Original Study

Real-World Treatment Patterns, Overall Survival, and Occurrence and Costs of Adverse Events Associated With First-line Therapies for Medicare Patients 65 Years and Older With Advanced Non–small-cell Lung Cancer: A Retrospective Study

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Abstract

This SEER-Medicare database analysis (n = 5931) for first-line platinum-based therapy of stage IV NSCLC describes real-world treatment patterns (2007 to mid-2013) by histologic subtype, adverse events (AEs), and associated costs. Carboplatin-doublets were most commonly prescribed; dyspnea/anemia were the most common AEs; mean per-patient-per-month cost was $11,909. Our findings confirm and expand previous study results regarding the AE-related costs of therapy by treatment regimen.

Purpose: This study sought to better understand real-world treatment patterns, overall and non–small-cell lung cancer (NSCLC)-specific survival, adverse event (AE) occurrence, and economic impact of first-line cancer therapies in Medicare patients. **Patients and Methods:** This retrospective cohort study identified patients ≥ 65 years in the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database who received a first-time advanced (stage IV) NSCLC diagnosis from 2007 to 2011, and who received first-line platinum-based chemotherapy from 2007 through mid-2013. First-line regimens, healthcare resource use, occurrence of AEs, and associated costs (2013 US dollars) were analyzed. Median survival was determined using the Kaplan-Meier method. **Results:** Surprisingly, only 46% of patients (n = 13,472) with stage IIIB/IV NSCLC received systemic therapy, and 5931 received platinum-based therapy. The mean age was 73 years, with 3354 (57%) males; 1489 (25%) had squamous and 4442 (75%) nonsquamous histology. The most common regimens were carboplatin doublets (70%), including carboplatin/paclitaxel (38%), carboplatin/pemetrexed (12%), carboplatin/gemcitabine (11%), and carboplatin/docetaxel (7%). The median overall survival from first-line therapy initiation was 7.2 months (95% confidence interval, 7.0-7.5 months). Dyspnea and anemia were the most common AEs of interest, whereas atypical pneumonia was associated with the greatest AE-related costs (mean, $5044). The mean total per-patient-per-month cost was $11,909, with AE-related costs comprising 9% of total costs. The highest costs and survival were observed for patients treated with carboplatin/pemetrexed and bevacizumab/carboplatin/paclitaxel. **Conclusions:** These real-world data illustrate the most common first-line regimens by histology, overall survival, AEs, and some of the high AE-related costs of therapy for advanced NSCLC, and provides extremely useful information for clinicians.

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Introduction

Lung cancer is the leading cause of cancer mortality among men and women in the United States (US) and accounts for about 27% of all cancer deaths. A total of 222,500 new cases of lung cancer and 155,870 lung cancer deaths were estimated for 2017.[1] Non–small-cell lung cancer (NSCLC), which accounts for about 85% of lung cancer cases, is usually not detected until after regional or distant metastasis (stage IIIB or IV), in which 5-year survival rates diminish to 5% or less.[1,2]

Lung cancer treatment options have vastly increased in recent years, with an expanding arsenal of targeted therapies guided by molecular testing for predictive biomarkers, immunotherapies, and precision local therapies such as stereotactic radiation.[3-5] Before the approval of first-line immunotherapy, the standard of care in the US for nonsurgical management of advanced/metastatic NSCLC was platinum doublet chemotherapy as first-line therapy, with or without molecular targeted therapy, and with or without maintenance therapy.[6] Platinum agents (cisplatin and carboplatin) have proven effective in combination with several other agents. Randomized controlled trials (RCTs) and meta-analyses have shown that chemotherapy, particularly first-line treatment with platinum-based doublets, is associated with statistically significantly better overall survival (OS) compared with palliative treatment only.[6] First-line chemotherapy is associated with an overall response rate of 30% percent, 4 months of median progression-free survival (PFS), and a median OS of 8 to 11 months.[7,8]

Agents used to treat advanced NSCLC are associated with various adverse event (AE) profiles and toxicities, including hematologic, gastrointestinal, and pulmonary-related toxic effects, among others.[9] These AEs may lead to higher utilization of healthcare resources and expenditures and, in extreme cases, may lead to substantial disability or mortality.[6,10-15] Although several real-world studies have examined treatment patterns, OS, and AE-related costs associated with lung cancer, most studies focused on all types of lung cancers combined,[12,16-20] or concentrated on all stages of NSCLC collectively[21-23] or a histologic subtype of NSCLC (ie, squamous or nonsquamous) with little information on OS or AE-related costs.[10,11,13-15,24-26]

The direct medical costs for lung cancer have reached a staggering $12.1 billion and are expected to increase to $15.2 billion by 2020.[17,27] Understanding current real-world treatment patterns and healthcare resource utilization (HCRU) is important for understanding the state of therapy and the potential impact of newer therapies, in addition to defining unmet medical needs.[28]

The aims of this retrospective observational study were to simultaneously examine real-world treatment patterns, overall and NSCLC-specific survival, AE occurrence, and costs associated with first-line platinum-based chemotherapy in a US Surveillance, Epidemiology, and End Results (SEER)-Medicare population with newly diagnosed advanced (stage IV) NSCLC. This paper describes our findings in the first-line setting, whereas a companion paper describes findings from the second-line setting.[29]

Patients and Methods

SEER-Medicare Database

This retrospective, observational cohort study utilized patient data from the SEER-Medicare linked database, which combines clinical, demographic, and cause of death information on incident cancer cases from the SEER cancer registry with longitudinal administrative Medicare claims.[30,31] The Medicare claims data (1991-2013) provided detailed information about covered health care services from the time of Medicare eligibility (at age 65, or younger if disabled or having end-stage renal disease) until death, including dates of service and coded diagnoses and procedures.[32] At the time of this study, the SEER cancer registry contained data on incident cancer cases between 1991 and 2011 that comprised approximately 28% of the US population. Medicare claims data were available through December 2013.[32]

Study Design and Patients

Data were collected from January 1, 2007, to December 31, 2013, for patients aged 65 years and older with a first-time diagnosis of advanced (stage IV) NSCLC from January 1, 2007, to December 31, 2011. Patients received platinum-based chemotherapy for advanced NSCLC between January 1, 2007, and June 30, 2013. The NSCLC diagnosis was based on the SEER collaborative stage, described in detail elsewhere,[33] and the date of NSCLC diagnosis was defined as the index date. Eligible patients had to have continuous enrollment in Medicare Part A (inpatient care) and Part B (outpatient services) with no health maintenance organization (HMO) enrollment during the entire observational period, namely, from 6 months before the index date (baseline period) until death, the date of HMO enrollment, the last date of follow-up in the SEER-Medicare database, or study completion (on December 31, 2013), whichever occurred first. Exclusion criteria included Stage IIIB lung cancer and multiple primary cancers, as reported in the SEER cancer registry, or a switch within the first 29 days of starting platinum-based chemotherapy to a tyrosine kinase inhibitor (TKI) targeting epidermal growth factor receptor mutations or anaplastic lymphoma kinase rearrangements. We did not include patient data from Medicare Part D, which thereby excluded most oral antineoplastic agents; however, information about a switch to a TKI (as an exclusion criterion) was obtained from National Drug Codes in the Durable Medical Equipment file.

The sponsor for this study (Merck & Co, Inc, Kenilworth, NJ) obtained Institutional Review Board approval for using the SEER-Medicare database. Informed consent was not required because this was a database analysis using de-identified claims.

Outcome Measures

Antineoplastic treatment regimens were captured from claims that utilized the Healthcare Common Procedures Coding System or National Drug Code numbers for specific agents (see Supplemental Table 1 in the online version).[34,35] First-line therapy was defined as platinum-based chemotherapy (monotherapy or in combination with other anticancer therapies) that began within 30 days before and 90 days after the diagnosis date, and included all therapy agents for which there was a claim during the next 29 days. First-line therapy ended when a 42-day period with no treatment was observed after the last dose of platinum-based chemotherapy, or if a second drug or regimen started on or after day 30 following the first dose of platinum-based chemotherapy, thus signifying a switch to second-line therapy.

Overall and NSCLC-specific survival were described at 1 year after initiation of first-line therapy (index therapy date) and at the