Diagnostic workup
- Patient evaluated by multi-disciplinary team
- Patient is candidate for systemic therapy
- Cisplatin-eligibility evaluated*
- Disease status confirmed: Advanced/mUC

Cisplatin-eligible
- Cisplatin-based chemotherapy
  - No disease progression
    - Avelumab maintenance
  - Disease progression
    - Pembrolizumab + enfortumab vedotin†

Cisplatin-ineligible
- Carboplatin-based chemotherapy
  - Disease progression
    - Pembrolizumab
    - Avelumab
    - Nivolumab
  - No disease progression
    - Pembrolizumab

Cisplatin- and carboplatin-ineligible
- Pembrolizumab†
- Pembrolizumab + enfortumab vedotin†

Disease progression on pembrolizumab monotherapy
- Clinical trial enrollment
- Guidelines-directed subsequent treatment

Disease progression
- Enfortumab vedotin
* Cisplatin eligibility criteria: Creatine clearance of ≥ 50-60ml/min calculated with the Cockgroft Gault formula, ECOG PS <2, no CTCAE grade ≥2 neuropathy, no heart failure, and no CTCAE grade ≥2 hearing loss
† Accelerated approvals contingent on confirmatory trials at the time of guideline publication