# Oncology Clinical Pathways
## Bladder Cancer

February 2023, V1.2023

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# Bladder Cancer – Presumptive Conditions

VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Vietnam Veterans – Agent Orange Exposure or Specified Locations

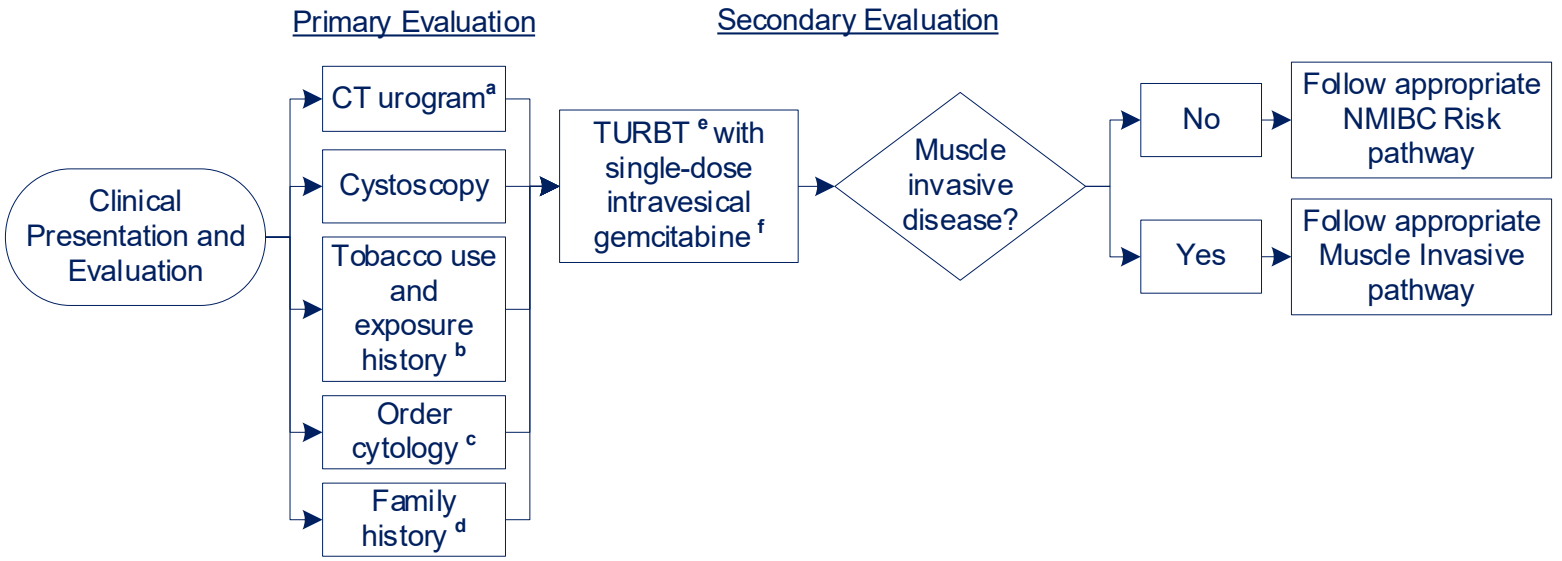
- Bladder cancer

Atomic Veterans – Exposure to Ionizing Radiation

- Cancer of the urinary tract

For more information, please visit U.S. Department of Veterans Affairs - Presumptive Disability Benefits (va.gov)

# Bladder Cancer – Clinical Presentation and Evaluation




Clinical trial(s) always considered on pathway.

[a] In patients unable to receive IV contrast, order alternative upper tract imaging.

[b] **Exposure** Agent Orange, burn pits, and other occupational/environmental toxins.

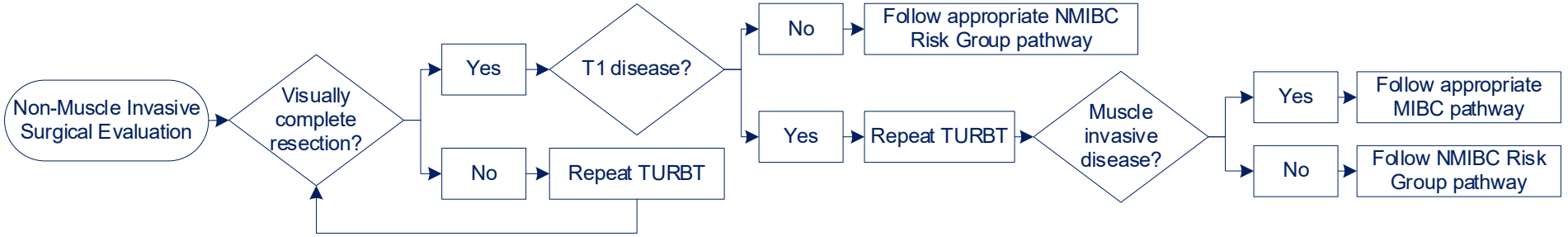
[c] **Cytology** order if results would change clinical management

[d] **Family History** family or personal malignancy history, suspicion for Lynch syndrome; age under 60 years

[e] **TURBT Transurethral Resection of Bladder Tumor (TURBT) with Exam Under Anesthesia (EUA)** and blue-light cystoscopy if clinically appropriate

[f] **Intravesical gemcitabine** for known or presumed low grade

# Bladder Cancer – Non-Muscle Invasive Surgical Evaluation

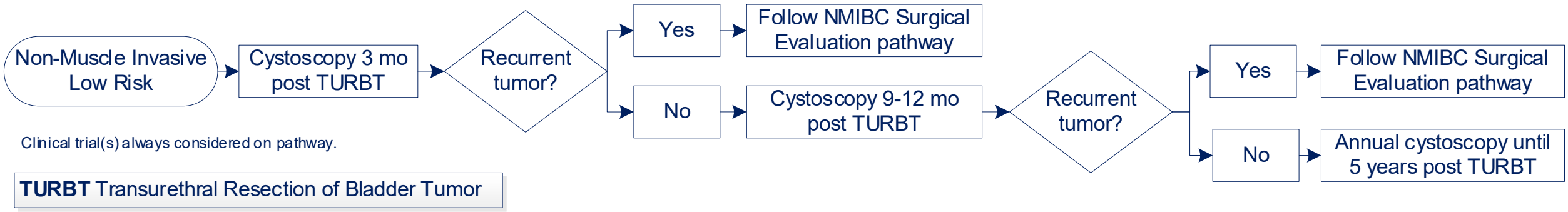



| American Urological Association Non-Muscle Invasive Risk Stratification | | |
|---|---|---|
| *Low Risk* | *Intermediate Risk* | *High Risk* |
| • Papillary urothelial neoplasm of low malignant potential<br><br>*Or*<br><br>• Low grade urothelial carcinoma<br>▪ Ta and<br>▪ ≤3 cm and<br>▪ Solitary | • Low grade urothelial carcinoma<br>▪ T1 or<br>▪ >3 cm or<br>▪ Multifocal or<br>▪ Recurrence within 1 year<br><br>*Or*<br><br>• High grade urothelial carcinoma<br>▪ Ta and<br>▪ <3 cm and<br>▪ Solitary | • High grade urothelial carcinoma<br>▪ CIS or<br>▪ T1 or<br>▪ >3 cm or<br>▪ Multifocal<br><br>*Or*<br><br>• Very high risk features (any)<br>▪ BCG unresponsive<br>▪ Variant histologies [a]<br>▪ Lymphovascular invasion<br>▪ Prostatic urethral involvement |

[a] **Variant histologies** includes micropapillary, nested, plasmacytoid, neuroendrocrine, sarcomatoid, squamous or glandular predominant.

**TURBT** Transurethral Resection of Bladder Tumor

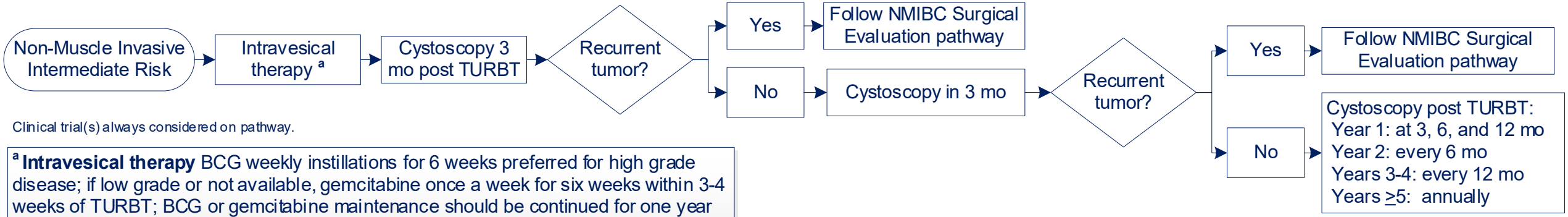
# Bladder Cancer – Non-Muscle Invasive Low Risk




Clinical trial(s) always considered on pathway.

**TURBT** Transurethral Resection of Bladder Tumor

# Bladder Cancer – Non-Muscle Invasive Intermediate Risk

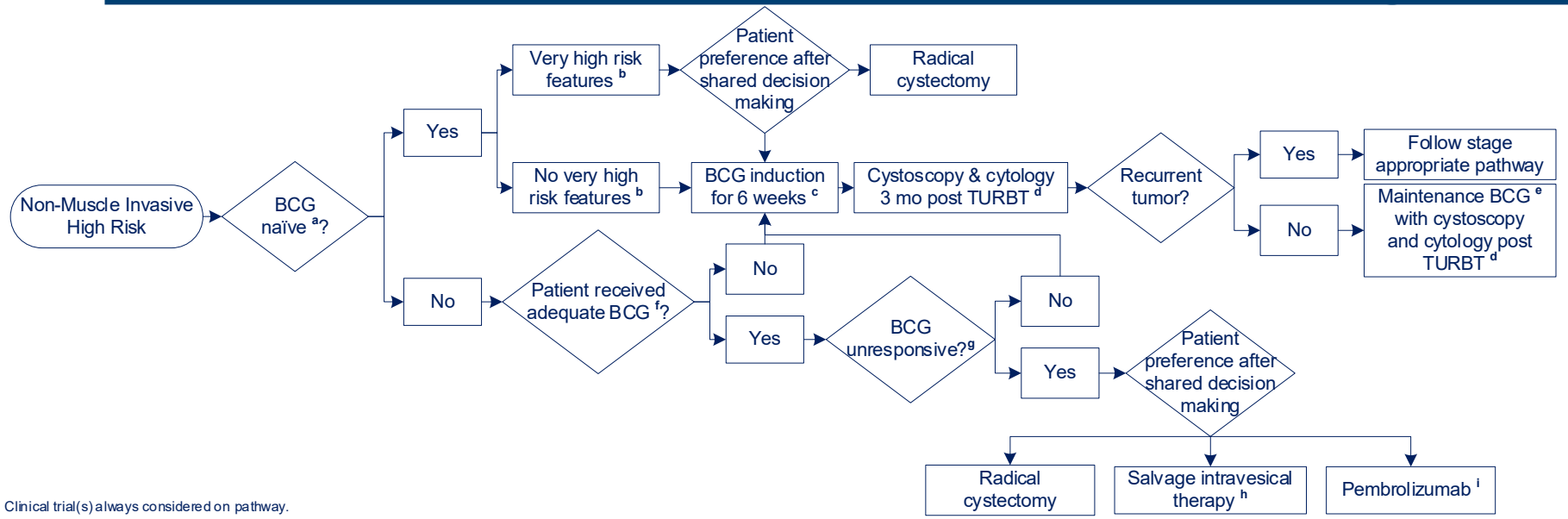



Clinical trial(s) always considered on pathway.

[a] **Intravesical therapy** BCG weekly instillations for 6 weeks preferred for high grade disease; if low grade or not available, gemcitabine once a week for six weeks within 3-4 weeks of TURBT; BCG or gemcitabine maintenance should be continued for one year

**TURBT** Transurethral Resection of Bladder Tumor

# Bladder Cancer – Non-Muscle Invasive High Risk




Clinical trial(s) always considered on pathway.

[a] **BCG naïve** BCG non-exposed or greater than one year since last BCG

[b] **Very high risk features** include BCG unresponsive, variant histologies, lymphovascular invasion, or prostatic urethral invasion

[c] **BCG Induction** only one repeat induction BCG course

[d] **Cystoscopy and Cytology Post TURBT** surveillance schedule: years 1-2: every 3 months; years 3-4: every 6 months; years ≥5: annually

[e] **BCG maintenance** 3 week instillations at 3, 6, 12, 18, 24, 30, and 36 months (3 years) after start of induction BCG

[f] **Adequate BCG** ≥5 induction doses and ≥2 maintenance doses

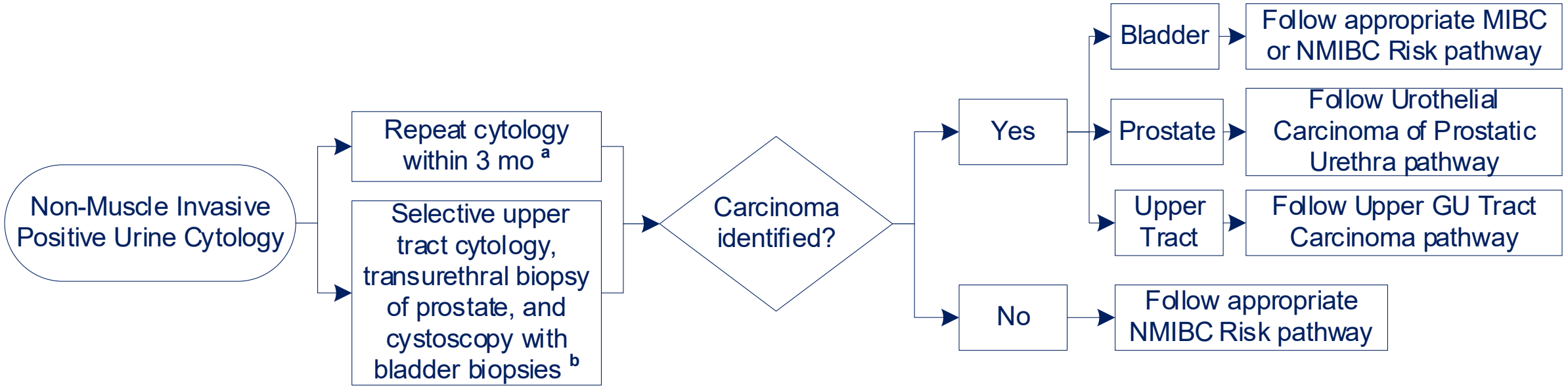
[g] **BCG unresponsive** Persistent high-grade disease or recurrence within 6 months of receiving at least 2 courses of intravesical BCG (at least 5 of 6 induction and at least 2 of 3 maintenance doses of BCG)

[h] **Salvage intravesical therapy** gemcitabine and docetaxel preferred

[i] **Pembrolizumab** indicated for treatment of patients with BCG-unresponsive, high-risk NMIBC with Tis tumors who are ineligible for or have elected not to undergo cystectomy

**TURBT** Transurethral Resection of Bladder Tumor

# Bladder Cancer – Non-Muscle Invasive Positive Urine Cytology

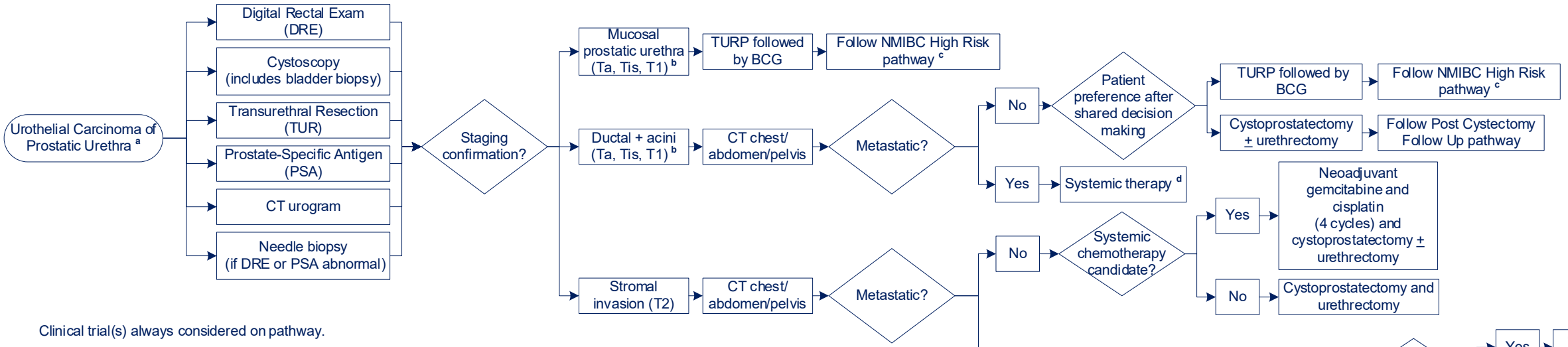



Clinical trial(s) always considered on pathway.

[a] **Cytology** Review clinical history with cytopathologist

[b] **Cystoscopy** Use enhanced technology if available

# Bladder Cancer – Urothelial Carcinoma of Prostatic Urethra




Clinical trial(s) always considered on pathway.

[a] **Urothelial Carcinoma of Prostatic Urethra** solely isolated prostatic urethra involvement

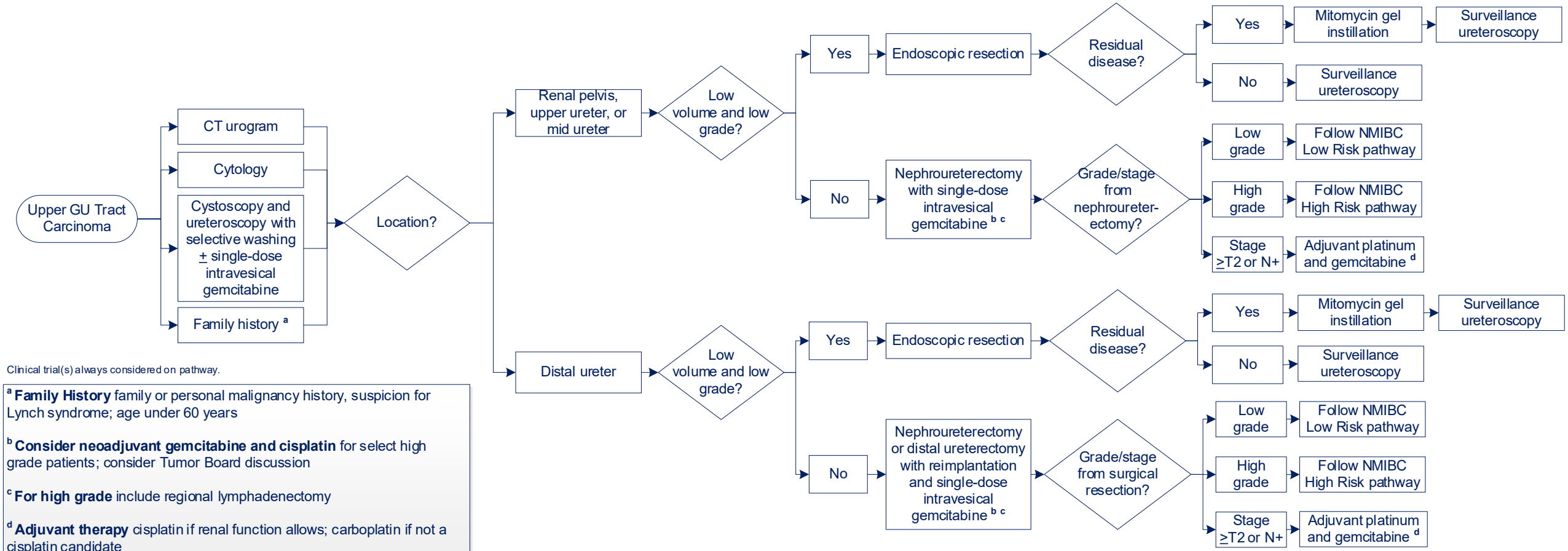
[b] **Ta, Tis, T1** based on TUR, confirm subepithelial involvement

[c] **Cystoscopy and Cytology Post TURBT** 6 months; surveillance schedule: years 1-2: every 3 months; years 3-4: every 6 months; years ≥5: annually

[d] **If cisplatin eligible**, prescribe gemcitabine and cisplatin followed by avelumab maintenance therapy; **if cisplatin ineligible**, prescribe gemcitabine and carboplatin followed by avelumab maintenance therapy

[e] **If only prior pelvic metastatic disease**, reimage with PET to ensure no metastatic disease prior to proceeding with surgery

# Bladder Cancer – Upper GU Tract Carcinoma




Clinical trial(s) always considered on pathway.

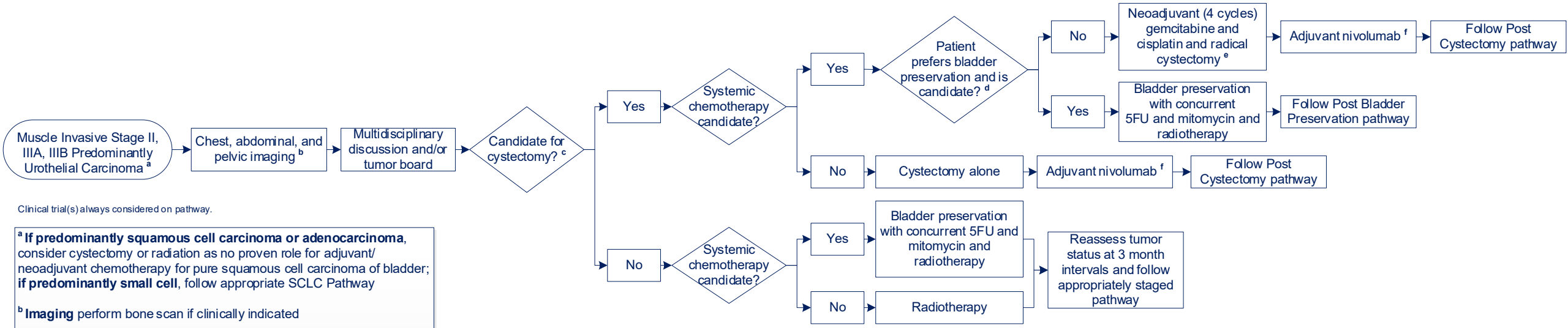
[a] **Family History** family or personal malignancy history, suspicion for Lynch syndrome; age under 60 years

[b] **Consider neoadjuvant gemcitabine and cisplatin** for select high grade patients; consider Tumor Board discussion

[c] **For high grade** include regional lymphadenectomy

[d] **Adjuvant therapy** cisplatin if renal function allows; carboplatin if not a cisplatin candidate

# Bladder Cancer – Muscle Invasive Stage II, IIIA, IIIB Predominantly Urothelial Carcinoma




Clinical trial(s) always considered on pathway.

[a] **If predominantly squamous cell carcinoma or adenocarcinoma**, consider cystectomy or radiation as no proven role for adjuvant/ neoadjuvant chemotherapy for pure squamous cell carcinoma of bladder; **if predominantly small cell**, follow appropriate SCLC Pathway

[b] **Imaging** perform bone scan if clinically indicated

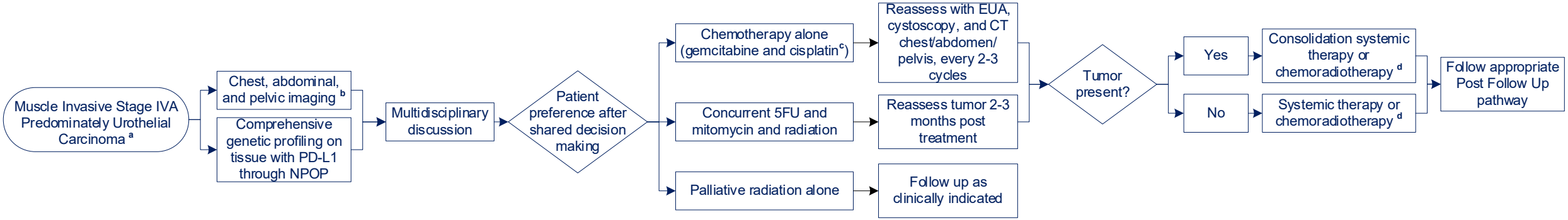
[c] **Patients with clinical node positive disease** should have resolution of adenopathy post chemo to become eligible for cystectomy

[d] **Candidate** Avoid bladder preservation in patients with hydronephrosis and extensive or multifocal carcinoma in situ

[e] **Consider Platinum-based chemotherapy** (4 cycles) if not given as neoadjuvant

[f] **Adjuvant nivolumab** for patients at high risk for recurrent MIBC following radical cystectomy with negative margins regardless of PD-L1 status

# Bladder Cancer – Muscle Invasive Stage IVA Predominately Urothelial Carcinoma




Clinical trial(s) always considered on pathway.

[a] **If predominantly squamous cell carcinoma or adenocarcinoma**, consider cystectomy or radiation as no proven role for adjuvant/neoadjuvant chemotherapy for pure squamous cell carcinoma of bladder; **if predominantly small cell**, follow appropriate SCLC Pathway

[b] **Imaging** perform bone scan if clinically indicated

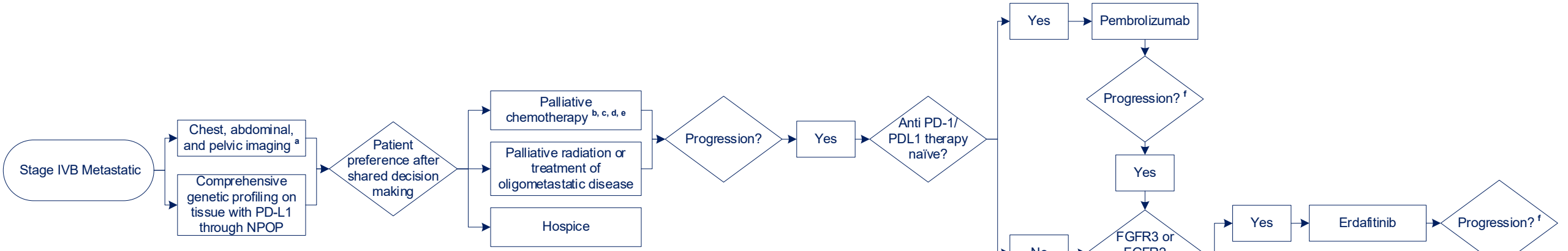
[c] **If patient not a cisplatin candidate,** recommend carboplatin

[d] **If no previous** radiation therapy and/or cystectomy

**EUA** Exam Under Anesthesia

**NPOP** National Precision Oncology Program

# Bladder Cancer – Stage IVB Metastatic




Clinical trial(s) always considered on pathway.

[a] **Imaging** perform bone scan if clinically indicated, imaging of Central Nervous System (CNS) as clinically indicated

[b] **If cisplatin eligible**, prescribe gemcitabine and cisplatin followed by avelumab maintenance therapy; **if cisplatin ineligible**, prescribe gemcitabine and carboplatin followed by avelumab maintenance therapy

[c] If **patient progresses on initial platinum-based chemotherapy** prior to avelumab, recommend pembrolizumab

[d] If **not a platinum-based chemotherapy candidate**, recommend pembrolizumab

[e] **Consider** platinum-based chemotherapy if not previously given

[f] If **patient not a candidate for these therapies,** consider hospice and/or palliative radiation

**NPOP** National Precision Oncology Program

**Criteria for Use**

**Erdafitinib:** exclude patients with retinal/corneal abnormality at baseline or serum phosphate greater than upper limits of normal at baseline; perform ophthalmological exams at baseline and then monthly for the first 4 months of therapy, then every 3 months thereafter

**Enfortumab Vedotin:** exclude patients with preexisting neuropathy ≥ Grade 2, baseline ocular disorders, or uncontrolled diabetes at baseline

# Bladder Cancer – Post Cystectomy Follow Up

Post Cystectomy Follow Up

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 5-10 | Year >10 |
|---|---|---|---|---|---|---|---|
| ***Imaging NMIBC*** | CT urogram at 3 &12 mo | Annual CT urogram | | | | Annual renal ultrasound | As clinically indicated |
| ***Imaging MIBC*** | CT chest and CT urogram every 3-6 mo | | Annual CT chest/abdomen/pelvis | | | Annual renal ultrasound | As clinically indicated |
| **Blood Tests** | CMP &CBC every 6 mo | Annual CMP and $B_{12}$ levels | | | | Annual $B_{12}$ levels | |
| ***Urine Tests*** | Urine cytology every 6-12 mo; consider urethral wash every 6-12 mo | Urine cytology as clinically indicated<br>Urethral wash cytology as clinically indicated | | | | | |

# Bladder Cancer – Muscle Invasive Post Bladder Preservation Follow Up

Muscle Invasive Post Bladder Preservation Follow Up

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 5-10 | Year >10 |
|---|---|---|---|---|---|---|---|
| ***Cystoscopy*** | Every 3 mo | | Every 6 mo | | Annually | | As clinically indicated |
| ***Imaging*** | CT chest and CT urogram every 3-6 mo | | Annual CT chest/abdomen/pelvis | | | As clinically indicated | |
| **Blood Tests** | CMP & CBC every 6 mo | Annual CMP | | | | | |
| ***Urine Tests*** | Urine cytology every 6-12 mo | | Urine cytology as clinically indicated | | | | |

# Questions?

Contact VHAOncologyPathways@va.gov