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Cost effectiveness of first-line pemetrexed plus platinum compared with other regimens in the treatment of patients with nonsquamous non-small cell lung cancer in the US outpatient setting☆,☆☆

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ABSTRACT

This retrospective observational study evaluated cost effectiveness of first-line treatment of advanced nonsquamous non-small cell lung cancer (NSCLC) with pemetrexed/platinum (Pem/Plat) relative to paclitaxel/carboplatin (Pac/Carbo) and paclitaxel/carboplatin/bevacizumab (Pac/Carbo/Bev). Patients initiating first-line treatment from 2006 to 2009 were identified in electronic medical records of 20 US oncology practices. Pem/Plat patients were matched 1:1 on important characteristics with Pac/Carbo and Pac/Carbo/Bev patients and followed for 1 year to assess progression, survival, and costs. Bootstrapping was used to calculate the probability of falling within quadrants of the incremental cost-effectiveness plane. Kaplan–Meier analysis and Cox proportional hazards regression modeling were also performed. Three hundred Pem/Plat patients (mean age, 67.6 years; male, 56.0%; PS 0/1, 71.0%) were matched with 300 patients in the other cohorts. Median PFS was 134 days (Pem/Plat) versus 106 days (Pac/Carbo) (hazard ratio [HR]: 0.67, $P < 0.001$) and 126 days (Pac/Carbo/Bev) (HR: 0.68, $P < 0.001$). Median OS was 298 days (Pem/Plat) versus 218 days (Pac/Carbo) (HR: 0.88, $P = 0.08$) and 271 days (Pac/Carbo/Bev) (HR: 0.93, $P = 0.31$). Pem/Plat therapy costs were higher versus Pac/Carbo ($21,841 higher PFS; $19,137 higher OS; $P \leq 0.05$) and lower versus Pac/Carbo/Bev ($15,160 lower PFS; $19,946 lower OS; $P \leq 0.05$). Pem/Plat had a greater probability of higher costs/higher effectiveness versus Pac/Carbo (PFS, 90.1%; OS, 96.3%) and lower costs/higher effectiveness versus Pac/Carbo/Bev (PFS, 69.5%; OS, 85.0%). Pem/Plat had higher cost and effectiveness than Pac/Carbo; depending on a payer's or society's willingness to pay, Pem/Plat may be considered cost effective compared with Pac/Carbo. Pem/Plat yielded greater effectiveness with lower costs than Pac/Carbo/Bev.

1. Introduction

Lung cancer is the second most commonly diagnosed cancer among both men and women in the United States (US) and is the leading cause of cancer deaths in both genders [1]. Non-small cell lung cancer (NSCLC) constitutes 80–85% of all lung cancers [2]. An estimated 78% of NSCLCs are detected as advanced (regional or distant) disease according to the US National Cancer Institute Surveillance and Epidemiology and End Results (NCI SEER) staging distribution data for 2002–2008 [3]. Among patients with advanced disease (stage IIIB/IV), prognosis remains poor, with 5-year survival estimated at 15.9% [3].

For patients with advanced (stage IIIB/IV) NSCLC, clinical guidelines recommend the use of 2-drug combination regimens as first-line therapy [4,5]. First-line treatment is often a combination therapy using platinum plus taxane-based chemotherapeutic agents with or without biologics or platinum plus targeted small-molecule therapy. Recent evidence from various phase III clinical trials has demonstrated the efficacy of specific combination treatments like pemetrexed/cisplatin (Pem/Cis) and paclitaxel/carboplatin/bevacizumab (Pac/Carbo/Bev) in the first-line setting for patients with advanced nonsquamous NSCLC [6,7]. Despite lack of data from phase III trials directly comparing

☆ Some of the study results (pemetrexed-platinum data) were presented at the 24th annual meeting of the Academy of Managed Care Pharmacy, San Francisco, CA, USA; April 18–20, 2012. The pemetrexed-cisplatin subgroup results were presented at the 37th Congress of the European Society for Medical Oncology, Vienna, Austria; September 28–October 2, 2012.

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clinical outcomes associated with Pem/Cis with Pac/Carbo and Pac/Carbo/Bev, these three regimens are frequently used in clinical practice as first-line treatment. Additionally, to our knowledge, few studies have used real-world data to compare the clinical and economic outcomes associated with these treatment strategies.

The primary objective of this retrospective observational study was to examine the real-world incremental cost effectiveness of a first-line chemotherapy regimen with pemetrexed plus platinum (Pem/Plat therapy) combination relative to the Pac/Carbo combination (doublet) and the Pac/Carbo/Bev combination (triplet) in patients with advanced nonsquamous NSCLC in the US outpatient medical oncology setting.

2. Patients and methods

2.1. Data source

This retrospective cohort study used data captured within the International Oncology Network (ION) clinical oncology database from January 2006 through December 2010. This electronic medical records (EMR) database captures outpatient-practice encounter history for patients under care of 175 geographically dispersed providers, representing 20 large, community-based practices across 13 states. The database includes laboratory results, diagnosis, disease profile, anthropomorphic measures, vital signs, treatment plan, specific therapy administrations associated with treatment plans, other medications such as supportive care agents, and performance status. The data elements described above are typically captured through either standardized fields or electronic progress notes. For purposes of this study, electronic progress notes were reviewed to abstract and/or verify information on necessary clinical and demographic characteristics, including advanced disease status, histology, and other inclusion criteria.

In addition to clinical EMR data, practice management system (PMS) data are incorporated within the EMR database; these data include patient demographics, treatment given, diagnosis information, dates, and billed transactions from the outpatient medical oncology setting. Utilization outside of this setting (e.g., hospitalizations and emergency department visits) is not captured. The Social Security Death Index (Social Security Administration's [SSA] Master Death File) was used to supplement documented vital status [8]. All data access, use, and reporting were conducted in a manner compliant with the Health Insurance Portability and Accountability Act, ensuring that confidentiality and privacy of patients were maintained. In addition, the use of patient data for this study was approved by an independent, central institutional review board.

2.2. Patient selection

The target population was patients with advanced nonsquamous NSCLC who initiated first-line treatment between January 2006 and December 2009 (i.e., study enrollment period). To be eligible for analysis, patients were required to meet the following criteria: (1) be at least 18 years of age, (2) have at least one International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code for lung cancer (162.2, 162.3, 162.4, 162.5, 162.8, 162.9, 197.0, or 231.2) along with documented advanced disease (stage IIIB/IV or early stage with evidence of progression to advanced disease), and (3) initiate first-line chemotherapy with or without targeted therapy (i.e., Pem/Plat, Pac/Carbo, or Pac/Carbo/Bev after documentation of advanced disease). The date of first-line treatment was defined as the index date. Patients were excluded based on the following criteria: (1) receiving care for another primary cancer during the study period, (2) squamous cell histology, (3) enrollment in clinical trials during the study period, (4) follow-up time of less than 1 year and no evidence of disease progression/death.

Table 1
Variables used to match cohorts.

Variable	Number of strata	Description
Index year	4	2006, 2007, 2008, 2009
AJCC stage	5	Stage I with subsequent progression to advanced disease Stage II with subsequent progression to advanced disease Stage IIIA with subsequent progression to advanced disease Diagnosed advanced stage IIIB Diagnosed advanced stage IV
Gender	2	Male Female
Performance status	3	ECOG 0 ECOG 1 ECOG 2+
Age, years	6	<40 40–49 50–59 60–69 70–79 80+

Abbreviations: AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group.

Eligible patients were placed into the following cohorts based on first-line treatment initiation: (1) Pem/Plat, (2) Pac/Carbo doublet, or (3) Pac/Carbo/Bev triplet. To mitigate any potential bias due to differences in patient characteristics, a matching strategy was employed. Patients in each cohort were placed into specific strata based on five key variables listed in Table 1. Within each strata (e.g., index year 2007, advanced stage IV, male, performance status score of 1, and age bracket 40–49), a Pem/Plat patient was randomly matched to one Pac/Carbo patient and one Pac/Carbo/Bev patient.

Table 2
Clinical and demographic characteristics of patients.

Variable	Pem/Plat $N = 300$		Pem/Cis $N = 78$	
	N	%	*N*	%
Platinum				
Carboplatin	222	74.0	0	0.0
Cisplatin	78	26.0	78	100.0
Age				
<40	4	1.3	2	2.6
40–49	21	7.0	6	7.7
50–59	66	22.0	17	21.8
60–69	101	33.7	26	33.3
70–79	91	30.3	23	29.5
80+	17	5.7	4	5.1
Gender				
Male	168	56.0	46	59.0
Female	132	44.0	32	41.0
Stage at diagnosis				
I	5	1.7	0	0.0
II	7	2.3	2	2.6
IIIA	10	3.3	3	3.8
IIIB	75	25.0	35	44.9
IV	203	67.7	38	48.7
Index ECOG PS[a]				
0	81	27.0	17	21.8
1	132	44.0	44	56.4
2	75	25.0	17	21.8
3	9	3.0	0	0.0
4	3	1.0	0	0.0

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; Pem/Cis, pemetrexed plus cisplatin; Pem/Plat, pemetrexed plus platinum.
[a] Index = date of first-line therapy initiation.