Palliative systemic therapy for advanced non-small cell lung cancer: Investigating disparities between patients who are treated versus those who are not

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ABSTRACT

Background: Palliative systemic therapy (ST) in advanced non-small cell lung cancer (NSCLC) is associated with improved overall survival (OS) and quality of life, yet many patients remain untreated. We explored differences between patients who did and did not receive palliative ST in order to gain evidence to support and advocate for the untreated.

Methods: We performed a retrospective analysis of newly diagnosed patients with advanced, incurable NSCLC seen as outpatients at our institution between 2009 and 2012. Demographics, treatment, and survival data were collected.

Results: 528 patients were seen: 291 (55%) received palliative ST, while 237 (45%) received none. Demographics were as follows: Median age 67, 55% male, 50% ECOG performance status (PS) 0–1, 48% with weight loss. Untreated patients were older (median 71 vs. 64, p < 0.01), less fit (PS 0–1 in 27% vs. 69%, p < 0.01), and more likely to have lost weight (57% vs. 41%, p < 0.01). Reasons for no treatment included poor PS (67%) and patient choice (23%). Median OS was shorter amongst untreated patients (3.9 vs. 10.7 months, HR 1.80 [95% CI 1.4–2.3], p < 0.01). In multivariate analysis, not receiving ST was associated with shorter OS.

Conclusion: Unsurprisingly, untreated patients had poorer prognostic features and worse OS. However, it is concerning that, despite being seen in an active academic center, nearly half of all referred patients with advanced NSCLC received no anti-cancer treatment. Current research primarily seeks to improve outcomes in treated patients with good PS. This review suggests that this is an inappropriate allocation of research effort. Our research should be more equitably split between good and poor performance patient groups if we are to improve the survival of all patients with advanced NSCLC. Potential strategies include more rapid diagnosis prior to functional decline, and the development of therapies effective and tolerated in a sicker population.

1. Background

Lung cancer is the leading cause of cancer-related death in North America and worldwide [1]. As evidence of the grave nature of this diagnosis, the five year overall survival for all patients diagnosed with any stage of non-small cell lung cancer (NSCLC) is only 17% [2]. Over the past three decades, and particularly in the last few years, there has been significant progress in the treatment of advanced NSCLC, with the advent of newer chemotherapeutic agents, targeted therapy, and immunotherapy [3]. Numerous phase III clinical trials have demonstrated that palliative systemic therapy for advanced NSCLC can be associated with improved outcomes, including longer survival [4–14] and better quality of life [15–17]. Despite this, retrospective analyses have demonstrated that only a fraction of patients diagnosed with advanced NSCLC receive any form of systemic therapy [18–20].

In an effort to understand the disparities between patients who do and do not receive palliative systemic therapy, as well as reasons for their treatment decisions, we undertook a retrospective analysis of all patients seen in outpatient consultation at our academic institution for advanced NSCLC. The proportion of patients who were untreated and the reasons for their lack of treatment

Table 1
Baseline patient characteristics.

	Untreated Patients N (%)	Treated PatientsN (%)	P value
Number of patients	237 (44.9)	291 (55.1)	
Age at diagnosis (years)			<0.01
median (range)	71 (43.6–89.7)	64.8 (34.9–86.7)	
Gender n (%)			0.87
male	132 (55.7)	160 (55.0)	
female	105 (44.3)	131 (45.0)	
Performance status			<0.01
0	10 (4.2)	36 (12.4)	
1	55 (23.2)	165 (56.7)	
2	57 (24.1)	54 (18.6)	
3	79 (33.3)	13 (4.5)	
4	18 (7.6)	1 (0.3)	
unknown	18 (7.6)	22 (7.6)	
Smoking			0.03
Current	108 (45.6)	120 (41.2)	
Ex-smoker	116 (49.0)	141 (48.5)	
Never smoker	9 (3.8)	28 (9.6)	
Unknown	4 (1.7)	2 (0.7)	
Weight loss (% of body weight)			<0.01
<5%	82 (34.6)	153 (52.6)	
>5%	135 (57.0)	120 (41.2)	
Unknown	20 (8.4)	18 (6.2)	
Creatinine (umol/L)			0.03
<120	203 (85.7)	273 (93.8)	
>=120	24 (10.1)	16 (5.5)	
Unknown	10 (4.2)	2 (0.7)	
Mode of referral			<0.01
Cancer assessment clinic	88 (37.1)	130 (44.7)	
Inpatient at other hospital	10 (4.2)	0 (0)	
Other out-patient	137 (57.8)	159 (54.6)	
Other medical oncologist	2 (0.8)	2 (0.7)	
Interval between symptoms and diagnosis			0.31
<2 weeks	10 (4.2)	18 (6.2)	
2–6 weeks	36 (15.2)	31 (10.6)	
6 weeks–6 months	126 (53.2)	140 (48.1)	
>6 months	47 (19.8)	64 (22.0)	
Unknown	18 (7.6)	38 (13.1)	
Histological subtype			0.03
Adenocarcinoma	125 (52.7)	183 (62.9)	
Large cell	10 (4.2)	17 (5.8)	
Mixed	1 (0.4)	0(0)	
Other NSCLC	17 (7.2)	12 (4.1)	
Squamous cell	63 (26.6)	55 (18.9)	
Unknown	21 (8.9)	24 (8.3)	
Stage			0.03
IIIB	22 (9.3)	13 (4.5)	
IV	215 (90.7)	278 (95.5)	

were investigated. Ultimately, with a better understanding of this phenomenon, we can begin to study and introduce supportive and treatment strategies that impact survival in the untreated, including those patients with a poor performance status.

2. Methods

2.1. Patient data

With ethics approval, we undertook a chart review of all patients seen in consultation in the outpatient setting for advanced, incurable NSCLC at The Ottawa Hospital Cancer Centre between 2009 and 2012. The Ottawa Hospital Cancer Centre, an academic centre in Canada's capital city, is the sole provider of medical and radiation oncology to a population of approximately 1.5 million in Eastern Ontario. At our cancer centre, there are several modes of referral to an oncologist: directly via a physician who has completed the diagnostic process, or via the Cancer Assessment Clinic, which organizes a rapid work-up of a suspected malignancy. Patient demographics,

disease characteristics, treatment details, and survival data were collected from hospital and pharmacy records. Patients included in the analysis were seen in consultation in the outpatient setting for a new diagnosis of confirmed stage IIIB (palliative) or stage IV NSCLC. Patients whose initial medical oncology consultation was performed as an in-patient at our institution, and patients who had relapsed following prior curative-intent therapy, were excluded.

2.2. Statistical methods

A retrospective analysis was performed. Descriptive analyses of treated versus untreated patients were undertaken with a goal of identifying underlying differences that could result in treatment disparities. Primary reasons for not receiving systemic therapy were also identified. Age at diagnosis was reported as median and range. Wilcoxon two-sample test was used to compare age at diagnosis between the groups. The other patient baseline characteristics were reported using frequency and percentage by group. Chi-square test or Fisher's exact test were applied where appropriate.