高 雄 榮 民 總 醫 院
威爾姆氏腫瘤診療原則

2022年03月15日 第一版

兒童癌症醫療團隊擬訂

注意事項：這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

修訂指引

- 本指引依下列參考資料制定版本
  – 台灣兒童癌症研究群(TPOG)
  TPOG WT2016 V2.0 (2017-3-27)

會議討論

上次會議：2021/02/19

本共識與上一版的差異

上一版	新版
1.依據TPOG WT2016 V2.0(2017-3-27)版本修訂威 爾姆氏瘤診療指引。	1.TPOG WT2016 V3.0(2021-3)修訂說明如下 (1)強調腎臟切除重量對very low-risk Wilms tumors (VLRWT)分級的重要 (ppt7); (2)刪除部分對術前 VAD 療程，針對小於 1 歲嬰兒劑量的描述(ppt21); (3)針對雙側 Wilms tumor 的治療作進一步說明建議(ppt27)

兒癌–Wilms Tumor

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腫瘤分級

Stage	COG (pre-chemotherapy)	SIOP (post-chemotherapy)
I	Tumor is limited to kidney and is completely resected	Tumor limited to kidney or surrounded with fibrous pseudocapsule if outside the normal contour of the kidney, the renal capsule or pseudocapsule may be infiltrated with the tumor, but it does not reach the outer surface, and it is completely resected (resection margins "clear")
	Renal capsule intact, not penetrated by tumor	The tumor may be protruding (bulging) into the pelvic system and "dipping" into the ureter, but it is not infiltrating their walls
	No tumor invasion of veins or lymphatics of renal sinus	The vessels of the renal sinus are not involved, but intrarenal vessel involvement may be present.
	No nodal or hematogenous metastases	Fine needle aspiration or percutaneous core needle biopsy ("tru-cut") do not upstage the tumor. The presence of necrotic tumor or chemotherapy-induced changes in the renal sinus/hilus fat and/or outside of the kidney should not be regarded as a reason for upstaging a tumor
	No prior biopsy	
	Negative margins	
II	Tumor extends beyond kidney but completely resected	The tumor extends beyond kidney or penetrates through the renal capsule and/or fibrous pseudocapsule into perirenal fat but is completely resected (resection margins "clear")
	Tumor penetrates renal capsule	The tumor infiltrates the renal sinus and/or invades blood and lymphatic vessels outside the renal parenchyma but it is completely resected
	Tumor in lymphatics or veins of renal sinus	The tumor infiltrates adjacent organs or vena cave but is completely resected
	Tumor in renal vein with margin not involved	
	No nodal or hematogenous metastases	
	Negative margin	

兒癌–Wilms Tumor

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腫瘤分級

III	Residual tumor or nonhematogenous metastases confined to abdomen	Incomplete excision of the tumor which extends beyond resection margins (gross or microscopic tumor remains postoperatively)
	Involved abdominal nodes	Any abdominal lymph nodes are involved
	Peritoneal contamination or tumor implant	Tumor rupture before or intraoperatively (irrespective of other criteria for staging)
	Tumor spillage of any degree occurring before	The tumor has penetrated through the peritoneal surface
	or during surgery	
	Gross residual tumor in abdomen	Tumor implants are found on the peritoneal surface
	Biopsy of tumor (including fine needle aspiration) prior to removal of kidney	The tumor thrombi present at resection margins of vessels or ureter, transected or removed piecemeal by surgeon
	Resection margins involved by tumor or transection of tumor during resection (i.e. piecemeal excision of tumor)	The tumor has been surgically biopsied (wedge biopsy) prior to preoperative chemotherapy or surgery
		The presence of necrotic tumor or chemotherapy-induced changes in a lymph node or at the resection margins should be regarded as stage III
IV	Hematogenous metastases or spread beyond abdomen	Hematogenous metastases or spread beyond abdomen
V	Bilateral renal tumors Each side's tumor should be substaged separately according to the above criteria	Bilateral renal tumors Each side's tumor should be substaged separately according to the above criteria

兒癌– Wilms Tumor

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*單側*威爾姆氏種類危險級分類

Patient age	Tumor weight	Stage, histology	LOH at both 1p and 16q	Rapid lung nodule response	Chemotherapy regimen	Radiation therapy
< 2 yrs	< 550 g	I, FH	Any	N/A	None	None
< 2 yrs	≥ 550 g	I, FH	None	N/A	EE4A	None
≥ 2 yrs	Any	I, FH	None	N/A	EE4A	None
Any	Any	II, FH	None	N/A	EE4A	None
Any	Any	I, FH	LOH*	N/A	DD4A	None
Any	Any	II, FH	LOH*	N/A	DD4A	None
Any	Any	III, FH	None	Any	DD4A	Local
Any	Any	III, FH	LOH*	Any	M	Local
Any	Any	IV, FH	None	Yes	DD4A	Local
Any	Any	IV, FH	None	No	M	Local, lung
Any	Any	IV, FH	LOH*	Any	M	Local, lung
Any	Any	I, FA or DA	Any	Any	DD4A	Local
Any	Any	II-III, FA	Any	Any	DD4A	Local
Any	Any	I-III CCSK	Any	Any	I	Local (RT omitted for stage I)
Any	Any	II-III, DA	Any	Any	rUH-1	Local
Any	Any	IV CCSK	Any	Any	rUH-1	Local
Any	Any	I-IV RTK	Any	Any	RTK	Local
Any	Any	IV, FA or DA	Any	Any	UH-2	Local, lung

This risk-stratification schema was modified from an existing risk stratification (Jeffrey et al 2014) and COG AREN0534.
*The detection of LOH at chromosomes 1p and 16q is optional if not applicable.

兒癌– Wilms Tumor

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評估	診斷	治療	追蹤

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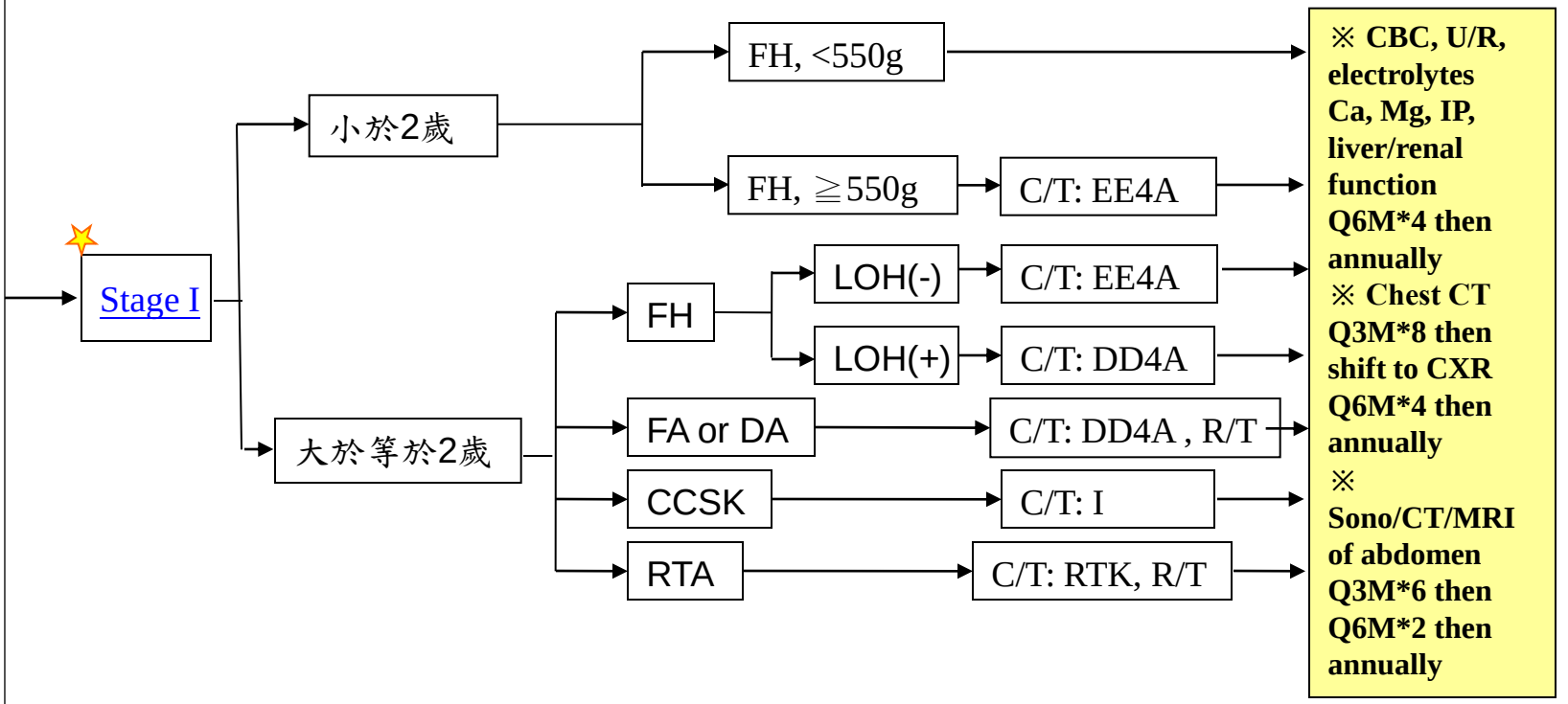
•血液常規
•電解質及肝腎功能
•凝血功能
•心臟超音波檢查
•腹部超音波
•聽力檢查
•腫瘤病理種類*
•骨頭掃描*
•胸部電腦斷層(CT)*
•腹部電腦斷層攝影(CT)* or 核磁共振檢查(MRI)*(擇一)
•腫瘤之LOH染色體檢測(外送臺大醫院)*

*與癌症期別相關之主要檢查



以COG stage I (pre-chemotherapy)為主，可手術完全切除且無先施行切片

兒癌– Wilms Tumor

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•腫瘤病理種類*
•骨頭掃描*
•胸部電腦斷層(CT)*
•腹部電腦斷層攝影(CT)* or 核磁共振檢查(MRI)*(擇一)
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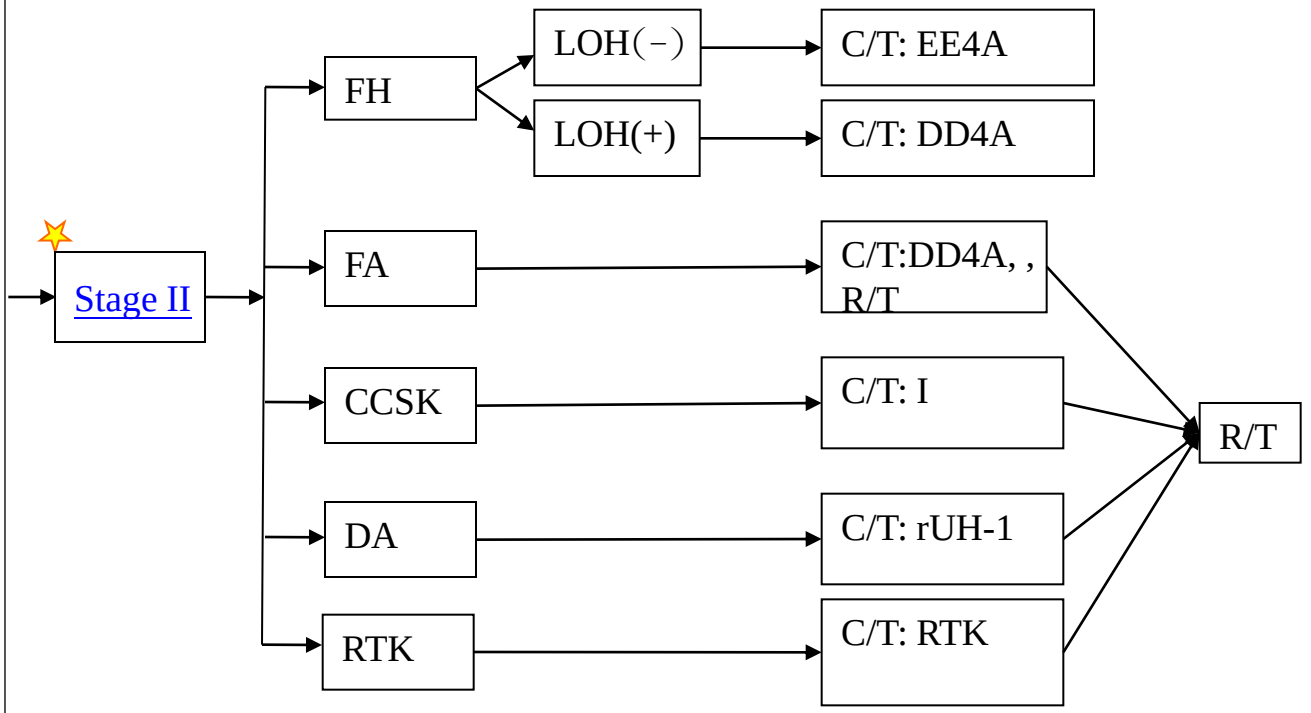

以COG stage II (pre-chemotherapy)為主

※ CBC, U/R, electrolytes Ca, Mg, IP, liver/renal function Q6M*4 then annually
※ Chest CT Q3M*8 then shift to CXR Q6M*4 then annually
※ Sono/CT/MRI of abdomen Q3M*6 then Q6M*2 then annually

兒癌– Wilms Tumor

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•凝血功能
•心臟超音波檢查
•腹部超音波
•聽力檢查
•腫瘤病理種類*
•骨頭掃描*
•胸部電腦斷層(CT)*
•腹部電腦斷層攝影(CT)* or 核磁共振檢查(MRI)*(擇一)
•腫瘤之LOH染色體檢測(外送臺大醫院)*

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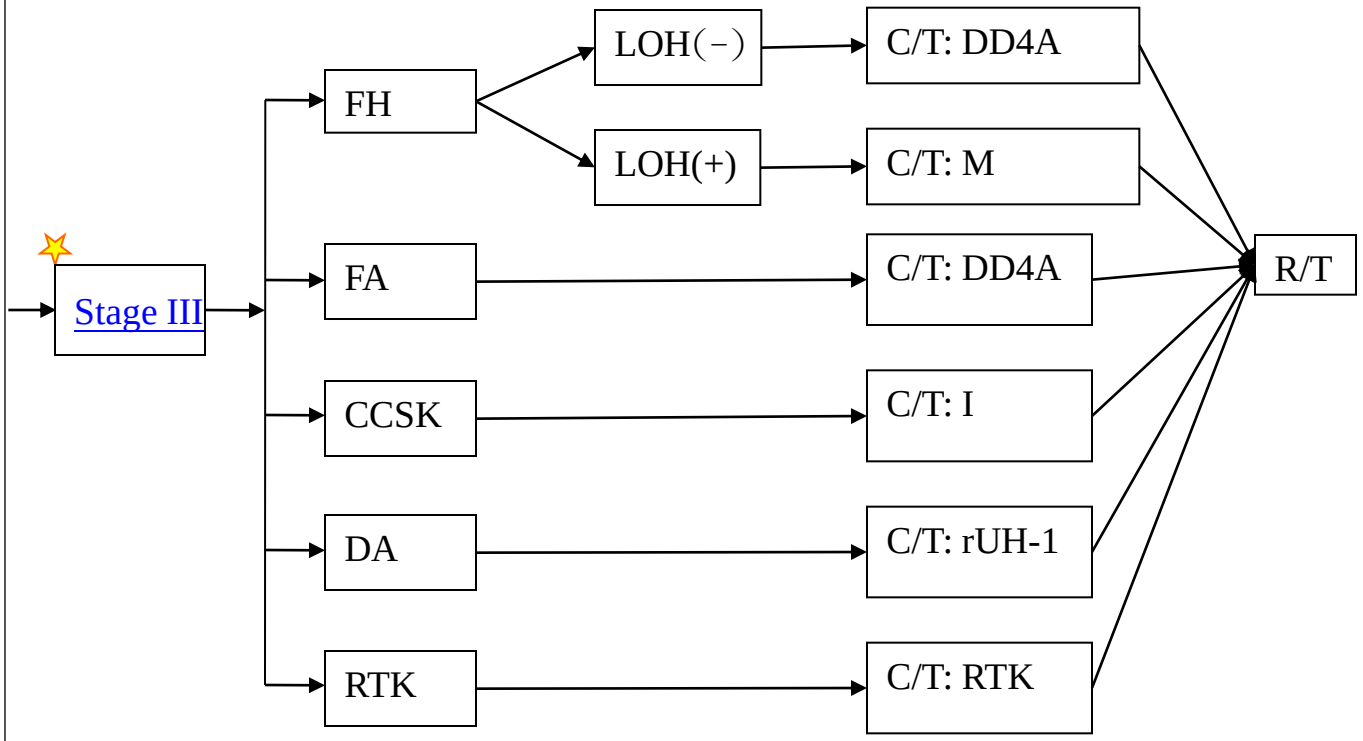

※ CBC, U/R, electrolytes Ca, Mg, IP, liver/renal function Q6M*4 then annually
※ Chest CT Q3M*8 then shift to CXR Q6M*4 then annually
※ Sono/CT/MRI of abdomen Q3M*6 then Q6M*2 then annually

☆ 以COG stage III (pre-chemotherapy)為主

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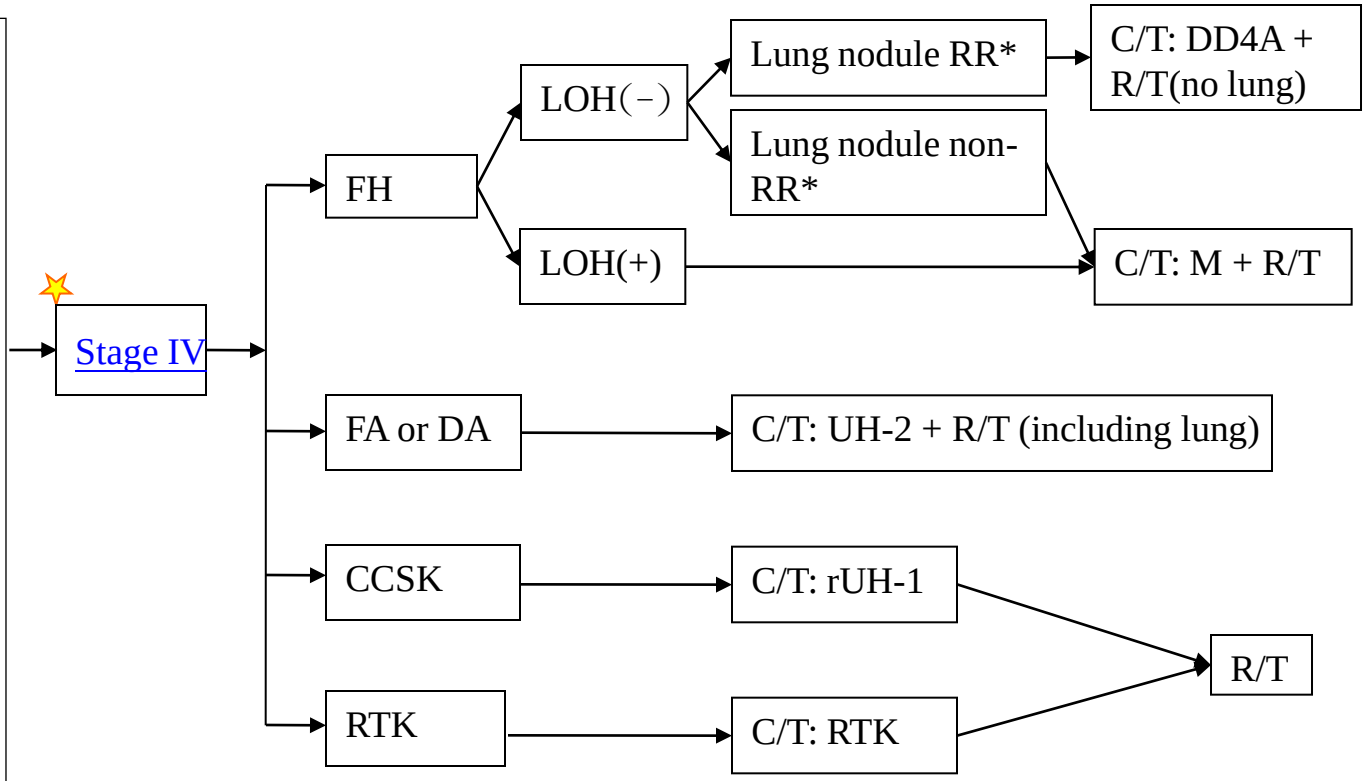

※ CBC, U/R, electrolytes Ca, Mg, IP, liver/renal function Q6M*4 then annually
※ Chest CT Q3M*8 then shift to CXR Q6M*4 then annually
※ Sono/CT/MRI of abdomen Q3M*6 then Q6M*2 then annually

☆以COG stage IV (pre-chemotherapy)為主
**RR: rapid responese

兒癌– Wilms Tumor

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治療原則及療程表表示方法

1. 若能手術切除，以nephrectomy為主要優先治療(並盡量不要經皮切片診斷)；若無法手術切除，先進行neo-adjuvant cgemotherapy
2. Nephrectomy: on day 0 of week 0.
3. For “biopsy only” patient, definitive surgery is undertaken at week 7 or week 13 after preoperative chemotherapy.
4. Chemotherapy should be administered within 14 days post-nephrectomy.
5. Week 1 = day 7 post nephrectomy.
6. Newborns and all <12 months old require a reduction in chemotherapy doses to 50% of those given to older children.
7. RT: over 5-7 days after nephrectomy

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化學治療處方建議表

Regimen	Agents
EE4A	vincristine and dactinomycin
DD4A	vincristine, dactinomycin, doxorubicin and possibly radiation therapy
Regimen I	vincristine, dactinomycin, doxorubicin, cyclophosphamide, and etoposide
Regimen M	vincristine, dactinomycin, doxorubicin, cyclophosphamide, and etoposide
revised UH-1	vincristine, dactinomycin, doxorubicin, cyclophosphamide, carboplatin, and etoposide
UH2	vincristine, dactinomycin, doxorubicin, cyclophosphamide, carboplatin, etoposide, and irinotecan
vincristine/irinotecan window therapy	vincristine and irinotecan in conjunction with revised UH-1 or UH-2 depending on response

兒癌– Wilms Tumor

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化學治療處方建議表 Regimen EE4A

Stage I / FH and stage II / FH: Nephrectomy, chemotherapy using Regimen EE4A

↓ reevaluate

WK	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
VCR	v	v	v	v	v	v	v	v	v	v			V*			V*			V*
AMD	v			v			v			v			v			v			v

Vincristine (VCR) 0.05 mg/kg IV push (maximum dose - 2 mg), beginning day 7 post-nephrectomy (week 1) if peristalsis has been established; then weekly for a total of 10 doses. The dose of vincristine is 1.5 mg/M^2 IV push for all patients who weigh more than 30 kg, but no single dose should exceed 2.0 mg.

Vincristine (VCR, V*) 0.067 mg/kg IV push (maximum dose - 2.0 mg) with dactinomycin at weeks 13, 16 and 19. The dose of vincristine is 2.0 mg/M^2 IV push with dactinomycin for all patients who weighed more than 30 kg, but no single dose should exceed 2.0 mg.

Dactinomycin (AMD) 0.045 mg/kg/dose IV push (maximum dose - 2.3 mg), beginning within 7 days post-nephrectomy (during week 0), and then at weeks 4, 7, 10, 13, 16, and 19. The dose of dactinomycin is 1.35 mg/M^2 for all patients who weighed more than 30 kg, but no single dose should exceed 2.3 mg.

Chemotherapy guidelines (Note: The day of nephrectomy will be considered day 0; the first dose of chemotherapy will be measured in days from that starting point.) No dose of dactinomycin should be initiated if the absolute neutrophil count is <1,000/mm^3 or the platelet count is <100,000/mm^3.

兒癌– Wilms Tumor

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化學治療處方建議表 Regimen DD4A

Stage III / FH; Stage I / Focal or diffuse anaplasia; Stage II or III / Focal anaplasia:
Nephrectomy, abdominal irradiation, chemotherapy using Regimen DD-4A

↓ reevaluate

WK	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
VCR	v	v	v	v	v	v	v	v	v	v			V*			V*			V*			V*			V*
AMD	v						v						v						v						v
EPI.				v						v						V*						V*			

Vincristine (VCR) 0.05 mg/kg IV push (maximum dose - 2 mg), beginning day 7 post-nephrectomy (week 1) if peristalsis has been established, then weekly for a total of 10 doses. The dose of vincristine is 1.5 mg/M^2 IV push for all patients who weighed more than 30 kg, but no single dose should exceed 2.0 mg.

Vincristine (VCR, V*) 0.067 mg/kg IV push (maximum dose - 2 mg) with dactinomycin or epirubicin at weeks 13, 16, 19, 22 and 25. The dose of vincristine is 2.0 mg/M^2 IV push for all patients who weighed more than 30 kg, but no single dose should exceed 2.0 mg.

Dactinomycin (AMD) 0.045 mg/kg/dose IV push (maximum dose - 2.3 mg), beginning within 7 days post-nephrectomy (during week 0), and then at weeks 7, 13, 19, and 25. The dose of dactinomycin administered at week 7 should be decreased by 50% (0.0225 mg/kg/dose) if whole lung or whole abdomen radiation therapy has been given. The dose of dactinomycin is 1.35 mg/M^2 for all patients who weighed more than 30 kg, but no single dose should exceed 2.3 mg. The dose of dactinomycin administered at week 7 should be decreased by 50% (0.675 mg/M^2) if whole lung or whole abdomen radiation therapy has been given.

Epirubicin (EPI) 1.5 mg/kg IV infusion over 1-2hours, is given at weeks 4 and 10; subsequently, 1.0 mg/kg IV push is given at weeks 16 and 22. The dose of epirubicin administered at week 3 should be decreased by 50% (0.75 mg/kg) if whole lung or whole abdomen radiation therapy has been given. The dose of epirubicin at weeks 4 and 10 is 45 mg/M^2 IV push, and at weeks 16 and 22 is 30 mg/M^2 IV push for all patients who weighed more than 30 kg. The dose at week 4 should be decreased by 50% (22.5 mg/M^2) if whole lung or whole abdomen radiation therapy has been given.

兒癌– Wilms Tumor

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化學治療處方建議表 Regimen M (modified DD4A) -1

a. Chest CT will be performed on all Stage IV patients with lung metastases at study enrollment and at Week 6.
b. Patients who have complete disappearance of their lung metastases (or who have tissue confirmation that the nodules do not contain viable tumor) at the Week 6 evaluation will be considered rapid responders and will continue with DD-4A.
c. Patients who do not have complete resolution of pulmonary nodules by Chest CT will undergo pulmonary irradiation and will be switched to regimen M (DD4A variation with dactinomycin and epirubicin given on the same day and alternating cyclophosphamide and etoposide)

WK	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
VCR		v	v		v	v	v			V*						V*						V*			V*
CTX[5]	v			v									v						v						
VP-16[5]	v			v									v						v						
AMD							v			v						v						v			v
EPI							v			v						v						v			v

Vincristine (VCR) 0.05mg/kg (1.5mg/M^2 if BW >30kg), iv push at weeks 8, 9, 11, 12,13. Maximal single dose is 2mg.

兒癌– Wilms Tumor

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化學治療處方建議表 Regimen M (modified DD4A) -2

Vincristine (VCR, V*) 0.067mg/kg (2mg/M^2 if BW >30kg) at weeks 16, 22, 28, 31. Maximal single dose is 2mg.

Cyclophosphamide[5] (CTX[5]) and Mesna with Etoposide (VP-16[5]): days 1-5, at weeks 7, 10, 19, 25.
Administration schedule:
-2 to 0 hr: Hydration at a rate of 200ml/M^2 /hr for 2 hours with D5 1/4 NS, IVF.
0 to 1 hr: **CTX[5]** 14.7 mg/kg (440mg/M^2 if BW >30kg) + **Mesna** 3mg/kg in 200ml/M^2 D5 1/2 NS IV infusion for 1 hour.
1-2 hr: **VP-16[5]** 3.3mg/kg in 200 ml NS /M^2 IV over 1 hr (100mg/M^2 if BW >30 kg)
3, 6, 9 hr: **Mesna** 3mg/kg (or 90mg/M^2 if BW >30kg) in 10ml NS IV infusion 15 min., q3h for 3 doses. Continue hydration at 150ml/M^2/hr for 6 hours with D5 1/2 NS
9-22 hr: D5 1/2 NS at 1000 ml/M^2 (total)
22-23 hr: same as –2 to 0 hrs.

Dactinomycin (AMD): 0.045mg/kg per dose, IV over 15 minutes. (1.35mg/M^2/dose if BW > 30 kg), (maximal single dose 2.3 mg) at weeks 13, 16, 22, 28, 31. Consider dose reduce by 50% at week 16, if delayed RT has been feasible at week 13.

Epirubicin (EPI): 1mg/kg IV in 200 ml/M^2 D5 1/2 NS, IV infusuin over 1-2 hours (30 mg/M^2 if BW >30 kg) at weeks 13, 16, 22, 28, 31. Dose should be reduced by 50% at week 16 if delayed RT has been feasible at week 13.

兒癌– Wilms Tumor

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化學治療處方建議表 Regimen I -1

Stage I-III / Clear cell sarcoma of the kidney(CCSK) : Nephrectomy, abdominal irradiation using 1080 cGy for Stage II & III patients, whole lung irradiation for patients with pulmonary metastases, chemotherapy with vincristine, epirubicin, etoposide, cyclophosphamide and mesna using Regimen I (see below).

WK	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
VCR	v	v	v		v	v	v	v	v		v	v	V*	V*					V*						V*
EPI	v						v						v						v						v
CTX[3]							v						v						v						v
CTX[5]				v						v						v						v			
VP-16[5]				v						v						v						v			

Vincristine (VCR) 0.05 mg/kg IV push (maximum dose - 2mg.), beginning day 7 post-nephrectomy (week 1) if peristalsis has been established, then at weeks 1-3, 5-9, 11-12. The dose of VCR is 1.5 mg/M^2 IV push for all patients who weighed more than 30 kg., but no single dose should exceed 2.0 mg.

Vincristine (VCR,V*) 0.067 mg/kg IV push (maximum dose - 2 mg) at week 13, 14, 19, 25. The dose of VCR is 2.0 mg/M^2 IV push for all patients who weighed more than 30 kg., but no single dose should exceed 2.0 mg.

Epirubicin (EPI) 1.5 mg/kg IV infusion over 1-2 hours, is given at weeks 1, 7, 13, 19 and 25. The dose of EPI administered at week 7 should be decreased by 50% (0.75 mg/kg) if whole lung or whole abdomen radiation therapy has been given. The dose of EPI at weeks 1, 7, 13, 19 and 25 is 45 mg/M^2 IV push for all patients who weighed more than 30 kg. The dose at week 7 should be decreased by 50% (22.5 mg/M^2) if whole lung or whole abdomen radiation therapy has been given.

兒癌– Wilms Tumor

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化學治療處方建議表 Regimen I -2

Cyclophosphamide (CTX[3]) and **Mesna** on days 1-3, with **Epirubicin (EPI)** day 1, at weeks 7, 13, 19, 25.

Administration schedule:

-2 to 0 hr: Hydration at a rate of 200 ml/M^2 /hr for 2 hours with D5 1/2 NS IVF.

0 to 1 hr: **CTX[3]** 14.7 mg/kg (440 mg/M^2 if BW >30kg) + **Mesna** 3 mg/kg in 200 ml/M^2 D5/ 1/2 NS IV infusion for 1 hour.

1-2 hr: **EPI:** 1.5mg/kg IV in 200 ml/M^2 D5 1/2 NS, iv over 1-2 hours (45 mg/M^2 if BW >30kg) at day 1

if RT has been given, or at week 19 if delayed tumor resection and RT is feasible at week 13.

3, 6, 9 hr: **Mesna** 3 mg/kg (or 90 mg/M^2 if BW >30kg) in 10ml NS iv infusion 15 min., q3h for 3 doses on days 1-3. Continue hydration at 150 ml/M^2/hr for 6 hours with D5 1/2 NS.

9-22 hr: D5/½ NS at 1000 ml/M^2 (total)

22-23 hr: same as –2 to 0 hrs.

Cyclophosphamide (CTX[5]), and **Mesna** with **Etoposide(VP-16[5])** on days 1-5, at weeks 4, 10, 16, 22.

Administration schedule:

-2 to 0 hr: Hydration at a rate of 200ml/M^2 /hr for 2 hours with D5 1/4 NS, IVF.

0 to 1 hr: **CTX[5]** 14.7 mg/kg (440mg/M^2 if BW >30kg) + **Mesna** 3mg/kg in 200ml/M^2 D5 1/2 NS IV infusion for 1 hour.

1-2 hr: **VP-16[5]** 3.3 mg/kg in 200 ml NS /M^2 IV over 1 hr (100 mg/M^2 if BW >30 kg)

3, 6, 9 hr: **Mesna** 3 mg/kg (or 90 mg/M^2 if BW >30kg) in 10ml NS IV infusion 15 min., q3h for 3 doses on days 1-5. Continue hydration at150 ml/M^2 for 6 hours with D5 1/2 NS

9-22 hr: D5 1/2 NS at 1000 ml/M^2 (total).

22-23 hr: same as –2 to 0 hrs.

兒癌– Wilms Tumor

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化學治療處方建議表 Regimen RTK

Stage I-IV / Rhabdoid tumor of the kidney: Nephrectomy, radiation therapy and chemotherapy with cyclophosphamide, mesna, etoposide and carboplatin

Babies <12 months of age should receive ONE-HALF of the recommended doses of all chemotherapeutic agents, as calculated on the basis of body weight. Full doses of chemotherapeutic agents should be administered to those patients when the child is ≥ 12 months of age.

WK	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
CBP^2	v			v						v			v						v			v			
VP-16^3	v			v						v			v						v			v			
CTX^4							v									v									v

Carboplatin (CBP^2) 16.7 mg/kg/day x 2 days, IV infusion over 60 minutes at weeks 1, 4, 10, 13, 19, 22. The dose of carboplatin is 500 mg/M^2/day x 2 days for all patients who weighed more than 30 kg.

Etoposide (VP-16^3) 3.3 mg/kg/day x 3 days in 200 ml/M^2 of D5 1/2 NS as an IV infusion over 60 minutes daily is given at weeks 1, 4, 10, 13, 19, 22 after carboplatin infusion. The dose of etoposide is 100 mg/M^2/day x 3 days for all patients who weighed more than 30 kg.

Cyclophosphamide (CTX^4) 14.7 mg/kg/day x 4 days (or 5 days) in 200 ml/M^2 of D5 1/2 NS as an IV infusion over 60 minutes daily is given at weeks 7, 16, 25. The dose of cyclophosphamide is 440 mg/M^2/day x 5 days for all patients who weighed more than 30 kg.

Mesna 3 mg/kg/dose x 4 doses in 10 ml IV over 15 minutes x 5 days, given after cyclophosphamide, at weeks 7, 16, and 25. The dose of mesna should be 90 mg/M^2/dose x 4 doses x 5 days for all patients who weighed more than 30 kg.

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手術前化學治療

符合下列條件者，考慮先進行neo-adjuvant chemotherapy：

1. Synchronous bilateral Wilms tumor
2. Wilms tumor in a solitary kidney
3. Extension of tumor thrombus in the inferior vena cava above the level of the hepatic veins
4. Tumor involved contiguous structures whereby the only means of removing the kidney tumor requires removal of the other structures (e.g. spleen, pancreas, or colon but excluding the adrenal gland).
5. Inoperable Wilms tumor
6. Pulmonary compromise due to extensive pulmonary metastases

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手術前化學治療處方建議表 Regimen VAD

Stage I-IV bilateral Wilms tumor (BWT) with biopsy revealing favorable histology or no preoperative biopsy; stage I-III BWT with focal anaplasia; stage I BWT with diffuse anaplasia; or high-risk, stage III-IV unilateral Wilms tumor with contralateral nephrogenic rest or predisposition syndrome.

WK	1	2	3	4	5	6
VCR	v	v	v	v	v	v
AMD	v			v		
EPI	v			v		

Vincristine (VCR): 0.05 mg/kg IV push if BW is < 30 kg; 1.5 mg/M^2 IV push if BW is > 30kg (maximal dose 2 mg) weeks 1 to 6.

Dactinomycin (AMD): 0.045 mg/kg IV push over 5 minutes, 1.35 mg/M^2 if BW is >30kg (maximal single dose 2.3 mg) on weeks 1 and 4. (打 1 天)

Epirubicin (EPI): 1.5mg/kg IV infusion over 2 hrs, 45 mg/M^2 if BW is >30kg on week 1 and 4.

** Calculating drug dosage on the basis of surface area probably leads to an overestimation in infants, so doses usually are calculated according to body weight instead.
** Reduction of all drugs for infants to 2/3 of the doses for older children. (<1y/o infant 除了用 kg 算之外，還要再減少 1/3 的劑量)

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化學治療處方建議表 Regimen Revised UH-1 -1

Stage IV BWT with Focal anaplasia; Stage II-IV BWT with Diffus anaplasia; Stage II or III / Diffus anaplasia; Stage IV CCSK

Nephrectomy followed by postoperative chemotherapy with revised UH-1 regimen and abdomen/flank irradiation, with a boost to residual tumor.

↓ reevaluate if primary tumor not yet resected

WK	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
VCR	v	v	v							v	v	v	v	v	v							v	v	v				v	v	v
EPI	v									v			v									v						v		
CTX[3]	v									v			v									v						v		
CBP				v			v									v			v						v					
CTX[low3]				v			v									v			v						v					
VP-16[3]				v			v									v			v						v					

Vincristine (VCR) : 0.025mg / kg for age < 1y , 0.05 mg / kg for age 1-3 yrs, 1.5mg / M^2 if age ≧3 yrs) IV over 1 minute (maximal dose 2 mg) on days 1, 8, and 15 (weeks 1-3) and weeks 10-15, 22-24, and 28-30.

Epirubicin (EPI) : 0.75 mg / kg for age < 1y , 1.5 mg / kg for age 1-3 yrs ; or 45mg/M^2 if BW > 30kg , in 200 ml/M^2 D5 1/2 NS IV infusion over 1-2 hours on day 1 (week 1) and on weeks 10, 13、22、and 28.

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化學治療處方建議表 Regimen Revised UH-1 -2

Cyclophosphamide (CTX[3]) : 14.7mg/kg, or 440mg/M^2 for BW ≧30kg in 200 ml/M^2 D5 1/2 NS IV infusion over 1 hr,-d 1,2,3 on weeks 1, 10, 13, 22, and 28.

Mesna : 20% cyclophosphamide dose at hour 0, hour 4 and hour 8 after cyclophosphamide (CTX[3]).

Carboplatin (CBP) : 500 mg/M^2 in 125-250mL D5W IV infusion over 1 hr, day 1. (For age <1y, 16.7 mg/kg) on weeks 4, 7, 16, 19, and 25.

Cyclophosphamide(CTX[low3]) : 10 mg/kg, or 300mg / M^2 if BW >30kg in 130ml /M^2 D5 1/2 NS IV over 15-30 minutes, days 1-3. on weeks 4, 7, 16, 19,and 25.

Etoposide (VP-16[3]) : 3.3mg/kg, or 100 mg / M^2 if BW >30kg in 200 ml / M^2 D5 1/2 NS IV infusion over 1 hr, days 1-3. on week 4, 7, 16, 19, and 25.

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化學治療處方建議表 Regimen UH-2 -1

Focal or diffuse anaplastic stage IV Wilms tumor: nephrectomy followed by postoperative chemotherapy with revised UH-1 regimen, or UH-2 regimen (revised UH-1 with additional vincristine and irinotecan) in patients with poor/partial response to chemotherapy and abdomen/flank irradiation with a boost to residual tumor [13]. Patients with lung metastasis receive whole lung irradiation.

Patients whose primary tumors were initially resected undergo radiotherapy as in regimen UH-2 beginning on day 1 in week 1. Patients with delayed primary tumor resection undergo radiotherapy as in regimen UH-2 beginning on day 1 in week 7. If the primary tumor was not previously resected, patients undergo resection, if feasible, in week 7.

↓ reevaluate if primary tumor not yet resected

WK	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
VCR	v	v	v							v	v					v	v	v	v	v	v				v	v		v	v	v				v	v	v
EPI	v															v			v									v						v		
CTX[3]	v															v			v									v						v		
CBP				v			v						v									v									v					
CTX[low3]				v			v						v									v									v					
VP-16[3]				v			v						v									v									v					
IRI[5]										v	v														v	v										

Vincristine (VCR) : 0.025mg / kg for age < 1y, 0.05 mg / kg for age 1-3 yrs, 1.5mg / M^2 if age ≧3 years) IV 1 minute (maximal dose 2 mg), ~~on~~ day 1 on weeks 1-3, 10, 11, 16-21, 25, 26, 28-30, and 34-36.

兒癌– Wilms Tumor

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化學治療處方建議表 Regimen UH-2 -2

Epirubicin (EPI): 0.75 mg / kg for age <1y, 1.5mg / kg for age 1-3 yrs, 45mg / M^2 if BW ≧ 30kg) in 200 ml / M^2 D5 1/2 NS IV infusion over 1-2 hours, day 1 on weeks 1, 16, 19, 28, and 34.

Cyclophosphamide (CTX[3]) 14.7mg/kg, or 440mg/M^2 if BW≧30kg in 200ml / M^2 D5 1/2 NS IV infusion over 1 hr, ~~on~~ days 1,2,3 on weeks 1, 16, 19, 28, and 34.

Mesna : 20% cyclophosphamide dose at hour 0, hour 4 and hour 8 after cyclophosphamide.

Carboplatine + CTX[low] + Etoposide on the weeks 4, 7, 13, 22, 31.
Carboplatin(CBP) : 500 mg / M^2 in 125-250ml D5W, IV infusion over 1 hr, day 1. (For age <1y, 16.7 mg/kg)

Cyclophosphamide(CTX[low3]) : 10 mg/kg in 130ml / M^2 D5 1/2 NS IV infusion over 30 minutes (300mg/M^2 if BW >30kg), ~~on~~ days 1, 2, 3.

Etoposide(VP-16[3]) : 3.3 mg/kg in 200 ml/M^2 D5 1/2 NS IV infusion over 1 hr (100mg/M^2 if BW >30kg), ~~on~~ days 1, 2, 3.

Irinotecan(IRI[5]) : 20 mg / M^2 / day IV infusion over 1 hr, ~~on~~ days 1-5 on the weeks 10, 11, 25, 26.

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*雙側*威爾姆氏腫瘤管理

- Approximately 5-7% of WT patients present with bilateral disease, either synchronously or metachronously. Bilateral WT usually occurs in younger children and more often in girls [14].
- In contrast to unilateral WT, there has not been uniform agreement about the therapeutic strategy in the management of BWT [15].
- After several multicenter trials, bilateral biopsies followed by pre-operative chemotherapy and then renal salvage surgery have been recommended. The management of BWT has evolved from primary surgery extirpation to kidney-preserving resection after preoperative chemotherapy.
- The NWTS-5 recommendation for the management of BWT includes initial biopsy and local staging followed by chemotherapy (according to abdominal stage and histological features) and second-look surgery at week 5.
- If needed, additional chemotherapy or radiation therapy is given, but definitive surgery is recommended within 12 weeks of diagnosis to limit the risk of chemoresistant clonal expansion [16].
- In recent study, radiotherapy was replaced by consolidation with high-dose melphalan and autologous hematopoietic stem cell rescue (AHSCR). They reported that on patients with BWT with pre-operative chemotherapy, late kidney-sparing surgery, and consolidation with high-dose melphalan plus AHSCR resulted in good preservation of kidney parenchymal and renal function [17].
- According to the NWTSG, metachronous bilateral WT has lower survival rates than synchronous BWT. Long-term survival rate for patients with synchronous BWT are approximately 70-80% [18].
- Survivors of BWT still have many chronic health issues and thereby need individualized long-term medical care [19]. The incidence of end-stage renal failure was 0.6% for unilateral tumors, 11.5% for BWT, and > 50% for Denys-Drash synrdrom/WAGR syndrome [20].
- Children younger than 12 months who have perilobar nephrogenic rests are at markedly increased risk of contralateral disease and require frequent and regular surveillance for several years [21].

兒癌– Wilms Tumor

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雙側威爾姆氏腫瘤治療

5.1 治療建議 回目錄

1. Image 診斷 BWT 後，可進行病理切片，若為 Favorable histology/focal anaplasia 則進入上述 VAD 6 週療程，或可不進行切片直接進入 VAD。若為 Stage IV focal anaplasia 或 Stage II-IV Diffuse anaplasia 則使用 rUH-1。
2. 6 週治療後，進行影像檢查以進行 definite surgery。考慮以下方式：
   a. unilateral total nephrectomy with contralateral partial nephrectomy
   b. bilateral partial nephrectomy
   c. unilateral total nephrectomy
   d. unilateral partial nephrectomy
   e. bilateral total nephrectomies

   若6週治療影像雖已達到Partial response但仍不適合進行bilateral partial nephrectomy，可再做 6 週 VAD。**definite surgery 最遲不超過 12 週。**
3. 術後依 SIOP staging，依兩側各自 Staging 及 Histology 結果較嚴重者，依 Table 1. for unilateral WT 安排 adjuvant chemotherapy and radiation therapy.
4. 若原先 6 週治療反應不理想 (less than PR)，應進行 Open biopsy 評估是否非 Wilms tumor，或需要更換化療療程。

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放射治療處方建議表

	Histology				
	Favorable	Focal anaplasia	Diffuse anaplasia	Clear cell sarcoma	Rhabdoid tumor
Stage I	0	10.8	10.8	10.8	10.8/19.8*
II	0	10.8	10.8	10.8	10.8/19.8*
III	10.8	10.8	19.8	10.8	10.8/19.8*
IV	Based on abdominal stage and histology				

* For patients aged > 1 year old

1. All patients except stage I and II favorable histology are irradiated.
2. Focal and diffuse anaplasia are distinguished in that Stage III diffuse anaplasia gets a higher dose
3. Whole lung RT is given only if pulmonary nodules are not in CR after week 6.
4. RT should start by day 10 post-op and not later than day 14.
5. Boost small areas of gross lung metastasis to 20 Cy.

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Drop off criteria

1. Incorrect diagnosis.
2. Patients and/or parents refuse to allow additional therapy.
3. The patient who, in the judgement of the Principal Investigator, could not or did not follow the assigned treatment, may be removed from study.
4. Patients who fail to meet all eligibility requirements of protocol (i.e., ineligible) will be taken off study, e.g., using other protocols, or not newly diagnosed patients.

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癌症藥物停藥準則

影像學檢查，若治療期間腫瘤有變大、轉移情況，或有嚴重藥物毒性出現，應停止或改變治療方式。

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