RESEARCH ARTICLE

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Treatment patterns and healthcare costs among patients with advanced non-small-cell lung cancer

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Summary Points

- Background
  - Treatment options for patients with advanced non-small-cell lung cancer (aNSCLC) have been expanding with the development of predictive biomarkers and biologically targeted treatments.
  - This study coupled US healthcare claims data with cell type and disease stage information from an oncology registry to assess contemporary systemic treatment patterns for patients with aNSCLC in clinical practice.
- Treatment patterns & healthcare costs
  - Platinum–taxane doublet regimens were the most common first-line treatment (29%), followed by bevacizumab plus platinum–taxane doublets (14%). Two or more newer agents (bevacizumab, erlotinib and/or pemetrexed) were included in 16% of first-line regimens.
  - The majority of second-line regimens (76%) included bevacizumab, erlotinib and pemetrexed.
  - Total healthcare costs varied widely depending on regimen, ranging from US$19,812 to US$167,847 for first-line regimens and US$35,737 to US$135,364 for second-line regimens.
  - Systemic therapy represented 20–55% of total first-line costs and 22–68% of total second-line costs.
- Conclusion
  - These results demonstrate the emerging use of targeted agents and the potential cost implications of systemic treatments for aNSCLC.

SUMMARY **Aim:** To identify contemporary first- and second-line treatment patterns for advanced non-small-cell lung cancer (aNSCLC) and associated costs. **Methods:** This study identified aNSCLC patients through an oncology registry linked to a large US commercial claims database. Patients with aNSCLC (stage IIIb or IV) and continuous enrollment in the health plan from diagnosis until death were included. First and second lines of therapy and their associated costs were determined. **Results:** The most common first-line regimens (n = 335) were platinum–taxane doublets alone (29%) or in combination with bevacizumab (14%) or pemetrexed (6%). Most second-line regimens (n = 74) contained pemetrexed, bevacizumab and/or erlotinib. Mean total healthcare costs ranged from US$19,182 to US$167,847 (first-line) and from US$35,737 to US$135,364 (second-line). Systemic therapy

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represented 20–55% of first-line and 22–68% of second-line total costs. **Conclusion:** Pemetrexed and targeted therapies are prevalent in both first- and second-line regimens. Total and systemic therapy-related costs exhibited considerable variability by regimen.

Cancer of the lung and bronchus is the leading cause of cancer death in the USA [1] and cost an estimated US$12 billion in 2010 [2]. Non-small-cell lung cancer (NSCLC) is one of two major types of lung cancer and accounts for 80–90% of all lung cancer cases. Based on 2002–2008 estimates, the majority of lung cancer patients had distant metastatic disease at diagnosis, with a 5-year relative survival rate of 4% [101]. Advanced NSCLC (aNSCLC) patients (i.e., stage IIIb/IV disease) have typically been treated with palliative systemic therapy, including those patients who present with disseminated metastases and those with a malignant pleural or pericardial effusion.

Between 2002 and 2006, platinum-based doublet chemotherapy agents were the most commonly prescribed first-line treatment regimens, and docetaxel, gefitinib and erlotinib were the most common second-line agents for patients diagnosed with lung cancer irrespective of cell type or disease stage [3]. However, aNSCLC treatment has evolved since 2006 with erlotinib as the only routinely available oral agent [102] (since modification of the gefitinib label in 2005 to restrict access [103]), revised National Comprehensive Cancer Network (NCCN) treatment guidelines [104] and the introduction of new agents for first-line use. Bevacizumab, a biologically targeted agent gained US FDA approval in 2006 [105], and pemetrexed, a novel chemotherapeutic agent [106], was approved in 2008. The elucidation of molecular pathways in cancer biology has led to personalized treatment strategies founded on molecular testing and targeted therapies [4]. New maintenance-based treatment paradigms have emerged for patients without disease progression after first-line platinum-based regimens [5]. The selection of treatment strategy requires consideration of multiple factors, such as patient performance status, cell histology and biomarkers predictive of therapeutic benefit. With expanding treatment options, the cost of contemporary aNSCLC cancer therapy warrants further investigation.

The literature on healthcare costs among aNSCLC patients is sparse due to the limited availability of databases containing both claims data and the clinical information necessary to distinguish between small-cell lung cancer and NSCLC, as well as early- and advanced-stage disease. The most recent real-world estimates of the cost of systemic treatment of aNSCLC in the USA are based primarily on data from 1998 to 2006 [6–8]. These studies either did not distinguish costs by treatment regimen [6] or were limited to first-line therapies (primarily platinum-based doublets) commonly prescribed during that period [7,8]. Studies of second-line therapy costs were limited to monotherapy treatment of all lung cancers [9], monotherapy treatment of aNSCLC (outpatient costs only) [10] or predated approval/clinical adoption of targeted therapies and pemetrexed [3].

With the evolving aNSCLC treatment landscape, there is a need to identify recent treatment utilization patterns and associated cost implications, including the contribution of systemic therapy costs to total costs. The objective of this analysis was to identify aNSCLC patients using clinical evidence of cell type and disease stage, assess contemporary first- and second-line aNSCLC treatment patterns and determine the associated real-world total and systemic treatment-related costs of aNSCLC patients with commercial insurance from the payer perspective.

Methods

Study design & data source

In this retrospective study, data were linked from three separate sources: healthcare claims, an oncology registry and Social Security Administration master death files. Healthcare claims were captured from the Optum Research Database, which represents a geographically diverse US health plan. The healthcare claims database represents approximately 14 million annual lives with medical and pharmacy benefits through commercial plans. Commercial health plan members with evidence of lung cancer in the Oncology Management (OM) database, an oncology registry, were included in the study. The OM database is a proprietary database containing clinical confirmation regarding lung cancer, including the date of diagnosis, cell type and stage provided by the treating physician. In addition, the Social Security Administration master death files were linked to patient

enrollment data in order to identify patients who died and the date of death. The combined dataset was used to identify treatment patterns and healthcare costs among patients with aNSCLC. All data were de-identified in accordance with established privacy guidelines under the Health Insurance Portability and Accountability Act [107]; therefore, Institutional Review Board approval was not sought.

Observation period

The study spanned two consecutive periods defined by the index date, which was the date of the initial lung cancer diagnosis in the OM database that occurred between 1 January 2006 and 30 April 2010. The baseline period was the 6 months prior to the index date and the follow-up period represented the interval from the index date until patient death, disenrollment from the health plan or the end of the study (30 April 2010), whichever occurred first.

Patients

Commercial health plan members with medical and pharmacy benefits and evidence of NSCLC who met all of the following criteria were included in the study sample: evidence of lung cancer in the OM database; evidence of advanced-stage (IIIb or IV) NSCLC; receipt of systemic therapy (chemotherapy or targeted agents); continuous enrollment for the 6-month baseline period; continuous enrollment for 6 months following the index date (patients who died prior to disenrolling from the health plan were retained); and being at least 18 years of age as of the index year.

Treatment patterns

Any systemic therapies commonly used in the first-line treatment of NSCLC were included: bevacizumab, carboplatin and cisplatin ('platinums'), cyclophosphamide, docetaxel and paclitaxel ('taxanes', including albumin-bound paclitaxel), doxorubicin, erlotinib, etoposide, gefitinib, gemcitabine, ifosfamide, irinotecan, mitomycin, pemetrexed, procarbazine, topotecan, vinblastine, vinorelbine and vincristine. Since claims data do not distinguish between first and second lines of therapy, lines of therapy were determined from an algorithm based on the date of receipt of agents and treatment gaps. The start date for first-line therapy was defined as the first claim for a systemic treatment after the index date; the end date was the last date of a claim for systemic therapy that occurred prior to a treatment gap of ≥60 days. Systemic therapies were not required to be given concomitantly (e.g., pemetrexed may be given as maintenance after four cycles of platinum-based chemotherapy among patients whose disease has not progressed [104]). Second-line therapy began on the first date of receipt of a systemic agent after first-line therapy ended and concluded 30 days after the receipt of the last second-line agent.

Measures

Patient age during the index year, gender and Charlson Comorbidity Score [11] during the baseline period were captured. Treatment regimen, number of cycles and duration of therapy during follow-up were determined. The treatment regimen represented all systemic therapy in a line of therapy. The number of cycles was defined as the number of days of drug administration. Treatment duration was computed for the interval from the start to the end date for each line of therapy. Costs are presented for the duration of each line of therapy. All-cause healthcare costs were computed as the sum of all health plan- and patient-paid amounts for all medical (ambulatory [office and outpatient hospitalization] visits, emergency room visits, inpatient hospitalization and other services) and retail pharmacy services. Total systemic therapy costs were computed as the sum of costs for chemotherapy and biologically targeted agents (except erlotinib), administration of the agents and all related resources (i.e., ambulatory, office and inpatient visits); thus, systemic therapy-related costs overlap with other components of total cost and do not represent a mutually exclusive category. Cost of erlotinib, an oral agent, was captured under pharmacy costs. All costs were adjusted to 2009 US dollars using the medical care component of the Consumer Price Index [108].

Analysis

Descriptive statistics were determined for all measures. Patient demographics and clinical characteristics and length of the follow-up period were computed for the entire study population. Total healthcare costs, systemic therapy costs and treatment duration are reported separately by line (first or second) of therapy for each treatment regimen. Data for patients who disenrolled from the health plan for reasons other than death or end of the study period were excluded from the analyses.

Results

Characteristics of the study population

A total of 4420 patients with lung cancer were identified in the OM database and 1213 patients met the continuous enrollment criteria. Of these 1213 patients, 817 were identified as having NSCLC and 527 as having aNSCLC (stage IIIb/IV), with 499 diagnosed between 1 January 2006 and 30 April 2010. Of these 499 patients, 397 initiated first-line treatment and 335 had complete first-line therapy data. A total of 95 patients initiated second-line therapy and 74 had complete second-line data. The majority of patients (n = 2705) were excluded due to a lack of continuous enrollment in the health plan 6 months prior to or 6 months following their diagnosis.

The mean (standard deviation [SD]) age of the aNSCLC population was 60.8 (9.1) years, approximately 69% of patients were between the ages of 45 and 64 years and nearly 59% of patients were men (Table 1). The mean (SD) Charlson Comorbidity Score at baseline was 4.1 (3.1). The mean (SD) length of follow-up was 385 (335) days and median follow-up was 276 days; 235 patients died during follow-up and the remaining were still enrolled at the end of the study period (n = 149) or disenrolled from the health plan (n = 115), in which case their data were censored.

Table 1. Baseline patient characteristics and length of follow-up.

Characteristic	aNSCLC (n = 499)	
	Mean	SD
Age (years)	60.8	9.1
Charlson Comorbidity Score†	4.1	3.1
Length of follow-up (days)	385	335
	n	Percentage
Age (years)		
▪ 18–44	13	2.6
▪ 45–64	344	68.9
▪ ≥65	142	28.5
Male	294	58.9
Length of follow-up		
▪ <3 months	77	15.4
▪ 3–<6 months	84	16.8
▪ 6–<9 months	80	16.0
▪ 9–<12 months	64	12.8
▪ 12–<24 months	110	22.0
▪ 24–<36 months	62	12.4
▪ ≥36 months	22	4.4

†At 6 months prior to diagnosis.
aNSCLC: Advanced non-small-cell lung cancer; SD: Standard deviation.

Treatment patterns

Treatment regimens during first- and second-line therapy are shown in Table 2. Complete first-line therapy information was available for 335 of the 397 aNSCLC patients who initiated first-line therapy. The only reasons for incomplete line of therapy data was disenrollment from the health plan for reasons other than death or end of the study period. The most common first-line regimen was platinum–taxane doublets, representing 29% of all patients undergoing first-line therapy. The second most common regimens were bevacizumab plus platinum–taxane doublets (14%), followed by pemetrexed plus platinum–taxane doublets (6%) and erlotinib monotherapy (5%). A total of 53 of the 335 (16%) first-line regimens included two or more newer agents (pemetrexed, bevacizumab and/or erlotinib). For platinum–taxane doublet-based regimens, the mean number of cycles of platinum–taxane doublets ranged from six to seven. For those platinum–taxane doublet-based regimens including a targeted agent or pemetrexed, the mean number of bevacizumab and pemetrexed cycles was seven and four, respectively; the mean supply of erlotinib was 75 days. The mean (median) duration of first-line therapy treatment ranged from 74 to 365 days (49 to 301 days) and regimens that included pemetrexed and/or bevacizumab were generally the longest.

Complete second-line therapy information was available for 74 aNSCLC patients. The majority of patients (76%) were treated with regimens containing pemetrexed, bevacizumab and/or erlotinib. The percentage of patients receiving regimens containing one of these agents was: pemetrexed, 24%; ertlotinib, 15%; and bevacizumab, 10%. A total of 27% of patients were treated with second-line therapies containing two or more of these agents. The mean (median) duration of second-line treatment ranged from 117 to 332 days (104 to 276 days).

Healthcare costs

Mean healthcare costs for first-line and second-line regimens are shown in Table 3. Total mean costs for first-line regimens ranged from US$19,182 (erlotinib monotherapy) to US$167,847 (regimens containing two or more of pemetrexed, bevacizumab and/or erlotinib). Ambulatory services (office and outpatient), which often include chemotherapy drug costs, accounted for the majority (70%) of total costs.

For all regimens, systemic therapy-related costs represented 38% of total costs and ranged from US$9307 for platinum–taxane doublet to US$79,552 for combinations containing at least two of the following: bevacizumab, erlotinib and/or pemetrexed. Mean inpatient hospitalization costs accounted for 19% of total costs for all regimens.

Total means costs for specified second-line regimens ranged from US$35,737 (regimens containing erlotinib) to US$135,364 (regimens containing two or more of pemetrexed, bevacizumab and/or erlotinib). Mean costs for ambulatory services represented 79% of total costs. Mean systemic therapy costs accounted for 50% of total costs and ranged from US$12,055 (regimens containing erlotinib) to US$91,118 (regimens containing bevacizumab). Mean inpatient hospitalization costs accounted for 11% of total costs for all regimens.

Discussion

This retrospective analysis linked confirmed aNSCLC diagnostic data with a commercial health claims database from 1 January 2006 to 30 April 2010 in order to identify contemporary first- and second-line treatment patterns and healthcare costs in the evolving aNSCLC treatment landscape. The most frequently used first-line treatments were platinum–taxane doublets (29%), combinations of two or more of bevacizumab, erlotinib and/or pemetrexed (16%) and platinum–taxane doublets plus bevacizumab (14%). Total healthcare costs for patients undergoing first-line therapy varied widely (US$19,182–167,847) across regimens, and systemic therapy-related costs represented 20–55% of total healthcare costs during first-line therapy. The predominant specified second-line therapies were combinations of two or more of bevacizumab, erlotinib and/or pemetrexed (27%), regimens containing pemetrexed (24%) and regimens containing erlotinib (15%). Total healthcare costs ranged from US$29,385 to US$135,364 during second-line therapy, with systemic therapy-related costs representing 22–68% of total costs.

Our results indicate that first-line treatment regimens have changed since the most recent reports based on data from 2006 and earlier. In a study of lung cancer patients (which did not distinguish between small-cell lung cancer and NSCLC diagnoses), all first-line therapies were platinum-based and 62% of these therapies were

Table 2. Treatment regimens by line of therapy.

	Patients		Duration (days)		Mean number of cycles†			Mean days of supply
	n	Percentage	Mean (SD)	Median	Platinum–taxane	Bevacizumab	Pemetrexed	Erlotinib
First-line (n = 335)								
Platinum–taxane doublet	98	29.3	99 (57)	87	6	–	–	–
Pemetrexed + platinum–taxane doublet	19	5.7	247 (107)	249	7	–	4	–
Pemetrexed + other combinations	14	4.2	178 (91)	152	2	–	4	–
Bevacizumab + platinum–taxane doublet	47	14.0	184 (185)	140	6	7	–	–
Erlotinib monotherapy	17	5.1	74 (82)	49	–	–	–	78
Erlotinib + platinum–taxane doublet	11	3.3	205 (161)	185	6	–	–	75
Pemetrexed, bevacizumab and/or erlotinib (≥2)‡	53	15.8	365 (252)	301	6	6	3	110
All other first-line regimens	76	22.7	147 (116)	136	4	–	–	2
Second-line (n = 74)								
Pemetrexed included	18	24.3	176 (132)	181	1	–	5	–
Bevacizumab included	7	9.5	223 (115)	273	8	9	–	–
Erlotinib included	11	14.9	117 (67)	104	1	–	–	73
Pemetrexed, bevacizumab and/or erlotinib (≥2)‡	20	27.0	332 (208)	276	2	5	5	59
All other second-line regimens	18	24.3	108 (59)	104	3	–	–	–

†Cycles identified from administration days for platinum–taxane doublets, bevacizumab and pemetrexed.
‡Contained two or more of these agents.
SD: Standard deviation.

Table 3. Healthcare costs associated with regimens by line of therapy.

Line of therapy	Mean costs (SD) in US$						
	Systemic treatment-related†	Ambulatory	Emergency room	Inpatient	Other	Pharmacy	Total
First-line							
Platinum–taxane doublet	9307 (7972)	29,573 (22,548)	166 (425)	13,047 (27,925)	934 (3340)	2190 (4263)	45,909 (39,064)
Pemetrexed + platinum–taxane doublet	27,098 (17,838)	65,368 (43,930)	462 (583)	26,253 (30,114)	841 (1245)	5628 (7671)	98,551 (68,693)
Pemetrexed + other combinations	29,491 (24,140)	53,193 (42,594)	255 (391)	8826 (22,621)	1362 (2580)	3762 (6113)	67,398 (46,878)
Bevacizumab + platinum–taxane doublet	68,100 (90,784)	102,379 (101,081)	442 (1330)	14,933 (27,703)	2761 (10,149)	2963 (6990)	123,477 (109,125)
Erlotinib monotherapy	8682 (8306)	4586 (7390)	17 (57)	3147 (5064)	1557 (5338)	9874 (8103)	19,182 (15,267)
Erlotinib + platinum–taxane doublet	15,028 (10,576)	34,615 (28,395)	298 (388)	21,139 (31,151)	916 (978)	16,712 (21,061)	73,680 (43,812)
Pemetrexed, bevacizumab and/or erlotinib (≥2)‡	79,552 (62,985)	118,223 (101,954)	3389 (20,445)	23,048 (56,331)	3900 (7739)	19,287 (25,063)	167,847 (132,113)
All other first-line regimens	15,434 (15,436)	46,580 (38,514)	237 (538)	17,978 (46,291)	1116 (2505)	2691 (3291)	68,602 (60,219)
Second-line							
Pemetrexed included	25,921 (24,738)	51,683 (51,201)	349 (656)	9595 (22,370)	647 (1063)	997 (935)	63,272 (66,139)
Bevacizumab included	91,118 (58,376)	127,384 (79,524)	109 (217)	934 (2472)	2303 (5175)	3724 (3365)	134,454 (80,556)
Erlotinib included	12,055 (6146)	18,492 (17,440)	191 (245)	6537 (8034)	259 (443)	10,258 (6556)	35,737 (20,959)
Pemetrexed, bevacizumab and/or erlotinib (≥2)‡	74,139 (72,938)	107,170 (87,315)	620 (816)	13,940 (21,848)	1816 (5356)	11,818 (8730)	135,364 (84,957)
All other second-line regimens	6563 (3995)	19,749 (20,626)	242 (502)	5086 (12,319)	702 (909)	3605 (8151)	29,385 (30,871)

†Sum of costs for chemotherapy and biologically targeted agents (except erlotinib, which is captured under pharmacy), administration of the agents and all related resources (i.e., ambulatory, office and inpatient visits). These costs may overlap with other cost components.
‡Contained two or more of these agents.
SD: Standard deviation.

platinum–taxane doublets [3]. In an analysis of aNSCLC patients, 52% of patients were treated with platinum–taxane doublets as first-line therapy, and the majority of the remaining patients were treated with other platinum doublets, vinorelbine (alone or in combination with gemcitabine or platinum) or taxane [8]. In our study, platinum–taxane doublets were also the most common first-line therapy, but represented only 29% of patients. Our results demonstrate the emerging use of biologically targeted therapies and pemetrexed in first-line therapy combinations: regimens containing bevacizumab, erlotinib and/or pemetrexed represented 48% of first-line regimens.

To our knowledge, this is the first study to report second-line therapy pattern utilization for aNSCLC patients. The majority of second-line therapies contained bevacizumab, erlotinib or pemetrexed or combinations of these agents. By contrast, a study of lung cancer patients based on data prior to 2007 identified docetaxel monotherapy and erlotinib monotherapy as the most common second-line regimens [3]. Our results suggest a shift in second-line therapy treatment patterns to combination therapy with newer agents. It is also possible that the prominent use of pemetrexed and erlotinib combinations in second-line therapy reflects maintenance or switch maintenance treatment strategies for patients whose disease has not progressed after platinum-based first-line chemotherapy [12], although the cost–effectiveness of maintenance strategies remains controversial [13,14].

Our costs results represent the entire episode of therapy and are a function of drug and administrations costs, duration of therapy and number of administrations. Higher costs generally reflected longer duration of treatment and the addition of bevacizumab, which appeared to contribute to higher first-line costs. For first-line regimens, the cleanest comparisons are for treatments that represent the addition of a single targeted agent (i.e., pemetrexed, bevacizumab or erlotinib) to platinum–taxane doublet therapy. The median duration of treatment and systemic treatment-related costs, respectively, for these combinations were: pemetrexed, 249 days, US$27,089; bevacizumab, 140 days, US$68,100; and erlotinib, 185 days, US$15,028. Thus, although median treatment duration was shortest for patients treated with bevacizumab plus platinum–taxane doublet therapy, systemic treatment-related costs were notably higher. Upon further investigation,

we find fewer pemetrexed administrations (four) than bevacizumab (seven). Using a crude calculation, the higher systemic treatment-related costs of bevacizumab are partially but not fully explained by the higher number of administrations. However, assuming patients were of similar body weight and surface area, the cost of each bevacizumab administration was approximately 1.5-times higher than the cost of each pemetrexed administration (based on average US sales prices for bevacizumab and pemetrexed [109]). The combination of more bevacizumab infusions at a higher per administration average US sales price explains the greater cost for bevacizumab plus platinum–taxane doublet regimens, even though duration of therapy is shorter.

Duration of treatment was generally longest for regimens containing pemetrexed and/or bevacizumab. For pemetrexed, this may reflect maintenance therapy for patients whose disease has not progressed after four cycles of platinum-based chemotherapy. Erlotinib is also indicated for maintenance therapy, and patients treated with erlotinib plus platinum–taxane doublet therapy had the third longest median duration of therapy. Patients who undergo maintenance therapy will likely have longer treatment durations than patients in clinical studies that do not include maintenance therapy. Maintenance therapy would be expected to extend treatment duration under two likely scenarios: the therapy is given only to patients who do not progress on a platinum-based regimen and thus have longer survival; and the therapy is given after platinum-based treatment, thus extending the duration of therapy.

Other aNSCLC studies reported costs of first-line therapy ranging from US$22,126 to US$31,104 [8] and US$28,562–34,516 [7] versus US$84,671 in this study. The costs results from the earlier studies are based primarily on chemotherapy doublet regimens for Medicare patients prior to 2004. Our costs results are based on aNSCLC patients with commercial insurance who are younger and more likely to be of working age than Medicare beneficiaries. In addition, provider payments under Medicare are significantly less than commercial insurance reimbursement rates [110]. In a study of metastatic lung cancer patients that did not distinguish costs between lines of therapy, the mean total healthcare costs averaged US$125,849 over 500 days in 2000–2006 [15]. The mean second-line therapy costs over 12 months were US$35,032–75,310 for lung cancer patients receiving treatment in 2002–2006 [3]. Our mean second-line therapy costs were higher (US$77,154), but represented only 197 mean days of treatment and exhibited a wide range. Second-line therapy costs likely reflect an individualized treatment approach based on tumor characteristics, patient performance status, comorbidities and tolerance of specific agents. Overall, our costs results exhibit the variability inherent in US healthcare costs data and are consistent with a diverse patient population. One overarching source of variation for patients in commercial plans is the diversity in negotiated reimbursement rates. Unlike Medicare, reimbursement rates are not standardized but negotiated at the provider level. Variation in costs for less frequently used services (e.g., inpatient) stems from the large number of patients who incurred zero cost for these services (e.g., have no hospitalizations) and the smaller number of patients who incurred large costs for these services. Finally, systemic treatment costs will vary depending on the cumulative dose for each patient.

Over the last decade, the identification of molecular markers to determine not only prognosis but also likelihood of response to a molecularly targeted agent is one of the major advances in oncology, but the addition of such targeted therapy is costly. The optimal regimen for second-line therapy remains controversial. Overall, the treatment patterns we identified are consistent with clinical practice guidelines. The diversity of treatments for both first- and second-line therapy is likely a reflection of an individualized treatment approach that incorporates patient clinical characteristics (e.g., histology, predictive biomarkers and performance status) and balances efficacy with tolerability.

There are several important limitations to our analysis and these results should be considered in this context. The algorithms we used to distinguish first- and second-line therapy may count some agents as second-line therapy but may, in fact, represent a combination of second- and third-line therapy or maintenance therapy utilized after lack of progression on four or more cycles of platinum-based chemotherapy. Pemetrexed, erlotinib and bevacizumab are the agents most likely to be affected by this practice. While a clear account of what is characterized as first-line therapy is not always possible, the use of these agents is accurate. The treatment patterns we identified do not provide the clinical rationale for decisions regarding

omission of a drug from a regimen or switching to another therapy. Patient clinical characteristics and tolerance of therapy are likely to influence treatment patterns and these data were not available. Our data source did not contain the relevant clinical information necessary to determine if or when progression or treatment failure occurred. We assume that clinicians are following guidelines and modifying treatment regimens accordingly; thus, our results reflect treatment patterns that occurred in actual clinical practice. We did not include two agents in our analysis, crizotinib and cetuximab, which are approved or included in NCCN guidelines for treatment of aNSCLC. Crizotinib was not approved or included in guidelines until after our study concluded. Cetuximab, although not approved for lung cancer, was present in 2009 NCCN guidelines, but this was during the late stage of our study. Furthermore, treatments received by patients enrolled in clinical trials may not generate insurance claims and, as a result, these treatments would not be captured in our analysis. Finally, our analysis was restricted to patients with commercial insurance; treatment patterns and healthcare costs in patients with Medicare, other insurance and the uninsured may differ from our results. However, the commercially insured population is sizable, and few databases contain both cost data and the clinical information necessary to identify aNSCLC patients. While the Surveillance and Epidemiology and End Results (SEER) database can be used to provide similar assessments for patients with Medicare and Medicaid insurance, the population and reimbursement practices are much more different compared with the commercially insured population.

Conclusion

Platinum and taxane combinations are still the mainstay of first-line treatment for aNSCLC, but combinations containing pemetrexed and biologically targeted therapies are increasingly prevalent in first- and second-line regimens.

Future perspective

Personalized medicine will continue to advance the treatment of NSCLC. Increased utilization of evidence-based clinical pathways, molecular testing and identification of patients eligible for targeted therapies and the development of more efficacious therapies may provide improved clinical and economic outcomes for the treatment of patients with aNSCLC.

Prior presentation

A portion of the results of this study were presented as a poster at the International Society for Pharmacoeconomics and Outcomes Research 14th Annual European Congress, Madrid, Spain, 5–8 November 2011.

Financial & competing interests disclosure

This study was sponsored by AbbVie (IL, USA). HJ Henk is an employee of OptumInsight Life Sciences (MN, USA), which is a health economics and outcomes research organization, retained by AbbVie to conduct this study. S Ray is an employee of AbbVie and holds stock in the company. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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- ▪ of interest
- ▪▪ of considerable interest

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▪▪ **Shows that between 2002 and 2006, the majority (62%) of lung cancer patients treated with systemic therapy received platinum–taxane doublet therapy as the first-line regimen. Docetaxel monotherapy and erlotinib monotherapy were the most common second-line regimens.**

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