***Patient1***

***Question1（The following is a replacement for Q1）：***

*I have detailed case information of a urothelial carcinoma patient, including his chief complaints, medical history, examination results, pathology findings, and treatment course. Please act as a professional multidisciplinary team (MDT) specializing in urological oncology, review the patient's information, and provide: A list of the current preferred treatment measures along with the reasons for each recommendation. A list of measures to avoid along with the reasons for each recommendation*

**(The following is a replacement for prompts1)+<Patient information1>**

***Anwser1（The following is a replacement for A1）***

### Preferred Treatment Measures

**Evaluation by Gynecologic Oncology:**

**Reason:** Given the vaginal bleeding and findings of abnormal metabolism in the cervix and anterior vaginal wall, assessment by a gynecologic oncologist is crucial to rule out concurrent primary gynecological malignancies or metastasis from the urothelial carcinoma.

**Systemic Therapy (Chemotherapy or Immunotherapy):**

**Reason:** Considering the history of high-grade invasive transitional cell carcinoma and the current evidence of potentially metastatic disease, systemic therapy might be needed to manage microscopic metastatic disease or overt metastases that are likely given the multiple sites of increased FDG metabolism.

**Targeted Radiation Therapy:**

**Reason:** For local control of any identified metastatic sites, particularly if they are symptomatic or at risk of causing complications (like the soft tissue masses and enlarged lymph nodes).

**Detailed Pathologic Review and Molecular Testing:**

**Reason:** A review of both the previous and current biopsies and performing molecular profiling to identify potential therapeutic targets and prognostic indicators.

**Palliative Care Consultation:**

**Reason:** To address symptoms and improve quality of life, considering the extensive disease and its impact on the patient's health.

### Measures to Avoid

**Avoid Delay in Treatment:**

**Reason:** Given the aggressive nature of recurrent urothelial carcinoma and evidence of widespread disease, prompt intervention is necessary to manage symptoms and disease progression.

**Avoid Non-Integrative Therapies:**

**Reason:** Unproven or alternative treatments could delay effective therapy and potentially worsen outcomes.

**Avoid Invasive Surgical Interventions:**

**Reason:** Without clear evidence of localized disease amenable to surgical resection, extensive surgeries might not provide benefit and could lead to significant morbidity given the current disease spread and patient’s past surgical history.

***Question2（The following is a replacement for Q2）：****prompt2+*

*1.What is the chemotherapy regimen?*

*2.How should vaginal bleeding be managed?*

*3.What is the most necessary examination for this patient at present? (Provide only one)*

*4.What surgery should be avoided, and why?*

### Chemotherapy Regimen

Given the patient's history of recurrent, high-grade urothelial carcinoma, a platinum-based chemotherapy regimen could be considered. A common choice would be:

* **Gemcitabine and Cisplatin (GC):** This combination is standard for treating advanced urothelial carcinoma. It typically involves Gemcitabine administered on Days 1, 8, and 15, and Cisplatin on Day 1 of a 28-day cycle.

### Management of Vaginal Bleeding

* **Local Measures and Symptomatic Treatment:** Including use of topical estrogens if atrophy is present, and tranexamic acid for bleeding control.
* **Hormonal Therapy:** If bleeding is related to hormonal imbalances or endometrial changes.
* **Gynecologic Evaluation:** Important to rule out other causes such as a new primary malignancy or metastatic disease, which might require specific interventions like targeted radiation or surgical procedures if localized and amenable.

### Most Necessary Examination

* **Biopsy of Vaginal/Cervical Lesions:** Given the patient’s history and current symptoms, a targeted biopsy of areas showing abnormal FDG uptake in the cervix and anterior vaginal wall is crucial. This will help confirm the diagnosis and guide specific treatment, particularly to differentiate between a new primary cancer and metastasis from the bladder cancer.

### Surgery to Avoid and Why

* **Avoid Radical Gynecological Surgery (e.g., Hysterectomy):** Unless a distinct, treatable gynecological malignancy is confirmed that could benefit from such an intervention. Radical surgery in this scenario may not significantly improve outcomes due to the metastatic nature of her condition and could significantly affect her quality of life by causing complications or delaying other necessary treatments like chemotherapy or radiation.

***Q3:****Are there any suitable clinical trials for this patient? Always include the NCT (ClinicalTrials.gov registration number) or PubMed ID, and indicate the level of evidence and clinical significance whenever possible.（The following is a replacement for prompt3）***EV-302 Trial** (NCT04223856): This Phase 3 study investigates the combination of enfortumab vedotin and pembrolizumab in patients with locally advanced or metastatic urothelial carcinoma who are ineligible for cisplatin-containing chemotherapy. The trial has shown promising results with a high percentage of patients experiencing significant tumor reduction​ ([Comprehensive Cancer Information](https://www.cancer.gov/news-events/cancer-currents-blog/2023/bladder-cancer-padcev-keytruda-doubles-survival" \t "_blank))​.

**CheckMate-901 Trial** (NCT03036098): This Phase 3 trial is evaluating nivolumab in combination with chemotherapy (cisplatin and gemcitabine) versus chemotherapy alone as a first-line treatment for patients with metastatic urothelial cancer. This trial might be an option if the patient has not previously received an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent​ ([Comprehensive Cancer Information](https://www.cancer.gov/news-events/cancer-currents-blog/2023/bladder-cancer-padcev-keytruda-doubles-survival" \t "_blank))​.

**DAD Trial** (NCT04724018): In this Phase 1 study, the combination of double antibody-drug conjugates sacituzumab govitecan and enfortumab vedotin is being tested in patients with metastatic urothelial carcinoma who have progressed on platinum-based chemotherapy and immunotherapy or are cisplatin ineligible. This could be considered if the patient has had prior lines of systemic therapy​ ([Targeted Oncology](https://www.targetedonc.com/view/updated-trials-at-esmo-reveal-new-frontline-combo-in-urothelial-carcinoma" \t "_blank))​.

***Patient2***

***Q1:****Prompts1+<Patient information2>*

***A1:***

### Preferred Treatment Measures

**Further Diagnostic Testing**:

**Repeat CT Urography**: Given the postoperative changes and mild dilatation of the ureters and renal pelvis, a repeat CT Urography is recommended to assess for any progression or new developments that might suggest a recurrence or complications such as strictures or fistulas.

**Cystoscopy with Biopsy**: Essential to visually inspect the ileal neobladder and ureteral-ileal anastomosis sites for any suspicious areas, followed by biopsy to confirm the presence of malignancy or other pathology.

**Management of Hematuria**:

**Hyperhydration**: To help flush the urinary system and potentially clear minor bleeding.

**Urine Alkalinization**: If uric acid or cystine stones are suspected contributors to hematuria.

**Pain Management**:

**Analgesics**: Appropriate pain management should be considered to handle intermittent flank pain, tailored to the intensity and frequency of the pain.

**Surveillance**:

**Regular Follow-Ups**: Continued surveillance through routine follow-up appointments for physical exams, urine tests, and imaging as deemed necessary by the progression and findings.

**Consultation with Multidisciplinary Team (MDT)**:

**Oncology, Urology, and Radiology Consultation**: Given the complexity of the patient’s history and recent findings, an MDT approach is essential for comprehensive care.

### Measures to Avoid

**Avoid Delays in Diagnostic Tests**:

Given the history of high-grade carcinoma and current symptoms indicative of possible recurrence, prompt diagnostic testing is crucial to avoid progression or complications.

**Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**:

These should be used cautiously, if at all, considering their potential to worsen renal function, especially if the patient's renal function is compromised.

**Avoid Invasive Procedures Without Prior Diagnostic Clarity**:

Any invasive procedures should be deferred until there is a clear diagnostic picture to avoid unnecessary complications and manage resources effectively.

**Avoid Routine Use of Antibiotics**:

Unless there is clear evidence of infection, routine use of antibiotics should be avoided to prevent antibiotic resistance and protect the patient’s microbiome.

### Reasons for Recommendations

* **Diagnostic Testing**: Essential to confirm the presence or absence of recurrence or complications, guiding further treatment.
* **Pain Management and Hyperhydration**: Aim to improve quality of life and manage symptoms effectively.
* **Consultation with MDT**: Ensures all potential complications and avenues for treatment are considered, providing a holistic approach to care.
* **Avoiding Certain Medications and Procedures**: Minimizes the risk of adverse effects and unnecessary interventions in a potentially complex clinical situation.

***Q2:****prompt2+*

*1.Which specific area should the CT urography primarily target?*

*2.Is there an indication for chemotherapy for the patient?*

*3.Is there an indication for surgery for the patient?*

*4.Is there an indication for radiotherapy for the patient?*

### Specific Area for CT Urography

The CT urography should primarily target:

* **Ileal Neobladder and Ureteral-Ileal Anastomosis Sites**: This area should be closely examined due to the patient's history of uneven thickening and enhancement in previous imaging studies, which could indicate potential complications such as strictures, recurrences, or anastomotic leaks.
* **Renal Pelvis and Ureters**: Given the mild dilation mentioned in the imaging studies, these areas should also be examined for signs of obstruction or upper urinary tract involvement.

### Indication for Chemotherapy

Currently, there might not be a direct indication for chemotherapy unless there is a confirmed diagnosis of recurrent or metastatic cancer. The detection of atypical cancer cells in urine cytology suggests a possibility of recurrence, but this needs to be confirmed with more definitive tissue diagnosis via biopsy before considering systemic treatment options like chemotherapy. If confirmed, chemotherapy might be considered depending on the stage and extent of disease.

### Indication for Surgery

Surgery might be indicated if there is:

* **Evidence of Recurrent Tumor at the Anastomosis Site**: Surgical intervention might be necessary to resect any recurrent tumor if it's localized and deemed resectable.
* **Structural Complications**: Such as strictures or fistulas at the anastomosis sites that are causing symptoms or affecting renal function.

### Indication for Radiotherapy

Radiotherapy is generally not a standard approach for the initial management of urothelial carcinoma post-cystectomy unless there is:

* **Pelvic Recurrence**: Radiotherapy might be considered if there is a localized recurrence where resection is incomplete or not possible, and the recurrence is confined to the pelvis.
* **Symptomatic Relief**: In cases of pain due to local disease, radiotherapy can be used for palliation.

*Q3*:*prompt3*

**Disitamab Vedotin Trial**: This phase 2 trial is evaluating the efficacy and safety of Disitamab Vedotin, alone or in combination with Pembrolizumab, for patients with locally-advanced unresectable or metastatic urothelial carcinoma that expresses HER2. The trial includes patients who have had only 1 or 2 lines of prior systemic treatment, making it potentially suitable for this patient if HER2 expression status is confirmed. This trial is ongoing, and more details can be found under NCT number NCT03507166.

***Patient3***

***Q1:****Prompts3+<Patient information3>* ***A1:***

### Preferred Treatment Measures for Urothelial Carcinoma

Based on the detailed case information you've provided, here are the current preferred treatment measures for the patient, along with the reasons for each recommendation:

**Systemic Therapy with Checkpoint Inhibitors:**

**Rationale:** Given the recurrence and metastatic nature of the urothelial carcinoma post multiple chemotherapy regimens and radiotherapy, systemic therapy with checkpoint inhibitors (e.g., pembrolizumab or atezolizumab) is recommended. These drugs have shown efficacy in advanced urothelial carcinoma, especially in cases where chemotherapy has been exhausted.

**Evidence:** Clinical trials have demonstrated that checkpoint inhibitors can extend survival in patients with advanced urothelial carcinoma, particularly in those who have not responded well to platinum-based chemotherapy.

**Continued Surveillance and Monitoring:**

**Rationale:** Regular follow-up using imaging studies such as CT or PET-CT scans is crucial to monitor the progression of the disease and assess the effectiveness of the current treatment plan.

**Method:** Schedule regular imaging studies every 3-6 months, or more frequently if symptoms suggest disease progression.

**Palliative Care and Symptom Management:**

**Rationale:** Due to the metastatic nature of the cancer and previous extensive treatments, focusing on the patient’s quality of life and symptom relief is essential. Palliative care can manage symptoms such as pain, urinary issues, and general discomfort.

**Components:** Include pain management, nutritional support, and psychological counseling to address the comprehensive needs of the patient.

**Clinical Trial Enrollment:**

**Rationale:** Considering the aggressive and recurrent nature of the cancer, enrolling the patient in clinical trials for new treatments could provide access to novel therapeutic options that are not yet widely available.

**Action:** Consult with research facilities and cancer treatment centers that are conducting trials focusing on advanced urothelial carcinoma.

### Measures to Avoid

**Avoidance of Additional Chemotherapy Regimens Similar to Previous Ones:**

**Reason:** The patient has already undergone multiple cycles of chemotherapy with limited success, indicating potential resistance to these drugs.

**Potential Outcome:** Further similar chemotherapy could increase toxicity without substantial benefit, deteriorating the patient's quality of life.

**Avoidance of Extensive Surgery:**

**Reason:** The extensive metastatic nature of the disease (e.g., involvement of the lungs and lymph nodes) makes curative surgery unlikely and could result in significant morbidity.

**Impact:** Surgical interventions in the context of widespread metastasis may not extend survival significantly and could impair quality of life.

**Avoidance of Aggressive Radiotherapy:**

**Reason:** The patient has already received targeted pelvic lymph node radiotherapy. Additional aggressive radiotherapy might lead to increased side effects such as radiation cystitis or bowel toxicity.

**Consideration:** Use radiotherapy judiciously to manage localized symptoms or for palliative purposes if specific problematic areas emerge.

### Conclusions

This multidisciplinary approach, emphasizing advanced systemic therapies, symptom management, and careful monitoring, aligns with the current understanding and treatment strategies for metastatic urothelial carcinoma. Each recommendation is made with the goal of balancing disease control with maintaining the patient's quality of life.

*Q2:prompt2+*

*1.How should the current hematuria and bladder irritation symptoms in the patient be managed?*

*2.How should the lymph node metastases be treated?*

*3.What chemotherapy regimen should be switched to?*

*4.How should the lung lesions be managed (choose only one treatment method)?*

*5.What surgical procedures should be avoided?*

A2:

### Management of Current Hematuria and Bladder Irritation Symptoms

**Intravesical Therapy:**

**Rationale:** Intravesical instillation of drugs such as hyaluronic acid or chondroitin sulfate can help soothe the bladder lining and reduce irritation symptoms and hematuria caused by cancer or previous treatments.

**Benefits:** These treatments are localized to the bladder and have minimal systemic side effects.

**Symptomatic Treatment:**

**Anticholinergics or Beta-3 agonists:** These can be used to manage symptoms of bladder irritation.

**Pain Management:** Non-steroidal anti-inflammatory drugs (NSAIDs) or opioids, as appropriate, to manage pain associated with irritation.

**Bladder Spasms:** Medications such as oxybutynin can help reduce spasms and discomfort.

### Treatment of Lymph Node Metastases

**Systemic Therapy:**

**Recommendation:** Continue with systemic therapies that target metastatic disease broadly, such as checkpoint inhibitors, which can address both primary tumor sites and metastatic nodes.

**Benefits:** These drugs can shrink metastases or stabilize disease, potentially reducing symptoms and slowing progression.

### Recommendations for Switching Chemotherapy Regimens

**Switch to an Alternative Chemotherapy or a Combination Regimen:**

**Options:** Consider switching to regimens such as MVAC (methotrexate, vinblastine, doxorubicin, cisplatin) if not previously used and if the patient's condition permits, or a combination involving a novel agent from a clinical trial.

**Rationale:** A different mechanism of action may overcome resistance to previous drugs and provide a therapeutic benefit.

### Management of Lung Lesions

**Systemic Therapy Alone:**

**Choice:** Due to the presence of multiple lung nodules and the overall metastatic burden, systemic therapy remains the best option.

**Rationale:** Systemic therapy, particularly newer targeted agents or immunotherapies, can address multiple metastatic sites simultaneously and is less invasive than surgical interventions or localized treatments like radiotherapy, which might be more appropriate for isolated or symptomatic lesions.

### Surgical Procedures to Avoid

**Radical Cystectomy:**

**Reason:** In the context of widespread metastatic disease and previous treatments, radical cystectomy is unlikely to provide curative benefit and can significantly impact the patient’s quality of life.

**Cocerns:** This surgery involves removing the bladder and nearby organs, which is a major operation with significant morbidity and recovery time.

**Major Resections of Lung Tissue:**

**Reason:** Given the metastatic nature of the lung lesions, major resections such as lobectomy or pneumonectomy are generally not advisable as they are unlikely to improve survival in the setting of widespread metastatic disease.

**Outcome:** These surgeries could severely affect pulmonary function and overall health without clear survival benefit.

*Q3*:*prompt3*

A3:  
**Clinical Trial with N-803 + Atezolizumab**

**Description:** This Phase II/III trial is evaluating the combination of N-803, an immunotherapy agent, with atezolizumab in patients who have experienced disease progression after initial response to checkpoint inhibitor therapy.

**Eligibility:** Suitable for patients with locally advanced or metastatic urothelial carcinoma who have progressed on or after standard of care therapies, including checkpoint inhibitors.

**Location:** Various sites in the United States, including the University of Tennessee Medical Center and Oncology Consultants of Houston.

**ClinicalTrials.gov ID:** NCT03022825

**Study of INO-5401 + INO-9012 in Combination with Atezolizumab**

**Description:** This Phase I/IIA trial investigates the safety, immunogenicity, and preliminary clinical efficacy of INO-5401 + INO-9012, delivered by intramuscular injection with electroporation, in combination with atezolizumab.

**Eligibility:** Targets patients with locally advanced unresectable or metastatic/recurrent Urothelial Carcinoma, divided into cohorts of those who have progressed during or following treatment with anti-PD-1/PD-L1 therapy and those who are treatment-naïve and ineligible for cisplatin.

**Location:** Multiple sites, including Scottsdale/Phoenix, AZ, and Jacksonville, FL.

**ClinicalTrials.gov ID:** NCT03493436

***Patient4***

***Q1:****Prompts1+<Patient information4>* ***A1:***

### Preferred Treatment Measures

**Continuation of Systemic Chemotherapy**:

Given the progression after initial chemotherapy, considering a change in the chemotherapy regimen might be beneficial if the patient's performance status allows. Agents like vinflunine or the inclusion of checkpoint inhibitors (e.g., pembrolizumab) could be considered based on recent clinical trials showing efficacy in advanced urothelial carcinoma.

**Targeted Therapy and Immunotherapy**:

Evaluate for eligibility for immunotherapy (e.g., pembrolizumab, atezolizumab) especially since the cancer is high-grade and there is evidence of progression. These agents have shown benefit in terms of response rates and survival in metastatic settings.

Molecular profiling of the tumor to identify potential targets for targeted therapies.

**Palliative Care and Symptom Management**:

Addressing symptoms such as pain, potential bleeding, and other symptomatic concerns through palliative interventions to maintain quality of life.

Consider palliative external beam radiation therapy if there is pain from metastatic sites, particularly bone metastases if confirmed.

**Management of Thromboembolism**:

Continue anticoagulation therapy for the internal jugular vein thrombosis. Monitor for effectiveness and adjust dosage as needed, considering potential interactions with chemotherapy.

**Regular Monitoring and Follow-ups**:

Frequent imaging and clinical evaluations to monitor disease progression, response to treatment, and early detection of complications such as further thrombosis or obstruction.

### Measures to Avoid

**Avoid Nephrotoxic Agents**:

Given the patient's age and presence of kidney cysts, it is advisable to avoid or minimize the use of nephrotoxic agents like high-dose cisplatin, if possible.

**Non-Essential Surgical Interventions**:

Considering the advanced stage of the disease and the presence of metastases, avoid aggressive surgical interventions that are unlikely to offer symptomatic relief or prolong survival but could increase morbidity.

**Limitation on Certain Chemotherapy Regimens**:

Avoid continuing with the same chemotherapy regimen if it has shown to be ineffective in controlling disease progression. Adjusting to a different regimen or introducing new agents based on emerging evidence should be considered.

**Avoid Invasive Diagnostic Procedures**:

Minimize invasive procedures that are not likely to influence the treatment outcome or are high-risk given the patient's current vascular complications.

### Conclusion

This approach balances aggressive management of advanced cancer with considerations for the patient's quality of life and potential side effects. The MDT should continue to adapt the treatment plan based on the patient's response to therapies and evolving clinical evidence in the field of urothelial carcinoma. Regular team discussions and patient consultations are essential to align treatment goals with the patient’s preferences and clinical status.

***Q2:****prompt2+**1.How to manage the patient's lymph node metastasis?*

*2.Can the patient undergo cytoreductive surgery?*

***A2:***

### Clear Conclusion on the Management Plan

**Treatment for Lymph Node Metastasis**:

The best approach for managing the lymph node metastasis in this patient would be **immunotherapy**. Considering the high-grade nature of the urothelial carcinoma and the progression despite chemotherapy, immunotherapy could provide a systemic treatment that targets the cancer more effectively, potentially improving both survival and quality of life. Drugs like pembrolizumab or atezolizumab are recommended, especially if the tumor expresses PD-L1, which is often associated with a better response to these agents.

**Feasibility of Cytoreductive Surgery**:

Given the patient’s age, extensive prior treatments, and the presence of widespread metastatic disease, **cytoreductive surgery is not recommended**. The risks and potential complications of such a major surgery outweigh the benefits in this case, as it is unlikely to significantly extend survival or improve quality of life in the context of metastatic disease.

### Rationale

These recommendations are guided by the need to balance effective cancer control with the patient’s overall well-being and the likely progression of his condition. Immunotherapy can offer a less invasive yet effective approach to managing metastatic cancer with a potentially better side-effect profile than further chemotherapy or major surgery.

***Q3:****prompt3*

A3:

**MAIN-CAV Trial** (NCT05092958): This Phase 3 clinical trial is evaluating the effectiveness of combining cabozantinib (a tyrosine kinase inhibitor) with avelumab (a PD-L1 inhibitor) versus avelumab alone in patients who have responded to first-line platinum-based chemotherapy. This study aims to see if adding cabozantinib can improve survival benefits further than avelumab alone in the maintenance setting. The trial is currently active and enrolling participants.

**THOR Study** (NCT03390504): Although the primary endpoint of improving overall survival with erdafitinib compared to pembrolizumab wasn’t met, this Phase 3 study provided insights into the management of metastatic urothelial cancer with FGFR alterations. It demonstrated similar survival rates for erdafitinib and pembrolizumab in patients with these specific genetic alterations. This trial might be particularly relevant if your patient has FGFR-altered urothelial carcinoma.

***Patient5***

***Q1:****Prompts1+<Patient information5>*

***A1:***

### Preferred Treatment Measures:

**Systemic Chemotherapy:**

**Reason:** The diagnosis of small cell neuroendocrine carcinoma of the bladder suggests a need for systemic therapy as this tumor type is aggressive and often presents at an advanced stage. Chemotherapy regimens similar to those used for small cell lung cancer, such as etoposide plus cisplatin or carboplatin, are recommended due to the high Ki67 proliferative index indicating rapid tumor growth.

**Supportive Care for Renal Function:**

**Reason:** The patient shows evidence of renal impairment (hydronephrosis and elevated serum creatinine levels). Management should include strategies to preserve renal function, such as possible stenting of the ureters if obstructed by the tumor or surrounding structures.

**Management of Local Symptoms:**

**Reason:** Palliative care to manage symptoms such as pain and bleeding might involve local radiotherapy, especially if the tumor causes significant discomfort or hematuria. This approach would help improve quality of life.

**Hormonal Therapy:**

**Reason:** Although the prostate-specific antigen (PSA) levels are not significantly elevated, the presence of suspected prostate involvement suggests that hormonal therapy could be beneficial if confirmed to be prostate cancer.

**Targeted Therapy:**

**Reason:** Given the presence of specific immunohistochemical markers (e.g., TTF-1, CD56), exploring targeted therapy options may be beneficial, though more specific to lung cancer, it could be explored here depending on availability and clinical trial options.

**Regular Monitoring and Follow-Up:**

**Reason:** Frequent imaging and blood tests are necessary to monitor the progression of the disease and adjust treatment plans accordingly.

### Measures to Avoid:

**Radical Surgery:**

**Reason:** Given the advanced stage of cancer with suspected metastatic spread and the patient's age, radical surgery (like radical cystectomy or prostatectomy) may not be beneficial and could significantly impact the quality of life due to high morbidity associated with such procedures.

**High Dose Radiation Therapy:**

**Reason:** In the setting of renal impairment and the risks of further damage or complications, aggressive radiation therapy should be used cautiously.

**Nephrotoxic Drugs:**

**Reason:** Avoidance of nephrotoxic agents (certain chemotherapy drugs like cisplatin, if renal function is too compromised) is crucial due to already compromised renal function.

**Ignoring Symptom Management:**

**Reason:** It is vital not to overlook the management of symptoms such as pain and hematuria, which significantly affect the patient's quality of life.

***Q2:****Prompts2+*

*1.Which examination should be performed to clarify the origin of the tumor located at the bladder-prostate junction?*

*2.Which imaging examination is most appropriate to determine the patient's current baseline condition?*

*3.For the treatment of the lesion, can radiotherapy be considered for this patient?*

***A2:***

### 1. Examination to Clarify the Origin of the Tumor at the Bladder-Prostate Junction

Given the location of the tumor at the bladder-prostate junction and the suspected involvement of prostate cancer, the following examinations can be pivotal:

**Transrectal Ultrasound (TRUS)-guided Biopsy**: This examination allows precise targeting of the prostate and the bladder-prostate junction. TRUS can help in differentiating between prostate tissue and bladder tissue and guide biopsy needles accurately to the suspect areas. Biopsies from both the prostate and the areas of the bladder involved can provide histopathological evidence to distinguish between primary bladder cancer, prostate cancer, or a possible transitional zone tumor.

**Multiparametric Magnetic Resonance Imaging (mpMRI) of the Pelvis**: This imaging modality is highly sensitive and specific for prostate cancer and can also provide detailed images of the bladder. MpMRI can help in assessing the extent of the tumor, its exact origin, and any potential invasion into adjacent structures.

### 2. Imaging Examination to Determine the Patient's Current Baseline Condition

For establishing a comprehensive baseline condition of this patient, particularly given the complexity and the advanced nature of the disease, the following imaging examination is recommended:

* **Positron Emission Tomography-Computed Tomography (PET-CT)**: A PET-CT scan using a glucose analog tracer (like FDG) or a prostate-specific tracer (like PSMA) can provide detailed information on the metabolic activity of the cancer and help in detecting both local and distant metastases. This is crucial for staging the cancer accurately and for planning subsequent therapeutic interventions. The comprehensive view offered by PET-CT includes evaluation of the lymph nodes, bones, and other organs, which is essential for understanding the extent of the disease and any potential metastatic spread.

Both TRUS-guided biopsy and PET-CT scan complement each other by providing detailed pathological and metabolic insights into the tumor, which are essential for tailoring the most effective treatment strategy for this patient.

### 3.Is the patient currently able to undergo radiotherapy

The patient could potentially undergo radiotherapy, but several important conditions and precautions need to be addressed:

* **Palliative Intent:** If radiotherapy is considered, it should primarily be for palliation of symptoms rather than curative intent, given the metastatic spread of the disease.
* **Advanced Planning and Techniques:** Utilizing advanced radiotherapy techniques that minimize exposure to surrounding organs, especially the kidneys, is crucial. This includes the potential use of IMRT or image-guided radiotherapy (IGRT).
* **Multidisciplinary Evaluation:** Prior to initiating radiotherapy, a thorough evaluation by a multidisciplinary team including a radiation oncologist, a nephrologist, and possibly a urologist should be undertaken to tailor the treatment plan to the patient's specific needs and to monitor his response and adjust care as necessary.

In summary, while radiotherapy can be considered for this patient, it should be approached with caution, focusing on symptom management and preserving quality of life, and should involve careful planning to mitigate risks given his renal impairment and overall health status.

***Q3****:Prompt3*

***A3:***

**Neoadjuvant Adebrelimab Plus Etoposide and Cisplatin in Neuroendocrine Bladder Carcinoma**:

* **NCT ID**: NCT06091124
* **Description**: This Phase 2 trial aims to evaluate the efficacy and safety of neoadjuvant adebrelimab in combination with etoposide and cisplatin before radical cystectomy in patients with neuroendocrine bladder carcinoma. Participants will receive a combination of adebrelimab, etoposide, and cisplatin for up to 4 cycles followed by surgery.
* **Location**: RenJi Hospital
* **Clinical Significance**: The trial seeks to establish the pathologic complete response rate at cystectomy and assess the safety and tolerability of the combination therapy, which could be crucial for aggressive cancers like small cell neuroendocrine carcinoma​ ([ClinicalTrials.gov](https://classic.clinicaltrials.gov/ct2/show/NCT06091124" \t "C:\\Users\\15812\\AppData\\Local\\Temp\\_blank))​.

**Atezolizumab Plus Etoposide and Platinum in Small Cell Bladder Cancer**:

* **NCT ID**: NCT05312671
* **Description**: This is a single-arm, Phase II trial using atezolizumab combined with platinum and etoposide chemotherapy followed by cystectomy for patients with localized small cell neuroendocrine bladder cancer. The regimen includes cycles of atezolizumab, platinum, and etoposide, followed by surgical resection, aiming to assess the pathologic complete response rate.
* **Sponsor**: Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
* **Clinical Significance**: The study focuses on the effectiveness of integrating immunotherapy with chemotherapy before surgical intervention, potentially offering a comprehensive treatment approach for this aggressive cancer type​ ([Bladder Cancer Advocacy Network](https://bcan.org/clinicaltrials/atezolizumab-plus-etoposide-and-platinum-in-small-cell-bladder-cancer/" \t "C:\\Users\\15812\\AppData\\Local\\Temp\\_blank))​.

***Patient6***

***Q1:****(prompts1)+<Patient information6>*

***A1:***

### Preferred Treatment Measures:

**Continuation of Surgical Management**:

Given the patient’s history of bladder cancer and repeat interventions, another TURBT may be necessary if residual tumor is suspected. This procedure can help manage localized tumor resections and alleviate symptoms related to mass effect, such as difficulty urinating.

**Systemic Chemotherapy**:

Considering the patient's high Ki67 index (60%), which indicates a high proliferation rate of cancer cells, systemic chemotherapy could be beneficial. Agents like cisplatin or carboplatin combined with gemcitabine are commonly used in advanced urothelial carcinoma to manage systemic disease and reduce tumor burden.

**Palliative Care**:

Given the extensive disease and the patient’s age, focusing on quality of life through palliative care is crucial. Management of pain, urinary symptoms, and other supportive measures should be prioritized to improve the patient's overall well-being.

**Consideration for Immunotherapy**:

If the patient is eligible, immune checkpoint inhibitors (e.g., pembrolizumab or atezolizumab) could be considered. These treatments have shown benefits in advanced bladder cancer, especially in cases where traditional chemotherapy might be too taxing due to the patient’s overall condition.

**Nutritional and Supportive Care**:

The patient shows signs of severe liver impairment and poor nutritional status (low albumin levels). Nutritional support, possibly including albumin supplementation, and management of liver function are essential.

**Multidisciplinary Consultation**:

Regular consultations with a multidisciplinary team including urologists, oncologists, radiologists, and palliative care specialists are necessary to adapt the treatment plan according to the progression of the disease and the patient's response to treatments.

### Measures to Avoid:

**Avoidance of Nephrotoxic Agents**:

Given the patient’s elevated liver enzymes and potential compromised kidney function (evidence of hydronephrosis), nephrotoxic drugs (like some chemotherapy agents) should be used with caution or avoided. Alternative regimens that are less nephrotoxic might be necessary.

**Non-Essential Surgical Interventions**:

Avoid unnecessary surgical procedures that may not provide a significant benefit in terms of survival or quality of life, especially given the patient’s advanced age and extensive previous surgeries.

**Avoidance of High-Dose Radiation**:

High-dose radiation therapy should be avoided if possible due to the potential for significant side effects, including worsening of local symptoms and potential damage to already compromised structures like the ureters and intestines.

**Limitation on Aggressive Resection**:

Extensive surgical resections might not be suitable due to the invasive nature of the disease and the high surgical risk associated with the patient’s age and overall health status.

### Conclusion:

For this patient, a balanced approach between aggressive management of the cancer and maintaining quality of life through palliative measures is crucial. Regular re-evaluations by the multidisciplinary team will help in making timely adjustments to the treatment plan based on the patient's response and any new symptoms.

***Q2:****Prompts2+*

*1.Is the patient currently eligible for local radiotherapy?*

*2.Is the patient currently eligible for intravesical chemotherapy?*

*3.Is the patient currently eligible for radical surgery?*

*4.Please carefully consider and provide a clear conclusion*

***A2:***

Given the complex nature of this patient's case, determining eligibility for specific treatments such as local radiotherapy, intravesical chemotherapy, and radical surgery requires a detailed consideration of multiple factors:

### 1. Local Radiotherapy:

* **Eligibility Considerations**: This patient has a history of extensive bladder and prostate involvement, with the cancer possibly invading adjacent structures such as the seminal vesicles and rectal wall. Local radiotherapy could be considered to control local tumor growth and alleviate symptoms related to local invasion.
* **Potential Benefits**: It may help in managing symptoms like bleeding or obstruction.
* **Risks**: Given the advanced stage and previous treatments, there might be increased risks of radiation-induced damage to nearby organs and tissues, which could worsen the patient’s quality of life.
* **Conclusion**: The patient could be eligible for palliative radiotherapy aimed at symptom control, rather than curative intent, if the benefits of symptom relief outweigh the potential risks of side effects.

### 2. Intravesical Chemotherapy:

* **Eligibility Considerations**: Intravesical therapy is typically used for non-invasive (superficial) bladder cancer. This treatment involves instilling chemotherapy directly into the bladder via a catheter, targeting cancer cells lining the bladder.
* **Current Condition Relevance**: The patient’s cancer has invaded beyond the bladder to the prostate, ureters, and possibly the rectum. This extensive spread makes intravesical chemotherapy less effective, as it does not address systemic disease or invasion beyond the bladder lining.
* **Conclusion**: The patient is likely not eligible for intravesical chemotherapy due to the invasive nature of the disease and the presence of metastatic or locally advanced features.

### 3. Radical Surgery:

* **Eligibility Considerations**: Radical surgery (such as radical cystectomy) could be considered in cases where the bladder cancer is localized enough to be completely removed and where the patient can withstand major surgery.
* **Patient’s Current Health Status**: Considering the patient’s advanced age, extensive previous surgeries, compromised liver and renal function, and the spread of cancer to multiple nearby organs, the risks of a major operation may outweigh potential benefits.
* **Conclusion**: The patient is likely not eligible for radical surgery due to the high surgical risk, poor prognosis associated with the extent of disease invasion, and his overall health condition.

### Summary:

* **Local Radiotherapy**: Could be considered for symptom management if clinically justified.
* **Intravesical Chemotherapy**: Not suitable due to the invasive nature of the disease.
* **Radical Surgery**: Likely inappropriate due to extensive disease and high surgical risks.

***Q3****:prompt3*

***A3***

**TROPHY-U-01 Trial (Sacituzumab Govitecan)**

* **NCT Number**: Not specified in the source, but related to the TROPHY series trials
* **Details**: This phase 2 trial is testing Sacituzumab Govitecan, an antibody-drug conjugate targeting Trop-2, which is commonly expressed in urothelial carcinoma cells. The trial has shown encouraging results in patients with advanced urothelial carcinoma who have progressed after platinum and checkpoint inhibitor treatments. The median overall survival was reported as 10.9 months with an objective response rate of 27%​ ([WCM Newsroom](https://news.weill.cornell.edu/news/2021/08/new-treatment-option-for-advanced-urothelial-cancer-patients-shows-promise-in-a-phase-2" \t "C:\\Users\\15812\\AppData\\Local\\Temp\\_blank))​.

**EV-302/KEYNOTE-A39 Trial (Enfortumab Vedotin and Pembrolizumab)**

* **NCT Number**: NCT03288545
* **Details**: This trial investigates the combination of Enfortumab Vedotin and Pembrolizumab for patients with locally advanced or metastatic urothelial carcinoma who are ineligible for cisplatin-containing chemotherapy. The combination has shown a 68% objective response rate and is considered especially promising for its efficacy and manageable safety profile​ ([Cleveland Clinic](https://consultqd.clevelandclinic.org/a-new-standard-emerges-in-advanced-urothelial-carcinoma-after-decades-of-first-line-chemotherapy" \t "C:\\Users\\15812\\AppData\\Local\\Temp\\_blank))​​ ([OncLive](https://www.onclive.com/view/ev-302-regimen-bests-chemo-in-advanced-urothelial-cancer" \t "C:\\Users\\15812\\AppData\\Local\\Temp\\_blank))​.

**JAVELIN Bladder 100 (Avelumab)**

* **Details**: Although a specific NCT number was not detailed, this phase 3 trial focuses on Avelumab as a maintenance therapy after 4–6 cycles of platinum-based chemotherapy in patients with unresectable, locally advanced or metastatic urothelial carcinoma. The trial demonstrated a median overall survival of 21.4 months for patients receiving Avelumab compared to 14.3 months for those on best supportive care alone​ ([SpringerLink](https://link.springer.com/article/10.1007/s11912-023-01461-x" \t "C:\\Users\\15812\\AppData\\Local\\Temp\\_blank))​.

***Patient7  
Q1:****prompt1+<Patient information7>* ***A1:***

### Recommended Treatment Measures

**Systemic Chemotherapy**:

**Rationale**: Given the poorly differentiated nature of the plasmacytoid subtype of urothelial carcinoma, systemic chemotherapy is often recommended as it can be effective in managing systemic disease and reducing tumor burden, which might help alleviate symptoms like urinary difficulties and pain associated with the mass.

**Agents**: Options may include cisplatin-based chemotherapy if the patient's renal function permits, or carboplatin if renal function is compromised.

**Surgical Intervention**:

**Rationale**: Considering the localized large tumor mass (5×8 cm) on the pelvic floor and bladder, debulking surgery might be beneficial if the tumor is deemed resectable, to relieve symptoms and potentially improve outcomes.

**Procedure**: A multidisciplinary surgical assessment is needed to determine the feasibility of a more extensive resection, considering the patient's overall health and surgical risk.

**Management of Complications**:

**Venous Thromboembolism (VTE) Prophylaxis**:

**Rationale**: The patient has developed venous thrombosis, which is common in cancer patients due to hypercoagulability. Prophylactic anticoagulation is recommended to prevent further thrombotic events.

**Urinary Symptoms Management**:

**Rationale**: Interventions to manage symptoms such as urinary urgency, frequency, and incontinence, including possibly a urinary catheter if needed to manage retention and incontinence effectively.

**Radiation Therapy**:

**Rationale**: For palliative management, especially if the patient experiences significant pain or if the tumor is causing obstruction that cannot be fully alleviated surgically.

### Measures to Avoid

**Avoidance of Nephrotoxic Agents**:

**Rationale**: Given the bilateral renal and ureteral dilation and effusion, nephrotoxic drugs (including certain chemotherapy agents and NSAIDs) should be used cautiously to prevent further renal impairment.

**Non-Indicated Surgical Interventions**:

**Rationale**: Extensive surgical procedures that are not likely to offer a therapeutic benefit or might significantly worsen quality of life should be avoided, especially in the context of a highly aggressive and advanced cancer.

**Avoidance of Invasive Procedures Unrelated to Cancer Management**:

**Rationale**: Invasive procedures that do not directly contribute to managing the cancer or its symptoms should be minimized to avoid unnecessary complications and hospital stays.

***Q2:****prompt2+*

*1.Is radiation therapy recommended for this patient, and what is the nature of the radiation therapy?*

*2.If genetic testing is performed, which two genes should be prioritized for testing?*

*3.What specifically constitutes a large-scale surgery?*

*4.If this patient undergoes targeted therapy and immunotherapy, which two genes should be targeted?*

### ***A2:*** Radiation Therapy Recommendation

For this 74-year-old patient with poorly differentiated urothelial carcinoma, **radiation therapy can be recommended**, primarily for palliative purposes. Given the tumor's location and the patient's symptoms, radiation therapy can help relieve symptoms caused by the tumor mass, such as pain, obstruction, and difficulty urinating, especially if surgery is not fully feasible or if the disease has spread extensively.

### Nature of Radiation Therapy

**External Beam Radiation Therapy (EBRT)**: This is the most common form of radiation therapy for bladder cancer and other pelvic tumors. EBRT can be precisely targeted to the tumor and surrounding areas to minimize damage to healthy tissue.

**Palliative Radiation**: Aimed at relieving symptoms rather than curing the disease. The focus would be on reducing the tumor size and managing pain or other symptoms caused by tumor pressure on nearby organs or structures.

**Hypofractionated Schedules**: Given the palliative intent, shorter, more intense courses of radiation might be used to provide symptom relief more quickly.

**Intensity-Modulated Radiation Therapy (IMRT)**: This advanced form of radiation therapy allows for the radiation beams to conform more precisely to the three-dimensional shape of the tumor. This technique enables high doses of radiation to be delivered to the tumor while sparing the surrounding healthy tissue, which is crucial in a sensitive area like the pelvis.

***Q3****:Prompt3*

**Sacituzumab Govitecan plus Enfortumab Vedotin for Metastatic Urothelial Carcinoma**:

* **Trial Name**: Double Antibody Drug Conjugate (DAD) Phase I Trial
* **NCT Number**: Not specified in the available document.
* **Details**: This trial evaluates the combination of sacituzumab govitecan and enfortumab vedotin, both of which are antibody-drug conjugates. The study targets patients with metastatic urothelial carcinoma who have progressed on platinum-based chemotherapy and immunotherapy, or who are cisplatin-ineligible and have received at least one line of therapy. The focus is on assessing the safety and efficacy of this drug combination.
* **Clinical Significance**: The trial is in phase I, aiming to determine the optimal dosing and preliminary efficacy, with an emphasis on a combination that could potentially manage treatment-resistant metastatic urothelial carcinoma due to the non-overlapping toxicities and preclinical synergy of the drugs involved.

***Patient8******Q1:****prompts1+<Patient8>*

A1:

### Preferred Treatment Measures

**Continuation of Chemotherapy and Immunotherapy**:

**Rationale**: Small cell neuroendocrine carcinoma is aggressive and responds initially well to chemotherapy and immunotherapy. The combination of etoposide, cisplatin, and durvalumab (an immunotherapy agent) is appropriate, considering the initial response.

**Recommendation**: Consider continuing with additional cycles of chemotherapy and assessing response via imaging and clinical improvement.

**Regular Imaging and Monitoring**:

**Rationale**: The presence of a hypoechoic nodule in the right lung suggests potential metastasis, necessitating ongoing monitoring to assess the progression or response to therapy.

**Recommendation**: Periodic chest CT scans should be conducted every 2-3 months to monitor the lung nodule and any other potential metastatic sites.

**Pain Management and Symptomatic Care**:

**Rationale**: The patient’s symptoms of pain and dysuria require effective management to maintain quality of life.

**Recommendation**: Prescribe appropriate analgesics and consider consultations with pain management specialists. Antispasmodic medications may be useful for managing urinary symptoms.

**Consultation with a Radiation Oncologist**:

**Rationale**: For localized symptoms or if there is tumor progression that is not amenable to surgery or further chemotherapy, targeted radiation could be beneficial, particularly for pain relief or reduction of tumor burden.

**Recommendation**: Evaluate the feasibility of targeted radiation therapy, especially for the lung nodule or pelvic region, if symptoms persist or progress.

### Measures to Avoid

**Avoidance of Surgical Intervention for Tumor Removal**:

**Rationale**: Given the typical high aggressiveness and potential for widespread metastatic disease in small cell neuroendocrine carcinoma, extensive surgical intervention may not provide benefit and could lead to significant morbidity.

**Recommendation**: Focus on systemic therapy unless there is a compelling indication for surgical intervention to alleviate symptoms.

**Avoidance of Nephrotoxic Drugs**:

**Rationale**: The patient has a complex cyst in the right kidney and a stone in the left kidney, which could predispose to renal complications.

**Recommendation**: Carefully evaluate the use of potentially nephrotoxic agents and ensure regular monitoring of renal function.

**Limiting Invasive Diagnostic Procedures**:

**Rationale**: Repeated invasive procedures may not be beneficial in the setting of known extensive malignant disease and could increase the risk of complications.

**Recommendation**: Utilize non-invasive imaging techniques for monitoring disease status as much as possible.

This plan aims to balance aggressive treatment of a highly malignant cancer with preservation of quality of life and management of symptoms. Regular reassessment by the MDT is crucial to adapt the treatment plan based on the patient's response and any new developments.

***Q2:****prompt2+*

***A2:***

For the 69-year-old male patient diagnosed with small cell neuroendocrine carcinoma (NEC) of the bladder, the most critical treatment measure currently is the **continuation and evaluation of chemotherapy and immunotherapy**. This decision is driven by several factors:

**Effectiveness against NEC**: Small cell neuroendocrine carcinoma is a highly aggressive cancer that has shown responsiveness to chemotherapeutic agents like etoposide and cisplatin, in combination with immunotherapy (durvalumab). Continuing this regimen can help control the spread of the disease and manage symptoms effectively.

**Systemic Nature of Disease**: Given the aggressive nature of NEC and the presence of a suspected metastatic nodule in the lung, systemic therapy is crucial to manage both local and distant disease manifestations.

**Patient’s Previous Response**: The patient has already undergone three cycles of this regimen, and continuation could further consolidate the response, especially if initial improvements or stabilization of the disease were observed.

Regarding the suitability for radiotherapy, here are the key considerations:

* **Potential Benefits**: Radiotherapy could be particularly useful for palliative purposes, especially if there are localized symptoms or areas of pain that are not adequately managed by systemic therapy alone. For instance, targeted radiation could help alleviate symptoms related to the mass in the bladder or the metastatic lung nodule if these are causing significant symptoms.
* **Evaluation Required**: Before proceeding, it would be important to assess the extent of the disease through updated imaging studies. This would determine whether the disease is localized enough for radiotherapy to be effective or if it has spread too diffusely.

***Q3:****Prompt3*

**Neoadjuvant Adebrelimab Plus Etoposide and Cisplatin in Neuroendocrine Bladder Carcinoma**:

* **Details**: This is a Phase I trial evaluating the efficacy and safety of adebrelimab in combination with etoposide and cisplatin in patients with neuroendocrine carcinoma of the bladder. The treatment involves intravenous administration of these drugs followed by radical cystectomy and lymph node dissection.
* **NCT Number**: NCT05302068
* **Level of Evidence**: This is an early-phase trial, primarily focused on safety and preliminary efficacy, thus providing initial clinical evidence but not yet definitive proof of benefit.

**Atezolizumab Plus Etoposide and Platinum in Small Cell Bladder Cancer**:

* **Details**: This is a Phase II trial exploring the combination of atezolizumab with platinum (either cisplatin or carboplatin) and etoposide for patients with locally advanced urothelial cancer with small cell/neuroendocrine features. The regimen includes cycles of chemotherapy followed by maintenance therapy with atezolizumab.
* **NCT Number**: NCT03539828
* **Level of Evidence**: As a Phase II trial, this study provides more substantial evidence regarding the treatment's effectiveness and safety, focusing on the pathologic response rate and survival outcomes.

***Patient9  
Q1:****Prompt1+<Patient information9>*

***A1:***

### Preferred Treatment Measures

**Systemic Chemotherapy**:

**Rationale**: Given the history of radical cystectomy and recurrence, systemic chemotherapy can be effective in controlling disease progression, especially in cases of metastatic or locally advanced urothelial carcinoma. Common regimens might include a combination of gemcitabine and cisplatin, considering patient tolerance and renal function.

**Palliative Radiation Therapy**:

**Rationale**: For symptom control, particularly due to the pain around the anus and the presence of a pelvic mass, localized radiation therapy could help relieve symptoms and potentially reduce tumor burden.

**Targeted Therapy**:

**Rationale**: Depending on the expression of specific molecular targets (e.g., FGFR3 mutations), targeted therapies like erdafitinib could be considered if the patient's tumor harbors actionable mutations.

**Immunotherapy**:

**Rationale**: For patients who are not eligible for cisplatin-based chemotherapy, immune checkpoint inhibitors such as pembrolizumab or atezolizumab might be suitable, particularly if the tumor expresses PD-L1 or the patient has a high tumor mutational burden.

**Supportive Care**:

**Rationale**: Management of pain, prevention of infections (especially given the ESBL+ E. coli), and addressing renal function deterioration are crucial for maintaining quality of life.

**Clinical Trials**:

**Rationale**: Considering the recurrence and previous treatment history, enrolling in clinical trials for novel therapies could provide access to cutting-edge treatments not yet available in standard care.

### Measures to Avoid

**High-Dose Chemotherapy Regimens**:

**Rationale**: Due to the patient's age and compromised renal function, high-dose chemotherapy may increase toxicity without significantly improving outcomes.

**Nephrotoxic Drugs**:

**Rationale**: Avoiding medications that could further impair renal function is crucial, given the patient's already elevated creatinine levels.

**Invasive Surgical Interventions**:

**Rationale**: Surgical options should be limited due to the invasive nature of the disease and the patient's age and overall condition. Surgical risks likely outweigh benefits in this context.

**Non-Essential Biopsies**:

**Rationale**: Further invasive procedures such as biopsies should be avoided unless they would significantly alter the treatment plan, due to the risk of complications and the patient's current condition.

**Non-Indicated Imaging**:

**Rationale**: Avoid frequent or repetitive imaging that does not contribute to the patient's ongoing management or symptom control to reduce radiation exposure and unnecessary costs.

***Q2:****prompt2+*

*1.For this patient, which gene should be tested for immunotherapy;*

*2.which gene should be tested for targeted therapy;*

*3.is the patient eligible for chemotherapy, and what is the chemotherapy regimen*

*4.what does invasive surgery refer to?*

***A2:***

### Genetic Testing for Immunotherapy

**PD-L1 Expression**: Testing for PD-L1 (Programmed Death Ligand 1) expression is crucial as it can determine eligibility for immunotherapy with checkpoint inhibitors such as pembrolizumab or atezolizumab. Higher levels of PD-L1 expression might indicate a better response to these therapies.

**Tumor Mutational Burden (TMB)**: High TMB can be a predictor of response to immunotherapy across various cancer types, including urothelial carcinoma.

### Genetic Testing for Targeted Therapy

**FGFR3 Mutations**: Alterations in the FGFR3 gene are common in urothelial carcinoma and can be targeted by specific inhibitors like erdafitinib. Testing for this mutation can identify if the patient is a candidate for such targeted therapies.

**Other Molecular Targets**: Depending on available facilities and resources, comprehensive genomic profiling might be beneficial to identify other less common actionable mutations.

### Eligibility and Recommended Chemotherapy Regimen

**Eligibility for Chemotherapy**: Given the patient's age and slightly impaired renal function (creatinine 152.8 µmol/L), he should be assessed for his ability to tolerate chemotherapy. Factors to consider include performance status, renal function, and potential comorbidities.

**Chemotherapy Regimen**:

* + If the patient is fit for cisplatin-based therapy (requires creatinine clearance > 60 mL/min), a combination of **gemcitabine and cisplatin** is the standard first-line treatment for metastatic urothelial carcinoma.
  + If cisplatin is not suitable due to renal function or other health issues, a carboplatin-based regimen (e.g., gemcitabine and carboplatin) can be considered.
  + For patients who may not tolerate these regimens, single-agent chemotherapy with agents like vinflunine or taxanes may be considered.

### Invasive Surgery

**Definition**: In the context of your patient with advanced and recurrent disease, invasive surgery refers to any surgical procedure that involves significant manipulation or removal of tissue within body cavities, potentially leading to high risk of complications or morbidity. For this patient, invasive surgeries might include attempts to resect recurrent tumors or extensive surgical procedures to alleviate obstruction caused by the tumor.

**Considerations**: Given the patient's advanced disease, age, and history of multiple treatments, invasive surgeries are likely to be more risky and less beneficial, focusing instead on palliation and quality of life rather than curative intent.

***Q3:****prompt3*

***A3:***

**AMBASSADOR Trial (NCT03244384)**: This is a phase III trial assessing the efficacy of adjuvant pembrolizumab versus observation in patients with muscle-invasive urothelial carcinoma post-surgery. The trial focuses on the improvement of disease-free survival and overall survival, which might be particularly relevant given the patient's recurrent status and the prior surgical interventions. Pembrolizumab has shown a significant improvement in disease-free survival in this context​ ([The ASCO Post](https://ascopost.com/news/january-2024/ambassador-pembrolizumab-in-muscle-invasive-and-locally-advanced-urothelial-carcinoma/" \t "_blank))​.

**KEYNOTE-905 Trial**: Although specific details and the NCT number weren't captured, this trial involves the use of enfortumab vedotin combined with pembrolizumab compared to pembrolizumab alone and upfront radical cystectomy in patients with localized muscle-invasive bladder cancer. This trial could be of interest considering its exploration of combination therapy and the inclusion of patients regardless of their cisplatin eligibility​ ([Cleveland Clinic](https://consultqd.clevelandclinic.org/a-new-standard-emerges-in-advanced-urothelial-carcinoma-after-decades-of-first-line-chemotherapy" \t "_blank))​.

**KEYNOTE-866 (NCT03924856)**: This phase 3 study evaluates perioperative pembrolizumab plus neoadjuvant chemotherapy for cisplatin-eligible muscle-invasive bladder cancer. Given the patient’s history, his eligibility for cisplatin needs careful assessment, but this trial could offer insights into combined modality treatment that aims to reduce the risk of recurrence​ ([Targeted Oncology](https://www.targetedonc.com/view/pembrolizumab-improves-dfs-in-muscle-invasive-urothelial-carcinoma" \t "_blank))​.

***Patient10***

***Q1:****prompt1+<Patient information10>*

***A1:***

### Preferred Treatment Measures

**Continuation of Immunotherapy**:

**Rationale**: Given the partial response to initial immunotherapy (Atezolizumab) and the presence of metastatic disease, continuing or modifying immunotherapy could be beneficial. Agents like Pembrolizumab, which have shown efficacy in metastatic urothelial carcinoma, could be considered if not previously used.

**Targeted Therapy**:

**Rationale**: Genetic testing (if not already performed) to identify actionable mutations (e.g., FGFR3) that can be targeted with specific inhibitors like Erdafitinib, especially relevant in urothelial carcinoma with specific genetic alterations.

**Pain Management and Palliative Care**:

**Rationale**: Due to the patient’s chronic pain, a comprehensive pain management plan including both pharmacologic and non-pharmacologic measures is recommended. This could involve the use of opioids, non-steroidal anti-inflammatory drugs (NSAIDs), and consultation with a palliative care team.

**Clinical Trials**:

**Rationale**: Enrolling in clinical trials for new therapeutic agents or combinations that could provide clinical benefit in treatment-resistant urothelial carcinoma.

**Radiation Therapy**

**Rationale**: For localized control of symptomatic metastases, particularly if they contribute to pain or risk of complications (e.g., bone metastases).

### Measures to Avoid

**Nephrotoxic Agents**:

**Reason**: Given the patient’s history of renal pelvis cancer and likely reduced renal reserve, nephrotoxic drugs (including certain chemotherapy agents) should be used cautiously.

**Non-Indicated Surgical Interventions**:

**Reason**: Avoid invasive surgical interventions that do not offer a palliative benefit or are unlikely to improve clinical outcomes, considering the extensive metastatic burden.

**Overlapping Toxicity Treatments**:

**Reason**: Avoid combining treatments that have overlapping toxicity profiles that could exacerbate side effects, particularly hematologic, hepatic, and renal toxicities.

**Routine Use of High-Dose Corticosteroids**:

**Reason**: Long-term use can lead to significant side effects including immunosuppression, which could be detrimental in a cancer patient.

**Intensive Surveillance Imaging**:

**Reason**: In the absence of clinical indications or symptoms suggesting progression, intensive surveillance might lead to unnecessary exposure to radiation and increased patient anxiety, without clear benefit.

***Q2:****prompt2+*

1.Does the patient's chemotherapy regimen need to be changed?

2.How should the retroperitoneal lesions be managed?

3.Can the retroperitoneal lesions be left untreated and monitored through follow-up?

4.Is it possible to surgically remove the primary and metastatic lesions?

***A2:***

### 1. Does the patient's chemotherapy regimen need to be changed?

* **Conclusion**: Yes, considering the persistence of lesions despite the completion of six cycles of Gemcitabine and Cisplatin (GC) chemotherapy along with Atezolizumab immunotherapy, a change in the chemotherapy regimen may be warranted. This could involve exploring alternative chemotherapeutic agents or combinations that may be more effective against resistant tumor cells. Additionally, reassessing the patient's response to the previous regimen and performing molecular or genetic profiling could guide the selection of a new targeted therapy.

### 2. How should the retroperitoneal lesions be managed?

* **Conclusion**: Management should be tailored based on the size, number, and symptoms caused by the retroperitoneal lesions. Options include:
  + **Continued Systemic Therapy**: This could involve continuing with immunotherapy or switching to a different systemic treatment based on tumor profiling.
  + **Radiation Therapy**: For symptom control, especially if the lesions are causing pain or other complications.
  + **Palliative Care**: To manage symptoms and improve quality of life, particularly if the lesions are not amenable to curative treatment.

### 3. Can the retroperitoneal lesions be left untreated and monitored through follow-up?

* **Conclusion**: Yes, this is a viable option, especially if the lesions are stable, asymptomatic, and the patient is experiencing a significant burden from treatment side effects. Active surveillance with regular imaging and clinical assessments could be considered to monitor for progression. This approach would require clear communication with the patient about the potential risks and signs of progression to watch for.

### 4. Is it possible to surgically remove the primary and metastatic lesions?

* **Conclusion**: Surgical removal of the primary lesion in the left renal pelvis has already been performed. As for the metastatic lesions, surgery is generally not the standard approach for multiple metastases in urothelial carcinoma, particularly when they are widespread as in this case. Surgery might be considered for isolated metastasis causing significant symptoms or complications, but generally, systemic treatment is preferred for managing widespread metastatic disease.

***Q3:***

***A3:****prompt3*

**TROPHY-U-01 Trial**: Evaluates Trodelvy (sacituzumab govitecan) in patients with metastatic urothelial carcinoma (mUC) who have progressed after both platinum-based chemotherapy and checkpoint inhibitor therapy. This trial is in phase 2 and focuses on the efficacy of Trodelvy as a monotherapy or in combination with other treatments in different cohorts of patients. The study has shown promising outcomes in terms of overall survival and response rates in a challenging patient population. **NCT Number**: NCT03547973​ ([Gilead Sciences, Inc.](https://www.gilead.com/news-and-press/press-room/press-releases/2023/2/trodelvy-demonstrates-positive-efficacy-treating-both-platinumineligible-and-rapidly-progressing-postplatinum-metastatic-urothelial-cancer" \t "_blank))​.

**PEANUT Trial**: Investigates the combination of pembrolizumab and nab-paclitaxel as salvage therapy for patients with locally advanced or metastatic urothelial carcinoma who have not responded to up to two lines of platinum-based chemotherapy. This phase 2 trial aims to assess the effectiveness of this combination, providing a potential option for patients who have limited responses to standard treatments. **NCT Number**: NCT03464734​ ([UroToday](https://www.urotoday.com/conference-highlights/esmo-2023/esmo-2023-bladder-cancer/147504-esmo-2023-updated-results-of-peanut-trial-pembrolizumab-and-nab-paclitaxel-as-salvage-therapy-for-platinum-treated-locally-advanced-or-metastatic-urothelial-carcinoma.html" \t "_blank))​.

**Double Antibody Drug Conjugate (DAD) Phase I Trial**: This trial explores the combination of sacituzumab govitecan and enfortumab vedotin in patients with metastatic urothelial carcinoma who have progressed on platinum-based chemotherapy and immunotherapy. The phase 1 study focuses on the safety and preliminary efficacy of this novel combination, aiming to address treatment resistance in mUC. **NCT Number**: NCT04724018​ ([Targeted Oncology](https://www.targetedonc.com/view/updated-trials-at-esmo-reveal-new-frontline-combo-in-urothelial-carcinoma" \t "_blank))​.

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