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Biosimilars engage in low levels of direct-to-physician marketing relative to reference biologics

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Abstract

Biosimilars have the potential to greatly reduce US spending on biologic drugs, but uptake of these competitor products varies. We used Open Payments data from 2014 to 2022 to proxy for direct-to-physician marketing and compared levels of activity between biologic and biosimilar drug manufacturers. Our analysis focused on 6 reference biologics that recently faced competition in the years immediately before and after the launch of the first biosimilar. We used Medicare Part B dosage units to measure market penetration of biosimilars and its relationship with biosimilar marketing activity. Last, we conducted a sensitivity test, comparing payments for primarily office- or hospital-based physicians, using affiliations constructed from Medicare Carrier claims. Reference biologic manufacturers greatly reduced the amount of direct-to-physician marketing in the post-launch period. Biosimilar manufacturers generally engaged in low levels of activity relative to the historic performance of reference biologics. These trends were consistent across office- and hospital-based physicians. The intensity of biosimilars' direct-to-physician marketing also had no apparent relationship with achieved market penetration. Our findings demonstrate that persistently high market shares of reference biologics cannot be explained by ongoing direct-to-physician marketing activities. At the same time, while such activities could educate physicians or induce switching, biosimilar entrants engaged in little direct-to-physician marketing.

Key words: biologics; biosimilars; direct-to-physician marketing; open payments; generic drugs; health economics.

Introduction

In recent years, over 40% of drug spending in the United States was for biologics, prescription therapies distinguished from small-molecule drugs by structural complexity and manufacturing methods.[1] Historically, many biologics had no close competitors, even after expiry of relevant patents and legal exclusivities.[2] In 2015, the Food and Drug Administration (FDA) first approved a "biosimilar," meaning a competitor to the original "reference biologic" that is verified to have no "clinically meaningful" differences.[3] As patients and physicians substitute with biosimilars, the savings in prescription drug spending could be substantial, both because biosimilars launch at lower prices and because competitive pressures may induce price reductions for the reference biologic.[4] However, substitution with biosimilars has been rather irregular across products and has lagged behind European countries.[4-7]

Marketing activities by reference biologics could explain this uneven substitution with biosimilars in the United States. Firms that manufacture reference biologics use direct-to-physician marketing activities, such as face-to-face visits, commonly accompanied by a free meal. These activities can serve an educational purpose; manufacturers often provide information about a drug's mechanism of action, clinical trial performance, and side effects. These interactions with physicians also increase prescribing, even after accounting for the targeting of payments on likely prescribers.[8-10] Following the launch of a biosimilar, the manufacturer of a reference biologic may sustain or redouble marketing activities to preserve physician preferences and deter substitution.

Biosimilar manufacturers could use these same marketing activities to promote substitution. A recent survey revealed physician uncertainty about the substitutability, indications, and regimen of biosimilars, as well as improved confidence after an informational intervention.[11] Therefore, direct-to-physician marketing encounters could reassure physicians that biosimilars have the same safety and efficacy as reference biologics and answer questions about the experience of patients who switch.

In this paper, we measured direct-to-physician marketing activities for 6 reference biologics that experienced the launch of 1 or more biosimilars, and the biosimilars themselves. We examined how payment records in Open Payments, our proxy for marketing activities, evolved for biosimilars and reference biologics in the periods before and after the launch of the first biosimilar. We also tested whether these trends differed for physicians based in an office or hospital setting. Finally, we probed the relationship between the intensity of biosimilar marketing payments and biosimilar market penetration in Medicare Part B.

Data and methods

To construct our sample of reference products and biosimilars, we used the FDA list of approved biosimilars and associated reference products, combined with industry reports for biosimilar launch dates.[12,13] To enable 8 quarters of follow-up, we included reference products with a launched biosimilar as of December 2020 and all biosimilars for those reference products launching within 8 quarters of the first. We excluded

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Amgen's Epogen (molecule epoetin alfa, also marketed by Johnson & Johnson as Procrit) because of disruptions due to changing clinical guidelines.[14] Our analysis sample included 22 distinct drugs: 6 reference products and 16 biosimilars (Appendix Table S1). These biosimilars constituted 95% of Part B biosimilar expenditures in 2021; although some drugs were also reimbursed through Part D, physician administrations under Part B comprised 93% of total drug spending in 2021. Most of the drugs in our sample treat cancer (Genentech's Avastin, Herceptin, Rituxan; and their biosimilars) or alleviate the side effects of cancer treatment (Amgen's Neupogen and Neulasta; and their biosimilars). Remicade (Johnson & Johnson) and its biosimilars are immunomodulators, commonly used for ulcerative colitis or Crohn's disease.

We identified Open Payments records containing the trade or nonproprietary name of each reference biologic and biosimilar. Open Payments is a database of mandatorily reported financial transfers between drug companies and health care providers, describing the date, recipient, and associated drug(s) for each transfer. Transfers can be cash or in-kind, typically in the form of meals, travel reimbursements, and consulting or speaking fees. We refer collectively to these transfers as "payments," which proxy for direct-to-physician marketing activities. To focus on interactions with physicians, we studied non–research-related general industry payments and excluded those made to teaching hospitals. The Open Payments data span from August 2013 to December 2022 and were downloaded on July 4, 2023.

We aggregated the number of payments to the drug-quarter level and defined time relative to the launch of the first biosimilar competitor to make comparisons around this key event. We chose the biosimilar date of launch (ie, first sales) rather than date of FDA approval to account for delays induced by patent disputes. We focused our analysis on the 4 quarters before, and up to 12 quarters after, the first biosimilar launch; thus, our sample period spans from July 2014 to December 2022. While this period captured the launch of more recent biosimilars, it included the COVID-19 pandemic. Appendix Figures S1 through S6 detail marketing activities by drug over time; payments were relatively low in 2020 but rebounded in subsequent periods.

We supplemented these marketing data with information from the Centers for Medicare and Medicaid Services (CMS). From the Medicare Part B Drug Dashboard (2016–2021), we collected annual dosage units by drug among the fee-for-service Medicare population; these results may not be representative of Medicare Advantage, commercial, or Medicaid populations. We referenced the 2 full calendar years available following the first biosimilar launch (Appendix Table S1). We also obtained quarterly average sales price by drug from published lists (2013–2021). Finally, to determine how marketing activities related to practice setting, we used individual-level Medicare Carrier claims (2014–2020) to determine whether physicians were predominantly office-based or hospital-affiliated.

This study was approved by the Institutional Review Board of Cornell University.

Results

Figure 1 depicts the average number of quarterly payments made by manufacturers of reference biologics in the 4 quarters prior (dark blue) and 8 quarters after (light blue) the launch of the first biosimilar, as well as manufacturer payments for the entering biosimilar(s) in the 8 quarters after launch (orange). We note that manufacturers of all 6 reference biologics reduced the intensity of direct-to-physician marketing activity following the biosimilar launch. The decline in reference activity from the pre- to post-launch period ranged from 25% (Neulasta) to 88% (Herceptin). These dynamics are further detailed in Appendix Figure S7, which depicts payments for reference biologics in the 12 quarters after first biosimilar launch, normalized by the payments in the 4 quarters before launch. Although reference payments declined across the board, 2 distinct patterns emerged. For one group (Neupogen, Remicade, Neulasta), payments gradually adjusted downward over time; in the year after launch, reference payments were 49% to 90% of pre-period levels. For the remaining reference products (Avastin, Herceptin, Rituxan), marketing payments were cut to less than 10% of pre-launch levels within the first year. The latter group shared a common manufacturer (Genentech),

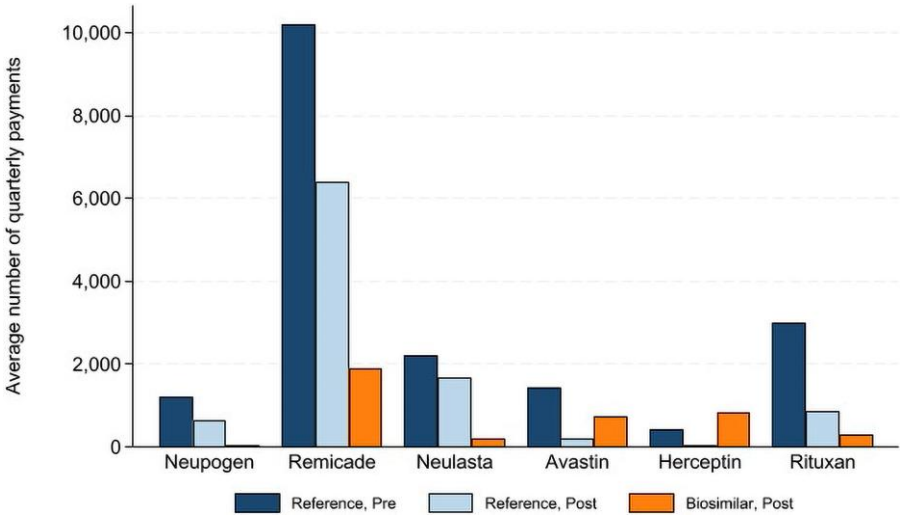

Figure 1. Average number of marketing payments in the periods before and after the launch of the first biosimilar. Biosimilar marketing payments reflect all products launched within 2 years of the first. The pre-period is only relevant for the reference product, and marketing payments are averaged over 4 quarters. In the post-period, marketing payments for reference and biosimilar products are averaged over 8 quarters.

which may explain similarities in the responses to biosimilar competition (see Appendix Table S1 for manufacturer information).

Figure 1 also shows that manufacturers of entrant biosimilars generally engaged in less direct-to-physician marketing activity. In the markets for Neupogen, Neulasta, and Rituxan, Open Payments encounters for biosimilars were low relative to the reference biologic (4% to 10% of pre-launch volume) and relative to the other launched biosimilars (the number of post-period payments averaged 182 vs 1160). This suggests that physicians interested in using these biosimilar products did not receive marketing visits that might have prompted them to transition patients to the biosimilar. Biosimilar activity was relatively more robust in the cases of Remicade, Avastin, and Herceptin, where 1 biosimilar among the early-launch cohort engaged in meaningful levels of marketing (Appendix Figure S8). However, among Remicade and Avastin biosimilars, the level was still well below that of the reference biologic in the year prior to launch (19% and 51%, respectively). Only the biosimilars for Herceptin exceeded the number of marketing payments made by the reference biologic manufacturer in the previous year by nearly 2-fold.

There is little apparent correlation between the intensity of biosimilar manufacturers' marketing activities and their success at inducing substitution away from reference biologics. Figure 2 shows the relationship between the relative intensity of biosimilars' direct-to-physician marketing activity and biosimilar Part B penetration. The *y*-axis plots biosimilar marketing payments in the 2 years after launch as a share of the payments made by the reference biologic manufacturer in the year prior to launch (ie, the ratio of the orange and dark blue bars in Figure 1). The *x*-axis plots the biosimilar market penetration rate, calculated as the number of dosage units for the biosimilar(s) as a share of the total dosage units for either the reference biologic or its biosimilar(s) in the 2 years following the first launch. Four reference biologics (Remicade, Neulasta, Rituxan, and Neupogen) faced little biosimilar marketing activity (low *y*-axis value), and biosimilar penetration rates remained between 10% and 36% of the market. Herceptin is the only drug in our sample for which biosimilar marketing intensity exceeded that of the reference biologic (*y*-axis value >1), and the biosimilar penetration rate was 48%. In comparison, the manufacturers for Avastin's biosimilars achieved a similar penetration rate (50%) while engaging in less marketing relative to the reference biologic. Appendix Figure S9 suggests that the biosimilar penetration rate was better explained by the ratio of the biosimilars' average sales price to that of the reference biologic.

Finally, we considered patterns of direct-to-physician marketing for office-based and hospital-affiliated physicians. Biosimilar uptake has been slower in hospital settings,[15,16] because physicians often are constrained to choosing products from a hospital formulary. As such direct-to-physician marketing for biosimilars might optimally target office-based physicians who face no such constraints. As shown in Appendix Figure S10, the setting-specific dynamics are largely similar to the marketing activities overall. In addition, the manufacturers of biosimilars and reference products target office-based physicians in similar proportion, and reference manufacturer behavior does not change much after the first launch (Appendix Figure S11).

Discussion

We assessed the potential role of direct-to-physician marketing in explaining the variable substitution towards biosimilars for 6 reference products that faced biosimilar competition. We documented two facts. First, reference biologic manufacturers generally curtailed their marketing activity after the launch of a biosimilar. Reference payments in the 2 years post-launch averaged 41% of pre-launch levels. This finding rules out the possibility that sustained or redoubled marketing efforts among reference biologic manufacturers contribute to their persistently high market shares.

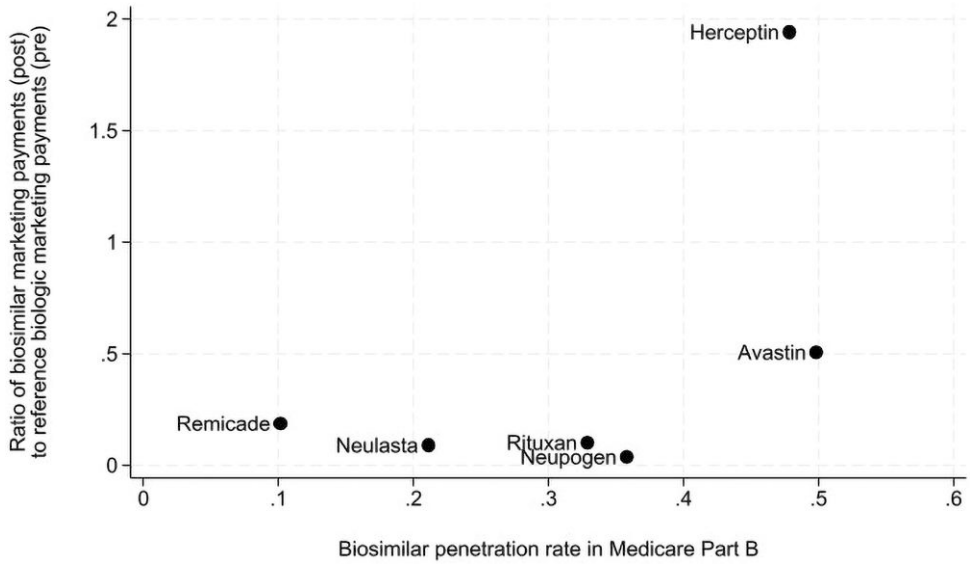

Figure 2. Relationship between the biosimilar marketing payment ratio and the penetration rate in Part B Medicare. The payment ratio numerator is the average quarterly biosimilar marketing payments in the 2 years after first launch, summed across all launched products; the denominator is the average quarterly marketing payments for the reference biologic in the year prior to first biosimilar launch. The penetration rate reports the Medicare Part B dosage units that were administered for the biosimilar as a share of all Part B dosage units administered for that molecule group during the first 2 calendar years following the launch of the first biosimilar (see Appendix Table S1 for the relevant period for each drug group).

Second, we showed that biosimilar manufacturers were engaged in direct-to-physician marketing but averaged 48% of reference biologic activity in the pre-launch period. These marketing efforts could have been used to overcome physician hesitancy. Direct-to-physician marketing might have been particularly useful for this set of non-interchangeable biosimilars, given the elevated role of the physician in prescribing decisions (rather than the pharmacist) and physician uncertainty about product comparability.

This study had several limitations in terms of its measurement of direct-to-physician marketing. First, reporting to Open Payments is not mandatory for marketing activities with no or low-dollar transfers of value. Second, the presence of a payment does not guarantee that the marketing representative met with the physician. Finally, Open Payments records may fail to list all drugs marketed in a particular encounter.

Our findings suggest two lesser-known ways that the biosimilar market differs from that of generic small-molecule drugs. Although the manufacturers of small-molecule drugs commonly reduce their marketing activities to zero once generic competitors become available,[8] we found a slower transition among the manufacturers of reference biologics. At least 1 reference product manufacturer continued moderate levels of marketing activities 3 years after the first biosimilar launched (Amgen, for Neupogen), and another resumed high levels of marketing 4 years after the onset of biosimilar competition (Johnson & Johnson, Remicade) (Appendix Figures S1 and S2). In addition, while the manufacturers of generic small-molecule drugs generally do not engage in direct-to-physician marketing, we found nontrivial amounts of such activity among biosimilars, consistent with the greater efforts among biosimilar manufacturers to brand their drugs and the greater need for physician education.

The biosimilars market is changing rapidly and, with it, the role of direct-to-physician marketing. The need to win over physicians individually may also fade as physicians gain experience with biosimilars and as more biosimilars are designated as "interchangeable." On the other hand, the existence of more biosimilar options for the same reference product could reinvigorate the use of marketing payments among manufacturers looking to build market share.[17,18] Finally, the launch of biosimilars for AbbVie's Humira and Amgen's Enbrel (expected in 2029) may shift the competitive dynamics of biosimilars in Part D, where the coverage and promotion of biosimilars has been limited by insurance formularies.[19]

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Supplementary material

Supplementary material is available at *Health Affairs Scholar* online.

Conflicts of interest

Please see ICMJE form(s) for author conflicts of interest. These have been provided as supplementary materials.

Notes

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