Received: 15 September 2025 | Revised: 7 October 2025 | Accepted: 22 October 2025

DOI: 10.3322/caac.70052

REVIEW ARTICLE

Advanced Urologic Cancer Consensus Conference (AUC3) 2025: Expert consensus on the management of renal cell and urinary tract cancers

Rana R. McKay MD[1] | Sumanta Pal MD[2] | Wanling Xie MS[3] | David Aggen MD, PhD[4] | Laurence Albiges MD, PhD[5] | Andrea Apolo MD[6] | Michael B. Atkins MD[7] | Rick Bangs MBA, PMP[8] | Kathryn E. Beckermann MD, PhD[9] | Joaquim Bellmunt MD, PhD[3] | Stephanie A. Berg DO[3] | Mehmet A. Bilen MD[10] | David Braun MD, PhD[11] | Maria I. Carlo MD[4] | Jason Efstathiou MD, DPhil[12] | Matthew Galsky MD[13] | Petros Grivas MD, PhD[14,15] | Shilpa Gupta MD[16] | Naomi Haas MD[17] | A. Ari Hakimi MD[4] | Hans Hammers MD, PhD[18] | Daniel Y. C. Heng MSC[19] | Michelle Hirsch MD, PhD[20] | Gopakumar Iyer MD[4] | Eric Jonasch MD[21] | Vadim S. Koshkin MD[22] | Oleksandr Kryvenko MD[23] | Bryan Lewis JD[24] | Roger Li MD[25] | Surena Matin MD[21] | Benjamin Maughan MD, PharmD[26] | David F. McDermott MD[27] | Bradley McGregor MD[3] | Joshua Meeks MD, PhD[28] | Matthew Milowsky MD[29] | Robert Motzer MD[4] | Andrea Necchi MD[30] | Dan Petrylak MD[11] | Sima Porten MD, MPH[22] | Thomas Powles MBBS, MRCP, MD[31] | Brian Rini MD[32] | Brian Shuch MD[33] | Arlene Siefker-Radtke MD[21] | Guru Sonpavde MD[34] | S. Srikala Sridhar MD[35] | Cristina Suarez MD, PhD[36] | Chad Tang MD[21] | Abhishek Tripathi MD[2] | Michiel S. Van Der Heijden MD, PhD[37] | Martin Voss MD[4] | Wenxin Xu MD[3] | Tian Zhang MD[18] | Jonathan Rosenberg MD[4] | Toni K. Choueiri MD[3]

Correspondence
Rana R. McKay, Medicine and Urology, University of California-San Diego, Moores Cancer Center, 3855 Health Sciences Drive, #0987, La Jolla, CA 92037, USA.
Email: rmckay@ucsd.edu

Abstract

The therapeutic landscape for renal cell carcinoma (RCC) and urinary tract cancer (UTC) has transformed dramatically, creating complexity in treatment selection and sequencing. The 2025 Advanced Urologic Cancer Consensus Conference was convened to establish evidence-based expert consensus recommendations for

Rana R. McKay and Sumanta Pal contributed equally to this article as co-first authors.

Jonathan Rosenberg and Toni K. Choueiri contributed equally to this article as co-senior authors.

optimal management. A multidisciplinary panel of 51 experts participated in a modified Delphi process addressing questions developed through iterative consensus-building covering RCC and UTC management. Voting occurred before and after the conference, and analyses focused on postmeeting responses. Consensus was defined as ≥75% agreement, with strong consensus as >90%. Strong consensus was found on the use of adjuvant pembrolizumab for higher risk RCC (pathologic T2 [pT2], grade 4; pT3–pT4, any grade; pTXN1; or fully resected metastatic disease) and on neoadjuvant therapy before cystectomy for localized UTC. There was strong consensus on the use of enfortumab vedotin plus pembrolizumab as frontline therapy for metastatic UTC and the use of platinum-based chemotherapy postprogression in biomarker-negative UTC. For RCC, there was consensus on the role of single-agent vascular endothelial growth factor receptor–tyrosine kinase inhibitor therapy after progression on frontline immune checkpoint inhibitor/vascular endothelial growth factor receptor–tyrosine kinase inhibitor therapy or dual immune checkpoint inhibitor therapy. However, there was a lack of consensus on other critical areas in the management of RCC and UTC. The 2025 Advanced Urologic Cancer Consensus Conference provides evidence-informed guidance for complex clinical scenarios while identifying critical research priorities. The group recognizes that the lack of consensus across multiple areas highlights the need for improved patient selection and prospective studies enabling optimal combination and sequencing approaches. This iterative annual process will address evolving treatment paradigms to optimize outcomes.

KEYWORDS
Delphi process, expert panel consensus, renal cell carcinoma, treatment optimization, urothelial carcinoma

INTRODUCTION

Renal cell carcinoma (RCC) and urinary tract cancers (UTCs) represent formidable global health challenges, imposing substantial morbidity and mortality worldwide.[1–3] Although the majority of patients with RCC present with localized disease amenable to curative nephrectomy, meaningful proportions develop metastatic disease. Although modern therapeutic approaches have enabled cure in select patients with advanced disease, most patients with metastatic RCC ultimately develop treatment resistance. Similarly, UTCs encompass a broad clinical spectrum, ranging from superficial disease with favorable outcomes to muscle-invasive and metastatic disease characterized by high recurrence rates and poor survival. This clinical heterogeneity underscores the critical need for enhanced therapeutic strategies and standardized management approaches across the entire disease continuum.

The therapeutic landscape for urologic cancers has transformed dramatically over the past decade, creating unprecedented opportunities and significant clinical complexity. In RCC, management has evolved substantially, with improved outcomes in both localized and advanced disease settings, including the first adjuvant therapy to achieve overall survival benefit[4] and landmark trials establishing immune checkpoint inhibitor (ICI)-based strategy as a standard of care in metastatic disease.[5–8] Similarly, trials have fundamentally altered UTC treatment, with perioperative ICI demonstrating overall survival benefit[9] and novel antibody–drug conjugate combinations replacing platinum-based therapy as the standard of care in the frontline therapy for metastatic UTC.[10] However, approval of multiple agents has created critical challenges in treatment selection and sequencing, which are further compounded by geographic variations in practice patterns and access to certain therapies. Clinical decision making has become increasingly complex as therapeutic options both expand quickly and move into less advanced disease stages, creating management nuances not prospectively addressed in clinical trials.

Beyond therapeutic advances, important considerations remain in diagnosis, risk assessment, and patient selection. Whereas available risk-stratification tools provide valuable clinical guidance, their application in practice requires further refinement to enhance and optimize treatment selection. Diagnosis and management of variant histologic subtypes present ongoing challenges, with such rare subtypes requiring specialized approaches still being defined by pathologists. In addition, promising biomarker candidates continue to

emerge from molecular profiling studies, yet their translation into routine clinical practice requires validation and standardization before adoption in routine care.

The complexity of modern urologic cancer care necessitates multidisciplinary input and robust collaboration to develop comprehensive recommendations that address diverse clinical contexts and patient populations. The Advanced Urologic Cancer Consensus Conference (AUC3) was convened to establish evidence-based expert consensus recommendations for optimal RCC and UTC management. The primary objective was to develop practical guidance for treatment selection, sequencing strategies, biomarker utilization, and management of challenging clinical scenarios by integrating the latest clinical trial data with top expert experience. A key secondary objective was to systematically identify areas lacking consensus that require future research prioritization, thereby focusing efforts on the most pressing clinical questions to ultimately improve patient outcomes through more informed and standardized treatment approaches.

METHODS

Conference structure and leadership

The conference used a scientific committee comprising four conference directors and 18 scientific chairs, with two chairs assigned to each of the nine sessions covering RCC and UTC diagnostics and management. Four sessions focused on RCC, and five sessions addressed UTC.

Expert panel composition

The expert panel representing North America and Europe consisted of 51 members representing diverse specialties within urologic cancer management, including medical oncologists ($n = 40$), urologists ($n = 6$), radiation oncologists ($n = 2$), pathologists ($n = 1$), and patient advocates ($n = 2$; see Table S1). Panelists were selected by the scientific chairs and conference directors for their extensive clinical experience in genitourinary malignancy management, contributions to guideline development, and research publications in the field. This multidisciplinary composition ensured comprehensive evaluation of evidence from various perspectives, including clinical efficacy and safety profiles, surgical considerations, pathologic assessment, as well as patient-centered outcomes and preferences.

Question selection and development

A modified Delphi process was used to develop consensus recommendations.[11] The two scientific chairs assigned to each topic developed initial draft questions, which underwent iterative review involving multiple rounds of refinement. Questions were first reviewed by all scientific chairs and conference directors, then revised based on feedback, and subsequently distributed to all panelists for additional review and refinement before finalization. This iterative process ensured clinical relevance, clarity, and appropriateness of response options for each question. In total, 188 questions were developed, with 91 and 97 questions addressing RCC and UTC, respectively.

The RCC sessions covered the management of locally advanced RCC ($n = 27$ questions), frontline systemic therapy for advanced/metastatic RCC ($n = 30$ questions), later-line treatments in advanced/metastatic RCC ($n = 18$ questions), and systemic therapy for advanced variant histology RCC ($n = 16$ questions). UTC sessions included nonmuscle-invasive bladder cancer (NMIBC; $n = 15$ questions), the management of locally advanced UTC ($n = 26$ questions), frontline systemic therapy for metastatic urothelial carcinoma (UC; $n = 18$ questions), later-line treatments for metastatic UC ($n = 19$ questions), and considerations for special populations ($n = 19$ questions).

Statistical analysis

Google Forms was used as the survey instrument. Panelists completed voting surveys at two timepoints: before the in-person meeting (January 23–24, 2025) and again after scientific presentations and panel discussions. Panelists were instructed to answer questions under the assumption that all therapies were available with no access restrictions. This analysis uses postmeeting survey responses, reflecting recommendations informed by the in-person scientific exchange. Given the diversity of specialties and expertise among panelists, experts were not mandated to answer every question and were encouraged to respond only within their domain of expertise, ensuring that responses reflected genuine expert judgment. Completion rates were tabulated for each question to assess response patterns and identify areas of uncertainty. Descriptive statistics were used to summarize panelist responses and demographic characteristics. Consensus was defined a priori as ≥75% agreement, with strong consensus defined as >90% agreement.[11] Response patterns were analyzed to identify areas in which expert opinion converged or diverged, providing insights into the strength of available evidence and clinical practice variation.

RESULTS

A listing of all the questions, including premeeting and postmeeting responses to all answer choices, is provided in Table 1 for RCC and in Table 2 for UTC. Consensus recommendations are highlighted in Figure 1.

TABLE 1 Preconference and postconference responses to questions regarding the management of renal cell carcinoma.

	Question	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
A01	For a patient with recently resected pT3bN1 disease (suggesting extension into the vena cava below the diaphragm and regional nodal involvement) with clear cell and sarcomatoid features, would you recommend adjuvant pembrolizumab for 1 year?	No	1	2.1	1	2.2	Yes
		Yes	46	97.9	44	97.8	
		Missing	3	—	4	—	
A02.A	Would you recommend adjuvant pembrolizumab for a patient with clear cell renal cell carcinoma (ccRCC) in the following clinical scenario (assuming the patient is fit and there are no contraindications): pT2 grade 4?	No	13	27.7	9	20.0	Yes
		Yes	34	72.3	36	80.0	
		Missing	3	—	4	—	
A02.B	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications):pT3a (renal sinus or perirenal invasion) grade 1–2?	No	17	37.0	20	45.5	No
		Yes	29	63.0	24	54.5	
		Missing	4	—	5	—	
A02.C	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications): pT3b (renal vein or inferior vena cava invasion) grade 1–2?	No	9	19.6	6	13.3	Yes
		Yes	37	80.4	39	86.7	
		Missing	4	—	4	—	
A02.D	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications): pT3a (renal sinus or perirenal invasion) grade 3–4?	No	3	6.7	2	4.5	Yes
		Yes	42	93.3	42	95.5	
		Missing	5	—	5	—	
A02.E	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications): pT3b (renal vein or inferior vena cava invasion) grade 3–4?	No	1	2.2	2	4.7	Yes
		Yes	45	97.8	41	95.3	
		Missing	4	—	6	—	
A02.F	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications): pT4 any grade?	No	1	2.2	2	4.4	Yes
		Yes	45	97.8	43	95.6	
		Missing	4	—	4	—	
A02.G	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications): pTxN1 any grade?	No	2	4.3	4	9.3	Yes
		Yes	45	95.7	39	90.7	
		Missing	3	—	6	—	
A02.H	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications): pTxNxM1 resected to no evidence of disease within 1 year of nephrectomy?	No	5	10.6	8	18.2	Yes
		Yes	42	89.4	36	81.8	
		Missing	3	—	5	—	
A02.I	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and	No	41	87.2	35	79.5	Yes
		Yes	6	12.8	9	20.5	

TABLE 1 (Continued)

	Question	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
	there are no contraindications): pTxNxM1 resected to no evidence of disease >1 year after nephrectomy?	Missing	3	—	5	—	
A02.J	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications): pTxNxM1 with SBRT to all metastases within 1 year of nephrectomy?	No	20	42.6	15	34.1	No
		Yes	27	57.4	29	65.9	
		Missing	3	—	5	—	
A02.K	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications): pTxNxM1 with SBRT to all metastases >1 year after nephrectomy?	No	46	97.9	37	84.1	Yes
		Yes	1	2.1	7	15.9	
		Missing	3	—	5	—	
A02.L	Would you recommend adjuvant pembrolizumab for a patient with ccRCC in the following clinical scenario (assuming the patient is fit and there are no contraindications): pT2G4, pT3GX, or pTxN1 with positive margins?	No	4	8.7	7	16.3	Yes
		Yes	42	91.3	36	83.7	
		Missing	4	—	6	—	
A03	For an older adult with clinically significant comorbidities that preclude nephrectomy and radiographic evidence of biopsy-proven, nonmetastatic RCC with a primary tumor that appears to be cT3a, initial management would constitute:	Ablation	5	10.6	6	13.3	No
		Observation	8	17.0	6	13.3	
		Stereotactic radiation	28	59.6	33	73.3	
		Systemic therapy	6	12.8	0	0.0	
		Missing	3	—	4	—	
A04	A patient with pT3bN1 ccRCC with sarcomatoid features did not receive adjuvant therapy. Nine months after surgery, he develops an isolated, potentially resectable lung metastasis. Would you recommend:	IO-combination systemic therapy	10	21.3	10	22.2	No
		IO-combination systemic therapy with metastasis directed therapy	7	14.9	7	15.6	
		Stereotactic ablative body radiotherapy alone	5	10.6	5	11.1	
		Stereotactic ablative body radiotherapy with adjuvant pembrolizumab	2	4.3	3	6.7	
		Surgical resection alone	2	4.3	2	4.4	
		Surgical resection with adjuvant pembrolizumab	21	44.7	18	40.0	
		Missing	3	—	4	—	
A05	Germline testing should be considered for which of these patients presenting with locally advanced kidney cancer (select ALL that apply)?	Patient diagnosed at age 45 years	47	97.9	44	97.8	Yes
A05.1		Patient diagnosed at age 50 years	15	31.3	14	31.1	No
A05.2		Patient with a first-degree relative with any histology RCC	37	77.1	38	84.4	Yes
A05.3		Patient with bilateral tumors independent of age	42	87.5	42	93.3	Yes
A05.4		Patient with nonclear cell histology	22	45.8	29	64.4	No
A05.5		Missing	2	—	4	—	

(Continues)

TABLE 1 (Continued)

	Question	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
A06	In a patient with cT3N0M0 renal mass who is fit for surgery, a biopsy should be performed before surgery _____.	Always	2	4.2	2	4.4	Yes
		Never	2	4.2	3	6.7	
		Rarely (<30%)	36	75	34	75.6	
		Usually (>60%)	8	16.7	6	13.3	
		Missing	2	—	4	—	
A07	In a patient with a cT3N0M0 renal mass, a retroperitoneal LN dissection should: (select ALL that apply)	A7.1 Be performed if suspicious LNs are seen preoperatively	28	59.6	29	64.4	No
		A7.2 Be performed if suspicious LNs are seen intraoperatively	35	74.5	26	57.8	
		A7.3 Not be performed	2	4.3	5	11.1	
		A7.4 Always be performed to improve staging	7	14.9	9	20.0	
		Missing	3	—	4	—	
A08	In patients who are eligible for adjuvant therapy, postoperative re-staging of the chest, abdomen, and pelvis should be performed _____ before consideration of adjuvant therapy.	Always	39	83.0	37	82.2	Yes
		Sometimes	1	2.1	3	6.7	
		Very Often	7	14.9	5	11.1	
		Missing	3	—	4	—	
A09	Do you obtain brain imaging in asymptomatic patients at intermediate-high or high risk of recurrence after ?	No	32	69.6	25	55.6	No
		Yes	14	30.4	20	44.4	
		Missing	4	—	4	—	
A10	Nephrectomy for T2N0M0 ccRCC (in an otherwise fit patient) that would render the patient anephric and dialysis-dependent should usually be avoided.	No	7	14.9	8	17.8	Yes
		Yes	40	85.1	37	82.2	
		Missing	3	—	4	—	
A11	In the current era, after surgery for high-risk, nonmetastatic ccRCC, postoperative ctDNA should be checked _____.	Always	1	2.1	1	2.2	No
		Never	19	40.4	18	40.0	
		Rarely	16	34.0	12	26.7	
		Sometimes	8	17.0	12	26.7	
		Very often	3	6.4	2	4.4	
		Missing	3	—	4	—	

TABLE 1 (Continued)

	Question	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
A12	In the current era, after surgery for high-risk, nonmetastatic ccRCC, tumor profiling should be performed _____.	Always	3	6.3	3	6.7	No
		Never	8	16.7	6	13.3	
		Rarely	16	33.3	13	28.9	
		Sometimes	13	27.1	16	35.6	
		Very Often	8	16.7	7	15.6	
		Missing	2	—	4	—	
A13	In the current era, after surgery for high-risk, nonmetastatic non-ccRCC, tumor profiling should be performed _____.	Always	13	27.1	11	24.4	No
		Never	3	6.3	4	8.9	
		Rarely	13	27.1	5	11.1	
		Sometimes	12	25.0	16	35.6	
		Very Often	7	14.6	9	20.0	
		Missing	2	—	4	—	
A14	In the current era, after surgery for high-risk, nonmetastatic ccRCC, a negative ctDNA should _____ influence decisions for adjuvant therapy.	Never	27	57.4	23	52.3	No
		Rarely	14	29.8	12	27.3	
		Sometimes	6	12.8	9	20.5	
		Missing	3	—	5	—	
A15	For a patient with cT2cN0M0 disease and a normal contralateral kidney/no chronic kidney disease, a partial nephrectomy should be performed _____.	Always	7	14.9	7	15.9	No
		Never	3	6.4	2	4.5	
		Rarely	6	12.8	3	6.8	
		Sometimes	12	25.5	15	34.1	
		Very often	19	40.4	17	38.6	
		Missing	3	—	5	—	
A16	For a patient who is nonsyndromic with large, bilateral/multifocal ccRCC (N0M0) who ultimately may lose one or both kidneys, the optimal approach is _____.	Integrated strategy of surgery and ablative techniques without systemic therapy	17	35.4	15	33.3	No
		Neoadjuvant systemic therapy followed by resection or ablative strategies to the extent feasible	18	37.5	19	42.2	
		Perform surgery on both sides (staged vs. together) with or without adjuvant therapy.	11	22.9	10	22.2	
		Systemic therapy alone without surgical or ablative techniques	2	4.2	1	2.2	
		Missing	2	—	4	—	

(Continues)

TABLE 1 (Continued)

	Question	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
B01	For a suspected ccRCC recurrence greater one year from the original nephrectomy, I routinely obtain a biopsy to confirm a diagnosis before starting systemic therapy.	No	10	21.7	7	15.6	Yes
		Yes	36	78.3	38	84.4	
		Missing	4	—	4	—	
B02	For ccRCC, I routinely use PD-L1 testing of the tumor to guide my front-line treatment decision making.	No	47	100.0	45	100.0	Yes
		Missing	3	—	4	—	
B03.A	For a patient who has asymptomatic, metastatic ccRCC with IMDC favorable-risk disease, the most important tumor related factor when opting for active surveillance is: Time to recurrence	1 (most important)	19	42.2	14	32.6	No
		2	10	22.2	11	25.6	
		3	16	35.6	16	37.2	
		4 (least important)			2	4.7	
		Missing	5	—	6	—	
B03.B	For a patient who has asymptomatic mccRCC with IMDC favorable risk disease, the most important tumor related factor when opting for active surveillance is: Specific sites of metastasis (eg, lung, pancreas, liver, and bone).	1 (most important)	7	15.9	7	16.3	No
		2	20	45.5	19	44.2	
		3	17	38.6	15	34.9	
		4 (least important)			2	4.7	
		Missing	6	—	6	—	
B03.C	For a patient who has asymptomatic, metastatic ccRCC with IMDC favorable-risk disease, the most important tumor-related factor when opting for active surveillance is: Burden of disease (low-volume vs. higher volume disease).	1 (most important)	21	46.7	22	51.2	No
		2	16	35.6	13	30.2	
		3	8	17.8	8	18.6	
		Missing	5	—	6	—	
B03.D	For a patient who has asymptomatic, metastatic ccRCC with IMDC favorable-risk disease, the most important tumor-related factor when opting for active surveillance is: molecular testing profile.	3			4	9.3	Yes
		4 (least important)	43	100.0	39	90.7	
		Missing	7	—	6	—	
B04	What defines oligometastatic disease in any histology RCC.	Three or less definitive metastases	23	50.0	26	60.5	No
		Five or less definitive metastases	12	26.1	10	23.3	
		No consensus definition exists.	10	21.7	7	16.3	
		One definitive metastasis	1	2.2	0	0.0	
		Missing	4	—	6	—	

TABLE 1 (Continued)

	Question	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
B05	Local/metastasis-directed therapies should not routinely be used for a single site of recurrence within 6 months of the original nephrectomy.	Agree	21	45.7	17	39.5	No
		Disagree	25	54.3	26	60.5	
		Missing	4	—	6	—	
B06	Local/metastasis-directed therapies should not routinely be used for a single site of recurrence within 12 months of the original nephrectomy.	Agree	11	23.9	9	20.9	Yes
		Disagree	35	76.1	34	79.1	
		Missing	4	—	6	—	
B07	ccRCC with an aggressive underlying biology (e.g., sarcomatoid/rhabdoid histology) and with limited sites of disease should NOT be considered for active surveillance or treated with metastasis directed therapy alone.	False	16	34.0	8	18.6	Yes
		True	31	66.0	35	81.4	
		Missing	3	—	6	—	
B08	For metastatic ccRCC with sarcomatoid differentiation, my preferred systemic therapy is ____.	Any approved anti–PD-1/VEGF combination	3	6.4	3	6.8	Yes
		Nivolumab + ipilimumab	44	93.6	41	93.2	
		Missing	3	—	5	—	
B09	I regard sarcomatoid and rhabdoid differentiation as equivalent and treat ccRCC tumors with each of these features the same.	False	16	34.8	14	33.3	No
		True	30	65.2	28	66.7	
		Missing	4	—	7	—	
B10	If there were no approval/insurance restrictions, I would use the IMDC risk stratification to guide my selection of first-line therapy for metastatic ccRCC.	No	20	43.5	25	59.5	No
		Yes	26	56.5	17	40.5	
		Missing	4	—	7	—	
B11	For most patients with IMDC favorable-risk disease requiring systemic therapy, my typical upfront therapy is _____.	IO + VEGF TKI	27	60.0	21	50.0	No
		Nivolumab + ipilimumab	16	35.6	21	50.0	
		VEGF monotherapy	2	4.4	0	0.0	
		Missing	5	—	7	—	
B12	I accept there is a group of “very favorable-risk” patients (3 years from diagnosis to systemic therapy; KPS >80; no brain, liver, or bone metastasis), which influences my clinical decision making.	False	9	19.6	10	23.8	Yes
		True	37	80.4	32	76.2	
		Missing	4	—	7	—	

(Continues)

TABLE 1 (Continued)

	Question	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
B13	For rapidly progressive and symptomatic, metastatic ccRCC without sarcomatoid or rhabdoid differentiation, my typical upfront systemic therapy regimen is _____.	IO + VEGF TKI	37	80.4	34	81	Yes
		Nivolumab + ipilimumab	8	17.4	6	14.3	
		Nivolumab + ipilimumab + cabozantinib	1	2.2	1	2.4	
		VEGF TKI alone	0	0.0	1	2.4	
		Missing	4	—	7	—	
B14	When I use an IO + VEGF TKI regimen upfront, I typically use _____.	Nivolumab + cabozantinib	20	45.5	18	45.0	No
		Pembrolizumab + axitinib	4	9.1	1	2.5	
		Pembrolizumab + lenvatinib	20	45.5	21	52.5	
		Missing	6	—	9	—	
B15	When I use an IO + VEGF TKI regimen upfront, I typically start the VEGF TKI at the recommended dose.	Agree	42	93.3	41	100.0	Yes
		Disagree	3	6.7	0	0.0	
		Missing	5	—	8	—	
B16	Among the approved IO + VEGF TKIs that you routinely use, do you consider them equivalent in their overall performance or is there a preferred regimen?	No preferred regimen	17	37.8	15	36.6	No
		Preferred regimen, nivolumab + cabozantinib	12	26.7	9	22.0	
		Preferred regimen, pembrolizumab + axitinib	16	35.6	1	2.4	
		Preferred regimen, pembrolizumab + lenvatinib	0	0	16	39	
		Missing	5	—	8	—	
B17	The presence of bone metastasis affects which regimen I will use.	No preferred regimen	19	43.2	17	41.5	No
		Yes, preferred regimen, nivolumab + cabozantinib	24	54.5	20	48.8	
		Yes, preferred regimen, nivolumab + ipilimumab	0	0.0	1	2.4	
		Yes, preferred regimen, pembrolizumab + lenvatinib	1	2.3	3	7.3	
		Missing	6	—	8	—	
B18	The presence of brain metastasis affects which regimen I will use:	No preferred regimen	23	51.1	19	46.3	No
		Yes, preferred regimen, nivolumab + cabozantinib	15	33.3	14	34.1	
		Yes, preferred regimen, nivolumab + ipilimumab	2	4.4	5	12.2	
		Yes, preferred regimen, pembrolizumab + lenvatinib	5	11.1	3	7.3	
		Missing	5	—	8	—	

TABLE 1 (Continued)

	Question	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
B19	A significant subset of patients (>25%) with metastatic ccRCC are cured with current immune checkpoint inhibitor-based therapy.	False	20	42.6	15	35.7	No
		True	27	57.4	27	64.3	
		Missing	3	—	7	—	
B20	In a patient who receives adequate exposure to adjuvant pembrolizumab, is immune checkpoint inhibitor re-challenge in some patients an acceptable practice?	No	10	21.7	3	7.1	Yes
		Yes	36	78.3	39	92.9	
		Missing	4	—	7	—	
B21.A	When would you re-challenge with immune checkpoint inhibitor at relapse after adequate exposure to adjuvant pembrolizumab? Relapse within 0–3 months of starting pembrolizumab?	No	37	82.2	35	85.4	Yes
		Yes	8	17.8	6	14.6	
		Missing	5	—	8	—	
B21.B	When would you re-challenge with immune checkpoint inhibitor at relapse after adequate exposure to adjuvant pembrolizumab? Relapse after 3 months and within 12 months of starting pembrolizumab?	No	35	77.8	28	68.3	No
		Yes	10	22.2	13	31.7	
		Missing	5	—	8	—	
B21.C	When would you re-challenge with immune checkpoint inhibitor at relapse after adequate exposure to adjuvant pembrolizumab? Relapse after 3 months and within 6 months of completing a year of adjuvant pembrolizumab?	No	37	82.2	32	78.0	Yes
		Yes	8	17.8	9	22.0	
		Missing	5	—	8	—	
B21.D	When would you re-challenge with immune checkpoint inhibitor at relapse after adequate exposure to adjuvant pembrolizumab? Relapse after 6 months and within 12 months of completing a year of adjuvant pembrolizumab?	No	24	53.3	14	34.1	No
		Yes	21	46.7	27	65.9	
		Missing	5	—	8	—	
B21.E	When would you re-challenge with immune checkpoint inhibitor at relapse after adequate exposure to adjuvant pembrolizumab? Relapse after 12 months and within 24 months of completing a year of adjuvant pembrolizumab?	No	5	11.1	3	7.3	Yes
		Yes	40	88.9	38	92.7	
		Missing	5	—	8	—	
B21.F	When would you re-challenge with immune checkpoint inhibitor at relapse after adequate exposure to adjuvant pembrolizumab? Relapse >24 months after completing a year of adjuvant pembrolizumab?	No	4	8.9	2	4.9	Yes
		Yes	41	91.1	39	95.1	
		Missing	5	—	8	—	

(Continues)

TABLE 1 (Continued)

	Question	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
B22	Does the IMDC risk score alter your choice of therapy at relapse?	No	29	63.0	30	73.2	No
		Yes	17	37.0	11	26.8	
		Missing	4	—	8	—	
C01	For a patient with IMDC favorable-risk ccRCC treated with axitinib + pembrolizumab with initial radiographic response followed by multisite disease progression after 18 months, what would you recommend as your second line regimen of choice?	Belzutifan	4	8.9	1	2.5	Yes
		Cabozantinib	34	75.6	34	85.0	
		Cabozantinib + nivolumab	2	4.4	1	2.5	
		Ipilimumab + nivolumab	3	6.7	3	7.5	
		Lenvatinib + everolimus	1	2.2	1	2.5	
		Tivozanib	1	2.2	0	0.0	
		Missing	5	—	9	—	
C02	For a patient with IMDC intermediate-risk ccRCC treated with ipilimumab + nivolumab with disease progression as best response, what do you recommend as a next step?	Belzutifan	1	2.2	0	0.0	Yes
		IO + TKI	5	10.9	3	7.5	
		Nivolumab maintenance and reimage in four to 6 weeks	2	4.3	1	2.5	
		TKI monotherapy	38	82.6	36	90.0	
		Missing	4	—	9	—	
C03	For a patient with IMDC intermediate-risk ccRCC treated with ipilimumab + nivolumab with a deep response lasting 18 months and a new solitary liver lesion, what is your next step?	Local therapy and continue nivolumab maintenance	39	86.7	36	85.7	Yes
		Re-dose ipilimumab with the next cycle	1	2.2	1	2.4	
		Switch to IO + TKI	3	6.7	1	2.4	
		Switch to TKI monotherapy	2	4.4	4	9.5	
		Missing	5	—	7	—	
C04	For a patient with IMDC favorable-risk ccRCC treated with TKI monotherapy for 5 years and has subsequent widespread disease progression what is your next choice in therapy?	Alternate TKI monotherapy	1	2.2	1	2.4	No
		IO + TKI therapy	12	26.7	12	29.3	
		Ipilimumab + nivolumab	21	46.7	19	46.3	
		Nivolumab monotherapy	11	24.4	9	22.0	
		Missing	5	—	8	—	

TABLE 1 (Continued)

	Question	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
C05	For a patient with IMDC intermediate-risk ccRCC treated with axitinib + pembrolizumab for 2 years with a response, then pembrolizumab discontinuation at 2 years and subsequent progression after pembrolizumab discontinuation, what is your next step?	Add back pembrolizumab	24	53.3	26	63.4	No
		Switch to belzutifan	2	4.4	2	4.9	
		Switch to cabozantinib monotherapy	18	40.0	13	31.7	
		Switch to lenvatinib + everolimus	1	2.2	0	0.0	
		Missing	5	—	8	—	
C06	A patient with ccRCC is treated in first-line lenvatinib + pembrolizumab and develops grade 4 hepatitis toxicity resulting in need to discontinue pembrolizumab and reduce lenvatinib dose. At the time of progression, what is your next choice in therapy?	Axitinib	5	11.1	2	5.0	No
		Belzutifan	13	28.9	10	25	
		Cabozantinib	23	51.1	23	57.5	
		Nivolumab	0	0.0	1	2.5	
		Tivozanib	4	8.9	4	10.0	
		Missing	5	—	9	—	
C07	A patient with IMDC intermediate-risk ccRCC is treated with cabozantinib + nivolumab for 3 months and experienced widespread progression at first assessment and no dose-limiting toxicity. How do you proceed?	Switch to belzutifan	3	6.7	0	0.0	Yes
		Switch to lenvatinib + everolimus	33	73.3	31	75.6	
		Switch to tivozanib	1	2.2	4	9.8	
		Treat beyond progression	1	2.2	2	4.9	
		Treat beyond progression, but increase cabozantinib dose to 60 mg	7	15.6	4	9.8	
		Missing	5	—	8	—	
C08	A patient with ccRCC was treated with lenvatinib + pembrolizumab as first-line therapy followed by cabozantinib as second-line therapy. What third-line agent would you choose in case of further progression?	Axitinib	3	6.7	1	2.4	Yes
		Belzutifan	35	77.8	34	81.0	
		Tivozanib	7	15.6	7	16.7	
		Missing	5	—	7	—	
C09	In advanced disease, do you usually reserve belzutifan for heavily pretreated patients?	No	20	44.4	15	36.6	No
		Yes	25	55.6	26	63.4	
		Missing	5	—	8	—	

(Continues)

TABLE 1 (Continued)

	Question	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
C10	I would be comfortable offering belzutifan after ipilimumab + nivolumab.	No	22	47.8	21	51.2	No
		Yes	24	52.2	20	48.8	
		Missing	4	—	8	—	
C11	I would be comfortable to offer tivozanib or axitinib or cabozantinib with equal enthusiasm after ipilimumab + nivolumab.	No	26	59.1	21	51.2	No
		Yes	18	40.9	20	48.8	
		Missing	6	—	8	—	
C12	When might you consider ipilimumab + nivolumab after the first line?	Later lines	12	26.7	13	32.5	No
		Never	19	42.2	19	47.5	
		Second line after TKI + IO	9	20.0	3	7.5	
		Third line after TKI + IO followed by TKI	5	11.1	5	12.5	
		Missing	5	—	9	—	
C13	Do you use darbepoetin to treat belzutifan-induced anemia?	No	15	33.3	6	15.4	Yes
		Yes	30	66.7	33	84.6	
		Missing	5	—	10	—	
C14	A patient receiving belzutifan has belzutifan induced hypoxia (to SPO_2 84%). What would you do next?	Arrange for supplemental home oxygen and continue belzutifan at full dose.	2	4.4	2	4.9	Yes
		Discontinue belzutifan permanently.	2	4.4	1	2.4	
		Hold belzutifan and dose reduce when oxygenation improves >92%.	41	91.1	38	92.7	
		Missing	5	—	8	—	
C15	A patient with metastatic ccRCC treated with IO-TKI followed by cabozantinib has baseline COPD requiring inhaler therapy. Would you treat with belzutifan?	No	6	13.3	5	11.9	No
		Yes, start belzutifan at attenuated dose, and have the patient monitor O_2 saturations.	15	33.3	16	38.1	
		Yes, start belzutifan at full dose, and have the patient monitor O_2 saturations.	24	53.3	21	50.0	
		Missing	5	—	7	—	
C16	You have a patient with IMDC poor risk ccRCC receiving first line ipilimumab + nivolumab with response in lung and liver metastases. He develops several new brain metastases. He receives radiotherapy to brain. Which agent would you switch to?	Cabozantinib	15	32.6	16	39.0	No
		I would not change systemic therapy.	29	63.0	24	58.5	
		Lenvatinib + everolimus	2	4.3	1	2.4	
		Missing	4	—	8	—	

TABLE 1 (Continued)

	Question	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
C17	In a patient who has previously progressed on three lines, including IO-containing therapy, what are you most likely to consider in fourth line?	Pursue a TKI the patient has not previously received	44	97.8	39	100	Yes
		Revisit a TKI the patient has received in earlier lines with good effect	1	2.2	0	0.0	
		Missing	5	—	10	—	
C18	In a fit patient pretreated with four different mechanisms of action drugs, which do you offer?	Best supportive care	6	13.3	2	4.9	Yes
		Fifth-line therapy	39	86.7	39	95.1	
		Missing	5	—	8	—	
D01	You have a patient with IMDC poor-risk ccRCC receiving first-line ipilimumab + nivolumab with response in lung and liver metastases. He develops several new brain metastases. He receives radiotherapy to brain. Which agent would you switch to?	No	4	8.5	5	11.6	Yes
		Yes	43	91.5	38	88.4	
		Missing	3	—	6	—	
D02	Which term do you prefer to characterize these tumors?	Nonclear cell	8	17.0	3	7.0	Yes
		The exact histology term, e.g., papillary RCC	39	83.0	39	90.7	
		Variant histology	0	0.0	1	2.3	
		Missing	3	—	6	—	
D03	When managing non-ccRCC, the revised WHO pathology classification of these tumors has helped in my management.	No	22	46.8	20	46.5	No
		Yes	25	53.2	23	53.5	
		Missing	3	—	6	—	
D04	When managing metastatic non-ccRCC, I obtain somatic genomic profiling.	No	6	13.0	5	11.9	Yes
		Yes	40	87.0	37	88.1	
		Missing	4	—	7	—	
D05	When managing metastatic non-ccRCC, my treatment choices differ based on the exact histology.	No	3	6.5	4	9.3	Yes
		Yes	43	93.5	39	90.7	
		Missing	4	—	6	—	
D06	When managing a patient with metastatic non-ccRCC, my threshold for offering local radiation therapy (as opposed to systemic therapy) in relevant situations is _____.	Higher than in ccRCC	19	41.3	16	38.1	No
		Lower than in ccRCC	14	30.4	8	19.0	
		The same as in ccRCC	13	28.3	18	42.9	
		Missing	4	—	7	—	

(Continues)

TABLE 1 (Continued)

	Question	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
D07	When managing a patient with metastatic non-ccRCC, my threshold for offering local surgery (as opposed to systemic therapy) in relevant situations is _____.	Higher than in ccRCC	19	41.3	21	48.8	No
		Lower than in clear cell renal cell carcinoma	13	28.3	10	23.3	
		The same as in clear cell renal cell carcinoma	14	30.4	12	27.9	
		Missing	4	—	6	—	
D08	TKI + IO is a well established standard of care for all nonclear cell histologies outside sarcomatoid de-differentiation.	No	18	39.1	15	35.7	No
		Yes	28	60.9	27	64.3	
		Missing	4	—	7	—	
D09	For a patient with localized, high-risk RCC (meeting entry definitions for KEYNOTE-564 by stage/grade), if the histology was papillary, would you recommend adjuvant pembrolizumab?	No	42	91.3	35	83.3	Yes
		Yes	4	8.7	7	16.7	
		Missing	4	—	7	—	
D10	For a patient with metastatic papillary RCC, what is your preferred option for first-line therapy?	Nivolumab + ipilimumab	4	8.9	6	14.6	No
		VEGF-TKI	6	13.3	7	17.1	
		VEGF-TKI + IO	35	77.8	28	68.3	
		Missing	5	—	8	—	
D11	For a patient with metastatic chromophobe RCC, what is your preferred option for first-line therapy?	Cabozantinib + nivolumab	5	11.1	2	5.0	No
		Lenvatinib + everolimus	14	31.1	7	17.5	
		Lenvatinib + pembrolizumab	23	51.1	29	72.5	
		Nivolumab + ipilimumab	3	6.7	2	5.0	
		Missing	5	—	9	—	
D12	For a patient with metastatic translocation RCC, what is your preferred option for first-line therapy?	Cabozantinib + nivolumab	13	29.5	8	20.0	No
		Lenvatinib + everolimus	1	2.3	2	5.0	
		Lenvatinib + pembrolizumab	25	56.8	25	62.5	
		Nivolumab + ipilimumab	5	11.4	5	12.5	
		Missing	6	—	9	—	
D13	For a patient with metastatic unclassified RCC, what is your preferred option for first-line therapy?	Cabozantinib + nivolumab	13	29.5	9	22.5	No
		Lenvatinib + pembrolizumab	20	45.5	22	55.0	
		Nivolumab + ipilimumab	11	25.0	9	22.5	
		Missing	6	—	9	—	

TABLE 1 (Continued)

	Question	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
D14	For a patient with metastatic collecting RCC, what is your preferred option for first-line therapy?	Cabozantinib + nivolumab	4	8.9	1	2.4	Yes
		Lenvatinib + pembrolizumab	2	4.4	4	9.8	
		Nivolumab + ipilimumab	2	4.4	2	4.9	
		Platinum-based chemotherapy	37	82.2	34	82.9	
		Missing	5	—	8	—	
D15	For a patient with metastatic renal medullary carcinoma, what is your preferred option for first-line therapy?	IO + IO	1	2.2	0	0.0	Yes
		Platinum-based chemotherapy	39	86.7	38	90.5	
		VEGF-TKI + IO	5	11.1	4	9.5	
		Missing	5	—	7	—	
D16	For a patient with metastatic, FH-deficient RCC, what is your preferred option for first-line therapy?	Bevacizumab + erlotinib	18	40.9	17	42.5	No
		Cabozantinib + nivolumab	12	27.3	10	25.0	
		Lenvatinib + pembrolizumab	10	22.7	9	22.5	
		Nivolumab + ipilimumab	4	9.1	4	10.0	
		Missing	6	—	9	—	

Abbreviations: cN, clinical lymph node classification; COPD, chronic obstructive pulmonary disease; cT, clinical tumor classification; ctDNA, circulating tumor DNA; FH, fumarate hydratase; G4, grade 4; GX, any grade; IMDC, International Metastatic RCC Database Consortium; IO, immunotherapy; KPS, Karnofsky performance status; LN, lymph node; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; pT, pathologic tumor classification; SBRT, stereotactic body radiation therapy; SPO_2, peripheral oxygen saturation; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor; WHO, World Health Organization.

TABLE 2 Preconference and postconference responses regarding the management of urinary tract cancer.

	Questions	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
E01	For low-risk bladder cancer (TaLG, < 3 cm), cystoscopy surveillance can be stopped at _____.	5 years	23	62.2	19	54.3	No
		3 years	5	13.5	10	28.6	
		2 years	2	5.4	1	2.9	
		Never	7	18.9	5	14.3	
		Missing	13	—	14	—	
E02	The current best treatment for intermediate-risk NMIBC is _____. Intermediate risk is defined as (1) low-grade tumor that is T1 or >3 cm or multifocal or recurs within 1 year; OR (2) high-grade tumor that is Ta and <3 cm and is solitary.	BCG	23	63.9	20	58.8	No
		Other agent	0	0.0	1	2.9	
		Single agent chemotherapy (gemcitabine, MMC, or other)	13	36.1	13	38.2	
		Missing	14	—	15	—	
E03	For patients unable to tolerate TURBT (for whatever reason), the best management of a low-grade bladder tumor is _____.	Neoadjuvant intravesical chemo-ablation	3	8.3	1	2.9	Yes
		Office-based fulguration	25	69.4	27	77.1	
		Surveillance	8	22.2	7	20.0	
		Missing	14	—	14	—	
E04	The optimal tumor characteristics for a single dose of intravesical therapy after TURBT followed by observation is _____.	<3 cm	15	40.5	8	23.5	No
		Negative cytology	1	2.7	4	11.8	
		No evidence of CIS	13	35.1	16	47.1	
		Solitary tumor	8	21.6	6	17.6	
		Missing	13	—	15	—	
E05	Urinary molecular markers are most useful in NMIBC for _____.	Adjudication of atypical cytology	8	21.6	9	26.5	No
		Alternating with surveillance cystoscopy	3	8.1	2	5.9	
		De-intensification of surveillance	3	8.1	2	5.9	
		I do not use urine molecular markers in NMIBC.	23	62.2	21	61.8	
		Missing	13	—	15	—	
E06	In patients with variant histology, early cystectomy should be offered for the following variant subtypes:	(A) Micropapillary	2	5.4	2	5.9	No
		(B) Plasmacytoid	1	2.7	0	0.0	
		(C) A and B	20	54.1	18	52.9	
		(D) Any subtype	5	13.5	6	17.6	
		(E) Depends on the % of variant histology	9	24.3	8	23.5	
		Missing	13	—	15	—	

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
E07	When possible, blue-light cystoscopy would benefit the best evaluation for NMIBC for _____.	All new tumors	11	28.9	10	29.4	No
		BCG unresponsive tumors	1	2.6	2	5.9	
		Tumors with suspected CIS	11	28.9	11	32.4	
		positive cytology and no visible lesions	15	39.5	11	32.4	
		Missing	12	—	15	—	
E08	In a BCG shortage, switching to other intravesical therapies in a patient with high-risk bladder cancer after 12 months of BCG could include _____.	Dual-agent chemotherapy	17	44.7	22	64.7	No
		New agents (nadofaragene firadenovec, interferon alfa-2b, nogapendekin alfa inbakicept, IL15R agonist)	7	18.4	4	11.8	
		Single-agent chemotherapy	7	18.4	5	14.7	
		Stopping therapy	7	18.4	3	8.8	
		Missing	12	—	15	—	
E09	In a patient with persistent CIS or TaHG after six doses (induction) BCG, the best treatment is _____.	Consider a clinical trial	3	7.9	2	5.9	No
		Cystectomy	10	26.3	3	8.8	
		Reinduction with six doses	13	34.2	14	41.2	
		Switch to another treatment	9	23.7	12	35.3	
		Three more doses	3	7.9	3	8.8	
		Missing	12	—	15	—	
E10	For patients with positive cytology and no evidence of bladder cancer, the best evaluation includes _____.	Blue-light cystoscopy	12	31.6	14	41.2	No
		Mapping bladder biopsies	6	15.8	7	20.6	
		Prostate urethral biopsies	2	5.3	3	8.8	
		Upper tract washings	18	47.4	10	29.4	
		Missing	12	—	15	—	
E11	If LVI is detected on TURBT for NMIBC, what would be your next step?	Abdominal imaging to evaluate for metastasis	10	26.3	15	44.1	No
		Radical cystectomy	3	7.9	3	8.8	
		ctDNA to evaluate for advanced cancer	1	2.6	1	2.9	
		Repeat TURBT	24	63.2	15	44.1	
		Missing	12	—	15	—	

(Continues)

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
E12	When is pembrolizumab the gold-standard treatment for BCG-unresponsive bladder cancer?	After anktiva and/or adstilidrin	2	5.3	4	11.8	No
		BCG unresponsive CIS	18	47.4	10	29.4	
		BCG unresponsive papillary (Ta) with CIS	2	5.3	6	17.6	
		Never	16	42.1	14	41.2	
		Missing	12	—	15	—	
E13	In patients treated with BCG, after a ___ disease-free interval, re-challenge with BCG again is a reasonable next step.	12 months	25	67.6	15	44.1	No
		6 months	8	21.6	15	44.1	
		3 months	3	8.1	2	5.9	
		Never	1	2.7	2	5.9	
		Missing	13	—	15	—	
E14	The choice of BCG-unresponsive treatment should be made based upon the end point of _____.	Cystectomy-free survival	8	21.6	8	23.5	Yes
		Recurrence-free survival	29	78.4	26	76.5	
		Missing	13	—	15	—	
E15	After BCG, the best treatment for BCG unresponsive bladder cancer is _____.	Gemcitabine-docetaxel	22	56.4	25	73.5	No
		Nadoferigene adstilidin	6	15.4	3	8.8	
		Nogapendekin alfa inbakicept-pmln + BCG	4	10.3	1	2.9	
		Pembrolizumab	7	17.9	5	14.7	
		Missing	11	—	15	—	
F01	How do you define locally advanced UC (choose as many as you think appropriate)?	F01.1: cT4b, N0, M0	36	85.7	36	90.0	Yes
		F01.2: cT3b–T4a, N0 M0	24	57.1	23	57.5	
		F01.3: T any, N1–N3, M0	34	81.0	36	90.0	
		F01.4: T any, N any, M1a	10	23.8	11	27.5	
		Missing	8	—	9	—	
F02	Is restaging transurethral resection of bladder tumor (TURBT) in patients with confirmed muscle invasive bladder cancer (MIBC) required?	May be used to assess for complete resection and to perform examination under anesthesia	24	61.5	20	51.3	No
		Never	6	15.4	13	33.3	
		Restaging TURBT is only needed for high-risk MIBC	3	7.7	2	5.1	
		Yes	6	15.4	4	10.3	
		Missing	11	—	10	—	

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
F03	Percutaneous nephrostomy tubes to facilitate neoadjuvant cisplatin-based chemotherapy for MIBC _____.	Are required in patients with MIBC and hydronephrosis but normal renal function before neoadjuvant cisplatin-based chemotherapy	3	7.5	5	13.5	Yes
		Are required in patients who have MIBC with hydronephrosis and elevated creatinine before neoadjuvant cisplatin-based chemotherapy	31	77.5	29	78.4	
		Required in patients who have MIBC with hydronephrosis and elevated creatinine	2	5.0	0	0.0	
		Should not be placed solely to facilitate neoadjuvant cisplatin-based chemotherapy	4	10.0	3	8.1	
		Missing	10	—	12	—	
F04	Ureteral stents are better than percutaneous nephrostomy in patients with elevated creatinine and hydronephrosis from tumor.	No	29	72.5	31	86.1	Yes
		Yes	11	27.5	5	13.9	
		Missing	10	—	13	—	
F05	Neoadjuvant therapy is recommended for eligible patients with MIBC undergoing trimodality therapy.	No	26	63.4	18	46.2	No
		Yes	15	36.6	21	53.8	
		Missing	9	—	10	—	
F06	Adjuvant chemotherapy is recommended for eligible patients with MIBC undergoing trimodality therapy.	No	34	82.9	31	81.6	Yes
		Yes	7	17.1	7	18.4	
		Missing	9	—	11	—	
F07	Trimodality therapy should not be offered to patients with multifocal tumors.	No	22	53.7	21	53.8	No
		Yes	19	46.3	18	46.2	
		Missing	9	—	10	—	
F08	Current standard-of-care neoadjuvant systemic therapy in patients with localized MIBC with adequate renal function is _____.	Cisplatin + gemcitabine + durvalumab	20	48.8	26	66.7	No
		Cisplatin-based combination chemotherapy	13	31.7	10	25.6	
		Dose-dense MVAC (methotrexate, vinblastine, doxorubicin, and cisplatin)	8	19.5	3	7.7	
		Missing	9	—	10	—	
F09	Split-dose neoadjuvant cisplatin should be offered as treatment for patients with creatinine clearance of 40–60 mL/minute.	No	2	5.0	2	5.1	Yes
		Yes	38	95.0	37	94.9	
		Missing	10	—	10	—	

(Continues)

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
F10	For patients with lymph node (LN)-positive (cN-positive, N1 [metastasis a single LN <2 cm in greatest dimension] or N2 [metastasis to a single LN 2–5 cm or multiple LNs all <5 cm]) UC, what is the optimal treatment prior to surgical consolidation or radiotherapy?	Initial systemic therapy with enfortumab vedotin (EV) + pembrolizumab	28	73.7	25	62.5	No
		Initial systemic therapy with gemcitabine + cisplatin + nivolumab	7	18.4	14	35.0	
		Systemic therapy alone and no consolidation therapy	3	7.9	1	2.5	
		Missing	12	—	9	—	
F11	For patients with cN3 (metastasis to LN >5 cm in greatest dimension), LN-positive disease, what is the optimal treatment before surgical consolidation or radiotherapy?	Initial systemic therapy with EV + pembrolizumab	30	76.9	30	76.9	Yes
		Initial systemic therapy with gemcitabine + cisplatin + nivolumab	3	7.7	5	12.8	
		Systemic therapy alone	6	15.4	4	10.3	
		Missing	11	—	10	—	
F12	For patients with LN-positive (cN-positive, N1 metastasis [single LN <2 cm in greatest dimension] or N2 [metastasis to a single LN 2–5 cm or multiple LNs all <5 cm]) UC, what is the optimal consolidative local therapy?	Radiotherapy	11	28.9	9	22.5	Yes
		Surgery	27	71.1	31	77.5	
		Missing	12	—	9	—	
F13	Lymphadenectomy at the time of radical cystectomy in a clinically node negative patient should _____.	Always follow a standard template	31	77.5	32	82.1	Yes
		Always follow an extended template	3	7.5	1	2.6	
		Yield at least 10 LNs	6	15.0	6	15.4	
		Missing	10	—	10	—	
F14	Lymphadenectomy at the time of radical cystectomy in a clinically node positive patient should _____.	Always follow a standard template	12	30.8	12	30.8	No
		Always follow an extended template	19	48.7	14	35.9	
		Resect all previously involved nodes if safe and feasible	8	20.5	13	33.3	
		Missing	11	—	10	—	
F15	Do you use ctDNA testing for minimal residual disease determination to guide adjuvant therapy after radical surgery for patients with UC?	For all patients	4	10.3	5	12.8	No
		For some patients	16	41.0	13	33.3	
		I do not order this test.	12	30.8	11	28.2	
		I order this test but do not use it to guide therapy selection.	7	17.9	10	25.6	
		Missing	11	—	10	—	
F16	If ctDNA testing is ordered, do you only administer therapy if it is positive regardless of the stage at surgery?	No	31	81.6	30	81.1	Yes
		Yes	7	18.4	7	18.9	
		Missing	12	—	12	—	

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
F17	In patients who have upper tract UC (UTUC) and high-risk disease after extirpative surgery without prior neoadjuvant chemotherapy, what is the most appropriate adjuvant therapy?	Adjuvant chemotherapy (cisplatin or carboplatin-based)	24	61.5	22	57.9	No
		Adjuvant cisplatin-based chemotherapy should be used for cisplatin-eligible patients and adjuvant nivolumab should be used for cisplatin-ineligible patients.	13	33.3	12	31.6	
		Adjuvant nivolumab	2	5.1	4	10.5	
		Missing	11	—	11	—	
F18	Should patients with UTUC receive neoadjuvant or adjuvant therapy?	Adjuvant therapy for high-risk disease after extirpative surgery	3	7.7	10	25.0	No
		Neoadjuvant therapy is the preferred approach for most patients with high grade UTUC.	13	33.3	12	30.0	
		The choice between neoadjuvant and adjuvant therapy for UTUC depends on individual factors (i.e., renal function, comorbidity)	23	59.0	18	45.0	
		Missing	11	—	9	—	
F19	For patients with pT3–pT4 or pN-positive disease after radical cystectomy who did not receive prior neoadjuvant cisplatin-based chemotherapy and have good renal function, the best next step is _____.	(A) Adjuvant cisplatin-based chemotherapy	16	40.0	18	45.0	No
		(B) Adjuvant nivolumab	10	25.0	6	15.0	
		(C) Surveillance only	0	0.0	1	2.5	
		(D) A or B	14	35.0	15	37.5	
		Missing	10	—	9	—	
F20	For patients with ypT2–ypT4 or ypN-positive disease after radical cystectomy who received prior neoadjuvant cisplatin-based chemotherapy, the best next step is _____.	(B) Adjuvant nivolumab	22	55.0	24	60.0	No
		(D) Surveillance only	1	2.5	2	5.0	
		(E) A or B	1	2.5	1	2.5	
		(F) B or C	16	40.0	13	32.5	
		Missing	10	—	9	—	
F21	For patients with muscle-invasive (cT2–cT4, N0–N2) plasmacytoid UC, what front-line treatment would you recommend (assume renal function is normal)?	Neoadjuvant cisplatin + gemcitabine + durvalumab	8	20.0	8	20.5	No
		Neoadjuvant cisplatin-based chemotherapy	13	32.5	14	35.9	
		Neoadjuvant EV + pembrolizumab	5	12.5	4	10.3	
		Neoadjuvant immunotherapy	0		1	2.6	
		Upfront radical cystectomy with lymphadenectomy if deemed resectable	14	35.0	12	30.8	
		Missing	10	—	10	—	

(Continues)

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
F22	For patients with muscle-invasive (cT2–cT4, N0–N2) sarcomatoid UC, what front-line treatment would you recommend (assume renal function is normal)?	Neoadjuvant cisplatin + gemcitabine + durvalumab	12	30.0	14	35.9	No
		Neoadjuvant cisplatin-based chemotherapy	8	20.0	9	23.1	
		Neoadjuvant EV + pembrolizumab	6	15.0	4	10.3	
		Neoadjuvant immunotherapy			2	5.1	
		Upfront radical cystectomy with lymphadenectomy if deemed resectable	14	35.0	10	25.6	
		Missing	10	—	10	—	
F23	For patients with muscle-invasive (cT2–cT4, N0–N2) micropapillary UC, what front-line treatment would you recommend (assume renal function is normal)?	Neoadjuvant cisplatin + gemcitabine + durvalumab	10	25.0	14	35.9	No
		Neoadjuvant cisplatin-based chemotherapy	16	40.0	15	38.5	
		Neoadjuvant EV + pembrolizumab	4	10.0	2	5.1	
		Neoadjuvant immunotherapy			1	2.6	
		Upfront radical cystectomy with lymphadenectomy if deemed resectable	10	25.0	7	17.9	
		Missing	10	—	10	—	
F24	For patients with invasive (cT2–cT4, N0–N2), pure squamous histology, what front-line treatment would you recommend (assume renal function is normal)?	Chemoradiation with chemotherapy regimen extrapolated from other disease paradigms			1	2.6	Yes
		Neoadjuvant chemotherapy regimen extrapolated from other disease paradigms	4	10.0	1	2.6	
		Neoadjuvant cisplatin-based chemotherapy	4	10.0	4	10.5	
		Neoadjuvant EV + pembrolizumab	1	2.5	2	5.3	
		Neoadjuvant immunotherapy			1	2.6	
		Upfront radical cystectomy with lymphadenectomy if deemed resectable	31	77.5	29	76.3	
		Missing	10	—	11	—	
F25	For patients with invasive (cT2–cT4, N0–N2) pure adenocarcinoma histology, what front-line treatment would you recommend (assume renal function is normal)?	Chemoradiation with chemotherapy regimen extrapolated from other disease paradigms			1	2.6	No
		Neoadjuvant chemotherapy regimen extrapolated from other disease paradigms	7	17.5	9	23.1	
		Neoadjuvant immunotherapy	2	5.0	1	2.6	
		Upfront radical cystectomy with lymphadenectomy if deemed resectable	31	77.5	28	71.8	
		Missing	10	—	10	—	
F26	For patients with invasive (cT2–cT4, N0–N2) pure small cell histology, what front-line treatment would you recommend (assume renal function is normal)?	Chemoradiation with chemotherapy regimen extrapolated from other disease paradigms	7	17.5	6	15.4	No

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
		Neoadjuvant chemotherapy regimen extrapolated from other disease paradigms	18	45.0	25	64.1	
		Neoadjuvant cisplatin-based chemotherapy	14	35.0	6	15.4	
		Neoadjuvant immunotherapy			1	2.6	
		Upfront radical cystectomy with lymphadenectomy if deemed resectable	1	2.5	1	2.6	
		Missing	10	—	10	—	
G01	Is platinum-based combination followed by switch maintenance avelumab a proper comparator control in randomized clinical trials?	No, it is not acceptable.	10	26.3	12	32.4	No
		Yes, but only in countries with no access to EV + pembrolizumab.	21	55.3	19	51.4	
		Yes, it is an acceptable option.	7	18.4	6	16.2	
		Missing	12	—	12	—	
G02	Cisplatin is a better partner for PD(L)-1 inhibition than carboplatin.	No, either platinum agent could be combined.	3	7.9	5	13.9	Yes
		Yes, based on available preclinical and clinical data	35	92.1	31	86.1	
		Missing	12	—	13	—	
G03	Are patient-reported outcomes and quality of life data relevant to therapy selection in the frontline setting?	No, such data are not able to differentiate between systemic therapy options.	5	13.2	7	17.9	No
		Yes, but only between regimens with similar efficacy.	17	44.7	20	51.3	
		Yes, such data are crucial for individual patient decision making.	16	42.1	12	30.8	
		Missing	12	—	10	—	
G04	What is the perception of continued pembrolizumab after discontinuation of EV when EV + pembrolizumab combination is used?	It has a major role driving progression-free survival and overall survival.	27	71.1	24	66.7	No
		It has a minor role; benefit is mainly driven from its concurrent administration with EV.	11	28.9	12	33.3	
		Missing	12	—	13	—	
G05	If a patient has received prior immune checkpoint inhibition (ICI) therapy in the localized or adjuvant setting, what is the first-line treatment recommendation?	EV + pembrolizumab only if there was no progression during prior ICI therapy	4	10.5	3	8.3	No
		EV + pembrolizumab only if there was progression 12 months after last ICI therapy dose	7	18.4	4	11.1	
		EV + pembrolizumab only if there was progression 3 months after last ICI therapy dose	2	5.3	5	13.9	
		EV + pembrolizumab only if there was progression = 6 months after last ICI therapy dose	14	36.8	14	38.9	

(Continues)

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
		EV + pembrolizumab regardless of timing of progression	9	23.7	9	25	
		EV + pembrolizumab should not be used in patients who had received prior ICI.	2	5.3	1	2.8	
		Missing	12	—	13	—	
G06	Should the presence of divergent histologic subtypes (pure or mixed with conventional urothelial histology) affect treatment recommendations for metastatic disease?	Histologic subtypes should be treated the same way as conventional urothelial histology.	5	12.8	7	18.4	No
		Histologic subtypes should be treated the same way as conventional urothelial histology as long as they are mixed (any %) with conventional urothelial histology	19	48.7	18	47.4	
		Histologic subtypes should be treated the same way as conventional urothelial histology as long as they represent a minority component (<50%).	15	38.5	13	34.2	
		Missing	11	—	11	—	
G07	Should small cell (high-grade neuroendocrine) UC be treated with a small cell carcinoma regimen regardless of the percentage of small cell?	No	6	15.4	5	13.5	Yes
		Yes	33	84.6	32	86.5	
		Missing	11	—	12	—	
G08	In patients who receive EV and pembrolizumab, _____.	EV should be continued until progression or unacceptable toxicity with dose adjustments as needed.	33	86.8	31	86.1	Yes
		EV should be used for a 'fixed' duration and then continue pembrolizumab monotherapy.	4	10.5	5	13.9	
		Plasma ctDNA is used to determine when to discontinue EV.	1	2.6			
		Missing	12	—	13	—	
G09	If EV + pembrolizumab moves to perioperative therapy, which frontline therapy would you use if patients rapidly relapse with metastatic disease (during therapy or shortly after)?	Cisplatin + gemcitabine + nivolumab in cisplatin-eligible patients	6	15.8	10	27.8	No
		Erdafitinib or T-DXd influenced by next-generation sequencing (NGS)/IHC	5	13.2	4	11.1	
		Platinum-based chemotherapy then switch maintenance avelumab	3	7.9	4	11.1	
		Platinum-based chemotherapy with no immune checkpoint inhibition	24	63.2	18	50.0	
		Missing	12	—	13	—	
G10	In situations without access to EV + pembrolizumab, which regimen is the preferred approach in cisplatin-eligible patients?	Cisplatin + gemcitabine + nivolumab	33	86.8	33	89.2	Yes
		Cisplatin-based chemotherapy followed by switch maintenance avelumab	5	13.2	4	10.8	
		Missing	12	—	12	—	

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
G11	Is chronic grade 2 peripheral neuropathy a contraindication for EV in your practice?	No	13	35.1	12	33.3	No
		Yes	24	64.9	24	66.7	
		Missing	13	—	13	—	
G12	Is uncontrolled diabetes mellitus (based on HbA1c level and/or symptoms) a contraindication for EV in your practice?	No	20	52.6	25	69.4	No
		Yes	18	47.4	11	30.6	
		Missing	12	—	13	—	
G13	Is cirrhosis liver dysfunction a contraindication for EV in your practice?	No	17	45.9	17	47.2	No
		Yes	20	54.1	19	52.8	
		Missing	13	—	13	—	
G14	What is the bilirubin cutoff to avoid using EV?	1.3 times ULN	1	2.7	2	5.6	No
		1.5 times ULN	22	59.5	19	52.8	
		2.0 times ULN	14	37.8	15	41.7	
		Missing	13	—	13	—	
G15	Do you wait for results of tumor NGS before you start frontline systemic therapy?	No, NGS results may affect only subsequent therapies (second line and beyond)	38	100.0	36	94.7	Yes
		Yes, NGS result may affect frontline therapy decision	0		2	5.3	
		Missing	12	—	11	—	
G16	When a patient receiving EV + pembrolizumab presents with mild neuropathy (sensory changes only) not interfering with activities of daily living, what is the optimal first maneuver?	Continue EV at same dose	13	35.1	10	27.0	No
		Hold EV and resume at same dose when neuropathy resolves	6	16.2	4	10.8	
		Hold EV and resume with one dose level reduction	18	48.6	23	62.2	
		Missing	13	—	12	—	
G17	When a patient receiving EV + pembrolizumab begins to notice changes with proprioception and balance, would you recommend physical therapy in addition to holding/reducing dose?	No	3	7.9	3	8.1	Yes
		Yes	35	92.1	34	91.9	
		Missing	12	—	12	—	
G18	When are oral steroids indicated with rash associated with EV + pembrolizumab (not blistering and not involving mucosa)?	At the first sign of grade 2 rash	7	18.9	13	36.1	No
		At the first sign of grade 3 rash	13	35.1	7	19.4	
		When high-potency topical steroids fail to control the rash after 7 days	17	45.9	16	44.4	
		Missing	13	—	13	—	

(Continues)

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
H01	For a cisplatin-ineligible patient with metastatic UC, after progression while on EV + pembrolizumab, what would be your next-line regimen in a biomarker-negative (*FGFR3*, HER2) patient eligible for aggressive therapy?	Platinum combination	29	76.3	32	91.4	Yes
		Sacituzumab govitecan	4	10.5	2	5.7	
		Taxane-based therapy	5	13.2	1	2.9	
		Missing	12	—	14	—	
H02	For a cisplatin-eligible patient with metastatic UC, after progression while on EV + pembrolizumab, what would be your next-line regimen in a biomarker-negative (*FGFR3*, HER2) patient eligible for aggressive therapy?	Cisplatin-gemcitabine-nivolumab	6	15.8	6	16.7	Yes
		Platinum combination	29	76.3	29	80.6	
		Sacituzumab govitecan	3	7.9	1	2.8	
		Missing	12	—	13	—	
H03	A cisplatin-ineligible patient with metastatic UC was treated with EV + pembrolizumab and developed peripheral neuropathy requiring discontinuing EV. He has progression and persistent grade 1 peripheral neuropathy. What would be your next-line regimen if he was biomarker-negative?	Platinum combination	18	47.4	24	66.7	No
		Re-institute EV, continue pembrolizumab	15	39.5	10	27.8	
		Sacituzumab govitecan	4	10.5	2	5.6	
		Taxane-based therapy	1	2.6	0		
		Missing	12	—	13	—	
H04	For a cisplatin-eligible patient with metastatic UC after progression on EV + pembrolizumab, what would be your next-line regimen in a biomarker-negative patient eligible for aggressive therapy with grade 1 neuropathy and in the absence of trials?	Cisplatin-gemcitabine-nivolumab	6	15.8	5	13.9	Yes
		Platinum combination	28	73.7	29	80.6	
		Sacituzumab govitecan	4	10.5	1	2.8	
		Taxane-based therapy			1	2.8	
		Missing	12	—	13	—	
H05	In a patient who has metastatic UC and is progressing after EV + pembrolizumab with HER2 IHC 3+, what is your preferred second-line therapy?	Platinum-combination	14	36.8	12	33.3	No
		Trastuzumab deruxtecan	24	63.2	24	66.7	
		Missing	12	—	13	—	
H06	In a patient who has metastatic UC and is progressing after EV + pembrolizumab with *FGFR3* mutation, what is your preferred second-line therapy?	Erdafitinib	27	71.1	24	66.7	No
		Gemcitabine-platinum	11	28.9	12	33.3	
		Missing	12	—	13	—	
H07	In a patients who has metastatic UC and is progressing after EV + pembrolizumab with both HER2 IHC 3+ and an *FGFR3* mutation, what is your preferred second-line therapy?	Erdafitinib	12	31.6	11	30.6	No
		Gemcitabine-platinum	9	23.7	10	27.8	
		Sacituzumab govitecan			1	2.8	
		Trastuzumab deruxtecan	17	44.7	14	38.9	
		Missing	12	—	13	—	

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
H08	For a fit patient with metastatic UC, after progression on cisplatin + gemcitabine followed by maintenance avelumab and is biomarker-negative (*FGFR3*, HER2), what is your next-line regimen?	EV	23	60.5	23	63.9	No
		EV + pembrolizumab	15	39.5	13	36.1	
		Missing	12	—	13	—	
H09	For a fit patient with metastatic UC, after progression on cisplatin + gemcitabine followed by maintenance avelumab with an *FGFR3* mutation, what would be your next-line regimen?	EV	12	31.6	18	50.0	No
		EV + pembrolizumab	10	26.3	8	22.2	
		Erdafitinib	16	42.1	10	27.8	
		Missing	12	—	13	—	
H10	For a fit patient with metastatic UC, after progression on cisplatin + gemcitabine followed by maintenance avelumab with HER2 IHC 3+, what would be your next-line regimen?	EV	17	44.7	18	50.0	No
		EV + pembrolizumab	8	21.1	9	25.0	
		Sacituzumab govitecan	1	2.6	0		
		Trastuzumab deruxtecan	12	31.6	9	25.0	
		Missing	12	—	13	—	
H11	For a platinum-ineligible patient with metastatic UC who is biomarker-negative (HER2, *FGFR3*), after progression on pembrolizumab single-agent, first-line therapy, what would be your next-line regimen?	EV	28	75.7	27	75.0	Yes
		EV + pembrolizumab	6	16.2	7	19.4	
		Platinum-combination	3	8.1	2	5.6	
		Missing	13	—	13	—	
H12	For a platinum-ineligible patient with metastatic UC who is *FGFR3* mutation-positive, after progression on prior single-agent pembrolizumab, what would be your next-line regimen?	EV	16	42.1	20	55.6	No
		EV + pembrolizumab	5	13.2	4	11.1	
		Erdafitinib	17	44.7	12	33.3	
		Missing	12	—	13	—	
H13	For a platinum-ineligible patient with metastatic UC who is HER2 IHC 3+, after progression on pembrolizumab single-agent, first-line therapy, what would be your next-line regimen?	EV	24	63.2	17	48.6	No
		EV + pembrolizumab	6	15.8	3	8.6	
		Platinum-combination	1	2.6	2	5.7	
		Trastuzumab deruxtecan	7	18.4	13	37.1	
		Missing	12	—	14	—	
H14	For a platinum-ineligible patient with metastatic UC who is *FGFR3* mutation-positive and is HER2 IHC 3+, after progression on first-line pembrolizumab, what would be your next-line regimen in a patient now eligible for chemotherapy?	EV	14	37.8	14	38.9	No
		EV + pembrolizumab	4	10.8	3	8.3	
		Erdafitinib	8	21.6	2	5.6	

(Continues)

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
		Platinum-combination	6	16.2	6	16.7	
		Trastuzumab deruxtecan	5	13.5	11	30.6	
		Missing	13	—	13	—	
H15	In a patient with metastatic UC who is post-EV + pembrolizumab as well as platinum combination therapy and both HER2 IHC 3+ and *FGFR3* mutation-positive, what is your preferred choice?	Erdafitinib	21	55.3	12	33.3	No
		Trastuzumab deruxtecan	17	44.7	24	66.7	
		Missing	12	—	13	—	
H16	In a patient with metastatic UC and HER2 IHC 3+, when do you treat with trastuzumab deruxtecan?	As fourth-line treatment after EV + pembrolizumab, platinum-based chemotherapy, and sacituzumab govitecan	1	2.6			No
		As second-line treatment after EV + pembrolizumab	13	34.2	15	41.7	
		As third-line treatment after EV + pembrolizumab and platinum-based chemotherapy	24	63.2	21	58.3	
		Missing	12	—	13	—	
H17	In a patient with metastatic UC and an *FGFR3* mutation, when do you treat with erdafitanib?	As second-line treatment after EV + pembrolizumab	14	36.8	13	37.1	No
		As third-line treatment after EV + pembrolizumab and platinum-based chemotherapy	24	63.2	22	62.9	
		Missing	12	—	14	—	
H18	In those with cisplatin-ineligible, metastatic UC progressing after adjuvant nivolumab, I will institute _____.	Biomarker-guided (T-DXd, erdafitinib)			2	5.6	No
		EV	6	15.8	6	16.7	
		EV + pembrolizumab	16	42.1	8	22.2	
		EV if progressing on or within 3–6 months of last nivolumab; otherwise, EV + pembrolizumab	14	36.8	16	44.4	
		Gemcitabine + carboplatin (or split dose cisplatin-gemcitabine)	2	5.3	4	11.1	
		Missing	12	—	13	—	
H19	Should sacituzumab govitecan continue to have a role in cancer treatment guidelines for UC?	No	17	44.7	11	31.4	No
		Yes	21	55.3	24	68.6	
		Missing	12	—	14	—	
I01	In a patient with advanced UC, what age do you consider as a contraindication to offering first-line EV and pembrolizumab?	85 years			2	5.6	Yes
		I do not consider any age threshold as a contraindication.	38	100.0	34	94.4	
		Missing	12	—	13	—	

TABLE 2 (Continued)

	Questions	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
I02	In older patients, do you start treatment with a lower dose of EV?	No, I offer full dose EV (1.25 mg/kg).	26	68.4	21	61.8	No
		Yes, I start with lower dose EV (0.75 mg/kg).	2	5.3	2	5.9	
		Yes, I start with lower dose EV (1 mg/kg).	10	26.3	11	32.4	
		Missing	12	—	15	—	
I03	In a frail patient with ECOG performance status of 3, what first-line treatment will you offer?	Best supportive care/hospice	11	28.9	8	24.2	No
		Enfortumab-vedotin and pembrolizumab	15	39.5	15	45.5	
		Gemcitabine-carboplatin followed by avelumab	1	2.6	1	3.0	
		Single-agent pembrolizumab	11	28.9	9	27.3	
		Missing	12	—	16	—	
I04	For a patient who has metastatic UC with predominant squamous cell carcinoma and is ineligible to receive cisplatin, what is the preferred first-line treatment?	EV and pembrolizumab	27	73.0	25	71.4	No
		Gemcitabine-carboplatin followed by avelumab maintenance	10	27.0	10	28.6	
		Missing	13	—	14	—	
I05	For a patient who has metastatic UC with predominant squamous cell carcinoma and is eligible to receive cisplatin, what is the preferred first-line treatment?	EV and pembrolizumab	23	62.2	24	68.6	No
		Gemcitabine-cisplatin and nivolumab	11	29.7	8	22.9	
		Gemcitabine-cisplatin followed by avelumab maintenance	3	8.1	3	8.6	
		Missing	13	—	14	—	
I06	For a patient who has metastatic UC with predominant sarcomatoid histology and is eligible to receive cisplatin, what is the preferred first-line treatment?	EV and pembrolizumab	30	78.9	25	71.4	No
		Gemcitabine-cisplatin and Nivolumab	6	15.8	9	25.7	
		Gemcitabine-cisplatin followed by avelumab maintenance	2	5.3	1	2.9	
		Missing	12	—	14	—	
I07	For a patient who has metastatic UC with predominant sarcomatoid histology and is ineligible to receive cisplatin, what is your preferred first-line treatment?	EV and pembrolizumab	35	94.6	32	91.4	Yes
		Gemcitabine-carboplatin followed by avelumab maintenance	2	5.4	3	8.6	
		Missing	13	—	14	—	
I08	For a patient who has metastatic UC with predominant plasmacytoid histology and is eligible to receive cisplatin, what is your preferred first-line treatment?	EV and pembrolizumab	29	76.3	28	80.0	Yes
		Gemcitabine-cisplatin and Nivolumab	6	15.8	7	20.0	
		Gemcitabine-cisplatin followed by avelumab maintenance	3	7.9			
		Missing	12	—	14	—	

(Continues)

TABLE 2 (Continued)

	Questions	Response	Preconference No.	Preconference %	Postconference No.	Postconference %	Consensus reached
I09	For a patient who has metastatic UC with predominant plasmacytoid histology and is ineligible to receive cisplatin, what is your preferred first-line treatment?	EV and pembrolizumab	35	92.1	32	91.4	Yes
		Gemcitabine-carboplatin followed by avelumab maintenance	3	7.9	3	8.6	
		Missing	12	—	14	—	
I10	For a patient with metastatic small cell neuroendocrine UC who is eligible to receive cisplatin, what is your preferred first-line treatment?	Cisplatin-etoposide	13	34.2	12	34.3	No
		Cisplatin-etoposide and durvalumab or atezolizumab	20	52.6	20	57.1	
		EV and pembrolizumab	1	2.6	1	2.9	
		Gemcitabine-cisplatin followed by avelumab maintenance	1	2.6			
		Ifosfamide + doxorubicin alternating with etoposide + cisplatin	3	7.9	2	5.7	
		Missing	12	—	14	—	
I11	For a patient who has metastatic UC with small cell neuroendocrine histology and is ineligible to receive cisplatin, what is your preferred first-line treatment?	Carboplatin-etoposide	14	36.8	11	32.4	No
		Carboplatin-etoposide and atezolizumab or durvalumab	20	52.6	19	55.9	
		EV and pembrolizumab	2	5.3	3	8.8	
		Gemcitabine-carboplatin followed by avelumab maintenance	2	5.3	1	2.9	
		Missing	12	—	15	—	
I12	For a patient who has metastatic UC with predominant micropapillary histology and is eligible to receive cisplatin, what is your preferred first-line treatment?	EV and pembrolizumab	30	78.9	29	82.9	No
		Gemcitabine-cisplatin and nivolumab	5	13.2	5	14.3	
		Gemcitabine-cisplatin followed by avelumab maintenance	3	7.9	1	2.9	
		Missing	12	—	14	—	
I13	For a patient who has metastatic UC with predominant micropapillary histology and is ineligible to receive cisplatin, what is your preferred first-line treatment?	EV and pembrolizumab	36	94.7	33	94.3	Yes
		Gemcitabine-carboplatin followed by avelumab maintenance	2	5.3	2	5.7	
		Missing	12	—	14	—	
I14	What is the recommended therapy for metastatic mucinous adenocarcinoma representing a primary bladder/urachal adenocarcinoma?	FOLFIRINOX (leucovorin calcium [folinic acid], fluorouracil, irinotecan, and oxaliplatin)	12	31.6	11	32.4	No
		FOLFOX (leucovorin calcium [folinic acid], fluorouracil, and oxaliplatin)	23	60.5	21	61.8	
		Gemcitabine, 5-fluorouracil, leucovorin, and cisplatin	3	7.9	2	5.9	
		Missing	12	—	15	—	

TABLE 2 (Continued)

	Questions	Response	Preconference		Postconference		Consensus reached
			No.	%	No.	%	
I15	What is the optimal therapy for invasive squamous cell carcinoma metastatic to distant LNs?	EV and pembrolizumab	9	25.7	8	25.0	No
		Gemcitabine and platinum	7	20.0	7	21.9	
		Ifosfamide, paclitaxel, and platinum	10	28.6	8	25.0	
		Platinum, paclitaxel, gemcitabine	9	25.7	9	28.1	
		Missing	15	—	17	—	
I16	In a patient with metastatic UC with HgbA1C >8%, would you offer EV and pembrolizumab treatment?	No, I will start platinum-based chemotherapy.	5	13.2	2	5.9	Yes
		Yes, I will offer EV and pembrolizumab without waiting for HbA1c to be <8%, with referral to endocrine to intensify treatment for diabetes mellitus.	33	86.8	32	94.1	
		Missing	12	—	15	—	
I17	In a patient with newly diagnosed, metastatic UC and a creatinine clearance < 30 mL/minute, what first-line treatment will you offer?	EV and pembrolizumab	32	84.2	32	94.1	Yes
		Gemcitabine-carboplatin followed by avelumab	3	7.9	2	5.9	
		Single-agent pembrolizumab	3	7.9			
		Missing	12	—	15	—	
I18	In a patient on hemodialysis with metastatic UC, what first-line treatment will you offer?	EV and pembrolizumab	31	81.6	31	91.2	Yes
		Gemcitabine-cisplatin and nivolumab			1	2.9	
		Gemcitabine-cisplatin followed by avelumab	1	2.6	1	2.9	
		Single-agent pembrolizumab	6	15.8	1	2.9	
		Missing	12	—	15	—	
I19	On the day of treatment, a patient has a glucose of >300 mg/dl. Do you still give EV?	No, I will hold EV and delay treatment until blood glucose is better controlled.	34	89.5	25	73.5	No
		Yes, I will administer EV along with insulin.	4	10.5	9	26.5	
		Missing	12	—	15	—	

Abbreviations: BCG, Bacillus Calmette–Guerin; CIS, carcinoma in situ; cN, clinical lymph node classification; cT, clinical tumor classification; ctDNA, circulating tumor DNA; ECOG, Eastern Cooperative Oncology Group; FGFR3, fibroblast growth factor receptor 3; HbA1c, hemoglobin A1C; HER2, human epidermal growth factor 2; IL-15R, interleukin 15 receptor; LVI, lymphovascular invasion; MMC, mitomycin C; pN, pathologic lymph node classification; pT, pathologic tumor classification; TaHG, high-grade Ta tumor; TaLG, low-grade Ta tumor; T-DXd, trastuzumab deruxtecan; ULN, upper limit of normal; ypN, pathologic lymph node classification after neoadjuvant therapy; ypT, pathologic tumor classification after neoadjuvant therapy.

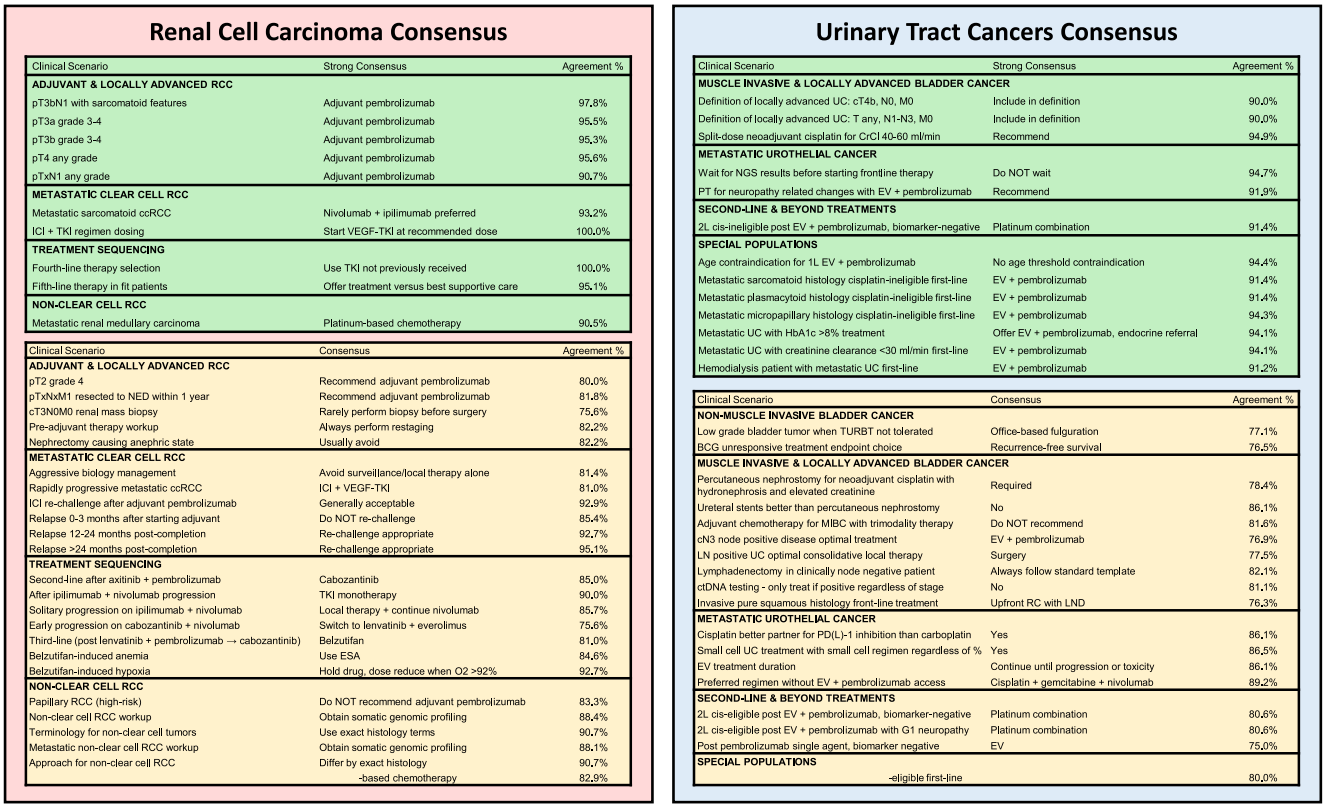

FIGURE 1 Consensus recommendations for renal cell carcinoma and urinary tract cancers. 2L indicates second line; BCG, Bacillus Calmette–Guerin; ccRCC, clear cell renal cell carcinoma; CrCl, creatinine clearance; cN, clinical lymph node classification; cT, clinical tumor classification; ctDNA, circulating tumor DNA; ESA, erythropoietin-stimulating agent; EV, enfortumab vedotin; G1, grade 1; ICI, immune checkpoint inhibitor; LN, lymph node; LND, lymph node dissection; MIBC, muscle-invasive bladder cancer; NED, no evidence of disease; NGS, next-generation sequencing; PD(L)-1, programmed death (ligand)-1; pT, pathologic tumor classification; PT, physical therapy; RC, radical cystectomy; RCC, renal cell carcinoma; TKI, tyrosine kinase inhibitor; TURBT, transurethral resection of bladder tumor; UC, urothelial carcinoma; VEGF, vascular endothelial growth factor.

1. Management of locally advanced RCC

A. Adjuvant pembrolizumab recommendations (questions A1, A2A–A2L)

Recommendations for adjuvant pembrolizumab largely aligned with the risk stratification demonstrated in KEYNOTE-564 (ClinicalTrials.gov identifier NCT03142334), in which pembrolizumab showed significant disease-free and overall survival benefit in patients at intermediate-high risk or high risk of recurrence postnephrectomy, although important areas of divergence and uncertainty emerged.[4] Strong consensus emerged for recommending adjuvant pembrolizumab across multiple scenarios, including pathologic T3a (pT3a) grade 3–4 disease (95.5%); pT3b disease regardless of grade (95.3%); pT4 tumors (95.6%); and node-positive disease (90.7%). This reflects confidence in the established efficacy and toxicity data in this curative-intent setting and recognition that these patients face a substantial risk of recurrence without adjuvant therapy.

For patients with completely resected metastatic disease, the panel reached consensus supporting adjuvant pembrolizumab when resection occurred within 1 year of nephrectomy (81.8%), consistent with the *M1 no evidence of disease* population included in KEYNOTE-564. Despite this voting outcome, expert discussions highlighted concerns regarding potential undertreatment in this population. Given the presence of metastatic disease, these patients would have received dual ICI or ICI plus a vascular endothelial growth factor receptor–tyrosine kinase inhibitor (VEGFR-TKI) as frontline therapy had they not undergone metastasectomy, raising questions about whether single-agent adjuvant pembrolizumab provides optimal treatment intensity despite its demonstrated benefit in KEYNOTE-564. Strong consensus against adjuvant therapy emerged when metastatic resection occurred more than 1 year after nephrectomy (79.5% opposed), reflecting concerns about diminishing benefit with prolonged intervals.

The expert recommendations extended beyond the specific KEYNOTE-564 eligibility criteria in several areas. Consensus supported adjuvant treatment for patients with positive surgical margins in the setting of high-risk disease (83.7%), acknowledging the increased recurrence risk associated with incomplete resection. Areas of uncertainty emerged around patients treated with stereotactic body radiation therapy (SBRT) to metastases, a scenario not specifically addressed in KEYNOTE-564. The lack of consensus for SBRT-treated

patients within 1 year of nephrectomy (65.9% in favor) highlights the challenge of extrapolating trial data to evolving treatment paradigms and the need for additional evidence in this population.

The panel was divided on adjuvant pembrolizumab for pT3a grade 1–2 disease (54.5% in favor), highlighting debate about whether patients with more favorable pathologic features derive sufficient benefit to justify potential toxicity and treatment burden. This uncertainty reflects the challenge of identifying patients with lower risk, resected RCC, who may experience a prolonged disease-free interval or a high likelihood of remaining free from recurrence without adjuvant therapy, raising concerns about exposing some patients with potentially indolent or more likely surgically cured disease to unnecessary ICI-related adverse events. Postoperative risk-stratification tools (such as nomograms and risk calculators) were not explicitly addressed and represent an important gap for future consensus work.

Although recommendations for adjuvant pembrolizumab largely aligned with KEYNOTE-564 eligibility criteria in high-risk populations, the pattern of responses reveals that experts do not uniformly accept trial eligibility as sufficient justification for treatment across all scenarios. The consensus pattern demonstrates expert preference for preventing undertreatment in high-risk patients while exercising caution about potential overtreatment in those with a more favorable prognosis. This approach reflects the desire to balance maximizing survival benefit and minimizing unnecessary exposure to immune-related adverse events in patients who may not experience recurrence.

B. Biopsy and staging approaches (questions A6, A8, A9)

The panel reached clear consensus against routine preoperative biopsy in surgical candidates with clinical T3 (cT3)N0M0 renal masses, with 75.6% recommending against biopsy. This approach reflects confidence in imaging-based diagnosis and surgical planning for appropriately selected patients, reserving biopsy for specific clinical scenarios in which tissue confirmation would alter management.

Strong consensus emerged for comprehensive postoperative restaging before adjuvant therapy consideration, with 82.2% of experts supporting routine chest, abdomen, and pelvis imaging. This systematic approach ensures accurate risk assessment and appropriate patient selection for adjuvant treatment by identifying occult disease that might have been missed on initial staging.

Brain imaging for asymptomatic patients at intermediate-high risk or high risk of recurrence remained controversial, with no consensus achieved. Notably, expert support for routine brain imaging shifted meaningfully between preconference and post-conference surveys (from 30.4% to 44.4%), suggesting that scientific presentations and discussions influenced opinions on the value of comprehensive surveillance in patients with high-risk disease, although uncertainty persists regarding optimal imaging strategy.

C. Molecular testing strategies (questions A5, A11–A14)

Consensus emerged for germline testing in populations at high risk for hereditary RCC syndromes, particularly patients diagnosed at age 45 years and younger (97.8%), those with bilateral tumors (93.3%), and patients with first-degree relatives affected by kidney cancer (84.4%). This targeted approach reflects current understanding of hereditary predisposition patterns while avoiding potential over-testing in sporadic disease.

The panel demonstrated significant skepticism regarding circulating tumor DNA (ctDNA) utility in nonmetastatic RCC, with a majority of experts (40%) recommending against routine testing and an additional 26.7% recommending it to be used rarely. This cautious stance reflects the well documented limitations of ctDNA sensitivity in early stage RCC without overt metastases on conventional imaging, in which nucleic acid shedding rates remain substantially lower than in other solid tumors.[12] The lack of consensus on incorporating negative ctDNA results into adjuvant treatment decisions underscores the current absence of validated clinical applications, with 52.3% indicating that negative ctDNA should never influence therapy choices.

Tumor profiling recommendations revealed a clear distinction between clear cell RCC (ccRCC) and variant RCC histologies. Experts showed limited enthusiasm for routine molecular profiling in ccRCC (28.9% rarely, 35.6% sometimes), reflecting the predominance of clinical and pathologic factors in treatment decisions, but had notably greater interest in profiling variant histologies (35.6% sometimes, 44.4% very often/always) in which actionable mutations may guide therapeutic choices.

D. Surgical decision making (questions A7, A10, A15, A16)

Retroperitoneal lymph node dissection approaches lacked consensus, although the majority of experts favored dissection when suspicious nodes are identified preoperatively (64.4%) or intraoperatively (57.8%). This selective approach reflects the balance between obtaining complete staging information and avoiding unnecessary operative morbidity in patients without apparent nodal disease.

Strong consensus emerged against surgery that would render patients anephric and dialysis-dependent (82.2%), emphasizing the importance of preserving renal function when feasible. This reflects the recognition that chronic dialysis significantly affects patient morbidity and mortality, making renal preservation a critical oncologic consideration.

Partial nephrectomy for cT2cN0M0 disease in patients with a normal contralateral kidney failed to reach consensus, with expert opinions distributed across sometimes (34.1%), very often (38.6%), and always (15.9%) categories. This reflects ongoing debate about the optimal balance between complete oncologic resection and

nephron preservation in intermediate-sized tumors. The diversity of expert opinion highlights the need for individualized decision making based on tumor characteristics, patient-related factors and preferences, and urologist experience.

Management of bilateral or multifocal ccRCC revealed significant uncertainty, with a slight majority voting in favor of neoadjuvant systemic therapy followed by resection or ablative strategies (42.2%) rather than integrating surgery and ablative techniques without systemic therapy (33.3%). This approach reflects the complex challenge of managing extensive disease while attempting to preserve renal function, although the lack of consensus also underscores the limited evidence base for this challenging clinical scenario.

2. Frontline systemic therapy for RCC

A. Treatment selection considerations (questions B1, B2, B17, B18)

Strong consensus emerged for obtaining tissue confirmation in suspected ccRCC recurrence occurring more than 1 year from original nephrectomy (84.4%). This reflects recognition that prolonged disease-free intervals raise questions about the nature of recurrent lesions and the importance of confirming histology before initiating systemic therapy.

The panel was unanimous in not routinely using programmed death ligand 1 (PD-L1) biomarker testing to guide frontline treatment decisions (100%), underscoring the lack of an established predictive value for PD-L1 expression in RCC treatment selection. This can contrast with several other tumor types in which PD-L1 expression may play a more defined role in ICI therapy selection.[13]

Site-specific metastatic disease considerations revealed uncertainty in treatment selection approaches. For bone metastases, no consensus was achieved, with experts divided between nivolumab plus cabozantinib (48.8%) and no preferred regimen (41.5%). Similarly, brain metastases failed to generate consensus on the optimal treatment approach. Discussions focused on the comparable efficacy of ICI plus VEGFR-TKI (ICI-VEGFR-TKI) combination regimens for both bone and brain metastases, as well as activity observed with nivolumab plus ipilimumab, in patients with central nervous system metastases in RCC.[14] The lack of strong preferences for specific regimens in these challenging presentations reflects limited comparative data and highlights the need for individualized decision making based on patient factors beyond metastatic sites alone.

B. International Metastatic RCC Database Consortium risk-stratification utility (questions B10, B22)

Expert opinion on the clinical utility of International Metastatic RCC Database Consortium (IMDC) risk stratification shifted meaningfully during the conference, with support for using the IMDC risk score to guide first-line therapy selection declining from 56.5% to 40.5%. Discussions reflected that IMDC parameters are prognostic rather than predictive, failing to effectively guide therapy selection among available treatment options. The panel showed even less enthusiasm for incorporating IMDC risk scores into recurrence/progression therapy decisions, with clear consensus that the IMDC score should not alter treatment choice at progression (73.2% opposed). Discussions focused on other parameters being more relevant at the time of progression, including prior treatment received, disease response and progression kinetics, toxicity profiles, route of administration, current disease burden, sites of metastases, etc. This reflects expert recognition that treatment selection at recurrence/progression requires consideration of dynamic factors specific to the progression event rather than traditional risk-stratification frameworks.

C. Favorable-risk disease management (questions B3, B11, B12)

For patients with IMDC favorable-risk, metastatic ccRCC, burden of disease emerged as the most important factor when considering active surveillance (51.2%), whereas molecular testing profile was consistently ranked least important (90.7%), reflecting its limited clinical utility in treatment selection.

Treatment selection for patients with favorable-risk, metastatic ccRCC requiring systemic therapy revealed significant uncertainty, with the panel evenly divided between ICI-VEGFR-TKI combinations (50%) and dual ICI with nivolumab plus ipilimumab (50%). This equipoise reflects contrasting efficacy profiles between regimens: ICI-VEGFR-TKI combinations demonstrate superior objective response rates and progression-free survival but no overall survival benefit in favorable-risk patients, whereas extended follow-up from CheckMate 214 (ClinicalTrials.gov identifier NCT02231749) has shown long-term overall survival advantage for nivolumab plus ipilimumab in this population.[15] Discussions reinforced that IMDC risk stratification alone is insufficient for treatment selection.

The panel reached consensus recognizing a distinct *very favorable*-risk subset (76.2%), defined by prolonged time to systemic therapy (≥3 years), excellent performance status, and absence of brain, liver, or bone metastases. This represents an important evolution in risk stratification because existing prognostic models have not formally recognized this exceptionally favorable subset. This acknowledgment suggests expert recognition that some patients may benefit from more conservative management approaches based on their indolent disease course, aiming to reduce toxicity and improve quality of life.

D. Sarcomatoid and rhabdoid ccRCC (questions B7, B8, and B9)

Strong consensus emerged that patients who have ccRCC with predominant sarcomatoid or rhabdoid histology should not be offered active surveillance or treated with metastasis-directed therapy alone,

even when limited sites of disease burden are present (81.4%). This reflects recognition that these aggressive histologic features may override traditional volume-based risk assessments and warrant immediate systemic intervention.

For metastatic ccRCC with sarcomatoid differentiation, there was overwhelming consensus favoring nivolumab plus ipilimumab as the preferred systemic therapy (93.2%). This reflects the particular efficacy of this dual-ICI regimen in sarcomatoid histology demonstrated in CheckMate 214, in which this subgroup showed enhanced durable responses with nivolumab plus ipilimumab.[16] Although a majority of the panel favored treating sarcomatoid and rhabdoid differentiation equivalently (66.7%), formal consensus was not achieved.

E. Oligometastatic disease and local therapies (questions B4, B5, and B6)

No formal consensus emerged on defining oligometastatic disease, although most experts favored three or less definitive metastases (60.5%) over five or less metastases (23.3%). When combined, experts supporting numerical thresholds (three or less or five or less metastases) represented 83.8% of responses, suggesting broad agreement on low-volume disease definitions despite various specific cutoffs. The minority acknowledging no consensus definition exists (16.3%) reflects ongoing debate in the literature about optimal oligometastatic disease criteria.

The role of metastasis-directed therapies revealed nuanced timing considerations based on disease-free interval from nephrectomy. For single-site recurrence within 6 months of nephrectomy, expert opinion was divided, with no consensus achieved (60.5% supporting use vs. 39.5% opposed). However, clear consensus emerged supporting metastasis-directed therapies for single-site recurrence occurring ≥12 months after nephrectomy (79.1% in favor). This pattern suggests expert recognition that early recurrence may reflect more aggressive biology, whereas a later, isolated recurrence may represent true oligometastatic recurrence more amenable to local intervention.

F. Dual ICI versus ICI-VEGFR-TKI regimens (questions B13–B16)

Despite broad acceptance of ICI-VEGFR-TKI combinations, no consensus was reached on specific regimen selection, with experts evenly divided between nivolumab plus cabozantinib (45%) and pembrolizumab plus lenvatinib (52.5%). Overall regimen preferences remained split (no preferred regimen [36.6%], pembrolizumab plus lenvatinib [39%], nivolumab plus cabozantinib [22%], or pembrolizumab plus axitinib [2.4%]). Notably, expert preference shifted between premeeting and postmeeting voting, highlighting genuine uncertainty about the preferred ICI-VEGFR-TKI combination. This equipoise reflects relatively comparable efficacy profiles of available combinations and lack of head-to-head comparisons among regimens. The panel supported starting VEGFR-TKI components at recommended doses (100% of respondents) rather than preemptive dose reduction, with dose modifications, e.g. delays and/or reductions implemented as needed postinitiation to manage treatment-emergent toxicities and therapy burden.

For rapidly progressive and symptomatic disease, strong consensus favored ICI-VEGFR-TKI combinations (81%) over dual ICI (14.3%), prioritizing rapid response rates and symptom palliation over potential long-term benefits of dual ICI in patients who may not have time to await potentially / relatively delayed response/benefit.

G. ICI rechallenge after adjuvant therapy (questions B20 and B21)

Strong consensus emerged supporting ICI re-challenge in appropriately selected patients who received adequate exposure to adjuvant pembrolizumab (92.9%), reflecting the data gap in CONTACT-03 and TiNivo-2 trials (ClinicalTrials.gov identifiers NCT04338269 and NCT04987203, respectively), with only very few patients having received prior adjuvant ICI.[17,18] Adequate exposure was not specifically defined in the survey, leaving interpretation to individual expert clinical judgment. There was consensus against re-challenge for early recurrence within 0–3 months of starting adjuvant pembrolizumab (85.4% opposed), reflecting concern about primary resistance. Support increased substantially for later recurrence, with strong consensus favoring re-challenge for recurrence occurring 3–6 months postcompletion of adjuvant pembrolizumab (78%) and even stronger support for recurrence after 12 months (92.7%) or after 24 months (95.1%) postcompletion of adjuvant pembrolizumab. This pattern reflects expert understanding that immunotherapy effects persist even beyond treatment completion, such that early relapse represents progression during effective drug exposure and likely indicates primary resistance. Conversely, longer treatment-free intervals may indicate that recurrence occurred after immune activation had subsided, potentially representing a treatment withdrawal effect that could make patients more amenable to ICI re-challenge.

3. Later-line treatments in RCC

A. Post–ICI-VEGFR-TKI progression management (questions C1 and C5–C7)

For postprogression treatment after ICI-VEGFR-TKI combinations, strong consensus favored single-agent VEGFR-TKI therapy, with cabozantinib monotherapy overwhelmingly preferred (85%). This reflects expert confidence in single-agent approaches after combination treatment failure, supported by CONTACT-3 data showing limited benefit of ICI re-challenge post-ICI failure in the CONTACT-3 and TiNivo-2 trials.[17,18]

In the context of stopping pembrolizumab at 2 years according to protocol and subsequently experiencing progression, no consensus emerged, with experts split between resuming pembrolizumab (63.4%) versus switching to cabozantinib (31.7%). This division reflects uncertainty about whether progression after planned ICI discontinuation represents true resistance or treatment withdrawal effect.

When ICI required discontinuation for toxicity, particularly hepatitis, and patients subsequently progressed, no formal consensus was achieved on the optimal treatment strategy between resuming ICI versus transitioning to a different treatment. However, experts generally favored VEGFR-TKI agents, with cabozantinib receiving the most votes (57.5%) and the sum of all tyrosine kinase inhibitor (TKI) options (axitinib, tivozanib, cabozantinib) totaling 75.0%, reflecting continued strategy of single-agent VEGFR-TKI targeting post-ICI-VEGFR-TKI failure.

For primary progression on ICI-VEGFR-TKI combinations, strong consensus supported switching to lenvatinib plus everolimus (75.6%), supported by phase 2 trial data demonstrating a meaningful response rate with this combination in heavily pretreated patients.[19]

B. Post–dual ICI progression management (questions C1 and C5–C7)

For patients experiencing progression on dual ICI therapy, strong consensus emerged favoring TKI monotherapy (90%), reflecting that the most robust data support VEGFR-TKI monotherapy as the optimal sequence after dual ICI. However, no consensus was achieved regarding specific TKI selection, with experts divided on whether tivozanib, axitinib, or cabozantinib could be offered with relatively equal enthusiasm (51.2% disagreed). This suggests that preferences exist for specific agents, reflecting the absence of head-to-head comparisons and differences in trial designs, provider experience, and the patient populations studied for each agent.

For mixed responses to dual ICI therapy (e.g., patients responding in visceral organs but developing new brain metastases controlled with radiation), no consensus emerged between continuing systemic therapy (58.5%) versus switching to cabozantinib (39%). Discussions reflected that the preference for continuing ICI recognizes control of oligoprogressive disease with SBRT and ongoing systemic benefit of ICIs, whereas support for cabozantinib was based on specific data demonstrating brain metastasis activity and its different mechanism of action versus ICIs.

C. Post–VEGFR-TKI progression management (question C4)

For patients experiencing progression after prolonged first-line TKI monotherapy, no consensus was achieved regarding optimal subsequent therapy. After 5 years of TKI treatment in favorable-risk disease, experts were divided between dual ICI with ipilimumab plus nivolumab (46.3%), ICI plus TKI (29.3%), and nivolumab monotherapy (22%). Notably, alternate TKI monotherapy was rarely favored (2.4%), with 75.6% of experts supporting introduction of an ICI in some form. The lack of consensus highlights the challenge of treatment selection in patients with TKI-experienced, ICI-naive disease, representing a clinical scenario analogous to the subsequent-line setting from the CheckMate 025 trial (ClinicalTrials.gov identifier NCT01668784), and should be distinguished from second-line scenarios after anti–VEGFR-TKI, in which an alternate VEGFR-TKI or belzutifan would be preferred options.

D. Integration of belzutifan (questions C9, C10, and C13–C15)

Belzutifan is a hypoxia-inducible factor (HIF)-2α inhibitor with demonstrated activity in treatment-refractory ccRCC after ICI and VEGFR-targeted therapy.[20] Expert opinions revealed uncertainty about optimal placement within current treatment sequences, with no consensus on reserving belzutifan for heavily pretreated patients (63.4%) or offering it immediately after dual ICI (48.8%). Discussions centered on its specific mechanism targeting HIF-2α, a key effector of Von Hippel–Lindau pathway dysregulation, suggesting potential advantage when used earlier in treatment before VEGFR-targeted treatment resistance emerges, although very limited data exist on predictive biomarkers for belzutifan response. This sequencing uncertainty reflects both the agent's recent regulatory approval and less real-world experience with optimal positioning/sequencing strategies.

The unique toxicity profile of belzutifan requires specialized management approaches that differ from traditional RCC therapies. Strong consensus emerged for using erythropoiesis-stimulating agents to manage belzutifan-induced anemia (84.6%), and near-universal agreement supported holding therapy and reducing dose upon resolution/improvement for patients wo develop hypoxia (92.7%). For patients with baseline pulmonary comorbidities, such as chronic obstructive pulmonary disease, no consensus was reached regarding dosing strategy, with experts divided between full-dose (50%) versus attenuated-dose (38.1%) initiation, although most supported belzutifan use with appropriate oxygen saturation monitoring. These management considerations highlight the importance of patient selection and proactive monitoring for belzutifan-distinct adverse events.

E. Third-line and later treatment options (questions C8, C12, C17, and C18)

Treatment decisions beyond second-line therapy demonstrated clear patterns of expert preference despite the complexity of heavily pretreated patients and the limited evidence guiding optimal sequencing strategies. In the setting of post–ICI-VEGFR first-line and post–VEGFR-TKI second-line, experts selected belzutifan as a

preferred third-line option (81% vs. 16.7% for tivozanib and 2.4% for axitinib), reflecting its novel/distinct mechanism of action and demonstrated efficacy in treatment-refractory disease.

The role of dual ICI with ipilimumab plus nivolumab in later-line settings remains controversial, with no consensus among experts. Nearly one half (47.5%) would never consider this combination after first-line treatment, whereas others supported its use in later lines (32.5%). This division reflects the evidence landscape because multiple studies have demonstrated limited activity of ICI after progression on prior ICI, although the FRACTION trial (ClinicalTrials.gov identifier NCT02996110) showed a modest objective response rate with nivolumab plus ipilimumab in the post-ICI setting.[21]

For fourth-line therapy selection, unanimous consensus supported pursuing a TKI that patients had not previously received (100%) rather than revisiting previously effective agents (0%). This approach prioritizes exposing patients to relatively different mechanisms of action over re-challenging with drugs that have already demonstrated resistance.

Expert commitment to continued active treatment in fit patients was evident, with strong consensus supporting fifth-line therapy (95.1%) over best supportive care (4.9%) in patients who had received four different therapy lines. This approach reflects the availability of multiple treatment options with distinct mechanisms of action, although patient fitness and preferences, treatment tolerance, quality-of-life considerations, and informed/shared decision making incorporating palliative care principles remain critical factors in treatment selection.

4. Systemic therapy for advanced variant histology RCC

A. Characterization and diagnostics of variant histology RCC (questions D1–D4)

Expert consensus strongly supports comprehensive diagnostic evaluation for patients with variant histology RCC, beginning with pathology re-review. Most experts (88.4%) ensure that pathology re-review is performed when managing patients with variant histology tumors, reflecting the importance of accurate histologic classification in guiding treatment decisions.

There was overwhelming consensus favoring specific histologic designation over generic categorization. Nearly all experts (90.7%) preferred exact histology terms, such as *papillary RCC*, rather than the broader *nonclear cell* classification. This preference emphasizes the recognition that different variant histologic subtypes may have distinct biologic behaviors and treatment sensitivities.

The effect of the revised World Health Organization pathology classification on clinical management showed mixed results, with no clear consensus among experts. A slight majority (53.5%) reported that the updated classification system has aided their patient management, whereas 46.5% found it less helpful in clinical decision-making.

Molecular characterization through somatic genomic profiling achieved strong consensus, with 88.1% of experts routinely obtaining this testing in metastatic variant histology RCC. This approach reflects the growing recognition of *potentially targetable* genomic alterations in variant histologic subtypes and the potential for precision oncology approaches, particularly given the limited evidence base for standard systemic therapies in these rare subtypes.

B. Treatment approaches for variant histology RCC

Expert consensus strongly affirmed that treatment choices should be tailored based on exact histologic subtype, with 90.7% of experts reporting that specific histology influences their management decisions. This approach reflects the growing recognition that variant RCC histologies have distinct behaviors and treatment sensitivities warranting individualized therapeutic strategies.

Strong consensus emerged against adjuvant pembrolizumab for high-risk papillary RCC, with 83.3% of experts not recommending this approach despite meeting stage/grade criteria equivalent to KEYNOTE-564 entry definitions (given that KEYNOTE-564 did not enroll patients with papillary RCC). This demonstrates caution in extrapolating adjuvant ICI benefit from ccRCC to papillary RCC given limited evidence in variant histologies. Thresholds for local interventions in metastatic variant histology RCC showed differed approaches among experts, with no clear consensus for either radiation or surgical intervention thresholds. Most experts use local intervention approaches at either the same rate or a higher rate than for ccRCC. Expert discussions around this approach acknowledge that variant histologies often demonstrate reduced sensitivity to standard systemic treatments compared with ccRCC.

Histology-specific first-line preferences

Treatment preferences varied significantly by specific histologic subtype:

- Papillary RCC: No consensus was achieved, although a majority (68.3%) favored ICI-VEGFR-TKI combinations.
- Chromophobe RCC: No consensus was achieved, although most selected lenvatinib plus pembrolizumab (72.5%), with 90% favoring lenvatinib-based combinations (with either pembrolizumab or everolimus).
- Translocation RCC: No consensus was achieved, although lenvatinib plus pembrolizumab was most favored (62.5%).
- Unclassified RCC: No consensus was achieved, with slight preference for lenvatinib plus pembrolizumab (55%) and remaining experts evenly split between cabozantinib plus nivolumab and nivolumab plus ipilimumab.
- Collecting duct RCC: Strong consensus favored platinum-based chemotherapy (82.9%), reflecting the aggressive nature and limited efficacy of targeted therapies in this subtype.

- Renal medullary carcinoma: Strong consensus supported platinum-based chemotherapy (90.5%), consistent with the aggressive clinical course requiring cytotoxic approaches.
- Fumarate hydratase-deficient RCC: No consensus emerged, with bevacizumab plus erlotinib as the most preferred (42.5%), followed by cabozantinib plus nivolumab (25%), and lenvatinib plus pembrolizumab (22.5%).

ICI-VEGFR-TKI combinations as standard of care for variant histologies (excluding sarcomatoid differentiation) did not achieve consensus, with 64.3% of experts considering this approach well established, whereas 35.7% disagreed, highlighting ongoing uncertainty about optimal first-line therapy across all variant histologies. These findings highlight the heterogeneity and high complexity of variant RCC management and the need for histology-specific treatment algorithms, particularly given limited evidence for many of these rare subtypes.

5. Management of nonmuscle-invasive bladder cancer

A. Diagnostic evaluation of nonmuscle-invasive bladder cancer (questions E1, E5, E7, E10, and E11)

Surveillance strategies for low-risk bladder cancer revealed no expert consensus regarding optimal cessation timing, with experts divided between stopping cystoscopy surveillance at 3 years (28.6%) or 5 years (54.3%) for low-risk disease (Ta low grade, <3 cm), whereas a minority (14.3%) supported indefinite surveillance.

Most experts (61.8%) reported no use of urinary molecular markers in NMIBC management. Among those using these assays, adjudication of atypical cytology was the most common application (26.5%), although no consensus emerged on optimal integration strategies. This limited adoption likely reflects insufficient evidence defining optimal patient selection criteria, timing of implementation, and integration with existing surveillance protocols.

Blue-light cystoscopy applications revealed varied expert preferences without consensus. The most commonly endorsed scenarios were positive cytology with no visible lesions (32.4%) and tumors with suspected carcinoma in situ (CIS; 32.4%), followed by evaluation of all new tumors (29.4%). This uncertainty reflects limited data on cost effectiveness, availability, and optimal implementation strategies across different clinical scenarios.

Evaluation approaches for patients with positive cytology but no evidence of bladder cancer demonstrated divergent preferences. Blue-light cystoscopy was most commonly selected (41.2%), followed by upper tract washings (29.4%), and mapping bladder biopsies (20.6%), reflecting the absence of standardized evaluation protocols and comparative effectiveness data for this challenging scenario.

Management of lymphovascular invasion detected on transurethral resection of bladder tumor (TURBT) for NMIBC revealed divided expert opinion between repeat TURBT (44.1%) and abdominal imaging for metastasis evaluation (44.1%), reflecting uncertainty about whether lymphovascular invasion by itself may be associated with occult invasive disease.

B. Treatment of nonmuscle-invasive bladder cancer (questions E2–E4, E6, E8, E9, and E12–E15)

Low-risk disease

For management of patients unable to tolerate TURBT, strong consensus emerged favoring office-based fulguration (77.1%) over surveillance or chemoablation. Optimal characteristics for single-dose intravesical therapy after TURBT showed no consensus, although most experts identified absence of CIS as the most important factor (47.1%) guiding treatment decisions.

Intermediate-risk disease

Treatment selection for intermediate-risk NMIBC demonstrated divided expert opinion between Bacillus Calmette–Guerin (BCG; 58.8%) and single-agent chemotherapy (38.2%), reflecting ongoing debate about optimal therapy for this risk category also in the relevant context of notable BCG shortage.

High-risk disease and BCG management

BCG shortage scenarios demonstrated preference for dual-agent chemotherapy (64.7%) over single-agent approaches in high-risk patients. Management of persistent CIS or high-grade Ta disease after BCG induction showed divided approaches between BCG reinduction with six doses (41.2%) and switching to alternative treatment (35.3%). BCG re-challenge timing showed no consensus, with experts equally divided between 6-month (44.1%) and 12-month (44.1%) disease-free intervals. This survey was performed before the availability of randomized data for ICI therapy in this setting.

BCG-unresponsive disease and systemic therapy

The role of intravenous pembrolizumab in BCG-unresponsive disease demonstrated no consensus, with experts divided between considering it never appropriate (41.2%) versus using it for BCG-unresponsive CIS (29.4%). For first-line treatment of BCG-unresponsive disease, intravesical gemcitabine-docetaxel (73.5%) was preferred over intravenous pembrolizumab (14.7%), although consensus was not achieved. Strong consensus emerged regarding treatment selection end points, with experts overwhelmingly favoring recurrence-free survival (76.5%) over cystectomy-free survival.

Surgical considerations

Management of histology subtype (variant) bladder cancer revealed no consensus regarding early cystectomy recommendations, with most experts (52.9%) supporting early cystectomy for both micropapillary and plasmacytoid subtypes.

6. Management of locally advanced urothelial cancer

A. Diagnostics and molecular testing (questions F1, F2, F15, and F16)

Strong consensus emerged regarding the definition of locally advanced UC, with experts overwhelmingly agreeing that cT4bN0M0 (90%) and TanyN1–N3M0 (90%) definitively represent locally advanced disease. A majority also included cT3b–cT4aN0M0 (57.5%), whereas oligometastatic disease was less commonly considered locally advanced (27.5%).

The role of restaging TURBT in confirmed that muscle-invasive bladder cancer (MIBC) showed no consensus among experts. The most common approach was selective use to assess for complete resection and perform examination under anesthesia (51.3%), although a substantial minority (33.3%) never performed restaging TURBT, reflecting varied institutional practices also depending on clinical scenarios.

The use of plasma ctDNA testing for minimal residual disease determination demonstrated no consensus, with only one third of experts using it for selected patients, whereas others either avoided the test or ordered it without using results for treatment decisions. Whereas data suggest potential utility, plasma ctDNA has not yet been established as a validated biomarker to guide therapy selection.[22] Strong consensus emerged that ctDNA results should not be the sole determinant of adjuvant therapy decisions. Most experts (81.1%) indicated that they would not base treatment decisions solely on positive ctDNA testing, emphasizing that pathologic and clinical staging remains a key consideration for treatment decisions regardless of ctDNA status.

B. Current neoadjuvant treatment (question F8)

Standard-of-care neoadjuvant systemic therapy for patients with localized MIBC and adequate renal function demonstrated no consensus among experts. The majority (66.7%) favored gemcitabine, cisplatin, and durvalumab, whereas others preferred traditional cisplatin-based combination chemotherapy (25.6%), e.g., dose-dense MVAC (methotrexate, vinblastine, doxorubicin, and cisplatin; 7.7%).

This division reflects the evolving treatment landscape after recent clinical trial results incorporating perioperative durvalumab into neoadjuvant gemcitabine/cisplatin. The preference for combination perioperative chemoimmunotherapy with durvalumab shows growing confidence, although a substantial minority support for conventional chemotherapy regimens suggests uncertainty about optimal regimen selection and the need for additional subsets and long-term efficacy and safety data.

C. Renal function considerations (questions F3, F4, and F9)

Neoadjuvant chemotherapy has become standard of care for localized MIBC, though renal dysfunction presents significant management challenges requiring careful consideration of both urinary diversion and dosing strategies.

Management of renal dysfunction in MIBC demonstrated clear expert consensus regarding urinary decompression approaches. Strong consensus emerged that decompression is required in patients who have MIBC with hydronephrosis and elevated creatinine before neoadjuvant cisplatin-based chemotherapy (78.4%). However, experts overwhelmingly preferred ureteral stents over percutaneous nephrostomy tubes (86.1%) in patients with elevated creatinine and hydronephrosis from tumor, reflecting the less invasive nature and improved quality of life associated with internal drainage. However, there are retrospective data suggesting a potential risk of upper tract tumor spread with stents, arguing in favor of a nephrostomy tube in such cases.[23]

For patients with borderline renal function, strong consensus emerged supporting split-dose neoadjuvant cisplatin for patients with creatinine clearance 40–60 mL per minute (94.9%). This approach demonstrates expert recognition of the importance of cisplatin-based chemotherapy while acknowledging the need for dose-modification strategies (e.g., split-dose cisplatin) to minimize nephrotoxicity in patients with compromised renal function.

D. Adjuvant treatment options (questions F19 and F20)

Adjuvant therapy selection for patients with high-risk UC after radical cystectomy varied based on prior treatment exposure. For patients with pT3–pT4 or pN0-positive disease who did not receive prior neoadjuvant cisplatin-based chemotherapy and had good renal function, consensus emerged around cisplatin-based chemotherapy when all cisplatin options were combined (over 80%). For patients with postneoadjuvant therapy T2–T4 (ypT2–ypT4) or ypN-positive disease after receiving neoadjuvant cisplatin-based chemotherapy, the majority selected adjuvant nivolumab (60%) as the preferred next step, although consensus was not achieved.[24]

E. Management of lymph node-positive disease (questions F10–F14)

Lymph node-positive UC represents a challenging clinical scenario with a historically poor prognosis, prompting evolving treatment approaches that incorporate recent advances in systemic therapy. The EV-302 trial (ClinicalTrials.gov identifier NCT04223856)

demonstrated a significant survival benefit with enfortumab vedotin (EV) plus pembrolizumab compared with standard platinum-based chemotherapy in advanced/metastatic disease, influencing treatment selection patterns also for locally advanced presentations.[10]

For patients with cN1–cN2 disease (single or multiple lymph nodes within the true pelvis), no consensus was achieved regarding optimal prepotential consolidation therapy, although the majority selected EV plus pembrolizumab (62.5%) over gemcitabine plus cisplatin plus nivolumab (35%). In contrast, strong consensus emerged for cN3 disease (lymph nodes along the common iliac arteries), with experts favoring EV plus pembrolizumab (76.9%) as initial systemic therapy before potential consolidation.

Consolidative local therapy preferences showed clear expert consensus favoring surgery over radiotherapy (77.5% vs. 22.5%) for cN1–cN2 disease. This surgical preference reflects confidence in the ability to achieve adequate locoregional control and pathologic staging information through operative intervention after initial systemic therapy.

Lymphadenectomy approaches varied significantly based on clinical node status. For clinically node-negative patients, strong consensus supported following a standard lymphadenectomy template (82.1%) rather than extended dissection or node count-based approaches. However, for clinically node-positive patients, no consensus emerged regarding optimal dissection extent, with experts divided between extended template (35.9%), standard template (30.8%), and targeted resection of previously involved nodes when safely feasible (33.3%).

F. Trimodality therapy (questions F5–F7)

Trimodality therapy, consisting of maximal transurethral resection followed by concurrent chemotherapy and radiation therapy, represents a bladder-preserving alternative to radical cystectomy for select patients with localized MIBC. Patient selection criteria for trimodality therapy remain controversial, with no consensus regarding multifocal tumor presentations. Experts were divided on whether trimodality therapy should be offered to patients with multifocal tumors (53.8% opposed vs. 46.2% supporting), highlighting ongoing uncertainty about tumor burden thresholds and technical feasibility considerations in organ-preservation approaches. Other variables discussed in the overall selection criteria included good bladder function/capacity, tumors that are completely resectable, and the absence of hydronephrosis and of extensive/diffuse CIS.

The integration of additional systemic therapy with trimodality approaches demonstrated varied expert opinions without clear consensus patterns. Neoadjuvant therapy for eligible patients undergoing trimodality therapy showed no consensus, with experts divided (53.8% supporting vs. 46.2% opposing), reflecting uncertainty about optimal sequencing and potential complications from combined modality approaches.

In contrast, strong consensus emerged against adjuvant chemotherapy for eligible patients with MIBC undergoing trimodality therapy (81.6% opposed), suggesting expert preference for chemotherapy-based, systemic therapy before rather than after radiation-based organ-preservation strategies. Discussions around this approach reflect the balance between maximizing systemic therapy benefit while minimizing treatment-related morbidity in bladder-preservation candidates.

G. Management of upper tract urothelial carcinoma (questions F17–F18)

No consensus regarding optimal adjuvant therapy approaches for the management of upper tract UC (UTUC) was reached. For patients who have high-risk disease after extirpative surgery without prior neoadjuvant chemotherapy, the majority (57.9%) favored adjuvant platinum-based chemotherapy, whereas others supported a stratified approach using cisplatin-based chemotherapy for eligible patients and adjuvant nivolumab for cisplatin-ineligible patients (31.6%). This preference for platinum-based adjuvant therapy is supported by the POUT trial (ClinicalTrials.gov identifier 01993979), which demonstrated improved disease-free survival with adjuvant chemotherapy in high-risk UTUC.[25]

The timing of systemic therapy in UTUC showed no consensus, with experts divided on the use of neoadjuvant or adjuvant approaches. The most common preference was individualizing the choice between neoadjuvant and adjuvant therapy based on patient-specific factors, such as renal function and medical comorbidities (45%). This individualized approach reflects the complexity of localized UTUC management and the unique anatomic, staging, and functional considerations affecting treatment sequencing decisions, as well as the lack of direct comparisons between neoadjuvant and adjuvant strategies.

H. Management of variant histologic subtypes (questions F21–F26)

Treatment approaches for histology subtypes of muscle-invasive UC demonstrated distinct patterns based on specific histologic subtypes. For plasmacytoid UC, no consensus emerged, with experts divided between neoadjuvant cisplatin-based chemotherapy (35.9%); upfront radical cystectomy with lymphadenectomy (30.8%); or cisplatin, gemcitabine, and durvalumab (20.5%). Similarly, sarcomatoid UC showed no consensus, although experts slightly favored neoadjuvant gemcitabine, cisplatin, and durvalumab (35.9%) over upfront radical cystectomy (25.6%).

Micropapillary UC management also lacked consensus, with preferences distributed between neoadjuvant gemcitabine, cisplatin, and durvalumab (35.9%), traditional cisplatin-based chemotherapy (23.1%), and upfront radical cystectomy (25.6%).

In contrast, pure squamous histology demonstrated strong consensus favoring upfront radical cystectomy with lymphadenectomy (76.3%), reflecting limited efficacy from neoadjuvant approaches. Pure

adenocarcinoma showed a similar pattern, with most experts (71.8%) preferring upfront surgery, although consensus was not achieved.

Small cell histology represented a unique paradigm, with no consensus but clear preference for systemic therapy approaches. The majority favored neoadjuvant chemotherapy regimens extrapolated from other small cell/neuroendocrine cancer paradigms (64.1%), recognizing the very aggressive nature and risk of early micrometastasis of small cell carcinoma and the potential benefit of systemic therapy approaches derived from small cell lung cancer treatment protocols.

7. Frontline systemic therapy for metastatic urothelial carcinoma

A. Treatment selection and management (questions G1–G5 and G8–G10)

The evolving treatment landscape for advanced UC recognized EV plus pembrolizumab as the new standard of care, but some uncertainty remains about alternative options in select scenarios. Expert opinion on platinum-based combination followed by switch maintenance avelumab as a clinical trial comparator showed no consensus, with most (51.4%) considering it acceptable only in countries without access to EV plus pembrolizumab. Strong consensus emerged favoring cisplatin over carboplatin in combinations with programmed death protein 1/PD-L1 inhibitors (86.1%) based on superior suggested immunomodulatory effects and results from the CheckMate 901 phase 3 trial (ClinicalTrials.gov identifier NCT03036098).[26] Regarding molecular profiling, strong consensus emerged that next-generation sequencing results should not delay frontline therapy initiation (94.7%), with experts viewing these results as most useful for selecting subsequent treatments rather than influencing first-line decisions.

Opinions varied on how to integrate patient-reported outcomes into therapy selection, with most (51.3%) finding them most valuable when comparing regimens that have relatively similar efficacy. For EV plus pembrolizumab management, strong consensus supported continuing treatment until progression or unacceptable toxicity (86.1%), whereas opinions were divided on continuing pembrolizumab after EV discontinuation, with the majority (66.7%) believing pembrolizumab can drive survival benefit.

Treatment selection after prior ICI exposure in the adjuvant setting showed no consensus, with most experts requiring progression ≥6 months after the last dose of prior ICI (38.9%) before using EV plus pembrolizumab. Regarding whether EV plus pembrolizumab should be used in the perioperative setting for patients experiencing rapid recurrence either during or shortly after EV plus pembrolizumab, experts were divided between platinum-based chemotherapy without ICI (50%) and cisplatin, gemcitabine, and nivolumab (27.8%).

In regions without access to EV plus pembrolizumab, strong consensus favored cisplatin, gemcitabine, and nivolumab (89.2%) in cisplatin-eligible patients, reflecting confidence in first-line ICI-based combination regimens.

B. Adverse event management and contraindications (questions G11, G13, G14, and G16–G18)

Expert approaches to EV contraindications varied based on the drug's mechanism as an antibody–drug conjugate targeting nectin-4 with a monomethyl auristatin E payload. Most (66.7%) considered chronic grade ≥2 peripheral neuropathy a contraindication because of microtubule-disrupting effects, with discussion emphasizing prolonged recovery time and potential irreversibility of neuropathic symptoms. Liver dysfunction opinions were divided, with a slight majority (52.8%) considering cirrhosis a contraindication and most favoring 1.5 times the upper limit of normal as the total bilirubin threshold in the absence of Gilbert syndrome.

Management strategies for treatment-emergent toxicities reflected the cumulative nature of antibody–drug conjugate side effects. For mild neuropathy, most experts (62.2%) preferred holding treatment and resuming with a dose reduction when feasible, whereas strong consensus supported adding physical therapy (91.1%) for proprioception and balance changes. Skin rash management approaches varied, with most (44.4%) adding systemic steroids when topical treatments fail after 7 days, reflecting concern for a potentially immune-mediated dermatologic toxicity profile or the nectin-4–driven cutaneous toxicity.

8. Later-line treatments for urothelial carcinoma

A. Biomarker-negative/unselected patients (questions H01–H04, H08, H11, H18, and H19)

Post-EV plus pembrolizumab progression

The management of patients progressing after first-line EV plus pembrolizumab demonstrated clear consensus patterns based on cisplatin eligibility. For cisplatin-ineligible patients with metastatic UC, there was strong consensus postconference (91.4%) favoring carboplatin-based combination therapy as the preferred next-line treatment, representing a shift from initial voting (76.3%). This overwhelming preference reflects the understanding that platinum-based chemotherapy may remain highly active in patients who have not previously received it, even after progression on other modern combinations.

Similarly, for cisplatin-eligible patients, consensus (80.6%) supported cisplatin-based combination therapy as the standard approach, with minimal consideration for cisplatin-gemcitabine-nivolumab combinations (16.7%) or sacituzumab govitecan (2.8%). The preference for standard platinum doublets over ICI-containing triplet regimens suggests that practitioners believe additional ICI may not provide meaningful benefit in the post-ICI setting, prioritizing the established efficacy and tolerability profile of conventional chemotherapy.

Management of patients who develop treatment-limiting peripheral neuropathy presented a much more complex scenario without clear consensus. For patients with persistent grade 1

neuropathy after EV discontinuation, most (66.7%) would still choose platinum-based combination therapy over re-instituting EV with continued pembrolizumab (27.8%). This preference suggests that the perceived risk-benefit ratio in most experts favors a chemotherapy approach rather than re-challenging with the agent that caused the neuropathy, even at a lower grade.

Postplatinum-based therapy with switch maintenance avelumab

After progression on first-line platinum plus gemcitabine with maintenance avelumab, treatment selection showed no clear consensus but demonstrated a strong trend toward EV monotherapy (63.9%) over the EV plus pembrolizumab combination (36.1%). Preference for single-agent EV reflects practical considerations, including the prior exposure to ICI and the established efficacy of EV monotherapy in platinum-refractory and ICI-refractory disease.

Postsingle-agent pembrolizumab (platinum-ineligible)

For platinum-ineligible patients who progress after single-agent pembrolizumab as first-line therapy, there was consensus (75%) favoring EV monotherapy over combination approaches. This clear preference reflects the efficacy of EV in platinum-naive, ICI-refractory UC, as demonstrated in cohort 2 from the phase 2 EV-201 trial (ClinicalTrials.gov identifier NCT03219333). The minority consideration for continuing pembrolizumab (19.4%) or using platinum-based combinations (5.6%) suggests that a few practitioners may consider the latter approach in select patients, possibly those with adequate performance status or specific clinical circumstances.

Postadjuvant nivolumab (cisplatin-ineligible)

The management of cisplatin-ineligible patients progressing after adjuvant nivolumab represents an emerging clinical scenario without clear consensus. The most frequently selected approach (44.4%) involves a timing-based strategy: using EV monotherapy if progression occurs within 3–6 months of the last nivolumab dose, otherwise using the EV plus pembrolizumab combination. This nuanced approach reflects the variable interpretation of ICI resistance based on the timing of progression, with early progression suggesting resistance that might not benefit from additional ICI therapy.

Role of sacituzumab govitecan

The ongoing role of sacituzumab govitecan in metastatic UC treatment guidelines remains controversial, with no clear consensus but a majority (68.6%) believing it should maintain its position in treatment algorithms despite large, well conducted, negative randomized trials. This represents a significant shift from initial voting (44.7% in support) to final consensus. The continued support likely reflects its response rate in heavily pretreated patients positive for fibroblast growth factor receptor 3/human epidermal growth factor 2 (*FGFR3*/HER2) expression. The role of granulocyte-colony–stimulating factor use as primary prophylaxis is critical with sacituzumab govitecan, as demonstrated in clinical trials.

B. Biomarker-selected patients (questions H05–H07, H09, H10, and H12–H17)

HER2 IHC 3+ tumors

HER2 IHC assessment in UC uses the gastric cancer scoring algorithm. The optimal timing of HER2-directed therapy remains an area of ongoing debate, with no clear consensus regarding whether trastuzumab deruxtecan (T-DXd) should be used as second-line or third-line therapy. Discussion reflected the growing recognition of HER2 as an actionable target in metastatic UC. In patients progressing after cisplatin/gemcitabine with switch maintenance avelumab or in platinum-ineligible patients progressing after single-agent pembrolizumab, panelists remain relatively divided between EV monotherapy, combination approaches, and T-DXd.

FGFR3 mutation/fusion–positive tumors

The optimal timing of *FGFR3*-targeted treatment shows no clear consensus, although the majority (62.9%) prefer erdafitinib as third-line therapy after both EV plus pembrolizumab and platinum-based chemotherapy rather than immediate second-line use. Treatment selection demonstrates lack of consensus across most clinical scenarios. After cisplatin/gemcitabine with switch maintenance avelumab and in platinum-ineligible patients after pembrolizumab monotherapy, panelists favor EV monotherapy over erdafitinib.

Dual-biomarker–positive (HER2 IHC 3+ and FGFR3 mutation/fusion–positive)

Patients harboring both HER2 overexpression and an *FGFR3* activating mutation or fusion represent a particularly complex management scenario with lack of consensus across all treatment settings. After progression on EV plus pembrolizumab, there is no consensus for erdafitinib (30.6%), platinum combination (27.8%), or T-DXd (38.9%). This distribution reflects the clinical uncertainty about which biomarker should take precedence as the oncogenic driver given the lack of established data comparing sequencing approaches in dual-biomarker–positive cases. In more heavily pretreated patients after both EV plus pembrolizumab and platinum-based chemotherapy, practitioners favor T-DXd (66.7%) over erdafitinib (33.3%) despite the lack of a phase 3 trial with T-DXd in metastatic UC.

9. Considerations for urinary tract cancer special populations

A. Older adults and individuals with select comorbidities (questions I01–I03 and I16–I19)

Age and dosing considerations

Strong consensus (94.4%) supported offering EV plus pembrolizumab at any chronologic age, with age alone not considered a contraindication. Dosing strategies showed no consensus, with most practitioners (61.8%) using full-dose EV (1.25 mg/kg), whereas others

(32.4%) preferred reduced dosing (1 mg/kg) in older patients. For frail patients with an Eastern Cooperative Oncology Group performance status of 3, no consensus exists, although EV plus pembrolizumab remains most frequently selected (45.5%), followed by best supportive care (24.2%), and single-agent pembrolizumab (27.3%).

Diabetes mellitus and renal impairment

Strong consensus (94.1%) supports offering EV plus pembrolizumab without waiting for glycemic optimization in patients who have hemoglobin A1C levels >8%, with endocrinology referral. For acute hyperglycemia >300 mg/dL, no consensus exists, although most (73.5%) prefer holding treatment until glucose control improves. Strong consensus supports EV plus pembrolizumab in patients with severe renal impairment, including a creatinine clearance <30 mL per minute (94.1%) and patients undergoing hemodialysis (91.2%). These treatment decisions also emphasized the importance of informed and shared decision making with patients and families regarding goals of therapy, balancing potential benefits against treatment-related risks in various vulnerable populations, especially with very limited data.

B. Special considerations for histologic subtypes/variants (questions I04–I15)

Urothelial carcinoma subtypes/variants

For squamous cell carcinoma, no consensus existed, although practitioners consistently favored EV plus pembrolizumab over platinum-based therapy regardless of cisplatin eligibility (71.4% cisplatin-ineligible, 68.6% cisplatin-eligible). Sarcomatoid histology showed strong consensus for EV plus pembrolizumab in cisplatin-ineligible patients (91.4%) and preference in cisplatin-eligible patients (71.4%). Both plasmacytoid and micropapillary histologies demonstrated consensus favoring EV plus pembrolizumab across all cisplatin eligibility groups (80%–94%).

Nonurothelial histologic subtypes

There was no consensus for treatment of small cell neuroendocrine carcinoma, but there was preference for platinum-etoposide with checkpoint inhibitor over chemotherapy alone (57.1% cisplatin-eligible, 55.9% cisplatin-ineligible), with minimal use of EV plus pembrolizumab. Mucinous adenocarcinoma showed no consensus with preference for FOLFOX (leucovorin calcium [folinic acid], fluorouracil, and oxaliplatin; 61.8%) over FOLFIRINOX (leucovorin calcium [folinic acid], fluorouracil, irinotecan, and oxaliplatin; 32.4%). In pure squamous cell carcinoma, there was consensus for various platinum-based combinations (75%) versus EV plus pembrolizumab (25%). These treatment preferences reflect the understanding that nectin-4 expression and localization may vary significantly across different histologic subtypes, with higher expression typically observed in conventional UC and some urothelial histologic subtypes versus pure nonurothelial urinary tract malignancies.[27]

DISCUSSION

AUC3 represents a unique, novel, and valuable contribution to the genitourinary oncology community, aiming to address critical gaps in clinical decision making that extend beyond the scope of traditional clinical trials, retrospective data sets, and practice guidelines. Although randomized controlled trials provide essential efficacy and safety data for regulatory approval, they often cannot address the nuanced clinical scenarios encountered in routine practice, including treatment sequencing decisions, management of special populations, and integration of rapidly evolving therapeutic options. Similarly, whereas professional society guidelines offer evidence-based recommendations, they may not capture the real-world complexity of treatment selection when multiple effective options exist or when facing scenarios with limited prospective data, and their implementation is often constrained by regional access patterns. A forum such as AUC3 fills this critical void by systematically gathering expert consensus on challenging clinical questions, providing practical guidance for practitioners navigating the increasingly complex landscape of modern urologic cancer care. The multidisciplinary composition of the expert panel, rigorous methodology using a modified Delphi processes, and focus on areas of clinical uncertainty make AUC3 a distinctive resource for guidelines-informed practice.

In RCC, the consensus recommendations highlight both the rapid evolution of the treatment landscape and the persistent areas requiring clinical judgment and further research. Strong consensus emerged around adjuvant pembrolizumab for high-risk disease, reflecting confidence in KEYNOTE-564 data, whereas uncertainty persists in scenarios not directly addressed by clinical trials, such as patients with advanced/metastatic, favorable-risk disease being considered for systemic therapy or those with prior adjuvant ICI exposure. The lack of consensus on specific first-line regimen selection despite multiple effective systemic therapy options underscores the need for improved predictive biomarkers and refined patient-selection strategies. Notably, expert recognition of treatment sequence–specific considerations, such as the preference for single-agent VEGFR-TKI therapy after dual ICI and ICI-VEGFR-TKI combinations, provides valuable guidance for real-world practice, in which patients frequently receive multiple lines of therapy. The integration of belzutifan and the management of variant histologies represent emerging areas in which expert consensus helps bridge the gap between limited clinical trial data and complex clinical practice needs.

For UTC, the consensus recommendations reflect the dramatic transformation of the treatment landscape after recent landmark trials, particularly the establishment of EV plus pembrolizumab as the new standard of care in the advanced/metastatic setting. The strong consensus supporting this combination across diverse patient populations, including those with medical comorbidities and selected variant histologic subtypes, demonstrates expert confidence in its broad applicability. However, the lack of consensus in later-line treatment selection, particularly regarding the optimal sequencing

of targeted therapies and the role of biomarker-directed treatment, highlights the complexity of modern, advanced UC management. The preference for platinum-based chemotherapy after EV plus pembrolizumab progression in *FGFR3*/HER2-negative patients provides crucial guidance for a common clinical scenario not directly addressed in registration trials. In addition, consensus regarding the management of special populations offers practical guidance for treatment decisions in vulnerable populations often underrepresented in clinical trials.

Several important limitations warrant acknowledgment. The panel composition was predominantly comprised of medical oncologists with primarily North American and European representation, which may limit generalizability to other geographic regions and bias consensus in areas requiring specialized surgical or radiation oncology expertise. Some questions used granular response categories that limited consensus achievement and reduced clinical interpretability. Although consensus thresholds (≥75% for consensus, >90% for strong consensus) are conventional in Delphi methodology, they remain somewhat arbitrary. Denominators varied across questions as panelists were not mandated to respond outside their domains of expertise. In some instances, voting patterns shifted between premeeting and postmeeting rounds, which may reflect the influence of scientific discussion on expert opinion. These findings are time-bound to January 2025 and assume availability of discussed therapies, which may not apply in all regions. These recommendations are intended to complement, not replace, established clinical practice guidelines and should be interpreted within local and regional healthcare contexts.

The identification of numerous areas lacking expert consensus serves as a valuable roadmap for future research priorities and clinical trial design. These gaps highlight the urgent need for predictive biomarkers, head-to-head comparisons of effective regimens, and prospective evaluation of treatment sequencing strategies. The dynamic nature of urologic cancer treatment, with ongoing clinical trials and emerging therapeutic approaches, necessitates regular reassessment of expert consensus as new evidence becomes available. AUC3 is planned as an annual conference to continuously address evolving treatment paradigms, emerging clinical questions, and areas in which practice patterns may benefit from expert guidance. This iterative approach will ensure that consensus recommendations remain current and relevant as the field continues to advance rapidly.

AFFILIATIONS

[1]Department of Medicine, Urology, and Radiation Medicine and Applied Sciences, University of California-San Diego, La Jolla, California, USA

[2]Department of Medical Oncology and Therapeutics Research, City of Hope Comprehensive Cancer Center, Duarte, California, USA

[3]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts, USA

[4]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, USA

[5]Department of Medical Oncology, Gustave Roussy, Villejuif, France

[6]Genitourinary Malignancies Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

[7]Department of Oncology, Georgetown Lombardi Comprehensive Cancer Center, Georgetown University, Washington, District of Columbia, USA

[8]Bladder Cancer Advocacy Network, Bethesda, Maryland, USA

[9]Department of Medicine, Tennessee Oncology, Nashville, Tennessee, USA

[10]Department of Hematology and Medical Oncology, Winship Cancer Institute, Emory University, Atlanta, Georgia, USA

[11]Section of Medical Oncology, Department of Medicine, Yale Cancer Center, Yale University, New Haven, Connecticut, USA

[12]Department of Radiation Oncology, Massachusetts General Hospital, Boston, Massachusetts, USA

[13]Division of Hematology and Medical Oncology, Department of Medicine, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, New York, USA

[14]Division of Medical Oncology, Department of Medicine, University of Washington, Seattle, Washington, USA

[15]Fred Hutchinson Cancer Center, Seattle, Washington, USA

[16]Department of Hematology and Medical Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, Ohio, USA

[17]Division of Hematology-Oncology, Department of Medicine, Abramson Cancer Center, University of Pennsylvania, Philadelphia, Pennsylvania, USA

[18]Division of Hematology-Oncology, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA

[19]Department of Medical Oncology, Tom Baker Cancer Center, University of Calgary, Calgary, Alberta, Canada

[20]Department of Pathology, Brigham and Women's Hospital, Boston, Massachusetts, USA

[21]Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

[22]Division of Hematology/Oncology, Department of Medicine, University of California-San Francisco, San Francisco, California, USA

[23]Department of Pathology and Laboratory Medicine, University of Miami Miller School of Medicine, Miami, Florida, USA

[24]KidneyCan, Philadelphia, Pennsylvania, USA

[25]Department of Genitourinary Oncology, Moffitt Cancer Center, Tampa, Florida, USA

[26]Division of Medical Oncology, Department of Medicine, Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah, USA

[27]Division of Medical Oncology, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA

[28]Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

[29]Division of Medical Oncology, Department of Medicine, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, North Carolina, USA

[30]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, University of Milan, Milan, Italy

[31]Department of Medical Oncology, Barts Cancer Institute, Queen Mary University of London, London, UK

[32]Division of Hematology/Oncology, Department of Medicine, Vanderbilt-Ingram Cancer Center, Vanderbilt University, Nashville, Tennessee, USA

[33]Department of Urology, University of California-Los Angeles, Los Angeles, California, USA

[34]Department of Genitourinary Oncology, AdventHealth Cancer Institute, Orlando, Florida, USA

[35]Division of Medical Oncology, Princess Margaret Cancer Center, University of Toronto, Toronto, Ontario, Canada

[36]Department of Medical Oncology, Vall d'Hebron Institute of Oncology, Hospital Universitari Vall d'Hebron, Barcelona, Spain

[37]Department of Medical Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands

ACKNOWLEDGMENTS

The authors thank Jennifer Colby for editorial and writing support in the preparation of this article

CONFLICT OF INTEREST STATEMENT

Rana R. McKay reports personal/consulting or advisory fees from Ambrx, Arcus, AstraZeneca, Aveo Pharmaceuticals, Bayer, Blue Earth Diagnostics, Boundless Bio, Bristol Myers Squibb Company, Calithera, Caris, Dendreon, Daiichi-Sankyo Company, Eli Lilly and Company, EISAI Inc., Exelixis, Janssen, Merck, Myovant, Neomorph, Nimbus, Novartis, Pfizer, Sanofi, SeaGen Inc., Sorrento Therapeutics, Telix, and Tempus outside the submitted work. Sumanta Pal reports support for travel, expenses, and accommodations from Crispr Therapeutics, Exelixis, and Ipsen outside the submitted work. Wanling Xie reports personal/consulting or advisory fees from Convergent Therapeutics and the Prostate Cancer Clinical Trials Consortium outside the submitted work. David Aggen reports grants/contracts from Astellas Pharma US Inc., EvolveImmune, Merck & Company Inc., and Pfizer Inc.; personal/consulting or advisory fees from AdaptImmune, Alpha Insights, Aptitude Health, Astellas Pharma, Boehringer Ingelheim, Bristol Myers Squibb Foundation, Century Therapeutics, Curio Science, Genentech Inc., Guidepoint Global Advisors, MJH Life Sciences, Natera, Pfizer Inc., Roche/Genentech, and Seattle Genetics/Pfizer; and travel support from Merck Sharp & Dohme outside the submitted work. Laurence Albiges reports research support/funding from Astellas Pharma, EvolveImmune, Merck, and Pfizer Inc.; personal/consulting or advisory fees from Amgen, Astellas Pharma, Bristol Myers Squibb Company, Daiichi-Sankyo Company, EISAI Inc., F. Hoffmann-La Roche, Janssen Pharmaceuticals, Pfizer Inc., Ipsen Pharma SAS, Novartis, Telix, and Xencor; and travel support from Bristol Myers Squibb Company, Ipsen Pharma SAS, and Merck Sharp and Dohme outside the submitted work. Andrea Apolo reports royalties from the University of Illinois-Urbana Champaign outside the submitted work. Michael B. Atkins reports grants/contracts from the National Cancer Institute; personal/consulting or advisory fees from AbbVie, Agenus, AstraZeneca, Aveo Pharmaceuticals, BeiGene, Boehringer-Ingelheim, Bristol Myers Squibb Company, EISAI Inc., Exelixis, Genentech, Immunocore, IO Biotech, Innovent, Jazz Pharmaceuticals, Merck, Novartis, OncoRena, Pfizer, Pliant Therapeutics, Pyxis Oncology, Roche, SAB Bio, Sanofi, SeaGen Inc., Simcha, Replimmune, Syncona, and Werewolf Pharmaceuticals; and data and safety monitoring for Novartis and Pfizer Pharmaceuticals LLC outside the submitted work. Rick Bangs reports personal/consulting or advisory fees from Astellas Pharma, AstraZeneca, Bladder Cancer Advocacy Network, Gilead Sciences Inc., Janssen Global Services LLC, Johnson & Johnson, and Pfizer; support for other professional activities from the Advanced Urologic Cancer Consensus Conference (AUC3), Astellas Pharma, AstraZeneca, Pfizer Pharmaceuticals, and SeaGen Inc.; and travel support from the International Bladder Cancer Group outside the supported work. Kathryn E. Beckermann reports grants/contracts from Aravive, Arsenal Bioscience, Bristol Myers Squibb Company, and Plonyr; and personal/consulting or advisory fees from Alpine Bioscience, Adicet, Aravive, Arcus, AstraZeneca, Aveo Pharmaceuticals, Bristol Myers Squibb Company, Exelixis, EISAI Inc., Nimbus, Merck, Novartis, Sanofi Pasteur Inc., SeaGen Inc., and Xencor outside the submitted work. Joaquim Bellmunt reports institutional research from Pfizer/EMD Serono; grants/contracts from Pfizer/Gilead Sciences Inc.; personal/consulting or advisory fees from AstraZeneca/MedImmune, Bristol Myers Squibb Company, EMD Serono/Merck, Merck, Novartis, Pfizer, and Pierre Fabre; honoraria from UpToDate; stock ownership in Bicycle Therapeutics; stock and other ownership interests in Rainier Therapeutics; royalties from UpToDate Bladder Cancer; and support for travel, accommodations, and expenses from Genentech/Roche and Ipsen outside the submitted work. Stephanie A. Berg reports personal/consulting or advisory board fees from Aptitude Health, Bristol Myers Squibb Company, Curio Sciences, EISAI Inc., Guardant Health, Natera, Targeted Oncology, and Xencor; and support for other professional activities from AVEO Pharmaceuticals Inc., EISAI Inc., Pfizer, and Sanofi outside the submitted work. Mehmet A. Bilen reports grants to his institution from AAA, AstraZeneca, Bayer, Bristol Myers Squibb Company, Genentech/Roche, Genome & Company, Incyte, Merck, Nektar, Peloton Therapeutics, Pfizer, SeaGen Inc., Tricon Pharmaceuticals, and Xencor; and personal/consulting or advisor fees from AstraZeneca, Bayer, Bristol Myers Squibb Company, Calithera Biosciences, EISAI Inc., EMD Serono, Exelixis, Genomic Health, Janssen Biotech, Nektar, Pfizer, SeaGen Inc., and Sanofi outside of the submitted work. David Braun reports research support from Exelixis and AstraZeneca; personal/consulting and advisory fees from AbbVie, Accolade 2nd MD, Adnovate Strategies, Aptitude Health, ASCO Post and Harborside, Cancer Expert Now, CancerNetwork, Catenion, Cello Health BioConsulting, Compugen, Daiichi-Sankyo Company, Dechert, DLA Piper, EISAI Inc., Elephas, Exelixis, AVEO Oncology, Haymarket Medical Network, Link Cell Therapies, MDedge, MedScape, Merck, NeoMorph, Nimbus, OncLive, Pfizer, PWW Consulting, Scholar Rock, and Targeted Oncology; and owns stock options in Elephas outside the submitted work. Jason Efstathiou reports personal/consulting or advisory fees from AngioDynamics Inc., Astellas Pharma US Inc., AstraZeneca, Bayer HealthCare Pharmaceuticals Inc., Bioprotect, Blue Earth Diagnostics Ltd., Boston Scientific Corporation, Clarity Pharmaceuticals, Elekta Inc., EMD Serono, Genentech USA Inc., Gilead Sciences Inc., IBA Proton Therapy Inc., Janssen Pharmaceuticals Inc., Johnson & Johnson, Lantheus Medical Imaging Inc., MDx Health, Merck, Myovant

Sciences, Pfizer Pharmaceuticals LLC, Progencis Pharmaceuticals Inc., and Roivant Pharma; and support for other professional activities from Merck, Myovant Sciences, and Roviant Pharma outside the submitted work. Matthew Galsky reports personal/consulting fees from AbbVie Inc., Aktis, Astellas Pharma, AstraZeneca, Bristol Myers Squibb Company, Daiichi-Sankyo Company, EMD Serono, Genentech, Gilead Sciences Inc., Incyte Corporation, Janssen Biotech, Merck, Pfizer, SeaGen Inc., Seattle Genetics Inc., and Veracyte outside the submitted work. Petros Grivas reports grants/contracts from Acrivon Therapeutics, ALX Oncology, Bristol Myers Squibb Company, EMD Serono Inc., G1 Therapeutics, Genentech, Gilead Sciences Inc., Merck Sharp & Dohme, Mirati Therapeutics, and QED Therapeutics; and personal/consulting fees from Aadi Bioscience, AbbVie, Asieris Pharmaceuticals, Astellas Pharma, AstraZeneca, Bicycle Therapeutics, Bristol Myers Squibb Company, CG Oncology, Daiichi-Sankyo Company, Eli Lilly and Company, EMD Serono Inc., F. Hoffmann-La Roche, Foundation Medicine Inc., Fresenius Kabi USA LLC, Gilead Sciences Inc., ImmunityBio, Janssen Scientific Affairs LLC, Merck Sharp & Dohme, Pfizer, PureTech Health, Replimune, Roche, Strata Oncology, Tyra Biosciences, and UroGen outside the submitted work. Shilpa Gupta reports institutional research funding from Bristol Myers Squibb Foundation, EMD Serono, Exelixis, Gilead Sciences, Merck, Moderna Therapeutics, Novartis, QED Therapeutics, Roche/Genentech, and SeaGen; personal/consulting or advisory fees from Astellas Pharma, Bayer, Bristol Myers Squibb Company/Medarex, EMD Serono, Foundation Medicine, Genzyme, Gilead Sciences, Merck, Natera, Pfizer, and SeaGen; speaking fees from Bristol Myers Squibb Company, Gilead Sciences, and SeaGen; stock and other ownership interests in BioNTech SE, Moderna Therapeutics, and Nektar; royalties from UpToDate; and support for travel, accommodations, and expenses from Pfizer outside the submitted work. Naomi Haas reports grants/contracts from the ECOG-ACRIN Cancer Research Group; personal/consulting or advisory fees from AVEO Pharmaceuticals, Calithera Biosciences, EISAI Inc., Exelixis, Merck Sharp & Dohme, Pfizer, and Roche/Genentech; and fees for expert testimony from Eli Lilly and Company outside the submitted work. Hans Hammers reports institutional research funding from Bristol Myers Squibb Company and Merck; personal/consulting or advisory fees from ARMO BioSciences, Bayer, Bristol Myers Squibb Company, Corvus Pharmaceuticals, Corvus Pharmaceuticals, Exelixis, Merck, Novartis, and Pfizer; honoraria from Bristol Myers Squibb Company; and support for travel, accommodations, and expenses from Bristol Myers Squibb Company, Eli Lilly and Company, Merck, Novartis, and Pfizer outside the submitted work. Daniel Y. C. Heng reports personal/consulting or advisory fees from Alberta Health Services, Bristol Myers Squibb Company, EISAI Inc., Exelixis Inc., Ipsen Pharma SAS, Merck, Novartis, and Pfizer Canada Inc. outside the submitted work. Gopakumar Iyer reports institutional research funding from AADi, Flare Therapeutics, Janssen, Loxo Oncology/Eli Lilly and Company, and Pfizer; personal/consulting or advisory fees from AstraZeneca, Bicycle Therapeutics, Daiichi-Sankyo Company. EMD Serono, Flare Therapeutics, Janssen Research and Development LLC, Loxo Oncology/Eli Lilly and Company, Mirati Therapeutics, and Pfizer outside the submitted work. Eric Jonasch reports personal/consulting fees from AVEO Pharmaceuticals Inc., Bristol Myers Squibb Company, EISAI Inc., Exelixis Inc., Ipsen Biopharmaceuticals Inc., Johnson & Johnson, Merck, Novartis Pharma, and Takeda Pharmaceuticals Inc. outside the submitted work. Vadim S. Koshkin reports grants/contracts from Tyra Biosciences; research funding from AstraZeneca/Pfizer, Curium US LLC, Eli Lily and Company, Gilead Sciences Inc., Merck, Nektar Therapeutics, Novartis, Pfizer, SeaGen Inc., and Taiho Oncology Inc.; and personal/consulting or advisory fees from Astellas Pharma, Bicycle Therapeutics, Bristol Myers Squibb Company, Genentech, Janssen Pharmaceuticals, Loxo Oncology, Merck Sharp & Dohme, Natera Inc., Pfizer, and Tempus outside the submitted work. Roger Li reports personal/consulting fees from AstraZeneca, Bristol Myers Squibb Company, CG Oncology, enGene, Johnson & Johnson, Merck, Pfizer, Predicine, UroGen, and Valar Labs outside the submitted work. Surena Matin reports grants/contracts from Helsinn/QED and UroGen Pharma Inc.; personal/consulting fees from Fujifilm Corporation, Johnson & Johnson, Mashup Media LLC, Merck, and *Urology Times* Clinical Forum Advancements; support for other professional activities from Ferring Pharmaceuticals (clinical trial); and is a fiduciary officer of Elsevier Publishing outside the submitted work. Benjamin Maughan reports grants/contracts or research funding to his institution for correlative studies and investigator-sponsored clinical trials from Bavarian-Nordic, Bristol Myers Squibb Company, Clovis Oncology, Exelixis, Genentech, and Merck; personal/consulting or advisory fees from AbbVie, Arcus, Astellas Pharma, AVEO Oncology, Bayer Oncology, Bristol Myers Squibb Company, Clovis Oncology, DAVA Oncology, EISAI Inc., Eli Lilly and Company, Exelixis, Janssen, Merck, Merck KgA, Peloton Therapeutics, Pfizer, Sanofi, Tempus, Telix, and Xencor; and is a member of a drug safety monitoring board for AVEO Oncology outside the submitted work. David F. McDermott reports research support from Bristol Myers Squibb Company, Genentech, Exelixis, and Pfizer; and personal/consulting fees or honoraria from Bristol Myers Squibb Company, Cullinan, EISAI Inc., Exelixis, Johnson & Johnson Health Care Systems Inc., Merck, and Pfizer outside the submitted work. Bradley McGregor reports institutional research funding from Bristol-Myers Squibb Company, Calithera Biosciences, Exelixis, Pfizer/EMD Serono, and Seattle Genetics/Astellas; grants/contracts from Gilead Sciences Inc.; and personal/consulting or advisory fees from Aptitude Health, Arcus Bioscience, Astellas Pharma, AstraZeneca, AVEO Pharmaceuticals, Bayer, Bristol Myers Squibb Company, Curio Science, Daiichi-Sankyo Company/AstraZeneca, Dava Oncology LP, EISAI Inc., Eli Lilly and Company, Exelixis, Genmab, Gilead Sciences Inc., Hexagon Bio, Loxo/Eli Lilly and Company, MJH Life Sciences, Pfizer, Prime Education, SeaGen Inc., Seattle Genetics/Astellas Pharma, and Targeted Oncology outside the submitted work. Joshua Meeks reports personal/consulting or advisory fees from AstraZeneca, Bristol Myers Squibb Company, Calibr, CG Oncology, Ferring, Immunity Bio, Imvax, Janssen, Merck, Pfizer, Photocure, Prokarium, Protara, SeaGen/Astellas Pharma, and

UroGen outside the submitted work. Matthew Milowsky reports institutional research funding from Accuray, Acrivon Therapeutics, Alliance for Clinical Trials in Oncology Foundation, ALX Oncology, Arvinas, Astellas Pharma, Bristol Myers Squibb Company, Clovis Oncology, Flare Therapeutics, G1 Therapeutics, Genentech, Loxo Oncology/Eli Lilly and Company, Merck, Mirati Therapeutics, Novartis, OncoC4, the Prostate Cancer Clinical Trials Consortium, Roche, and SeaGen; personal/consulting or advisory fees from Loxo Oncology/Eli Lilly and Company; support for other professional activities from Elsevier, Medscape, and Research to Practice; and stock and other ownership interests in Gilead Sciences and Pfizer outside the submitted work. Robert J. Motzer reports grants/contracts from AVEO Pharmaceuticals, Bristol Myers Squibb Company, EISAI Inc., Exelixis, Pfizer, and Merck; and personal/consulting or advisory fees from Merck outside the submitted work. Andrea Necchi reports institutional research funding from AstraZeneca and Merck Sharp & Dohme; grants/contracts from Bristol Myers Squibb Company, Gilead Sciences Inc., and Ipsen; personal/consulting or advisory fees from Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb Company, Clovis Oncology, Daiichi-Sankyo Inc., F. Hoffman-La Roche, Ferring, Gilead Sciences Inc., GlaxoSmithKline, Incyte Corporation, Janssen Cilag EMA, Merck Sharp & Dohme, Rainier Therapeutics, Roche, and Seattle Genetics/Astellas; honoraria from AstraZeneca, Bristol Myers Squibb Company, Foundation Medicine, Janssen, Merck, and Roche; support for other professional activities from Bayer; support for travel, accommodations, and expenses from AstraZeneca, Janssen, Merck Sharp & Dohme, Rainier Therapeutics, and Roche; and stock and other ownership interests in Bayer outside the submitted work. Dan Petylak reports institutional grants/contracts or research funding from Advanced Accelerator Applications, Agensys, Astellas, AstraZeneca, Bayer, Bicycle Therapeutics, BioXCel Therapeutics, Bristol Myers Squibb Company, Clovis Oncology Inc., EISAI Inc., Eli Lilly and Company, Endocyte, Genentech, Gilead Sciences, Innocrin Pharma, MedImmune, Merck, Mirati Therapeutics, Novartis Pharma, Pfizer, Progenics, Replimune, Roche Laboratories, Sanofi, Seattle Genetics, and SeaGen; personal/consulting or advisory fees from Advanced Accelerator Applications, Amgen, Astellas Pharma, AstraZeneca, Bayer, Bicycle Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb Company, Clovis Oncology Inc., Eli Lilly and Company, Exelixis, Gilead Sciences, Incyte Corporation, Ipsen, Janssen Global Services LLC, Mirati Therapeutics, Monopteros Therapeutics, Pfizer, Pharmacyclics LLC (an AbbVie Company), Regeneron, Roche Laboratories, Seattle Genetics, SeaGen, and UroGen Pharma; support for other professional activities from Bicycle Therapeutics and Merck; fees for expert testimony from Celene and Sanofi; and owns stock in Tyme Inc. outside the submitted work. Sima Porten reports institutional research funding from Photocure Inc.; personal/consulting or advisory fees from AstraZeneca, Ferring Inc., Natrea, Oncuria, Photocure Inc., and Stryker; support for other professional activities from Janssen Pharmaceuticals Inc.; and honoraria from the American Urologic Association, Exact Sciences, and Pacific Edge outside the submitted work. Tom Powles reports research funding from Astellas Pharma, AstraZeneca, Bristol Myers Squibb Company, EISAI Inc., Exelixis, Ipsen, Johnson & Johnson, Merck Serono, Merk Sharp and Dohme, Novartis, Pfizer, Roche, and SeaGen; personal/consulting or advisory fees from Astellas Pharma, AstraZeneca, Bristol Myers Squibb Company, EISAI Inc., Exelixis, Incyte Corporation, Ipsen, Johnson & Johnson, MashupMD, Merck, Merck Serono, Merck Sharp and Dohme, Novartis, Pfizer, Roche, and SeaGen; honoraria from Astellas Pharma, AstraZeneca, Bristol Myers Squibb GmbH & Company KG, EISAI Inc., Exelixis, Incyte, Ipsen, Johnson & Johnson/Janssen, MashupMD, Merck, Merck Serono, Novartis, Pfizer, Roche, and SeaGen; and support for travel, accommodations, and expenses from AstraZeneca, Ipsen, Merck Sharp and Dohme, Pfizer, and Roche outside the submitted work. Brian Rini reports institutional research funding from Adela, Arcus, AstraZeneca, AVEO, Bristol Myers Squibb Company, Daiichi-Sankyo Company, Genentech, Exelixis, HiberCell, Incyte, Janssen, Merck, Pfizer, POINT Biopharma, Regeneron, Surface Oncology, and Tempus; grants/contracts from Arcus; and personal/consulting or advisory fees from AstraZeneca, Aveo, Bristol Myers Squibb Company, Debiopharm, EISAI Inc., Exelixis Inc., Formedics, Johnson & Johnson, Merck, and Xencor outside the submitted work. Brian Shuch reports personal/consulting fees from Histosonics and Veracyte Inc. and support for other professional activities from Merck and Telix outside the submitted work. Arlene Siefker-Radtke reports institutional research funding from Basilea Pharmaceutical, Bristol Myers Squibb Company, Janssen Pharmaceuticals Inc., Merck, the National Institutes of Health, and Nektar; personal/consulting or advisory fees from AstraZeneca, Basilea Pharmaceutical, Bavarian Nordic, Bristol Myers Squibb Company, G1 Therapeutics, Genentech, Gilead Sciences, Ideeya Biosciences, Immunomedics Inc., Janssen Pharmaceuticals Inc., Loxo, Merck, Mirati Therapeutics, the National Comprehensive Cancer Network, Nektar Therapeutics, SeaGen Inc., and Taiho Pharmaceutical; support for other professional activities from AbbVie, Astellas Pharma US Inc., Bicycle Therapeutics, Biohaven Pharmaceuticals Inc., Bristol Myers Squibb Company, EMB Serono, Ideeya Biosciences, Pfizer, Seattle Genetics Inc., and Taiho Oncology Inc.; and has a patent "Methods of characterizing and treating molecular subsets of muscle-invasive bladder cancer" outside the submitted work. Guru Sonpavde reports institutional research support/grants or contracts from Bayer, Blue Earth Diagnostics, Dainippon Sumitomo Pharma, EMD Serono, and Jazz Pharmaceuticals; personal/consulting or advisory fees from Aktis, Astellas Pharma, AstraZeneca, Bicycle Therapeutics, Bristol Myers Squibb Company, Daiichi-Sankyo Company, Eli Lilly and Company, Ellipses Pharma, EMD Serono, G1 Therapeutics, Gilead Sciences Inc., GlaxoSmithKline, Janssen Pharmaceuticals, Loxo Oncology, Merck, Pfizer, Scholar Rock, SeaGen Inc., Seattle Genetics, Servier Pharmaceuticals LLC, Synapse, Syncorp, Tempus, and Vial; speaking fees from Astellas Pharma, AstraZeneca, Aveo, Bayer, Exelixis, Gilead Sciences Inc., Janssen Biotech, Merck, Natera, Pfizer, and SeaGen Inc.; a family member who is employed by Myriad/Exact

Sciences; and data and safety monitoring for Mereo outside the submitted work. S. Srikala Sridhar reports institutional research funding from Bayer, Janssen, and Pfizer; and personal/consulting or advisory fees from Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb Company, EMD Serono, Immunomedics, Hoffmann-La Roche Limited, Janssen, Merck & Company, Merck Sharp & Dohme, Pfizer, Roche/Genentech, Sanofi, and SeaGen outside the submitted work. Cristina Suarez reports institutional grants/research support from Bristol Myers Squibb International, Ipsen, Merck Sharp & Dohme, Pfizer, and Roche; personal/consulting or advisory fees from Astellas, Bayer, Bristol Myers Squibb Company, Ipsen Fund, Merck, Novartis, Pfizer, and Roche; support for other professional activities from AstraZeneca, Bristol Myers Squibb Company, Ipsen Fund, and Roche; fees for expert testimony from Astellas and Merck Sharp & Dohme; and travel support from Bristol Myers Squibb International, Ipsen Fund, and Roche outside the submitted work. Chad Tang reports grants/contracts from Merck and Myriad Genetics Laboratories Inc.; personal/consulting or advisory fees from Diffusion Pharmaceuticals, Siemens USA, and Telix; honoraria from Bayer, Boston Scientific Corporation, Elekta, Lantheus, Molli Surgical, and Vision RT; royalties from Wolters Kluwer; and travel support from VisionRT outside the submitted work. Abhishek Tripathi reports personal/consulting or advisory fees from AADi, Bayer, Exelixis Deka Biosciences, Gilead Sciences, and Seattle Genetics/Astellas; and speaking fees from Sanofi outside the submitted work. Michiel S. Van Der Heijden reports institutional grant support from 4SC AG, AstraZeneca, Bristol Myers Squibb Company, F. Hoffmann-La Roche, and Merck Sharp & Dohme; and consulting fees (paid to institution) from Astellas Pharma, Bristol Myers Squibb Company, Daiichi-Sankyo Company, F. Hoffmann-La Roche, Janssen Pharmaceuticals, Merck Sharp & Dohme Corporation, Pfizer, and SeaGen Inc. outside the submitted work. Martin Voss reports research funding from Pfizer; grants/contracts from Eli Lilly and Company, Exelixis Inc., Pfizer Inc., and Regeneron; personal/consulting or advisory fees from Affimed Therapeutics, Arcus Bioscience, AVEO Pharmaceuticals Inc., EISAI Inc., Exelixis Inc., Genentech Inc., Kura Oncology, Merck, MicuRx Pharmaceuticals, Oncorena, and Pfizer; and stock and other ownership interest in Cell Genix outside the submitted work. Xu Wenxin reports institutional research support from Arsenal Biosciences, Merck, and Oncohost; grants/contracts from the Department of Defense (DoD grant W81XWH2210951); personal/consulting or advisory fees from AVEO Pharmaceuticals Inc., Celdara, Deciphera Pharmaceuticals, Jazz Pharmaceuticals, and Merck; and support for other professional activities from Broadcastmed, CEA Group Holding Company, EISAI Inc., Exelixis Inc., Jazz Pharmaceuticals, Medical Logix, MJH Life Sciences, Prime Education, WebMD Health, and Xencor outside the submitted work. Zhang Tian reports grants/contracts from Astellas Pharma and Janux Therapeutics; research funding from ALX Oncology, AstraZeneca, Bayer Pharmaceuticals, Eli Lilly & Company, Janssen/Johnson & Johnson, Merck, OncoC4, and Pfizer; personal/consulting or advisory fees from Aravive, Bayer Pharmaceuticals, Dava Oncology LP, Dendreon Pharmaceuticals LLC, Gilead Sciences Inc., Mashup Media, MJH Associates, Peerview, and Aravive; and support for other professional activities from ALX Oncology, AstraZeneca Pharmaceuticals LP, Aveo Oncology, Bristol Myers Squibb Company, EISAI Inc., Eli Lilly & Company, EMD Serono Inc., Janssen Pharmaceuticals Inc., Kura Oncology, Merck, Novartis Pharmaceuticals Corporation, OncoC4, Pfizer, Sanofi and Genzyme US Companies, SeaGen Inc., Tempus, and Xencor outside the submitted work. Jonathan Rosenberg reports institutional research funding from Acrivon Therapeutics, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb Company, Eli Lilly and Company, Genentech/Roche, and SeaGen Inc.; personal/consulting or advisory fees from Aadi Bioscience, Aktis Oncology, Astellas Pharma US Inc., Astellas Pharma Global Development, AstraZeneca Pharmaceuticals LP, Bayer, Boehringer Ingelheim International, Bristol Myers Squibb Company, Celgene Corporation, Century Therapeutics, Eli Lilly and Company, EMD Serono, Emergence Therapeutics, E.R. Squibb & Sons LLC, Generate Biosciences, Genentech Inc., Gilead Sciences Inc., Hengrui Therapeutics, Imvax, Janssen Oncology, Loxo Oncology, Merck & Company. Merck Sharp & Dohme, Mirati Therapeutics, MJH Life Sciences, Natera, Page AI, Pfizer, Roche/Genentech, Samsung Bioepis, SeaGen Inc., and Tyra Biosciences; honoraria from MashupMD, the National Comprehensive Cancer Network, Pfizer, and UpToDate; support for other professional activities from Alligator Bioscience, Arcus Bioscience, Arsenal Bio, Astellas Pharma, Astellas Pharma Global Development, AstraZeneca Pharmaceuticals LP, AstraZeneca UK Ltd., AVEO Pharmaceuticals Inc., Bayer, Bicycle Therapeutics, Boehringer Ingelheim, Clinical Care Options LLC, Exelixis Inc., Eli Lilly and Company, EMD Serono, Genentech Inc., Esai, Ideology Health, Infinity Pharmaceuticals, Inzio Medical, Mashup Media, Medical Educator Consortium, Medscape, Natera, Neomorph, Physicians Education Resources LLC, PSL Group Services, QED Therapeutics, Research to Practice, Samsung Bioepis, Scholar Rock, SeaGen Inc., Signify MD, Telix, and Touch Oncology; support for travel expenses and accommodation from Astellas Pharma, AstraZeneca Pharmaceuticals LP, E.R. Squibb & Sons LLC, and SeaGen Inc.; and has patents licensed to his institution "Amplification of chromosome 1q23 to predict cancer outcomes" and "Predictor of platinum sensitivity" outside the submitted work. Toni K. Choueiri reports institutional research funding from Agensys, Arcus Biosciences, AstraZeneca, AVEO, Bayer, Bristol Myers Squibb Company, Calithera Biosciences, EISAI Inc., Exelixis, GlaxoSmithKline, Ipsen, Merck, NiKang Therapeutics, Novartis, Peloton Therapeutics, Pfizer, Roche, Roche/Genentech, Seattle Genetics/Astellas, Takeda, and TRACON Pharma; honoraria from Alkermes, Analysis Group, Aravive, Arcus Biosciences, the American Society for Clinical Oncology, AstraZeneca, Bayer, Bristol Myers Squibb Company, Clinical Care Options, EISAI Inc., Eli Lilly and Company; EMD Serono, the European Society for Medical Oncology, Exelixis, Foundation Medicine, Gilead Sciences, Gilead Sciences, GlaxoSmithKline, Harborside Press, HiberCell, Infinity Pharmaceuticals, Ipsen, Janssen Oncology, Kanaph

Therapeutics, *Lancet Oncology*, MashupMD, Merck, Michael J. Hennessy Associates, Navinata Health, the National Comprehensive Cancer Network, NiKang Therapeutics, Novartis, Peloton Therapeutics, Pfizer, PlatformQ Health, Precede Bio, Prometheus, Roche/Genentech, Sanofi/Aventis, Scholar Rock, Tempest Therapeutics, *The New England Journal of Medicine*, and UpToDate; personal/consulting or advisory fees from Alkermes, Analysis Group, Aravive, Arcus Biosciences, the American Society for Clinical Oncology, AstraZeneca, Bayer, Bicycle Therapeutics, Bristol Myers Squibb Company, Clinical Care Options, Curesponse, EISAI Inc., EMD Serono, the European Society for Medical Oncology, Exelixis, Foundation Medicine, Gilead Sciences, GlaxoSmithKline, Harborside Press, Infinity Pharmaceutical, Ipsen, Janssen Oncology, Kanaph Therapeutics, *Lancet Oncology*, Merck, Michael J. Hennessy Associates, Navinata Health, the National Comprehensive Cancer Network, Neomorph, NiKang Therapeutics, Novartis, Peloton Therapeutics, Pfizer, PlatformQ Health, Precede Bio, Prometheus, Roche/Genentech, Sanofi/Aventis, Scholar Rock, Tempest Therapeutics, *The New England Journal of Medicine*, and UpToDate; has applied for institutional patents for "Biomarkers of Clinical Response and Benefit to Immune Checkpoint Inhibitor Therapy" (International Patent Application No. PCT/US2018/058430), circulating tumor DNA technologies, and "PBRM1 Biomarkers Predictive of Anti-Immune Checkpoint Response" (International Patent Application No. PCT/US2018/12209); support for travel, accommodations, and expenses from Alexion Pharmaceuticals, Alligent, Analysis Group, AstraZeneca, Bayer, Bristol Myers Squibb Company, Cerulean Pharma, Clinical Care Options, Corvus Pharmaceuticals, EISAI Inc., Eli Lilly and Company, EMD Serono, the European Society for Medical Oncology, Exelixis, Foundation Medicine, GlaxoSmithKline, Harborside Press, HERON, Ipsen, Kidney Cancer Association, Lancet Oncology, Lpath, Merck, Michael J. Hennessy Associates, Navinata Health, National Comprehensive Cancer Network, Novartis, Peloton Therapeutics, Pfizer, PlatformQ Health, Prometheus, Roche/Genentech, Sanofi/Aventis, *The New England Journal of Medicine*, and UpToDate; and has relationships with other medical communication companies outside the submitted work. The remaining authors disclosed no conflicts of interest.

ORCID

Rana R. McKay https://orcid.org/0000-0002-0581-7963
Wanling Xie https://orcid.org/0000-0001-5995-8000
David Aggen https://orcid.org/0000-0003-3963-5751
Laurence Albiges https://orcid.org/0000-0002-5734-3480
Andrea Apolo https://orcid.org/0000-0001-9409-1836
Michael B. Atkins https://orcid.org/0000-0003-3901-9924
Rick Bangs https://orcid.org/0000-0002-0706-8775
Kathryn E. Beckermann https://orcid.org/0000-0002-4616-6140
Joaquim Bellmunt https://orcid.org/0000-0003-2328-3421
Stephanie A. Berg https://orcid.org/0000-0001-6193-5350
Mehmet A. Bilen https://orcid.org/0000-0003-4003-1103
David Braun https://orcid.org/0000-0003-4543-5553
Maria I. Carlo https://orcid.org/0000-0002-4786-7408
Jason Efstathiou https://orcid.org/0000-0003-0996-0350
Matthew Galsky https://orcid.org/0000-0001-7655-9378
Petros Grivas https://orcid.org/0000-0003-3965-3394
Naomi Haas https://orcid.org/0000-0001-8907-7968
A. Ari Hakimi https://orcid.org/0000-0002-0930-8824
Hans Hammers https://orcid.org/0000-0002-6224-4559
Michelle Hirsch https://orcid.org/0000-0002-8767-8564
Eric Jonasch https://orcid.org/0000-0003-0943-2806
Vadim S. Koshkin https://orcid.org/0000-0003-2277-8668
Roger Li https://orcid.org/0000-0003-1274-7200
Surena Matin https://orcid.org/0000-0003-1638-1445
Benjamin Maughan https://orcid.org/0000-0002-0010-8551
David F. McDermott https://orcid.org/0000-0002-2675-5095
Bradley McGregor https://orcid.org/0000-0002-8298-0289
Joshua Meeks https://orcid.org/0000-0001-8535-5545
Matthew Milowsky https://orcid.org/0000-0002-8965-8129
Robert Motzer https://orcid.org/0000-0001-6925-2327
Andrea Necchi https://orcid.org/0000-0002-3007-2756
Sima Porten https://orcid.org/0000-0002-3948-4968
Thomas Powles https://orcid.org/0000-0001-7760-4724
Brian Rini https://orcid.org/0000-0002-2212-080X
Arlene Siefker-Radtke https://orcid.org/0000-0002-6328-9599
Guru Sonpavde https://orcid.org/0000-0002-1010-9611
S. Srikala Sridhar https://orcid.org/0000-0002-6994-1285
Chad Tang https://orcid.org/0000-0002-5915-1327
Michiel S. Van Der Heijden https://orcid.org/0000-0002-4407-7881
Wenxin Xu https://orcid.org/0000-0002-8450-2037
Jonathan Rosenberg https://orcid.org/0000-0003-2637-4249
Toni K. Choueiri https://orcid.org/0000-0002-9201-3217

REFERENCES

1. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. *CA Cancer J Clin*. 2025;75(1):10-45. doi:10.3322/caac.21871
2. Cirillo L, Innocenti S, Becherucci F. Global epidemiology of kidney cancer. *Nephrol Dial Transplant*. 2024;39(6):920-928. doi:10.1093/ndt/gfae036
3. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229-263. doi:10.3322/caac.21834
4. Choueiri TK, Tomczak P, Park SH, et al. Overall survival with adjuvant pembrolizumab in renal-cell carcinoma. *N Engl J Med*. 2024;390(15):1359-1371. doi:10.1056/nejmoa2312695
5. Choueiri TK, Powles T, Burotto M, et al. Nivolumab plus cabozantinib versus sunitinib for advanced renal-cell carcinoma. *N Engl J Med*. 2021;384(9):829-841. doi:10.1056/nejmoa2026982
6. Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus pembrolizumab or everolimus for advanced renal cell carcinoma. *N Engl J Med*. 2021;384(14):1289-1300. doi:10.1056/nejmoa2035716
7. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. *N Engl J Med*. 2018;378(14):1277-1290. doi:10.1056/nejmoa1712126
8. Rini BI, Plimack ER, Stus V, et al. Pembrolizumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. *N Engl J Med*. 2019;380(12):1116-1127. doi:10.1056/nejmoa1816714
9. Powles T, Catto JWF, Galsky MD, et al. Perioperative durvalumab with neoadjuvant chemotherapy in operable bladder cancer. *N Engl J Med*. 2024;391(19):1773-1786. doi:10.1056/nejmoa2408154

10. Powles T, Valderrama BP, Gupta S, et al. Enfortumab vedotin and pembrolizumab in untreated advanced urothelial cancer. *N Engl J Med*. 2024;390(10):875-888. doi:10.1056/nejmoa2312117
11. Gillessen S, Turco F, Davis ID, et al. Management of patients with advanced prostate cancer. report from the 2024 Advanced Prostate Cancer Consensus Conference (APCCC). *Eur Urol*. 2025;87(2):157-216. doi:10.1016/j.eururo.2024.09.017
12. Jani C, Abdallah N, Tan A, McKay RR. Liquid biopsy for renal cell carcinoma: a comprehensive review of techniques, applications, and future prospects. *Kidney Cancer*. 2024;8(1):205-225. doi:10.1177/24684570241303346
13. Reck M, Rodriguez-Abreu D, Robinson AG, et al. Pembrolizumab versus chemotherapy for PD-L1–positive non-small-cell lung cancer. *N Engl J Med*. 2016;375(19):1823-1833. doi:10.1056/nejmoa1606774
14. Emamekhoo H, Olsen MR, Carthon BC, et al. Safety and efficacy of nivolumab plus ipilimumab in patients with advanced renal cell carcinoma with brain metastases: CheckMate 920. *Cancer*. 2022;128(5):966-974. doi:10.1002/cncr.34016
15. Choueiri TK, Escudier B, McDermott DF, et al. Nivolumab plus ipilimumab vs sunitinib for first-line treatment of advanced renal cell carcinoma: final analysis from the phase 3 CheckMate 214 trial [abstract]. *J Clin Oncol*. 2025;43(16 suppl):4505. doi:10.1200/jco.2025.43.16_suppl.4505
16. Tannir NM, Signoretti S, Choueiri TK, et al. Efficacy and safety of nivolumab plus ipilimumab versus sunitinib in first-line treatment of patients with advanced sarcomatoid renal cell carcinoma. *Clin Cancer Res*. 2021;27(1):78-86. doi:10.1158/1078-0432.ccr-20-2063
17. Pal SK, Albiges L, Tomczak P, et al. Atezolizumab plus cabozantinib versus cabozantinib monotherapy for patients with renal cell carcinoma after progression with previous immune checkpoint inhibitor treatment (CONTACT-03): a multicentre, randomised, open-label, phase 3 trial. *Lancet*. 2023;402(10397):185-195. doi:10.1016/s0140-6736(23)00922-4
18. Choueiri TK, Albiges L, Barthelemy P, et al. Tivozanib plus nivolumab versus tivozanib monotherapy in patients with renal cell carcinoma following an immune checkpoint inhibitor: results of the phase 3 TiNivo-2 Study. *Lancet*. 2024;404(10460):1309-1320. doi:10.1016/s0140-6736(24)01758-6
19. Motzer RJ, Hutson TE, Glen H, et al. Lenvatinib, everolimus, and the combination in patients with metastatic renal cell carcinoma: a randomised, phase 2, open-label, multicentre trial. *Lancet Oncol*. 2015;16(15):1473-1482. doi:10.1016/s1470-2045(15)00290-9
20. Choueiri TK, Powles T, Peltola K, et al. Belzutifan versus everolimus for advanced renal-cell carcinoma. *N Engl J Med*. 2024;391(8):710-721. doi:10.1056/nejmoa2313906
21. Choueiri TK, Kluger H, George S, et al. FRACTION-RCC: nivolumab plus ipilimumab for advanced renal cell carcinoma after progression on immuno-oncology therapy. *J Immunother Cancer*. 2022;10(11):e005780. doi:10.1136/jitc-2022-005780
22. Powles T, Assaf ZJ, Davarpanah N, et al. ctDNA guiding adjuvant immunotherapy in urothelial carcinoma. *Nature*. 2021;595(7867):432-437. doi:10.1038/s41586-021-03642-9
23. Sountoulides P, Pyrgidis N, Brookman-May S, Mykoniatis I, Karasavvidis T, Hatzichristou D. Does ureteral stenting increase the risk of metachronous upper tract urothelial carcinoma in patients with bladder tumors? A systematic review and meta-analysis. *J Urol*. 2021;205(4):956-966. doi:10.1097/ju.0000000000001548
24. Bajorin DF, Witjes JA, Gschwend JE, et al. Adjuvant nivolumab versus placebo in muscle-invasive urothelial carcinoma. *N Engl J Med*. 2021;384(22):2102-2114. doi:10.1056/nejmoa2034442
25. Birtle AJ, Jones R, Chester J, et al. Improved disease-free survival with adjuvant chemotherapy after nephroureterectomy for upper tract urothelial cancer: final results of the POUT Trial. *J Clin Oncol*. 2024;42(13):1466-1471. doi:10.1200/jco.23.01659
26. van der Heijden MS, Sonpavde G, Powles T, et al. Nivolumab plus gemcitabine-cisplatin in advanced urothelial carcinoma. *N Engl J Med*. 2023;389(19):1778-1789. doi:10.1056/nejmoa2309863
27. Ghali F, Vakar-Lopez F, Roudier MP, et al. Metastatic bladder cancer expression and subcellular localization of Nectin-4 and Trop-2 in variant histology: a rapid autopsy study. *Clin Genitourin Cancer*. 2023;21(6):669-678. doi:10.1016/j.clgc.2023.05.014

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: McKay RR, Pal S, Xie W, et al. Advanced Urologic Cancer Consensus Conference (AUC3) 2025: expert consensus on the management of renal cell and urinary tract cancers. *CA Cancer J Clin*. 2026;e70052. doi:10.3322/caac.70052