Carboplatin/Cisplatin • Cyclophosphamide • Doxorubicin • Ifosfamide • Paclitaxel • Melphalan • Capecitabine • Irinotecan • Oxaliplatin • Vinorebine	• 5FU+leucovorin+oxaliplatin± bevacizumab (mucinous) • Capecitabine+ oxaliplatin± bevacizumab (mucinous) • Irinotecan+ cisplatin (clear cell carcinoma)
		Targeted therapy
		• Entrectinib (for NTRK gene fusion- positive tumor) • Trametinib (for low grade serous carcinoma)
Targeted therapy	**Targeted therapy**	**Immunotherapy**
• Bevacizumab • Olaparib • Niraparib	• Pazopanib	• Pembrolizumab
	Hormone therapy	**Hormone therapy**
	• Aromatase inhibitor • Leuprolide acetate • Megestrol acetate • Tamoxifen	• Fulvestrant (low grade serous carcinoma)

Ovary, Fallopian Tube and Peritoneal Carcinoma

全身性藥物處方建議

Recurrent or persistent disease after primary treatment: Combination if platinum sensitive

Regimens	Dosage	Route	Day	Interval
1. **Paclitaxel + Carboplatin**				
Paclitaxel Carboplatin	175 mg/m^2 AUC 5 ~7.5	IVD 3 hrs IVD 1 hr	Day 1 Day 1	Q3W
2. **Weekly paclitaxel + Carboplatin**				
Paclitaxel Carboplatin	80 mg/m^2 AUC 1.5	IVD 1 hr IVD 1 hr	Day 1 Day 1	QW
3. **Docetaxel /Carboplatin**				
Docetaxel Carboplatin	60 mg/m^2 AUC 5 -7.5	IVD 1 hr IVD 1 hr	Day 1 Day 1	Q3W
4. **Gemcitabine + Platinum**				
Gemcitabine Carboplatin, or Cisplatin	1000 mg/m^2 AUC 4 30 mg/m^2	IVD 30 mins IVD 1 hr IVD 1 hr	Day 1, 8 Day 1 Day 1, 8	Q3W
5. **Liposomal doxorubicin/platinum**				
Pegylated liposomal doxorubicin Carboplatin, or Cisplatin	30-40 mg/m^2 AUC 5 30-50 mg/m^2	IVD 90 mins IVD 1 hr IVD 1 hr	Day 1 Day 1 Day 1	Q4W
6. **Gemcitabine/Carboplatin**, x6 cycles, 最多10 cycles, 合併使用Bevacizumab直到疾病惡化				
Gemcitabine Carboplatin Bevacizumab	1000mg/m^2 AUC 4 15mg/kg	IVD IVD IVD 30-90 mins	Day 1, 8 Day 1 Day 1	Q3W

全身性藥物處方建議

Recurrent or persistent disease after primary treatment: Single-agent if platinum sensitive

Regimens	Dosage	Route	Day	Interval
Carboplatin	AUC 5-7.5	IV 1 hr	Day 1	
Cisplatin	50-75 mg/m^2	IV 1 hr	Day 1	

全身性藥物處方建議

Recurrent or persistent disease after primary treatment: if platinum resistant

Preferred regimen	Other recommended Regimen	Useful in certain circumstances
Chemotherapy	**Chemotherapy**	**Targeted therapy**
• Liposomal doxorubicin± bevacizumab • Paclitaxel(weekly) ± bevacizumab • Topotecan± bevacizumab • Gemcitabine • Cyclophosphamide+ Bevacizumab • Docetaxel • Etoposide	• Capecitabine • Cyclophosphamide • Ifosfamide • Irinotecan • Melphalan • Oxaliplatin • Paclitaxel • Pemetrexed • Sorafenib+ topotecan • Vinorelbine	• Entrectinib (for NTRK gene fusion- positive tumor) • Trametinib (for low grade serous carcinoma)
Targeted therapy	**Targeted therapy**	**Immunotherapy**
• Bevacizumab • Olaparib • Niraparib	• Pazopanib	• Pembrolizumab
	Hormone therapy	**Hormone therapy**
	• Aromatase inhibitor • Leuprolide acetate • Megestrol acetate • Tamoxifen	• Fulvestrant (low grade serous carcinoma)

全身性藥物處方建議

Recurrent or persistent disease after primary treatment: Single-agent if platinum resistant

Regimens	Dosage	Route	Day	Interval
1. Docetaxel	100 mg/m^2	IVD 1 hr	Day 1	Q3W
2. Melphalan	0.2 mg/kg/day	PO	Day 1-5	Q4-6W
3. Gemcitabine	800 mg/m^2	IVD 1 hr	Day 1	QW
4. Liposomal doxorubicin	40-50 mg/m^2	IVD 90 mins	Day 1	Q4W
5. Paclitaxel, weekly	60-80 mg/m^2	IVD 1 hr	Day 1	QW
6. Paclitaxel	175 mg/m^2	IVD 3 hrs	Day 1	Q3W
7. Topotecan	1.00-1.25 mg/m^2/day	IVD 30 mins	Day 1-3~5	Q3W or Q4W
8. Topotecan, weekly	2.5-4 mg/m^2	IVD 90 mins	Day 1, 8, 15	Q4W
9. Pazopanib (需團隊共識討論)	400-800 mg		Day 1	QD
10. Pembrolizumab# (需團隊共識討論)	成人建議劑量200mg	IVD 30 mins		Q3W

#if Microsatellite instability-H or mismatch repair-deficient

全身性藥物處方建議

Recurrent or persistent disease after primary treatment: Combined bevacizumab and non-platinum agent

Regimens	Dosage	Route	Day	Interval
Liposomal doxorubicin + Bevacizumab				
Bevacizumab Liposomal doxorubicin	10 mg/kg 40 mg/m^2	IVD 30-90 mins IVD	Day 1 Day 1	Q2W Q4W
Paclitaxel + Bevacizumab				
Bevacizumab Paclitaxel	10 mg/kg 80 mg/m^2	IVD 30-90 mins IVD	Day 1 Day 1, 8, 15, 22	Q2W Q4W
Topotecan (Q4W) **+ Bevacizumab**				
Bevacizumab Topotecan	10 mg/kg 4 mg/m^2	IVD 30-90 mins IVD	Day 1 Day 1, 8, 15	Q2W Q4W
Topotecan (Q3W) **+ Bevacizumab**				
Bevacizumab Topotecan	15 mg/kg 1.25 mg/m^2	IVD 30-90 mins IVD	Day 1 Day 1-5	Q3W Q3W

全身性藥物處方建議

Acceptable maintenance therapy (Front line, second line use)*

Regimens	Dosage	Route	Day	Interval
1. **Bevacizumab** If used previously as part of a combination & partial or complete remission following primary therapy for stage II-IV disease or recurrence therapy for platinum-sensitive disease				
Bevacizumab	7.5-15mg/kg	iv		Q3W
2. **Paclitaxel** Monthly and if clinical complete remission following primary therapy for stage II-IV disease				
Paclitaxel				
3. **Olaparib** If platinum-sensitive disease with partial or complete response, Germline or somatic BRCAm If HRD(+)→ consider combine with bevacizumab				
Olaparib	300mg	po		BID
4. Niraparib+				
Niraparib	200mg	po		QD
4. **Pazopanib** If clinical complete remission following primary therapy for stage II-IV disease without prior bevacizumab				
Pazopanib	400-800 mg	po		QD

*Maintenance therapy is suitable for stage II-IV disease
+ The recommended starting dose of Zejula is 200 mg (two 100-mg capsules), taken once daily

全身性藥物處方建議›非上皮性卵巢癌

Treatment for Germ Cell Tumor of the Ovary

- Stage I dysgerminoma or stage I, grade 1 immature teratoma: observe
- High risk patients (any stage embryonal tumor ; any stage yolk sac tumor ; stage II-IV dysgerminoma ; Stage I, grade 2 or grade 3 or stage II-IV immature teratoma ; any stage nongestational choriocarcinoma)

Chemotherapy for Germ Cell Tumor of the Ovary

Regimens	Dosage	Route	Day	Interval
1. BEP, x3-4 cycles, Bleomycin累積劑量不可＞225mg				
Etoposide Bleomycin Cisplatin	100 mg/m^2 15mg /30mg 100 mg/m^2	IVD 1 hr IVD IVD	Day 1-3 Day 1-3/Day 1 Day 1	Q3W or Q4W Q3W or Q4W Q3W or Q4W
2. Etoposide/carboplatin, x3 cycles				
Etoposide carboplatin	120 mg/m^2 400 mg/m^2	IVD 1 hr IVD 1 hr	Day 1-3 Day 1	Q4W

全身性藥物處方建議›非上皮性卵巢癌

Recurrence Therapy for Germ Cell Tumor of the Ovary

1. Platinum based chemotherapy

   TIP (paclitaxel /ifosfamide/cisplatin)

   VIP (etoposide/ifosfamide/cisplatin) (palliative)

2. High dose chemotherapy

   → consult medical oncology for C/T with stem cell transplantation

3. Radiation therapy (palliative localized RT)

全身性藥物處方建議›非上皮性卵巢癌

Treatment for Sex cord-Stromal tumor of the ovary

1. Stage I low risk → observe
2. Stage I high risk (ruptured stage IC or poorly differentiated), stage I intermediate risk (eg. Heterologous elements) → observe or platinum based chemotherapy
3. Stage II-IV: Platinum based chemotherapy or Radiation for limited disease

Chemotherapy for Sex cord-Stromal tumor of the ovary

Regimens	Dosage	Route	Day	Interval
1. Paclitaxel + Carboplatin/Cisplatin				
Paclitaxel Carboplatin , or Cisplatin	175 mg/m^2 AUC 5 75 mg/m^2	IVD 3 hrs IVD 1 hrs IVD	Day 1 Day 1 Day 1	Q3W
2. Etoposide/carboplatin, x3 cycles				
Etoposide carboplatin	120 mg/m^2 400 mg/m^2	IVD 1 hr IVD 1 hr	Day 1-3 Day 1	Q4W
3. BEP, x3-4 cycles, Bleomycin累積劑量不可＞225mg				
Etoposide Bleomycin Cisplatin	100 mg/m^2 15mg / 30mg 100 mg/m^2	IVD 1 hr IVD IVD	Day 1-3 Day 1-3 / Day1 Day 1	Q3W or Q4W Q3W or Q4W Q3W or Q4W

全身性藥物處方建議›非上皮性卵巢癌

Recurrence therapy for Sex cord-Stromal tumor of the ovary

1. Chemotherapy
   Paclitaxel/carboplatin
   Etoposide/cisplatin (EP)
   Etoposide/carboplatin (EP)
   Paclitaxel/Ifosfamide
   Docetaxel
   Paclitaxel
2. Bevacizumab may be considered for granulosa cell tumors
3. Hormone therapy
   Leuprolide may be considered as hormone therapy for granulosa cell tumors
   Aromatase inhibitor (anastrozole, letrozole)
   Tamoxifen
4. Palliative localized RT/ablation

持續性或復發性疾病

- 評估疾病的程度和進展
  - Clinical symptoms and signs
  - Imaging studies
    Chest / Abdominal / Pelvic CT, MRI or PET as clinically indicated.
  - Tumor marker
- 完成化療後完全緩解，但 <6個月復發；或第二、三、四期部分緩解，考慮復發性或持續性上皮性卵巢癌化療治療處方。
- 完成化療後完全緩解，但6~12個月內復發；或完全緩解>6個月疑似復發情形。
  - Consider secondary cytoreductive surgery / PET scan followed by chemotherapy (可同first line C/T regimen；或platinum-based + 非paclitaxel類agent；或non-platinum-based agent)
  - Consider secondary cytoreductive surgery followed by clinical trial
- 完成化療後完全緩解，但 >12個月後復發
  - Consider secondary cytoreductive surgery followed by platinum-based combination chemotherapy (同first line C/T regimen)
  - Consider secondary cytoreductive surgery followed by clinical trial
- 無臨床復發，但CA-125上升
  - Delay treatment until clinical relapse
  - Immediate treatment as recurrent disease

追蹤

門診追蹤

- 第一年每2個月1次
- 第二年每3個月1次
- 此後每6個月追蹤1次

追蹤建議

- 身體檢查如骨盆腔檢查。若腫瘤指數一開始即高於正常值，建議每次追蹤。
- 依臨床表徵需要可行影像學檢查如：Abdominal / Pelvic CT, MRI, or Chest x-ray。

Borderline Ovarian Cancer

邊緣性卵巢腫瘤診療指引

1. Primary Treatment
   - Standard treatment
   - Surgical cytoreduction
2. Chemotherapy/Targeted therapy: Individualized
3. Salvage Therapy
   - Secondary cytoreductive surgery
   - Whole abdominal radiation (WAR)
   - 2nd look surgical reassessment
4. Palliative Therapy
   - Palliative chemotherapy
   - Palliative surgery
   - Hospice care

邊緣性卵巢腫瘤診療指引

術前準備

- Ultrasound and /or abdominal CT
- Chest imaging
- CBC/DC
- Chemistry profile with liver and renal function tests
- Institutional pathology review (if diagnosis by previous surgery or tissue biopsy)
- CA-125 or other tumor markers as clinically indicated
- Upper/Lower GI endoscopy if clinically indicated

Borderline Ovarian Cancer

邊緣性卵巢腫瘤診療指引

Adjuvant Treatment for Ovarian Borderline Tumors				
Prior complete surgical resection	Residual disease by image studies	Invasive implants or unknown	Fertility desired	Adjuvant treatment options
Yes		No		• Observe
		Yes		• Observe • Treat as low-grade serous epithelial cancer
No	No	No		• Observe
	Yes	No	Yes	• Observe • Fertility-sparing surgery & resection of residual disease
			No	• Observe • completion surgery & resection of residual disease
		Yes	Yes	• Fertility-sparing surgery & maximally deb resection of residual disease • Observe • Treat as low-grade serous epithelial cancer
			No	• Completion of surgery & resection of residual disease • Observe • Treat as low-grade serous epithelial cancer

附錄

1. 卵巢癌(Ovary borderline tumor, low malignant potential)癌症登記申報原則分述如下:

情況	Ovary borderline tumor (Low malignant potential) 病理報告描述	5th 性態碼	是否申報
一	with intraepithelial carcinoma	2	是
二	with micro-invasion	3	是
三	with intraepithelial carcinoma and micro-invasion	3	是
四	無intraepithelial carcinoma 亦無micro-invasion	1	否

2. 組織病理報告 Granulosa cell tumor (M8620/1、 8621/1、 8622/1)因臨床醫療專家認為屬於惡性，5th性態碼依矩陣概念由1改變為3(惡性)予以申報癌登,唯其癌症診斷依據不可摘錄為組織病理學確診。
3. (子宮頸癌)組織切片病理報告記錄為 CIN 2-3，視為CIN3組織病理編碼為8077/2(Squamous intraepithelial neoplasia, grade III)

卵巢癌核心測量指標

指標類型	測量指標	分子	分母
1	卵巢惡性腫瘤確診病人，治療前有接受骨盆腔和腹部電腦斷層(CT)檢查的比率。	分母中，治療前一個月內有接受骨盆腔和腹部電腦斷層(CT)檢查的人數。	所有確診為原發性卵巢惡性腫瘤的人數。
2	術後病理診斷為卵巢癌之病患，首次手術紀錄有詳細記載殘存腫瘤狀態及大小的比率。	分母中，SSF3編碼為000、010、020、030、040的人數。	上皮性卵巢癌病患首次治療有接受治療性手術，術後分期為第Ⅱ、Ⅲ、Ⅳ期的人數。(扣除非上皮及GERM CELL, SEX CORD-STROMAL)
3	術後病理診斷為卵巢癌之病患，首次手術紀錄無殘存腫瘤狀態及大小的比率。	分母中，SSF3 編碼為000 的人數。	上皮性卵巢癌病患首次治療有接受治療性手術，術後分期為第II、III、IV期的人數。(扣除非上皮及GERM CELL, SEX CORD-STROMAL)

Vulva Cancer

Vulva Cancer

分期

TNM	FIGO	Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor confined to the vulva and/or perineum Multifocal lesions should be designated as sch. The largest lesion or the lesion with the greatest depth of invasion will be the target lesion identified to address the highest pT stage. Depth of invasion is defined as the measurement of the tumor from the epithelial-stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion.
-T1a	IA	Lesions 2 cm or less, confined to the vulva and/or perineum, and with stromal invasion of 1.0 mm of less
-T1b	IB	Lesions more than 2cm, or any size with stromal invasion of more than 1.0 mm, confined to the vulva and/or perineum
T2	II	Tumor of any size with extension to adjacent perineal structures (lower/distal third of the urethra, lower/distal third of the vagina, anal involvement)
T3	IVA	Tumor of any size with extension to any of the following – upper/proximal two thirds of the urethra, upper/proximal two thirds of the vagina, bladder mucosa, or rectal mucosa – or fixed to pelvic bone
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
N1	III	Regional lymph node metastasis with one or two lymph node metastases each less than 5 mm, or one lymph node metastasis =5 mm
-N1a*	IIIA	One or two lymph node metastases each less than 5 mm
-N1b	IIIA	One lymph node metastasis=5mm
N2		Regional lymph node metastasis with three or more lymph node metastases each less than 5 mm, or two or more lymph node metastases =5 mm, or lymph node(s) with extra-nodal extension
-N2a	IIIB	Three or more lymph node metastases each less than 5 mm
-N2b	IIIB	Two or more lymph node metastases =5 mm
-N2c	IIIC	Lymph node(s) with extra-nodal extension
N3	IVA	Fixed or ulcerated regional lymph node metastasis
M0		No distant metastasis (no pathologic M0; use clinical M to complete stage group)
M1	IVB	Distant metastasis (including pelvic lymph node metastasis)

外陰癌診療指引

術前準備

- Blood analysis
- Pathology proved
- Tumor marker
- CT scan/MRI/PET-CT (小心健保剔退) if clinically indicated
- Cystoscopy/Colonoscopy if clinically indicated
- Cervical HPV and cytology testing

Vulva Cancer

外陰癌診療指引

Stage	Choice of Treatment
IA	• Simple partial vulvectomy (margin at least 1cm) • Radiotherapy • CCRT
IB	• Radical vulvectomy + unilateral inguinofemoral lymphadenectomy (≥2 cm from the vulvar midline) or SLN biopsy • Radical vulvectomy + bilateral inguinofemoral lymphadenectomy (for midline lesion) or SLN biopsy • Radical vulvectomy ± radiation to the groin areas • Radiotherapy • CCRT
Smaller II (≤4 cm)	• Radical vulvectomy + bilateral groin dissection or SLN biopsy • Neoadjuvant chemotherapy + (Radical vulvectomy + bilateral groin dissection) or Radiotherapy • Radiotherapy ± Chemotherapy • CCRT
Larger II (>4 cm)	• EBRT with concurrent chemotherapy ± IFLN dissection ± interstitial RT • Radical surgeries such as en bloc radical vulvectomy with bilateral inguinofemoral lymphadenectomy or pelvic exenteration (less favored)

Candidates for SLN biopsy:
- Negative clinical groin examination and imaging
- A primary unifocal vulvar tumor size of <4 cm
- No previous vulvar surgery that may have impacted lymphatic flow to the inguinal region.

A complete inguinofemoral lymphadenectomy is recommended if an ipsilateral SLN is not detected.

Vulva Cancer

外陰癌診療指引

Stage	Choice of Treatment
III	• Radical vulvectomy + bilateral inguinofemoral lymphadenectomy ± (Radiotherapy or CCRT) • CCRT • Neoadjuvant chemotherapy + (Radical vulvectomy + bilateral inguinofemoral lymphadenectomy) or Radiotherapy • Radiotherapy ± Chemotherapy
IV	• CCRT • Radiotherapy ± systemic therapy • Radical vulvectomy/possible exenteration + bilateral inguinofemoral lymphadenectomy± (Radiotherapy or CCRT) • Neoadjuvant chemotherapy + (Radical vulvectomy + bilateral inguinofemoral lymphadenectomy) or Radiotherapy • Supportive care

Treatment consideration:

- Central or lateral location
- Local or multifocal lesion

Unresectable LN regardless of T stage: Fine needle aspiration for enlarged LN-> CCRT

外陰癌診療指引›輔助治療

手術後的輔助治療(FIGO stage I-II)			
Margin	LN	Risk factor	Management
(−)	(−)	(−)	• Observation
		(+)	• Radiotherapy or • CCRT
	(+)	(−) or (+)	• CCRT or • Radiotherapy
(+)	(−) or (+)	(−) or (+)	• Reoperation • Radiotherapy • CCRT

- Risk factor: close tumor margins, lympho-vascular invasion, tumor size, depth of invasion, and pattern of invasion (spray or diffuse), Nodal involvement (as an indicator of lympho-vascular space invasion)
- Pathologic close margin has also varied from 1–8 mm for formalin-fixed tissue, observation with regular close follow-up is reasonable

外陰癌診療指引›輔助治療

手術後的輔助治療	
Node (-) (SLN or inguinofemoral node)	Observe
SLN (+)	EBRT ± concurrent chemotherapy
	Completion inguinofemoral node dissection → EBRT ± concurrent chemotherapy
Inguinofemoral node dissection (+)	EBRT ± concurrent chemotherapy (especially if ≥2 LNs positive or 1 LN positive with >2 mm metastasis)

全身性藥物處方建議

外陰癌化療處方適應症

- Neoadjuvant chemotherapy for bulky tumor and advanced disease
  Followed by surgery or RT
- Concurrent chemoradiotherapy
  Early bulky tumor followed by surgery
  Postoperative with lymph node metastasis Advanced cancer
  Primary treatment
- Palliative chemotherapy for distant, recurrent, or metastatic cancer
- If distant metastasis or recurrence → Systemic Chemotherapy ± Palliative Radiotherapy

Vulva Cancer

Chemoradiation	
Preferred regimens	Cisplatin
Other recommended regimens	1. Cisplatin+5-FU 2. 5-FU+mitomycin C 3. Others

Advanced or Recurrent/Metastatic disease	
Systemic therapies	
Preferred regimens	1. Cisplatin/Carboplatin 2. Cisplatin/Carboplatin+ Paclitaxel 3. Cisplatin+ Paclitaxel+ bevacizumab
Other recommended regimens	1. Paclitaxel 2. Cisplatin+ Vinorelbine 3. Erlotinib 4. Cisplatin+ gemcitabine 5. Carboplatin+ paclitaxel+ bevacizumab 6. Others
Biomarker directed systemic therapy for second-line treatment	
Pembrolizumab	TMB-H, PD-L1-positive, or MSI-H/MMR deficient
Nivolumab	
Larotrectinib or entrectinib	NTRK gene fusion positive tumors

Vulva Cancer

全身性藥物處方建議

Neoadjuvant Chemotherapy (先輔助化療)

Regimens	Dosage	Route	Day	Interval
1. **Cisplatin** Only (QW x3 cycles) Surgery performed on 3rd day after completing chemotherapy				
Cisplatin	40 mg/m^2 (at least 25 mg/m2)	IVD 1 hr	Day 1	QW
2. **Paclitaxel + Cisplatin Regimen** (q10d x3 cycles) Surgery performed within 3 weeks after completing chemotherapy				
Paclitaxel Cisplatin	60 mg/m^2 60 mg/m^2	IVD 1.5 hrs IVD 1 hr		Q10D
3. **5-FU + Cisplatin** x3 cycles				
5-FU Cisplatin	100 mg/m^2 50 mg/m^2	IVD 24 hrs IVD 1 hr	Day 1-5 Day 1	Q3W

CCRT regimen (同步化學放射治療)

Regimens	Dosage	Route	Day	Interval
1. **Cisplatin** Only (QW)				
Cisplatin	40 mg/m^2	IVD 1 hr	Day 1	QW
2. **5-FU + Cisplatin**				
5-FU Cisplatin	250 mg/m^2 4 mg/m^2	IVD 96 hrs IVD 96 hrs		QW
3. **5-FU + Mitomycin-C**				
5-FU Mitomycin-C	750 mg/m^2 15 mg/m^2	IVD 24 hrs Single bolus	Day 1-5 Day 1	Q2W
4. **POB Regimen** Bleomycin累積劑量不可＞150mg				
Cisplatin Vincristine Bleomycin	50 mg/m^2 1 mg/m^2 15 mg	IVD 1 hr IVD 15-30 mins IVD 15 mins	Day 1 Day 1 Day 1-3	Q3W

Vulva Cancer

臺北榮民總醫院婦女醫學部婦癌團隊
Version 2021.10

全身性藥物處方建議

Regimens	Dosage	Route	Day	Interval
Cisplatin/carboplatin Regimen				
Cisplatin Carboplatin	40 mg/m^2 AUC 2	IVD 1 hr IVD 1 hr	Day 1 Day 1	QW QW
Paclitaxel + Cisplatin/carboplatin Regimen, x6 cycles				
Paclitaxel Cisplatin	135 mg/m^2 50 mg/m^2	IVD 3 hrs IVD 1 hr	Day 1 Day 1	Q3W
Paclitaxel + Cisplatin/carboplatin + Bevacizumab(自費)				
Paclitaxel Cisplatin Bevacizumab	175 or 135 mg/m^2 50 mg/m^2 7.5-15 mg/kg	IVD 3 hrs IVD 1 hr IVD 30-90 mins	Day 1 Day 1 Day 1	Q3W
Paclitaxel				
Paclitaxel	175 mg/m^2 135 mg/m^2 if prior RT	IVD 3 hrs IVD 3 hrs	Day 1	Q3W
Cisplatin+ Vinorelbine				
Cisplatin Vinorelbine	50 mg/m^2 25 mg/m^2		Day 1 Day 1, 8	Q3W
Erlotinib				
Erlotinib	100 and 150 mg/day	PO		QD
Gemcitabine + Cisplatin Regimen, x6 cycles				
Gemcitabine Cisplatin	1000 mg/m^2 50 mg/m^2	IVD 30 mins IVD 1 hr	Day 1, 8 Day 1	Q3W

Regimens	Dosage	Route	Day	Interval
Paclitaxel + Ifosfamide + Cisplatin Regimen, x6 cycles				
Paclitaxel Ifosfamide Cisplatin	175 mg/m^2 1 gm/m^2 50 mg/m^2	IVD 3 hrs IVD 24 hr IVD 1 hr	Day 1-3	Q3W
Irinotecan + Cisplatin Regimen, x6 cycles				
Irinotecan Cisplatin	60 mg/m^2 60 mg/m^2	 IVD 1 hr	Day 1, 8, 15 Day 1	
Topotecan + Cisplatin weekly Regimen, x6 cycles				
Topotecan Cisplatin	2 or 2.5 mg/m^2 40 mg/m^2	IVD 90 mins IVD 1 hr	Day 1, 8, 15 Day 1, 8, 15	
Topotecan + Cisplatin Regimen, x6 cycles				
Topotecan Cisplatin	0.75 mg/m^2 50 mg/m^2	IVD 30 mins IVD 1 hr	Day 1-3 Day 1	Q3W
Ifosfamide + Cisplatin Regimen, x6 cycles				
Ifosfamide Cisplatin	5 gm/m^2 50 mg/m^2	IVD 24 hrs IVD 1 hr		Q3W
Epirubicin + Ifosfamide + Cisplatin Regimen, x6 cycles				
Epirubicin Ifosfamide Cisplatin	50 mg/m^2 1 gm/m^2 50 mg/m^2	IVD 24 hr IVD 1 hr	Day 1-3	Q3W

全身性藥物處方建議

備註：

1. Cisplatin 為外陰癌治療化學治療首選藥物，若 (CCr < 60)，Carboplatin可做為替代藥物取代 (婦癌個案注 Cisplatin若因CCR ≤ 60，weekly Cisplatin 40 mg/m^2，可改為Carboplatin AUC 2；若非weekly用法，Cisplatin Q3W使用，則為75 mg/m2改為Carboplatin AUC 5。)

2. Platinum + Topotecan (D1~3) (Q3W)用法：
   - Cisplatin 50 mg/m2 (D1) + Topotecan 0.75 mg/m^2 (D1~D3)，Cisplatin 用於第一天；
   - Carboplatin (AUC 5) (D3) + Topotecan 0.75 mg/m^2 (D1~D3)，Carboplatin用於第三天，
   - 是因要降低骨髓抑制副作用。

持續性或復發性疾病

考慮因素

- Status of disease and patient's condition
- Performance status
- Palliative or Curative treatment

Treatment of recurrent vulvar cancer may include the following

1. Wide local excision with or without radiation therapy to treat cancer that has come back in the same area.
2. Radical vulvectomy and pelvic exenteration to treat cancer that has come back in the same area.
3. Radiation therapy ± concurrent chemotherapy.
4. Chemotherapy and palliative supportive care
5. Radiation therapy as palliative treatment to relieve symptoms and improve quality of life.
6. A clinical trial of a new treatment.
7. Pembrolizumab, second-line therapy for PD-L1–positive, MSI-H/dMMR, or TMB-H tumors vulvar tumors

持續性或復發性疾病

Vulvar confined recurrence	
1. Radical excision ± unilateral or bilateral IFLN dissection 2. Pelvic exenteration for select cases with a central recurrence	Margin (-), node (-): • observation or EBRT
	Margin (+), node (-): • re-excision or EBRT ±brachytherapy ± concurrent chemotherapy
	Margin (-), node (+): • EBRT ± chemotherapy
	Margin (+), node (+): • EBRT ± brachytherapy ± concurrent chemotherapy ± re-excision as needed/appropriate.
EBRT ± brachytherapy ± concurrent chemotherapy	Resection can be considered for patients with gross residual tumor

持續性或復發性疾病

Nodal Recurrence or Distant Metastasis	
Multiple positive pelvic nodes or distant metastasis ± pelvic R/T history	1. Systemic therapy ±Selected EBRT if feasible 2. Palliative/best supportive care 3. Clinical trial enrollment
Isolated groin/pelvic recurrence + R/T history	1. Resection followed by systemic therapy 2. Systemic therapy ±Selected EBRT if feasible 3. Palliative/best supportive care
Limited to the groin, no R/T history	1. Resection of positive nodes followed by EBRT ± concurrent chemotherapy 2. Unresectable nodes, EBRT with or without concurrent chemotherapy

追蹤

門診追蹤

- 前兩年每3個月1 次
- 第三至四年每6個月1次
- 第五年每年

追蹤建議

身體檢查如骨盆腔檢查, 抹片檢查(90天)，若SCC或其他腫瘤指數一開始即高於正常值，建議每次追蹤。依個人狀況若有臨床需求可行抽血(CBC或生化功能)，依臨床表徵需要可行影像學檢查如：CXR, CT chest/abdomen/pelvis or whole-body PET/CT.

Vagina Cancer

Vaginal Cancer

分期

TNM	FIGO	Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor confined to the vagina
-T1a	I	Tumor confined to the vagina, measuring ≦2.0 cm
-T1b	I	Tumor confined to the vagina, measuring >2.0 cm
T2	II	Tumor invading paravaginal tissues but not to pelvic sidewall
-T2a	II	Tumor invading paravaginal tissues but not to pelvic wall, measuring ≦2.0 cm
-T2b	II	Tumor invading paravaginal tissues but not to pelvic wall, measuring >2.0 cm
T3	III	Tumor extending to the pelvic sidewall* and/or involving the lower third of the vagina and/or causing hydronephrosis or nonfunctioning kidney
T4	IVA	Tumor invading the mucosa of the bladder or rectum and/or extending beyond the true pelvis (bullous edema is not sufficient evidence to classify a tumor as T4)
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
N1	III	Pelvic or inguinal lymph node metastasis
M0		No distant metastasis
M1	IVB	Distant metastasis

陰道癌診療指引

Vaginal cancer definition:

Vaginal cancer is strictly defined as a cancer found in the vagina without clinical or histologic evidence of cervical or vulvar cancer, or a prior history of these cancers within five years.

*Edge SB, Compton CC The American Joint Committee on Cancer: The 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol. 2010;**17**:1471–1474.*

術前準備

Blood analysis

- Pathology proved
- Tumor marker
- CT scan/MRI/PET-CT (小心健保剔退) if clinically indicated
- Cystoscopy/Colonoscopy if clinically indicated

Vaginal Cancer

陰道癌診療指引

Stage	Choice of Treatment
I	· Surgical management† · Brachytherapy ± external beam RT · External beam RT ± brachytherapy ± chemotherapy · CCRT*
II	· CCRT + brachytherapy · Neoadjuvant chemotherapy + Radical hysterectomy + PLND ± PALNS
III	· External beam RT ± brachytherapy ± chemotherapy · CCRT*
IV	· External beam RT ± brachytherapy ± chemotherapy · Pelvic exenteration ± radiotherapy ± chemotherapy · Supportive care ± palliative chemotherapy or radiotherapy · CCRT*

Treatment consideration: (upper or lower location; local or multifocal lesion)
†Surgical management (location: upper vagina)
1. RH+ lymph node dissection + partial or total vaginectomy
2. Partial or total vaginectomy + parametrectomy + lymph node dissection (for patients who had undergone hysterectomy)

* 仍未定論

陰道癌診療指引

手術後的輔助治療(FIGO Stage I)			
Margin	LN	Bulky size (>2cm)	Management
(−)	(−)	(−)	Observation
		(+)	Observation or IVRT
	(+)	(−) or (+)	CCRT or Radiotherapy ±chemotherapy
(+)	(−) or (+)	(−) or (+)	CCRT or Radiotherapy ±chemotherapy

全身性藥物處方建議

陰道癌化療處方適應症

- Neoadjuvant chemotherapy for bulky tumor and advanced disease
- Concurrent chemoradiotherapy
  - Postoperative with lymph node metastasis or margin (+)
  - Primary treatment*
- Palliative chemotherapy for distant, recurrent, or metastatic cancer
- If distant metastasis or recurrence → Systemic Chemotherapy ± Palliative Radiotherapy

*仍未定論

Vaginal Cancer

全身性藥物處方建議

CCRT (同步化學放射治療)

Regimens	Dosage	Route	Day	Interval
1. **Cisplatin** Only (QW)				
Cisplatin	40 mg/m^2	IVD 1 hr	Day 1	QW
2. **POB Regimen** Bleomycin累積劑量不可＞150mg				
Cisplatin Vincristine Bleomycin	50 mg/m^2 1 mg/m^2 15 mg	IVD 1 hr IVD 15-30 mins IVD 15 mins	Day 1 Day 1 Day 1-3	Q3W
3. **5-FU + Cisplatin**				
5-FU Cisplatin	250 mg/m^2 4 mg/m^2	IVD 96 hrs IVD 96 hrs		QW
4. **5-FU + Mitomycin-C**				
5-FU Mitomycin-C	750 mg/m^2 15 mg/m^2	IVD 24 hrs Single bolus	Day 1-5 Day 1	Q2W

Vaginal Cancer

全身性藥物處方建議

Adjuvant or Disseminated or Recurrent Disease Chemotherapy Regimen

Regimens	Dosage	Route	Day	Interval
Paclitaxel + Cisplatin Regimen, x6 cycles				
Paclitaxel Cisplatin	135 mg/m^2 50 mg/m^2	IVD 3 hrs IVD 1 hr		Q3W
Topotecan + Cisplatin Regimen, x6 cycles				
Topotecan Cisplatin	0.75 mg/m^2 50 mg/m^2	IVD 30 mins IVD 1 hr	Day 1-3 Day 1	Q3W
Ifosfamide + Cisplatin Regimen, x6 cycles				
Ifosfamide Cisplatin	5 gm/m^2 50 mg/m^2	IVD 24 hrs IVD 1 hr		Q3W
Gemcitabine + Cisplatin Regimen, x6 cycles				
Gemcitabine Cisplatin	1000 mg/m^2 50 mg/m^2	IVD 30 mins IVD 1 hr	Day 1, 8 Day 1	Q3W

Regimens	Dosage	Route	Day	Interval
Epirubicin + Ifosfamide + Cisplatin Regimen, x6 cycles				
Epirubicin Ifosfamide Cisplatin	50 mg/m^2 1 gm/m^2 50 mg/m^2	IVD 24 hr IVD 1 hr	Day 1-3	Q3W
Paclitaxel+ Ifosfamide + Cisplatin Regimen, x6 cycles				
Paclitaxel Ifosfamide Cisplatin	175 mg/m^2 1 gm/m^2 50 mg/m^2	IVD 3 hrs IVD 24 hr IVD 1 hr	Day 1-3	Q3W
Irinotecan + Cisplatin Regimen, x6 cycles				
Irinotecan Cisplatin	60 mg/m^2 60 mg/m^2	 IVD 1 hr	Day 1, 8, 15 Day 1	
Topotecan + Cisplatin weekly Regimen, x6 cycles				
Topotecan Cisplatin	2 or 2.5 mg/m^2 40 mg/m^2	IVD 90 mins IVD 1 hr	Day 1, 8, 15 Day 1, 8, 15	

備註：

- Cisplatin 為陰道癌治療化學治療首選藥物，若 (CCr < 60)，Carboplatin可做為替代藥物取代 (婦癌個案注射Cisplatin若因CCR ≤ 60，weekly Cisplatin 40 mg/m^2，可改為Carboplatin AUC 2；若非weekly用法，如Cisplatin Q3W使用，則為75 mg/m^{2}改為Carboplatin AUC 5。)
- Platinum + Topotecan (D1~3) (Q3W)用法：
  Cisplatin 50 mg/m^2 (D1) + Topotecan 0.75 mg/m^2 (D1~D3)，Cisplatin 用於第一天；
  Carboplatin (AUC 5) (D3) + Topotecan 0.75 mg/m^2 (D1~D3)，Carboplatin用於第三天，
  是因要降低骨髓抑制副作用。

持續性或復發性疾病

考慮因素：

- Prior therapy
  - Surgery → Radiotherapy
  - Radiotherapy → Surgery
- Status of disease and patient's condition
- Performance status
- Palliative or Curative treatment

Treatment of recurrent vaginal cancer may include the following

- Local recurrence → radiotherapy or pelvic exenteration
- Distant recurrence → Chemotherapy

Vaginal Cancer

持續性或復發性疾病

Stage	Management
Stage I	• Small localized disease (depth ≦5mm, size ≦2cm) ➢ Upper vagina: surgical management ➢ Lower vagina: Brachytherapy ± external beam RT • Large or multifocal disease → External beam RT • CCRT*
Stage II	• External beam RT ± brachytherapy ± chemotherapy • CCRT*
Stage III	• External beam RT ± brachytherapy ± chemotherapy • CCRT*
Stage IVA	• pelvic exenteration ± radiotherapy ± chemotherapy • External beam RT ± brachytherapy ± chemotherapy • CCRT*
Stage IVB	• Supportive care ± palliative chemotherapy or radiotherapy • CCRT*

*仍未定論

追蹤

門診追蹤

- 第一年每3個月1次
- 第三年每6個月1次
- 第五年後每年追蹤1次

追蹤建議

身體檢查如骨盆腔檢查，若SCC或其他腫瘤指數一開始即高於正常值，建議每次追蹤。依個人狀況若有臨床需求可行抽血(CBC或生化功能)，依臨床表徵需要可行影像學檢查如：

- Abdominal/Pelvic CT
- MRI
- Chest x-ray。

Chorionic Disease, and Tumor

分期	診療指引 Hydatidiform Mole GTN	Guideline	化療處方	持續或 復發性疾病	追蹤

Chorionic Disease, or Chorionic Tumor

分期

TNM	FIGO	Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor confined to uterus
T2	II	Tumor extends to other genital structures (ovary, tube, vagina, broad ligaments) by metastasis or direct extension
M0		No distant metastasis
M1		Distant metastasis
-M1a	III	Lung metastasis
-M1b	IV	All other distant metastases

Chorionic Disease, or Chorionic Tumor

絨毛膜癌診療指引

Terminology

- 絨毛膜疾病(Gestational Trophoblastic Disease, GTD):
  GTD is pregnancy-related disorder, a proliferative disorder of trophoblastic cells
- 絨毛膜腫瘤(Gestational Trophoblastic Neoplasia, GTN):
  GTN refers to the subset of GTD that develops malignant sequelae

Panel: Gestational trophoblastic diseases
Benign trophoblastic lesions • Exaggerated placental reaction • Placental-site nodule
Hydatidiform moles (abnormally formed placentas) • Complete mole • Partial mole
Trophoblastic neoplasia • Invasive mole • Choriocarcinoma • Placental-site trophoblastic tumor (PSTT) • Epithelioid trophoblastic tumor (ETT)

Chorionic Disease, or Chorionic Tumor

絨毛膜癌診療指引

FIGO/WHO Scoring system based on prognostic factor				
	0	1	2	4
Age	<40	>40	-	-
Antecedent pregnancy	Mole	Abortion	Term	
Interval from index pregnancy,months	<4	4-6	7-12	>12
Pretreatment hCG mIU/mL	$<10^3$	$>10^3$-10^4	$>10^4$-10^5	$>10^5$
Largest tumor size including uterus, cm	-	3-4	≧5	-
Site of metastases including uterus	Lung	Spleen, kidney	GI tract	Brain, liver
Number of metastases identified	-	1-4	5-8	>8
Previous failed chemotherapy	-	-	Single drug	≧Two drugs

Chorionic Disease, or Chorionic Tumor

絨毛膜癌診療指引

Diagnosis and Clinical Workup

- β-hCG, CBC
- Ultrasonography
- CXR
- Chest CT/abdomen CT if GTN; brain MRI (preferred) or CT if pulmonary metastasis

絨毛膜癌診療指引›Hydatidiform Mole

Diagnosis

- Ultrasonography
- Suction evacuation and curettage

Treatment

- Suction evacuation and curettage: oxytocin infusion, cervical dilation, suction curettage, sharp curettage
- Hysterectomy: alternative, if childbearing has been completed
- Prophylactic chemotherapy: at the time of evacuation is controversial

Follow-up after evacuation

- Weekly β-hCG levels, until these levels are normal for 3 consecutive weeks
- Monthly β-hCG levels, until the levels are normal for 6 consecutive months
- Contraception with oral contraceptives for 6 months

絨毛膜癌診療指引›GTN

Diagnostic criteria (FIGO recommendation)

- β-hCG should either plateau, with at least four persistently elevated β-hCG values on days 1, 7, 14 and 21, or rise sequentially for 2 weeks on days 1, 7 and 14 or longer
- Pathology diagnosis confirming invasive mole, choriocarcinoma, PSTT, ETT

Risks

- Low-risk disease:
  - Stage I, nonmetastatic
  - Stage II-III, score ≤6
- High-risk metastatic disease
  - Stage II-III, score ≥7
  - Stage IV
  - Ultra-high-risk or very-high-risk, score ≥12

絨毛膜癌診療指引›GTN

Treatment

Treatment is based on classification into risk groups defined by the stage and scoring system

Low-risk GTN

- Single-agent chemotherapy, Methotrexate or Actinomycin D
- Chemotherapy is continued until hCG values have returned to normal and 3 courses has been administered after the first normal hCG level

High-risk GTN

- Primary intensive combination chemotherapy and the selective use of radiation therapy and surgery
- Combination chemotherapy: EMA/CO, EMA/EP
- EMA/EP as primary treatment of very-high-risk GTN

Ultra-high risk GTD with chest, liver or brain metastasis

- Induction low dose E+P for 1-3 cycles before commencing EMA/CO or EMA/EP
- Low dose E+P: Etoposide 100mg/m^2, Cisplatin 20mg/m^2 on Day 1 & 2, every 7 days for 1-3 cycles

絨毛膜癌診療指引›GTN

Hysterectomy for GTN

Primary treatment

- Placental site trophoblastic tumor
- Epithelioid trophoblastic tumor
- Severe uncontrollable uterine bleeding, sepsis
- Decrease tumor burden
- Relieve bowel or urinary obstruction

Adjuvant treatment

- Coincident with the initiation of chemotherapy to shorten the duration of treatment if fertility preservation is not desired
- Persistent chemotherapy-resistant disease in the uterus

GTN/GTD Guidelines

Workup

- Complete history & PE
- CBC
- Coagulation studies
- Serum chemistries
- Blood type & antibody screen
- β-hCG
- Ultrasonography
- CXR
- Suction evacuation and curettage

Optional

- Chest CT
- Abdomen CT
- Brain CT

Diagnosis

- Hydatidiform mole → see GTD/GTN-2
- Choriocarcinoma → see GTD/GTN-3

GTD/GTN-2

Primary treatment of Hydatidiform mole

Suction evacuation and curettage

- Oxytocin infusion
- Cervical dilation
- Suction curettage
- Sharp curettage

Hysterectomy

- Alternative, if childbearing has been completed

Follow up

→ See GTD/GTN-3

Prophylactic chemotherapy

- At the time of evacuation is controversial

→ See GTD/GTN-5

GTD/GTN-3

Follow-up After Evacuation

β-hCG level

- weelky β-hCG, until these levels are normal for 3 consecutive weeks
- monthly β-hCG, until the levels are normal for 6 consecutive months

→ Fails to return to normal

- plateauing β-hCG level over at least 3 weeks
- a 10 percent or greater rise in β-hCG for three or more values over at least two weeks

GTN/GTD-4

Contraception

- for 6 months
- oral contraceptives

GTD/GTN-4

CLINICAL WORKUP OF GTN

- Metastatic workup
- β-hCG
- CXR- Chest CT
- Abdomen/pelvic CT or ultrasonography
- Brain CT or MRI

Evaluation for risk factors

- age
- antecedent pregnancy- pretreatment β-hCG level
- largest tumor size
- site of metastases
- number of metastases- previous failed chemotherapy

- Low risk disease → See GTD/GTN-5
- High risk disease
  Very high risk disease → See GTD/GTN-6

Chorionic Disease, or Chorionic Tumor

臺北榮民總醫院婦女醫學部婦癌團隊
Version 2021.10

GTD/GTN-5

Treatment of low risk GTN

Single-agent chemotherapy

- Methotrexate (MTX)
- Actinomycin D (ACT-D)

Change Agent

- if hCG level plateaus above normal during treatment
- if toxicity precludes an adequate dose or frequency of treatment

→ If significant elevation of hCG → GTD/GTN-6

- metastases
- resistance to single-agent

Chorionic Disease, or Chorionic Tumor

GTD/GTN-6

Treatment of High-Risk GTN

Combination chemotherapy

- EMA/CO
- EMA/EP for very high risk GTN

Selective radiation therapy

Follow Up

- Weekly hCG to normal for 3 weeks
- Monthly hCG for 12 months
- Contraception for 12 months

Resistant or relapsed

Selective surgery

See GTD/GTN-7

GTD/GTN-7

Management of Resistant or Relapsed GTN

Chemotherapy

- EMA/EP
- TP/TE

Surgery

- Resection of localized lesion in uterus
- Hysterectomy:
  ovarian removal is not required
  uncontrollable uterine bleeding
  sepsis
  PSTT, ETT
- Thoracotomy
- Craniotomy
- Excision of vaginal/liver metastasis

Chorionic Disease, or Chorionic Tumor

化療處方建議

Chemotherapy for low-risk gestational trophoblastic neoplasia	
Chemotherapy regimen	**Primary remission rate (%)**
MTX 0.4 mg/kg (maximum 25 mg)/d IV or IM for 5 d; repeat every 14 d	87-93
MTX 1 mg/kg IM d 1, 3, 5, 7; folinic acid 0.1 mg/kg IM (15mg PO) 30 hr after each MTX on d 2, 4, 6, 8; repeat every 14 d	74-90
Act-D 10-12 μg/kg IV QD for 5d; repeat every 14 d	77-94
Act-D 1.25 mg/m^2 (max 2mg) IV pulse every 2 wk	69-90

Act-D, actinomycin D; D5W, dextrose 5% in water; IM, intramuscular; IV, intravenous; IVP, intravenous push; MTX, methotrexate; PO, by mouth; QD daily.

Chorionic Disease, or Chorionic Tumor

化療處方建議

Protocols for EMA/CO and EMA/EP regimens		
Day	Drug	Dose
Protocol for EMA/CO		
1	Etoposide Act D MTX	100 mg/m^2 by infusion in 200 mL saline over 30 min 0.5 mg IVP 100 mg/m^2 IVP 200 mg/m^2 by infusion over 12 h
2	Etoposide Act D Folinic acid	100 mg/m^2 by infusion in 200 mL saline over 30 min 0.5 mg IVP 15 mg every 12 h x 4 doses PO (preferred) or IM beginning 24 h after starting MTX
8	Cyclophosphamide Vincristine	600 mg/m^2 by infusion in saline over 30 min 1 mg/m^2 IV over 5-10min
Protocol for EMA/EP regimens (preferred regimens for PSTT and ETT)		
1	Etoposide Act D MTX Folinic acid	100 mg/m^2 by infusion in 200mL saline over 30 min 0.5 mg IVP 100 mg/m^2 IVP 200 mg/m^2 by infusion over 12h 15 mg every 12 h x 4 doses PO (preferred) or IM beginning 24 h after starting MTX
8	Cisplatin Etoposide	75 mg/m^2 IV with prehydration 150 mg/m^2 by infusion in 200 mL saline over 30 min (Filgrastim 5mcg/kg SC on days 9-14)

Chorionic Disease, or Chorionic Tumor

化療處方建議

Protocol for TP/TE regimens	
Day 1 (TP)	
Dexamethasone	20 mg orally (12 h before paclitaxel)
Dexamethasone	20 mg orally (6 h before paclitaxel)
Cimetidine	30 mg in 100ml normal saline intravenous for 30 min
Chlorphenamine	10 mg intravenous bolus
Paclitaxel	135 mg/m^2 in 250 ml normal saline intravenous for 3 h
Mannitol	10% in 500 ml intravenous for 1 h
Cisplatin	75 mg/m^2 in 1 L normal saline intravenous for 3 h
Post-hydration	1L normal saline, 20 mmol potassium chloride, and 1 g magnesium sulphate intravenous for 2 h
Day 15 (TE)	
Dexamethasone	20 mg orally (12 h before paclitaxel)
Dexamethasone	20 mg orally (6 h before paclitaxel)
Cimetidine	30 mg in 100ml normal saline intravenous for 30 min
Chlorphenamine	10 mg intravenous bolus
Paclitaxel	135 mg/m^2 in 250 ml normal saline intravenous for 3 h
Etoposide	150 mg/m^2 in 1 L normal saline intravenous for 1 h
(Pegfilgrastim)	(6mg SC on days 2 and 16)
TP=paclitaxel-cisplatin. TE=paclitaxel-etoposide	
Table 3: TP-TE schedule for relapsed gestational trophoblastic neoplasia	

Chorionic Disease, or Chorionic Tumor

持續性或復發性疾病

Treatment of resistant GTN

- Chemotherapy combined with surgery
- EMA/EP, TP/TE,
- BEP (Bleomycin, Etoposide, Cisplatin), every 3 weeks
  - Bleomycin 15 mg IVD on D1-3 or 30 mg IVD on D1 (total dose <150mg)
  - Etoposide 100 mg/m2 IVD 1 hr on D1-3
  - Cisplatin 100 mg/m2 IVD on D1
- VIP (Etoposide, Ifosfamide, Cisplatin), every 3 weeks
  - Etoposide 75mg/m2/day IV on D1-5*
  - Ifosfamide 1.5g/m2/day IV on D1-5*
  - Mensna 120mg/m2/day bolus just prior to ifosfamide, then 1.2g/m2/day IV infusion over 12 hours after ifosfamide dose on D1-5*
  - Cisplatin 20mg/m2/day IV on D1-5*
  - (Pegfilgrastim 6mg SC on day 5; or Filgrastim 300 mcg SC on D6-14)

持續性或復發性疾病

Treatment of resistant GTN

- ICE (Ifosfamide, Carboplatin, Etoposide), every 3 weeks
  - Ifosfamide 1.2g/m2/day IV on d1-3
  - Mesna 120mg/m2/day IV bolus prior to ifosfamide, then 1.2g/m2/day IV infusion over 12 hours after ifosfamide dose on D1-3
  - Carboplatin AUC 4 IV on D1
  - Etoposide 75mg/m2/day IV on D1-3
  - Pegfilgrastim 6mg SC on D4; or or Filgrastim 300mg SC on D6-14
- TIP (Paclitaxel, Ifosfamide, Cisplatin), every 3 weeks
  - Paclitaxel 250mg/m2 IV on D1
  - Ifosfamide 1500mg/m2 IV on D2-5
  - Mesna 300mg/m2 IV before ifosfamide, then at 4 hours and 8 hours from the start of each ifosfamide dose on D2-5
  - Cisplatin 25mg/m2/day IV on D2-5

持續性或復發性疾病

Treatment of resistant GTN

- Pembrolizumab (200 mg IV every 3 weeks)
- Nivolumab (240 mg IV every 2 weeks)
- Avelumab 800mg IV every 2 weeks
- Gemcitabine ± carboplatin (repeat every 3 weeks)
  - Gemcitabine 600-1000 mg/m2/day IV on D1 and 8
  - Carboplatin AUC 4 or 5 IV on D1
- Gemcitabine ± cisplatin (repeat every 4 weeks)
  - Gemcitabine 600-800 mg/m2/day IV on D1, 8 and 15
  - Cisplatin 25-30 mg/m2/day IV on D1, 8 and 15
- 5-fluorouracil 1200 mg/m2/day continuous infusion over 3 days
- Capecitabine 1250mg/m2 PO twice daily for 2 weeks on and 1 week off (repeat cycle every 3 weeks)

Chorionic Disease, or Chorionic Tumor

追蹤

Follow-up after treatment for GTN

After hCG regression to normal and completion of chemotherapy:

- hCG, 1-month intervals for 12 months
- Physical examinations, 6-12 months interval
- Chest X-ray
- Consider abdominal sonography or PET/CT at the completion of C/T and then every 6 to 12 months for 2 to 3 years
- Contraception should be maintained during treatment and for 1 year after completion of chemotherapy, preferably using oral contraceptives

附錄

化療的毒性

化療藥物是醫師治病中最具毒性的處方，不管劑量、療程、給藥方式，都是相當重要。嚴重時，即使正確使用藥物、劑量、與適當的療程，仍有1-3%的病人，因其藥物毒性或併發症造成病人死亡，不可不慎！

1. 血液毒性

骨髓抑制是大部份化學藥物的毒性，最大副作用通常發生在治療10天前後，而在第21天至28天會恢復正常。顆粒白血球過低及血小板過低是大部份使用混合性化學治療(combination chemotherapy)可預期到的副作用這些副作用的嚴重度及持續期相當不一致依據藥物種類、劑量、使用方法，以及病人曾接受放射或化學治療而定。通常急性顆粒白血球過低發生在化學治療後6-12天，而在21-24天恢復，血小板的影響通常慢4-5天，而恢復也在白血球恢復後4-5天才恢復。貧血通常是經過幾次療程治療後產生慢性毒性才發生的。

通常病人顆粒白血球少於500/mm3達5天以上，容易發生敗血症，臨床醫師應該考慮使用有力的廣效的抗生素預防最近使用血球生長激素如G-CSF或GM-CSF，可降低白血球過低的情況。

化療的毒性

血小板在少於20000/mm3，會增加自動出血的機會，尤其是腸胃道的出血。通常在血小板低於20000/mm3輸血小板6-10單位。在必要時2-3天後再輸血小板，如果病患有急性腸胃道出血或要實施手術前血小板低於50000/mm3，也應該輸血小板。對於經發生白血球或血小板過低者，化學藥物劑量應該調整(表2)。

表2. 白血球及 血小板抑與化學藥物調整的關係

血球數(mm3)	劑量調整
白血球	
>4000	100%劑量
3999-3000	100%劑量(非骨髓抑制藥) 50%劑量(骨髓抑制藥)
2999-2000	100%劑量(非骨髓抑制藥) 25%劑量(骨髓抑制藥)
1999-1000	50%劑量(非骨髓抑制藥) 25%劑量(骨髓抑制藥)
≦999	不可使用
血小板	
>100,000	100%劑量(非骨髓抑制藥)
50,000-100,000	100%劑量(非骨髓抑制藥) 50%劑量(骨髓抑制藥)
<50,000	不可使用

化療的毒性

2. 噁心及嘔吐

噁心及嘔吐是化學治療相當常見的副作用。在治療婦癌有效的化學藥物如cyclophosphamide、ifosfamide、cisplatin、adriamycin都會引起很嚴重的噁心和嘔吐。如何抑制噁心和嘔吐，應該視為化學藥物治療整體的一部份。

以前使用dexamethasone和metoclopramide混合使用，最近幾年在發展出5HT3(5-hydroxy-tryptaminetype-3)接受器的拮抗劑(antagonists)如ondansetron、granisetron、trosetron，若再加上混合上述藥物可抑制80%使用cisplatin所產生的立即性的噁心及嘔吐，但是對延遲性噁心和嘔吐並沒有如期望的效果「可是不同的作用機轉引起的。

3. 腸胃道毒性

腸胃道毒性也是一種常見的化學藥物的副作用，黏膜炎是因黏膜上皮細胞是快速分裂的細胞，會受到直接影響，受傷的黏膜若加上白血球過低，常常會導致細菌或黴菌的侵入。上腸胃的黏膜炎通常發生在骨髓抑制前3到5天，若發生口腔黴菌感染，使用抗黴菌藥物都非常有效。下腸胃的黏膜炎一定伴隨下痢。更嚴重的併發症會發生腸穿孔、及壞死性腸炎(necrotizing entero-colitis)。

化療的毒性

4. 抑制免疫能力

大部份化學治療藥物都會產生抑制細胞性或體液性(humoral)的免疫能力，其免疫抑制的能力受到藥物使用的方法及劑量而有所差異，但是在治療結束後2-3天就會恢復，不會持續存在。

5. 皮膚反應

包括落髮及過敏性皮膚反應，也是很常見的副作用。靜脈注射滲漏發生的皮膚壞死

和脫落，則常見於adriamycin、actinomycin D、mitomycin C、vinblastine、vincristine，和nitrogen mustard，壞死的程度受到藥物滲漏的量來決定。處理，包括馬上拿掉點滴，局部注射類團醇和冰敷至少三天。落髮雖然不會有何傷害，但是會影病人的情緒。在化學藥物治療結束後10至20天頭髮都會開始再度長出。使用冰帽試圖減少落髮，其效果不一。過敏性皮膚反應有時是很嚴重的，bleomycin會引起皮膚色素沈澱，對光敏感(photosensitivity reaction)以及指甲脫落；actimocycin D和methotrexate則會引起毛炎；adriamycin則會引起所謂放射恢復反應(radiation recall reactions)的副作用；liposomal doxorubicin會產生手足脫疼痛性皮膚症狀。

化療的毒性

6. 肝臟毒性

肝臟毒性較不常見，會引起一些酵素如transaminase，alkaline phosphatase和bilirubin中度上升，然而長期使用methotrexate(MTX)，會導致嚴重反應以致肝硬化。其處理原則如同其它原因引起的肝炎或肝硬化同樣支持性療法。本身存在肝病的病人更會增加危險性。當肝功能不良，需要調整化學藥物劑量(表3)。Venook發現taxol引起的副作用與其劑量和血液肝功能bilirubin等值有關。建議當肝功能，AST高於正常二倍且bilirubin ≦ 1.5mg/dl，taxol的劑量不超過135 mg/m^2，bilirubin 1.6-3.0 mg/m^2，劑量為75mg/m^2，bilirubin 3 mg/m^2，劑量為50mg/m^2。

表3. 肝功能與藥物劑量調整的關係

Bilirubin	SGOT	Adriamycin	Daunorubicin	Vinblastine Vincristine VP-16	Cyclophosphamide Methotrexate	5-FU
<1.5	<60	100%	100%	100%	100%	100%
1.5-3.0	60-180	50%	75%	50%	100%	100%
3.1-5.0	>180	25%	50%	Omit	75%	100%

化療的毒性

7. **肺臟毒性**

某些特定的化學藥物會引起間質性肺炎(interstitial pneumonitis)及肺纖維化

(pulmonany fibrosis)，這些藥物包括bleomycin、alkylating和nitrosoureaso處理原則包括停藥及支持性療法，類固醇可能有些幫助。

8. **心臟毒性**

心臟毒性主要發生在使用adriamycin，累積劑量達500mg/m^2，其危險性會很顯著的

增加，因此500mg/m^2被定為我們能忍受的最大劑量。在我們了解這個限度，已經很少發生了在很少情況下，cyclophosphamide使用大劑量時也有發生心臟毒性的報告，mitomycin C也曾有類似的報告。

化療的毒性

9. 泌尿系統的毒性

化學治療藥物會引起腎臟的損傷，包括：

- Cisplatin：會產生腎小管的毒性，引起氮血症(azotemia)及鎂離子流失，可以用利用尿劑來減低這種副作用。
- Methotrexate：會沈澱到腎小管，引起無尿性腎衰竭，這種毒性可以用維持大量尿量及使尿液鹼性化來避免。
- Nitrosoureas：會引起慢性間質性腎炎及慢性腎衰竭。
- Mitomycin C：會引起全身性微血管病變性的溶血和急性腎衰竭。
- Cyclophosphamide、ifosfamide：會刺激膀胱黏膜引起慢性出血性膀胱炎，特別是使用高劑量或長期治療，大量灌水及利尿可以減少這種副作用。在腎功能不好時，化學藥物的劑量依腎功能(CCr)來決定減少其劑量。治療化學藥物已引起泌尿系統的毒性時，必須使用有腎毒性的藥物，以及增加體液來增加腎小球的過濾，以增加尿量。假如這樣處理，仍然發生尿量減需考慮短期間的洗腎。對MTX不容易用洗腎方法排出，唯可用leukovorin (calcium folinate)救濟法，直到MTX血中濃度低於5x108M。最近，mesna (sodium mercaptoethane-sulfonate)可用來和高劑量cyclophosphamide或ifosfamide合用，避免膀胱的毒性(表4)。

化療的毒性

表4. 腎功能(CCr)與藥物劑量調整的關係				
	>60 ml/min	30-60 ml/min	10-30 ml/min	<10 ml/min
Bleomycin	NC	75	75	50
Cisplatin	NC	50	Omit	Omit
Cyclophosphamide	NC	NC	NC	50
Methotrexate	NC	50	Omit	Omit
Mithramycin	NC	75	75	50
Mitomycin	NC	75	75	50
NC=no change				

化療的毒性

10. 神經毒性

大部的化學治療藥都有某些中樞神經或周邊神經的毒性，通常都是微的副作用，嚴重的較少。Vinca alkaloids如vincristine、vinblastine和vindesine會引起周邊神經包括運動、感覺神經和自主神經的毒性，尤其是vincrinstine，首先是深部肌鍵反射的消失，以及遠端感覺的麻木。這些神經毒性在停用後都會慢慢恢復。Cisplatin會引起耳毒性以及周邊神經病變，尤其是高劑量會造成漸進性及延遲性周邊神經病變，以感覺神經為主，往往在二至三次療程後才發生，並持續到停藥二、三個月後。其它的藥物如5-FU會引起急性小腦毒性；hexamethylmelamine會產生周邊神經及大腦神經病變；ifosfamide會產生大腦神經病變。

11. 過敏性反應

有時化學藥物會引起嚴重的立即性過敏反應(anaphylaxis)，曾見於使用cyclophosphamide、adriamycin、cisplatin、melphalan靜脈注射，及高劑量MTX。Bleomycin會引起顯著發燒、過敏反應、雷氏現象(Raynaud's phenomenon)和慢性硬皮樣反應。Etoposide(VP-16)也曾有這樣的益以告。Taxol造成嚴重過敏反應，相信是由劑溶劑cremphor引起的，事前使用dexamethasone 20mg、diphenhydramine 50mg和cimetidine 300mg等預防，是使用taxol的例行工作。

化療的毒性

12. 生殖功能不良

很多化學藥物長期使用會影響睪丸及卵巢的功能，尤其是alkylating藥物會引起無精蟲及無月經。第二性微通常較不受影響。短期使用化學藥物如antimetabolites、vinca alkaloids或antitumor antibiotics較不影響生殖系統。發生無月經都伴隨升高FSH，和LH以及降低E2的低清值，尤其在三十歲以上的婦女會發生早期性卵巢衰竭。

至於化學治療在懷孕中引起先天性異常主要是發生在早期懷孕時，尤其是antimetabolites和alkylating藥物。中期及晚期懷孕使用化學治療因個案不多，不足證實它的影響。

13. 代謝功能不良

使用vinca alkaloid的化學藥物有報告過會引起抗利尿性(antidiuretics hormone, ADH)的分泌 。化學治療後造成腫瘤分解症候群(tumor lysis syndrome)會產生致命的高鉀、高酸、低鈣，以高尿酸而引起腎衰竭。

14. 精神性副作用

化學治療引起精神上的作用 很難有定論，也比生理上的副作用較少去注意。毫無疑問地，化學治療會引起許多病人憂鬱、焦慮，而影響到他們的預後。

化療的毒性

15. **造成次發性癌病(second malignancies)**

很多化學藥物都有致突變性，以及致畸性(teratogenic)，依藥物種類而有很的差別。Alkylating藥物，尤其是melphalan、procarbazine和nitrosoureas，似乎最會發生；antimetabolites則較少會發生。較會發生的因素有：廣泛性放射治療加上混合性化學治療，使用alkylating藥物治療超過一年，長期維持性化學治療，治療開始時的年齡超過40歲。

總之，化學治療既然本身是以毒攻毒的治療方式，如何使用化學治療而不導致病患因而死亡，是臨床醫師必須了解的。尤其有藥物劑量美制的藥物，很有可能會引起病人致死，請格外小心(表5)。

表5. 有劑量限制的化學藥物及毒物

藥物	毒性
Adriamycin	心臟壞死
Daunorubicin	心臟壞死
Bleomycin	肺纖維化
Nitrosoureas	腎毒性病變
Cisplatin	腎毒性病變
Carboplatin	骨髓抑制
Vincristine	周邊神經病變

化療的毒性

化學治療效果的評定，可分為病人的主觀感覺及醫師的客觀檢查兩方面。以客觀檢查及生命延長來評定，是最可靠的方法。一個適當的評定，必須是曾經在一個月之內接受兩個以上的療程的化學治療，而且在次一個月詳細追蹤檢查後而定。

a. 完全緩解(complete remission)：所有可測量大小的腫瘤病灶，全部消失，無症狀，並且維持一個月以上

b. 部份緩解(partial remission)：所有可測量大小的腫瘤，全部小於50%以上，沒有新的腫瘤發生，並且維持一個月以上。

c. 改善(improvement)：至少有一個腫瘤的病灶縮小25%以上，沒有新的腫瘤發生，並維持一個月以上。

d. 穩定(stable)：腫瘤大小改變不超過25%以上，沒有新腫瘤發生，並維持一個月以上。

e. 惡化(prorgression)：所有可測量大小的腫瘤，全部增加在25%以上，或有新的腫瘤出現。

另外有一個臨床常用的名詞－反應率(response rate)是泛指化學治療後，腫瘤的體積減小到50%以下，並且沒有新的腫瘤在其它部位出現，占全部治療人數的百分率而言。

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