PD-1 Inhibitor Prescribing Patterns and Utilization Trends in a Large National Health Plan

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Background

The accelerated approval of nivolumab and pembrolizumab, both programmed death-1 (PD-1) inhibitors, provides new treatment options for several cancers. PD-1 agents will continue to be tested in many different disease states and are likely to be used off-label. Given the recency of PD-1 agents, little is known about the manner in which they will be prescribed by physicians and utilized by patients.

Objective

To track utilization and describe patterns of use of nivolumab and pembrolizumab within a large national health plan

Methods

Analysis: Retrospective observational

Data Source: Medical and pharmacy claims, and enrollment data, for individuals with commercial, Medicaid or Medicare health plan coverage from Humana Inc.; a healthcare company providing insurance for 14.2 million individuals in all 50 states (2016).[1]

Analysis Period: September 4, 2014 to March 31, 2016

- This analysis is a part of a recurring quarterly report. The results reflect data from the third quarter of 2014 through the first quarter of 2016.
- Index date: Date of PD-1 treatment initiation (i.e., nivolumab or pembrolizumab) as indicated by National Drug Codes (NDC)
- Pre-index period:
  - None required
  - For calculation of metastatic disease and cancer diagnosis (i.e., melanoma, lung cancer, kidney cancer), 6 months of continuous enrollment prior to index date was required.
  - Calculation of pretreatment(s) was identified from patients' entire claims data history.
- Follow-up period:
  - None required
  - Patients were followed post-index, until the earlier of disenrollment, death, or discontinuation, to identify outcome measures.

Measures:

- Index drug: Initiation of PD-1 therapy (i.e., nivolumab or pembrolizumab) indicated by NDC
  - Patients were assigned to the drug cohort associated with their index drug regardless of post-index switching.
- Patient demographics: Age, gender, race/ethnicity, geographic region, and health plan category, as indicated on index date

Measures continued:

- Baseline clinical characteristics: Index drug (i.e., nivolumab or pembrolizumab) and initiation quarter, as indicated on index date; metastatic disease, cancer diagnosis, pretreatment, measured during pre-index period
  - Metastatic disease: Identified by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM [196.xx, 197.xx, 198.xx]) and ICD-10-CM (C77.xx, C78.xx, C79.xx)
  - Cancer diagnosis: Melanoma (ICD-9-CM 172.xx, ICD-10-CM C43.xx) , lung cancer (ICD-9-CM 162.xx, ICD-10-CM C34.xx) and kidney cancer (ICD-9-CM 189.0, ICD-10-CM C64.xx)
  - Pretreatment: Drug therapy related to existing cancer diagnosis, identified by NDC, Current Procedural Terminology, and the Healthcare Common Procedure Coding System codes
- Outcome measures: Measured during follow-up period
  - Discontinuation: Gap in index drug therapy of at least 45 days without evidence of death or disenrollment during the 45 day window
  - Emergency department (ED) utilization: Identified by medical claims indicating ED as place of service; claims with the same service date as, or service date adjacent to, a hospitalization were not considered ED utilization
  - Inpatient utilization: Identified by medical claims indicating inpatient hospital facility as place of service; transfers (i.e., claims with the same discharge and admission date) were considered a single inpatient hospitalization
  - Outpatient utilization: Identified by medical claims indicating a non-physician office, outpatient facility, as place of service
  - Physician office visit: identified by medical claims indicating physician's office as place of service
  - Mortality: Total deceased patients; tabulated for the Medicare Advantage Prescription Drug population only

Inclusion Criteria and Exclusion Criteria: Those who initiated PD-1 therapy between September 4, 2014 and March 31, 2016 were included in the study sample. Continuous enrollment during the study period, including 6 month pre-index period, was required for analysis of pre-existing conditions, and pretreatment measures.

Statistical Analyses: Descriptive statistics were used to measure patient demographics, baseline clinical characteristics, and outcome measures. Outcome measures were measured per patient per month to account for varying follow-up.

Results

Table 1. Patient Demographics

Characteristic	Overall
N	1,133
Age in years, mean (SD)	68.7 (10.0)
Gender, *n* (%)	
Male	692 (61)
Race/ethnicity, *n* (%)	
White	822 (72.5)
African American/Black	114 (10.1)
Hispanic	7 (0.6)
Other	28 (2.5)
Unknown	162 (14.3)
Geographic region, *n* (%)	
Northeast	29 (2.6)
Midwest	224 (19.8)
South	775 (68.4)
West	105 (9.3)
Health plan category, *n* (%)	
Commercial	140 (12.4)
Medicare	974 (86.0)
MAPD	876 (77.3)
PDP	98 (8.6)
Medicaid	19 (1.7)

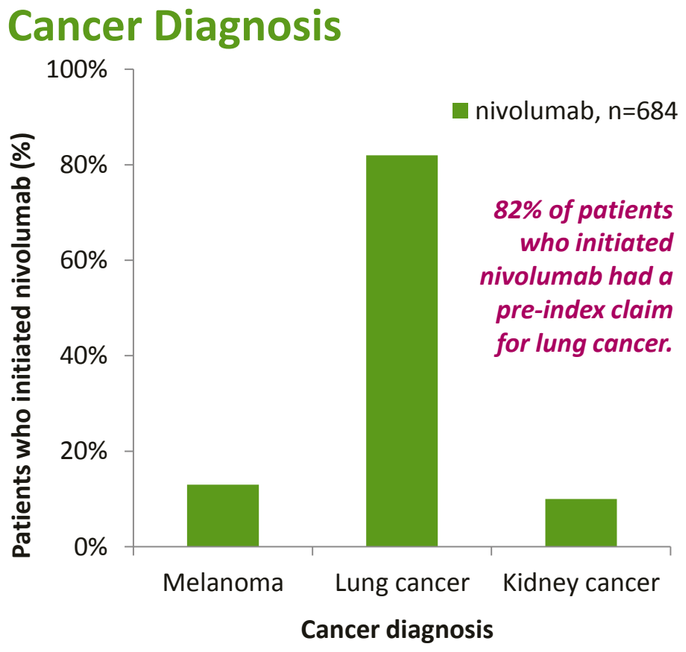
MAPD= Medicare Advantage Health and Prescription Drug; PDP= Prescription Drug Plan

Table 2. Baseline Clinical Characteristics

Diagnosis	Overall
N	1,133
Index drug, *n* (%)	
nivolumab	998 (88)
pembrolizumab	135 (12)
Presence of metastatic disease, *N*=762*	
Yes, *n* (%)	642 (84.0)
Cancer diagnosis, *N*= 762*	
Melanoma, *n* (%)	157 (20.6)
Lung cancer, *n* (%)	580 (76.1)
Kidney cancer, *n* (%)	66 (8.7)
Melanoma pretreatment, *N*=170**	
dabrafenib, *n*(%)	10 (5.9)
vemurafenib, *n*(%)	5 (2.9)
ipilimumab, *n* (%)	59 (34.7)
Lung cancer pretreatment, *N*=611**	
cisplatin, *n*(%)	47 (7.7)
carboplatin, *n*(%)	365 (59.7)
EGFR inhibitors, *n* (n%)	64 (10.5)
Kidney cancer pretreatment, *N*=68**	
anti-angiogenic or interferon therapy, *n* (%)	43 (63.3)

*Excludes PDP and those without 6 month pre-index enrollment;
**Includes the PDP line of business; cancer diagnoses are not mutually exclusive; EGFR= epidermal growth factor receptor

Figure 1. Nivolumab Initiation by Cancer Diagnosis



Excludes PDP and those without 6 month pre-index enrollment; cancer diagnoses are not mutually exclusive

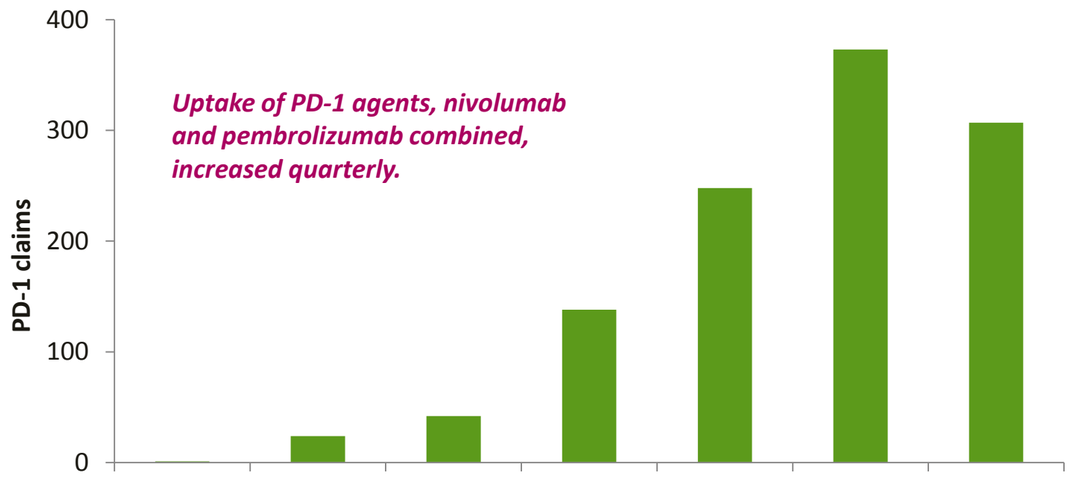
PD-1 agents appear to be used differently; nivolumab more frequently for lung cancer, and pembrolizumab more for melanoma.

Table 3. Outcome Measures

Measure	Overall
PD-1 drug claims PPPM , mean (SD)	1.8 (1.2)
nivolumab	1.8 (1.3)
pembrolizumab	1.4 (1.1)
Discontinuation, *n* (%)*	105 (14)
ED visits PPPM, median (IQR)	0.0 (0-0.7)
Inpatient visits PPPM, median (IQR)	0.0 (0-0.3)
Outpatient visits PPPM, median (IQR)	1.9 (0.3-3.5)
Physician visits PPPM, median (IQR)	2.7 (0.9-4.1)
Mortality, *n* (%)**	324 (37)

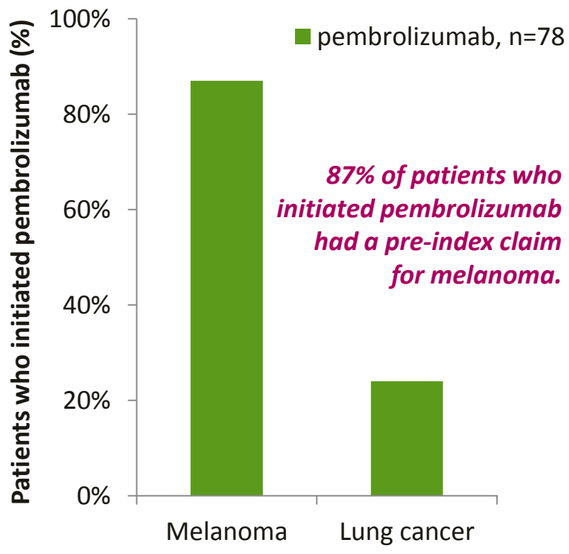
N=746; **N*=876, MAPD only; SD= standard deviation; IQR= interquartile range; PPPM= per patient per month; ED= emergency department

Figure 2. PD-1 Initiation by Quarter



*Due to the expected delay in medical claims processing, Q1, 2016 may not reflect all PD-1 claims

Figure 3. Pembrolizumab Initiation by Cancer Diagnosis



Excludes PDP and those without 6 month pre-index enrollment; cancer diagnoses are not mutually exclusive of one another

Conclusions

- Use of PD-1 therapy increased quarterly; more patients initiated therapy with nivolumab than pembrolizumab.
- Nivolumab was more commonly used to treat lung cancer, and pembrolizumab more often used to treat melanoma; which was likely due to differences in FDA labeling between nivolumab and pembrolizumab regarding program death ligand-1 expression testing for lung cancer.
- Continued review of prescribing trends is essential to ensure proper use of PD-1s.

Limitations

- This study utilized data for a population insured by a single health plan, and may not be generalizable to other populations.
- Findings are subject to limitations inherent to retrospective claims-based studies (e.g., coding errors, missing data, fixed variables, delays in claims adjudication).
- The descriptive nature of the analysis prevents inference of a temporal or causal relationship between measures.
- Given the nature of the structure of this analysis, follow-up period varied by measure, which could affect interpretation of results.

References

1. Humana Inc. Humana reports second quarter 2016 financial results; Reaffirms recent 2016 financial guidance increase. Available at: http://phx.corporate-ir.net/External.File?item=UGFyZW50SUQ9NjQyMzc2fFNoaWxkSUQ9MzQ3OTI2fFR5cGU9MQ==&t=1. Published August 3, 2016. Accessed August 31, 2016.

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