Assessing Resource Use in Oncology Patients: A Comparison of Analyses Based on Claims Data and Medical Chart Review

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ABSTRACT

BACKGROUND: Provider claims data are used to make medical analyses and decisions, but such databases typically lack important clinical information.

OBJECTIVE: To compare the patterns of use of filgrastim in analyses of a claims database and a medical chart review.

METHODS: We extracted data from the Medicare 5% sample claims database for the years 1996 through 1998 and from a medical chart review of the Oncology Practice Pattern Survey (OPPS) for the same period to determine the patterns of use of filgrastim in patients with non-Hodgkin's lymphoma treated with cyclophosphamide, doxorubicin, vincristine, and prednisone. The analyses were restricted to the first 3 cycles of the chemotherapy.

RESULTS: A total of 414 patients in the Medicare database were treated with 1,360 cycles of chemotherapy. The mean duration of filgrastim use in these patients was 6.6 days. In the OPPS database, 80 patients were treated with 152 cycles of chemotherapy, with a mean duration of filgrastim use of 9.3 days.

CONCLUSION: The mean duration of filgrastim use in the OPPS database was greater than that in the Medicare database and was closer to that shown in clinical trials to produce optimal results (approximately 11 days). The actual use of resources may be underestimated in claims databases, owing to their limitations and potential for bias.

KEYWORDS: Claims database, Resource use, Medical chart review

Public and private payers frequently use provider claims databases to track health care expenditures, analyze patterns of medical resource utilization, and provide a basis for making plan-level treatment decisions (eg., drug coverage, treatment guidelines or restrictions, and medication formulary status). While claims-based analyses are increasingly used by decision makers due to low costs, rapidity of results, and large sample size, the sole reliance on claims data for making plan-level decisions is associated with notable challenges, limitations, and potential biases.

The most significant limitations of claims data arise from deficiencies in the information that is available. Claims data typically lack critical data such as illness severity, the indication for drug use, the criteria used in making the treatment choice, and outcomes.¹⁻⁴ In complex disease areas such as cancer, claims data present additional challenges such as a lack of information about the chemotherapy regimen used, the instances of and reasons for changes in the chemotherapy dose or schedule, and the cancer stage.^{1,2} Further, claims databases may be subject to inconsistency over time as a result of ongoing editing and changes in coding and may contain invalid data due to a lack of edit checks.³ Missing or incorrect data can introduce serious bias, producing inaccurate and misleading results. Medical record review or linking of claims and registry databases can resolve many of these discrepancies but is sometimes considered too costly and difficult.^{1,2} Finally, all data derived from administrative databases contain a non-random patient sample, which may introduce unknown bias into an analysis.^{3,4}

Because of these limitations, clinical guidelines and other important medical decisions should ideally be based on validated, methodologically sound data sources such as clinical trial results, medical chart reviews, or prospective studies. To illustrate the challenges and limitations of claims-based analyses compared with more methodologically rigorous techniques, we selected the use of granulocyte colony-stimulating factor (ie., filgrastim) in oncology as a case study. Filgrastim is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of severe neutropenia with fever.⁵ In a decision-analytic model, the high costs of febrile neutropenia favored prophylactic filgrastim use compared with no use or therapeutic use.⁶ In randomized controlled clinical trials, filgrastim was administered for a mean of 11 days, beginning 24 hours after chemotherapy to reach an absolute neutrophil count (ANC) of $10 \times 10^9/L$ —the level consistent with current prescribing information in the chemotherapy-induced neutropenia (CIN) setting. In these trials, the costs of purchasing and administering filgrastim were partially or completely offset by a reduction in the costs of febrile neutropenia.⁷⁻⁹

This article reports filgrastim use patterns based on analyses of

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FIGURE 1 Medicare 5% Analysis Process Flow Chart

the physician and outpatient files. Claims for filgrastim were identified using 2 HCFA Common Procedure Coding System (HCPCS) J-Codes (which include all non-self-administered injectable drugs): J1440 (the filgrastim 300-µg vial) and J1441 (the filgrastim 480-µg vial). Approximately 95% of filgrastim use occurred in the physician's office setting, while 4% occurred in the hospital outpatient setting (hospital-administered medications are not reported in the Medicare SAFs).

Utilization for most patients was captured by merging the files into one analysis file containing 2.9 million claims (Figure 1). However, the records were incomplete for some patients who had either entered the analysis period after initiation of their cancer chemotherapy treatment (i.e., initiation began prior to January 1996) or exited the analysis before their cancer chemotherapy treatment ended (i.e., treatment ended after December 1998).

Medicare SAFs do not include the number of vials used or the dosage patients received from a physician-administered chemotherapy agent or supportive medication. Dose was calculated using an algorithm that assigns a dose based on the corresponding J-Code multiplied by number of units associated with the claim (eg, 2 units of J1440 = filgrastim 600 µg).

For a claims-based analysis to yield clinically meaningful results on which valid, reliable plan- or program-level decisions can be based, medically relevant time frames that accurately capture resource use patterns (eg, cycles of chemotherapy) must be defined.¹¹ Three analytical approaches were considered for the claims-based analysis. These approaches were: (1) use-per-time, (2) episode-of-treatment, and (3) per-chemotherapy-cycle. The use-per-time approach involved aggregating filgrastim doses per patient and reporting the average over each year (1996, 1997, 1998) and over the 1996 to 1998 3-year period. However, this approach uses

arbitrarily defined time periods, which is not considered appropriate in oncology, where treatment is typically characterized by periods of intense resource use during an episode, followed by little or no use in the interepisode periods.^{11,12} The episode-of-treatment approach is clinically more appropriate than the use-per-time approach since it does capture intense resource use during an episode. Under this approach, the length of an episode of treatment (including primary and secondary prophylaxis and treatment) is defined as a period where there was a minimum of 2 months before and 2 months after any month (or contiguous month) with claims for filgrastim, where no use occurred. However, the episode-of-treatment approach failed to link filgrastim utilization to chemotherapy regimens, which is the medically appropriate

claims data from the Medicare 5% sample and compares the findings to those obtained by medical chart review from Amgen's Oncology Practice Pattern Study (OPPS).¹⁰

Methods

Claims Data Analysis

Claims data analyses of filgrastim utilization were conducted using the Medicare 5% sample claims database from 1996 through 1998. The database contains data from the Medicare Standard Analytical Files (SAFs) developed by the Centers for Medicare and Medicaid Services (CMS, formerly the Health Care Financing Administration [HCFA]). All files for patients with one or more claims for filgrastim between 1996 and 1998 were extracted from

method for assessing filgrastim utilization. The per-chemotherapy-cycle approach was selected for this analysis because it linked daily filgrastim utilization to a specific chemotherapy regimen. This approach is described in greater detail below.

For the per-chemotherapy-cycle analysis, patients receiving 21-day cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy were selected for the following reasons:

- CHOP is used for both early and advanced stages of non-Hodgkin's lymphoma (NHL)
- CHOP has moderately high CIN rates
- CHOP dose intensity is particularly significant because NHL is a curative tumor
- Prophylaxis of CIN with filgrastim can help allow for increased CHOP dose intensity.^{13,14}

In this analysis an algorithm was created that assigned an index date to the first claim for CHO (cyclophosphamide, doxorubicin, vincristine). Prednisone-related claims were not found in the Medicare 5% sample database. Primary (prophylactic) filgrastim use was defined as filgrastim therapy initiated within the first 5 days of a cycle of CHOP chemotherapy. Filgrastim utilization was included in the analysis if the first claim began on or between the CHO index date (day 1 of the chemotherapy regimen) and the fifth day after the index date (day 5).

Medical Chart Review

A similar cycle-based approach as outlined above was applied to a medical chart review of patients with a diagnosis of NHL. This database included patient information abstracted from 12 community and academic oncology practice settings in the United States that participated in the OPPS between 1991 and 1999.¹⁰ The practice settings included 2 academic centers, 5 integrated hospital systems, and 5 community practices. Data were collected by clinical staff at each site on standard case report forms. Patients were included if they had a diagnosis of NHL, were aged at least 18 years and had received CHOP chemotherapy and filgrastim at any time between 1996 and 1998.

Results

Medicare 5% Analysis

A total of 414 cancer patients who had received a total of 1,360 cycles of CHO(P) chemotherapy were included in the analysis. Patients included in this analysis received a range of 1 to 16 (mean, 2.4) cycles of CHO(P) and filgrastim therapy during the study period; however, the analysis was restricted to the first 3 cycles based on historical data showing that the largest percentage of neutropenic events in patients receiving CHO(P) therapy occur during this time.¹⁰ During the first 3 cycles of CHO(P), the overall mean duration of filgrastim usage per cycle was 6.6 days, approximately 4.4 days shorter than the 11 days reported in clinical trials.⁷⁻⁹

TABLE 1 Per-Cycle Duration of Filgrastim Use in Patients Undergoing CHO(P) Chemotherapy

Days of Filgrastim Use, Mean (Range)			
CHO(P) Cycle	Medicare 5% Sample*	OPPS†	Difference
1	6.3 (1-14)	9.5 (5-13)	3.2
2	6.8 (1-13)	9.3 (2-14)	2.5
3	6.9 (1-13)	9.2 (3-14)	2.3
All	6.6 (1-14)	9.3 (2-14)	2.7

*This analysis was limited to claims for C, H, and O because prednisone-related claims were not found in the Medicare 5% sample database.

†OPPS NHL patients, all ages, 1996–1998.

OPPS

A total of 80 patients who received a total of 152 cycles of CHO(P) were included in the analysis. As in the Medicare 5% data analysis, the OPPS analysis was based on the first 3 cycles of CHO(P) therapy. Analysis of the OPPS data indicated an overall mean of 9.3 days (range, 2 to 14 days) of primary filgrastim use (Table 1). The results of the analysis of OPPS data more closely correspond to the average 11 days duration of filgrastim therapy observed in clinical trials. These results suggest that a claims-based analysis may underestimate the actual average per-cycle duration of filgrastim use when patients are dosed consistent with filgrastim prescribing recommendations for CIN.

Discussion

This study was designed to compare 2 sources of data for analysis of resource utilization of filgrastim in the CIN setting: claims data and medical chart review. A comparison of findings from analyses based on the 2 data sources revealed consistently lower (ranging from 2.3 to 3.2 days lower) estimates of the duration of primary filgrastim per chemotherapy cycle use from the Medicare 5% data as compared with the OPPS data. The result of the Medicare 5% data analysis is a mean duration of filgrastim use per chemotherapy cycle that is approximately 4.4 days less than appropriate use consistent with the prescribing information.

The estimation of mean duration of filgrastim use in the analysis of the Medicare 5% data may have been biased from the following limitations of claims data, some of which required assumptions as noted:

- Complete information on patient, tumor, and other factors involved in making treatment decisions were not captured in the claims, thus increasing the difficulty of interpreting mean duration of filgrastim use per chemotherapy cycle from a medical perspective.
- Cancer chemotherapy regimens could not be identified; therefore, we assumed that separate claims for C, H, and O represented CHOP chemotherapy.

- The purpose of filgrastim use (primary prophylaxis or treatment) was not documented; thus, filgrastim use beginning within the first 5 days of a cycle of CHOP chemotherapy was assumed to represent primary prophylaxis use.
- Because reasons for the gaps in filgrastim therapy were absent from the claims database, gaps of 2 to 3 days were assumed to represent typical treatment interruptions, such as failure to receive filgrastim during the weekend, and were ignored when counting the duration of an episode of filgrastim use.
- Filgrastim use in other care settings such as the hospital inpatient or home health care setting was not captured by the Medicare 5% sample, thus contributing to the bias of the sample.

In a separate preliminary analysis, Chrischilles et al. (written communication, January 2003) compared filgrastim utilization from the OPDS database with corresponding Medicare claims for 1994 through 1996 present in both databases; 8 patients received primary prophylactic filgrastim (early filgrastim, defined as within 8 days after the start of the first cycle of chemotherapy) according to the OPDS database. Of these, 5 had at least one filgrastim claim in the Surveillance, Epidemiology, and End Results (SEER)-Medicare database. Utilization across databases was further examined by incorporating the start date of filgrastim use, and a match was indicated if the filgrastim start date (first use) from SEER-Medicare was within 3 days of that reported in OPDS. Of the 8 early filgrastim patients in OPDS, 4 did not match because they were hospitalized during that period, and filgrastim could not be identified from inpatient claims (there are no specific codes for filgrastim in the ICD9 procedure list used for hospital claims). Among those not hospitalized (n=4), Chrischilles et al. were able to confirm OPDS-reported early filgrastim in the Medicare claims data for 3 patients and found that while the OPDS database indicated that filgrastim was ordered for the fourth patient, a chart review was not able to confirm whether it had been administered. Hence, while Medicare claims may be valid for identifying early filgrastim use in some epidemiologic studies (eg., factors associated with neutropenia hospitalization), claims data result in substantial underestimation of total filgrastim utilization.

Because of the limitation of the claims data and the assumptions that were required, the results of the analysis of the Medicare 5% sample may provide an underestimate of filgrastim usage on a per-chemotherapy-treatment-cycle basis. Thus, as others have shown previously,¹⁵ the results shown here strongly suggest that claims-based analyses should not serve as a sole source guide to plan-level treatment choice decisions.

Conclusion

This analysis shows the difficulty in analyzing claims data to accurately describe medical resource use on a per-chemotherapy-cycle basis. A comparison of the duration of filgrastim use based on analysis of claims data from the Medicare 5% sample and medical chart review (OPDS data) indicated that claims data analyses may underestimate the duration of primary filgrastim use per chemotherapy cycle due to potentially significant limitations of the databases. Although the claims-based analysis was based on

Medicare claims data, the implications may be relevant to other medical claims databases. Medications such as filgrastim that are used episodically and for several indications pose unique challenges in estimating of resource use based on analysis of medical claims data as a sole source of information.

DISCLOSURES

The development of this manuscript was funded, in part, by Amgen. Funding was obtained by authors Georgette N. Semroc and Jonathan C. Tierce. Author Moshe Fridman is a consultant to Amgen. Semroc served as principal author of this study. Study concept and design and drafting of the manuscript were primarily the work of Semroc and Tierce. Critical revision of the manuscript, analysis and interpretation of data, and statistical expertise were the work of Semroc, Tierce, and Fridman.

REFERENCES

1. Fleming ST, Kohrs FP. Linking claims and cancer registry data: is it worth the effort? *Clin Perform Qual Health Care*. 1998;6:88-96.
2. Potosky AL, Riley GF, Lubitz JD, Mentnech RM, Kessler LG. Potential for cancer related health services research using a linked Medicare-tumor registry database. *Med Care*. 1993;31:732-48.
3. Paul JE, Tilson HH. Use and opportunities for administrative data bases in pharmaco-economic research. In: Spilker B, ed. *Quality of Life and Pharmacoeconomics in Clinical Trials*. 2nd ed. Philadelphia, PA: Lippincott-Raven Publishers; 1996:1165-71.
4. Berndt ER, Russell JM, Miceli R, et al. Comparing SSR treatment costs for depression using retrospective claims data: the role of nonrandom selection and skewed data. *Value Health*. 2000;3:208-21.
5. Neupogen (filgrastim) prescribing information. Thousand Oaks, CA: Amgen; 2001.
6. Lyman GH, Lyman CG, Sanderson RA, Balducci L. Decision analysis of hematopoietic growth factor use in patients receiving cancer chemotherapy. *J Natl Cancer Inst*. 1993;85:48-93.
7. Glaspy JA, Bleecker G, Crawford J, Stoller R, Strauss M. The impact of therapy with filgrastim (recombinant granulocyte colony-stimulating factor) on the health care costs associated with cancer chemotherapy. *Eur J Cancer*. 1993;23A(suppl 7):S23-S30.
8. Holmes FA, O'Shaughnessy JA, Vukelja S, et al. Blinded, randomized, multicenter study to evaluate single administration pegfilgrastim once per cycle versus daily filgrastim as an adjunct to chemotherapy in patients with high-risk stage II or stage II/IV breast cancer. *J Clin Oncol*. 2002;20:727-31.
9. Crawford J, Ozer H, Stoller R, et al. Reduction by granulocyte colony-stimulating factor of fever and neutropenia induced by chemotherapy in patients with small-cell lung cancer. *N Engl J Med*. 1991;325:164-70.
10. Morrison VA, Picozzi V, Scott S, et al. The impact of age on delivered dose intensity and hospitalizations for febrile neutropenia in patients with intermediate-grade non-Hodgkin's lymphoma receiving initial CHOP therapy: a risk factor analysis. *Clin Lymphoma*. 2001;2:47-56.
11. Mitchell JB, Bubolz T, Paul JE, et al. Using Medicare claims for outcomes research. *Med Care*. 1994;32(7 suppl):JS38-JS51.
12. Huse D, Portnoy M. Constructing episodes of care from claims data: applications to pharmaco-economic and outcomes research. Paper presented at: Sixth Annual International Meeting of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) May 21-23, 2001; Washington, DC.
13. Miller TP, Dahlberg S, Cassady R, et al. Chemotherapy alone compared with chemotherapy plus radiotherapy for localized intermediate- and high-grade non-Hodgkin's lymphoma. *N Engl J Med*. 1998;339:21-26.
14. Fisher RI, Gaynor ER, Dahlberg S, et al. Comparison of a standard regimen (CHOP) with three intensive chemotherapy regimens for advanced non-Hodgkin's lymphoma. *N Engl J Med*. 1993;328:1002-06.
15. Lave JR, Pashos CL, Anderson GR, et al. Costing medical care: using Medicare administrative data. *Med Care*. 1994;32:JS77-JS89.