Published in final edited form as:

J Urol. 2009 November ; 182(5): 2164–2171. doi:10.1016/j.juro.2009.07.049.

Cytoreductive Nephrectomy for Kidney Cancer With Sarcomatoid Histology—Is Up-Front Resection Indicated and, if Not, is it Avoidable?

Brian Shuch, Jonathan Said, Jeff C. La Rochelle, Ying Zhou, Gang Li, Tobias Klatte, Fairouz F. Kabbinaavar, Allan J. Pantuck, and Arie S. Belldegrun*

Departments of Urology (BS, JCL, TK, FFK, AJP, ASB), Pathology (JS), Medicine (FFK) and Biostatistics (YZ, GL), David Geffen School of Medicine at UCLA, Los Angeles, California

Abstract

Purpose—Cytoreductive nephrectomy has a survival advantage in select patients. Patients with sarcomatoid features are known to have poor outcomes. We reviewed the role of surgery in this population to see if these patients could be identified preoperatively.

Materials and Methods—Cytoreductive nephrectomy cases identified as having sarcomatoid features or spindle cells were reviewed. The histology, grade, and the presence and percentage of sarcomatoid elements were recorded. Clinicopathological characteristics, survival and systemic therapy were compared to cases without sarcomatoid histology.

Results—A total of 62 tumors with sarcomatoid histology were identified, accounting for 14.9% of the 417 patients undergoing cytoreductive nephrectomy. The percentage of sarcomatoid transformation widely varied with a range of 2% to 100% and a mean/median of 49.8%/50%. An increased percentage of sarcomatoid features is associated with a worse prognosis. Patients with and those without sarcomatoid features had similar clinical characteristics. In the sarcomatoid group a higher T stage ($p < 0.001$) and increased incidence of nonclear cell histology ($p < 0.001$) were noted. Median survival of patients with sarcomatoid features was 4.9 vs 17.7 months for nonsarcomatoid histology ($p < 0.001$). Use of postoperative therapy was significantly worse for patients with sarcomatoid histology.

Conclusions—Patients with sarcomatoid histology undergoing cytoreductive nephrectomy have a dire prognosis despite aggressive surgery and postoperative therapy. The variability in the sarcomatoid component and the lack of specific clinical features make preoperative identification challenging. Research should focus on identifying biomarkers for this subset of tumors that may allow up-front systemic therapy with surgery reserved for responding patients.

Keywords

carcinoma; renal cell; nephrectomy; histology; biological markers

Sarcomatoid renal tumors were initially described as an aggressive subtype of renal cell carcinoma that had spindle cells similar to sarcomas.¹ However, sarcomatoid features can be found within all histological subtypes and are considered to be a common pathway of

dedifferentiation.² As such, classifications now consider sarcomatoid histology to be a poorly differentiated, aggressive characteristic and not a distinct subtype.³⁻⁵

The incidence of renal tumors having sarcomatoid features has been estimated at 1% to 8%⁶⁻⁸ but is highly stage dependent.⁹ With many patients undergoing cytoreductive nephrectomy in the recent era of RCC treatment the frequency of these features appears to have increased in modern series. In patients undergoing cytoreductive nephrectomy the frequency can be up to 20%.¹⁰

Cytoreductive nephrectomy followed by systemic therapy emerged as the standard of care after 2 phase III trials demonstrated a survival advantage.^{11,12} However, both trials excluded patients who would not likely benefit from surgery and/or systemic therapy such as those with poor performance status and brain metastasis. Several retrospective series have demonstrated that poor patient selection may limit the usefulness of cytoreduction because high risk patients frequently cannot receive or respond to systemic therapy.^{13,14} Therefore, careful selection for surgery may maximize the response to systemic therapy.¹⁵

Despite the identification of sarcomatoid histology as a high risk feature, no study excluded these patients from cytoreductive nephrectomy. We critically assessed up-front cytoreductive nephrectomy in patients with sarcomatoid features and compared the results to those of patients with nonsarcomatoid features. Additionally we looked at patient and tumor characteristics that might aid preoperative identification.

MATERIALS AND METHODS

An approved pathological database identified patients with documentation of sarcomatoid or spindle shaped cells in the pathology report. The database was cross-referenced with a prospective database of clinicopathological data including patients undergoing cytoreductive nephrectomy at the University of California-Los Angeles from 1989 to 2006. Patients were included in study based on radiographic or pathological documentation of distant metastatic disease (M1). During the analyzed period no patient was offered neoadjuvant therapy at our institution. Postoperatively patients with measurable residual disease and adequate performance status were considered for systemic therapy which consisted most frequently of interleukin-2 based therapy. After 2004 a gemcitabine/doxorubicin combination was given to patients with sarcomatoid histology after observed responses were reported.¹⁶

All cases with reported sarcomatoid histology were re-reviewed by an experienced genitourinary pathologist (JS). Tumors were designated as having sarcomatoid features based on the World Health Organization classification.⁵ Primary histological subtype, PSF and Fuhrman grade of the carcinomatous component were recorded. The type of sarcomatoid component was described as fibrosarcomatous or malignant histiocytoma-like.⁶ Other patterns were described and if no uniform feature was present it was considered not otherwise specified.¹⁷ The PSF was retrospectively estimated by a single genitourinary pathologist (JS) by summation of all slides.

Clinical information was reviewed for age, gender, race, ECOG PS, anemia, and number and sites of metastases. Pathological information included tumor size, T classification, grade, histological subtype and presence of lymph node metastases. All tumors that had confirmed sarcomatoid histology were reclassified as having grade 4 disease regardless of the total PSF or the grade of the carcinoma component.⁸

Clinicopathological variables of those patients identified with sarcomatoid histology were compared to those without these features. Categorical patient characteristics were compared by chi-square tests. When the expected frequency was less than 5 Fisher's exact tests were

used. Continuous variables were analyzed with the Student t test. The study end point was overall survival measured from the date of nephrectomy to the date of last followup or death. Survival probabilities were calculated with the Kaplan-Meier method and groups were compared using log rank tests. Cox regression analysis was used to confirm the role of sarcomatoid histology in determining survival, controlling for potential confounders including age, gender, ECOG PS (0, 1 or greater), grade (1, 2, 3 and 4), histology (clear vs nonclear), T classification (1/2, 3 and 4), size, the presence of anemia, number of metastatic sites (1, 1 or more) and lymph node metastases (N0, N1 or greater). Univariate and multivariate analyses were conducted, and the multivariate model was built using the stepwise model section with a significant cutoff of 0.1. The α -level of 5% was used to determine statistical significance. Statistical analyses were conducted using SAS® v. 9.1.

RESULTS

Of 68 patients reported to have sarcomatoid histology 62 had sarcomatoid features confirmed on review. Primary histological subtype was clear cell, papillary type I, papillary type II, chromophobe, collecting duct and unclassified in 42 (67.7%), 3 (4.8%), 6 (9.7%), 4 (6.5%), 1 (1.6%) and 6 patients (9.7%), respectively. The percentage of the sarcomatoid component was 1% to 20% in 18 patients (29%), 21% to 50% in 16 (25.8%) and 51% to 100% in 28 (45.2%). The grade of the carcinoma component was grade 2 in 5 patients (8.1%), grade 3 in 24 (38.7%) and grade 4 in 29 (46.8%). Four cases (6.5%) did not have identifiable carcinoma components and, therefore, were considered unclassified RCC. The pattern of the sarcomatoid regions was fibrosarcomatous in 2 (3.2%) patients, malignant fibrous histiocytoma-like in 12 (19.4%) and not otherwise specified in 46 (74.2%). Two additional cases had other features (3.2%), 1 with a leiomyosarcoma appearance and the other with myxoid features. Mean and median PSF was 49.8% and 50%, respectively. However, the distribution varied widely, ranging from 2% to 100% (fig. 1).

A total of 417 patients underwent cytoreductive nephrectomy, of which the sarcomatoid group accounted for 14.9%. Overall cohort characteristics and features of patients with routine and sarcomatoid histology are shown in table 1. Patients with and without sarcomatoid features had similar age, gender, ECOG PS and nodal involvement. In addition, patients with sarcomatoid histology had marginally larger tumors but this failed to reach significance (mean size 9.7 vs 9.0 cm, $p = 0.181$). The presence of anemia was more frequent with sarcomatoid histology (59.3% vs 45.9%) but this also did not reach statistical significance ($p = 0.057$). The extent and location of metastatic sites were similar between the 2 groups. The presence of miscellaneous sites of metastasis was increased with sarcomatoid histology (27.9% vs 18.3%) but did not reach significance ($p = 0.085$). The pathological T classification in the sarcomatoid group was higher with up to 25.8% of patients demonstrating T4 disease compared to 7.1% ($p < 0.001$). Nonclear histology was more frequently observed in the sarcomatoid group (32.3% vs 15.8%, $p = 0.002$).

Median survival in the overall cohort was 14.7 months (95% CI 11.9–17.7). A total of 314 patients died during the followup period (75.3%). Median followup of surviving patients was 12.9 months. Survival of patients with sarcomatoid histology (median 4.9 months, 95% CI 3.0–8.1) was significantly worse than for those with routine histology (median 17.7 months, 95% CI 14.8–23.4) ($p < 0.001$) (fig. 2). One, 2 and 5-year overall survival was 25%, 15% and 2% in the sarcomatoid group, and 60%, 43% and 21% in the routine histology group, respectively. Analysis of the subset of patients in both groups able to receive systemic therapy also demonstrated worse survival for those with sarcomatoid histology. Patients with sarcomatoid histology had a median survival of 10.7 months (95% CI 5.6–24.1) compared to 23.4 months (95% CI 17.7–28.8) ($p = 0.0044$) (fig. 3).

Univariate Cox regression models were fitted for each covariate respectively. To study the relative risk between sarcomatoid and routine groups by adjusting for potential confounders we built a multivariate model using the stepwise process to select main effect variables. In addition the interaction terms between sarcomatoid and other selected covariates were studied. None of them could be added to the main effect model at the significant level of 0.1. The final model is presented in table 2. The multivariate Cox regression model demonstrated a significant difference (HR 1.88, $p = 0.014$) in survival rates between sarcomatoid and routine histology groups after adjustment for patient age, gender, ECOG PS, grade, size, anemia, and number and sites of metastases. In addition to sarcomatoid histology multiple metastatic sites (HR 1.66, $p < 0.001$), worse ECOG PS (HR 1.72, $p < 0.001$), higher grade (risk of death for grade 1, 2 and 3 vs grade 4 was 0.34 [$p = 0.053$], 0.55 [$p = 0.015$] and 0.66 [$p = 0.077$], respectively), larger tumor size (HR 1.05, $p = 0.007$) and female gender (HR 1.37, $p = 0.019$) were all significant predictors of worse overall survival. While anemia and older age were associated with worse survival they failed to reach significance. After controlling for the 8 covariates in the multivariate model, T stage and the presence of lymph node metastases were no longer significant, although they were significant on univariate analysis (table 2).

Several graphical techniques were used to check for the proportional hazards assumption for the covariate sarcomatoid after adjusting for all other relevant covariates in the multivariate model. No gross departure from the proportionality assumption was found. We used a Cox-Snell residuals plot to assess the overall fit of the model. The estimated cumulative hazard rate lies on the 45-degree line except in the tail, suggesting the model fits well (not shown).

The association of survival and PSF was assessed but the results were limited due to the small number of patients. Analysis by quartiles demonstrated that each quartile had worsened survival compared to cases without sarcomatoid histology (not shown). However, analyses of quartiles provided limited results as the groups were small and had wide confidence intervals. With analysis of PSF as a continuous variable the risk of dying tended to increase with increasing PSF (HR 1.08, 95% CI 1.01–1.014, $p = 0.0018$). A distinct cut point to stratify patients could not be found with the limited data set.

The use of postoperative systemic therapy for patients with sarcomatoid histology was significantly lower ($p = 0.004$). Only 41.9% of patients proceeded to systemic therapy in the context of a strategy of up-front surgery followed by systemic therapy compared to 61.3% of those without sarcomatoid features (table 1).

DISCUSSION

We present one of the largest series evaluating the outcome of cytoreductive nephrectomy followed by systemic therapy in the setting of sarcomatoid histology. Our study is unique in that we compared clinicopathological characteristics and outcomes to those of patients without sarcomatoid features. While many series have confirmed the poor outcome of patients with sarcomatoid histology, only Mian et al questioned if cytoreductive nephrectomy in this population is beneficial.¹⁸ As patients with sarcomatoid features made up 15% of our overall cohort of patients this question affects a significant patient population.

The importance of careful patient selection for cytoreductive nephrectomy should not be underestimated. If patients cannot receive systemic therapy they receive limited benefit from cytoreductive surgery alone. Bennett et al presented their experience highlighting the importance of patient selection.¹³ In a consecutive series of cytoreductive nephrectomy including patients with multiple sites of metastases, brain metastases and poor performance status, only 23% proceeded to systemic therapy. Other series including those by Levy¹⁹ and

Fallick¹⁵ et al used strict criteria for selection and demonstrated that the majority (82% to 93%) of carefully selected patients can proceed to systemic therapy. Both series used strict criteria and excluded patients from analysis for reasons such as poor performance status, the presence of liver or brain metastasis, or high risk for surgery.

The survival of patients with advanced sarcomatoid tumors is known to be poor. Several series have demonstrated that median survival after nephrectomy for stage IV or M1 disease is 6 to 12 months, with few long-term survivors.^{7,8,18,20,21} While several centers have developed strict criteria for performing cytoreductive nephrectomy, few require a biopsy and/or exclude patients with known sarcomatoid features.

Despite evidence of poor survival only Mian et al questioned the role of cytoreduction in this patient population.¹⁸ In this report the authors described the outcome of 60 patients with sarcomatoid features who underwent cytoreductive nephrectomy. Median survival was 7 months overall and 8.5 months in those who received systemic therapy.¹⁸ The majority of patients (72%) were able to receive systemic therapy. The 50% improvement in survival and ability to receive systemic therapy compared to our cohort can be explained by differences in study design. In the series by Mian et al 47% of patients had surgery performed elsewhere and later presented for treatment. This survivorship bias excluded those with rapidly progressing disease with poor survival who could not have received systemic therapy.

In the series by Mian et al patients undergoing cytoreductive nephrectomy and receiving systemic therapy appeared to have improved survival compared to those who had systemic therapy alone (8.5 vs 5.3 months).¹⁸ Despite selection biases the authors concluded that resection likely provided no clear survival benefit. Patients with preoperatively identified histology were recommended to undergo up-front systemic therapy.

If patients with sarcomatoid histology do not benefit from resection we must consider methods of preoperative identification. While Mian et al discussed the role of renal biopsy there are problems with this strategy.¹⁸ It is unclear whether a small gauge needle can provide adequate tissue and preserve cellular architecture to reliably determine sarcomatoid features. Additionally, as demonstrated in figure 1 half the patients in our cohort contained less than 50% sarcomatoid histology. Sampling a single tumor region could produce a sampling error leading to false-negative biopsies. This histological heterogeneity also may hinder radiographic methods aimed at preoperative identification. Another identification strategy could be to resect/biopsy a distant site of metastasis to assess the presence of sarcomatoid features. However, metastases may contain only a carcinoma component or mixed features.²²

Clinical features would be useful in preoperative identification. However, we did not demonstrate significant differences in gender, age, tumor size, anemia, lymph node involvement or performance status. Mian et al recommended biopsy in patients with multiple sites of metastases, or brain, liver or bone metastases.¹⁸ However, patients with sarcomatoid features appeared to have a similar frequency of multiple sites and organ specific metastases compared to those with routine features. On the pathological specimen those with sarcomatoid features had an increased incidence of T4 disease (25.4%). While preoperative identification of clinical T4 disease could heighten suspicion, the radiographic ability to discern extension beyond Gerota's fascia or invasion into adjacent organs is poor. Due to an intense desmoplastic reaction, Margulis et al demonstrated that even intraoperative inspection and resection of adjacent organs may not reliably predict pathological T4 disease.²³

As biopsy and radiographic identification may not accurately identify patients with a limited sarcomatoid component, a different strategic approach must be developed. Identification of a

sarcomatoid specific antigen could be useful if shed into the serum or urine. Additionally, a radiolabeled antibody against such an antigen could be used in a similar fashion as the G250 antibody currently in clinical trials for the detection of clear cell tumors.²⁴

With poor survival and limited ability to receive therapy after nephrectomy, up-front surgery needs to be reconsidered in this population. If patients can be reliably preoperatively identified, neoadjuvant therapy may be preferable to up-front surgery. The era of targeted agents has brought renewed interest in neoadjuvant therapy due to clinical responses in the primary tumor.^{25,26} Unfortunately these agents may have worse efficacy with sarcomatoid histology and up-front administration of these agents may not be sufficient.²⁷ Combination therapy may be useful as responses in the primary tumor have been observed with the administration of gemcitabine.²⁸ This agent can be safely administered even in the setting of poor performance status and has been used in conjunction with doxorubicin in this population.^{16,29} Based on the poor outcome of patients undergoing cytoreductive nephrectomy we believe that if identification is confirmed preoperatively surgery should likely be reserved for those patients with an objective response or disease stabilization with up-front systemic therapy. Again current methods of identification are not sufficient and, therefore, future efforts should focus on reliable methods aimed at preoperative identification.

Several notable limitations of this study must be addressed including its retrospective nature. The majority of our series was during the cytokine era with the last third including the chemotherapy era. As our study period ended in 2006 targeted agents were not available. We hoped that the introduction of targeted agents would improve survival after cytoreductive nephrectomy, providing support for up-front surgical resection. However, based on the available data it does not appear that tyrosine kinase inhibitors provide a dramatic response in this population.²⁷ Additionally, while we routinely offered aggressive therapy to all patients regardless of histology, perhaps the poor response and survival of patients with sarcomatoid features biased the use of systemic therapy.

CONCLUSIONS

Sarcomatoid transformation is present in 15% of patients undergoing cytoreductive nephrectomy. Patients with RCC with sarcomatoid features undergoing resection have extremely poor survival and frequently cannot proceed to systemic therapy. Preoperative identification of these patients based on clinical features is challenging. Future efforts should be aimed at discovering reliable serum or urine based markers. If identified, patients should undergo up-front systemic therapy and reserve surgery for those who respond. The variability in the percentage of sarcomatoid components hinders future biopsy or radiographic strategies to identify patients before surgery.

Abbreviations and Acronyms

ECOG PS	Eastern Cooperative Oncology Group performance status
PSF	percentage sarcomatoid features
RCC	renal cell carcinoma

REFERENCES

1. Farrow GM, Harrison EG Jr, Utz DC. Sarcomas and sarcomatoid and mixed malignant tumors of the kidney in adults. 3. Cancer. 1968; 22:556. [PubMed: 4299778]

2. Delahunt B. Sarcomatoid renal carcinoma: the final common dedifferentiation pathway of renal epithelial malignancies. *Pathology*. 1999; 31:185. [PubMed: 10503259]
3. Storkel S, Eble JN, Adlakha K, et al. Classification of renal cell carcinoma: Workgroup No. 1. Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). *Cancer*. 1997; 80:987. [PubMed: 9307203]
4. Kovacs G, Akhtar M, Beckwith BJ, et al. The Heidelberg classification of renal cell tumours. *J Pathol*. 1997; 183:131. [PubMed: 9390023]
5. Eble, J.; Sauter, G.; Epstein, J., et al. *Pathology and Genetics, Tumors of the Urinary System and Male Genital Organs*. World Health Organization, International Agency for Research on Cancer; Lyon, France: 2004.
6. Tomera KM, Farrow GM, Lieber MM. Sarcomatoid renal carcinoma. *J Urol*. 1983; 130:657. [PubMed: 6887392]
7. de Peralta-Venturina M, Moch H, Amin M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. *Am J Surg Pathol*. 2001; 25:275. [PubMed: 11224597]
8. Chevillet 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]
9. Sella A, Logothetis CJ, Ro JY, et al. Sarcomatoid renal cell carcinoma. A treatable entity. *Cancer*. 1987; 60:1313. [PubMed: 2441841]
10. Margulis V, Matin SF, Tannir N, et al. Surgical morbidity associated with administration of targeted molecular therapies before cytoreductive nephrectomy or resection of locally recurrent renal cell carcinoma. *J Urol*. 2008; 180:94. [PubMed: 18485389]
11. Mickisch GH, Garin A, van Poppel H, et al. Radical nephrectomy plus interferon-alfa-based immuno-therapy compared with interferon alfa alone in metastatic renal-cell carcinoma: a randomised trial. *Lancet*. 2001; 358:966. [PubMed: 11583750]
12. Flanigan RC, Salmon SE, Blumenstein BA, et al. Nephrectomy followed by interferon alfa-2b compared with interferon alfa-2b alone for metastatic renal-cell cancer. *N Engl J Med*. 2001; 345:1655. [PubMed: 11759643]
13. Bennett RT, Lerner SE, Taub HC, et al. Cytoreductive surgery for stage IV renal cell carcinoma. *J Urol*. 1995; 154:32. [PubMed: 7776449]
14. Shuch B, La Rochelle J, Wu J, et al. Performance status and cytoreductive nephrectomy: redefining management in patients with poor performance. *Cancer*. 2008; 113:1324. [PubMed: 18661529]
15. Fallick ML, McDermott DF, LaRock D, et al. Nephrectomy before interleukin-2 therapy for patients with metastatic renal cell carcinoma. *J Urol*. 1997; 158:1691. [PubMed: 9334580]
16. Nanus DM, Garino A, Milowsky MI, et al. Active chemotherapy for sarcomatoid and rapidly progressing renal cell carcinoma. *Cancer*. 2004; 101:1545. [PubMed: 15378501]
17. Yang XJ, Tan MH, Kim HL, et al. A molecular classification of papillary renal cell carcinoma. *Cancer Res*. 2005; 65:5628. [PubMed: 15994935]
18. 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]
19. Levy DA, Swanson DA, Slaton JW, et al. Timely delivery of biological therapy after cytoreductive nephrectomy in carefully selected patients with metastatic renal cell carcinoma. *J Urol*. 1998; 159:1168. [PubMed: 9507824]
20. Bertoni F, Ferri C, Benati A, et al. Sarcomatoid carcinoma of the kidney. *J Urol*. 1987; 137:25. [PubMed: 3025462]
21. 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]
22. Ro JY, Ayala AG, Sella A, et al. Sarcomatoid renal cell carcinoma: clinicopathologic. A study of 42 cases. *Cancer*. 1987; 59:516. [PubMed: 3791160]
23. Margulis V, Sanchez-Ortiz RF, Tamboli P, et al. Renal cell carcinoma clinically involving adjacent organs: experience with aggressive surgical management. *Cancer*. 2007; 109:2025. [PubMed: 17420980]

24. Divgi CR, Pandit-Taskar N, Jungbluth AA, et al. Preoperative characterisation of clear-cell renal carcinoma using iodine-124-labelled antibody chimeric G250 (124I-cG250) and PET in patients with renal masses: a phase I trial. *Lancet Oncol.* 2007; 8:304. [PubMed: 17395103]
25. Shuch B, Riggs SB, LaRochelle JC, et al. Neoadjuvant targeted therapy and advanced kidney cancer: observations and implications for a new treatment paradigm. *BJU Int.* 2008; 102:692. [PubMed: 18410444]
26. Margulis V, Matin SF, Tannir N, et al. Surgical morbidity associated with administration of targeted molecular therapies before cytoreductive nephrectomy or resection of locally recurrent renal cell carcinoma. *J Urol.* 2008; 180:94. [PubMed: 18485389]
27. Golshayan AR, George S, Heng DY, et al. Meta-static sarcomatoid renal cell carcinoma treated with vascular endothelial growth factor-targeted therapy. *J Clin Oncol.* 2009; 27:235. [PubMed: 19064974]
28. Fujiwara Y, Kiura K, Tabata M, et al. Remarkable shrinkage of sarcomatoid renal cell carcinoma with single-agent gemcitabine. *Anticancer Drugs.* 2008; 19:431. [PubMed: 18454054]
29. Ferrigno D, Buccheri G. Front-line weekly chemotherapy with gemcitabine for unfit patients with non-small cell lung cancer (NSCLC). *Lung Cancer.* 2004; 45:373. [PubMed: 15301878]

Figure 1.
Histogram demonstrating wide variability in percentage of sarcomatoid histology in primary tumor

Figure 2. Kaplan-Meier analysis of overall survival (months) of sarcomatoid and nonsarcomatoid groups

Figure 3. Kaplan-Meier analysis of overall survival (months) of sarcomatoid and nonsarcomatoid groups able to proceed to systemic therapy.

Table 1

Patient characteristics

Category	Overall	Routine Histology	Sarcomatoid Histology	p Value*
No. gender (%):				
M	295 (70.7)	252 (71.0)	43 (69.4)	0.795
F	122 (29.3)	103 (29.0)	19 (30.6)	
Mean $\pm$ SD age (median)	60.3 $\pm$ 10.6 (61)	60.4 $\pm$ 10.7 (61)	59.2 $\pm$ 9.6 (59)	0.378
No. ECOG PS (%):				
0	116 (27.9)	102 (28.7)	14 (23.0)	0.352
1 or Greater	300 (72.1)	253 (71.3)	47 (77.0)	
No. histology (%):				
Clear	338 (81.1)	299 (84.2)	42 (67.7)	0.002
Nonclear	79 (18.9)	56 (15.8)	20 (32.3)	
No. T class (%):				
1/2	108 (26.0)	98 (27.7)	10 (16.1)	
3	267 (64.2)	231 (65.3)	36 (58.1)	<0.001
4	41 (9.9)	25 (7.1)	16 (25.8)	
No. node (%):				
0	298 (71.6)	256 (72.3)	42 (67.7)	0.461
(+)	118 (28.4)	98 (27.7)	20 (32.3)	
Mean $\pm$ SD tumor size (median)	9.1 $\pm$ 4.1 (9.0)	9.0 $\pm$ 4.1 (8.5)	9.7 $\pm$ 3.6 (9.0)	0.181
No. grade (%):				
1/2	134 (32.2)	134 (37.9)	0 –	
3	183 (44.0)	183 (51.7)	0 –	<0.001
4	99 (23.8)	37 (10.5)	62 (100.0)	
No. anemia (%):				
Yes	192 (47.9)	157 (45.9)	35 (59.3)	0.057
No	209 (52.1)	185 (54.1)	24 (40.7)	
No. multiple sites (%):				
Yes	183 (44.2)	152 (43.1)	31 (50.8)	0.260
No	231 (55.8)	201 (56.9)	30 (49.2)	

Category	Overall	Routine Histology	Sarcomatoid Histology	p Value [*]
No. lung (%):				
Yes	317 (76.2)	271 (76.3)	46 (75.4)	0.875
No	99 (23.8)	84 (23.7)	15 (24.6)	
No. bone (%):				
Yes	124 (29.9)	103 (29.1)	21 (34.4)	0.401
No	291 (70.1)	251 (70.9)	40 (65.6)	
No. brain (%):				
Yes	30 (7.2)	25 (7.0)	5 (8.2)	0.788
No	386 (92.8)	330 (93.0)	56 (91.8)	
No. liver (%):				
Yes	62 (14.9)	55 (15.5)	7 (11.5)	0.416
No	354 (85.1)	300 (84.5)	54 (88.5)	
No. miscellaneous (%):				
Yes	82 (19.8)	65 (18.4)	17 (27.9)	0.085
No	333 (80.2)	289 (81.6)	44 (72.1)	
No. systemic therapy (%):				
Yes	240 (58.4)	214 (61.3)	26 (41.9)	0.004
No	171 (41.6)	135 (38.7)	36 (58.1)	

* Bold type indicates statistical significance.

Table 2

Cox regression model of overall survival for patients undergoing cytoreductive nephrectomy

	Parameter Estimate	Standard Error	HR (95% CI)	p Value
Sarcomatoid	0.6295	0.2561	1.660 (1.309–2.105)	0.0140
No. sites	0.5067	0.1211	1.718 (1.281–2.304)	<0.0001
ECOG PS	0.5413	0.1497	1.718 (1.281–2.304)	0.0003
Grade:				
1	−1.0814	0.5583	0.339 (0.114–1.013)	0.0527
2	−0.6040	0.2484	0.547 (0.336–0.889)	0.0150
3	−0.4158	0.2348	0.660 (0.416–1.045)	0.0766
4 (reference)				
Size	0.0432	0.0159	1.371 (1.054–1.784)	0.0065
Gender	0.3155	0.1343	1.239 (0.969–1.584)	0.0188
Anemia	0.2139	0.1254	1.010 (0.998–1.021)	0.0881
Age	0.0098	0.0058	1.010 (0.998–1.021)	0.0945