UPPER URINARY TRACT UROTHELIAL CARCINOMA

General Overview

- UC arising in pyelocaliceal cavities or ureter
- Mostly men, age 70-90, often found upon staging/follow-up of lower urinary tract cancer
- Risk factors: urinary tract cancer, smoking, Lynch syndrome (5%)
- Often multifocal (10-20%) or synchronous UTUC Tis (10-35%)
- Histology: almost always urothelial

Diagnostic work up and staging

- Familial/personal anamnesis for Lynch-associated cancer (colorectal, endometrium, small bowel, UTUC)
- CT urography
- Flexible cystoscopy + ureteroscopy with selective cytology, biopsies, tumor mapping
- CT Tx-abdomen
- Test microsatellite instability on resection specimen or biopsy if no resection, especially if >60yrs or (familial) Lynch-assiocated cancer. If present: germline screening

Muscle-invasiveness is often underestimated with clinical staging, but the majority of patients (50-70%) presents with muscle-invasive disease. UTUC are categorized as h (probable pT2) based on a combination of factors:

- G3 (biopsy and/or cytology)
- Non-urothelial histology
- cT3-4 on CT
- Low-grade UCC associated with (after expert discussion):
    - Hydronephrosis
    - ≥2cm
    - Multifocality

Primary Tumor (T)	Regional Lymph Nodes (N)	Distant Metastasis (M)
Tx: Primary tumor cannot be assessed **T0**: No evidence of primary tumor **Ta**: Noninvasive papillary carcinoma **Tis**: Carcinoma in situ **T1**: Invasion subepithelial connective tissue **T2**: Invasion muscularis **T3**: (rena pelvis) Invasion beyond muscularis into peripelvic fat or renal parenchyma. (urether) Invasion beyond muscularis into perinephric fat **T4**: Tumor invades adjacent organs or through the kidney into perinephric fat	**Nx**: LN cannot be assessed **N0**: No regional LN **N1**: Single regional LN < 2 cm in the greatest dimension **N2**: Single regional LN > 2cm, or multiple LN Reg LN: hilar and retroperitoneal and, for mid- and distal ureter, pelvic. Laterality has no influence.	**M0**: No distant M+ **M1**: Distant M+

Prognostic stage group	TNM	5y survival (%)
0a	Ta N0 M0	94
0is	Tis N0 M0	94
I	T1 N0 M0	91
II	T2 N0 M0	75
III	T3 N0 M0	54
IV	T4 Nx, N0 M0	12
	Any T, N1, M0	
	Any T, N2, M0	
	Any T, any N, M1	

Treatment

Low risk localized UTUC

- Laser ablation
- Resection, kidney-sparing if possible (several techniques exist)
- Chemo ablation or adjuvant instillation to discuss

High risk localized UTUC

Resection:

- Radical nephro-ureterectomy (RNU) + lymphadenectomy
  - kidney-sparing surgery if nephrectomy is unacceptable (especially distal UTUC)
- Single post-operative bladder instillation with chemotherapy

(Neo-)adjuvant treatment:

- If pT2 or cT3-4 and cisplatinum-eligible: neo-adjuvant
  - 4x cisplatinum-gemcitabine (consider split-dose cisplatinum if eGFR 45-55ml/min)
  - Alternative in very fit pts: 6x dd-MVAC
  - Same if very high risk and pt expected to become cisplatinum-ineligible after RNU
- If cTa-2 or cis-ineligible: RNU followed by adjuvant if pT2-4 and/or pN+
  - Cisplatinum-eligible: 4x cis-gem (split-dose if eGFR 45-55 ml/min) or 6x dd-MVAC
  - Carboplatinum-eligible: 4x carbo-gem
- If platinum-ineligible, pT3-4 and/or N+ and TPS ≥1%: consider 12x nivolumab

Clinical N+ UTUC

- N1: same as localized, with neo-adjuvant chemotherapy if possible
- N2: treat like metastatic, consider RNU + lymphadenectomy if downstaging.

Metastatic UTUC

- Same as MIBC

Follow-up after treatment with curative intent

- Via urologist, for frequent cystoscopic follow up
- If adjuvant treatment: refer for cystoscopy at 3mo post-op, avoid nadir
- High risk UTUC: CT Tx-abdomen every 6mo year 1-2, every 12mo year 3-5