INCTR Wilms Tumor Proposed Protocol

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Objective

- To develop a protocol for countries wherein majority of Wilms tumor present with large size tumors.

Eligibility Criteria

- **Inclusion Criteria**
  - All newly diagnosed untreated cases of **unilateral** renal tumors in age 6 months- 18 years.
- **Exclusion Criteria**
  - Syndromic children (WAGR, BWS)
  - Bilateral WT

Reason: Form <10% of cases and require individualized therapy including nephron sparing surgery.

Baseline Investigations

- Baseline Examination of Nutrition and syndromic features
- Complete Hemogram; LFT; RFT
- USG Abdomen/Pelvis and/or Contrast Enhanced CT scan of Abdomen and Pelvis
- Chest radiograph and/or CT chest

- In countries where CT is not routinely available, ultrasound abdomen and chest radiograph may be done

No need for baseline Doppler

Optional Testing

- Fine needle aspiration cytology or biopsy of the tumor may be done as per the individual institutional practice.
- Proving a renal tumor by histology is Not a prerequisite to be enrolled on the protocol.

What should abdominal radiology provide?

- Size of tumor in maximum dimension
- Presence of necrosis: <25%, 25-50%, 50-75%, >75%
- **Laterality with a comment on contralateral kidney**
- Presence of thrombus
- Lymph node status
- Liver nodules
- Relationship with aorta and inferior vena cava: **pushed, engulfed, none.**
- **Origin of tumor: Upper pole, lower pole or hilum**

Metastases

- Chest radiograph/ CT Chest
  - Yes/No
  - Unilateral/Bilateral
  - Number on each side: upto five or >5
- If Chest radiograph is showing a doubtful lesion, then a CT Chest would be desirable.

Preoperative Chemotherapy in Non Metastatic WT

6 weeks of chemotherapy (No diff in 4 vs 8 weeks)

Wk 0	VCR	ACD
Wk 1	VCR	
Wk 2	VCR	
Wk 3	VCR	ACD
Wk 4	VCR	
Wk 5	VCR	

Reevaluation After 6 weeks

CT or USG and comment on the same radiology criteria as at baseline

Proceed for Surgery

Surgical Principles

- Nephroureterectomy to be done by TA/TP approach. Mention whether done outside or within the Gerota's fascia (as per the institutional practice)
- Lymph node sampling to include supra and infra hilar paracaval/paraaortic, iliac nodes and aotocaval nodes on the side of the renal tumor.
- ***Comment on spillage***
- ***Evaluation of contralateral kidney not needed with CT imaging (If USG is used as imaging alone, then this may be incorporated for those centers)***

Pathology

Whole Specimen to be examined (Not just a biopsy)

- Favorable histology vs Unfavorable histology (Anaplasia and or blastema)
- Necrosis will not be part of this study as it requires extensive tissue sectioning
- Other type of renal tumor such as CCSK* or rhabdoid tumor*).

  * CCSK/Rhabdoid tumors go off study

Staging Based on Pathology

Classify as Stage 1-3 based on:

- Involvement of renal capsule and sinuses
- Intraoperative spillage
- Transected tumor thrombus
- Lymph node involvement as evidenced by presence of tumor or necrosis

Central Review of the slides to be done either by email or sending slides; blocks to be preserved for biological studies.

Post Op Therapy of Favorable Histology Wilms Tumor

Stage 1 FH WT

Wk 6	VCR	ACD
Wk 7	VCR	
Wk 8	VCR	
Wk 9	VCR	ACD
Wk 10	VCR	
Wk 12	VCR*	ACD
Wk 15	VCR*	ACD
Wk 18	VCR*	ACD

Stage 2 FH WT

Wk 6	VCR	ADR
Wk 7	VCR	
Wk 8	VCR	
Wk 9	VCR	ACD
Wk 10	VCR	
Wk 12	VCR*	ADR
Wk 15	VCR*	ACD
Wk 18	VCR*	ADR*
Wk 21	VCR*	ACD
Wk 24	VCR*	ADR*

Stage 3 FH WT

Chemotherapy plus Abdominal RT

Wk 6	VCR	ADR
Wk 7	VCR	
Wk 8	VCR	
Wk 9	VCR	ACD
Wk 10	VCR	
Wk 12	VCR*	ADR
Wk 15	VCR*	ACD
Wk 18	VCR*	ADR*
Wk 21	VCR*	ACD
Wk 24	VCR*	ADR*

Post Op Therapy of unfavorable Histology Wilms Tumor:

Focal Anaplasia

- **Stage 1 as Stage 1 FH**
- **Stage 2 and 3 as Stage 3 FH**

Post Op Therapy of unfavorable Histology Wilms Tumor:
Diffuse Anaplasia

Chemotherapy and Radiotherapy for all stages 1-3.

Wk 6	VCR	ADR		
Wk 7	VCR			
Wk 8	VCR			
Wk 9			CYCLO	VP-16
Wk 12	VCR*	ADR	CYCLO*	
Wk 15			CYCLO	VP-16
Wk 18	VCR*	ADR	CYCLO*	
Wk 21			CYCLO	VP-16
Wk 24	VCR*	ADR	CYCLO*	
Wk 27			CYCLO	VP-16
Wk 30	VCR*	ADR	CYCLO*	

Metastatic Disease

Pre Op Chemotherapy for Metastatic Disease

- Wk 0 VCR ACD
- Wk 1 VCR
- Wk 2 VCR
- Wk 3 VCR ADR
- Wk 4 VCR
- Wk 5 VCR ACD
- Wk 6 VCR
- Wk 7 VCR
- Wk 8 VCR ADR

Reevaluation after 6 or 9 weeks

- CT or USG Abdomen and comment on the same radiology criteria as at baseline.
- Chest radiograph or Chest CT

- Proceed for Surgery with same surgical and pathology principles.

If lung metastases:

- Disappeared: No RT
- Present: RT to lungs
- Doubtful: Confirm by metastatectomy and if positive, give RT and if negative then no RT

Post Op Chemo for FH and focal anaplasia Stage 4 WT

Wk 9	VCR	ACD
Wk 10	VCR	
Wk 12	VCR*	ADR
Wk 15	VCR*	ACD
Wk 18	VCR*	ADR*
Wk 21	VCR*	ACD
Wk 24	VCR*	ADR*

Post Op Chemo for Diffuse anaplasia Stage 4 WT

Chemotherapy and RT locally for all stages

Wk 9			CYCLO	VP-16
Wk 12	VCR*	ADR	CYCLO*	
Wk 15			CYCLO	VP-16
Wk 18	VCR*	ADR	CYCLO*	
Wk 21			CYCLO	VP-16
Wk 24	VCR*	ADR	CYCLO*	
Wk 27			CYCLO	VP-16
Wk 30	VCR*	ADR	CYCLO*	

Doses

VCR 1.5 mg/m2 (Max 2mg) (0.05 mg/kg for weight <30 kg)

ACD 1.35 mg/m2 (Max 2.3 mg) (45 mcg/kg for weight <30 kg)

ADR 45 mg/m2 (1.5 mg/kg for weight <30 kg)

ADR* 30 mg/m2 (1.0 mg/kg for weight <30 kg)

CYCLO 440mg/m2 d1-5

CYCLO* 440mg/m2 d1-3

VP-16 100mg/m2 d1-3

Radiation Therapy

To be started within 2 weeks after surgery.