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| **PROTOCOL TITLE:** Kidney/Pancreas Pre-Transplant Evaluation Candidates with History of Urologic Malignancies: Adenocarcinoma of the Prostate, Renal Cell Carcinoma, Urothelial Carcinoma of the Bladder |
| **APPLICABLE FACILITIES:**[ ] EHC [ ] EDH [ ] EHH [ ] EHI [ ] EHN [ ] EJCH [ ] ELTAC [x] ESJH[x] EUH [ ] EUHM [ ] EUHS [ ] EUOSH [ ] EWWH [ ] RJV-ERH [ ] RJV-ESOP [ ] TEC/ESA |
| **EFFECTIVE DATE:**  | **ORIGINATION DATE:**  |

**CATEGORY:**

Choose One or More: Diagnostic/Therapeutic/Preventive

**LEVEL:**

Choose One: Independent

**CONTENT:**

**Policy Statement**:
The Emory Kidney/Pancreas Transplant Program will consider candidates for kidney/pancreas transplantation in the setting of a known history of localized (non-metastatic) and successfully treated prostate cancer (adenocarcinoma), renal cell carcinoma, or urothelial carcinoma of the bladder. Both end-stage renal disease and the post-transplant immunosuppressed state are associated with an increased incidence [and lethality] of some urologic malignancies. Nevertheless, it is acknowledged that the benefits of transplantation significantly outweigh the risks associated with the aforementioned urologic malignancies, provided that key selection criteria are met. The following tables outline a general guideline for the timing of listing/transplant in the setting of treated, localized urologic malignancies.

**Prostate Cancer (Adenocarcinoma)**

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| **Risk Group** | **Tumor Criteria** | **Acceptable Treatment** | **When to List/ Transplant** |
| **Very Low Risk** | cT1c *and*PSA < 10 *and*PSA density <0.15 *and*GS 3+3=6 (GG1)***with***<3 positive cores *and*<50% involvement of any positive core | 1. Active Surveillance | - May list or transplant while on active surveillance after confirmatory biopsy*(i.e., second biopsy after initial diagnosis, usually within 3-6 months; preferably, but not necessarily, MRI-guided)* |
| **Low** | cT1-T2a, *and*PSA < 10 *and*GS 3+3=6 (GG1) | 1. Active Surveillance (preferred)2. Surgery3. Radiotherapy | - May list or transplant while on active surveillance after confirmatory biopsy- No delay after successful treatment*🡪 After surgery, PSA should be undetectable; positive margins OK if pT2, GG1-2; if adverse pathology (pT3, +margin), consider adjuvant RT +/- genomic testing to guide its use* *🡪 After radiotherapy, PSA nadir should be <2.0 ng/mL* *(can take 12 months)* |
| **Intermediate (Favorable)** | ***Only one*** intermediate factor:cT2b-c, *or*PSA 10-19.9 *or*GS 3+4=7 (GG2)***and***<50% cores positive with cancer | 1. Surgery (recommended)2. Radiotherapy (recommended)3. Whole-gland cryoablationψ (selected patients)4. Active surveillance (selected patients) | - No delay after successful treatment*🡪 After surgery, PSA should be undetectable; positive margins OK if pT2, GG1-2; if adverse pathology (pT3, +margin), consider adjuvant RT +/- genomic testing to guide its use**🡪 After radiotherapy, PSA nadir should be <2.0 ng/mL* *(can take 12 months after ADT)**🡪 AS: recommend MRI guided confirmatory biopsy followed by genomic testing confirming lower-risk tumor; this should be decided in conjunction with treating urologist* |
| **Intermediate (Unfavorable)** | ***More than one*** intermediate factor:cT2b-c, *or*PSA 10-19.9 *or*GS 3+4=7 (GG2)***or any one of***GS 4+3=7 (GG3) *or*>50% cores positive with cancer | 1. Surgery2. Radiotherapy + short-term androgen deprivation therapy (3-6 months) | - No delay after successful treatment*🡪 After surgery, PSA should be undetectable; if adverse pathology (pT3, +margin), consider adjuvant RT +/- genomic testing to guide its use**🡪 After radiotherapy, PSA nadir should be <2.0 ng/mL* *(can take 12 months after ADT)* |
| **High** | ≥cT3, *or*PSA >20 *or*Gleason score 8-10 (GG4 and 5) | 1. Surgery2. Radiotherapy + long-term androgen deprivation therapy (18-24 months) | - 2 year waiting period after surgery; 3 years after radiotherapy; without biochemical recurrence*ϒ**🡪 After surgery, PSA should be undetectable; if adverse pathology (pT3, +margin), consider adjuvant RT +/- genomic testing to guide use of RT**🡪 After radiotherapy, PSA nadir should be <2.0 ng/mL* *(can take 12 months after ADT)* |

\*Radiotherapy may consist of different forms of radiation delivery, including external beam, brachytherapy, etc.

δRemission after radiotherapy is defined as nadir <2.0 ng/mL with testosterone levels recovered if patient received ADT

ψWhole gland cryosurgery is an acceptable treatment option in low or intermediate risk disease for patients with a life expectancy >10 years and contraindications to surgery or radiotherapy; however, it currently receives only a conditional recommendation (Grade C) in AUA guidelines because comparative mortality data is lacking. As such, patients treated with this modality would have to be discussed on a case-by-case basis.

ϒDefinition of biochemical recurrence i) after surgery: ≥ 2.0 ng/mL on two consecutive tests; ii) after radiotherapy: PSA at nadir + 2.0 ng/mL

**Note:** PSA screening in the waitlisted population should be performed in accordance with AUA screening guidelines (<https://www.auanet.org/guidelines/prostate-cancer-early-detection-guideline>). As part of the initial pre-transplant evaluation, PSA testing is performed in all men aged 55-69 or in younger men who are at high risk for prostate cancer (e.g. family history).

**Renal Cell Carcinoma**

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| **Tumor Stage** | **Acceptable Treatment** | **When to List/Transplant** |
| **T1a**≤ 4 cm, confined to kidney | 1. Active Surveillance\*2. Partial Nephrectomy3. Radical Nephrectomy4. Radiofrequency ablationε | - May list on active surveillance\*🡪 *Consider biopsy to ensure favorable histology*- *No delay after successful treatment* - May undergo concomitant transplant and surgical treatment, or delayed surgical treatment in appropriately selected cases🡪 *Consider biopsy to ensure favorable histology* |
| **T1b**> 4 cm but ≤ 7 cm, confined to kidney | 1. Partial Nephrectomy2. Radical Nephrectomy | - If tumor is low grade (WHO/ISUP 1 or 2)🡪 *No delay after successful treatment* *-* If tumor is high grade (WHO/ISUP 3 or 4)🡪 *3 year waiting period after successful treatment*- May undergo concomitant transplant and surgical treatment🡪 *Requires biopsy to ensure favorable histology* |
| **T2**- T2a: > 7 cm but ≤ 10 cm, confined to the kidney- T2b: > 10 cm, confined to kidney | 1. Radical Nephrectomy | - If tumor is low grade (WHO/ISUP 1 or 2)🡪 *No delay after successful treatment* -If tumor is high grade (WHO/ISUP 3 or 4)🡪 *3 year waiting period after successful treatment*  |
| **T3**- Invasion beyond the kidney but not beyond Gerota’s**T4**- Invasion beyond Gerota’s or into contiguous adrenal gland | 1. Radical nephrectomy with resection of tumor thrombus (T3) / resection of adjacent invaded organs (T4) | - Waiting period after successful treatment to be determined based on careful decision-making in conjunction with the treating urologist- If node positive disease, not a candidate for transplant |

**Note 1:** Histology is a key considerationin the prognosis of RCCs. The most common histologies include clear cell (70%), papillary (10-15%), and chromophobe (5%)*.* Rare and/or aggressive sub-types (eg. medullary, rhabdoid, sarcomatoid, collecting duct) are not covered by these guidelines and should be carefully discussed with the treating urologist.

**Note 2: \***Active surveillance for a small renal mass is acceptable for a patient with CKD IV/V in order to delay the initiation of dialysis and should not preclude waitlisting for transplantation. If the patient undergoes transplant, a concomitant radical nephrectomy would be indicated or could be done later in a staged fashion.

**Note 3:** εAblative therapy (RFA or Cryotherapy) is considered an acceptable treatment modality for small renal masses ≤ 3 cm in patients with comorbidities, high surgical risk, and those wishing to avoid surgery. However, using this treatment modality there is an increased need for re-treatment (2-10%) and risk of progression (13%), which would require subsequent surgical treatment. As such, we do not recommend ablative therapy for treatment of small renal masses prior to transplantation. In addition, comorbidities precluding surgical treatment for a small renal mass would also likely preclude renal transplantation. However, if a patient has already undergone ablative therapy, then listing may proceed provided that there is documentation of pre-treatment biopsy and no evidence of viable tumor on follow-up scan at 3-6 months.

**Bladder Cancer (Urothelial)**

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| **Risk Group** | **Tumor Criteria** | **Acceptable Treatment** | **When to List/ Transplant** |
| **Low** | Ta *and*Low grade *and*Solitary < 3 cmPNLMP\* | 1. TURε +/- intravesical chemotherapy (single dose) | - No delay after successful treatment🡪 *Requires cystoscopy at 3 months to assess for recurrence; no delay if small low-grade recurrence* |
| **Intermediate** **or** **High** | Any recurrent *or*Any multifocal *or*Any > 3 cm *or*Any T1 *or*Any CIS *or*Any high grade | 1. Low grade: TUR +/- intravesical chemotherapy2. High grade/CIS: TUR +/- BCGψ +/- intravesical chemotherapy (for BCG-unresponsive or BCG-intolerant patients)3. Any grade: Radical cystectomy with urinary diversion |  - 2 year waiting period after last positive biopsy/resection  |
| **Muscle-Invasive** | ≥ T2 | 1. Radical cystectomy with urinary diversion +/- adjuvant or neoadjuvant chemotherapy or immunotherapy | - Minimum 2 year waiting period after successful treatment with careful decision-making involving treating urologist-Negative urine cytology and urethral wash are recommended prior to listing |

\*PUNLMP = papillary urothelial neoplasm of low malignant potential

εTUR = trans-urethral resection

ψBCG = Baceillus Calmette-Guerin

**RELATED POLICIES / PROCEDURES:**

**DEFINITIONS:**

**REFERENCES AND SOURCES OF EVIDENCE:**

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**KEY WORDS:**

Adenocarcinoma of the Prostate

Renal Cell Carcinoma

Urothelial Carcinoma of the Bladder