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NCCN Clinical Practice Guidelines in Oncology™

Kidney Cancer

V.2.2010

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NCCN Kidney Cancer Panel Members

* Robert J. Motzer, MD/Chair † Þ
Memorial Sloan-Kettering Cancer Center

Neeraj Agarwal, MD ‡
Huntsman Cancer Institute at the University of Utah

Clair Beard, MD §
Dana-Farber/Brigham and Women's Cancer Center

Sam Bhayani, MD ω
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Graeme B. Bolger, MD †
University of Alabama at Birmingham Comprehensive Cancer Center

Barry Boston, MD † £
St. Jude Children's Research Hospital/University of Tennessee Cancer Institute

Michael A. Carducci, MD † Þ
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Sam S. Chang, MD ω
Vanderbilt-Ingram Cancer Center

Toni K. Choueiri, MD † Þ
Dana-Farber/Brigham and Women's Cancer Center

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Robert A. Figlin, MD †
City of Hope Comprehensive Cancer Center

Mayer Fishman, MD, PhD † ‡ Þ
H. Lee Moffitt Cancer Center & Research Institute

Steven L. Hancock, MD § Þ
Stanford Comprehensive Cancer Center

Gary R. Hudes, MD † ‡
Fox Chase Cancer Center

Eric Jonasch, MD †
The University of Texas M. D. Anderson Cancer Center

Timothy M. Kuzel, MD † ‡
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Paul H. Lange, MD ω
Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance

Ellis G. Levine, MD †
Roswell Park Cancer Institute

Kim A. Margolin, MD † ‡
Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance

M. Dror Michaelson, MD, PhD †
Massachusetts General Hospital Cancer Center

Continue

Thomas Olencki, DO ‡
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Roberto Pili, MD †
Roswell Park Cancer Institute

Bruce G. Redman, DO †
University of Michigan Comprehensive Cancer Center

Cary N. Robertson, MD ω
Duke Comprehensive Cancer Center

Charles J. Ryan, MD †
UCSF Helen Diller Family Comprehensive Cancer Center

Lawrence H. Schwartz, MD ф
Memorial Sloan-Kettering Cancer Center

Joel Sheinfeld, MD ω
Memorial Sloan-Kettering Cancer Center

Jue Wang, MD †
UNMC Eppley Cancer Center at The Nebraska Medical Center

† Medical oncology
‡ Hematology/hematology oncology
§ Radiotherapy/Radiation oncology
ф Diagnostic Radiology
£ Supportive Care including Palliative, Pain Management, Pastoral care and Oncology social work
Þ Internal medicine
ω Urology
* Writing committee member

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See NCCN Categories of Evidence and Consensus

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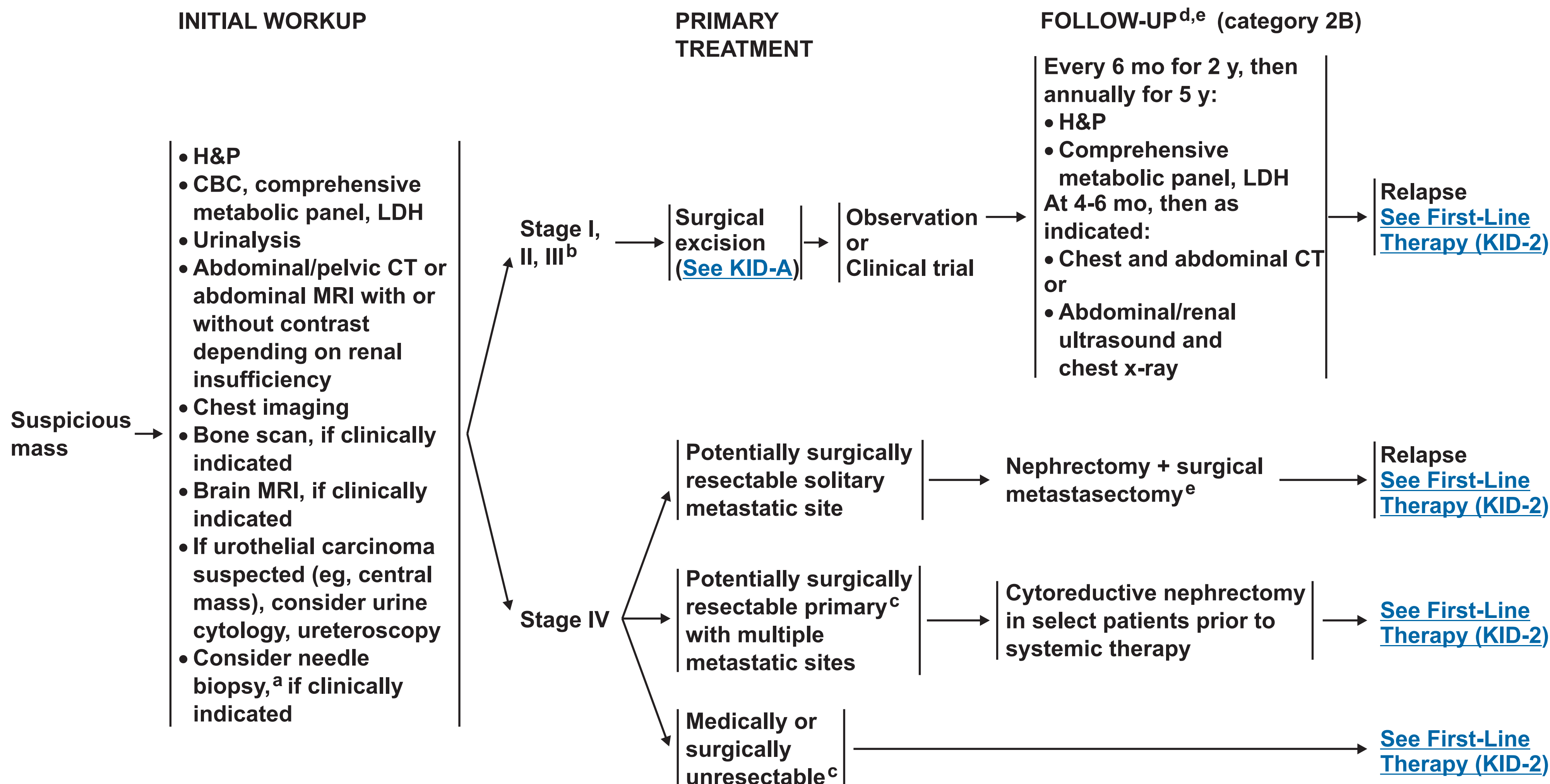

[a] Biopsy of small lesions may be considered to confirm diagnosis of malignancy and guide surveillance strategies.
[b] Patients are encouraged to participate in clinical trials.
[c] Individualized treatment based upon symptoms and extent of metastatic disease.
[d] UCLA Integrated Staging System (UISS) surveillance protocol based on risk group stratification of high, intermediate, low, or nodal status has been published and may be considered as an alternate to the listed follow-up for patients with localized or locally advanced RCC. See Surveillance Protocol Based on UISS Risk (KID-B)
[e] No single follow-up plan is appropriate for all patients. Follow-up should be individualized based on patient and tumor characteristics.

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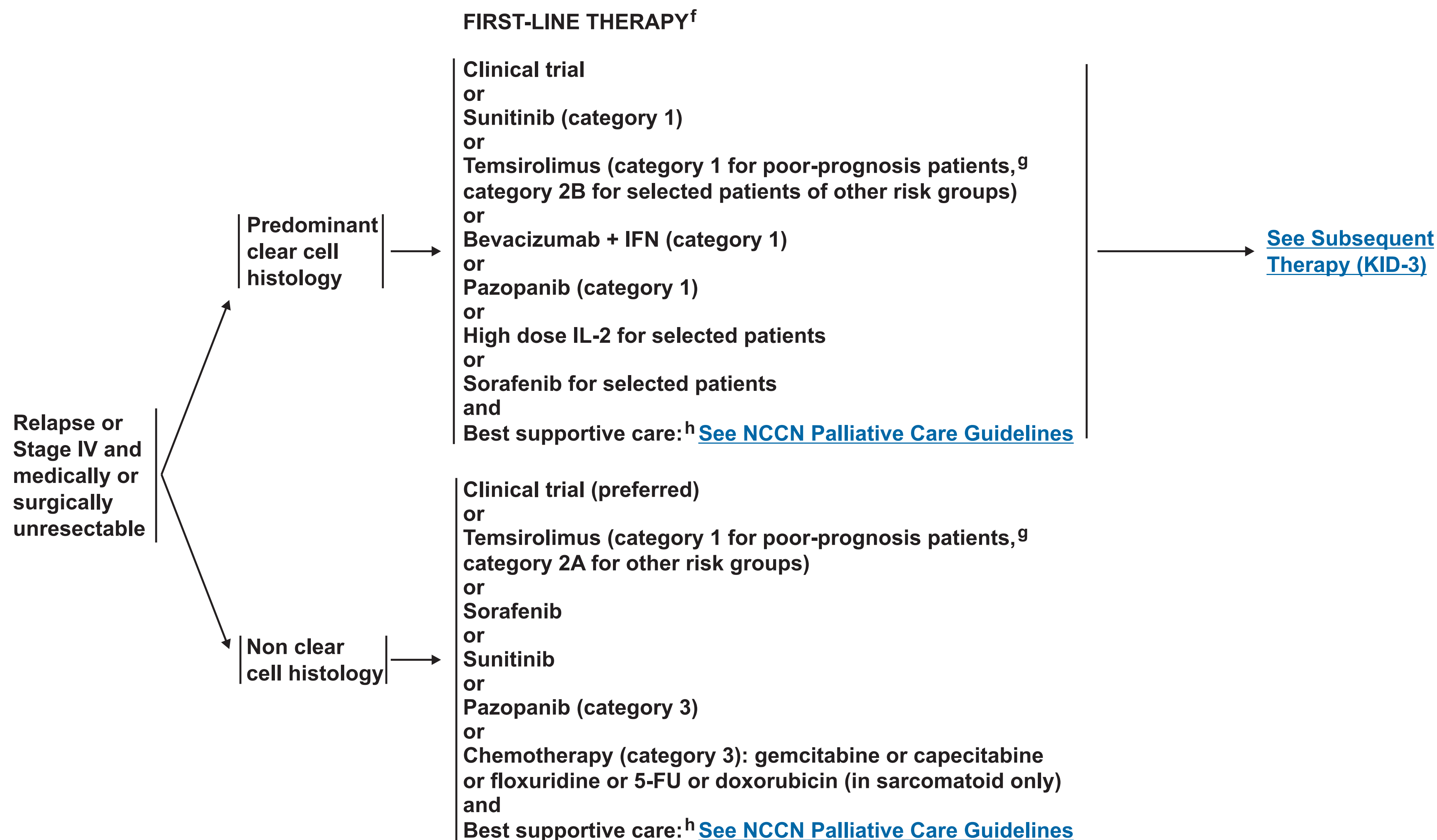

[f] Category 1 recommendations are listed in order of FDA approval.

[g] Poor-prognosis patients, defined as those with ≥ 3 predictors of short survival. See Predictors of Short Survival (KID-C).

[h] Best supportive care can include palliative RT, metastasectomy, or bisphosphonates for bony metastases.

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SUBSEQUENT THERAPY[i]

Predominant clear cell histology

Clinical trial
or
Everolimus (category 1 following tyrosine kinase inhibitor[j])
or
Sorafenib (category 1 following cytokine therapy and category 2A following other tyrosine kinase inhibitor[j])
or
Sunitinib (category 1 following cytokine therapy and category 2A following other tyrosine kinase inhibitor[j])
or
Pazopanib (category 1 following cytokine therapy and category 3 following other tyrosine kinase inhibitor[j])
or
Temsirolimus (category 2A following cytokine therapy and category 2B following tyrosine kinase inhibitor[j])
or
Bevacizumab (category 2B)
or
IFN or IL-2 (category 2B)
and
Best supportive care:[h] See NCCN Palliative Care Guidelines

[h] Best supportive care can include palliative RT, metastasectomy, or bisphosphonates for bony metastases.
[i] Tyrosine kinase inhibitors with a category 1 designation are listed in order of FDA approval.
[j] For example, sorafenib, sunitinib, or pazopanib.

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PRINCIPLES OF SURGERY

- Nephron-sparing surgery is appropriate in selected patients, for example:
  - Multiple primaries
  - Uninephric state
  - Renal insufficiency
  - Selected patients with small unilateral tumors
- Regional lymph node dissection is optional.
- Adrenal gland may be left if uninvolved and tumor is not high risk, on the basis of size and location.
- Special teams may be required for extensive inferior vena cava involvement.
- Observation or emerging energy ablative techniques (eg, cryosurgery or radiofrequency ablation) can be considered for patients who are not surgical candidates.
- Emerging energy ablative techniques (eg, cryosurgery or radiofrequency ablation) are currently considered an option by some experts for selected small tumors. Though a rigorous comparison with surgical resection (ie, total or partial nephrectomy by open or laparoscopic techniques) has not been done. Biopsy of small lesions may be considered to confirm diagnosis of malignancy and guide surveillance stragegies.

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SURVEILLANCE PROTOCOL BASED ON UISS RISK[1] (1 of 2)

UISS Risk Group Based Surveillance Protocol for Patients Following Surgical Resection for Localized and Locally Advanced Renal Cell Cancer See Risk Group Stratification (KID-B 2 of 2)

	Months Follow-up										
	3	6	12	18	24	30	36	48	60	84	108
Low risk:											
• History and physical examination			●		●		●	●	●		
• Laboratory studies*			●		●		●	●	●		
• Chest CT			●		●		●	●	●		
• Abdominal CT					●			●			
Intermediate risk:											
• History and physical examination		●	●	●	●	●	●	●	●	●	●
• Laboratory studies*		●	●	●	●	●	●	●	●	●	●
• Chest CT†		●	●	●	●	●	●	●	●	●	●
• Abdominal CT			●				●		●	●	●
High risk:											
• History and physical examination		●	●	●	●	●	●	●	●	●	●
• Laboratory studies*		●	●	●	●	●	●	●	●	●	●
• Chest CT†		●	●	●	●	●	●	●	●	●	●
• Abdominal CT		●	●	●	●		●	●	●	●	●
Nodal disease:											
• History and physical examination	●	●	●	●	●		●	●	●	●	●
• Laboratory studies*	●	●	●	●	●		●	●	●	●	●
• Chest CT†	●	●	●	●	●		●	●	●	●	●
• Abdominal CT	●	●	●	●	●		●	●	●	●	●

* Includes complete blood count, serum chemistries and liver function tests.

† A chest radiograph can be alternated with a chest CT after 3 years of follow-up.

[1] Lam J, Shvarts O, Leppert J, et al. Postoperative surveillance protocol for patients with localized and locally advanced renal cell carcinoma based on a validated prognostic nomogram and risk group stratification system. J Urol 2005;174:466-472.

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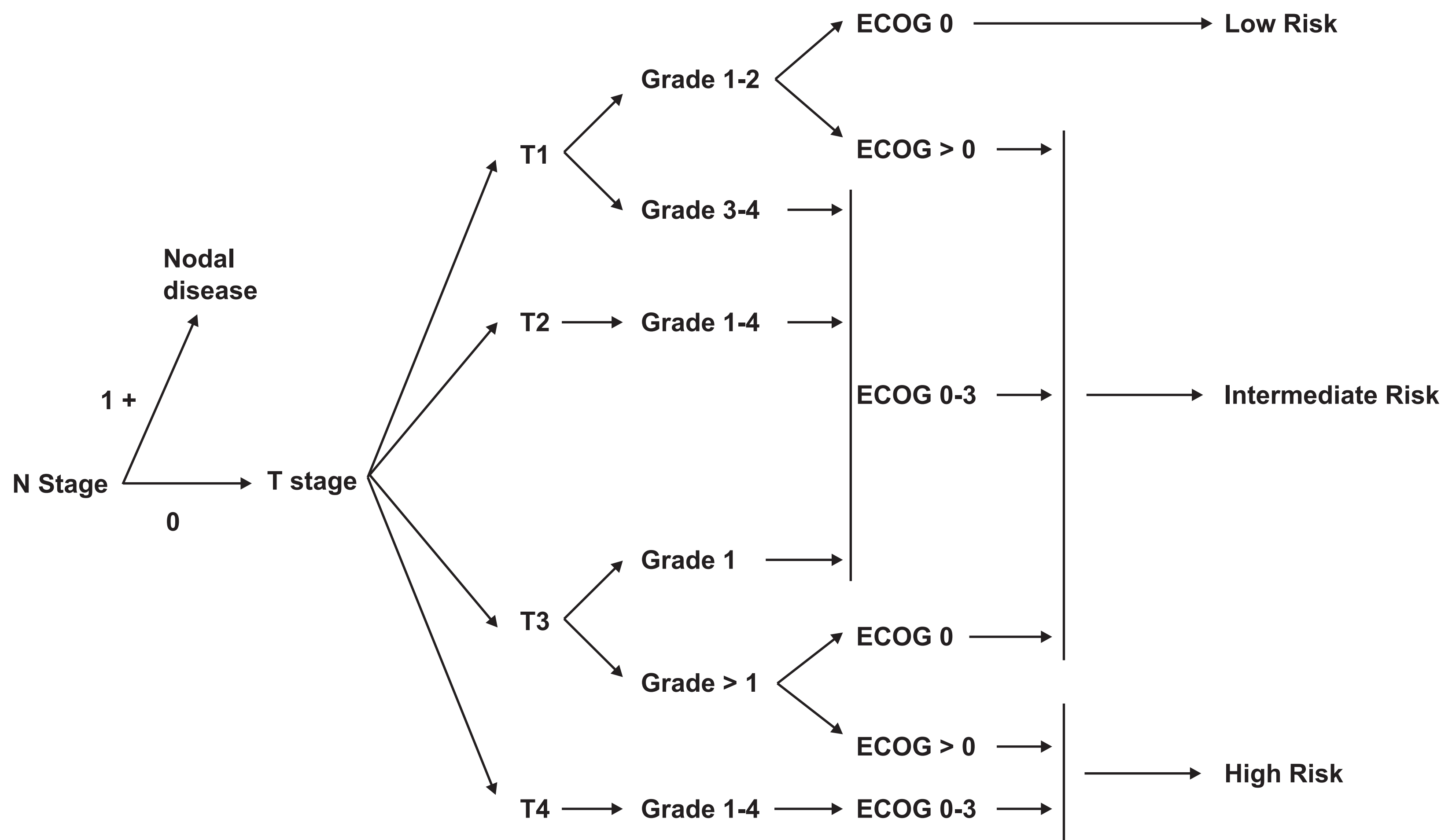
SURVEILLANCE PROTOCOL BASED ON UISS RISK[1] (2 of 2)

RISK GROUP STRATIFICATION



Flow chart for determination of UISS risk group assignment of patients with localized or locally advanced RCC.
Start from left to right using 1997 AJCC N stage and T stage, Fuhrman grade, and ECOG-PS.

[1] Lam J, Shvarts O, Leppert J, et al. Postoperative surveillance protocol for patients with localized and locally advanced renal cell carcinoma based on a validated prognostic nomogram and risk group stratification system. J Urol 2005;174:466-472.

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PREDICTORS OF SHORT SURVIVAL[1]

Poor-prognosis patients are defined as those with ≥ 3 predictors of short survival.

- **Lactate dehydrogenase level > 1.5 times upper limit of normal**
- **Hemoglobin level < lower limit of normal**
- **Corrected serum calcium level > 10 mg/dl (2.5 mmol/liter)**
- **Interval of less than a year from original diagnosis to the start of systemic therapy**
- **Karnofsky performance score ≤ 70**
- **≥ 2 sites of organ metastasis**

[1] Hudes G, Carducci M, Tomczak P et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. N Engl J Med 2007; 356(22):2271-2281.

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Staging (2002 AJCC 6th Edition)

Table 1

AJCC Staging of Renal Cell Carcinoma

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 7 cm or less in greatest dimension, limited to the kidney
T1a	Tumor 4 cm or less in greatest dimension, limited to the kidney
T1b	Tumor more than 4 cm but not more than 7 cm in greatest dimension, limited to the kidney
T2	Tumor more than 7 cm in greatest dimension, limited to the kidney
T3	Tumor extends into major veins or invades adrenal gland or perinephric tissues but not beyond Gerota's fascia
T3a	Tumor directly invades the adrenal gland or perirenal and/or renal sinus fat but not beyond Gerota's fascia
T3b	Tumor grossly extends into the renal vein or its segmental (muscle-containing) branches, or vena cava below the diaphragm
T3c	Tumor grossly extends into vena cava above diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond Gerota's fascia

Regional Lymph Nodes (N)*

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastases in a single regional lymph node
N2	Metastases in more than one regional lymph node

* *Note:* Laterality does not affect the N classification
Note: If a lymph node dissection is performed, then pathologic evaluation would ordinarily include at least eight nodes.

Distant Metastasis (M)

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage Grouping

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0	M0
	T3	N1	M0
	T3a	N0	M0
	T3a	N1	M0
	T3b	N0	M0
	T3b	N1	M0
	T3c	N0	M0
	T3c	N1	M0
Stage IV	T4	N0	M0
	T4	N1	M0
	Any T	N2	M0
	Any T	Any N	M1

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Category 1: The recommendation is based on high-level evidence (e.g. randomized controlled trials) and there is uniform NCCN consensus.

Category 2A: The recommendation is based on lower-level evidence and there is uniform NCCN consensus.

Category 2B: The recommendation is based on lower-level evidence and there is nonuniform NCCN consensus (but no major disagreement).

Category 3: The recommendation is based on any level of evidence but reflects major disagreement.

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