COG-AREN03B2: Renal Tumors Classification, Biology, and Banking Study

FAST FACTS

Eligibility Reviewed and Verified By

_____ MD/DO/RN/LPN/CRA Date _____

_____ MD/DO/RN/LPN/CRA Date _____

Consent Version Dated_____

PATIENT ELIGIBILITY:

Important note: The eligibility criteria listed below are interpreted literally and cannot be waived (per COG policy posted 5/11/01). All clinical and laboratory data required for determining eligibility of a patient enrolled on this trial must be available in the patient's medical/research record which will serve as the source document for verification at the time of audit.

___1. **AREN03B2 enrollment is mandatory prior to enrollment on therapeutic studies. Consult the relevant therapeutic study for renal tumors. Physicians are encouraged not to begin treatment until an initial risk assignment is made on AREN03B2.**

___2. Renal tumors

Patients with the first occurrence of any tumor of the kidney identified on CT scan or MRI are eligible for enrollment on the banking component of this study.

As of Amendment 8, only patients with an institutional diagnosis of Stage I-IV focal or diffuse anaplasia will be eligible for central review and return of an Initial Risk Assignment and/or subsequent central pathology review. All other patients will not undergo a central review of pathology, imaging, or surgical reports, and Initial Risk Assignment will not be entered. These patients will be eligible only for the banking portion of the study.

Eligible tumors include (but are not limited to):

Nephroblastic Tumors	Nephroblastoma (Wilms Tumor) • Favorable histology • Anaplasia (Diffuse, Focal) Nephrogenic rests and Nephroblastomatosis Cystic Nephroma and Cystic Partially Differentiated Nephroblastoma Metanephric Tumors • Metanephric Adenoma • Metanephric Adenofibroma • Metanephric Stromal Tumor
Mesoblastic Nephroma	Cellular, Classic, Mixed
Clear Cell Sarcoma	
Rhabdoid Tumor	
Renal Epithelioid Tumors of Childhood	Papillary renal cell carcinoma Renal medullary carcinoma Renal tumors associated with Xp11.2 translocations Oncocytic renal neoplasms following neuroblastoma
Angiolipoma	
Ossifying renal tumor of infancy	

___3. Extrarenal tumors

Patients with the first occurrence of the following tumors are also eligible:

- Extrarenal nephroblastoma or extrarenal nephrogenic rests
- Malignant rhabdoid tumor occurring anywhere outside the Central Nervous System

___4. Required Submissions

Required specimens, reports, forms, and copies of imaging studies must be available or will become available for submission and the institution must intend on submitting them as described in the protocol procedures.

___5. For ALL patients, the following submissions are required:

- A complete set of recut H & E slides (including from sampled lymph nodes, if patient had upfront nephrectomy)*#
- Representative formalin-fixed paraffin-embedded tissue block or if a block is unavailable, 10 unstained slides from a representative block of tumor, if available.*
- Institutional pathology report, Specimen Transmittal Form, and Pre-Treatment Pathology Checklist
- Copies of images and institutional reports of CT and/or MRI abdomen and pelvis, and Pre-Treatment Imaging Checklist
- Copies of images and institutional report of chest CT for all malignant tumors
- Institutional surgical report(s) and Pre-Treatment Surgical Checklist
- CRFs: Staging Checklist and Metastatic Disease Form (if metastatic disease is noted on imaging)

* Tissue must be from diagnosis, prior to any renal tumor directed chemotherapy or radiation (only exception is for presumed FHWT patients discovered to have FAWT or DAWT at delayed nephrectomy and plan to enroll at delayed nephrectomy or second biopsy, see Section 3.1.5.1.1).

If there are concerns with limited availability of diagnostic slides, please contact the study chair or study pathologist.

For patients with bilateral, bilaterally predisposed, multicentric, or unilateral tumor in solitary kidney, required slides and tissue may be submitted for banking at the time of their first post-chemotherapy surgical procedure.

Please note: if the above required items are not received within 120 days of study enrollment, the patient will be considered off study per Section 7.1 criteria.

___6. Age

Patients must be < 30 years old at the time of diagnosis.

___7. Required Pathology Materials for All Patients

All patients enrolling on AREN03B2 must have pathology specimens submitted (see Section 5.1). ONLY patients with (focal or diffuse) anaplastic Wilms Tumor (WT) identified at initial diagnostic procedure (biopsy or nephrectomy) will receive rapid central review. These patients must submit pre-chemotherapy tissue for central pathology review.

Patients initially diagnosed with Favorable Histology WT (FHWT) at initial, pre-chemotherapy biopsy and who have anaplasia identified at a later procedure (delayed nephrectomy or second biopsy) must submit tissue from the delayed procedure for central review. In such cases, it is highly recommended and encouraged, but not required, to submit original diagnostic pre-chemotherapy tissue from initial biopsy.

The following patient groups will now be eligible for Rapid Central Review:

1. Patients with institutional pre-chemotherapy diagnosis of Stage I-IV focal or diffuse anaplasia at initial biopsy or nephrectomy
2. Patients identified with anaplasia at delayed nephrectomy or second biopsy, after an initial diagnosis of FHWT (Stage I-IV) from a pre-treatment biopsy.

___8. Central Review

As soon as possible following registration and strongly recommended by Day 7 after surgery/biopsy, the patient's baseline diagnostic images (CT, MRI) must be sent to IROC Rhode Island. Also see Section 5.5.2

___9. Required Institutional surgical report(s) for Central Review

All patients enrolling on AREN03B2 (with the exception of patients with bilateral, bilaterally predisposed, multicentric, or unilateral tumor in a solitary kidney planning to enroll on AREN03B2 without biopsy or surgery) must submit institutional surgical reports for central review. Submission of institutional surgical reports and the Pre-Treatment Surgical Checklist is required for initial risk assignment to occur.

For patients who have upfront nephrectomy, lymph node sampling is required. If upfront nephrectomy occurred and lymph nodes are not submitted, the patient will not be eligible for a COG renal therapeutic trial. See Section 3.1.4.2 for details.

The following schema displays the prognostic factors that will be used to define eligibility requirements for COG therapeutic studies:

For Patients with Favorable Histology Wilms Tumor:

Patient Age	Tumor Weight	Stage	Initial Risk Group	LOH 1p/16q	Lung Metastases Response	Extra-Pulmonary Mets	Final Risk Group
< 2 yrs	< 550 g	I[#]	Very Low	Any	N/A	N/A	Very Low
Any	≥ 550 g	I	Low	No	N/A	N/A	Low
≥ 2 yrs	Any	I	Low	No	N/A	N/A	Low
Any	Any	II	Low	No	N/A	N/A	Low
Any	≥ 550 g	I	Low	Yes	N/A	N/A	Standard
≥ 2 yrs	Any	I	Low	Yes	N/A	N/A	Standard
Any	Any	II	Low	Yes	N/A	N/A	Standard
Any	Any	III	Standard	No	N/A	N/A	Standard
Any	Any	IV	Higher	No	Complete	No	Standard
Any	Any	III	Standard	Yes	N/A	N/A	Higher
Any	Any	IV	Higher	Yes	Any	Any	Higher
Any	Any	IV	Higher	Any	Partial	Any	Higher
Any	Any	IV	Higher	Any	Any	Yes	Higher
Any	Any	V	Bilateral	Any	Any	Any	Bilateral

Lymph node biopsy is **required** to confirm Stage I disease in Very Low Risk patients.

Summary of Submission Requirements and Recommendations. **See specific guidelines in Section 5.2.**

SUBMISSION REQUIREMENTS FOR PATIENTS POTENTIALLY ENROLLING ON A COG RENAL THERAPEUTIC STUDY THAT REQUIRES PRIOR ENROLLMENT ON AREN03B2	
Pathology Specimens for Central Review: See Sections 3.1.4.1, 3.1.5 and 5.2.2 . • A complete set of recut H & E slides (including from sampled lymph nodes, if patient had upfront nephrectomy) • Representative formalin-fixed paraffin-embedded tissue block or if a block is unavailable, 10 unstained slides from a representative block of tumor, if available. o For anaplastic tumors, the tissue block or unstained slides submitted must contain anaplasia, with the maximum volume of anaplasia from the entire tumor. • Institutional pathology report, Specimen Transmittal Form and Pre-Treatment Pathology Checklist	• **REQUIRED from primary diagnostic tissue,** at enrollment prior to any chemotherapy.* • Requested from any biopsied metastatic site at any time point (if not already submitted as the primary diagnostic tissue) • **REQUIRED** at nephrectomy: o If delayed nephrectomy, only required from patients who received an initial risk assignment of FHWT or those who are planning to enroll on AREN03B2 at delayed nephrectomy or second biopsy with diagnosis of focal or diffuse anaplastic Wilms tumor. Refer to Sections 3.1.5 and 4.2. o If patient had upfront nephrectomy, H&E slides from sampled lymph nodes are required to be submitted, otherwise an initial risk assignment will not be issued. • Requested at RELAPSE
Snap Frozen Tumor Tissue from diagnostic tissue (primary tumor or metastatic site) • At least 1 gram and up to 10 grams if available, in 1 gram aliquots. • See Section 5.2.1.2.1 for details.	• Requested at enrollment prior to any chemotherapy* o Every effort should be made to secure sufficient tissue at the time of diagnostic surgical procedure. • Requested for all other tumors. • Requested at any surgery and at RELAPSE.
Snap Frozen Normal Kidney Tissue • Up to 10 grams if available, in 1 gram aliquots. See Section 5.2.1.2.1 for details.	• Requested at enrollment (prior to any chemotherapy*) AND at any surgery
Snap Frozen Tumor Tissue from biopsied metastatic areas (if obtained in addition to primary diagnostic site) • At least 1 gram and up to 10 grams if available, in 1 gram aliquots.	• Requested at enrollment prior to any chemotherapy* AND at any surgery
10-20 mL of whole blood in a Streck Cell-Free DNA tube • See Section 5.2.1.2.3 for details.	• Requested at enrollment prior to any chemotherapy*
Institutional surgical report(s) • **Pre-Treatment Surgical Checklist –** this form is required at enrollment.	• **REQUIRED** at enrollment (prior to any chemotherapy*) • **REQUIRED** at nephrectomy (if relevant) • Requested at any subsequent surgery
Diagnostic Imaging: See Section 5.5 for details • Copies of films and institutional reports of CT/MRI abdomen, pelvis, chest. • Pre-Treatment Imaging Checklist	• **REQUIRED** at enrollment prior to any chemotherapy*
Additional Required Forms: Staging Checklist and Metastatic Disease Form (if metastatic disease noted at imaging)	• **REQUIRED** at enrollment prior to any chemotherapy*
• **Formalin Fixed FFPE Block** – See Section 5.2.1.2.2 for details. For anaplastic tumors, the tissue block or unstained slides submitted must contain anaplasia.	• Requested at enrollment prior to any chemotherapy*
Serum (PRE NEPHRECTOMY) - spun from 6 mL of whole blood in red top tube. • See Section 5.2.1.2.4 for details.	• Requested at enrollment prior to any chemotherapy*
Urine (PRE NEPHRECTOMY) - 5-15 mL: See Section 5.2.1.2.5 for details.	• Requested at enrollment prior to any chemotherapy*
Whole blood (5-10 mL) in EDTA tube: See Section 5.2.1.2.3 for details.	• Requested at end of therapy AND at one year after end of therapy**

*The phrase ‘prior to any chemotherapy’ used throughout this table is not intended to prohibit prior chemotherapy when given for a previous or different cancer, for example, in patients with renal cell carcinoma who developed renal cell carcinoma as a second cancer.
**End of therapy blood work should be sent as close as possible to completion of therapy (i.e., at recovery from final therapy); permissible to submit within 4 months of completing therapy for end of therapy sample, and within 10 -16 months of end of therapy for one year after end of therapy sample. Please document the timing of the sample in relationship to last therapy given.
NOTE: If the required materials and forms at enrollment as listed in Section 3.2.2 are not received within 120 days of study enrollment, the patient will be considered off study per Section 7.1 criteria.