Renal Cell Carcinoma

Disease State

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https://medical.emdserono.com/en_US/medinfo/therapeutic-areas/oncology.html

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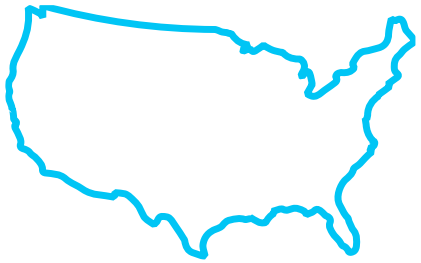
Content

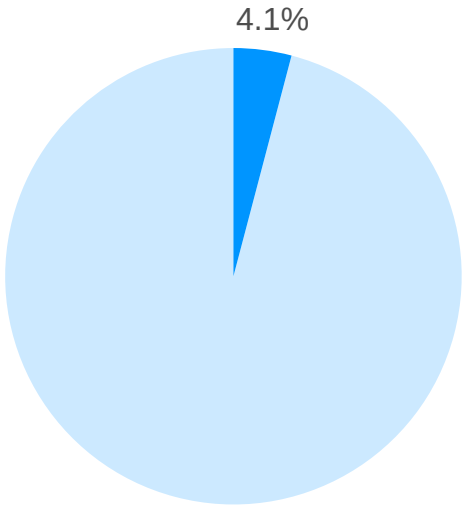
Incidence and prevalence



In the United States,

~81,610

new cases of kidney and renal pelvis cancer
were estimated for 2024[1,*]



Kidney and renal pelvis cancer represents

4.1%

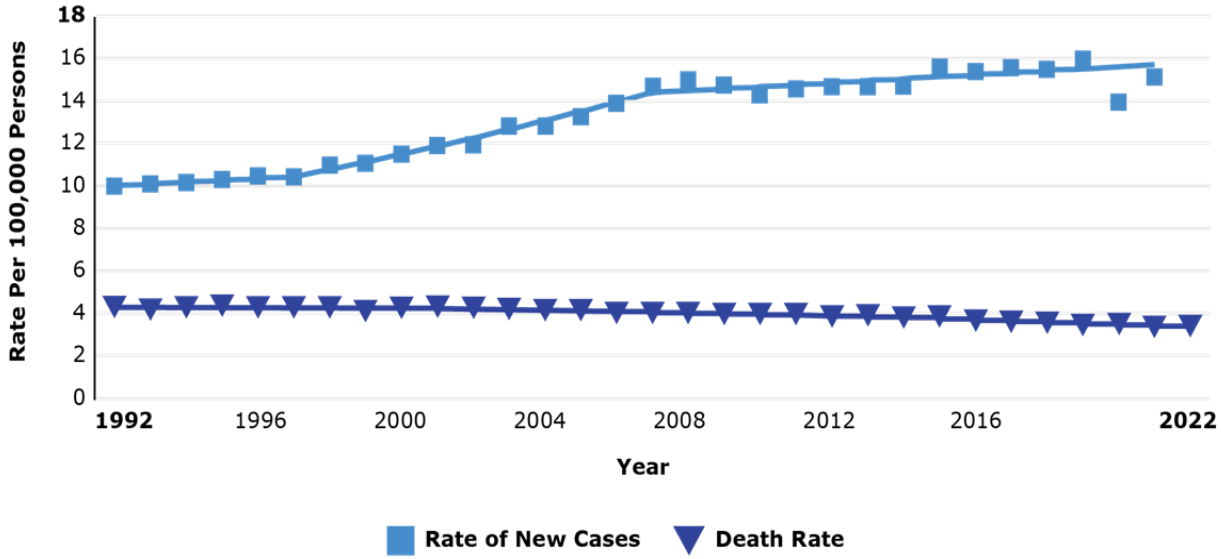
of all new cancer cases in the United States

CHANGE IN INCIDENCE AND DEATH RATES PER 100,000 PERSONS OVER TIME IN THE UNITED STATES[1,*]

Approximately

646,960

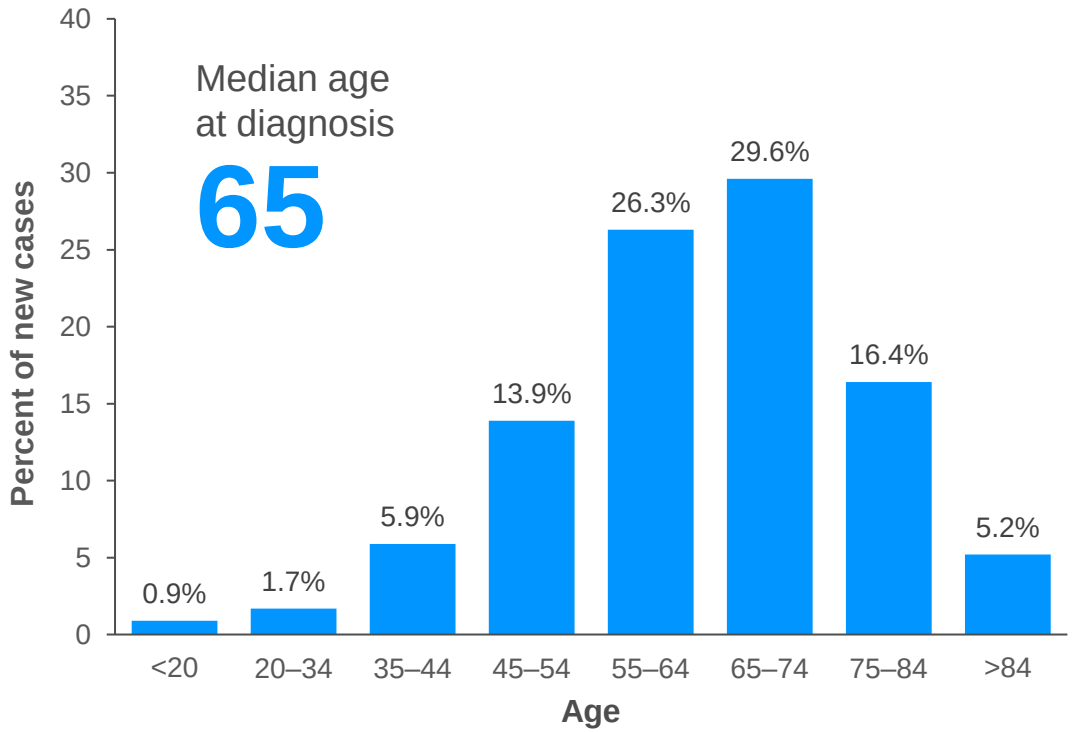
people in the United States were living with kidney and renal pelvis cancer in 2021, with increasing incidence each year (on average) over 2010-2019[1]



*New cases derived from SEER 12. Deaths derived from US Mortality. All Races, Both Sexes. Rates are Age-Adjusted.
1. SEER Stat Fact Sheets: Kidney and Renal Pelvis Cancer. https://seer.cancer.gov/statfacts/html/kidrp.html (Accessed 7 October 2024).

Incidence by age and demographics

KIDNEY AND RENAL PELVIS CANCER ARE MOST FREQUENTLY DIAGNOSED AMONG PEOPLE AGED 65–74[1,*]



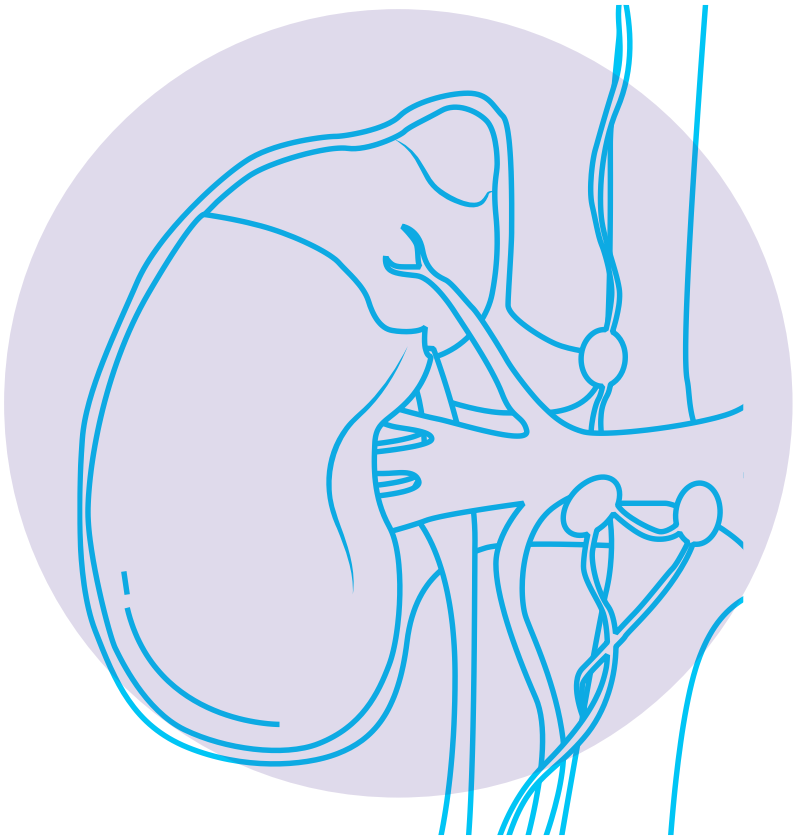
NUMBER OF NEW CASES PER 100,000 PERSONS BY RACE/ETHNICITY AND SEX: KIDNEY AND RENAL PELVIS CANCER[1,†]

	Males	Females
All races	23.4	11.9
Non-Hispanic White	24.2	11.8
Non-Hispanic Black	25.3	13.0
Non-Hispanic Asian/Pacific Islander	12.1	5.8
Non-Hispanic American Indian/Alaska Native	39.5	19.8
Hispanic	23.9	13.9

*SEER 22 2017-2021, All Races, Both Sexes. †SEER 22 2017–2021, Age-Adjusted.

1. SEER Stat Fact Sheets: Kidney and Renal Pelvis Cancer. https://seer.cancer.gov/statfacts/html/kidrp.html (Accessed 7 October 2024).

RCC subtypes



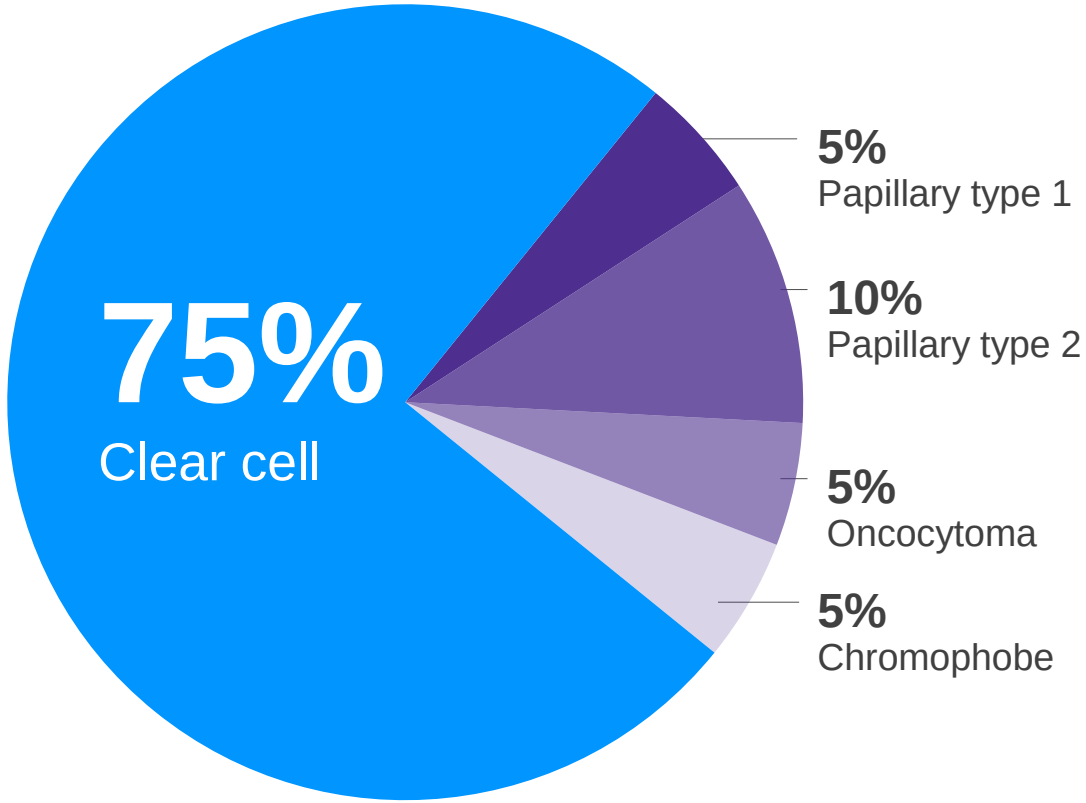
- RCC arises from the renal epithelium, representing **>90%** of renal malignancies[1]
- RCC is composed of several different subtypes, which differ in several ways[1]
  - **Major subtypes include[1]**
    - **Clear cell RCC (ccRCC)**
    - **Papillary RCC (pRCC)**
    - **Chromophobe RCC (chRCC)**
  - Unclassified RCC (uRCC)
  - Other subtypes are very rare, each with ≤1% total incidence[1]
  - RCC with sarcomatoid differentiation (sRCC), characterized by a spindle-like morphology, high cellularity, and atypia, is a highly aggressive form of RCC.[2] These features are found in 5–8% ccRCC, 8–9% of chRCC, and 2–3% of pRCC[2]
- There is significant intra- and intertumor heterogeneity in ccRCC, which could contribute to observed heterogeneous clinical outcomes[1]

ccRCC, clear cell renal cell carcinoma; chRCC, chromophobe renal cell carcinoma; pRCC, papillary renal cell carcinoma; RCC, renal cell carcinoma; uRCC, unclassified renal cell carcinoma.

1. Hsieh JJ, et al. Nat Rev Dis Primers. 2018;3:17009; 2. Pichler R, et al. Cancers (Basel). 2019;11(3):422.

Most common RCC subtypes

INCIDENCE (%)[1,2]



- RCC is a heterogeneous group of diseases[1]
- Of all kidney tumors, >90% are RCC[1]
- Different neoplasms of the kidney are characterized by distinct histologies, genetic alterations, clinical course, and response to therapy[1,2]

RCC, renal cell carcinoma.

1. Hsieh JJ, et al. Nat Rev Dis Primers. 2018;3:17009; 2. Linehan WM, et al. Clin. Cancer Res 2004;10:6282s–6289s.

Morphological and clinical differences in RCC subtypes

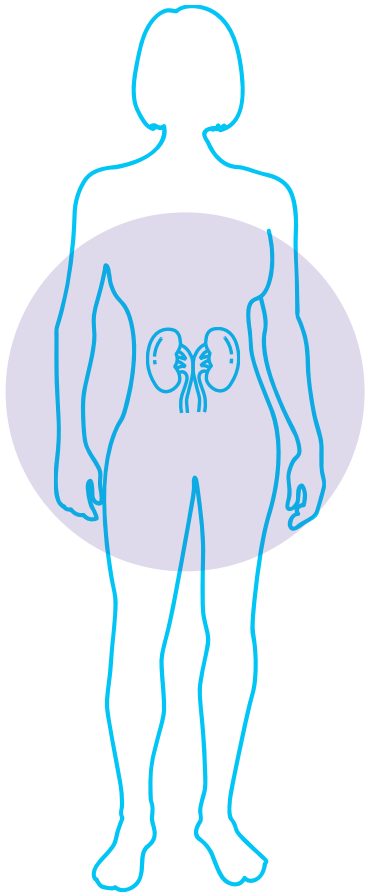
RCC subtype	Clinical features[1–4]	Morphological/ immunohistochemical features[1,5*]
ccRCC	65%–70% of adult RCCs (5% associated with hereditary syndromes)	Clear/eosinophilic cells, branched vasculature like the antlers on a deer Positive for CAIX and CD10, negative for CK7 and AMACR
pRCC	15%–20% of adult RCCs; Type 1 shows a better prognosis than Type 2 as it is detected earlier at lower grades; CIMP-RCC is associated with early-onset disease and poor survival	Finger-like structure, foamy macrophages; Type 1: scanty, basophilic cytoplasm (takes up the basic hematoxylin dye) Type 2: abundant eosinophilic cytoplasm (takes up the acidic eosin dye) Positive for CD10, CK7 and AMACR, negative for CAIX
chRCC	5%–7% of adult RCCs; favorable prognosis; most frequent subtype in patients in 6th decade of life; associated with Birt–Hogg–Dubé syndrome with an *FLCN* mutation	Cells with prominent cell membrane, irregular nuclei with perinuclear halos (vacuolated area surrounding nucleus), pale to eosinophilic cytoplasm Positive for KIT and CK7, negative for CAIX and CD10

*Immunohistochemistry is one of the most valuable diagnostic tools for categorizing diverse subtypes of renal tumors. CAIX, CD10, CK7, AMACR, and KIT are commonly used immunomarkers for diagnosis of RCC subtypes. CAIX is a well-described enzyme in RCC and is highly expressed at the tumor cell surfaces of ccRCC.

AMACR, alpha-methylacyl-CoA racemase; BAP1, BRCA1-associated protein 1; CAIX, carbonic anhydrase 9; ccRCC, clear cell renal carcinoma; chRCC, chromophobe renal cell carcinoma; CD10, neprilysin; CIMP-RCC, CpG island methylator phenotype renal cell carcinoma; CK7, cytokeratin-7; FLCN, folliculin; HIF, hypoxia-inducible factor; MET, mesenchymal-epithelial transition; mTOR, mechanistic target of rapamycin kinase; pRCC, papillary renal cell carcinoma; PTEN, phosphatase and tensin homolog; SETD2, SET domain containing 2; TP53, tumor protein p53; VHL, Von Hippel-Lindau.

1. Inamura K, et al. Int J Mol Sci. 2017;18:2195; 2. Linehan WM, et al. Clin. Cancer Res 2004;10:6282s–6289s.; 3. Muglia VF, et al. Radiol Bras. 2015;48:166–74; 4. Ricketts CJ, et al. Cell Rep. 2018;23(1):313–26; 5. Shanmugasundaram K, et al. Antioxid Redox Signal. 2016;25(12):685-701.

Metastasis



Approximately

30%

of patients who are thought to have non-metastatic disease, based on initial clinical and pathological evaluation, have occult metastases that will eventually become clinically evident[1]

Patients with ccRCC are believed to have the highest risk of metastasis, and the poorest survival after the pRCC subtype CIMP-RCC[2,3]

83–88%

of metastatic disease demonstrates a clear cell histology, and all other metastatic tumors are denoted non-clear cell RCC (nccRCC)[1]

Despite morphological similarities, there are molecular differences between the primary and metastatic tumors. The relevance of these differences to disease management has yet to be understood[4]

ccRCC, clear cell renal cell carcinoma; CIMP-RCC, CpG island methylator phenotype renal cell carcinoma; nccRCC, non-clear cell renal cell carcinoma; pRCC, papillary renal cell carcinoma; RCC, renal cell carcinoma.

1. Hsieh JJ, et al. Nat Rev Dis Primers. 2018;3:17009; 2. Patard JJ, et al. J Clin Oncol. 2005;23(12):2763–71; 3. Ricketts CJ, et al. Cell Reports. 2018;23:313–26; 4. Semeniuk-Wojtaś A, Stec R, Szczylik C. Urol Oncol. 2016;34(5):215–20.

Common chromosomal alterations and key mutations in RCC

RCC subtype	Chromosomal alteration[1,2]	Gene mutation[3,4]
ccRCC	LOH in 3p (most common), chromosomes 14, 8, 9 and 6 (20–40%) and chromosomes 1, 4, 10q, 13q, 17p, and 18q (less frequent)	• *VHL* (most common) • *PBRM1* • *SETD2* • *BAP1* • *KDM5C* • *MTOR*
pRCC	Trisomy of chromosomes 7 and 17 and loss of the Y chromosome; LOH in 9p and in chromosomes 6, 8, and 14	*MET* and *fumarate hydratase* mutations
chRCC	Monosomy of chromosomes 1, 2, 6, 10, 13, 17, and 21 in 75–100% of tumors; deletion of 3p, 8p, and 9p in up to 25% of tumors	*Folliculin* gene mutation

- LOH (loss of heterozygosity) in 3p in ccRCC leads to haploinsufficiency of multiple tumor suppressors (*VHL*, *PBRM1, SETD2, BAP1)*[5]

Loss of heterozygosity[6]	Haploinsufficiency[7]
A genetic event where one copy of an entire gene and its surrounding chromosomal region are lost	A situation when because of inactivation or deletion of one copy of a gene, the remaining functional copy of the gene is not able to produce the needed gene product to preserve normal function

ccRCC, clear cell renal cell carcinoma; chRCC, chromophobe renal cell carcinoma; LOH, loss of heterozygosity; pRCC, papillary renal cell carcinoma; RCC, renal cell carcinoma.

1. Cairns P. Cancer Biomark. 2011;9(1–6):461–73; 2. Lindgren D, et al. Cell Reports. 2017;20:1476–89; 3. Beksac AT, et al. Urologic Oncology. 2017;35(8):507-15; 4. Nabi S, et al. F1000Research 2018;7(F1000 Faculty Rev):307; 5. Hsieh JJ, et al. Nat Rev Dis Primers. 2018;3:17009; 6. Gorringe KL. In eLS , John Wiley & Sons, Ltd (Ed.). 2016; 7. Berger aH, et al. J Pathol. 2011;223:137–46

Biomarkers

- Unlike other cancers, RCC does not carry a high mutational load; analysis by MSKCC Score suggested no trend with stratification by risk group[1]
- No differences in expression of T cell effector molecules (granzyme A and perforin) or checkpoint expression were observed by MSKCC risk group[2]

PROGNOSTIC AND PREDICTIVE BIOMARKERS IN RCC[1]

Biomarker	Association	Biomarker	Association
Gene alterations in *BAP1*	Worse overall survival	**Negative IHC expression for BAP1**	Better mTOR inhibitor response
Gene alterations in *PBRM1*	Better overall survival		
PBRM1 wild type + gene alterations *BAP1*	Worse overall survival	**Negative IHC expression for PBRM1**	Better mTOR inhibitor response
Gene alterations in *KDM5C*	Better overall survival		
PDCD1, CTLA4 and TLR9	Worse overall survival	**SETD2, TP53, and VHL**	Not associated with prognosis
9p deletion	High risk of recurrence and RCC-specific mortality		

BAP1, BRCA1-associated protein 1; *KDM5C*, lysine demethylase 5C; MSKCC, Motzer score for renal cell carcinoma; mTOR, mammalian target of rapamycin; PBRM1, protein polybromo-1; RCC, renal cell carcinoma; SETD2, SET Domain Containing 2; TP53, tumor protein p53; VHL, Von Hippel-Lindau.

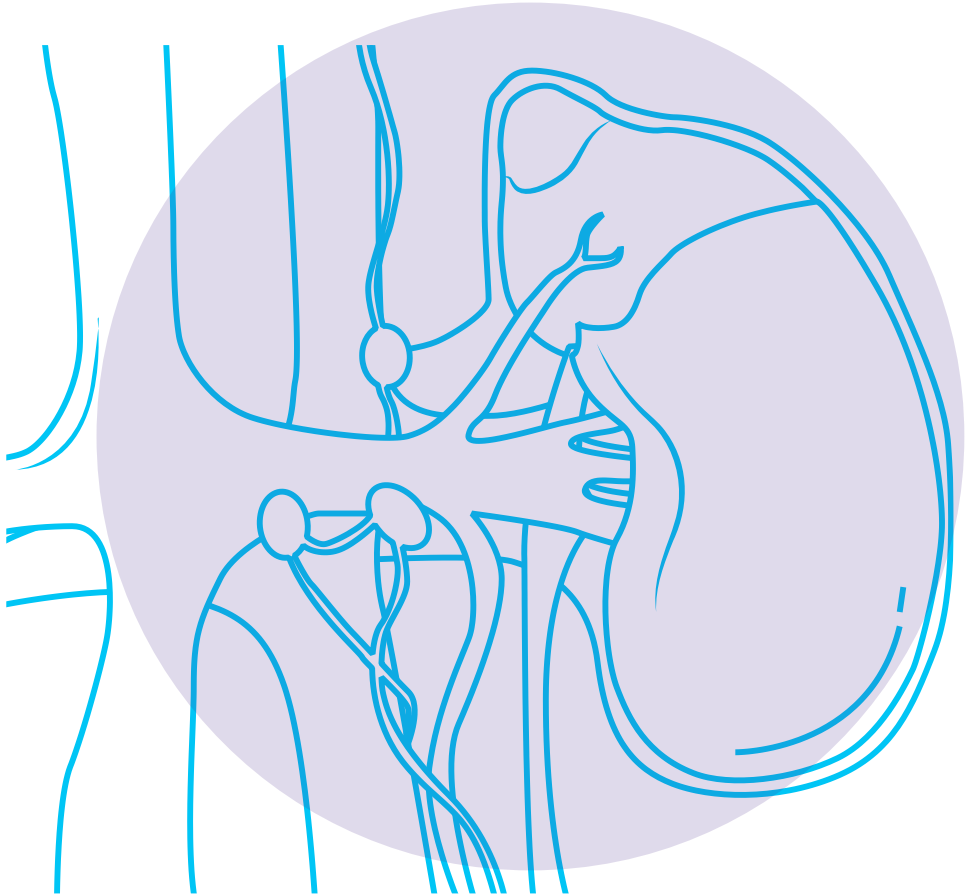
1. Lopez-Beltran A, et al. Front Oncol. 2018;8. doi:10.3389/fonc.2018.00456; 2. de Velasco G, et al. Cancer Immunol Res. 2016;4(10):820–2.

Signs and symptoms

Kidney cancer rarely causes visible signs or symptoms in its early stages. However, symptoms might become apparent in the later stages of the disease.[1]

POSSIBLE SIGNS AND SYMPTOMS OF KIDNEY CANCER MAY INCLUDE[1]:

- Blood in the urine (hematuria)
- Lower back pain on one side
- A mass (lump) on the side or lower back
- Fatigue
- Loss of appetite
- Weight loss
- Persistent fever that is not caused by infection
- Anemia



1. ACS. Revised February 2023. Kidney cancer signs and symptoms. https://www.cancer.org/cancer/kidney-cancer/detection-diagnosis-staging/signs-and-symptoms.html (Accessed 7 October 2024).

Diagnosis[1] (1/2)

- >50% of RCC cases are currently detected incidentally; however, suspicion of RCC should prompt the following laboratory examinations:

Serum creatinine	Hemoglobin	Leukocyte and platelet counts	Lymphocyte-to-neutrophil ratio
Lactate dehydrogenase	C-reactive protein	Serum-corrected calcium	

RCC, renal cell carcinoma.

1. Escudier B, et al. Ann Oncol 2016;27(Suppl 5):v58–v68.

Diagnosis[1] (2/2)

- The following imaging and biopsy tests should be done for detection of RCC :

Ultrasonography and CT scans are typically used to diagnose RCC, and allow assessment of local invasiveness, lymph node involvement, and distant metastases

MRI might provide additional information on local advancement and venous involvement by tumor thrombus

Biopsy provides histopathological confirmation of malignancy

Contrast-enhanced chest, abdominal, and pelvic CT is mandatory for accurate staging

RCC, renal cell carcinoma.

1. Escudier B, et al. Ann Oncol 2016;27(Suppl 5):v58–v68.

Disease classification – grade and stage

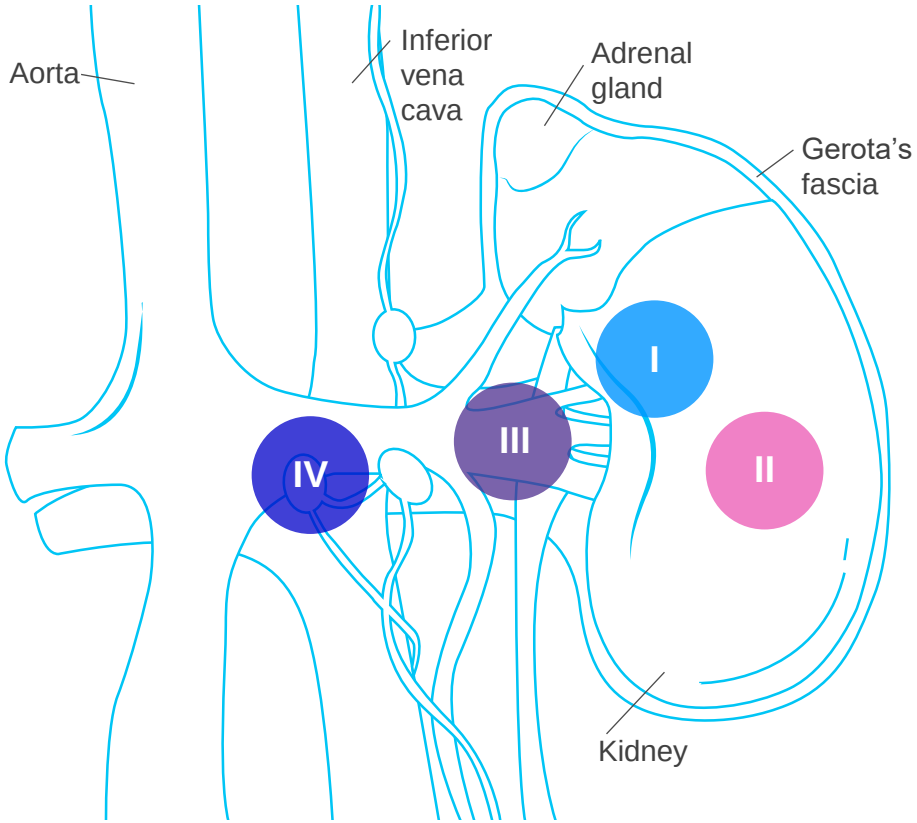
Staging of RCC is based on size, position, and lymph node involvement, and treatment is largely guided by stage[1]

STAGE I

- Tumor <7 cm in the largest dimension
- Limited to the kidney

STAGE III

- Tumor in the major veins or adrenal gland with an intact Gerota's fascia
- Or one regional lymph node involved



STAGE II

- Tumor >7 cm in the largest dimension
- Limited to the kidney

STAGE IV

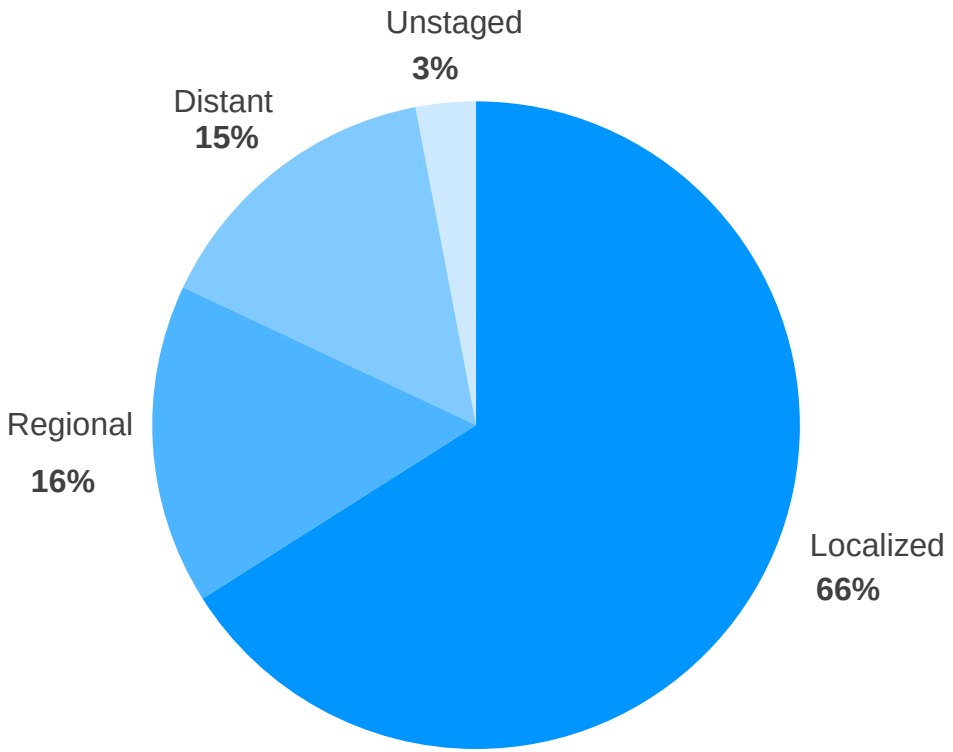
- Tumor beyond Gerota's fascia
- Or more than one regional lymph node involved
- Distant metastases

RCC, renal cell carcinoma.

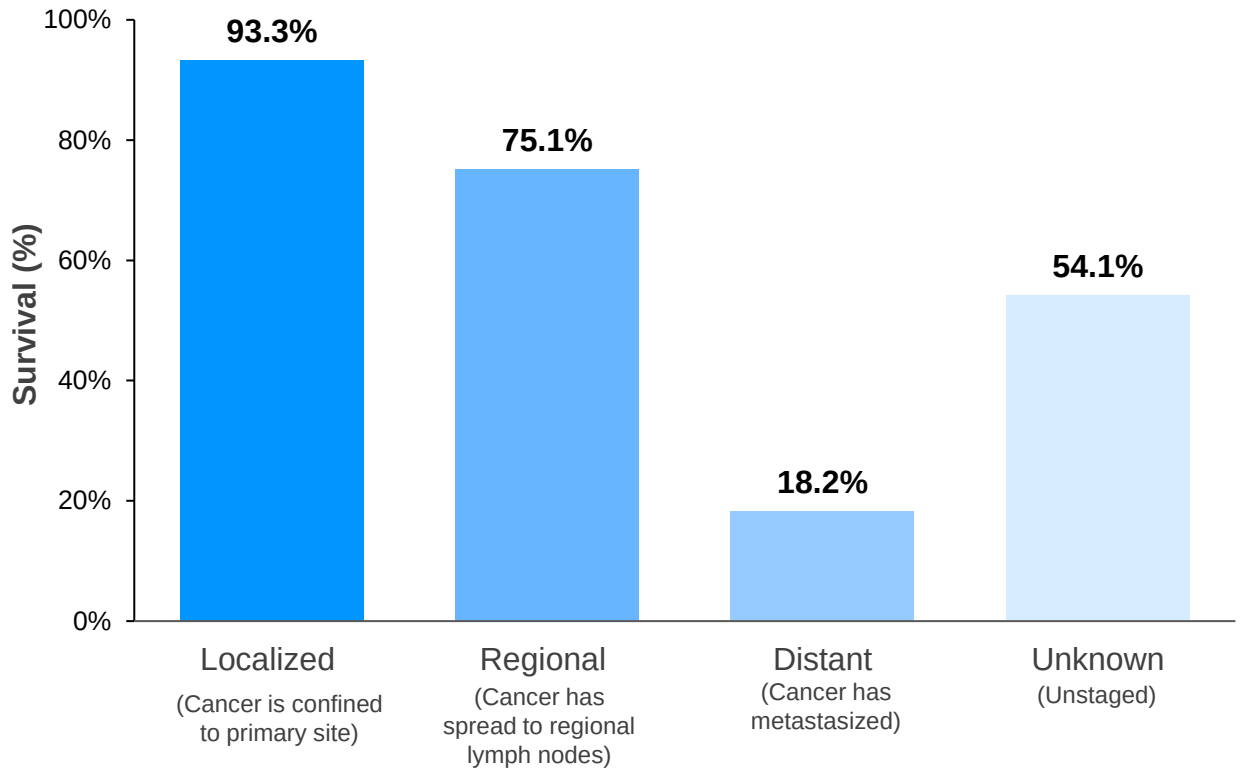
1. Hsieh JJ, et al. Nat Rev Dis Primers. 2018;3:17009.

Stage at diagnosis of kidney and renal pelvis cancer is linked with survival[1]

PROPORTION OF PATIENTS WITH DIFFERENT DISEASE STAGES AT DIAGNOSIS[1,*]



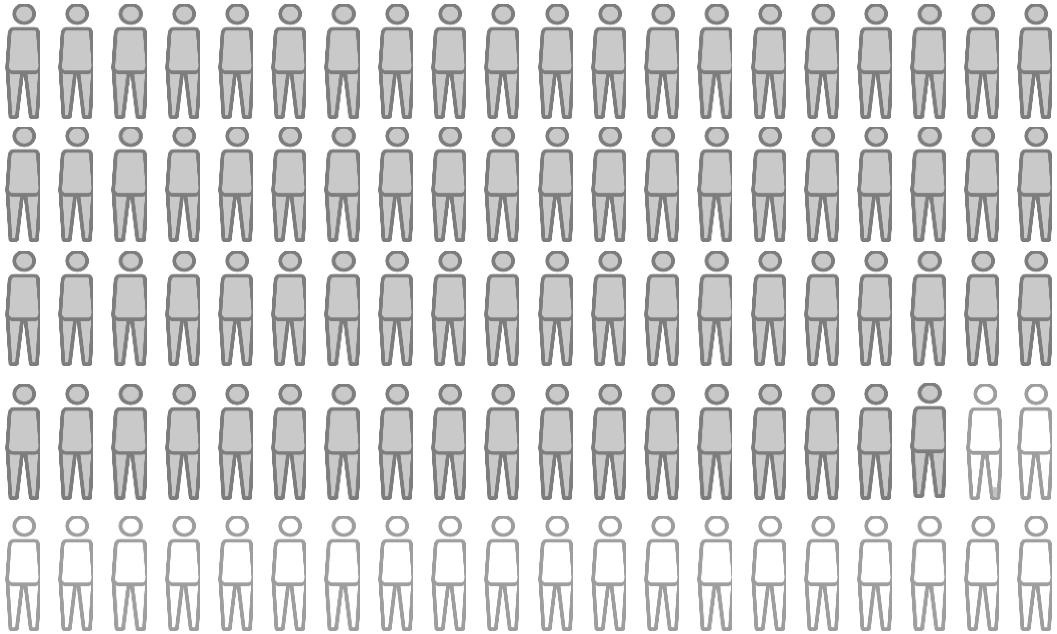
5-YEAR RELATIVE SURVIVAL VARIES ACCORDING TO DISEASE STAGE AT DIAGNOSIS[1,*]



*SEER 22 (Excluding IL/MA) 2014–2020, All races, Both Sexes by SEER Combined Summary Stage.

1. National Cancer Institute. SEER stat fact sheets: kidney and renal pelvis cancer. http://seer.cancer.gov/statfacts/html/kidrp.html (Accessed 7 October 2024).

Relative survival



5-Year Relative Survival (All Stages Combined)*,†

78.1%

NUMBER OF DEATHS PER 100,000 PERSONS BY RACE/ETHNICITY AND SEX: KIDNEY AND RENAL PELVIS CANCER[1,‡]

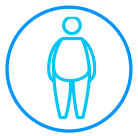
	Males	Females
All races	5.1	2.1
Non-Hispanic White	5.3	2.2
Non-Hispanic Black	4.9	2.1
Non-Hispanic Asian/Pacific Islander	2.3	1.0
Non-Hispanic American Indian/Alaska Native	10.1	4.1
Hispanic	4.7	2.1

*Kidney and renal pelvis cancer. Unshaded figures represent those who have died from kidney and renal pelvis cancer. Shaded figures represent those who have survived 5 years or more.
†SEER 22 (Excluding IL/MA) 2014–2020. ‡US 2018–2022, age-adjusted.

1. SEER Stat Fact Sheets: Kidney and Renal Pelvis Cancer. https://seer.cancer.gov/statfacts/html/kidrp.html (Accessed 7 October 2024).

Key risk factors[1,2]

SMOKING
Smokers are at greater risk than non-smokers



OBESITY
Strong link between excess weight (in men and women) and RCC

AGE[2]
The median age of people at diagnosis is 65 years

GENDER
RCC is twice as common in men as in women

RACE[2]
Non-Hispanic Americans/Indian Alaska Natives have higher rates of RCC than other races

GENETICS
Genetic risk factors and several rare inherited conditions can cause RCC (see next slide)

FAMILY HISTORY
- People with a family history of RCC have an increased risk
- Risk is highest in individuals with a sibling with RCC

HIGH BLOOD PRESSURE
Those with high blood pressure have a higher risk of RCC; it is not known whether this is due to the condition or antihypertensive medication (or both)

ADVANCED KIDNEY DISEASE
Those requiring dialysis are especially at risk

WORKPLACE EXPOSURES
Exposure to cadmium, some herbicides, and organic solvents (particularly trichloroethylene) can increase the risk of RCC

DRUG EXPOSURES
Exposure to acetaminophen, NSAIDS, aristolochic acid etc can increase the risk of RCC

RCC, renal cell carcinoma.

1. ACS. Revised February 2023. Risk factors for kidney cancer. https://www.cancer.org/cancer/kidney-cancer/causes-risks-prevention/risk-factors.html (Accessed 7 October 2024);
2. National Cancer Institute. SEER stat fact sheets: kidney and renal pelvis cancer. http://seer.cancer.gov/statfacts/html/kidrp.html (Accessed 7 October 2024).

Hereditary syndromes associated with RCC[1]

Syndrome	Gene	Renal cancer type
BAP1 mutant disease	*BAP1*	Clear cell
Birt–Hogg–Dubé syndrome	*FLCN*	Oncocytic, chromophobe
Familial clear cell renal cancer with Chromosome 3 translocation	Transloc chr 3	Clear cell
Hereditary leiomyomatosis and RCC	*FH*	Papillary type 2
Hereditary papillary renal cancer	*MET*	Papillary type 1
PTEN hamartoma syndrome	*PTEN*	Clear cell
SDH-associated renal cancer	*SDHB* *SDHC* *SDHD*	Clear cell, chromophobe, oncocytoma
Tuberous sclerosis complex	*TSC1* *TSC2*	Angiomyolipoma Epitheliod angiomyolipoma
Von Hippel-Lindau syndrome	*VHL*	Clear cell

Hereditary kidney cancer accounts for

3–5%

of all kidney cancer

10

inherited cancer susceptibility syndromes are associated with inherited risk of kidney cancer, **with 12 genes identified**

BAP1, BRCA1-associated protein 1; FH, familial hypercholesterolemia; FLCN, folliculin; MET, mesenchymal-epithelial transition; PTEN, phosphatase and tensin homolog; RCC, renal cell carcinoma; SDH, succinate dehydrogenase; SDHB, succinate dehydrogenase complex B; SDHC, succinate dehydrogenase complex C; SDHD, succinate dehydrogenase complex D.

1. Haas NB, Nathanson KL. Adv Chronic Kidney Dis. 2014;21(1):81–90.

Genetic and hereditary risk factors

The four major, autosomal-dominant, heritable RCC syndromes recognized by the National Cancer Institute[1-3]

Syndrome	Gene locus, gene type (protein)	Renal tumor pathology type	Non-renal tumors and associated abnormalities	Cumulative lifetime cancer risk
Von Hippel-Lindau (VHL) syndrome[1]	VHL 3p26, tumor suppressor (pVHL)	Clear-cell RCC (multifocal)	CNS hemangioblastoma, retinal hemangioblastomas, pheochromocytoma, pancreatic neuroendocrine tumor, endolymphatic sac tumor, cystadenoma of the pancreas, the epididymis, and the broad ligament	24%–45%
Hereditary papillary renal carcinoma[2]	MET 7q31.2, proto-oncogene (hepatocyte growth factor receptor)	Papillary type 1	None known	Approaching 100%
Birt–Hogg–Dubé syndrome[1]	FLCN 17p11.2, tumor suppressor (folliculin)	Chromophobe, hybrid oncocytic, papillary, clear-cell, oncocytoma	Cutaneous: fibrofolliculomas/ trichodiscomas Pulmonary: lung cysts, spontaneous pneumothoraces	15%–30%
Hereditary leiomyomatosis and RCC[3]	FH 1q42.3-43, tumor suppressor (fumarate hydratase)	'HLRCC-type RCC' may be new entity (formerly called papillary type 2)	Cutaneous leiomyomas, uterine leiomyomas (fibroids)	Up to 30%

These pathogenic variants are estimated to account for

5–8%

of RCC cases[1]

FH, familial hypercholesterolemia; FLCN, folliculin; HLRCC, hereditary leiomyomatosis renal cell carcinoma; MET, mesenchymal-epithelial transition; RCC, renal cell carcinoma; VHL, Von Hippel-Lindau.

1. Genetics of Renal Cell Carcinoma. National Cancer Institute website. Revised April 2023. https://www.cancer.gov/types/kidney/hp/kidney-genetics-pdq#section/_24 (Accessed 7 October 2024); 2. Hereditary Papillary Renal Carcinoma. National Cancer Institute website. Revised December 2022. https://www.cancer.gov/types/kidney/hp/renal-cell-carcinoma-genetics/hprc-syndrome (Accessed 7 October 2024); 3. Hereditary Leiomyomatosis and Renal Cell Cancer. National Cancer Institute website. Revised December 2022. https://www.cancer.gov/types/kidney/hp/renal-cell-carcinoma-genetics/hlrcc-syndrome (Accessed 7 October 2024)

Other inherited syndromes with increased risk of renal cancer[1]

BAP1 mutations and familial renal cancer	• BAP1 mutations have been associated with a higher tumor grade and decreased overall survival • Studies have suggested that BAP1 mutations predispose to familial clear cell renal cancer, along with uveal, cutaneous melanoma, and mesothelioma[2]
Chromosome 3 translocations	• Inherited susceptibility due to balanced translocations involving chromosome 3 have been described, caused by loss of the rearranged chromosome during mitosis. • Multiple genes involved in the pathogenesis of clear cell renal cancer including *VHL*, *PBRM1*, *BAP1*, and *SETD2* are located on chromosome 3
PTEN hamartoma tumor syndrome (Cowden disease)	• Sporadic renal cancers and cell lines have shown that mutations in PTEN are present, particularly in late stage and clear cell renal cancers. ccRCC is reported more frequently in patients with Cowden disease
SDH-associated paraganglioma / pheochromocytoma	• Mutations in three of the four proteins (SDHB/C/D) comprising the succinate dehydrogenase complex, have been associated with an increased risk of renal cancer, including clear cell, chromophobe, and oncocytomas
Tuberous sclerosis complex	• An autosomal dominant genetic disorder characterized by the formation of hamartomas in multiple organs, including the brain, kidney, skin, and lungs

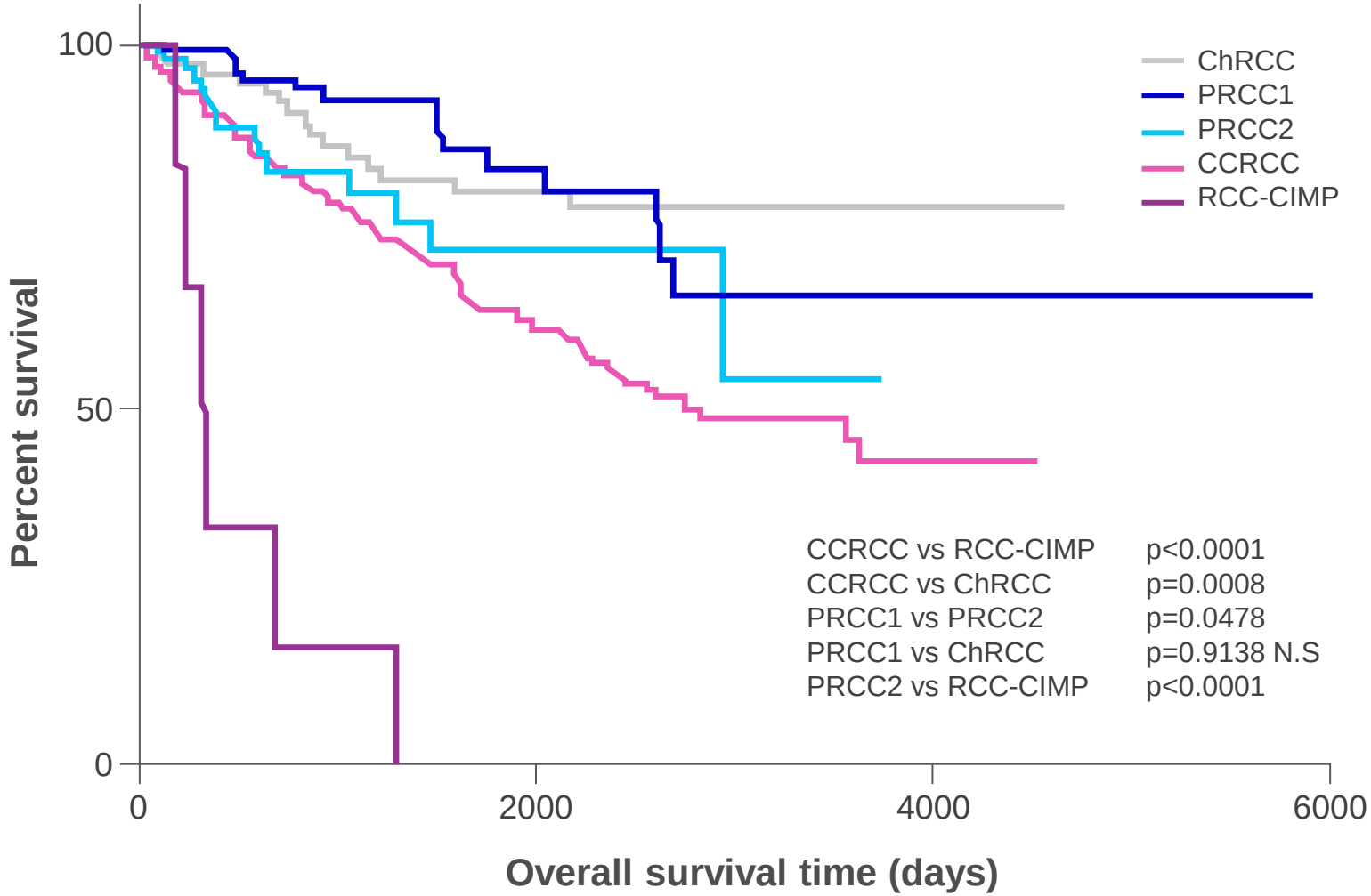
BAP1, BRCA1-associated protein 1; PBRM1, polybromo 1; SDH, succinate dehydrogenase; SETD2, SET Domain Containing 2; VHL, Von Hippel-Lindau.

1. Haas NB, Nathanson KL. Adv Chronic Kidney Dis. 2014;21(1):81–90. 2. Walpole S, et al. J Natl Cancer Inst. 2018;(12):1328–41.

Menu

Survival by subtype

- The TCGA assessed survival in 894 patients with RCC.[1] Patients with ccRCC and with the RCC-CIMP subtype of pRCC were reported to have the worst survival[1]
- In another clinical study, recurrence post partial nephrectomy also varied by subtype, with ccRCC having the highest rate of recurrence as compared to chRCC or pRCC[2]



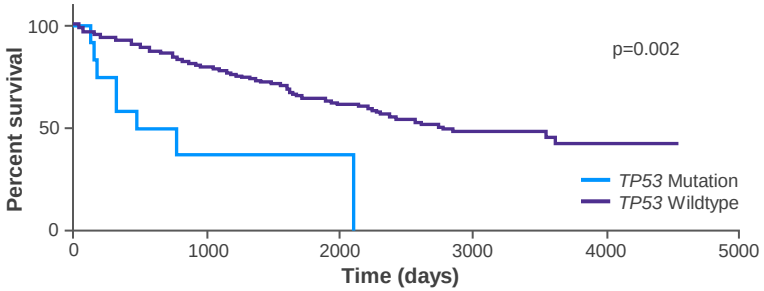
Based on data from a cohort of 843 TCGA-RCC patients consisting of 488 ccRCC, 274 pRCC (including 160 type 1 PRCC, 70 type 2 PRCC, and 10 CIMP-RCC), and 81 ChRCC.
ccRCC, clear cell renal carcinoma; chRCC, chromophobe renal cell carcinoma; pRCC, papillary renal cell carcinoma; RCC-CIMP, CpG island methylator phenotype renal cell carcinoma; TCGA, The Cancer Genome Atlas.

1. Ricketts CJ, et al. Cell Reports. 2018;23:313–26; 2. Nguyen DP, et al. Urol Oncol. 2016;34(6):259.e1–8.

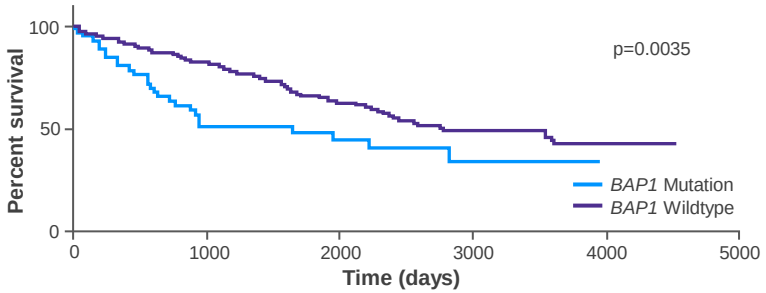
Survival and mutation status

ccRCC: Decreased survival with *TP53* and *BAP1* mutations

ccRCC *TP53* MUTATION

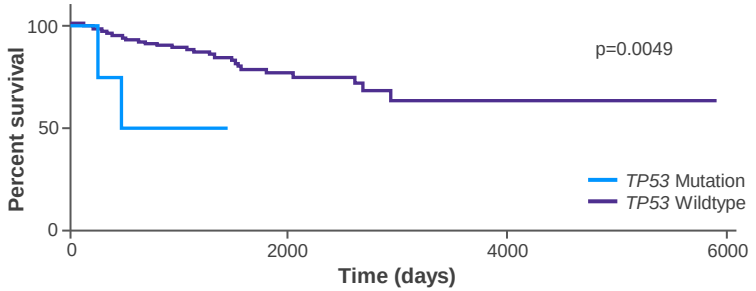


ccRCC *BAP1* MUTATION

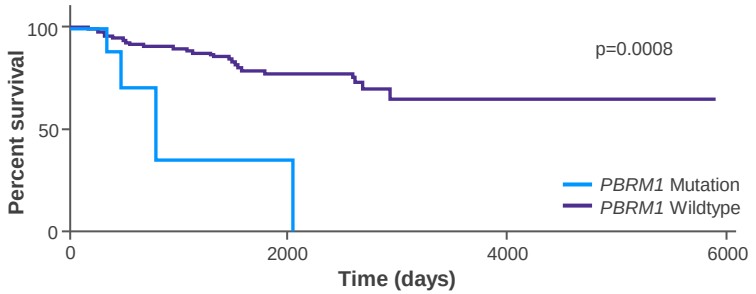


pRCC: Decreased survival with *TP53* and *PBRM1* mutations

pRCC *TP53* MUTATION

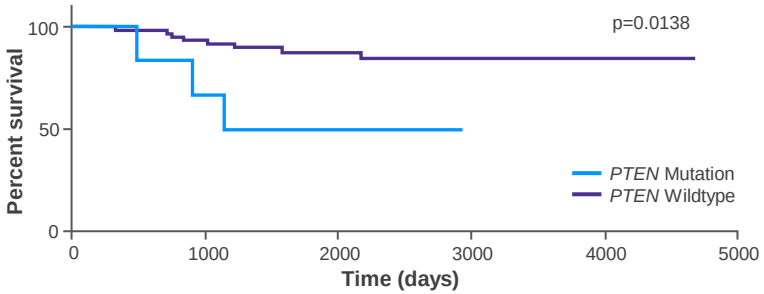


pRCC *PBRM1* MUTATION



chRCC: Decreased survival with PTEN mutation

chRCC *PTEN* MUTATION



Higher overall mutation rate suggested for ccRCC and pRCC vs chRCC, with pRCC having the highest overall mutation rate[1]

Based on data from a cohort of 843 TCGA-RCC patients consisting of 488 ccRCC, 274 pRCC, and 81 ChRCC.
BAP1, BRCA1-associated protein 1; ccRCC, clear cell renal cell carcinoma; *CDKN2A*, cyclin-dependent kinase inhibitor 2A; chRCC, chromophobe renal cell carcinoma; *PBRM1*, polybromo 1; pRCC, papillary renal cell carcinoma; *PTEN*, phosphate and tensin homolog; *TP53*, tumor protein p53.

1. Ricketts CJ, et al. Cell Reports. 2018;23:313–26.

Prognostic measures

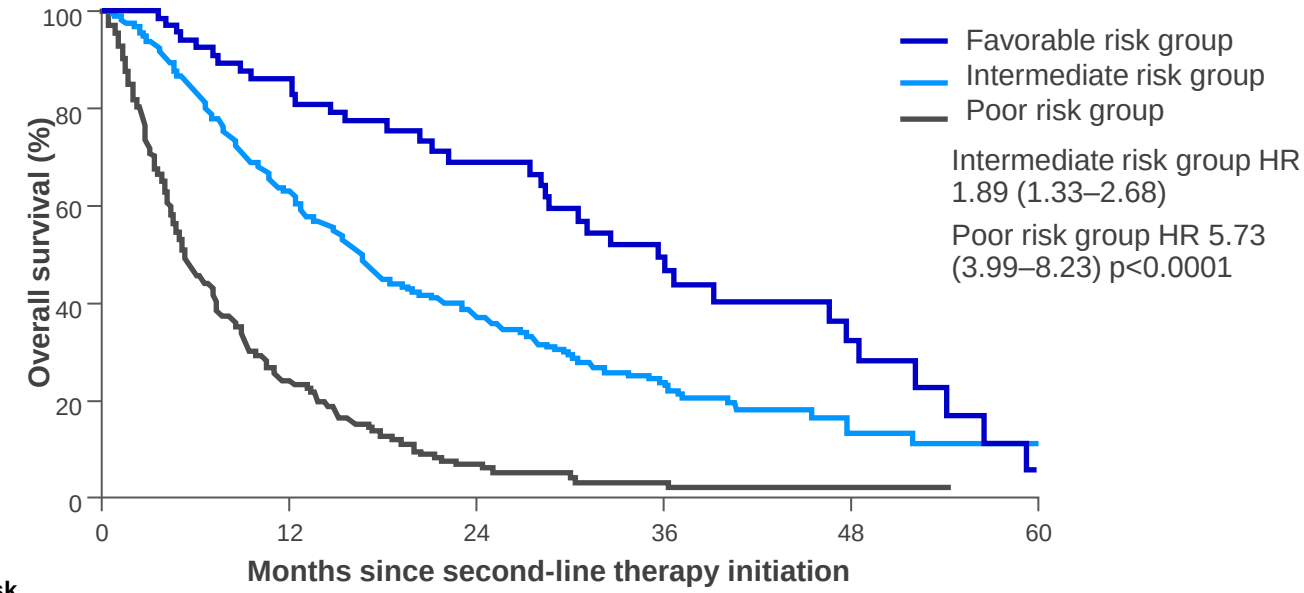
THE INTERNATIONAL mRCC CARCINOMA DATABASE CONSORTIUM MODEL (IMDC) FOR PROGNOSIS IN FIRST-LINE TREATMENT FOR mRCC

Criteria

- Karnofsky performance status <80%
- Time from diagnosis to treatment <1 year
- Hemoglobin < LLN
- Calcium concentration > ULN
- Neutrophils > ULN
- Platelets > ULN

Number of criteria	Group	Median overall survival
0	Favorable	35.3 months (95% CI 28.3–47.8)
1–2	Intermediate	16.6 months (95% CI 14.9–17.9)
3–6	Poor	5.4 months (95% CI 4.7–6.8)

OVERALL SURVIVAL ACCORDING TO THE IMDC MODEL[1]



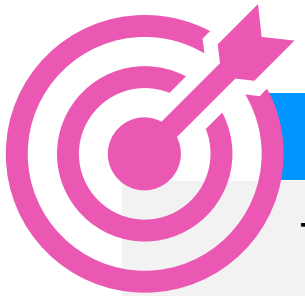
No. at risk						
Favorable risk group	76	52	31	19	8	1
Intermediate risk group	529	257	97	37	9	4
Poor risk group	261	49	9	3	1	0

Patients who received second-line targeted therapy after progressing on first-line targeted therapy for mRCC were included in the study. Patients who had immunotherapy before their first targeted therapy were included.[1]

CI, confidence interval; HR, hazard ratio; IMDC, International mRCC Database Consortium; LLN, lower limit of normal; mRCC, metastatic renal cell carcinoma; ULN, upper limit of normal.

1. Ko JJ, et al. Lancet Oncol. 2015;16(3):293–300.

Goals of treatment for RCC



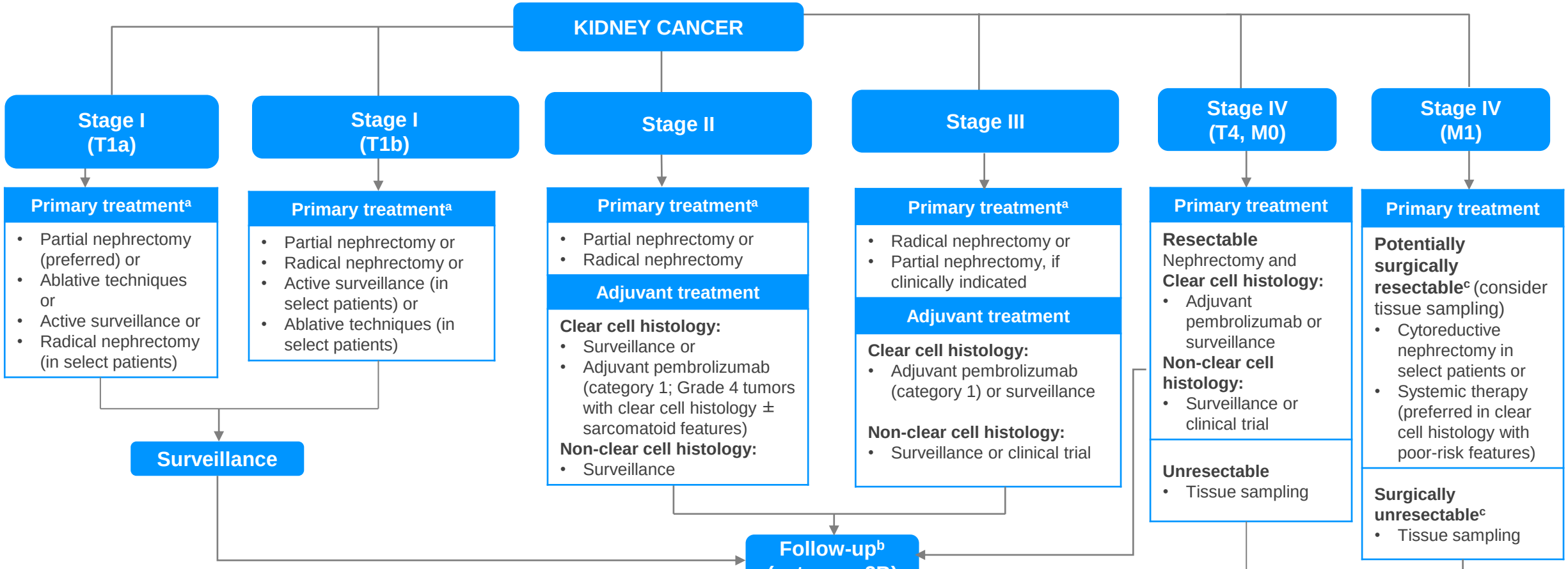
The treatment goals for RCC are to

- Slow disease progression
- Alleviate symptoms
- Improve quality of life
- Increase lifespan

RCC, renal cell carcinoma.

Cardenas LM, et al. CMAJ. 2024;196(7):E235–E240.

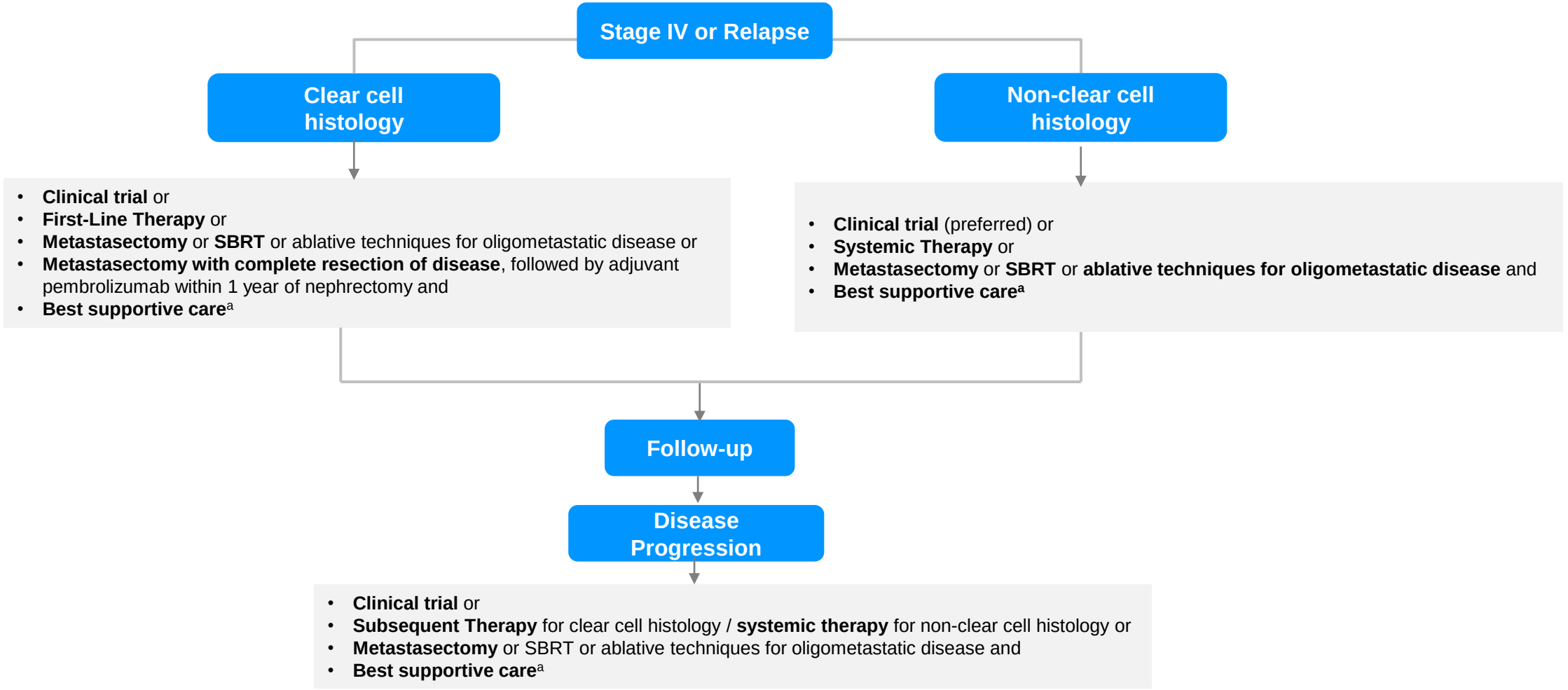
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Principles of RCC management (1/2)[1]



All recommendations are category 2A unless otherwise indicated. [a]Stereotactic body radiation therapy (SBRT) may be considered for non-optimal surgical candidates with stage I kidney cancer (category 2B) or with stage II/III kidney cancer (both category 3). [b]No single follow-up plan is appropriate for all patients. Follow-up should be individualized based on patient requirements. [c]Individualize treatment based on symptoms and extent of metastatic disease.

1. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Kidney Cancer V.2.2025.

NCCN Guidelines®: Principles of RCC management (2/2)[1]



[a]Best supportive care can include radiation therapy where SBRT is the preferred approach, bisphosphonates, or receptor activator of nuclear factor kappa-B (RANK) ligand inhibitors for bony metastases. An FDA-approved biosimilar is an appropriate substitute for denosumab.
SBRT, stereotactic body radiation therapy
1. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Kidney Cancer V.2.2025. © 2024 National Comprehensive Cancer Network, Inc. All rights reserved. Accessed date: November 8, 2024. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available.

Conclusions

- RCC is a heterogenous disease, composed of several different subtypes, including ccRCC, pRCC, chRCC, and unclassified RCC; each subtype has distinct clinical and morphological characteristics
- ccRCC is the main subtype of RCC; *VHL* gene alteration plays a key role in its pathogenesis
- Apart from lifestyle, health, and drug related factors, genetic and rare inherited conditions can also cause RCC
- Molecular and genetic characterization of various RCC subtypes facilitates understanding of its evolution which is needed for the development of appropriate therapies to treat this disease
- Various mutation types also affect the survival in patients with RCC
- A number of targeted agents (TKIs, anti-VEGF antibodies, ICIs) have been approved by the FDA for the treatment of advanced RCC in the first and/or subsequent lines of therapy

ccRCC, clear cell RCC; chRCC, chromophobe ICI, immune checkpoint inhibitors; RCC; pRCC, papillary RCC; RCC, renal cell cancer, TKI, tyrosine kinase inhibitor; VHL, Von Hippel-Lindau; VEGF, vascular endothelial growth factor.