

Appendix V

Primary Studies for Adjuvant Systemic Therapy for Patients with UTUC.				
Author, Year Sample size Study Design	Key Inclusion Criteria	Interventions Comparisons	Oncologic Results (95% CI, unless otherwise indicated)	Harms (95% CI, unless otherwise indicated)
<p>Bajorin,¹³⁸ 2021 709 (149 with UTUC) RCT (CheckMate 274)</p> <p>Risk of Bias Moderate</p>	<p>HR of recurrence (pathologic stage [p or yp] T3-4a, or N+), negative surgical margins, and disease- free within 4 weeks before randomization Allowed cisplatin- based NAC</p>	<p>A. Nivolumab</p> <p>B. NU alone: radical NU, placebo</p>	<p>Nivolumab vs. placebo <i>overall sample (bladder UC & UTUC)</i></p> <p>DFS 6 months: 74.9% vs. 60.3% Median, months: 20.8 vs.10.8 HR 0.70 (98.22% CI 0.55 to 0.90), p<0.001 <i>by initial tumor origin</i> Urinary bladder: HR 0.62 (0.49-0.78) Renal pelvis: HR 1.23 (0.67-2.23) Ureter: HR 1.56 (0.70- 3.48)</p> <p>Survival free from recurrence outside the urothelial tract 6 months: 77.0% vs. 62.7% Median, months: 22.9 vs. 13.7 HR 0.72 (0.59 to 0.89)</p> <p>Distant MFS 6 months: 82.5% vs. 69.8% Median, months: 40.5 vs. 29.5 HR 0.75 (0.59 to 0.94)</p>	<p><u>Nivolumab vs. placebo overall sample (bladder UC & UTUC)</u></p> <p>Adverse Events any: 98.9% vs. 95.4% grade ≥3: 42.7% vs. 7.2% Discontinuation due to treatment-related AE: 12.8% vs. 2.0%</p> <p><u>Nivolumab group</u> most common treatment- related AE <i>any grade</i> pruritus: 23.1% fatigue: 17.4% diarrhea: 16.8% <i>grade ≥3</i> increased serum lipase: 5.1% increased amylase level: 3.7% diarrhea: 0.9% colitis: 0.9% pneumonitis: 0.9%</p> <p>Treatment-related deaths pneumonitis: n=2 bowel perforation: n=1</p>
<p>Bellmunt,¹³⁷ 2021 809 (54 with UTUC)</p> <p>RCT (IMvigor010)</p> <p>Risk of Bias Moderate</p>	<p>muscle-invasive, pathologic stage (p or yp stage) T2-4a or N+ tumors</p>	<p>A. Atezolizumab</p> <p>B. NU alone: NU with LND, observation</p>	<p>Atezolizumab vs. observation</p> <p>DFS <i>Overall sample (bladder UC & UTUC)</i> 18 months: 51% vs. 49% Median DFS, months: 19.4 vs.16.6 stratified HR 0.89 (0.74- 1.08), log-rank p=0.24</p> <p><i>UTUC patients</i> Median DFS, months: 14.2 vs. 28.1 HR 1.25 (0.57-2.74)</p>	<p><u>Atezolizumab vs. observation overall sample (bladder UC & UTUC)</u></p> <p>AE, any cause Any grade: 94% vs. 79% Grade 3-4: 37% vs. 20% Serious AE: 31% vs. 18% immune mediated AE: 46% vs. 8%</p> <p><u>Atezolizumab group</u> treatment-related AEs Any grade: 71% Grade 3-4: 16% Serious AE: 11% AE leading to discontinuation: 16% AE leading to dose interruption: 33%</p> <p>Treatment related death</p> <p>Multisystem organ failure 1</p>