Published in final edited form as:

Am J Clin Oncol. 2016 April ; 39(2): 126–131. doi:10.1097/COC.0000000000000029.

The effect of receiving treatment within a clinical trial setting on survival and quality of care perception in advanced stage non-small cell lung cancer

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Abstract

Objectives—Treatment outcomes of advanced stage (IIIB and IV) non-small cell lung cancer (NSCLC) are poor. In this study, we explore the survival outcomes and the perception of the quality of care delivered in stage IIIB and IV NSCLC patients treated within vs. outside a clinical trial.

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Conflict of interest statement:

The authors have no conflicts of interest to disclose. None declared.

Methods—Data were obtained from the Cancer Care Outcomes Research and Surveillance Consortium (CanCORS). Baseline characteristics according to clinical trial participation were determined. The association between clinical trial enrollment and survival was assessed using a Cox proportional hazard model after adjusting for age, income, primary data collection and research site, comorbidities, self-reported performance status, presence of brain metastasis, stage IIIB vs. IV, and cancer histology.

Results—Of 815 stage IIIB and IV NSCLC patients, 56 (7%) were enrolled in clinical trials. Median survival for the patients treated within vs. outside a clinical trial was 20.5 vs. 16.7 months, respectively ($P=0.21$). Using a multivariate survival model, clinical trial enrollment did not correlate with longer survival ($P=0.81$). Comparing patients according to clinical trial enrollment, patients treated within a clinical trial setting perceived a better overall quality of care ($P<0.01$).

Conclusions—Management of stage IIIB and IV NSCLC patients within a clinical trial setting conveyed a perception of superior care that did not translate into survival benefit. These findings suggest that providing cancer care within a clinical trial should not imply a survival benefit when counseling stage IIIB and IV NSCLC patients about entering clinical trials.

Keywords

Lung cancer; Clinical trials; Quality of care; Chemotherapy; Radiation therapy

Introduction

Lung cancer is the leading cause of cancer death in the United States and the world¹. In spite of the progress made in managing and treating this disease, outcomes for advanced stage non-small cell lung cancer (NSCLC), which comprises the majority of the cases, are poor². Consequently, enrolling lung cancer patients in clinical trials is viewed as potentially the best available treatment whenever possible.

Although clinical trials are primarily designed to test an experimental intervention, there is an argument that participation in a clinical trial may confer survival benefit through enhancing quality of care, stringent patient selection criteria, and adapting aggressive measures for treating patients in trials³. This favorable gain from being in a trial is often referred to as the “trial effect” or “inclusion benefit”. Although survival advantage for patients in clinical trials was noticed in various cancers⁴⁻¹¹, including small cell lung cancer (SCLC) and resectable NSCLC, this association is not established in advanced stage NSCLC. Also, most studies that explored the “trial effect” did not adjust for important survival covariates, and suffered from small sample size.

Boosting patient accrual to cancer clinical trials has been a major challenge for research institutions^{12,13}. Recognizing the crucial need to enroll more patients in trials, it is important to ensure that patients have realistic expectations of the benefits from trial.

The purpose of this study is to examine the survival outcomes, the specifics of the care delivered and the patient perception of the quality of care provided for advanced stage (IIIB and IV) NSCLC patients managed within versus outside a clinical trial. The study used the Cancer Care Outcomes Research and Surveillance Consortium (CanCORS) database, which

represents a large cohort of patients across the United States¹⁴. We believe this study will improve our understanding of the “trial effect” in stage IIIB and IV NSCLC, and will be of benefit when counseling patients about entering clinical trials.

Materials and Methods

Study Population

The study population included all CanCORS participants with advanced stage NSCLC (stage IIIB or IV per the American Joint Committee on Cancer “AJCC” staging, 6th edition) who had completed a full baseline interview. CanCORS is a broadly representative¹⁴, large study of care and outcomes in lung and colorectal cancer patients who were diagnosed between September 2003 and June 2005. The study is funded by the National Cancer Institute (NCI) and involves seven primary data collection and research (PDCR) sites which include geographically defined areas, health-care delivery systems and Veterans Administration Hospitals across the United States.

The CanCORS instruments for data collection include baseline and follow up patient and surrogate interviews, medical record abstraction by trained abstracters and physician surveys. The baseline interviews were either full-length or brief where the latter were for ill patients unable to take the full interview. The surrogate interviews were used if death or sickness prevented the patient from completing the initial interview. All baseline interviews were completed an average of 4 months after diagnosis. The follow up interviews/surveys were completed 11-14 months after diagnosis (detailed methodology for CanCORS has been previously described)¹⁴. Of the 5207 patients in CanCORS with lung cancer, 2941 had advanced stage NSCLC and 815 completed the full baseline survey.

Study Measures

Data collected from the surveys and the abstracted medical records included socio-demographic and clinical characteristics, symptom management, quality of care delivered, and participation in a clinical trial. All variables were obtained from the full baseline interviews except for location of patient death, following patients’ wishes in the last month of life, time spent in place of death before dying and the patient/surrogate respondent perception of quality of cancer care received which were obtained from the follow up surveys. Comorbidities, receipt of chemotherapy treatment, disease stage, histology, presence of brain metastasis, and survival details were collected from medical records. Comorbidity at the time of diagnosis, was classified as none, mild, moderate or severe per the Adult Comorbidity Evaluation 27 Index (ACE-27)¹⁵. Survival data were obtained from medical records and was updated over time from surveys of patients and surrogates and data from participating cancer registries

Statistical analysis

Frequencies of categorical variables were calculated according to enrollment in clinical trial. A Monte Carlo approximation to the Fisher’s exact test and chi-squared tests were used to assess the association between covariates and enrollment in a clinical trial. Kaplan-Meier curves were used to plot the univariate association between the status of enrolling in a

clinical trial and survival. The log rank test was used to compare the two Kaplan-Meier curves. Thereafter, a Cox proportional hazard model was used to determine the association between enrollment in a clinical trial and survival adjusting for age, income, PDCR site, comorbidities, self-reported performance status, presence of brain metastasis, stage IIIB vs. IV, and cancer histology. The survival analyses had a 90% power to detect a true hazard ratio of 0.645 for the effect of enrolling in a clinical trial on survival as compared to no clinical trial. A Cox proportional hazard model was also used to determine the association between enrollment in a clinical trial and survival only for the patients who received chemotherapy adjusting for the same covariates as in the above model. All analyses were performed in SAS 9.3.

Results

A total of 56 (7%) participants reported having enrolled in clinical trials which included chemotherapy 38 (68%), radiation therapy 8 (14%) or surgery 1 (2%).

Baseline patient demographics and clinical characteristics for those who enrolled vs did not enroll in a clinical trial are summarized in Table 1. Although patients 75 years were less likely to receive treatment in a clinical trial (7, 13% vs. 170, 22%), this was not statistically different ($P=0.21$). Patients who received treatment outside a clinical trial were more likely to have lower income ($P=0.02$) and to suffer from brain metastasis ($P=0.02$). There was no significant difference in comorbidities, baseline performance status, PDCR site, cancer stage (IIIB vs. IV), cancer histology or educational level.

Enrollment in a clinical trial was not associated with improved survival. As shown in the Kaplan-Meier survival curves (Figure 1), the median survival time for the patients treated within versus outside a clinical trial was 20.5 vs 16.7 months, respectively (Log Rank Test: $P=0.21$). Assessing survival after adjusting for several covariates using a Cox proportional hazard model (Table 2) also showed no survival benefit for the patients enrolled in clinical trials (Hazard Ratio (HR):1.05, 95% CI: 0.71-1.55). In the same model, worse survival was noticed in patients with severe comorbidities (HR:1.54, 95% CI: 1.17-2.02) and stage IV disease (HR:1.49, 95% CI: 1.23-1.81). The presence of brain metastasis was not associated with worse survival (HR:1.14, 95% CI: 0.82-1.57). We repeated these analyses after restricting the cohort to the patients who received chemotherapy and still showed no survival advantage for the patients in clinical trials (HR:1.01, 95% CI: 0.63-1.63) (data in the supplementary material, Supplemental Digital Content 1, <http://links.lww.com/AJCO/A43>).

Table 3 shows the patient-reported symptom management and end-of-life care received according to clinical trial enrollment. There was no significant difference between patients receiving care within vs. outside a clinical trial with regard to receiving the needed help for pain ($P=0.93$), mood changes ($P=0.68$), nausea and/or vomiting ($P=0.98$), cough ($P=0.14$) or breathing ($P=0.21$). Being in a clinical trial did not result in significant differences in the frequency of discussing and receiving hospice care ($P=0.18$ and 0.79, respectively), addressing resuscitation preferences ($P=0.31$), location of death ($P=0.33$) or following patient's wishes in the last month of life ($P=0.87$) (Table 4). However, the patients in clinical

trials and their surrogate respondents perceived a superior quality of care compared to the other patients ($P<0.01$) (Table 5).

Discussion

To our knowledge, this is the largest population-based study of stage IIIB and IV NSCLC exploring the survival outcomes and the patients' perception of the care received according to the status of enrollment in a clinical trial. Historically, identifying a comparison group of patients not enrolled in trials has been challenging¹⁶. However, utilizing the robust CanCORS database, we were able to define stage IIIB and IV NSCLC patients treated within and outside clinical trials with comparable baseline characteristics, and to adjust for important covariates known to be associated with survival in advanced stage NSCLC.

Examining the patients' baseline characteristics (Table 1) showed that those in clinical trials had higher income ($P=0.02$) and were less likely to have brain metastasis ($P=0.02$), where the latter is mostly due to the common practice of excluding NSCLC patients with brain metastasis from clinical trials. However, other variables associated with survival in NSCLC such as age, performance status, comorbidities, and cancer stage were not statistically different between the patients treated within vs. outside trials. This similarity in the baseline characteristics is likely related to our study methods because to achieve comparability we intentionally included only the patients who completed the full baseline survey, who were known to have better baseline performance status and be more likely candidates for trials. Of note, previous studies showed that selecting healthier patients to enroll in clinical trials has been progressively increasing with time¹⁷.

In our study, there was no significant difference in the survival of advanced stage NSCLC patients who received care within versus outside a clinical trial even after adjusting for age, income, primary data collection and research site, comorbidities, self-reported performance status, presence of brain metastasis, stage IIIB vs. IV, and cancer histology. The only covariates associated with worse survival were cancer stage IV and higher level of comorbidity. The finding that brain metastasis was not associated with worse survival, even though exclusively seen in non-trial patients, is consistent with the report by Sperduto and colleagues which showed that prognosis of NSCLC patients with brain metastasis is variable¹⁸. Because of the selection process in our study, it is likely that our patient population was fit to receive aggressive treatment for brain metastasis such as surgical resection.

Of interest, survival was not statistically different for the patients according to trial enrollment status after restricting the analysis to those who received chemotherapy. It is noteworthy that most of the recent advances in treating NSCLC have been in the chemotherapy/targeted treatment fields. Of the 56 patients enrolled in clinical trials, 38 (67%) indicated that chemotherapy was involved in the trial. Although this patient-reported item might be limited by the level of the patient's understanding of the research protocol, it does shed a light on the general nature of the clinical trials involved.

Various reasons might be put forward to explain the similar survival outcomes. First, advanced stage NSCLC remains a fatal disease where there have been relatively modest improvement in therapy except for a small subset of patients with specific genetic abnormalities lending them candidates for novel targeted therapies^{19,20}. Thus it is crucial not to take our results out of context to discourage patient participation in clinical trials that might potentially introduce new and effective treatments. Second, due to lack of information on the specifics of the trials involved, it is unclear if the trials' outcomes were superior or inferior to standard care. Third, our study might have been underpowered to show a survival difference as the number of patients in trials was relatively small. However, given our results and considering that published studies on the trial effect in advanced stage NSCLC either did not show survival benefit or failed to assign a representative comparison group¹⁶, it is essential that survival benefit from enrolling in a clinical trial is not implied in efforts to enroll advanced stage NSCLC patients in trials.

The patient-reported cancer care elements including symptom management and end-of-life related issues were similar regardless of the status of enrollment in a clinical trial. This suggests, in contrast to published reports, that patients in trials do not receive preferential treatment^{3,21}. However, it was noted that the patients treated within a trial perceived a superior quality of care compared to others ($P<0.01$). Although the basis for this perception is unclear, it is likely to be multi-factorial. Patients interested in clinical trials may be inherently more optimistic and likely to hope for successful treatment. Expectations of personal benefit are one reason why patients participate in clinical trials, even if the chances of direct benefit are low²². In dose-finding phase I clinical trials, hope for therapeutic benefit was shown to be a strong motivator for participation²³. Another potential reason for the perceived superior care is that large teams take care of trial patients including physicians, nurses and research coordinators, which might confer a sense of special care.

Concern about the tendency of research participants to overestimate the benefits of clinical trials has been prominent in discussions of the ethics of cancer trials as well as other studies in which the likelihood of direct benefit is low²⁴. Some experts consider this tendency to overestimate the benefits of clinical trials an example of "therapeutic misconception (TM)," an often-documented failure by research participants to appreciate the differences between research and treatment^{25,26}. In spite of efforts to fully guard against TM, the risk of TM remains noticeable, particularly in trials for highly serious and fatal disorders^{27,28}. Strategies for addressing TM have included efforts to separate the investigators or researchers from control of the clinical care of research patients, clear communication about the differences between on and off trial treatment before and during the informed consent process, and decision monitoring following the consent process²⁸. Efforts to address perceived inclusion benefit need not eliminate participants' hope for a positive outcome, but, rather, seek to contextualize this hope.

Some limitations should be pointed out when interpreting our results. The number of patients enrolled in trials was relatively small. The trials involved were heterogeneous and included chemotherapy, radiation therapy and surgery trials without information about the therapeutic agents used or the number of treatments delivered. Only participants who were healthy enough to complete the full baseline interview were included. Finally, the trial type

and participation were patient-reported. In spite of these limitations, the population-based nature and the large geographic area represented by CanCORS, the ability to adjust for important covariates and the medical abstraction of clinical variables are unique features that add to the strength of our study.

Conclusion

This study advances the knowledge on the association between receiving treatment within vs. outside a clinical trial, survival outcomes, and patients' perception of quality of care in advanced stage NSCLC. Our findings are insightful for researchers conducting clinical trials as well as for patients. This study supports the notion that survival benefit in NSCLC trials is unlikely related to the ancillary care delivered in trials. On the other hand, our study highlights the potential for misperceptions among patients participating in NSCLC trials with respect to the benefits that may confer on them.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments and Financial Disclosure

The work of the CanCORS Consortium was supported by grants from the National Cancer Institute (NCI) to the Statistical Coordinating Center (U01 CA093344) and the NCI supported Primary Data Collection and Research Centers (Dana-Farber Cancer Institute/Cancer Research Network U01 CA093332, Harvard Medical School/Northern California Cancer Center U01 CA093324, RAND/UCLA U01 CA093348, University of Alabama at Birmingham U01 CA093329, University of Iowa U01 CA093339, University of North Carolina U01 CA093326) and by a Department of Veterans Affairs grant to the Durham VA Medical Center CRS 02-164.

We also would like to thank Nicholas Rudzianski, BS, a CanCORS project manager for the invaluable support he provided to complete this work.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA: a cancer journal for clinicians*. 2012; 62:10–29. [PubMed: 22237781]
2. Schiller JH, Harrington D, Belani CP, et al. Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. *N Engl J Med*. 2002; 346:92–98. [PubMed: 11784875]
3. Braunholtz DA, Edwards SJ, Lilford RJ. Are randomized clinical trials good for us (in the short term)? Evidence for a “trial effect”. *J Clin Epidemiol*. 2001; 54:217–224. [PubMed: 11223318]
4. Feuer EJ, Frey CM, Brawley OW, et al. After a treatment breakthrough: a comparison of trial and population-based data for advanced testicular cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 1994; 12:368–377. [PubMed: 7509384]
5. Roy P, Vaughan Hudson G, Vaughan Hudson B, et al. Long-term survival in Hodgkin's disease patients. A comparison of relative survival in patients in trials and those recorded in population-based cancer registries. *European journal of cancer*. 2000; 36:384–389. [PubMed: 10708941]
6. Sorbye H, Pfeiffer P, Cavalli Björkman N, et al. Clinical trial enrollment, patient characteristics, and survival differences in prospectively registered metastatic colorectal cancer patients. *Cancer*. 2009; 115:4679–4687. [PubMed: 19562777]
7. Robinson WR, Ritter J, Rogers AS, et al. Clinical trial participation is associated with improved outcome in women with ovarian cancer. *International Journal of Gynecological Cancer*. 2009; 19:124–128. [PubMed: 19258953]

8. 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*. 1999; 10:809–815. [PubMed: 10470428]
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; 56:1710–1718. [PubMed: 3896460]
10. Schea RA, Perkins P, Allen PK, et al. Limited-stage small-cell lung cancer: patient survival after combined chemotherapy and radiation therapy with and without treatment protocols. *Radiology*. 1995; 197:859–862. [PubMed: 7480770]
11. Quoix E, Finkelstein H, Wolkove N, et al. Treatment of small-cell lung cancer on protocol: potential bias of results. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 1986; 4:1314–1320. [PubMed: 3018183]
12. Klabunde CN, Keating NL, Potosky AL, et al. A population-based assessment of specialty physician involvement in cancer clinical trials. *J Natl Cancer Inst*. 2011; 103:384–397. [PubMed: 21317382]
13. 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; 20:2109–2117. [PubMed: 11956272]
14. Catalano PJ, Ayanian JZ, Weeks JC, et al. Representativeness of Participants in the Cancer Care Outcomes Research and Surveillance Consortium Relative to the Surveillance, Epidemiology, and End Results Program. *Med Care*. 2012 [Ahead of print].
15. Piccirillo J, Costas I, Claybour P, et al. The measurement of comorbidity by cancer registries. *J Registry Manage*. 2003; 30:8–14.
16. Peppercorn JM, Weeks JC, Cook EF, et al. Comparison of outcomes in cancer patients treated within and outside clinical trials: Conceptual framework and structured review. *Lancet*. 2004; 363:263–270. [PubMed: 14751698]
17. Hotta K, Fujiwara Y, Matsuo K, et al. Recent improvement in the survival of patients with advanced nonsmall cell lung cancer enrolled in phase III trials of first-line, systemic chemotherapy. *Cancer*. 2007; 109:939–948. [PubMed: 17285602]
18. Sperduto PW, Kased N, Roberge D, et al. Summary report on the graded prognostic assessment: an accurate and facile diagnosis-specific tool to estimate survival for patients with brain metastases. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2012; 30:419–425. [PubMed: 22203767]
19. Rosell R, Carcereny E, Gervais R, et al. Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial. *Lancet Oncol*. 2012; 13:239–246. [PubMed: 22285168]
20. Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. *N Engl J Med*. 2010; 363:1693–1703. [PubMed: 20979469]
21. Stiller CA. Centralised treatment, entry to trials and survival. *Br J Cancer*. 1994; 70:352–62. [PubMed: 8054285]
22. Wright JR, Whelan TJ, Schiff S, et al. Why cancer patients enter randomized clinical trials: exploring the factors that influence their decision. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2004; 22:4312–4318. [PubMed: 15514372]
23. Daugherty C, Ratain MJ, Grochowski E, et al. Perceptions of cancer patients and their physicians involved in phase I trials. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 1995; 13:1062–1072. [PubMed: 7738612]
24. Henderson GE, Churchill LR, Davis AM, et al. Clinical trials and medical care: defining the therapeutic misconception. *PLoS Med*. 2007; 4:e324. [PubMed: 18044980]
25. Lidz CW, Appelbaum PS. The therapeutic misconception: problems and solutions. *Med Care*. 2002; 40:V55–63. [PubMed: 12226586]
26. Joffe S, Weeks JC. Views of American oncologists about the purposes of clinical trials. *J Natl Cancer Inst*. 2002; 94:1847–1853. [PubMed: 12488478]

27. Appelbaum PS. Clarifying the ethics of clinical research: a path toward avoiding the therapeutic misconception. *Am J Bioeth.* 2002; 2:22–23. [PubMed: 12189066]
28. Arkin LM, Sondhi D, Worgall S, et al. Confronting the issues of therapeutic misconception, enrollment decisions, and personal motives in genetic medicine-based clinical research studies for fatal disorders. *Hum Gene Ther.* 2005; 16:1028–1036. [PubMed: 16149901]

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Figure 1. Survival analysis for stage IIIB and IV NSCLC patients receiving cancer care within vs. outside a clinical trial. Median overall survival after diagnosis of NSCLC was 20.5 vs 16.7 months, respectively (Log Rank Test: $P=0.21$).

Table 1

Stage IIIB and IV NSCLC patient demographics and clinical characteristics

Variable	In clinical trial		Not in clinical trial		p-value
	(N = 56)		(N = 759)		
	N	%	N	%	
Gender					0.88
Female	25	45	331	44	
Male	31	55	428	56	
Age					0.21
<= 64	31	55	358	47	
65-74	18	32	231	30	
>= 75	7	13	170	22	
Ethnicity					0.37 [†]
White	38	68	543	72	
Hispanic	4	7	40	5	
African-American	5	9	97	13	
Asian	5	9	31	4	
Other	4	7	48	6	
Marital Status					0.46 [†]
Married	37	66	418	55	
Living With Partner	4	7	33	4	
Widowed	7	13	123	16	
Divorced	5	9	131	17	
Separated	1	2	17	2	
Never Married	2	4	33	4	
Don't know	0	0	1	<1	
Missing	0	0	3	<1	
Region of the country					0.17
Northeast	2	4	6	<1	
Midwest	14	25	154	20	
South	11	20	164	22	
West	29	52	435	57	
Health Insurance					0.20
Yes	53	95	677	89	
No	3	5	82	11	
Income (\$)					0.02
<20,000	7	13	212	28	
20,000-<40,000	19	34	204	27	
40,000-<60,000	6	11	121	16	

Variable	In clinical trial		Not in clinical trial		p-value
	(N = 56)		(N = 759)		
	N	%	N	%	
>=60,000	16	29	139	18	
Missing	8	14	83	11	
Education Level					0.08
Did Not Finish High School	7	13	135	18	
High School Diploma	19	34	241	32	
Some College	12	21	223	29	
College Degree	7	13	83	11	
Grad or Professional School	11	20	68	9	
Missing	0	0	9	1	
Speaks English at home					0.35 [†]
Yes	53	95	730	96	
No	3	5	22	3	
Not applicable	0	0	2	<1	
Missing	0	0	5	<1	
PDCR site					0.44
Cancer Research Network	5	9	114	15	
VA Hospital	7	13	97	13	
Other	44	79	548	72	
Comorbidity score at diagnosis					0.58
None	9	16	150	20	
Mild	17	30	244	32	
Moderate	8	14	116	15	
Severe	4	7	122	16	
Missing	18	32	127	17	
Recalled Performance Status					0.17
Not limited at all	28	50	302	40	
Limited a lot/Limited a little	28	50	442	58	
Missing	0	0	15	2	
Brain Metastasis					
Present	0	0	64	8	0.02 [†]
Absent	56	100	695	92	
Stage					0.56
IIIB	18	32	273	36	
IV	38	68	486	64	
Histology					0.81
Adenocarcinoma	14	25	221	29	
Other	24	43	411	54	

Variable	In clinical trial		Not in clinical trial		p-value
	(N = 56)		(N = 759)		
	N	%	N	%	
Missing	18	32	127	17	

[†]Fisher's Exact Test

Table 2

Cox Proportional Hazard model of overall survival for stage IIIB and IV NSCLC patients. N = 603

Effect	Hazard Ratios (95% CL)	Parameter Estimates (s.e)	Wald Chi-Square (df)	value
Enrolled in Clinical Trial–Yes	1.05 (0.71, 1.55)	0.05 (0.20)	0.06 (1)	0.81
Age			2.53 (2)	0.28
<=64	1			
65-74	0.99 (0.80, 1.23)	−0.01 (0.11)	0.01 (1)	0.94
>=75	1.18 (0.94, 1.50)	0.17 (0.12)	1.96 (1)	0.16
Income (\$)			4.05 (3)	0.26
<20,000	1			
20,000-<40,000	0.93 (0.75, 1.16)	−0.07 (0.11)	0.39 (1)	0.53
40,000-<60,000	0.88 (0.68, 1.15)	−0.12 (0.13)	0.85 (1)	0.36
>=60,000	0.75 (0.56, 1.00)	−0.29 (0.15)	3.92 (1)	0.05
PDCR site			3.10 (2)	0.21
Cancer Research Network	1			
VA Hospital	1.29 (0.92, 1.80)	0.25 (0.17)	2.19 (1)	0.14
Other	1.25 (0.97, 1.63)	0.23 (0.13)	2.91 (1)	0.09
Comorbidity score at diagnosis			12.38 (3)	<0.01
None	1			
Mild	1.03 (0.82, 1.31)	0.03 (0.12)	0.07 (1)	0.79
Moderate	1.12 (0.85, 1.47)	0.11 (0.14)	0.62 (1)	0.43
Severe	1.54 (1.17, 2.02)	0.43 (0.14)	9.44 (1)	<0.01
Recalled Performance Status			0.36 (1)	0.55
Not limited	0.94 (0.78, 1.14)	−0.06 (0.10)	0.36 (1)	0.55
Limited a lot/a little	1			
Brain Metastasis			0.62 (1)	0.43
Absent	1			
Present	1.14 (0.82, 1.57)	0.13 (0.16)	0.62 (1)	0.43
Stage			16.34 (1)	<0.01
IIIB	1			
IV	1.49 (1.23, 1.81)	0.40 (0.10)	16.34 (1)	<0.01
Histology			0.36 (1)	0.55
Adenocarcinoma	0.94 (0.78, 1.14)	−0.06 (0.10)	0.36 (1)	0.55
Others	1			

Table 3

Symptom management, hospice care, and revival status characteristics of stage IIIB and IV NSCLC patients

Variable	In clinical trial		Not in clinical trial		p-value
	(N = 56)		(N = 746)		
	N	%	N	%	
Received wanted help for symptom					
Pain					0.93 [†]
Yes	19	34	267	36	
No	1	2	21	3	
Not Applicable	36	64	457	61	
Don't Know	0	0	1	<1	
Low Energy					0.54
Yes	13	23	193	26	
No	8	14	66	9	
Not Applicable	34	61	479	64	
Don't Know	1	2	8	1	
Mood					0.68 [†]
Yes	10	18	130	17	
No	3	5	26	3	
Not Applicable	43	77	588	79	
Refused	0	0	2	<1	
Nausea and/or Vomiting					0.98
Yes	14	25	190	25	
No	1	2	11	1	
Not Applicable	41	73	545	73	
Cough					0.14 [†]
Yes	11	20	209	28	
No	0	0	35	5	
Not Applicable	45	80	501	67	
Don't Know	0	0	1	<1	
Breathing					0.21 [†]
Yes	14	25	239	32	
No	2	4	33	4	
Not Applicable	39	70	472	63	
Don't Know	1	2	2	<1	
Hospice was discussed					0.18 [†]
Yes	6	11	132	18	
No	49	88	606	81	

Variable	In clinical trial		Not in clinical trial		p-value
	(N = 56)		(N = 746)		
	N	%	N	%	
Don't Know	0	0	6	<1	
Not applicable	1	2	1	<1	
Refused	0	0	1	<1	
Received hospice care					0.79 [†]
Yes	1	2	21	3	
No	2	4	19	3	
Not applicable	53	95	706	95	
Discussed revival or use of life-sustaining machines					0.31 [†]
Yes	18	32	258	35	
No	37	66	472	63	
Refused	0	0	6	<1	
Don't Know	0	0	8	1	
Not Applicable	1	2	1	<1	
Missing	0		1		

[†] Fisher's Exact Test

Table 4

End of life care characteristics for stage IIIB and IV NSCLC patients (from follow up surveys)

Variable	In clinical trial		Not in clinical trial		p-value
	(N = 39)		(N = 551)		
	N	%	N	%	
Location of patient death					0.33 [†]
Hospital	8	21	63	11	
Nursing Home	0	0	8	1	
Hospice In Patient Unit	1	3	19	3	
Home	3	8	91	17	
Someplace Else	1	3	8	1	
Not Applicable	26	67	362	66	
Patients' wishes followed during last month of life					0.87 [†]
A great deal	11	28	122	22	
Somewhat	1	3	27	5	
Not at all	0	0	8	1	
Refused	0	0	1	<1	
Don't Know	0	0	3	<1	
Not Applicable	27	69	390	71	
Time spent in place of death before death					0.78 [†]
< 48 hours	1	3	28	5	
48 hours - 1 week	2	5	49	9	
> 1 week	10	26	111	20	
Don't Know	0	0	1	<1	
Not Applicable	26	67	362	66	

[†] Fisher's Exact Test

Table 5

Perceived quality of care by stage IIIB and IV NSCLC patients or their surrogate respondent (from follow up surveys)

“Would you say that you received medical care that was better than, about the same, or worse than other patients?”	In clinical trial		Not in clinical trial		p-value
	(N = 56)		(N = 759)		
	N	%	N	%	<0.01 [†]
Better than	17	30	106	14	
About the same	16	29	245	32	
Worse than	0	0	17	2	
Refused	0	0	3	<1	
Don't Know	5	9	179	24	
Not Applicable	1	2	1	<1	
Missing	17	30	208	27	

[†] Fisher's Exact Test