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Physician-Industry Interactions and Anti-Vascular Endothelial Growth Factor Use Among US Ophthalmologists

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Abstract

Importance—The publication of the US Physician Payments Sunshine Act provides insight into the financial relationship between physicians and the pharmaceutical industry. This added transparency creates new opportunities of using objective data to better understand prior research that implicates pharmaceutical promotions as an important factor in a physician's decision-making process.

Objective—To assess the association between reported industry payments and physician-prescribing habits by comparing the use of anti–vascular endothelial growth factor (VEGF) intravitreal injections by US ophthalmologists to the industry payments these same physicians received.

Design, Setting, Participants—This study reviews data from the Centers for Medicare & Medicaid Services (CMS) 2013 Medicare Provider Utilization and Payment Data: Physician and Other Supplier Public Use File and the CMS-sponsored August through December 2013 Open Payments program (Physician Payments Sunshine Act). Ophthalmologists who prescribe anti-VEGF injections for all indications were analyzed.

Main Outcomes and Measures—Association between industry payments reportedly received and the number and type of anti-VEGF injections administered.

Results—A total of 3011 US ophthalmologists were reimbursed by CMS for 2.2 million anti-VEGF injections in 2013. Of these physicians, 38.0% reportedly received $1.3 million in industry payments for ranibizumab and aflibercept. Analysis revealed positive associations between increasing numbers of reported industry payments and total injection use (r = 0.24; 95% CI, 0.22–

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Study concept and design: Taylor, Vollman, Apte.

Acquisition, analysis, or interpretation of data: All authors.

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0.26; P < .001), aflibercept and ranibizumab injection use (r = 0.32; 95% CI, 0.29–0.34; P < .001), and percentage of injections per physician that were aflibercept or ranibizumab (r = 0.27; 95% CI, 0.25–0.29; P < .001). A smaller association was noted between greater number of industry payments and bevacizumab injection use (r = 0.07; 95% CI, 0.04–0.09; P < .001). Similar associations were found between the total dollars of reported industry payments received to injection use. Subgroup analysis further revealed that physicians receiving $1 to $25 in reported industry benefits were more likely than those not receiving industry payments to perform a greater percentage of their injections with aflibercept and ranibizumab.

Conclusions and Relevance—Among ophthalmologists who prescribe anti-VEGF medications, there is a positive association between reported pharmaceutical payments and increased use of aflibercept and ranibizumab injections. As is inherent to the design of correlation studies, this analysis cannot determine whether the payments reported caused the increased use, are a result of the increased use, or are merely associated with some other factor that causes the increased use.

Introduction

In an effort to increase the transparency of physician-industry relationships, the Physician Payments Sunshine Act was signed into law in 2010 in the United States and mandates public posting of all payments to physicians by the pharmaceutical industry. The Physician Payments Sunshine Act registry began tracking industry payments to physicians beginning August 2013, and it provides unique insight into the financial relationship between physicians and industry in the United States. For example, during the last 5 months of 2013, a total of 470 000 US health care professionals received $3.4 billion in industry payments.[1] Although this registry provides valuable understanding into the extent of physician-industry interactions, it does little to assess whether physician-industry relationships influence physician practice habits.

Within ophthalmology, the treatment of neovascular eye disease by intravitreal injections that block vascular endothelial growth factor (VEGF) provides a unique cohort to analyze this complex physician-industry relationship. Aflibercept (Eylea, Regeneron Pharmaceuticals Inc), bevacizumab (Avastin, Genentech), and ranibizumab (Lucentis, Genentech) are the primary anti-VEGF injections used. During the past decade, these drugs have significantly improved visual acuity outcomes in many common vision-threatening eye diseases, including neovascular age-related macular degeneration[2–4] and diabetic macular edema.[5–7] Two of these medications, aflibercept and ranibizumab, are approved by the US Food and Drug Administration (FDA) for intraocular use. Bevacizumab, a medication originally approved for treatment of colorectal cancer, is used off-label in ophthalmology and is usually prepared through compounding pharmacies with a mean price per dose of $60. This price is substantially less than the Centers for Medicare & Medicaid Services (CMS) allowable charges for ranibizumab ($1985 per dose) or aflibercept ($1960 per dose) in the treatment of neovascular age-related macular degeneration. Although bevacizumab has not gone through the same FDA approval process as aflibercept or ranibizumab, multiple randomized clinical trials reveal that bevacizumab has noninferior visual acuity outcomes and an analogous adverse effect profile compared with ranibizumab in the treatment of

neovascular age-related macular degeneration.[8–12] Given the substantially lower cost and equivalent visual acuity outcomes, many ophthalmologists use bevacizumab as first-line therapy for neovascular eye disease.

Because aflibercept and ranibizumab were specifically designed and FDA approved for intravitreal injection, they are marketed by their parent companies for that indication. In contrast, intraocular bevacizumab is used off-label and so is not marketed for ophthalmic use. Thus, analyzing prescribing habits of anti-VEGF injections among ophthalmologists provides a unique opportunity to assess the effect of physician-industry interactions on medication use because randomized clinical trials have demonstrated equivalence of the 3 most commonly used injections, 2 of which (aflibercept and ranibizumab) are extensively marketed to physicians and 1 of which (bevacizumab) is not marketed to ophthalmologists by the pharmaceutical industry.

Key Points

Question

Is there an association between industry payments and physician choice of anti–vascular endothelial growth factor injections?

Findings

Review of data from the US Centers for Medicare & Medicaid Services Open Payments reveal a positive association between increasing numbers of industry payments reported and proportion of aflibercept and ranibizumab injections used. Increasing numbers and amounts of industry payments correlated with correspondingly higher use of total aflibercept and ranibizumab injections more so than with bevacizumab.

Meaning

Although pharmaceutical payments to physicians are associated with increased use of aflibercept and ranibizumab, the study design cannot determine whether the payments reported caused increased use, resulted in increased use, or were associated with other factors that caused increased use.

Methods

Study Design and Participants

We performed a review of the CMS 2013 Medicare Provider Utilization and Payment Data: Physician and Other Supplier Public Use File[13] and the CMS-sponsored August through December 2013 Open Payments program (Physician Payments Sunshine Act).[14] Ophthalmologic uses of Healthcare Common Procedure Coding System (HCPCS) codes J2778 (ranibizumab injection) and J0178 (aflibercept injection) for all indications were reviewed and categorized as aflibercept or ranibizumab injections. All ophthalmologic uses of HCPCS codes J9035 (bevacizumab injection), J3490 (unclassified drugs), and J3590 (unclassified biologics) were reviewed and categorized as bevacizumab injections.

Through the open payments data set, all reported industry payments from Genentech and Regeneron Pharmaceuticals to ophthalmologists for “Lucentis” or “Eylea aflibercept injection” were assessed. Ophthalmologists with the same name and practice location in the 2 data sets were then merged into a single record. Physicians with the same name but different practice locations in the 2 data sets were queried through the American Society of Retina Specialists directory, and those who had a history of living or training in both the cities listed were merged into a single record and included in the analysis. Data were obtained on multiple variables, including injection type, physician location, injection reimbursement, and number and amount of reported payments from Genentech and Regeneron Pharmaceuticals.

Procedures

Prior research has demonstrated that nearly all J3490 (unclassified drugs) and J3590 (unclassified biologics) HCPCS codes used for patients with macular degeneration by ophthalmologists are for intravitreal bevacizumab.[15] To ensure that most of these injections in our cohort represented bevacizumab, we compared and found a similar mean reimbursement per injection of HCPCS codes J9035 (bevacizumab injection, $52.08), J3490 (unclassified drugs, $54.00), and J3590 (unclassified biologics, $49.95). Furthermore, we performed the overall study analysis 3 different ways to ensure that the small number of injections not bevacizumab billed with J3490 and J3590 codes did not alter the results. In the first analysis, J9035 (bevacizumab injection) alone was used to represent bevacizumab injections. In the second analysis, physicians with mean reimbursements of J3490 and J3590 injections less than $30 or greater than $80 were excluded, but all other J9035, J3490, and J3590 codes were incorporated as bevacizumab injections. In the third analysis, and represented in this article, are the results of all J9035, J3490, and J3590 injections, representing total bevacizumab injections. Similar correlation coefficients and significance values were found in each of the analyses.

The Medicare Provider Utilization and Payment Data: Physician and Other Supplier Public Use File data set tracks anti-VEGF injections by units of medication reimbursed and office visits associated with a reimbursement of an anti-VEGF medication. Because the dose of ranibizumab much more so than aflibercept or bevacizumab can vary by disease indication, use of the units of medication reimbursed as a surrogate for total injections administered is not ideal. Instead, our study uses the number of office visits associated with each intravitreal injection as a marker for total injections administered. However, this method fails to account for half of the injections in cases in which the same medication is injected into both eyes on a given day. In our analysis, we compared the total units reimbursed and total office visits associated with aflibercept and bevacizumab and found a 7.29% and 8.75% difference, respectively, between the 2 groups. This comparable decrease between aflibercept and bevacizumab was not thought to be substantial, and it was assumed that ranibizumab had a similar percentage of injections performed bilaterally.

The CMS characterizes payments from the pharmaceutical industry to physicians using 5 different categories: travel, food and beverage, consultation, education, and other compensation. Payments listed under the other compensation category typically represent

payments for serving as faculty or as a speaker at an event other than a continuing education program. Payments from Genentech and Regeneron Pharmaceuticals for “Lucentis” and “Eylea aflibercept injection” were categorized and defined by the number of industry payments (0, 1, 2, 3–5, >5) or dollars of industry payments received (grouped into 6 levels from $0 to >$1000).

Outcomes and Statistical Analysis

Statistical analysis was performed using SAS statistical software, version 9.3 (SAS Institute Inc). Testing was performed separately for industry-promoted medications (aflibercept and ranibizumab) and those not promoted by the pharmaceutical industry (bevacizumab). Descriptive statistics, nonparametric Wilcoxon 2-sample tests, and Kendall τ correlations were performed (95% CIs for rank order correlations) to analyze for the association between reported industry payments and use of intravitreal injections. The percent injections formulas were performed by calculating each physician’s percentage of injections per medication category and then taking the average of that value for each experimental group. Results are presented as the mean, SD, and correlation coefficient. A subgroup analysis using the nonparametric Kruskal-Wallis test was used to determine whether the association was consistent at each level of industry payments. Results of this analysis are presented as medians and interquartile ranges (IQRs).

Results

A total of 3011 different physicians were reimbursed by CMS for 2 201 127 anti-VEGF injections in 2013 for all indications. A total of 1835 physicians performed 476 885 aflibercept injections, 2854 physicians performed 1 082 279 bevacizumab injections, and 1629 physicians performed 641 963 ranibizumab injections. A total of 1144 of the physicians received $1 320 783.60 in reported industry payments from Genentech or Regeneron Pharmaceuticals for “Lucentis” or “Eylea aflibercept injection” (Table 1).

Analysis was then directed at testing the primary hypothesis: whether there is a nonzero association between reported industry payments and aflibercept and ranibizumab vs bevacizumab use. Physicians accepting industry benefits performed a median of 53.6% (IQR, 23.0%−82.67%) of their injections with aflibercept or ranibizumab. In comparison, the 1867 physicians who did not receive industry benefits performed a median of 16.5% (IQR, 0%−54.0%) of their injections with aflibercept or ranibizumab ($P < .001$).

The review next compared the association between increasing numbers of reported industry payments to the amount and percentage of injections used (Table 2). Analysis revealed a correlation between increasing numbers of industry payments to increasing amounts of total injections ($r = 0.24$; 95% CI, 0.22–0.26; $P < .001$), aflibercept and ranibizumab injections (r = 0.32; 95% CI, 0.29–0.34; $P < .001$), and percentage of injections per physician that were aflibercept or ranibizumab ($r = 0.27$; 95% CI, 0.25–0.29; $P < .001$). The percentage of bevacizumab injections per physician was inversely correlated with the number of industry payments reported ($r = −0.27$; 95% CI, −0.25 to −0.29; $P < .001$). A small correlation between increasing numbers of industry payments and bevacizumab injections was also noted ($r = 0.07$; 95% CI, 0.04–0.09; $P < .001$).

We then analyzed dollars of industry payments reported to the injection use of the 2 experimental groups (Table 3) and determined the correlation coefficient between total injections and dollars of reported industry payments ($r = 0.22$; 95% CI, 0.20–0.24; $P < .001$). Likewise, as the dollars of industry payments per physician increased so, too, did the use of aflibercept and ranibizumab injections ($r = 0.29$; 95% CI, 0.27–0.31; $P < .001$). We also determined the correlation between percentage of injections that were aflibercept or ranibizumab and the dollars of industry payments reported ($r = 0.25$; 95% CI, 0.23–0.28; $P < .001$). In addition, physicians in this cohort receiving greater than $1000 in reported industry payments had the highest use of anti-VEGF injections overall but the lowest use of bevacizumab injections of any of the groups. There was a small correlation between bevacizumab injection use and dollars of industry payments reported ($r = 0.06$; 95% CI, 0.04–0.09; $P < .001$).

Next, the use of injections by ophthalmologists who had minimal interaction with the pharmaceutical industry compared with those who received no reported industry payments was assessed. Analysis revealed a difference in the percentage of aflibercept and ranibizumab medications used in physicians receiving $1 to $25 in industry payments when compared with those not accepting industry benefits ($P < .001$). A similar association was also noted when comparing the percentage of aflibercept and ranibizumab injections in those who received no reported industry payments to those accepting a single payment from the pharmaceutical industry ($P < .001$).

Finally, a subgroup analysis comparing the proportion of aflibercept and ranibizumab injections to bevacizumab injections per physician at each of the levels of reported industry payments in Table 2 and Table 3 was performed to determine the consistency of the overall effects noted in the global analyses. The median proportion of aflibercept and ranibizumab injections was different from bevacizumab injections in the 0, 1, 3 to 5, and greater than 5 payments groups (67.0%, 26.0%, 28.8%, and 56.2% difference in each group, respectively; $P < .001$). A difference was not identified in the median proportion of aflibercept and ranibizumab compared with bevacizumab injections in the 2 payments group (7.8% difference, $P = .81$) (Table 4). When the cohort by dollars of industry payments is analyzed, the median proportion of aflibercept and ranibizumab injections was different from bevacizumab in the $0 (67.0%), $1 to $24.99 (10.4%), $200 to $999.99 (35.2%), and greater than $1000 (58.0%) groups ($P < .001$, .02, .006, and <.001, respectively). A difference in the proportion of aflibercept and ranibizumab injections in the $25 to $99.99 (4.6%) and $100 to $199.99 (5.8%) groups was not identified ($P = .84$ and $P = .45$, respectively) (Table 5).

Discussion

Each of the primary analyses within this study had similar results. As the amount of interactions between physicians and the pharmaceutical industry increased so, too, did the use of aflibercept and ranibizumab. This correlation was most pronounced when comparing aflibercept and ranibizumab injection totals and percentage of aflibercept and ranibizumab injections per physician to the number of industry interactions recorded. Our findings further indicate an association between increasing numbers and dollars of industry benefits to numbers of bevacizumab injections administered. This correlation was smaller than any of

the other analyses and, given the large sample size of the overall study, may not be clinically meaningful, even though statistically significant. Overall, the study results indicate that increasing numbers and dollars of industry interactions correlated with a correspondingly higher use of aflibercept and ranibizumab injections much more so than bevacizumab. Because of the organization of observational studies, the noted correlation cannot prove whether the payments reported caused the increased use, are a result of the increased use, or are merely associated with some other factor that causes the increased use.

The purpose of the subgroup analysis (Table 4 and Table 5) was to assess whether there was consistency within groups of the overall study results reported in Table 2 and Table 3. The finding that there were similar proportions of aflibercept and ranibizumab injections compared with bevacizumab injections in the groups representing moderate amounts of industry interactions was not surprising because they corresponded to where physician preferences transitioned from predominately bevacizumab to aflibercept or ranibizumab injections. Thus, although the aggregate trend was a positive association between industry payments and aflibercept and ranibizumab injection use, those subgroups captured where the proportion of injections between groups was different.

Although some would have analyzed each anti-VEGF medication separately, we chose to group aflibercept and ranibizumab into a single category for a variety of reasons. First, the data analyzed were from the first reporting of industry payments to physicians through the Physician Payments Sunshine Act, and so without being able to compare year-to-year variability in amount and type of industry reimbursements, it is difficult to determine whether different pharmaceutical companies are uniform in how they report payments to physicians. Second, a substantial proportion of intravitreal injections are used for diabetic macula edema, and aflibercept was not FDA approved for that indication in 2013. This had a meaningful effect on aflibercept prescribing by physicians and could have covered any observable effect of physician-industry interactions on the use of aflibercept. Third, aflibercept was still relatively new to the market in 2013, and more factors, such as accessibility, likely influenced its use more than the more established anti-VEGF medications bevacizumab and ranibizumab.

Because of the organization of the CMS databases, this study has several limitations. To protect patient privacy, physicians administering any of the injections analyzed to fewer than 10 patients are not included, which likely had little effect on our analysis because most participating physicians have many patients receiving injections. Another limitation of the study is that the results do not include injections reimbursed by insurance plans aside from the CMS. Furthermore, our analysis of the CMS data revealed that some retina specialists billed CMS for HCPCS code 67028 (injection of drug into eye) but did not additionally bill with HCPCS codes that specify drug type. This practice likely occurs more frequently in large multi-physician groups, where injection charges are sometimes managed through a single physician, and raises concerns about whether the database accurately associates injections to the physician performing the procedure. However, institutions that bill in this manner are considered the exception rather than the rule, and the large number of physicians analyzed in our cohort likely minimizes any potential bias this could introduce.

Bevacizumab is also different than aflibercept or ranibizumab in that it is a repackaged medication. As such, there are ancillary factors in some locations, such as state pharmacy laws or institutional physician practice plan regulations, that may skew anti-VEGF use away from bevacizumab injections by restricting the ability to use repackaged anti-VEGF medications. The effects of these potentially confounding variables, although important at an individual physician level, are likely to be minimal in our large global analysis. Use of a repackaged medication could also potentially increase the risk of developing endophthalmitis. Although this possibility exists, it is a procedural risk universal to every physician in our cohort and so would not be expected to affect physicians differently between our experimental categories. An additional difference between the medications is that rebate programs exist for 1 of the industry-promoted medications. This program provides financial incentive for physicians who perform large numbers of injections to choose that medication and so would be expected to disproportionately influence high injection users to use injections in the aflibercept and ranibizumab category. This potentially confounding factor is difficult to account for and should be considered while viewing the results of our analysis.

Despite the strong correlation between reported industry payments and aflibercept and ranibizumab use, the results are unable to prove how each variable affects the other. One possible conclusion is that physician-industry interactions influence physician-prescribing behavior. Alternatively, the findings can be seen as the outcome of the pharmaceutical industry involving physicians who prescribe their medications in activities for which payments are provided. Finally, the findings may be the result of a separate factor that causes increased aflibercept and ranibizumab use to which these 2 variables are independently associated. As future iterations of the CMS Medicare Provider Utilization and Payment Data: Physician and Other Supplier Public Use File data sets are published, comparing past pharmaceutical payments to subsequent physician-prescribing habits may help clarify how each variable affects the other. Furthermore, the process through which physicians arrive at a decision on what therapeutic route to pursue in the treatment of a given disease is complicated and often multifactorial, especially when multiple treatment options exist that reveal similar outcomes. During the past several years, multiple authors[16–27] have studied and commented on the effect of industry interactions on physician-prescribing habits. These articles[16–27] reveal the extent of physician-industry interactions and often find that gifts to physicians from the pharmaceutical industry correlate to altered prescribing behavior. We believe our study adds to this knowledge by revealing a positive association between physician-industry interactions and a preference for industry-promoted medications in a large national cohort. As in prior studies,[17–20,22–27] our work fails to prove a causative relationship, but it implicates industry interactions as a possible contributory factor on a physician's decision making.

Conclusions

Although unable to prove a causal relationship, this analysis reveals a positive association between reported pharmaceutical payments to ophthalmologists and use of aflibercept and ranibizumab injections. In addition, the claim by prior authors[25]that small gifts may be as influential as large gifts is supported by revealing differences in practice patterns with even 1

reported payment or reported payments less than $25 from industry. Not only does this study reveal how the Physician Payments Sunshine Act can be used in connection with other data sets to understand physician-industry relationships in ophthalmology, it illustrates the types of studies that can be performed within many disciplines of medicine to understand complex relationships.

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Table 1.

Reported Industry Payments to Physicians Prescribing Anti – VEGF Injections for Ranibizumab and Aflibercept

	Genentech			Regeneron Pharmaceuticals			Industry Total		
Payment Type	**No. of Physicians**	**No. of Payments**	**Payment Amount, $**	**No. of Physicians**	**No. of Payments**	**Payment Amount, $**	**No. of Physicians**	**No. of Payments**	**Payment Amount, $**
Consultation	50	78	191 753.56	34	56	163 737.25	74	134	355 490.81
Education	67	69	5 902.00	63	82	816.72	129	151	6 718.72
Food and beverage	681	1339	71 680.56	798	1608	64 719.95	1104	2947	136 400.51
Other compensation	37	106	301 926.87	44	129	306 547.55	71	235	608 474.42
Travel	53	180	127 246.96	97	410	86 452.18	136	590	213 699.14
Total	720	1772	698 509.95	827	2285	622 273.65	1144	4057	1 320 783.60

Abbreviation: VEGF, vascular endothelial groeth factor.

Table 2.

Injection Use by Number of Reported Industry Payments[a]

	Mean (SD)			Injections by Category, %		
No. of Reported Industry Payments	**Total Injections**	**Aflibercept and Ranibizumab Injections**	**Bevacizumab Injections**	**Mean Aflibercept and Ranibizumab**	**Mean Bevacizumab**	**SD**
0 (n = 1867)	583.07 (690.54)	242.75 (455.00)	340.33 (425.54)	29.6	70.4	33.6
1 (n = 434)	786.21 (758.76)	404.56 (573.50)	381.64 (431.75)	42.0	58.0	33.3
2 (n = 274)	930.47 (789.83)	517.42 (589.27)	413.05 (444.66)	50.6	49.4	32.7
3–5 (n = 278)	1147.84 (852.14)	727.74 (691.25)	420.10 (482.96)	58.0	42.0	31.5
>5 (n = 158)	1248.52 (840.37)	923.91 (757.74)	324.61 (330.22)	67.6	32.4	28.5
Correlation coefficient (95% CI)[a]	0.24 (0.22 to 0.26)	0.32 (0.29 to 0.34)	0.07 (0.04 to 0.09)	0.27 (0.25 to 0.29)	−0.27 (−0.25 to −0.29)	NA

Abbreviation: NA, not applicable.

[a] $P < .001$ for all comparisons. Correlation coefficients, 95% Cls, and significance calculations were derived using continuous variables.

Table 3.

Injection Use by Dollars of Reported Industry Payments[a]

	Mean (SD)			Injections by Category, %		
Reported Industry Payments, $	**Total Injections**	**Aflibercept and Ranibizumab Injections**	**Bevacizumab Injections**	**Mean Aflibercept and Ranibizumab**	**Mean Bevacizumab**	**SD**
0 (n = 1867)	583.07 (690.54)	242.75 (455.00)	340.33 (425.54)	29.6	70.4	33.6
1–24.99 (n = 264)	841.08 (789.62)	442.86 (572.63)	398.21 (425.54)	45.5	54.5	32.8
25–99.99 (n = 343)	974.44 (792.91)	546.90 (615.63)	427.54 (448.90)	49.8	50.2	32.5
100–199.99 (n = 282)	906.96 (791.41)	536.96 (667.21)	370.00 (398.62)	48.8	51.2	33.8
200–999.99 (n = 140)	1097.38 (861.50)	717.31 (669.11)	380.07 (489.98)	58.6	41.4	33.5
>1000 (n = 115)	1277.00 (893.26)	950.39 (791.61)	326.61 (314.66)	68.4	31.6	28.1
Correlation coefficient (95% CI)[a]	0.22 (0.20 to 0.24)	0.29 (0.27 to 0.31)	0.06 (0.04 to 0.09)	0.25 (0.23 to 0.28)	−0.25 (−0.23 to −0.28)	NA

Abbreviation: NA, not applicabl e.

[a] $P < .001$ for all comparisons. Correlation coefficients, 95% Cls, and significance calculations were derived using continuous variables.

Table 4.

Proportion of Aflibercept and Ranibizumab Injections to Bevacizumab Injections by Number of Reported Industry Payments

	Injections by Category, Median, %		
No. of Reported Industry Payments	**Aflibercept and Ranibizumab**	**Bevacizumab**	***P* Value**
0 (n = 1867)	16.5	83.5	<.001
1 (n = 434)	37.0	63.0	<.001
2 (n = 274)	53.9	46.1	.81
3–5 (n = 278)	64.4	35.6	<.001
>5 (n = 158)	78.1	21.9	<.001

Table 5.

Proportion of Aflibercept and Ranibizumab Injections to Bevacizumab Injections by Dollars of Reported Industry Payments

	Injections by Category, Median, %		
Reported Industry Payments, $	**Aflibercept and Ranibizumab**	**Bevacizumab**	***P* Value**
0 (n = 1867)	16.5	83.5	<.001
1–24.99 (n = 264)	44.8	55.2	.02
25–99.99 (n = 343)	52.3	47.7	.84
100–199.99 (n = 282)	47.1	52.9	.45
200–999.99 (n = 140)	67.6	32.4	.006
>1000 (n = 115)	79.0	21.0	<.001