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#### Research paper

## Clinical outcomes of black vs. non-black patients with locally advanced non-small cell lung cancer



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#### ABSTRACT

*Objectives*: The black population remains underrepresented in clinical trials despite reports suggesting greater incidence and deaths from locally advanced non-small cell lung cancer (NSCLC). We determined outcomes for black and non-black patients in a well-annotated cohort treated with either definitive chemoradiation (CRT; bimodality) or CRT followed by surgery (trimodality therapy).

Materials and Methods: A retrospective analysis of 355 stage III NSCLC patients treated with curative intent at the University of Maryland, Medical Center, between January 2000-December 2013 was performed. The Kaplan–Meier approach and the Cox proportional hazards models were used to analyze overall survival (OS) and freedom-from-recurrence (FFR) in black and non-black patients. The chi-square test was used to compare categorical variables.

Results: Black patients comprised 42% of the cohort and were more likely to be younger (p < 0.0001), male (p = 0.030), single (p < 0.0001), reside in lower household income zipcodes (p < 0.0001), have an Eastern Cooperative Oncology Group (ECOG) performance status > 0 (p < 0.001), and less likely to undergo surgery (p < 0.0001). With a median follow-up of 15 months for all patients and 89 months for surviving patients (range:1–186 months), median OS times for black and non-black patients were 22 and 24 months, respectively (p = 0.698). FFR rates were also comparable between the two groups (p = 0.468). Surgery improved OS in both cohorts. Race was not a significant predictor for OS or FFR even when adjusted for other factors.

Conclusions: We found similar oncologic outcomes in black and non-black NSCLC patients when treated with curative intent in a comprehensive cancer center setting, despite epidemiologic differences in presentation and receipt of care. Future efforts to improve outcomes in black patients could focus on addressing modifiable social disparities.

#### 1. Introduction

Lung cancer remains the leading cause of cancer death in the United States (US) and worldwide [1]. Non-small cell lung cancer (NSCLC) accounts for 80% of the lung cancer diagnoses in the US and a quarter of patients present with locally advanced disease [2]. The non-Hispanic black population comprises about 12% of the US population, and while

black patients experience a higher incidence and mortality rate of lung cancer [3], they remain underrepresented in prospective randomized clinical trials [4–6]. In 1993, the National Institutes of Health (NIH) Revitalization Act prioritized the inclusion of women and minorities in NIH-funded clinical research. Although this policy has improved recruitment of women with NSCLC into clinical trials, a significant enrollment disparity has remained for minorities [4,5].

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Patients with stage III NSCLC are typically treated with a combination of platinum-based chemotherapy with concurrent radiation [7,8] with or without surgical resection [9]. The modern trials that have guided our treatment paradigms for locally advanced NSCLC (LA-NSCLC) have included < 15% black/African-American participants thereby giving very little information about racial outcome differences [8–11]. Furthermore, there are scant data in the literature describing outcomes using modern treatment paradigms specifically for stage III NSCLC in the black population, although some institutional studies suggest poorer survival for black patients [12]. Complex socio-economic, environmental, and possibly biologic factors may account for differences in survival [13.14]. While, large population-based databases may provide national trends involving access to care and general outcomes for the black population, they lack information on various disease and treatment-specific details to analyze outcomes that might be achieved in a standardized setting. Therefore, large-institutional analysis with a predominant black population are needed, wherein such data could be analyzed in the backdrop of pursuing uniform, guidelinesdriven, standard-of-care treatment paradigms. The overall objective of this report is to report oncological outcomes; overall survival (OS) and freedom-from-recurrence (FFR) in black patients with LA-NSCLC treated with curative intent from 2000 to 2013. In the setting of a National Cancer Institute (NCI)-designated cancer center with a large black patient population, a detailed multivariate analysis of patient, disease and treatment-specific factors is performed to compare outcomes in comparison to non-black patients similarly treated during the same time period.

#### 2. Material and methods

From January 2000 to December 2013, 355 patients with American Joint Committee on Cancer (AJCC) 7th edition clinical stage III NSCLC were treated at our center. Two previous AJCC staging editions (5th and 6th) were used during this time period; however, all patients were re-assigned a clinical stage according to the 7th edition staging for this analysis. Clinical data were retrospectively analyzed under institutional review board approval. Patient's race was self-reported in our electronic medical records system and we divided the cohorts as "non-Hispanic black" (referred to as 'black' in rest of the manuscript) and "non-black," predominantly white, patients (96.6% white, 1% Latino, 1.5% Asian, 0.9% other). All patients were treated with curative intent with chemotherapy and radiation (overall median dose, 64.8 Gy; range, 10.8-81.6 Gy), primarily delivered concurrently (Table 1) with or without surgical resection. Concurrent chemoradiation was generally administered with weekly carboplatin/paclitaxel (area under the curve [AUCs] of 2 and 50 mg/m<sup>2</sup>, respectively) and was typically followed with two cycles of consolidative treatment with definitive doses of carboplatin/paclitaxel (AUCs of 5-6 and 200-225 mg/m<sup>2</sup>, respectively).

The study covers a span of 13 years, where general treatment paradigms shifted from sequential CRT to concurrent, decrease utilization of elective nodal irradiation and greater use of intensity-modulated radiation therapy (IMRT) over 3D-conformal radiation therapy (3D-CRT) as well as 4D CT scans, the latter three being more common in our institution after 2009. For follow up, patients were typically monitored with serial CT or PET/CT scans as clinically indicated every three months for the first year, 4–6 months for the next 2–5 years, then yearly thereafter with both medical and radiation oncologists.

The Pearson's chi-square test was used to compare categorical variables. OS was calculated from the date of diagnosis (confirmatory biopsy of primary or mediastinal nodes) to the time of death or date of last follow-up. Patients were only censored if they were lost to follow-up. FFR was determined by the date of diagnosis to the time of first failure, either distant or local/regional disease progression and patients were censored at the time of their last follow-up or death. Progression-free-survival (PFS) was analyzed by the date of diagnosis to the time of

Table 1 Baseline patient and treatment characteristics between cohorts (N = 355).

Characteristic	Black (N = 150) No. (%)	Non-Black (N = 205) No. (%)	p-value
Age (years)			
Median/Range	57(30-81)	63 (36–86)	< 0.0001
< 60	87 (58.0)	80 (39.0)	1 0.0001
≥60	61 (40.7)	125 (61.0)	
Missing	2 (1.3)	0 (0)	
Gender			
Male	96 (64.0)	107 (52.2)	0.030
Female	54 (36.0)	98 (47.8)	0.030
Marital Status			
Married	E2 (2E 2)	122 (64.4)	< 0.0001
Single	53 (35.3) 97 (64.7)	132 (64.4) 73 (35.6)	< 0.0001
_	37 (04.7)	75 (55.0)	
Median Income <sup>b</sup>	00 (00 6)	400 (40 <b>=</b> )	
≥\$43, 723	33 (22.6)	139 (68.5)	< 0.0001
Insurance Status			
Yes	118 (78.7)	180 (87.8)	0.021
No	26 (17.3)	18 (8.8)	
Missing	6 (4.0)	7 (3.4)	
ECOG PS			
0	54 (36.0)	111 (54.1)	0.001
≥1	95 (63.3)	91 (44.4)	
Missing	1 (0.67)	3 (1.5)	
Charlson Score			
≤6	88 (58.7)	101 (49.3)	0.088
> 7	62 (41.3)	103 (50.2)	
Missing	0 (0)	1 (0.5)	
Diagnosis of COPD			
No	114 (76.0)	136 (66.3)	0.031
Yes	33 (22.0)	67 (32.7)	0.001
Missing	3 (2.0)	2 (1.0)	
-			
Smoking (pack-years Median/Range	35/0-160	40/0-212	0.006
Histology			
Adenocarcinoma	53 (35.3)	60 (29.3)	0.345
Squamous Cell	37 (24.5)	67 (32.7)	
NSCLC (NOS)	50 (33.3)	62 (30.2)	
Other	10 (6.7)	16 (7.8)	
T stage <sup>c</sup>			. =
TX	7 (4.7)	11 (5.4)	0.740
≤T2 ≥ T3	65 (43.6) 77 (51.7)	96 (46.8) 97 (47.5)	
	// (31./)	97 (47.3)	
N stage <sup>c</sup>			
NX	1 (0.7)	2 (1.0)	0.853
≤ N1	24 (16.1)	32 (15.7)	
N2 N3	95 (63.8) 29 (19.5)	123 (60.3) 47 (23.0)	
113	29 (19.3)	47 (23.0)	
Stage	05 (5( 5)	115 (56.1)	0.015
IIIA	85 (56.7)	115 (56.1)	0.915
IIIB	65 (43.3)	90 (43.9)	
Γrimodality vs. Bimα	odality		
Trimodality	23 (15.3)	65 (31.7)	< 0.0001
Bimodality	127 (84.7)	140 (68.3)	
Surgery Type			
Lobectomy	20 (87.0)	56 (86.2)	0.923
Pneumonectomy	3 (13.0)	9 (13.8)	
Type of chemoradiat	ion		
Concurrent	136 (90.7)	191 (93.2)	0.387
Sequential	14 (9.3)	14 (6.8)	
Radiation Dose preso Median/Range		66/45–79	0.022
_		30, 10 / 3	0.022
Radiation Dose deliv Median/Range	ered (Gy) <sup>d</sup> 61.6/31–81.6	64.8/10.8-70.2	0.042
Radiation Technique			
3D-CRT	99 (66)	136 (66.3)	0.908

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