Administrative Data Algorithms to Identify Diagnosis- and Treatment-Related Measures in Patients With Multiple Myeloma: A Validation Study

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BACKGROUND

- It is estimated that multiple myeloma (MM) accounts for 0.8% (114,000) of all new cancer cases annually and 0.9% (63,000) of all cancer deaths annually worldwide[1,2]
- In the USA, an estimated 30,280 patients were diagnosed with MM and 12,590 patients died from MM in 2017[3]
- Although the long-term prognosis of MM is poor, developments in new therapies, including immunomodulatory drugs and proteasome inhibitors, have improved overall survival to a median of 5 years[4,5]
- Despite these advances in therapies, virtually all patients with MM eventually relapse and die from disease progression[6]
- Analyses of secondary administrative data (e.g. insurance claims) are frequently required to generate real-world evidence on current MM-related treatment patterns, costs, and outcomes of patients with MM in routine clinical practice
- Without access to definitive clinical information from patients' medical records, various claims-based algorithms have been used to identify and define key measures (e.g. diagnosis date, receipt of therapy)

OBJECTIVE

- To systematically assess the validity of claims data-based algorithms used to identify MM diagnosis- and treatment-related measures

METHODS

Study Design

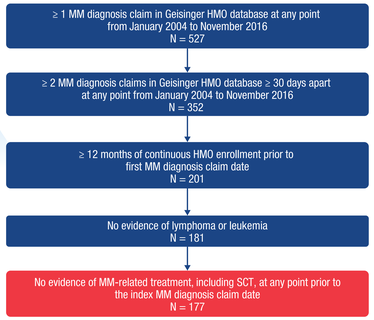
- A retrospective, noninterventional, observational study was implemented using administrative claims data from Geisinger Health, a large, integrated health-care delivery network in central, south-central, and northeast Pennsylvania, as well as in southern New Jersey
- In a cohort of patients with MM, specific algorithms were implemented to identify and define study measures
- Once defined in the claims data, these measures were adjudicated against a medical record review to assess the validity of the specific claims-based algorithms used to construct the measures
- The sample cohort was refined from an initial search of patients with ≥ 1 MM diagnosis claim in the database (Figure 1)

Claims-Based Algorithms

- The first MM-related drug administration date on or after the index MM diagnosis date was considered the start of first-line treatment; Table 1 provides the MM-related drug list and specific cycle requirements that were used for each drug
- All MM treatments of interest administered within the first 60 days after the first-line start date were considered part of the first-line regimen until the line ended under any of the following conditions (whichever occurred first):
  - Addition of (or switch to) a new MM drug (from the drug list presented in Table 1) after ≥ 60 days on the first-line regimen, unless the new drug was for maintenance therapy
  - A gap in all therapy of ≥ 180 days
- Initiation of a second-line treatment (except switching or initiation of a new steroid, i.e. either dexamethasone or prednisone monotherapy) was defined as progression

METHODS (cont.)

Figure 1. Sample Flow Chart



HMO, Health Maintenance Organization; MM, multiple myeloma; SCT, stem cell transplantation.

Table 1. Multiple Myeloma Drug List and Cycle Definitions

Drug[a]	Administration Route	Threshold for ≥ 1 Cycle, When Used in a Doublet Regimen[b]	Threshold for ≥ 1 Cycle, When Used in a Triplet Regimen[c]
Lenalidomide	Oral	21 days of supply in the first 30 days or 42 days of supply in the first 60 days	42 days of supply in the first 90 days
Bortezomib	Infusion/injection	4 doses in the first 30 days or 8 doses in the first 60 days	8 doses in the first 90 days
Thalidomide	Oral	21 days of supply in the first 30 days or 42 days of supply in the first 60 days	42 days of supply in the first 90 days
Melphalan	Infusion/ injection or oral	4 doses in the first 30 days (if oral, 4 days of supply) or 8 doses in the first 60 days (if oral, 8 days of supply)	8 doses in the first 90 days (if oral, 8 days of supply)
Cyclophosphamide	Infusion/ injection or oral	1 dose in the first 30 days (if oral, 4 days of supply) or 2 doses in the first 60 days (if oral, 8 days of supply)	2 doses in the first 90 days (if oral, 8 days of supply)
Doxorubicin	Infusion/injection	4 doses in the first 30 days or 8 doses in the first 60 days	8 doses in the first 90 days
Vincristine	Infusion/injection	4 doses in the first 30 days or 8 doses in the first 60 days	8 doses in the first 90 days
Steroid (dexamethasone or prednisone)	Oral	Any exposure	Any exposure

[a]Drugs like melphalan, cyclophosphamide, and steroids may also be used as monotherapy, and relatively uncommon drugs like etoposide, bendamustine, cisplatin, rituximab, pomalidomide, arsenic trioxide, busulfan, vorinostat, daratumumab, elotuzumab, ixazomib, carfilzomib, and panobinostat were considered part of the regimen if administered for at least 1 cycle. [b]Doublet regimens include: melphalan + prednisone; lenalidomide + dexamethasone; thalidomide + dexamethasone; and bortezomib + dexamethasone. [c]Triplet regimens include: cyclophosphamide + prednisone + lenalidomide; melphalan + prednisone + lenalidomide; melphalan + prednisone + thalidomide; bortezomib + cyclophosphamide + dexamethasone; bortezomib + melphalan + prednisone; bortezomib + lenalidomide + dexamethasone; bortezomib + thalidomide + dexamethasone; and vincristine + doxorubicin + dexamethasone.

Medical Record Review

- An in-field medical record review was conducted for the 177 patients identified using claims data, with the following elements captured using a data collection form: date of initial MM diagnosis, start and stop dates of each drug administered, and date of progression/recurrence (if observed)

METHODS (cont.)

- Using the abstracted data from the medical record review, treatment lines were defined using the following criteria:
  - Any MM-related drug was required to be administered for ≥ 30 days to be considered part of the first-line regimen, and for combination regimens, drugs were required to have an overlap of ≥ 30 days
  - The end of the first line was defined as either addition of (or switch to) a new MM-related drug (except steroids) or end of the study follow-up

Analyses

- Descriptive analysis was conducted for patient demographics and treatment patterns
- The validity of each claims-based study measure was assessed by computing agreement proportions and positive predictive values (PPVs):
  - Agreement proportion was defined as: (1) the proportion of patients with a claims-based algorithm-observed MM diagnosis date, first-line start date, and first-line stop date within 30 days of those ascertained from the medical record review; and (2) the proportion of patients with the same regimen observed from the claims-based algorithms and medical record review
  - PPV was defined as the number of true positives divided by the combined total of true positives and false positives
    - It was computed for: (1) diagnosis of MM, (2) receipt of first-line treatment, (3) disease progression after first-line treatment, and (4) receipt of second-line treatment

RESULTS

- At initial MM diagnosis, 68.9% of patients were aged ≥ 65 years; 54.8% of patients were male, and mean (standard deviation) duration of follow-up was 30.5 (30.3) months
- Of the 177 patients for whom medical record review was conducted, 74.0% were found to have evidence of MM; additional details on diagnosis from medical record review are shown in Table 2

Table 2. Evidence of Multiple Myeloma Diagnosis

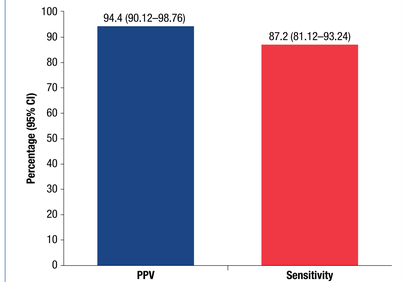
	Administrative Claims Database	Medical Record Review
Total patients, N (%)	177 (100)	177 (100)
Evidence of MM diagnosis (active disease), n (%)	177 (100)	131 (74.0)
MM only	NA	117 (66.1)
MM and smoldering	NA	10 (5.6)
MM and MGUS/plasmacytoma	NA	4 (2.3)
No evidence of MM diagnosis (active disease), n (%)	0	46 (26.0)
MGUS only	NA	6 (3.4)
Plasmacytoma only	NA	2 (1.1)
Smoldering only	NA	20 (11.3)
More than 1 of MGUS, plasmacytoma, or smoldering	NA	4 (2.3)
No evidence of MGUS, plasmacytoma, or smoldering	NA	14 (7.9)
PPV with medical record review as standard, % (95% CI)	74.0 (67.55–80.47)	

CI, confidence interval; MGUS, monoclonal gammopathy of undetermined significance MM, multiple myeloma; NA, not applicable; PPV, positive predictive value.

RESULTS (cont.)

- Among patients with confirmed MM diagnoses (n = 131), 84.7% (95% confidence interval [CI] 78.6–90.9) of patients had an initial MM diagnosis date from claims data within 30 days of the initial MM diagnosis date as ascertained from the medical record review
  - For 66.4% of patients, the difference in date of MM diagnosis was ≤ 7 days
- From the medical record review, 89.3% of patients were confirmed to receive first-line treatment, and 82.4% of patients were identified using the claims-based algorithms as receiving first-line treatment; the resulting PPV and sensitivity are shown in Figure 2

Figure 2. PPV and Sensitivity for Receipt of First-Line Treatment



CI, confidence interval; PPV, positive predictive value.

- Figure 3 and Table 3 show the distribution of broad categories and specific first-line regimens identified from the claims data and abstracted from the medical record review
- Among patients who received lenalidomide- or bortezomib-based first-line treatment, the difference in the start date of first-line treatment from the claims database and medical record review was ≤ 30 days for 84.5% of patients (95% CI 76.1–92.9), whereas the difference in stop date was ≤ 30 days for 45.1% of patients (95% CI 33.5–56.6)

Figure 3. First-Line Treatment Regimen Categories

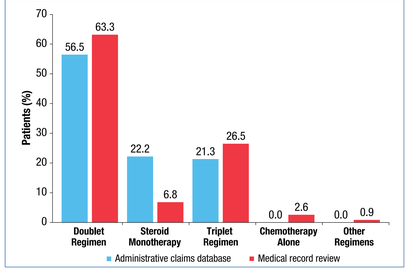


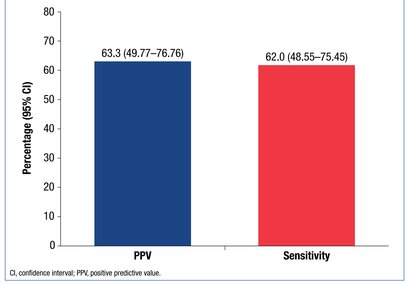
Table 3. First-Line Treatment Regimens and Agreement Proportions From the Administrative Claims Database and Medical Record Review

First-Line Treatment Regimens (n [%]) and Agreement Proportions (95% CI)	Administrative Claims Database (N = 108)	Medical Record Review (N = 117)
Lenalidomide- and bortezomib-based, n (%)	8 (7.4)	12 (10.3)
Bortezomib + lenalidomide + dexamethasone	8 (7.4)	12 (10.3)
Lenalidomide-based, n (%)	11 (10.2)	12 (10.3)
Lenalidomide + dexamethasone	11 (10.2)	12 (10.3)
Bortezomib-based, n (%)	53 (49.1)	58 (49.6)
Bortezomib + dexamethasone	37 (34.3)	43 (36.8)
Bortezomib + cyclophosphamide + dexamethasone	10 (9.3)	9 (7.7)
Bortezomib + thalidomide + dexamethasone	4 (3.7)	4 (3.4)
Bortezomib + thalidomide + dexamethasone + doxorubicin	1 (0.9)	0
Bortezomib + dexamethasone + carfilzomib	1 (0.9)	0
Bortezomib + melphalan + prednisone	0	1 (0.9)
Bortezomib + dexamethasone + doxorubicin	0	1 (0.9)
Agreement proportion for lenalidomide-based or bortezomib-based treatments, % (95% CI)	77.8 (68.17–87.38)	–
Non-bortezomib- or lenalidomide-based, n (%)	36 (33.3)	35 (29.9)
Agreement proportion for all treatments, % (95% CI)	66.7 (57.78–75.56)	–

CI, confidence interval.

- After receipt of first-line treatment, disease progression was observed among 45.4% of patients from the claims database and 48.7% of patients from the medical record review; PPV and sensitivity for disease progression are shown in Figure 4

Figure 4. PPV and Sensitivity for Disease Progression After First-Line Systemic Therapy



CI, confidence interval; PPV, positive predictive value.

- Second-line treatment was observed among 37.4% of patients from the claims database and 45.8% of patients from the medical record review
  - Resulting PPV was 71.4% (95% CI 58.8–84.1), and sensitivity was 58.3% (95% CI 45.9–70.8)

DISCUSSION

- A PPV of 74.0% (95% CI 67.6–80.5) was observed for identification of true MM diagnosis
  - A study by Whyte et al.[7] found that PPVs for identification of metastatic breast, lung, or colorectal cancer ranged from 55.0% to 82.0%
- High PPV and sensitivity were observed for the receipt of first-line systemic therapy
- Based on the claims database and medical record review, most patients received doublet regimens
  - As compared with the medical record review, analysis of the claims database showed a relatively greater proportion of patients identified as having received steroid monotherapy
- For lenalidomide- or bortezomib-based first-line treatment, the agreement for exact agents was 77.8% (95% CI 68.2–87.4)
  - A study by Carroll et al.[8] found that 82.8% of patients with breast cancer, 87.0% with colorectal cancer, and 95.0% with lung cancer had the same composition of first-line regimen when claims-based algorithms were compared with medical record review

CONCLUSIONS

- The claims-based algorithms assessed had a PPV or agreement proportion of > 70% for identifying true MM diagnoses, receipt of first-line therapy, and first-line lenalidomide- or bortezomib-based regimens
- Further understanding of discrepancies observed between the claims data and medical record review is needed to refine and improve the value of using claims data in conducting MM-related research

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DISCLOSURES

- R.P., S.C.: RTI Health Solutions, which received research funding from Celgene Corporation to perform this study – employment
- Z.C., K.P.: Celgene Corporation – employment, equity ownership

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