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Outcomes of Patients with Renal Cell Carcinoma and Sarcomatoid Dedifferentiation Treated with Nephrectomy and Systemic Therapies Over Three Decades: Comparison Between the Cytokine (1987–2005) and the Targeted Therapy (2006–2015) Eras

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Abstract

Purpose—To study the overall survival and prognostic factors of patients with sarcomatoid renal cell carcinoma treated with nephrectomy and systemic therapy in the cytokine and targeted therapy eras.

Materials and Methods—This is a retrospective study of patients with sarcomatoid renal cell carcinoma who had nephrectomy and received systemic therapy at our center in the cytokine era (1987–2005) or the targeted therapy era (2006–2015). Multivariate regression models were used to determine the association of covariables with survival.

Results—Among 199 patients with sarcomatoid renal cell carcinoma, 167 (83.9%) have died (median overall survival 16.5 months; 95% CI: 15.2, 20.9). Survival of patients with clear-cell histology was significantly longer vs. those with non-clear cell histology ($p = 0.034$). Patients with synchronous metastatic disease had a significantly shorter survival compared with patients with metachronous metastatic disease (median 12.1 months vs. 23.3 months; $p = 0.0064$). Biopsy of the

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primary tumor or a metastatic site could detect the presence of sarcomatoid features in only 7.5% of cases. Although a significant improvement in survival rate was observed in the first year for patients treated in the targeted therapy era ($p = 0.011$), this effect was attenuated at year 2, disappeared at years 3–5 after diagnosis, and was not evident in patients with poor risk features.

Conclusions—Patients with sarcomatoid renal cell carcinoma still have poor prognosis with no clear long-term benefit of targeted therapy, underscoring the need to develop more effective systemic therapies for these patients.

Keywords

Sarcomatoid renal cell carcinoma; targeted therapies

INTRODUCTION

There are approximately 63,000 new renal cell carcinoma (RCC) cases and almost 14,000 deaths from RCC each year in the US¹. Nephrectomy for clinically localized disease is the gold standard treatment for curative intent, with nephron-sparing surgery (partial nephrectomy) preferred in appropriately selected cases based on the extent of disease. However, RCC recurs in 20% to 40% of patients who undergo nephrectomy for clinically localized disease². In addition, approximately 20% to 30% of patients with RCC present with metastatic disease².

Sarcomatoid dedifferentiation can be an associated feature with any RCC histologic subtype. It is found in approximately 5% of all RCCs but accounts for 15–20% of patients with advanced disease. Histologically, renal cell carcinomas with sarcomatoid dedifferentiation (sRCC) contain pleomorphic spindle cells and giant cells interposed with an epithelial component³. Most sRCCs present with metastatic disease and are historically associated with a poor prognosis and a median overall survival of 4 to 9 months^{4–6}.

Due to the rarity of sRCC, there is paucity of data on the optimal management of patients with advanced disease. Treatment with cytotoxic chemotherapy and/or cytokines historically produced very minimal responses and survival benefit^{3, 4, 7–10}. Targeted therapies directed against the vascular endothelial growth factor (VEGF) and mammalian target of rapamycin (mTOR) pathways have revolutionized the treatment of advanced, clear-cell RCC; however, only small series exist that investigated the particular entity of sarcomatoid RCC^{6, 11–21}. Herein, we present a retrospective analysis of our institutional sRCC database and describe the clinical and pathological characteristics of advanced sRCC. The study objective was to analyze the outcome of patients with metastatic sRCC in different therapeutic eras (before 2006 versus 2006 and later) and to explore factors associated with patient survival.

PATIENTS AND METHODS

Patients with sRCC who had nephrectomy, and received systemic therapy for metastatic disease at The University of Texas MD Anderson Cancer Center from 1987 to 2015 were retrospectively identified from a secure database. The study was approved by our institutional review board and was conducted in accordance with the Declaration of Helsinki

and good clinical practice guidelines. Patients had to have sarcomatoid features in their nephrectomy pathology specimen to be included in this analysis, regardless of the underlying histological RCC subtype.

Demographics, clinical features, performance status, symptoms at diagnosis, laboratory values, operative notes, pathological features, post-operative evaluation, systemic therapies and follow ups were recorded, and the Charlson comorbidity index (CCI) was calculated using this information. The CCI was not age-adjusted and no points were given for localized or metastatic sRCC. Points were added to the CCI if patients had localized or metastatic malignancies other than sRCC. Risk stratification was performed using both the international metastatic renal cell carcinoma database consortium (IMDC) and Memorial Sloan Kettering Cancer Center (MSKCC) prognostic models^{22, 23}.

Systemic therapies were grouped as ‘targeted’ (sunitinib, sorafenib, bevacizumab, axitinib, pazopanib, erlotinib, temsirolimus, or everolimus), ‘immunotherapy’ (IL-2, IFN α , dendritic cells pulsed with tumor lysate vaccination, heat shock protein peptide complex-96 vaccination, nivolumab, ipilimumab), ‘chemotherapy’ (cyclophosphamide, doxorubicin, 5-fluorouracil, gemcitabine, cisplatin, capecitabine), or ‘combinations’ (this group consisted of two subgroups: one including targeted therapies, and another including therapies other than targeted therapies).

Statistical Methods

Unless otherwise specified, overall survival (OS) was measured from time of diagnosis until death of any cause or last follow-up. Patients who were alive at the time of last contact were censored on that date. OS curves were estimated by the Kaplan-Meier method and were compared using the log-rank test. Median follow-up time was calculated using the reverse Kaplan-Meier method. Cox regression models were used to determine the association of variables with OS. A p value <0.05 was considered statistically significant. A multivariate analysis was conducted using backward variable selection, and cut-points for numeric variables were selected based on univariate analysis of terciles. Plots of median OS, and OS probabilities at selected times as smooth functions of year of diagnosis, were generated using nonparametric quantile regression adapted for right censored data²⁴.

RESULTS

Clinical and pathological characteristics

We identified 199 patients with sRCC who had undergone nephrectomy and received systemic therapy. The median age of all patients at initial diagnosis was 57 years, with a 2:1 male preponderance (Table 1). The vast majority of patients were symptomatic at initial diagnosis (92%), with pain being the most common symptom (52.3%), followed by hematuria (34.7%). The majority of the patients were Caucasian (79.9%). The median time to initiation of systemic therapy from nephrectomy was 3.7 months (range 0 – 88 months). Median follow-up was 8.8 years from diagnosis and 8.6 years from nephrectomy.

Preoperative biopsy was performed on 133 patients (76 patients had a biopsy of their primary tumor, and 57 patients had a biopsy of a metastatic site), but the diagnosis of sRCC

was made in only 10 cases (3 kidney biopsies and 7 biopsies of a metastatic site) based on this biopsy. Out of the 199 patients, 139 (69.9%) had metastatic disease at initial presentation, and 60 (30.1%) developed metastatic disease after nephrectomy was performed with curative intent. All 199 patients had confirmed sarcomatoid features in their nephrectomy specimens; 181 patients had their nephrectomy at MDACC, and 18 patients had it elsewhere but received systemic therapy and were followed at MDACC. The primary epithelial component was clear-cell RCC in the majority of cases (80.9%).

Overall survival of patients with metastatic sRCC

Of the total cohort of 199 patients, 167 (83.9%) patients have died during the study follow-up (median OS 16.5 months, 95% CI: 15.2, 20.9). The OS rates were 94% (95% CI: 91%, 98%) at 6 months, 67% (95% CI: 61%, 74%) at 12 months, 38% (95% CI: 31%, 45%) at 2 years, and 14% (95% CI: 10%, 21%) at 5 years (Figure 1). Compared with those who were diagnosed with localized disease, patients who presented with metastatic disease at initial diagnosis had a significantly shorter median OS (12.1 months vs. 23.3 months; $p=0.0064$).

Two preoperative laboratory values were found to be significantly associated with OS on multivariable analysis: preoperative corrected serum calcium (Ca) greater than 9.2 mg/dL [hazard ratio (HR) = 2.17, 95% CI: 1.4–3.35, $p=0.0005$] and preoperative white blood cell count (WBC) greater than 9.3 K/ μ L (HR = 1.64, 95% CI: 1.05–2.58, $p=0.030$). The neutrophil/lymphocyte ratio prior to nephrectomy was evaluable in 153 patients. Only 4 patients (2.6%) had a neutrophil/lymphocyte ratio < 3.0. However, when this ratio was dichotomized at the median of 3.23, it was significantly associated with OS (HR=2.0, 95% CI: 1.1 – 3.3, $p=0.021$). Tumor stage at presentation (localized vs regional/distant metastases) and histology of the epithelial component (clear-cell vs non-clear cell) were also independently associated with OS on the multivariable analysis (HR=1.94, 95% CI 1.16–3.22, $p=0.011$, and HR=1.76, 95% CI 1.11–2.77, $p=0.015$ respectively). The OS for clear-cell vs. non-clear cell patients was similar during the first 12 months, but afterwards favored patients with underlying clear-cell histology ($p=0.026$) (Figure 2). Most patients had a large primary tumor (median tumor size 11 cm) staged as pT3 or pT4 (79.4%) (Table 1). Tumor size was not significantly associated with OS. The IMDC and MSKCC prognostic classification systems were able to distinguish OS differences between poor-risk and intermediate-risk groups in metastatic sRCC patients. Patients classified as “poor-risk” did significantly worse than those classified as “intermediate-risk” ($p=0.017$ by IMDC, and $p=0.061$ by MSKCC). There were patients with missing data (43 patients by IMDC, 60 patients by MSKCC) in both groups. Only four patients were classified as having favorable-risk by IMDC criteria, and none by MSKCC criteria (Figure 5).

Effect of systemic therapies on survival

As first-line therapy, 77 patients (38.6%) received targeted therapies, whereas 122 patients (61.3%) received chemotherapy or immunotherapy. Patients who received a combination of therapies were classified in two subgroups: A subgroup that included targeted therapies ($n=13$) and a subgroup that did not ($n=43$). Overall, there was no significant OS difference according to the type of first-line systemic therapy that patients received (Supplemental Figures 1 and 2).

To assess the potential impact of targeted therapy on OS, we compared the OS for patients in two eras: those diagnosed in 1987–2005, and those diagnosed in 2006–2015. As shown in Table 2, the baseline characteristics, including histology and tumor stage, were very similar between the two groups. There was no significant difference in the rates of stage IV disease ($p=0.3$) or of clear cell vs non-clear cell histology ($p=0.62$) between patients diagnosed in 1987–2005 compared with those diagnosed in 2006–2015. There was a significant improvement in OS at 12 months for patients diagnosed in the targeted therapy era ($p = 0.011$), but this effect was attenuated at year 2 and disappeared at years 3–5 after diagnosis (Figures 3&4 and Table 3). Of note, the improvement in OS was seen in patients with intermediate-risk by MSKCC or IMDC but not in patients with poor-risk (Supplementary Figure 3). Supplementary Figure 4 shows the association between sarcomatoid percentage and OS.

DISCUSSION

The majority of our patients (69.9%) presented with metastatic disease at initial diagnosis, while the rest developed metastasis after nephrectomy. This is consistent with prior literature suggesting that sRCC patients are more likely to be diagnosed at a higher clinical stage than those with clear-cell RCC without sarcomatoid dedifferentiation²⁵. In addition, the vast majority of our patients (92%) presented with symptoms related to their primary tumor or metastatic disease. Consistent with previous reports,²⁶ our analysis suggested that patients with higher percentages of sarcomatoid component have shorter median OS (Supplementary Figure 4). Detecting sarcomatoid features by biopsy of the primary renal tumor or a metastatic site prior to nephrectomy is challenging. Currently, there are no biochemical or immunologic markers specific to sRCC, and the sensitivity of preoperative biopsies for sRCC is low, although it may improve by multiquadrant biopsies²⁷. Indeed, in our large cohort, only 7.5% of sRCC patients were identified by biopsy prior to nephrectomy. Some authors have accordingly suggested the use of preoperative imaging modalities, such as MRI, to identify sRCC, although these approaches have not yet significantly improved diagnostic accuracy²⁸. Of note, we did not include in our analysis patients diagnosed with biopsy-proven sRCC that did not undergo nephrectomy.

Although various cytotoxic chemotherapeutics have been studied in metastatic sRCC, none has shown a clear benefit. An earlier series published in 1987 from our institution, did not find any significant advantage of any particular chemotherapy, although doxorubicin-based chemotherapy did produce complete responses in 2/8 patients³. In 2011, the Eastern Cooperative Oncology Group (ECOG) published the results of a phase II trial of doxorubicin and gemcitabine in 39 patients with metastatic sRCC, and reported a 16% response rate, with significant toxicity associated with the regimen²⁹. In the present study, 7% of patients received cytotoxic chemotherapy, with no observed meaningful survival benefit compared with other therapeutic modalities (Supplemental Figure 1).

There are few studies (listed in Supplementary Table 1) focusing on the treatment modalities of sRCC in the targeted therapy era. In the present manuscript, we report the largest single-institution experience studying the management and outcomes of patients with metastatic sRCC, who had nephrectomy as part of their treatment and who received systemic therapy.

One of the goals of our study was to determine whether the introduction of targeted therapies has led to improved survival outcomes in these patients. Since VEGF-directed therapies and mTOR inhibitors entered the clinic in 2005, there has been a dramatic improvement in the outcomes of RCC patients in general, mainly those harboring the clear-cell RCC subtype. Published studies investigating targeted therapies alone or in combination with cytotoxic chemotherapy for sRCC have shown modest or no improvement in survival outcomes^{16, 18–20}. In this report, we have shown a 1-year OS benefit for patients diagnosed after 2005, compared with those who were diagnosed before 2005. However, this improvement in OS was not durable, as the 3-year and 5-year overall survival rates were very similar for patients diagnosed in the cytokine era and those diagnosed in the targeted therapy era. Of note, we were unable to detect a statistically significant difference in OS among patients treated with first-line targeted therapies compared with other treatments. Therefore, it is clear that novel and more effective therapies are needed to achieve better clinical outcomes and prolong survival in patients with sRCC. The outcomes of patients with sRCC may be different from between studies, as we only included patients with sRCC who had nephrectomy. At present, it is unclear how much nephrectomy affects survival outcomes of patients with sRCC.

Potential confounders such as earlier diagnosis and improved supportive care may also account for the improved outcomes over time and may explain why the improvement in survival began in 2000, before targeted therapies became common practice, rather than 2005 (Figure 3). Indeed, Table 2 suggests a trend towards lower rates of Stage IV disease in patients diagnosed in the targeted therapy era, although this did not reach statistical significance. In addition, patients with poor-risk classification by either the MSKCC or IMDC criteria have not experienced any improvement in survival outcomes in over 2 decades (Supplementary Figure 3). These patients carry the worst prognosis and are in dire need for novel treatment strategies.

Our study differs from prior data in terms of longer follow up time and in being the largest single-institution cohort to date. In addition, we were able to study systemic therapies used over a long period of time, therefore allowing us to compare therapies in different eras. The limitations of our study include its retrospective nature and heterogeneous systemic therapies that patients received over the years. However, we controlled for several clinical and pathological variables known to influence survival outcomes, including the CCI, a validated risk adjustment tool that accounts for the effect of comorbidities on mortality³⁰. We were unable to specifically control for the survival effect of targeted therapies when given beyond the first-line setting. Despite these limitations, we confirmed that the survival of sRCC patients without poor-risk features, who had nephrectomy, has improved over time in a large single-center analysis of sRCC spanning 3 decades of experience.

In conclusion, we have shown that the survival of patients with advanced sRCC who had nephrectomy has been steadily improving since 2000. The reasons for this may be the introduction of targeted therapies, earlier diagnosis, and improved supportive care. This survival benefit, however, does not extend beyond the first 2 years after diagnosis, and is not seen in patients with poor-risk features. Therefore, there is an unmet need to develop more effective therapies for patients with sRCC. The availability of immune checkpoint inhibitors

for the salvage of patients with RCC after first-line therapy with VEGF directed therapies, and the launch of several phase 3 trials in the first-line setting combining two immune checkpoint inhibitors, or an immune checkpoint inhibitor with a VEGF directed agent, may hopefully improve the outcome of patients with sRCC.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin*. 2016; 66:7. [PubMed: 26742998]
2. Chin AI, Lam JS, Figlin RA, et al. Surveillance strategies for renal cell carcinoma patients following nephrectomy. *Rev Urol*. 2006; 8:1. [PubMed: 16985554]
3. Sella A, Logothetis CJ, Ro JY, et al. Sarcomatoid renal cell carcinoma. A treatable entity. *Cancer*. 1987; 60:1313. [PubMed: 2441841]
4. Mian BM, Bhadkamkar N, Slaton JW, et al. Prognostic factors and survival of patients with sarcomatoid renal cell carcinoma. *J Urol*. 2002; 167:65. [PubMed: 11743277]
5. Cheville JC, Lohse CM, Zincke H, et al. Sarcomatoid renal cell carcinoma: an examination of underlying histologic subtype and an analysis of associations with patient outcome. *Am J Surg Pathol*. 2004; 28:435. [PubMed: 15087662]
6. Pal SK, Jones JO, Carmichael C, et al. Clinical outcome in patients receiving systemic therapy for metastatic sarcomatoid renal cell carcinoma: a retrospective analysis. *Urol Oncol*. 2013; 31:1826. [PubMed: 22608544]
7. Escudier B, Droz JP, Rolland F, et al. Doxorubicin and ifosfamide in patients with metastatic sarcomatoid renal cell carcinoma: a phase II study of the Genitourinary Group of the French Federation of Cancer Centers. *J Urol*. 2002; 168:959. [PubMed: 12187199]
8. Shuch B, Said J, La Rochelle JC, et al. Cytoreductive Nephrectomy for Kidney Cancer With Sarcomatoid Histology-Is Up-Front Resection Indicated and, if Not, is it Avoidable? *Journal of Urology*. 2009; 182:2164. [PubMed: 19758641]
9. Shuch B, Said J, LaRochelle JC, et al. Histologic evaluation of metastases in renal cell carcinoma with sarcomatoid transformation and its implications for systemic therapy. *Cancer*. 2010; 116:616. [PubMed: 19998348]
10. Nanus DM, Garino A, Milowsky MI, et al. Active chemotherapy for sarcomatoid and rapidly progressing renal cell carcinoma. *Cancer*. 2004; 101:1545. [PubMed: 15378501]
11. Battelli C, Cho DC. mTOR inhibitors in renal cell carcinoma. *Therapy*. 2011; 8:359. [PubMed: 21894244]
12. Bradshaw MJ, Cheville JC, Croghan GA. A 51-year-old man with rapidly progressive metastatic sarcomatoid renal cell carcinoma: an apparent complete clinical response to second-line therapy with sunitinib and low-dose interferon-alpha. *Clin Adv Hematol Oncol*. 2011; 9:61. [PubMed: 21326149]
13. Juan MJ, Climent MA. Long stabilization of sarcomatoid renal cell carcinoma treated with sorafenib. *Actas Urol Esp*. 2012; 36:385. [PubMed: 22266253]

14. Golshayan AR, George S, Heng DY, et al. Metastatic sarcomatoid renal cell carcinoma treated with vascular endothelial growth factor-targeted therapy. *J Clin Oncol.* 2009; 27:235. [PubMed: 19064974]
15. Molina AM, Tickoo SK, Ishill N, et al. Sarcomatoid-variant renal cell carcinoma: treatment outcome and survival in advanced disease. *Am J Clin Oncol.* 2011; 34:454. [PubMed: 21127411]
16. Voss MH, Bastos DA, Karlo CA, et al. Treatment outcome with mTOR inhibitors for metastatic renal cell carcinoma with nonclear and sarcomatoid histologies. *Ann Oncol.* 2014; 25:663. [PubMed: 24458473]
17. Castillo M, Petit A, Mellado B, et al. C-kit expression in sarcomatoid renal cell carcinoma: potential therapy with imatinib. *J Urol.* 2004; 171:2176. [PubMed: 15126780]
18. Staehler M, Haseke N, Roosen A, et al. Sorafenib after combination therapy with gemcitabine plus doxorubicine in patients with sarcomatoid renal cell carcinoma: a prospective evaluation. *Eur J Med Res.* 2010; 15:287. [PubMed: 20696639]
19. Michaelson MD, McKay RR, Werner L, et al. Phase 2 trial of sunitinib and gemcitabine in patients with sarcomatoid and/or poor-risk metastatic renal cell carcinoma. *Cancer.* 2015; 121:3435. [PubMed: 26058385]
20. Kyriakopoulos CE, Chittoria N, Choueiri TK, et al. Outcome of Patients With Metastatic Sarcomatoid Renal Cell Carcinoma: Results From the International Metastatic Renal Cell Carcinoma Database Consortium. *Clinical Genitourinary Cancer.* 2015; 13:e79. [PubMed: 25450036]
21. Kunene V, Misorcia M, Pirrie S, et al. Sarcomatoid renal cell carcinoma: clinical outcome and survival after treatment with sunitinib. *Clin Genitourin Cancer.* 2014; 12:251. [PubMed: 24560086]
22. Motzer RJ, Mazumdar M, Bacik J, et al. Survival and prognostic stratification of 670 patients with advanced renal cell carcinoma. *J Clin Oncol.* 1999; 17:2530. [PubMed: 10561319]
23. Ko JJ, Xie W, Kroeger N, et al. The International Metastatic Renal Cell Carcinoma Database Consortium model as a prognostic tool in patients with metastatic renal cell carcinoma previously treated with first-line targeted therapy: a population-based study. *The Lancet Oncology.* 16:293.
24. Bowman AW, Wright EM. Graphical exploration of covariate effects on survival data through nonparametric quantile curves. *Biometrics.* 2000; 56:563. [PubMed: 10877317]
25. Cangiano T, Liao J, Naitoh J, et al. Sarcomatoid renal cell carcinoma: biologic behavior, prognosis, and response to combined surgical resection and immunotherapy. *J Clin Oncol.* 1999; 17:523. [PubMed: 10080595]
26. Adibi M, Thomas AZ, Borregales LD, et al. Percentage of sarcomatoid component as a prognostic indicator for survival in renal cell carcinoma with sarcomatoid dedifferentiation. *Urol Oncol.* 2015; 33:427 e17.
27. Abel EJ, Heckman JE, Hinshaw L, et al. Multi-Quadrant Biopsy Technique Improves Diagnostic Ability in Large Heterogeneous Renal Masses. *J Urol.* 2015; 194:886. [PubMed: 25837535]
28. Takeuchi M, Kawai T, Suzuki T, et al. MRI for differentiation of renal cell carcinoma with sarcomatoid component from other renal tumor types. *Abdominal Imaging.* 2014; 40:112.
29. Haas NB, Lin X, Manola J, et al. A phase II trial of doxorubicin and gemcitabine in renal cell carcinoma with sarcomatoid features: ECOG 8802. *Med Oncol.* 2012; 29:761. [PubMed: 21298497]
30. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987; 40:373. [PubMed: 3558716]

Figure 1.
Probability of survival from time of diagnosis in patients with sRCC

A

OS by Stage

Number at risk							
Local disease	58	46	30	22	17	10	10
Regional/distant metastasis	141	81	45	28	18	12	11

Figure 2.
Overall survival (OS) after nephrectomy in patients with sRCC stratified by A. stage at presentation and B. underlying histology

Figure 3. Association between year of diagnosis and median overall survival (OS) from time of diagnosis.

Figure 4.
Association between year of diagnosis and overall survival (OS) at 1 year, 3 years and 5 years

Number at risk							
Good	4	4	3	1	0	0	0
Intermediate	81	40	22	10	7	6	4
Poor	71	23	8	6	4	3	2

Figure 5. Overall survival (OS) in patients with sRCC stratified by A. the Memorial Sloan Kettering Cancer Center (MSKCC) and B. the international metastatic renal cell carcinoma database consortium (IMDC) criteria

Table 1

Clinical and pathological characteristics of study patients (N=199)

Age – Median, years (range)	57 (22–82)
Gender	
Female	69 (34.7%)
Male	130 (65.7%)
Race	
White	159 (79.9%)
Hispanic	25 (12.6%)
Black	8 (4%)
Other	7 (3.5%)
ECOG Performance Status	
0	35 (17.6%)
1	126 (63.3%)
2	38 (19.1%)
Symptoms Any Relevant	183 (92%)
Pain	104 (52.3%)
Hematuria	69 (34.7%)
Weight Loss	45 (22.6%)
Night Sweats	25 (12.6%)
Fever	21 (10.6%)
Charlson Comorbidity Index	
0	130 (65.3%)
1	42 (21.1%)
2	18 (9.0%)
3	6 (3.0%)
4	1 (0.5%)
6	1 (0.5%)
Missing	1 (0.5%)
Smoking History	
Yes	117 (59%)
No	82 (41%)
Tumor Size – Median, cm (range)	11 (1.8 – 27)
Pathologic Tumor Stage	
T1/T2	38 (19.1%)
T3	131 (65.8%)
T4	27 (13.6%)
Missing	3 (1.5%)
Primary Epithelial Histology	
Clear cell	161 (80.9%)
Non-clear cell	38 (19.1%)
Pathological Nodal Stage	

N0/Nx	127 (63.8%)
N1	63 (31.7%)
Missing	9 (4.5%)
Positive Surgical Margins *	
Yes	35 (17.6%)
No	162 (81.4%)

* Soft tissue and/or vein wall margins

Table 2

Baseline characteristics of patients diagnosed during the cytokine therapy era (1987–2005) and the targeted therapy era (2006–2015)

	1987–2005	2006–2015
Number Of Patients	116	83
Median age	55	58
AJCC Stage		
I	5 (4%)	2 (2%)
II	9 (8%)	1 (1%)
III	25 (21%)	31 (38%)
IV	77 (67%)	49 (59%)
Pathological Tumor Stage		
T1a	4 (4%)	2 (2%)
T1b	8 (7%)	2 (2%)
T2a	9 (8%)	3 (3%)
T2b	10 (9%)	1 (1%)
T3a	56 (50%)	47 (58%)
T3b	10 (9%)	15 (18%)
T3c	1 (1%)	0 (0)
T4	13 (12%)	13 (16%)
Histology		
Clear Cell	87 (74.5%)	65 (78.3%)
Non-Clear Cell	29 (25.5%)	18 (21.7%)

Table 3

Comparison of overall survival (OS) rates with 95% confidence intervals for patients diagnosed during the cytokine era (1987–2005) and the targeted therapy era (2006–2015)

	1987–2005	2006–2015
1-year OS	61% (53%, 70%)	79% (70%, 89%)
2-year OS	33% (26%, 42%)	46% (36%, 60%)
3-year OS	26% (20%, 36%)	29% (19%, 43%)
4-year OS	17% (12%, 26%)	19% (11%, 34%)
5-year OS	14% (9%, 22%)	13% (6%, 28%)

Numbers in parentheses represent 95% confidence intervals