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The use of bevacizumab and ranibizumab for branch retinal vein occlusion in medicare beneficiaries

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ABSTRACT

Purpose: To describe the frequency and variation of intravitreal bevacizumab and ranibizumab use for branch retinal vein occlusion (BVO) in the United States (US).

Methods: We obtained a 5% random sample of Medicare beneficiaries from the Medicare Denominator and Physician/Supplier Part B claims files from 2010 to 2013 and identified all beneficiaries with an ICD-9-CM code for branch retinal vein occlusion (BVO, 362.36). Patient age, gender, race, state of residence and Charlson Comorbidity Index (CCI) scores were collected. *Healthcare Common Procedure Coding System* (HSCPS) codes for bevacizumab (J3590, J9035, and J3490) and for ranibizumab (J2778) were used to identify the mode of treatment for each patient. Patients who met the following criteria were excluded from this study: (1) under 65 years of age; (2) residence outside of the 50 United States or the District of Columbia; (3) no Part-B coverage or with HMO coverage that was not processed by Centers for Medicare & Medicaid Services (CMS); (4) concomitant diagnosis of diabetic edema (ICD-9: 362.07) or central retinal vein occlusion (ICD-9: 362.35); and (5) received both or none of the above two treatments. Geographic variation was examined by comparing injection frequencies across the nine US census divisions using Chi-squared analysis.

Results: During 2010–2013, a majority of the 3944 BVO patients who met the inclusion criteria received bevacizumab compared to ranibizumab (76.7% vs 23.3%). Most patients were aged 75–79 (22.0%) or 80–84 (22.0%), female (61.5%), white (88.3%), and had a CCI score of 1–2 (39.8%). The frequencies of bevacizumab and ranibizumab injections for BVO varied significantly between the US census divisions ($p < 0.0001$). The highest frequencies of bevacizumab use were in the Mountain (90.6%) and Pacific (82.7%) divisions while the highest frequencies of ranibizumab use were in the West North Central (37.9%) and Mid Atlantic (32.7%) divisions.

Conclusions and Importance: A majority of Medicare beneficiaries with BVO received bevacizumab compared to ranibizumab from 2010 to 2013, with significant geographic variation in the use of the two anti-VEGF agents. Future research into factors driving geographic variation in the use of these agents may help direct cost-effective strategies for the management of BVO.

1. Introduction

Retinal vein occlusion (RVO) is the second most prevalent retinal vascular disease after diabetic retinopathy and can lead to ocular neovascularization and visually-threatening macular edema.[1,2] Prior studies have demonstrated the efficacy of anti-vascular endothelial growth factor (anti-VEGF) agents including bevacizumab (Avastin®, Genentech), ranibizumab (Lucentis®, Genentech), and aflibercept (Eylea®, Regeneron Pharmaceuticals Inc) in treating macular edema secondary to RVO and maximizing visual improvement in these patients.[3–8] However, across all disease states, the cost of intravitreal anti-VEGF agents alone accounted for more than $2.6 billion annually within the fee-for-service (FFS) Medicare population by 2014.[9]

Significant cost differences exist between agents; in 2015, per unit,

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bevacizumab cost on average $67.50 while ranibuzmab cost $387.25, and aflibercept cost $962.85 (5 units of ranibizumab and 2 units of aflibercept are typically administered in treating RVO).[9] In addition, considerable variation exists with respect to the use of intravitreal anti-VEGF agents for the management of RVO.[10–12] Previous studies have identified regional and provider factors associated with overall variation in anti-VEGF use.[10–15] However, the geographic variation of anti-VEGF use for the treatment of RVO has not been well described. The public release of FFS Medicare claims data by the Centers for Medicare and Medicaid Services (CMS) in 2014 has enabled greater transparency in drug and payment variation.[16] Herein, we used a 5% Medicare Denominator and Physician/Supplier Part B claims database obtained from the CMS to evaluate the frequency and geographic variation of bevacizumab and ranibizumab for branch retinal vein occlusion (BVO) among beneficiaries from 2010 to 2013. We omitted aflibercept from the study as its approval for use in BVO did not take effect until 2014.

2. Materials and methods

2.1. Data collection

We obtained a 5% random sample of Medicare beneficiaries from the Medicare Denominator and Physician/Supplier Part B claims files maintained by the CMS from 2010 to 2013. All Medicare beneficiaries with BVO were identified using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis code for 362.36 and were extracted from the 5% Physician/Supplier Part B claims files.[15] The study was approved by the institutional review board of the University of California, Los Angeles.

All BVO patients were then merged with the 5% Denominator files, and their demographics, including age, gender, race, and state of residence, were extracted. The Charlson Comorbidity Index (CCI) scores were calculated based on the selected systemic diseases identified using ICD-9 diagnosis codes from the 5% Physician/Supplier Part B claims files. *Healthcare Common Procedure Coding System* (HCPCS) codes for bevacizumab (J3590, J9035, and J3490) and for ranibizumab (J2778) were used to identify the mode of treatment for each patient. The anti-VEGF agent aflibercept had not been approved by the US Food and Drug Administration (FDA) for use in BVO management until after the study period (October 2014) and was thus excluded from the present study.

Patients who met the following criteria were excluded from this study: (1) patients who were under 65 years of age; (2) patients who did not reside in the 50 United States or the District of Columbia; and (3) patients who did not have Part-B coverage or with HMO coverage that was not processed by CMS; (4) patients who had concomitant diagnosis of diabetic edema (ICD-9: 362.07) or central retinal vein occlusion (ICD-9: 362.35); and (5) patients who did not receive either of the above two treatments or if they received both types of treatment. All US regions were appropriately represented in the final sample.

2.2. Statistical analysis

Data analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC). Descriptive statistics were used to describe the characteristics for the study population. Geographic variation was examined by comparing injection frequencies across the nine US census divisions; Chi-square tests were used to calculate statistical significance of overall comparisons. Subgroup comparisons between two divisions were performed using Fisher exact test.

3. Results

A sample of 3944 patients was obtained (Table 1). Most patients were aged 75–79 (22.0%) or 80–84 (22.0%), female (61.5%), white (88.3%), and had a CCI score of 1–2 (39.8%).

Table 1
Baseline characteristics of patients receiving bevacizumab and ranibizumab injections for BVO from 2010 to 2013 (n = 3944).

Patient Characteristic	n (%)
Age (years)	
65–69	607 (15.4)
70–74	672 (17.1)
75–79	869 (22.0)
80–84	868 (22.0)
85–89	617 (15.6)
≥90	311 (7.9)
Sex	
Male	1520 (38.5)
Female	2424 (61.5)
Race	
White	3482 (88.3)
Black	262 (6.6)
Hispanic	59 (1.5)
Asian	71 (1.8)
Other or unknown	70 (1.8)
CCI score	
0	1100 (27.9)
1–2	1569 (39.8)
3–4	790 (20.0)
≥5	485 (12.3)
Anti-VEGF factor	
Bevacizumab	3025 (76.7)
Ranibizumab	919 (23.3)

BVO = branch retinal vein occlusion.
CCI = Charlson comorbidity index.
VEGF = vascular endothelial growth factor.

Table 2
Frequency of bevacizumab and ranibizumab injections within each United States Census Division[a] among patients with branch retinal vein occlusion (BVO) from 2010 to 2013 (n = 3944).

United States Census Division	Bevacizumab n (%)	Ranibizumab n (%)
New England	115 (78.8)	31 (21.2)
Mid Atlantic	380 (67.3)	185 (32.7)
East North Central	504 (79.0)	134 (21.0)
West North Central	190 (62.1)	116 (37.9)
South Atlantic	676 (76.0)	213 (24.0)
East South Central	205 (78.9)	55 (21.1)
West South Central	311 (81.0)	73 (19.0)
Mountain	213 (90.6)	22 (9.4)
Pacific	431 (82.7)	90 (17.3)

Data are no. (%).
[a] The census divisions are defined as follows: New England Division: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont; Middle Atlantic Division: New Jersey, New York, Pennsylvania; East North Central Division: Illinois, Indiana, Michigan, Ohio, Wisconsin; West North Central Division: Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, South Dakota; South Atlantic Division: Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia; East South Central Division: Alabama, Kentucky, Mississippi, Tennessee; West South Central Division: Arkansas, Louisiana, Oklahoma, Texas; Mountain Division: Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, Wyoming; Pacific Division: Alaska, California, Hawaii, Oregon, Washington.

From 2010 to 2013, the frequencies of bevacizumab and ranibizumab injections for BVO varied significantly between the US census divisions ($p < 0.0001$; Table 2). Among the sample population, a majority received bevacizumab compared to ranibizumab (76.7% vs 23.3%; see Table 3). The highest frequencies of bevacizumab use for BVO were in the Mountain (90.6%) and Pacific (82.7%) divisions while the highest frequencies of ranibizumab use were in the West North Central (37.9%) and Mid Atlantic (32.7%) divisions ($p < 0.0001$ for frequency distributions of Mountain v. West North Central, Mountain v.