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Trends in the Use of Cytoreductive Nephrectomy in the United States

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Abstract

Cytoreductive nephrectomy had been considered a standard in the treatment of metastatic renal cell carcinoma in the cytokine era, but with the introduction of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors (TKIs) an ‘evidence void’ for this approach has been created. In this study, we found that the use of cytoreductive nephrectomy (CyNx) has declined in the VEGFR TKI era, and in addition, potential racial and socioeconomic disparities exist.

Background—Two randomized trials published in 2001 established CyNx for patients with metastatic renal carcinoma (mRCC) as a treatment standard in the cytokine era. However, first-line systemic therapy for mRCC changed in 2005 with FDA approval of VEGFR TKIs. We evaluated the patterns of use of CyNx from 2000 to 2008.

Materials and Methods—The National Cancer Database was queried for patients diagnosed with mRCC. Patients who underwent CyNx were identified and were further categorized by pre-VEGFR versus VEGFR TKI era, race, insurance status, and hospital. For these subcategories, prevalence ratios (PRs) were generated using the proportion of patients with mRCC undergoing CyNx versus those not undergoing CyNx.

Results—Of the 47,417 patients (pts) identified with mRCC, the prevalence of cytoreductive nephrectomy increased 3% each year from 2000 to 2005 ($P < .0001$), then decreased 3% each year from 2005 to 2008 ($P = .0048$), with a significant difference between the eras (0.97 vs. 1.025; $P < .0001$). Black and Hispanic pts were less likely than Caucasian pts to undergo CyNx. Pts with Medicaid, Medicare, and no insurance were less likely than pts with private insurance to undergo

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Disclosure

The authors have no relevant conflict of interest.

CyNx. Pts diagnosed at community hospitals were significantly less likely than pts at teaching hospitals to undergo CyNx.

Conclusion—The use of CyNx has declined in the VEGFR-TKI era. In addition, racial and socioeconomic disparities exist in the use of CyNx. The results of pending randomized trials evaluating the role of CyNx in the VEGFR-TKI era are awaited to optimize use of this modality and address potential disparities.

Keywords

Kidney cancer; Renal cell carcinoma; Socioeconomic differences; Tyrosine kinase inhibitor

Introduction

Metastatic renal cell carcinoma (mRCC) is generally resistant to cytotoxic chemotherapy, but unlike most other solid tumors, has historically been treated with immunotherapy.¹ For years, the role of surgical removal of the primary tumor in the setting of metastatic disease, also known as cytoreductive nephrectomy (CyNx), was viewed as controversial, with potential for delay of systemic treatment and perioperative mortality cited as major reasons for concern.^{2,3} Subsequently, 2 prospective, randomized trials conducted by the Southwest Oncology Group (SWOG) and European Organization for the Research and Treatment of Cancer (EORTC) demonstrated that CyNx was generally safe, and improved overall survival, in patients with mRCC treated with interferon- α 2b, establishing CyNx as a treatment standard.^{4,5}

The use of CyNx in treatment of mRCC had been steadily increasing, particularly after the reporting of the SWOG and EORTC randomized trials in 2001.⁶ However, the systemic treatment paradigm for mRCC drastically changed in 2005, with FDA approval of the vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors (TKIs) which were rapidly adopted as standard first-line therapy. A shift in systemic therapy, from interferon to VEGFR TKIs, has resulted in an ‘evidence void’ regarding the utility of CyNx as the SWOG and EORTC trials were performed in the age of immunotherapy, and the appropriateness of extrapolation of those results to newer generation systemic therapies, with different mechanisms of action, is unclear. We sought to investigate patterns in the use of CyNx in the pre-VEGFR TKI and VEGFR TKI eras, as well as explore factors associated with the use of this treatment modality.

Materials and Methods

Data derived for this study were obtained from the public National Cancer Data Base (NCDB) (http://cromwell.facs.org/BMarks/BMPub/Ver10/bm_reports.cfm). The NCDB is a national, hospital-based cancer registry jointly sponsored by the American College of Surgeons and the American Cancer Society. Beginning in 1996, Commission on Cancer (CoC)-accredited programs were required to report cancers diagnosed or treated at their facilities to the NCDB. Since 2001, data collection was restricted only to CoC-accredited programs. The NCDB contains standardized data elements on patient demographics, tumor characteristics, type of surgery performed, and the first course of treatment in common with

population-based registries. In addition, the NCDB contains information on patient insurance status, geographic location of residence, type of treatment facility, and income level. The public NCDB allows queries of data categorized by several variables but generates aggregate results rather than raw data, and therefore without individual data elements. Because no patient, provider, or hospital identifiers are included in the research dataset and no protected health information is present, institutional review board approval was not required for this study.

Patients undergoing CyNx were defined as those presenting with stage IV kidney cancer that underwent nephrectomy. The impact of several variables on the likelihood of nephrectomy was also explored. These variables were divided into 4 categories: patient-level demographics, clinical characteristics, area characteristics, and facility characteristics. These variables were extracted from the public NCDB, but are standardized in the NCDB as previously described⁷ and as briefly reviewed herein.

Patient-Level Demographic

Race/ethnicity was categorized as white, black, Hispanic, Asian-Pacific Islander, and other/unknown, and sex was categorized as male and female. Age at diagnosis was a continuous variable. Primary payer/insurance type at diagnosis was determined using Facility Oncology Registry Data Standards codes, which were grouped into the following categories: Medicaid, Medicare (Medicare alone or Medicare with supplement), uninsured (for not insured-not otherwise specified, not insured-charity write-off, and not insured-self-pay), managed care, Veterans Administration, Indian Health Service/Public Health Service, military, and private insurance plans (health maintenance organization, preferred provider organization, private insurance).

Clinical Characteristics

Staging information in the NCDB is collected according to American Joint Committee on Cancer staging.⁸ The pathologic stage group is used where documented, and augmented by the clinical stage group where pathologic stage is not recorded. Data regarding stage, patient age, year of diagnosis, and type of surgery were extracted.

Area-Level Variables

Area-based indicators of patient socioeconomic status, specifically education and income, were derived from US census data at the Zip code level, and divided into quartiles based on the observed distribution in the US population. The proportions of the population in the patient's Zip code of residence without a high school degree are divided into the following groups: 29%, from 20% to 28.9%, from 14% to 19.9%, <14%, and missing.

Facility-Level Characteristics

Three types of treatment facilities are described: community facilities, community cancer centers, and teaching/research centers. Community hospitals treat at least 300 cancer cases each year and have a full range of services for cancer care, but patients need referral for portions of their treatment. Community cancer centers are facilities that offer the same range of services as the community hospitals but have at least 750 annual cancer cases and conduct

weekly cancer conferences. Teaching/research facilities differ from community cancer facilities in that the teaching/research facilities have residency programs and ongoing cancer research. National Cancer Institute-designated Comprehensive Cancer Programs that participate in the CoC approvals program are included as teaching/research facilities in this study.

Statistical Analyses

Log-binomial regression was used to estimate prevalence ratios (PRs) and corresponding 95% confidence intervals (CIs) relating the proportions of patients having no surgical treatment of their metastatic renal carcinoma among categories of various socioeconomic and demographic variables. In addition, the prevalence of no surgical treatment was estimated per 1 year increase in the year of diagnosis and compared between pre- and post-TKI periods (2000–2005 vs. 2005–2008). Age at diagnosis was divided into 9 groups (eg, <20, 20–30, >90) for purposes of this analysis, with each interval being replaced with its median value, and tested for a linear trend the percentage without surgery. Similarly, for the proportions of the population in the patient's Zip code of residence without a high school degree as described, each interval was replaced with its median value, and tested for a linear trend the percentage without surgery. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc).

Results

A total of 292,668 patients diagnosed with kidney and renal pelvis cancer between years 2000–2008 were extracted, and all patients with stage IV disease who received all or part of their first course treatment at a CoC-accredited facility were selected from the NCDB ($n = 47,417$). Importantly, approximately 10% ($n = 4748$) of identified patients had transitional cell carcinoma (TCC) on histologic reporting. Also, 1.4% of patients underwent surgical procedures other than nephrectomy (local tumor excision/destruction, surgery not otherwise specified; $n = 814$). Of the 47,417 patients with stage IV mRCC diagnosed between 2000 and 2008, 25,616 patients (54%) did not undergo CyNx.

Impact of Year of Diagnosis on CyNx

The prevalence of cytoreductive nephrectomy increased 3% each year from 2000 to 2005 ($P < .0001$). However, with FDA approval of VEGFR TKIs in 2005 as first-line therapy for mRCC, the use of CyNx decreased 3% each year from 2005 to 2008 ($P = .0048$), with a significant difference between the pre-VEGFR TKI (2000–2005) and the VEGFR TKI (2005–2008) era prevalence ratios ($P < .0001$) (Figure 1).

Impact of Other Variables on CyNx

The impact of several variables on the prevalence of CyNx are detailed in Tables 1 and 2 and described herein.

Impact of Race/Ethnicity on CyNx

Black and Hispanic pts were significantly less likely to have undergone CyNx compared with Caucasian pts [PR (black) = 0.85; 95% CI, 0.83–0.88; $P < .0001$; PR (Hispanic) = 0.95;

95% CI, 0.93–0.99; $P < .008$]. Caucasian pts were less likely than Asian Pacific Islanders to undergo surgical treatment (PR = 0.90; 95% CI, 0.84–0.97; $P < .0001$).

Impact of Healthcare Insurance on CyNx

People insured with Medicaid (PR = 0.8; 95% CI, 0.76–0.83; $P < .0001$), Medicare (PR = 0.71; 95% CI, 0.69–0.74; $P < .0001$), no health insurance (PR = 1.42; 95% CI, 0.67–0.70; $P < .0001$), Indian/Public Health (PR = 0.70; 95% CI, 0.58–0.84; $P < .0001$), and Veterans Administration coverage (PR = 0.67; 95% CI, 0.66–0.71; $P < .0001$) were significantly less likely to have undergone CyNx compared with patients with private insurance ($P < .0001$). However, compared with private insurance, no significant differences were observed for patients with military or managed care plans.

Impact of Age on CyNx

With every 10 year increase in age, the prevalence of undergoing CyNx decreased by 15% (PR 0.85; 95% CI, 0.85–0.86; $P < .0001$).

Impact of Education on CyNx

With every 5% increase in areas where the population did not have a high school education, the prevalence of undergoing CyNx decreased by 4% (PR = 0.96; 95% CI, 0.96–0.97; $P < .0001$).

Treatment Facility

Patients diagnosed at community hospitals (PR = 0.78; 95% CI, 0.76–0.79; $P < .0001$), comprehensive cancer centers (PR = 0.79; 95% CI, 0.78–0.81; $P < .0001$) and Veterans Administration hospitals (PR = 0.71; 95% CI, 0.68–0.75; $P < .0001$) were significantly less likely to have undergone CyNx compared with patients diagnosed at teaching hospitals.

Discussion

The shift in standard first line systemic therapy for metastatic renal carcinoma, from immunotherapy to VEGFR TKIs, has resulted in an ‘evidence void’ regarding the role of CyNx. Despite lack of supporting Level 1 evidence in the VEGFR TKI era, CyNx is still commonly practiced. Several randomized trial are ongoing, with the goal of generating definitive evidence to guide the use of this treatment modality in the setting of newer generation systemic therapies (Table 3). Pending the results of these studies, we sought to determine if practice patterns regarding CyNx have changed over the past decade, as well as to identify characteristics that might influence the use of CyNx.

The results of our study suggest that the use of CyNx has decreased in the era of targeted therapy. This trend is not surprising, given the lack of definitive evidence pending the completion and reporting of ongoing randomized trials.⁹ In addition, the decreased likelihood of CyNx in older, compared with younger, patients is not unexpected given concerns for increased operative morbidity and mortality in this patient population, particularly in the setting of an incurable malignancy.¹⁰ More surprising, and concerning, was the potential racial and socioeconomic differences observed. While the findings of this

analysis can only be viewed as hypothesis-generating, within the limitations of our analysis Black, Hispanic, and Indian American patients were less likely to undergo CyNx compared with Caucasian and Asian Pacific Islander pts who were more likely to undergo CyNx. Notably, prior studies have demonstrated that Black pts have a higher incidence of renal carcinoma and lower survival rates, while Asian Pacific Islander pts showed the opposite trend compared with Caucasian pts.^{11,12} Whereas the underlying biology of disease may play a role, decreased accessibility and/or acceptability of CyNx in racial and ethnic minorities may also be critical factors, as has been demonstrated with multiple other therapeutic modalities in studies of other solid tumors.^{13,14} Decreased levels of education and income likely contribute to poor accessibility and acceptability and have previously been correlated with worse outcomes in patients with cancer.¹⁵

The impact of insurance status on outcomes of cancer-related surgery has also been well documented.^{16,17} Incorporating CyNx in the treatment of mRCC requires careful planning and monitoring from a team of subspecialty practitioners, and thus, may be associated with the quality of insurance coverage. Again, though our findings can only be considered hypothesis-generating because of the limitations of the analysis, private insurance, compared with most other types of coverage, was associated with increased use of CyNx. Also, the use of CyNx was more prevalent in academic hospitals versus other types of care facilities.

Strengths of our study include a very large data set representing a diverse population of patients drawn from hospital-based registries throughout the United States, during a time period when randomized trials both established the utility of CyNx and subsequently altered the systemic therapy landscape for renal carcinoma. However, our study also has several important limitations. First, and foremost, we only had access to the public NCDB and did not have access to individualized patient data. The public NCDB allows queries of data categorized by several variables but generates aggregate results rather than raw data. Therefore, without individual data elements, we could not perform multivariable analysis to determine the relationships among the various factors associated with decreased use of CyNx and clearly, several of the variables associated with decreased use of CyNx may not retain independent significance in such an analysis. However, the primary goal of our analysis was to examine trends in the pre- and postcytokine era, and though the data also demonstrate that differences do exist in the implementation of CyNx across populations, these latter findings are hypothesis-generating and the exact nature of these disparities requires further analysis. Second, also as a result of aggregate-level data, our data-set of >47,000 patients includes a subset of patients with TCC (accounting for approximately 10% of patients, approximately 60% of whom underwent nephrectomy) and a small subset of patients that underwent surgical procedures other than nephrectomy (eg, local tumor destruction; accounting for approximately 3.88% of patients who underwent surgery) that could not be excluded from the analysis. However, the prevalence of patients undergoing CyNx with both parameters pre- and post-2005 was comparable (TCC: 9.65% vs. 10.46%, undefined surgical procedures: 3.96% vs. 3.78%). Third, as we only had 'total stage' information, and not information regarding tumor-node-metastasis (T, N, and M) status, our practical definition of CyNx for this analysis relied on selection of patients with stage IV kidney cancer who had undergone nephrectomy, acknowledging that stage IV kidney cancer is not synonymous with distant metastases. However, the total proportion of patients with

stage IV renal cancer undergoing CyNx in our analysis is in line with prior studies using individual patient data.¹⁸ Fourth, our findings may not be generalized to non-CoC approved hospitals. Although the NCDB includes data for >75% of new cancer cases in the United States annually, CoC-approved hospitals are more often larger, urban centers that provide more cancer-related services (including cancer screening, chemotherapy, and radiation) than non-CoC-approved hospitals. Finally, details regarding the specific systemic therapies administered, and clinical outcomes, were not available.

Conclusion

Cytoreductive nephrectomy may play both diagnostic and therapeutic roles, in patients presented with mRCC, particularly in patients with large primary tumors and limited metastatic burden, and for whom control of the primary may prevent imminent morbidity. Several retrospective studies have explored the role of CyNx in the era of VEGFR TKIs including the safety, and potential utility, of this approach.^{18–24} In the absence of results from randomized trials, the ultimate role CyNx remains undefined in the era of VEGFR TKIs. However, given the utility of CyNx to alleviate disease burden, lack of data to support VEGFR TKI use alone without nephrectomy, and concern for surgical complications by starting antiangiogenesis therapy first, it is reasonable to consider initial nephrectomy as the default approach, especially if patients are considered an appropriate surgical candidate, with good performance status. The results of our study are hypothesis-generating, and warrant validation with individual patient level data of a comparable study population. To our knowledge, our study is the first to describe changes in the patterns of use of this modality over the past decade and to identify potential racial/ethnic and socioeconomic differences in the application of CyNx. The results of ongoing randomized trials evaluating the role of CyNx in the VEGFR TKI era are awaited in an effort to optimize use of this treatment modality, and to address barriers to accessibility and acceptability should CyNx be proven beneficial.

References

1. Coppin C, Porzolt F, Awa A, et al. Immunotherapy for advanced renal cell cancer. *Cochrane Database Syst Rev*. 2005;CD001425. [PubMed: 15674877]
2. Bennett RT, Lerner SE, Taub HC, et al. Cytoreductive surgery for stage IV renal cell carcinoma. *J Urol*. 1995; 154:32–34. [PubMed: 7776449]
3. 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; 159:1168–1173. [PubMed: 9507824]
4. 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; 345:1655–1659. [PubMed: 11759643]
5. Mickisch GH, Garin A, van Poppel H, et al. Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: a randomised trial. *Lancet*. 2001; 358:966–970. [PubMed: 11583750]
6. Jeldres C, Baillargeon-Gagne S, Liberman D, et al. A population-based analysis of the rate of cytoreductive nephrectomy for metastatic renal cell carcinoma in the United States. *Urology*. 2009; 74:837–841. [PubMed: 19616828]
7. National Cancer Data Base Benchmark Report 2011. Available at: <http://www.facs.org/cancer/ncdb/index.html>.

8. Edge, SB.; Byrd, BR.; Compton, CC., et al., editors. AJCC Cancer Staging Manual. 7th ed.. New York, NY: Springer; 2010.
9. Richey SL, Culp SH, Jonasch E, et al. Outcome of patients with metastatic renal cell carcinoma treated with targeted therapy without cytoreductive nephrectomy. *Ann Oncol.* 2011; 22:1048–1053. [PubMed: 21115604]
10. Sun M, Abdollah F, Schmitges J, et al. Cytoreductive nephrectomy in the elderly: a population-based cohort from the USA. *BJU Int.* 2011 Sep 27. published online.
11. Stafford HS, Saltzstein SL, Shimasaki S, et al. Racial/ethnic and gender disparities in renal cell carcinoma incidence and survival. *J Urol.* 2008; 179:1704–1708. [PubMed: 18343443]
12. Vaishampayan UN, Do H, Hussain M, et al. Racial disparity in incidence patterns and outcome of kidney cancer. *Urology.* 2003; 62:1012–1017. [PubMed: 14665346]
13. Newman LA, Carolin K, Simon M, et al. Impact of breast carcinoma on African- American women: the Detroit experience. *Cancer.* 2001; 91:1834–1843. [PubMed: 11335911]
14. Hoffman RM, Gilliland FD, Eley JW, et al. Racial and ethnic differences in advanced- stage prostate cancer: the prostate cancer outcomes study. *J Natl Cancer Inst.* 2001; 93:388–395. [PubMed: 11238701]
15. Albano JD, Ward E, Jemal A, et al. Cancer mortality in the United States by education level and race. *J Natl Cancer Inst.* 2007; 99:1384–1394. [PubMed: 17848670]
16. Trinh QD, Schmitges J, Sun M, et al. Morbidity and mortality of radical prostatectomy differs by insurance status. *Cancer.* 2012; 118:1803–1810. Published online August 25, 2011. [PubMed: 22009603]
17. Kwok J, Langevin SM, Argiris A, et al. The impact of health insurance status on the survival of patients with head and neck cancer. *Cancer.* 2010; 116:476–485. [PubMed: 19937673]
18. Zini L, Capitanio U, Perrotte P, et al. Population-based assessment of survival after cytoreductive nephrectomy versus no surgery in patients with metastatic renal cell carcinoma. *Urology.* 2009; 73:342–346. [PubMed: 19041122]
19. O'Malley RL, Brewer KA, Hayn MH, et al. Impact of cytoreductive nephrectomy on eligibility for systemic treatment and effects on survival: are surgical complications or disease related factors responsible? *Urology.* 2011; 78:595–600. [PubMed: 21777963]
20. Abdollah F, Sun M, Thuret R, et al. Mortality and morbidity after cytoreductive nephrectomy for metastatic renal cell carcinoma: a population-based study. *Ann Surg Oncol.* 2011; 18:2988–2996. [PubMed: 21499808]
21. You D, Jeong IG, Ahn JH, et al. The value of cytoreductive nephrectomy for metastatic renal cell carcinoma in the era of targeted therapy. *J Urol.* 2011; 185:54–59. [PubMed: 21074811]
22. Choueiri TK, Xie W, Kollmannsberger C, et al. The impact of cytoreductive nephrectomy on survival of patients with metastatic renal cell carcinoma receiving vascular endothelial growth factor targeted therapy. *J Urol.* 2011; 185:60–66. [PubMed: 21074201]
23. Wood CG, Margulis V. Neoadjuvant (presurgical) therapy for renal cell carcinoma: a new treatment paradigm for locally advanced and metastatic disease. *Cancer.* 2009; 115:2355–2360. [PubMed: 19402066]
24. Chapin BF, Delacroix SE Jr, Culp SH, et al. Safety of presurgical targeted therapy in the setting of metastatic renal cell carcinoma. *Eur Urol.* 2011; 60:964–971. [PubMed: 21621907]

Clinical Practice Points

- Although cytoreductive nephrectomy had previously been considered a treatment standard in patients with metastatic renal cell carcinoma in the cytokine era, FDA approvals of VEGFR TKIs since 2005 has created an 'evidence void' in this approach.
- Delayed systemic treatment and associated surgical complications have become major concerns, and the appropriateness of extrapolation of those results to newer generation systemic therapies, with different mechanisms of action, is unclear.
- We sought to investigate patterns in the use of CyNx in the cytokine and VEGFR TKI eras, as well as explore factors associated with the use of this treatment modality.
- In our retrospective study using the NCDB, we found the use of cytoreductive nephrectomy has indeed decreased in the era of the VEGFR TKI therapy.
- In addition, racial and socioeconomic disparities exist in the use of CyNx.
- The findings of our study are hypothesis-generating, and the results of pending randomized trials evaluating the role of CyNx in the VEGFR TKI era are awaited to optimize use of this modality and address potential disparities.

Figure 1. Prevalence of CyNx by Year of Diagnosis
Abbreviation: CyNx = cytoreductive nephrectomy.

Table 1

Impact of Patient Level Demographics on the Use of Cytoreductive Nephrectomy

Variable	Unit	Prevalence Ratio ^a	Confidence Limits		P Value
Age	Every 10 year of increasing age	0.85	0.85	0.86	<.0001
Median Income	Every \$10,000 increment of increasing income	1.05	1.04	1.06	<.0001
No HS Education, %	Every 5% increment of region without HS education	0.96	0.96	0.97	<.0001
Race	API vs. white	1.11	1.03	1.19	.0069
	Black vs. white	0.85	0.83	0.88	<.0001
	Hispanic vs. white	0.95	0.93	0.99	.0081
	Native American vs. white	0.88	0.79	0.99	.0282
	Other vs. white	1.03	0.96	1.11	.3980
	White	Reference			
Insurance	Indian/Public Health Service vs. private	0.70	0.58	0.84	.0001
	Managed care vs. private	1.03	0.99	1.06	.1381
	Medicaid vs. private	0.80	0.76	0.83	<.0001
	Medicare vs. private	0.71	0.69	0.74	<.0001
	Military vs. private	1.09	0.95	1.23	.2359
	None vs. private	0.70	0.67	0.74	<.0001
	Unknown vs. private	0.87	0.83	0.92	<.0001
	VA vs. private	0.67	0.66	0.71	<.0001
	Private	Reference			

Abbreviations: API = Asian Pacific islander; HS = High School; VA = Veterans Affairs.

^aPrevalence of surgery at primary site.

Table 2

Impact of Treatment Facility on the Use of Cytoreductive Nephrectomy

Variable	Type of Hospital	Prevalence Ratio (Prevalence of No Surgery at Primary Site Increase)	Confidence Limits	P Value	Overall P Value
Hospital Type	Community vs. teaching and research	0.78	0.76 0.79	< .0001	< .0001
	Comprehensive vs. teaching and research	0.79	0.78 0.81	< .0001	
	Other vs. teaching and research	0.83	0.79 0.87	< .0001	
	VA vs. teaching and research	0.71	0.68 0.75	< .0001	
	Teaching and research	Reference			

Abbreviation: VA = Veterans Affairs.

Table 3
Randomized Phase III Clinical Trials Evaluating Use of CyNx With Targeted Therapy

Study	Population	Intervention	Primary Outcome	Primary Completion Date
NCT00930033 (CARMENA)	n = 576, metastatic	Nephrectomy + sunitinib vs. sunitinib alone	Overall survival	May 2013
NCT01099423 (EORTC)	n = 458, metastatic	Nephrectomy => sunitinib vs. sunitinib => nephrectomy	Progression-free survival	October 2014

Abbreviations: CARMENA = Clinical Trial to Assess the Importance of Nephrectomy; CyNx = cytoreductive nephrectomy; EORTC = European Organization for Research and Treatment of Cancer.