Published in final edited form as:
J Am Coll Surg. 2013 April ; 216(4): 774–781. doi:10.1016/j.jamcollsurg.2012.12.036.

Does Enrollment in Cancer Trials Improve Survival?

Christopher J. Chow, MD[1,*], **Elizabeth B. Habermann, PhD, MPH**[2], **Anasooya Abraham, MD, MS**[1], **Yanrong Zhu, MS**[1], **Selwyn M. Vickers, MD, FACS**[1], **David A. Rothenberger, MD, FACS**[1], and **Waddah B. Al-Refaie, MD, FACS**[3]

[1]Department of Surgery, University of Minnesota, Minneapolis, MN

[2]Division of Health Care Policy and Research, Mayo Clinic, Rochester, MN

[3]Department of Surgery, Georgetown University Hospital and Lombardi Comprehensive Cancer Center, Washington, DC

Abstract

Background—Stakeholders derive many benefits from cancer clinical trials, including guidance for future oncologic treatment decisions. However, whether enrollment in cancer trials also improves patient survival independently of trial outcomes remains under-investigated. We hypothesized that cancer trial enrollment is not associated with patient survival outcomes.

Methods—Using the 2002–2008 California Cancer Registry, we identified 555,469 patients with stage I–IV solid organ tumors. Baseline characteristics were compared by trial participation status. Logistic regression determined predictors of trial enrollment. Multivariate Cox proportional hazards regression examined the impact of trial participation on overall and cancer specific mortality with adjustment for covariates.

Results—Only 0.33% of our cohort was enrolled in clinical trials. Trial participants were likely to be younger than 65 (OR 2.13; 95% CI 1.90–2.38), Hispanic rather than non-Hispanic white (OR 0.78; 95% CI 0.67–0.90) and have breast cancer (OR 3.14; 95% CI 2.62–3.77). Multivariate survival analyses demonstrated that enrollment in cancer trials predicted a lower hazard of death. However, when stratified by disease site, this survival benefit was only observed in lung, colon and breast cancers (Table). Sensitivity and interaction analyses confirmed these relationships.

Conclusions—In this first population-based study examining trial effect in solid organ cancers, enrollment into cancer trials predicted lower overall and cancer specific mortality among common cancer sites. While these findings may demonstrate a survival benefit due to trial enrollment, they likely also reflect the favorable attributes of trial enrollees. Once corroborated, stakeholders must consider broader cancer trial designs representative of the cancer burden treated in the real world.

Corresponding author: Waddah B. Al-Refaie, MD, FACS, Division of Surgical Oncology, Department of Surgery, Georgetown University Hospital and Lombardi Comprehensive Cancer Center, 3800 Reservoir Road NW, PHC, 4th Floor, Washington, DC 20007, Tel: 612-625-2991. Fax: 612-625-4406., waddah.b.al-refaie@gunet.georgetown.edu.

*Supported by NIH NCI T32 CA132715

Presented at the Southern Surgical Association, 124th Annual Meeting, Palm Beach, 2012

INTRODUCTION

Randomized clinical trials (RCTs) provide superior evidence to help establish which treatments will benefit cancer patients. By their design, they help minimize the impact that both confounding and certain types of bias can have on reported results. RCTs remain the gold standard method to evaluate whether novel treatments are efficacious, and therefore, tremendous resources are devoted to their conduct. The ultimate goal of these efforts is to improve the survival of all cancer patients, but this requires generalizability and the implementation of trial findings into everyday practice.

To date, cancer clinical trials in the United States are faced with significant challenges. Accrual to clinical trials remains quite poor, and trial enrollees tend to be white, younger in age, insured and breast cancer patients [1–5]. As a result, the generalizability of cancer clinical trials to real world settings has been questioned[6–8]. Proponents of clinical trials often encourage patient participation due to perception of enrollment benefit. However, whether enrollment in cancer trials actually improves patient survival independently of treatment outcomes remains under-investigated. Some investigations have observed a cancer clinical trial effect [9–12] while others have not [13–16]. Unfortunately, this question of trial effect does not lend itself to be tested in a direct experimental manner due to ethical concerns [17].

Informed by both our previous work and that of others, we hypothesized that cancer trial enrollment was not associated with a patient's survival outcomes. The aim of our study was to examine the independent contribution of enrollment to cancer trials on survival rates in a large and diverse cohort of patients with stage I–IV of various solid tumors.

METHODS

Study Design and Data Source

To test our hypothesis, we conducted a retrospective cohort study using the California Cancer Registry (CCR), one of the largest population-based cancer registries in the US [18]. As of December 2009, case reporting for cases diagnosed in 2008 were estimated to be 97% complete [19]. Information regarding data abstraction by the registrars as well as reporting standards have been previously published [20–22].

Cohort Selection

Cases included all tumors of the breast, lung, stomach, esophagus, liver, biliary tree, pancreas and skin as defined by ICD-O-3 site codes. Patients younger than age 18 or older than 94 years were excluded. Cases with histologic types consistent with Kaposi's sarcoma, leukemia and lymphoma were also excluded. Although CCR case data were available beginning in 1988, reporting of patient trial enrollment was not available until after 2001. Therefore, our final cohort was composed of patients diagnosed between 2002 and 2008 (n=553,688).

Trial Participation

Trial participation was designated by the registry based on a patient's enrollment in national, regional or institutional study protocols for cancer care. For the purposes of this study, any

protocol participation was considered trial enrollment regardless of the sponsoring organization.

Unadjusted Analyses

Patient- , tumor- and treatment-related factors (age, gender, marital status, race, insurance status, tumor stage, and tumor grade, treatment modality, hospital CoC status) were compared by enrollment status using chi squared analysis. Age was categorized into the following groups: 18–65 and 65+. Payers were grouped by similar payment sources: private, underinsured/other, military and uninsured. Each case's treatment modality (surgery, radiation, chemotherapy) was dichotomized into received versus not received. These then were categorized into the following groups: no treatment, chemotherapy only, radiotherapy only, surgery only, chemoradiotherapy, combined surgery and chemotherapy, combined surgery and radiotherapy and a combination of surgery, chemotherapy and radiotherapy. Patients with missing treatment modality data were considered not to have received that particular modality.

Adjusted Analyses

To better understand the trend of enrollees into clinical trials, we conducted multivariate analyses of predictors of enrollment into clinical trials. To examine the impact of trial participation on cancer specific survival, multivariate Cox proportional hazards regression analyses were performed adjusting for covariates. These covariates included age, gender, marital status, race, payer, rural residence, CoC facility, treatment modality, tumor grade, tumor stage and year of diagnosis. We also performed interaction analyses between enrollment status and race, payer, age and stage. Finally, we performed sensitivity analyses as described in the results section below. All statistical analyses were performed using SAS 9.2 (Cary, NC).

The University of Minnesota Institutional Review board reviewed this study (HSC# 1206E15881) and deemed it exempt from further review.

RESULTS

Bivariate Analysis

Of the entire cohort of 553,688 patients, only 1846 (0.33%) were enrolled in a trial protocol. Trial participants were more likely to differ from non-participants by age, gender, residence, marital status, race, insurance status, tumor grade, tumor stage and treatment modality (for all, $p<0.0001$) (TABLE 1).

Multivariate Logistic Regression of Predictors of Trial Enrollment

Enrollees were more likely to be non-Hispanic whites than non-Hispanic Black, Hispanic, or Asian/Pacific Islanders (TABLE 2). Patients younger than 65 were more likely to be trial participants (OR 2.13; 95% CI 1.90–2.38). Payer type did not predict enrollment. However, persons with tumors of certain organ sites were more likely to be trial participants: breast, melanomas, biliary tree/liver and pancreas (see TABLE 2).

Multivariate Cox Proportional Hazards Regression of Mortality

After adjusting for covariates, trial enrollment predicted lower cancer specific death (HR 0.74; 95% CI 0.66–0.83) and overall death (HR 0.74; 95% CI 0.67–0.81) (TABLE 3). Because of individual impact of a disease site on its care and survival, further organ-specific stratification was performed. When stratified by organ site, the positive impact of trial enrollment on cancer specific mortality and overall mortality was only seen in lung, colon and breast cancer sites (TABLE 3). However, enrollment into cancer trial did not impact mortality for persons treated for melanoma, esophagus/stomach or liver/biliary/pancreas cancers. Other predictors of cancer specific death are shown in TABLE 4.

Finally, we performed various sets of interaction and sensitivity analyses. First, we identified no significant interaction between trial enrollment as a variable and race (p=0.23), payer type (p=0.10), age (p=0.12) or stage (p=0.53). Second, our estimates remained unchanged during our repeated sensitivity analyses using different age groupings or payer categorizations. Third, we found that our estimates remained unchanged when stage IV patients were excluded.

DISCUSSION

In this large and diverse population-based study of cancer patients, enrollment in a clinical trial predicted improved overall and cancer-specific survival. The current findings represent one of the first studies examining the impact of cancer trial enrollment on survival at the population level. While these findings may demonstrate a survival benefit due to trial enrollment, they likely also reflect the otherwise known favorable attributes of trial enrollees.

The literature exploring the role of trial enrollment on survival is conflicting, largely due to variation in confounder adjustment. Investigators who performed unadjusted analyses frequently found no survival benefit to trial enrollment in small cell lung, local breast or rectal cancers [13–16]. On the other hand, others who did perform adjusted analyses found that survival benefits to trial enrollment sometimes disappeared after adjustment for socioeconomic status or treatments received [9–12]. In our present study, we were able to adjust for multiple patient, tumor and treatment characteristics and still demonstrate cancer specific survival benefit with patient enrollment.

Despite the known relationship between underinsurance and enrollment into clinical trials[1,23,24] and cancer specific mortality [25,26] our current study found that payer was not a significant independent predictor of trial enrollment or of cancer specific death. We speculate that our study may have been underpowered to delineate these specific relationships seen elsewhere in the literature.

The impact of organ site on trial benefit is worthy of discussion. Our study found that when stratified by organ site, the protective effect of trial enrollment was seen only in three sites: breast, lung and colon. This may be due to enrollment of more advanced stage melanoma, pancreatic and hepatobiliary cancers--patients who already have poor prognoses.

We acknowledge several limitations to our study inherent to the use of large tumor registry data. First, our study design compared trial enrollees to non enrollees. We did not have information for whether our non-enrollees refused clinical trial participation, were ineligible for participation or even had access to trial enrollment. Second, the CCR does not compile information on patient performance status or comorbidities, which certainly can influence eligibility for trial enrollment. Third, although the CCR provides information regarding the sponsoring organization for a given case's treatment protocol, it does not provide information about the type of study was enrolled in. Finally, the CCR does not compile detailed information about provider or hospital attributes that may influence enrollment patterns.

Despite these limitations, our study has several positive aspects. First, the use of the California Cancer Registry allowed for assessment of cases from a large and diverse population based registry with a comparison group that included all cancer patients in the state of California during the study period. Second, the ability to examine a wide spectrum of common and complex cancer sites from early to advanced cancer stage is an additional strength given the NCI's initiatives for larger and broader cancer clinical trials.

The implications of our work are as follows: First, future clinical trials should be designed to investigate cancer treatment modalities for the cancer burden that occurs in the community: the cancer population is expected to be older and increasingly of minority ethnicity over the next twenty years [27]. Second, it will be increasingly critical to involve cancer patients in all stages of trial development in order to provide these crucial stakeholders with insight into the need for participation. Finally, while cancer clinical trials are crucial in guiding the practice of oncology, the promotion of clinical trials due to survival benefit must be done with caution.

CONCLUSION

In this first US population-based study, enrollment into cancer trials predicted lower overall and cancer specific mortality for patients with common cancers. While these findings demonstrate a survival benefit due to trial enrollment, they likely also reflect the favorable attributes of trial enrollees. Once corroborated, stakeholders must consider broader cancer trial designs representative of the cancer burden treated in the real world.

References

1. Al-Refaie WB, Vickers SM, Zhong W, Parsons H, Rothenberger D, Habermann EB. Cancer trials versus the real world in the United States. Annals of surgery. 2011; 254(3):438–42. discussion 442–3. [PubMed: 21775882]
2. Ford JG, Howerton MW, Lai GY, et al. Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. Cancer. 2008; 112(2):228–42. [PubMed: 18008363]
3. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. JAMA_: the journal of the American Medical Association. 2004; 291(22):2720–6. [PubMed: 15187053]
4. Stewart JH, Bertoni AG, Staten JL, Levine EA, Gross CP. Participation in surgical oncology clinical trials: gender-, race/ethnicity-, and age-based disparities. Annals of surgical oncology. 2007; 14(12): 3328–34. [PubMed: 17682824]

5. Lara PN, Higdon R, Lim N, et al. Prospective evaluation of cancer clinical trial accrual patterns: identifying potential barriers to enrollment. Journal of clinical oncology_: official journal of the American Society of Clinical Oncology. 2001; 19(6):1728–33. [PubMed: 11251003]
6. Rothwell PM. External validity of randomised controlled trials: "to whom do the results of this trial apply?". Lancet. 2005; 365(9453):82–93. [PubMed: 15639683]
7. Elting LS, Cooksley C, Bekele BN, et al. Generalizability of cancer clinical trial results: prognostic differences between participants and nonparticipants. Cancer. 2006; 106(11):2452–8. [PubMed: 16639738]
8. Al-Refaie WB, Habermann EB, Dudeja V, et al. Extremity soft tissue sarcoma care in the elderly: insights into the generalizability of NCI Cancer Trials. Annals of surgical oncology. 2010; 17(7): 1732–8. [PubMed: 20354801]
9. Davis S, Wright PW, Schulman SF, et al. Participants in prospective, randomized clinical trials for resected non-small cell lung cancer have improved survival compared with nonparticipants in such trials. Cancer. 1985; 56(7):1710–8. [PubMed: 3896460]
10. Marubini E, Mariani L, Salvadori B, et al. Results of a breast-cancer-surgery trial compared with observational data from routine practice. Lancet. 1996; 347(9007):1000–3. [PubMed: 8606561]
11. Cottin V, Arpin D, Lasset C, et al. Small-cell lung cancer: patients included in clinical trials are not representative of the patient population as a whole. Annals of oncology_: official journal of the European Society for Medical Oncology/ESMO. 1999; 10(7):809–15. [PubMed: 10470428]
12. Schea RA, Perkins P, Allen PK, Komaki R, Cox JD. Limited-stage small-cell lung cancer: patient survival after combined chemotherapy and radiation therapy with and without treatment protocols. Radiology. 1995; 197(3):859–62. [PubMed: 7480770]
13. Schmoor C, Olschewski M, Schumacher M. Randomized and non-randomized patients in clinical trials: experiences with comprehensive cohort studies. Statistics in medicine. 1996; 15(3):263–71. [PubMed: 8643884]
14. Ward LC, Fielding JW, Dunn JA, Kelly KA. The selection of cases for randomised trials: a registry survey of concurrent trial and non-trial patients. The British Stomach Cancer Group. British journal of cancer. 1992; 66(5):943–50. [PubMed: 1419641]
15. Dahlberg M, Glimelius B, Påhlman L. Improved survival and reduction in local failure rates after preoperative radiotherapy: evidence for the generalizability of the results of Swedish Rectal Cancer Trial. Annals of surgery. 1999; 229(4):493–7. [PubMed: 10203081]
16. Burgers JA, Arance A, Ashcroft L, Hodgetts J, Lomax L, Thatcher N. Identical chemotherapy schedules given on and off trial protocol in small cell lung cancer: response and survival results. British journal of cancer. 2002; 87(5):562–6. [PubMed: 12189557]
17. Peppercorn JM, Weeks JC, Cook EF, Joffe S. Comparison of outcomes in cancer patients treated within and outside clinical trials: conceptual framework and structured review. Lancet. 2004; 363(9405):263–70. [PubMed: 14751698]
18. Parikh-Patel A, Bates JH, Campleman S. Colorectal cancer stage at diagnosis by socioeconomic and urban/rural status in California, 1988–2000. Cancer. 2006; 107(5 Suppl):1189–95. [PubMed: 16835910]
19. [Accessed October 7, 2012] No Title. Available at: http://www.ccrcal.org/Inside_CCR/FAQ.shtml#how complete is ccr data
20. Ayanian JZ, Zaslavsky AM, Fuchs CS, et al. Use of adjuvant chemotherapy and radiation therapy for colorectal cancer in a population-based cohort. Journal of clinical oncology_: official journal of the American Society of Clinical Oncology. 2003; 21(7):1293–300. [PubMed: 12663717]
21. Kunz PL, Gubens M, Fisher GA, Ford JM, Lichtensztajn DY, Clarke CA. Long-term survivors of gastric cancer: a california population-based study. Journal of clinical oncology_: official journal of the American Society of Clinical Oncology. 2012; 30(28):3507–15. [PubMed: 22949151]
22. Masoomi H, Ziogas A, Lin BS, et al. Population-based evaluation of adenosquamous carcinoma of the colon and rectum. Diseases of the colon and rectum. 2012; 55(5):509–14. [PubMed: 22513428]
23. Parsons HM, Harlan LC, Seibel NL, Stevens JL, Keegan THM. Clinical trial participation and time to treatment among adolescents and young adults with cancer: does age at diagnosis or insurance

make a difference? Journal of clinical oncology_: official journal of the American Society of Clinical Oncology. 2011; 29(30):4045–53. [PubMed: 21931022]

24. Sateren WB, Trimble EL, Abrams J, et al. How sociodemographics, presence of oncology specialists, and hospital cancer programs affect accrual to cancer treatment trials. Journal of clinical oncology_: official journal of the American Society of Clinical Oncology. 2002; 20(8): 2109–17. [PubMed: 11956272]
25. Robbins AS, Pavluck AL, Fedewa SA, Chen AY, Ward EM. Insurance status, comorbidity level, and survival among colorectal cancer patients age 18 to 64 years in the National Cancer Data Base from 2003 to 2005. Journal of clinical oncology_: official journal of the American Society of Clinical Oncology. 2009; 27(22):3627–33. [PubMed: 19470927]
26. Sabik LM, Bradley CJ. Differences in Mortality for Surgical Cancer Patients by Insurance and Hospital Safety Net Status. Medical care research and review_: MCRR. 2012
27. Smith BD, Smith GL, Hurria A, Hortobagyi GN, Buchholz TA. Future of cancer incidence in the United States: burdens upon an aging, changing nation. Journal of clinical oncology_: official journal of the American Society of Clinical Oncology. 2009; 27(17):2758–65. [PubMed: 19403886]

Table 1

Patient, Tumor and Treatment Factors, by Trial Participation

Factors	Not Enrolled	Enrolled	χ^2 p-value
Age			
18–64	253707 (45.9%)	1276 (69.1%)	<0.0001
65+	298135 (54.0%)	570 (30.9%)	
Sex			
Male	197754 (35.8%)	494 (26.8%)	<0.0001
Female	354088 (64.2%)	1342 (73.24%)	
Residence			
Rural	87961 (15.9%)	240 (13%)	<0.0001
Urban	464151 (84.1%)	1606 (87%)	
Marital Status			
Single	74092 (13.4%)	264 (14.3%)	
Married	301276 (54.5%)	1171 (63.4%)	<0.0001
Separated/Divorced/Widowed	147882 (26.9)	404 (21.9%)	
Unknown	28592 (5.2%)	7 (0.4%)	
Race/ethnicity			
Non-Hispanic White	380635 (69.0%)	1390 (75.3%)	
Non-Hispanic Black	32368 (5.9%)	79 (4.3%)	
Hispanic	73214 (13.3%)	218 (11.8%)	<0.0001
Asian/Pacific Islander	54358 (9.9%)	152 (8.2%)	
Non-Hispanic American Indian	1726 (0.3%)	5 (0.3%)	
Other/Unknown	9541 (1.7%)	2 (0.1%)	
Insurance Status			
Private	264097 (47.9%)	1071 (58%)	
Underinsured/Other	274807 (49.8%)	737 (39.9%)	<0.0001
Uninsured	8752 (1.6%)	29 (1.6%)	
Military	4184 (0.8%)	9 (0.5%)	
CoC Hospital			
Approved	197172 (35.7%)	1194 (58.8%)	<0.0001
Not Approved	348292 (63.1%)	732 (39.7%)	
Unknown	6378 (1.2%)	10 (0.5%)	
Grade			
Low	208143 (37.7%)	819 (44.4%)	<0.0001
High	130331 (23.6%)	514 (28.8%)	
Unknown	213368 (38.7%)	513 (27.8%)	
Stage			<0.0001

Factors	Not Enrolled	Enrolled	χ^2 p-value
I	203508 (36.9%)	618 (33.5%)	
II	90897 (16.5%)	504(27.3%)	
III	71205 (12.9%)	290 (15.7%)	
IV	92985 (16.9%)	187 (10.1%)	
Unknown	93247 (16.9%)	247 (13.4%)	
Organ Site			
Lung	116727 (21.2%)	167 (9.1%)	
Colon	104482 (18.9%)	186 (10.1%)	
Melanoma	73544 (13.3%)	327 (17.7%)	<0.0001
Breast	188884 (34.2%)	1031 (55.9%)	
Stomach/Esophagus	26828 (4.9%)	40 (2.2%)	
HPB	41337 (7.5%)	85 (5.2%)	
Treatment			
None	99567 (18.0%)	30 (1.6%)	
Chemo Only	35073 (6.4%)	143 (7.6%)	
Radiation Only	15978 (2.9%)	8 (0.4%)	
Surgery Only	228881 (41.5%)	461 (25.0%)	<0.0001
Chemo + Radiation	27392 (5.0%)	87 (4.7%)	
Chemo + Surgery	50144 (9.1%)	359 (19.5%)	
Radiation + Surgery	51346 (9.3%)	295 (16.0%)	
Chemo + Surgery + Radiation	43461 (7.9%)	463 (25.1%)	

Table 2

Logistic Regression Predicting Trial Enrollment (n=553688, c=0.770)

Factor	Adjusted OR*	95% CI	p-value
Age			
18–64 vs 65+	2.125	1.896–2.382	<0.001
Gender			
Female vs Male	0.849	0.738–0.977	0.022
Marital Status			
Married vs Single	1.184	1.033–1.357	0.015
Divorced/Separated/Widowed vs Single	1.078	0.917–1.266	0.363
Unknown vs Single	0.110	0.052–0.235	<0.001
Race			
Non-Hispanic Blacks vs Non-Hispanic White	0.735	0.583–0.926	0.009
Hispanic vs Non-Hispanic White	0.778	0.671–0.901	<0.001
Asian/Pacific Islander vs Non-Hispanic White	0.763	0.643–0.907	0.002
American Indian vs Non-Hispanic White	0.849	0.351–2.052	0.716
Unknown vs Non-Hispanic White	0.121	0.030–0.487	0.003
Payer			
Underinsured vs Private	1.037	0.933–1.152	0.504
Military vs Private	0.578	0.299–1.118	0.103
Uninsured vs Private	0.948	0.933–1.152	0.779
Grade			
High vs Low Grade	0.885	0.789–0.993	0.037
Unassessed vs Low Grade	0.519	0.435–0.619	<0.001
CoC Hospital			
CoC Approved vs Not Approved	3.147	2.851–3.473	<0.001
Unknown vs Not Approved	0.722	0.385–1.351	0.308
Stage			
I vs IV	0.612	0.508–0.737	<0.001
II vs IV	1.073	0.887–1.297	0.468
III vs IV	1.351	1.116–1.636	0.002
Unknown vs IV	0.685	0.550–0.852	<0.001
Residence			
Rural vs Urban	0.864	0.752–0.992	0.039
Organ Site			
HPB vs Colon	1.903	1.460–2.482	<0.001
Breast vs Colon	3.144	2.620–3.773	<0.001

Factor	Adjusted OR*	95% CI	p-value
Lung vs Colon	1.011	0.809–1.262	0.924
Melanoma vs Colon	6.539	5.089–8.402	<0.001
Stomach/Esophagus vs Colon	1.040	0.739–1.480	0.829

Table 3

Cancer Trial Enrollment and Mortality

Trial Enrollment	Overall Mortality Enrolled vs Not Enrolled HR* (95% CI)	Cancer Specific Mortality Enrolled vs Not Enrolled HR* (95% CI)
All Sites Included	0.74 (0.67–0.81)	0.74 (0.66–0.83)
Stratified By Disease Site		
Lung	0.74 (0.62–0.88)	0.73 (0.60–0.87)
Colon	0.59 (0.45–0.78)	0.57 (0.42–0.77)
Breast	0.75 (0.59–0.94)	0.69 (0.52–0.90)
Melanoma	0.83 (0.61–1.12)	0.97 (0.69–1.37)
Esophagus/Stomach	0.86 (0.53–1.39)	0.77 (0.46–1.30)
Liver/Biliary/Pancreas	1.01 (0.82–1.26)	1.03 (0.82–1.28)

*Adjusted for age, gender, marital status, race, payor, rurality of residence, year of diagnosis, organ site, tumor stage, tumor grade, care at a CoC hospital and treatment modalities received.

Table 4

Predictors of Cancer Specific Mortality

Factor	Overall Mortality HR* (95% CI)
Trial Enrollment	
Enrolled vs Not Enrolled	0.74 (0.66–0.83)
Gender	
Female vs Male	0.86 (0.85–0.87)
Marital Status	
Married vs Single	0.88 (0.87–0.89)
Divorced/Separated/Widowed vs Single	1.06 (1.04–1.08)
Unknown vs Single	0.71 (0.69–0.74)
Race	
Non-Hispanic Blacks vs Non-Hispanic White	1.03 (1.01–1.05)
Hispanic vs Non-Hispanic White	0.93 (0.91–0.94)
Asian/Pacific Islander vs Non-Hispanic White	0.81 (0.79–0.82)
American Indian vs Non-Hispanic White	1.07 (0.99–1.15)
Unknown vs Non-Hispanic White	0.39 (0.36–0.43)
Payer	
Underinsured vs Private	1.11 (1.10–1.13)
Military vs Private	1.12 (1.06–1.18)
Uninsured vs Private	1.15 (1.11–1.19)
Grade	
High vs Low Grade	1.55 (1.53–1.57)
Unassessed vs Low Grade	1.29 (1.27–1.30)
CoC Hospital	
CoC Approved vs Not Approved	0.92 (0.91–0.93)
Unknown vs Not Approved	1.09 (1.04–1.13)
Stage	
I vs IV	0.16 (0.15–0.16)
II vs IV	0.32 (0.31–0.32)
III vs IV	0.55 (0.54–0.56)
Unknown vs IV	0.47 (0.46–0.47)
Residence	
Rural vs Urban	1.02 (1.00–1.031)

*Adjusted for age, year of diagnosis, organ site, tumor grade, and treatment modalities received.