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ORIGINAL REPORT

Trajectories of Injectable Cancer Drug Costs After Launch in the United States

Noa Gordon, Salomon M. Stemmer, Dan Greenberg, and Daniel A. Goldstein

Author affiliations and support information (if applicable) appear at the end of this article.

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Corresponding author: Daniel A. Goldstein, MD, Davidoff Cancer Center, Rabin Medical Center, Petach Tikvah, Israel; e-mail: dgolds8@emory.edu.

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ABSTRACT

Purpose

Cancer drug prices at launch have increased in recent years. It is unclear how individual drug prices change over time after launch and what market determinants influence these changes. We measured the price trajectories of a cohort of cancer drugs after their launch into the US market and assessed the influence of market structure on price changes.

Methods

We studied the changes in mean monthly costs for a cohort of 24 patented, injectable anticancer drugs that were approved by the US Food and Drug Administration between 1996 and 2012. To account for discounts and rebates, we used the average sales prices published by the Centers for Medicare and Medicaid Services. Costs were adjusted to US general and health-related inflation rates. For each drug, we calculated the cumulative and annual drug cost changes. We then used a multivariable regression model to evaluate the association between market and cost changes over time.

Results

With a mean follow-up period of 8 years, the mean percent change in cost for all drugs was +25% (range, −14% to +96%). After adjusting for inflation, the mean cost change was +18% (range, −16% to +59%). Rituximab and trastuzumab followed a similar pattern in cost increases over time, and the inflation-adjusted monthly costs rose since approval by 49% and 44%, respectively. New supplemental US Food and Drug Administration approvals, new off-label indications, and new competitors did not influence the annual cost change rates.

Conclusion

Anticancer drug costs may change substantially after launch. Regardless of competition or supplemental indications, there is a steady increase in costs of patented anticancer agents over time. New regulations may be needed to prevent additional increases in drug costs after launch.

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INTRODUCTION

In recent years, there have been growing concerns regarding increasing drug prices, particularly in oncology. Some patients face severe financial distress as a result of high out-of-pocket treatment costs, which may affect their adherence to treatment and subsequent treatment outcomes.[1-3] It has been clearly demonstrated that severe financial hardship leads to increased mortality.[4] Furthermore, health care payers are experiencing a growing economic burden and facing resource allocation challenges while dealing with budget constraints.[5,6]

Over recent decades, launch prices of anticancer drugs, at the time of market entrance, have increased substantially.[7] Howard et al[8] assessed the trends of launch prices for 58 anticancer drugs that were approved between 1995 and 2013 in the United States and found that the average launch price, adjusted for inflation and health benefits, had increased by 10% annually. However, high anticancer drug prices are not only a result of new drugs being launched at high prices. They are also a result of changes in prices after launch. Imatinib, for example, considerably changed the treatment outcomes of patients with chronic myelogenous leukemia,[9] and its monthly cost almost tripled in the last decade. This was despite second-generation tyrosine kinase inhibitors entering the market as competitors and despite an increase in market size resulting from patients' increased survival and treatment durations.[10]

One can argue that in a healthily functioning market, when competition enters the market prices should decrease. However, the market for

ASSOCIATED CONTENT

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Data Supplement

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drugs in the United States is currently not functioning healthily for a variety of reasons.[11] In this report, we seek to understand whether cost trajectories of chronic myelogenous leukemia treatments and other outliers are representative of all anticancer drugs.

Growing evidence on price trajectories of anticancer drugs have accumulated in recent years. Bennette et al[12] used a large commercial claims database and examined time trends in monthly costs of oral anticancer drugs. Between 2007 and 2013, there was an average inflation-adjusted annual increase in cost of 5%.[12] In general, for each drug, the cost rose after US Food and Drug Administration (FDA) approval for supplemental indications and decreased when a competitor entered the market. Another analysis of changes in monthly spending for 18 orally administered anticancer drugs revealed that there were increases in most drug costs. Annual cost increases varied between 15% and 30%.[13]

Medicare Part B covers infusible and injectable drugs that are administered in outpatient settings and physician offices. Average sales prices (ASPs) are baseline benchmarks for Medicare reimbursement after accounting for discounts and rebates.[14] Medicare Part B drug spending increased from $9.4 billion in 2005 to $18.5 billion in 2014, and anticancer drugs accounted for 42.1% of all Medicare Part B expenditures in 2014.[15]

The objective of this study was to systematically measure the cost trajectories of individual anticancer drugs after their launch into the US market. We aimed to understand average cost changes over time from the Medicare payer's perspective and how market structure influences these changes.

Table 1. Drug Characteristics

Generic Name	FDA-Approved Indications*	First FDA Approval	Dosing†	Patent Holder	Biologic Properties
Arsenic trioxide	APL	2000	0.15 mg/kg daily	Cephalon	Arsenic
Bendamustine	CLL, NHL	2008	120 mg/m^2 on days 1 and 2 of 28-day cycle	Cephalon	Alkylating agent
Bevacizumab	Colon, lung (2006), breast (2008)‡, GBM (2009), kidney (2009), cervix (2014), ovary (2014),	2004	5 mg/kg every 2 weeks	Roche-Genentech	VEGF-directed antibody
Bortezomib	Multiple myeloma, MCL	2003	1.3 mg/m^2 twice per week	Millennium Pharmaceuticals	Proteasome inhibitor
Brentuximab	Lymphoma	2011	1.8 mg/kg every 3 weeks	Seattle Genetics	CD30-directed antibody-drug conjugate
Cabazitaxel	Prostate	2010	25 mg/m^2 every 3 weeks	Sanofi	Microtubule inhibitor
Cetuximab	Colon, head and neck (2011)	2004	250 mg/m^2 weekly	ImClone	EGFR-directed antibody
Clofarabine	ALL	2004	52 mg/m^2 daily for 5 days every 28 days	Genzyme	Purine nucleoside metabolic inhibitor
Denosumab	Bone metastasis, prophylaxis in cancer (2011), osteoporosis (2012), giant-cell tumors (2013), hypercalcemia (2014)	2010	120 mg every 4 weeks	Amgen	RANKL-directed antibody
Eribulin	Breast, liposarcoma (2016)	2010	1.4 mg/m^2 on days 1 and 8 of 21-day cycle	Eisai	Microtubule inhibitor
Ipilimumab	Melanoma, adjuvant (2015)	2011	3 mg/kg every 3 weeks for total of 4 doses	Bristol-Myers Squibb	CTLA-4–directed antibody
Ixabepilone	Breast	2007	40 mg/m^2 every 3 weeks	Bristol-Myers Squibb	Microtubule inhibitor
Liposomal vincristine	ALL	2012	2.25 mg/m^2 weekly	Talon	Liposomal vinca alkaloid
NAB-paclitaxel	Breast, lung (2012), pancreas (2013)	2005	260 mg/m^2 every 3 weeks	Celgene	Microtubule inhibitor
Nelarabine	ALL, lymphoma	2005	1,500 mg/m^2 on days 1, 3, and 5 of 21-day cycle	GlaxoSmithKline	Nucleoside metabolic inhibitor
Ofatumumab	CLL	2009	1,000 mg on day 1 of 28-day cycle	GlaxoSmithKline	CD20-directed antibody
Panitumumab	Colon	2006	6 mg/kg every 2 weeks	Amgen	EGFR-directed antibody
Pemetrexed	Mesothelioma, NSCLC (2009)	2004	500 mg/m^2 on day 1 of 21-day cycle	Eli Lilly	Folate analog metabolic inhibitor
Pertuzumab	Breast, adjuvant (2015)	2012	420 mg every 3 weeks	Genentech	HER2-directed antibody
Pralatrexate	Lymphoma	2009	30 mg/m^2 weekly for 6 weeks in 7-week cycle	Allos	Folate analog metabolic inhibitor
Rituximab	NHL, RA (2009), CLL (2010), WG (2011)	1997	375 mg/m^2 every 3 weeks	Roche-Genentech	CD20-directed antibody
Temsirolimus	Kidney	2007	25 mg weekly	Pfizer	mTOR inhibitor
Trastuzumab	Breast, adjuvant (2006), gastric (2010)	1998	2 mg/kg weekly	Roche-Genentech	HER2-directed antibody
Ziv-aflibercept	Colon	2012	4 mg/kg every 2 weeks	Sanofi	VEGF-directed antibody

Abbreviations: ALL, acute lymphoblastic leukemia; APL, acute promyelocytic leukemia; CD, classification determinant; CLL, chronic lymphocytic leukemia; CTLA-4, cytotoxic T-cell lymphocyte-4; EGFR, epidermal growth factor receptor; FDA, US Food and Drug Administration; GBM, glioblastoma; HER2, human epidermal growth factor receptor 2; MCL, mantle cell lymphoma; mTOR, mammalian target of rapamycin; NAB, nanoparticle albumin bound; NHL, non-Hodgkin lymphoma; NSCLC, non–small-cell lung cancer; RA, rheumatoid arthritis; RANKL, receptor activator of nuclear factor kappa-B ligand; VEGF, vascular endothelial growth factor; WG, Wegener granulomatosis.

*Includes supplemental indications.

†Dosing for first indication approved.

‡Bevacizumab approval for metastatic breast cancer was revoked in November 2011.

METHODS

Description of Anticancer Drug Price Changes Over Time

We included in our analysis all Medicare Part B anticancer drugs that received their initial FDA approval between 1996 and 2012. These data were obtained from CenterWatch.[16] We excluded all medications for the treatment of pain or adverse effect management, as well as cytokine therapies, hormonal therapies, autologous T-cell immunotherapies, and drugs that subsequently lost their FDA approval. We also excluded drugs if their patents expired during the follow-up period.

For each drug, we calculated the mean single dose and monthly dose (4 weeks) according to the prescribing instructions included in the product label for the first indication of the drug. An average body weight of 82 kg (180 lbs) and an average body-surface area of 1.86 m^2 were used, as described in a previous economic analysis.[17] To account for discounts and rebates, we used the ASPs published by the Centers for Medicare and Medicaid Services (CMS) for all Part B drugs.[18] We calculated the mean monthly cost of each drug using the mean dose and the quarterly ASP per drug unit for each quarter during the period between January 2005 and January 2017. Finally, we calculated the annual and cumulative cost changes during this follow-up period. We used annual inflation rates and health-related inflation rates published by the US Department of Labor[19] to calculate the inflation-adjusted annual and cumulative cost changes.

Association Between Changes in Drug Market Over Time and Price Trajectories

To evaluate the association between market and cost changes, we used a repeated-measures multivariable mixed-effects linear regression analysis. The output variable was the change in the mean monthly cost of each drug throughout the follow-up period of 2005 to 2017 for all 24 drugs in our cohort. Three models were created for three versions of the output variable: percent change in price, percent change in general inflation-adjusted price, and percent change in health-related inflation-adjusted price. For all models, the following variables were included as covariates. Time from start of follow-up (in years), number of new FDA supplemental indications (obtained from the Drugs@FDA database[20]), number of new competitors for the FDA-approved indications of the drugs (obtained from the CenterWatch database[16]), and number of new off-label indications (obtained by scanning off-label compendium-approved indications each year, with class I to IIB strength of recommendation and evidence category A or B; these data were obtained from the Micromedex 2.0 DRUGDEX compendium[21]). Three models were created for the market structure changes in the same year (one for each output variable), and three were created for market structure changes in the previous year. In addition, three models were created to account for market volume changes, which were measured using data on annual numbers of beneficiaries and claims that were available only for 11 drugs between 2011 and 2015 in the Medicare Drug Spending Dashboard.[22] For all models, to control for the price at launch, we used this variable as a fixed effect. Missing data for a given output variable or time point were excluded from the analysis. Data were analyzed using SPSS statistical software (version 22; SPSS, Chicago, IL).

RESULTS

Anticancer Drug Cohort

Twenty-four Medicare Part B anticancer drugs were included in the analysis. Six drugs received their initial FDA approval in the

Table 2. Cost Changes

Generic Name	Mean Monthly Dose (mg)*	Mean Monthly Cost at Launch (US$)	Follow-Up Years (No.)	Percent Change			
				Mean Annual (SD)	Cumulative	Cumulative Inflation Adjusted	Cumulative Health Related Inflation Adjusted
Arsenic trioxide	344	11,455	2005-2017 (12)	6 (4)	+95	+57	+39
Bendamustine	372	6,924	2009-2017 (8)	5 (5)	+50	+32	+21
Bevacizumab	820	4,680	2005-2017 (12)	2 (2)	+29	+4	−8
Bortezomib	19	5,490	2005-2017 (12)	4 (3)	+63	+31	+16
Brentuximab	197	19,482	2013-2017 (4)	8 (0.1)	+35	+ 29	+22
Cabazitaxel	62	8,382	2012-2017 (5)	3 (1)	+14	+9	+0
Cetuximab	1,860	9,232	2005-2017 (12)	1 (1)	+14	−8	−19
Clofarabine	484	56,486	2006-2017 (11)	3 (3)	+31	+8	−4
Denosumab	120	1,731	2012-2017 (5)	3 (3)	+14	+8	−4
Eribulin	7	6,253	2012-2017 (5)	4 (2)	+20	+13	+5
Ipilimumab	328	41,016	2012-2017 (5)	3 (2)	+14	+8	+0
Ixabepilone	99	6,310	2009-2017 (8)	2 (2)	+20	+5	−3
Liposomal vincristine	17	34,602	2014-2017 (3)	8 (0.5)	+21	+18	+14
NAB-paclitaxel	645	5,375	2006-2017 (11)	2 (2)	+24	+3	−9
Nelarabine	11,160	18,513	2007-2017 (10)	6 (2)	+83	+55	+39
Ofatumumab	1,000	4,538	2011-2017 (6)	3 (2)	+17	+8	−0.5
Panitumumab	984	8,154	2008-2017 (9)	3 (2)	+30	+14	+2
Pemetrexed	1,240	5,026	2005-2017 (12)	4 (2)	+57	+27	+12
Pertuzumab	560	5,718	2014-2017 (3)	2 (2)	+7	+4	−2
Pralatrexate	191	31,684	2011-2017 (6)	6 (4)	+43	+31	+21
Rituximab	930	4,111	2005-2017 (12)	5 (0.5)	+85	+49	+32
Temsirolimus	100	4,791	2009-2017 (8)	4 (2)	+42	+24	+14
Trastuzumab	656	3,476	2005-2017 (12)	5 (0.5)	+78	+44	+27
Ziv-aflibercept	656	6,147	2014-2017 (3)	−4 (14)	−13	−15	−20

Abbreviations: NAB, nanoparticle albumin bound; SD, standard deviation.
*Average single dose and monthly dose (four weeks) according to the label dosing instruction. Average body weight was 82kg (180lb) and an average body surface area (BSA) was 1.86m^2.

defined timeframe but were excluded from our analysis because they lost their patents during the follow-up period. Table 1 summarizes the basic characteristics of the drugs, including biologic properties, first FDA approval year, FDA-approved indications (including supplemental indication), dosing for the first approved indication, and patent holder.

Price Trajectories

Overall, for the follow-up period of 12 years (mean, 8 years), the mean cumulative cost increase of all 24 drugs was +36.5% (95% CI, 24.7% to 48.3%). When normalizing to annual general and health-related inflation rates, the mean cumulative increases were +19.1% (95% CI, 11.0% to 27.2%) and +8.4% (95% CI, 1.4% to 15.4%), respectively. Although the mean annual general inflation rate in our follow-up period was +1.09% and the health-related inflation rate was +1.15%, the mean annual change in monthly cost was +3.73%. Individual results, including the mean monthly cost at launch and the cumulative and annual changes in monthly cost from baseline, are summarized in Table 2. Additional information regarding cost changes is available in the Data Supplement.

The following drugs incurred high cost changes over time: arsenic trioxide, which was approved by the FDA in 2000 for the treatment of acute promyelocytic leukemia (95.5% cost increase from baseline in 12 years); nelarabine, which was approved in 2005 for the treatment of patients with T-cell acute lymphoblastic leukemia (83.2% increase from baseline in 12 years); rituximab, which was approved in 1997 for non-Hodgkin lymphoma (85.2% increase from baseline in 12 years); and trastuzumab, which was approved for metastatic human epidermal growth factor receptor 2–positive breast cancer in 1998 (78.4% increase from baseline in 12 years). Ziv-aflibercept, which was approved for metastatic colorectal cancer in 2012, was the only anticancer drug for which cost decreased after launch (−12.8% from baseline in 3 years).

Of the 24 drugs that were included in the analysis, 13 were targeted therapies. Figure 1 shows the cumulative percent change in the mean monthly cost from baseline throughout the follow-up period. Cost trajectories of these drugs can be divided into two clusters according to the gradients of the slopes. The first includes drugs with steadily rising costs—trastuzumab, rituximab, bortezomib, and brentuximab—with a mean cumulative increase of 66% and mean annual increase of 5%. The second cluster includes drugs for which costs did not steadily rise or for which the increases in cost started after periods of stable cost; the mean annual increase in this cluster was 2%. Ziv-aflibercept was considered to be an outlier because it is the only drug with a price that decreased with time, with a total decrease of −13% and mean annual decrease of 4%. Additionally, 11 cytotoxic chemotherapies were included in the analysis. Descriptions of price trajectories are provided in the Data Supplement. Cost trajectory patterns in this group of drugs

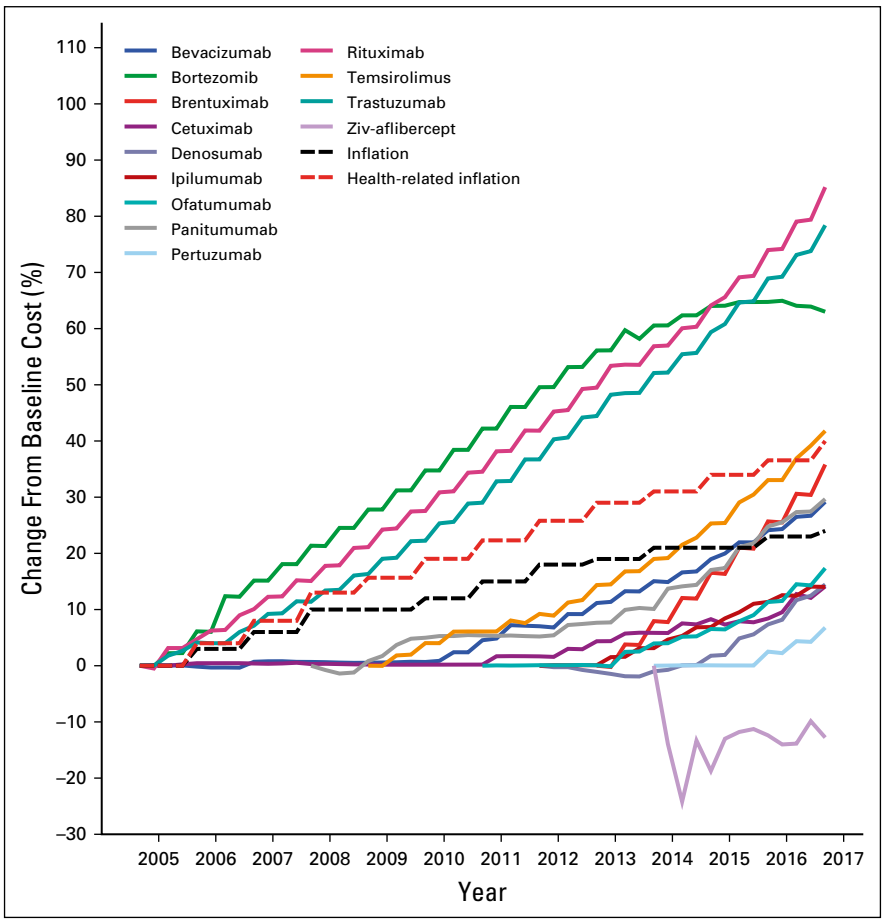

Fig 1. Cost trajectories of targeted therapies. Cumulative change (%) from baseline mean monthly cost by year. General inflation rates are plotted as black dotted line; health-related inflation is plotted as red dotted line.

were heterogeneous and varied from large increases to drugs that are not steadily rising or in which the increase starts after a period of cost stability.

Association Between Changes in Drug Market Over Time and Price Trajectories

When examining the influence of market structure changes on price changes, we found that no time-dependent variable—the addition of FDA supplemental approvals, the addition of compendium off-label indications, or introduction of new competitors into the market—influenced the rates of price changes. Table 3 summarizes the three repeated-measures mixed-effects linear regression models. The first model used the actual drug price as the output variable, and the two other models used prices adjusted to inflation and health-related inflation. Addition of FDA supplemental approvals, addition of compendium off-label indications, and introduction of competitors into the market did not influence the rates of price change. The only variable that was significant in these models and may have influenced price change rates was the time lapse from launch. For every additional year, there was an additional increase of 0.308% in inflation-adjusted price change and a 0.211% increase in health-related inflation-adjusted price change rates. Similar results were found in a sensitivity analysis that examined the influence of market changes in the previous year. The results are summarized in the Data Supplement. Additional regression models were created to examine the influence of number of claims and number of beneficiaries on the price change rates. Data were available for only 11 drugs from our cohort and for the years of 2011 to 2015. The results are summarized in the Data Supplement. As previous models showed, these models did not find any additional influence of market volume changes on the rates of price change.

Table 3. Influences of Market Changes on Cost Changes: Repeated-Measures Regression Model

Covariate Regression Variable	Mean Monthly Price Change (%)	95% CI	*P*
Model one			
Actual price			
Follow-up year	0.164	−0.233 to 0.351	.085
New supplemental indication	−0.203	−0.943 to 0.536	.585
New off-label indication	0.092	−0.488 to 0.673	.752
New competitor	−0.106	−0.398 to 0.186	.468
Model two			
General inflation-adjusted price			
Follow-up year	0.308	0.120 to 0.497	.002
New supplemental indication	−0.744	−1.610 to 0.120	.091
New off-label indication	−0.503	−1.201 to 0.194	.156
New competitor	−0.063	−0.417 to 0.289	.718
Model three			
Health-related inflation adjusted price			
Follow-up year	0.211	−0.030 to 0.391	.023
New supplemental indication	−0.106	−0.840 to 0.627	.773
New off-label indication	0.065	−0.274 to 0.405	.702
New competitor	−0.170	−0.466 to 0.125	.253

NOTE. Three models were created for three output variables: percent change in price, percent change in general inflation-adjusted price, and percent change in health-related inflation-adjusted price. For all models, the following variables were included as covariates: time from start of follow-up (years), number of new US Food and Drug Administration (FDA) supplemental indications in the same year, number of new compendium off-label indications in the same year, and number of new competitors for the FDA-approved indications of the drug in the same year. For all models, drug launch price was used as a fixed-effect covariate. All models were created for a sample size of 24 drugs and for the timeframe of 2005 to 2017.

DISCUSSION

In this study, we examined the cost trajectories of a cohort of 24 patented Medicare Part B injectable anticancer drugs. We used ASPs, which are baseline indicators for Medicare reimbursement.[18] Our findings suggest that costs increase over time and that there are some specific drugs in which costs rise substantially. To our knowledge, this is the first study that systematically analyzed the discounted cost changes over time of branded injectable anticancer drugs in the US market and the associations between market structure and cost trajectories.

Howard et al[8] previously examined changes in the prices of 19 anticancer drugs that were covered by Medicare Part B. The average annualized postlaunch growth rate of inflation-adjusted prices was 1%, and the 75th percentile was 4%. They concluded that the prices of innovative drugs do not change much after launch and that launch prices are the main focus when examining high drug prices. Our findings are different, possibly because we excluded all six drugs approved since 1996 and because patent expiration resulted in price decreases (eg, gemcitabine, irinotecan, oxaliplatin, docetaxel, liposomal doxorubicin, and epirubicin). We also believe that an average annual inflation-adjusted 4% increase will lead to a substantial cumulative increase after a decade.

The cohort of anticancer drugs that we examined included drugs from different pharmaceutical companies; however, four drugs were manufactured by Roche-Genentech. A notable resemblance in cost trajectory was observed in two of these drugs, rituximab and trastuzumab, which received their FDA approval in consecutive years (1997 and 1998) and followed an almost identical pattern, with total cumulative increases of 85.2% and 78.4%, respectively, in a total follow-up period of 12 years. The annual cost increase of both drugs was 5%, with a low variation between years (standard deviation, 0.5%); both had major medical effects and no competition in those years.

We also examined the association between cost trajectories of drugs that were approved for the same indication and might function as competitors. Four anticancer drugs in our cohort were approved for metastatic colorectal cancer. Figure 2 shows the cumulative percent change in the mean monthly cost from baseline throughout the follow-up period for four anticancer drugs. Bevacizumab and cetuximab gained their initial FDA approval in 2003 and 2004, respectively. Until 2010, the costs of these two drugs did not increase substantially, but in 2010, they started to rise together. The parallel increases in the costs of these two drugs might have been a result of the entrance into the market in 2006 of panitumumab, a direct competitor of

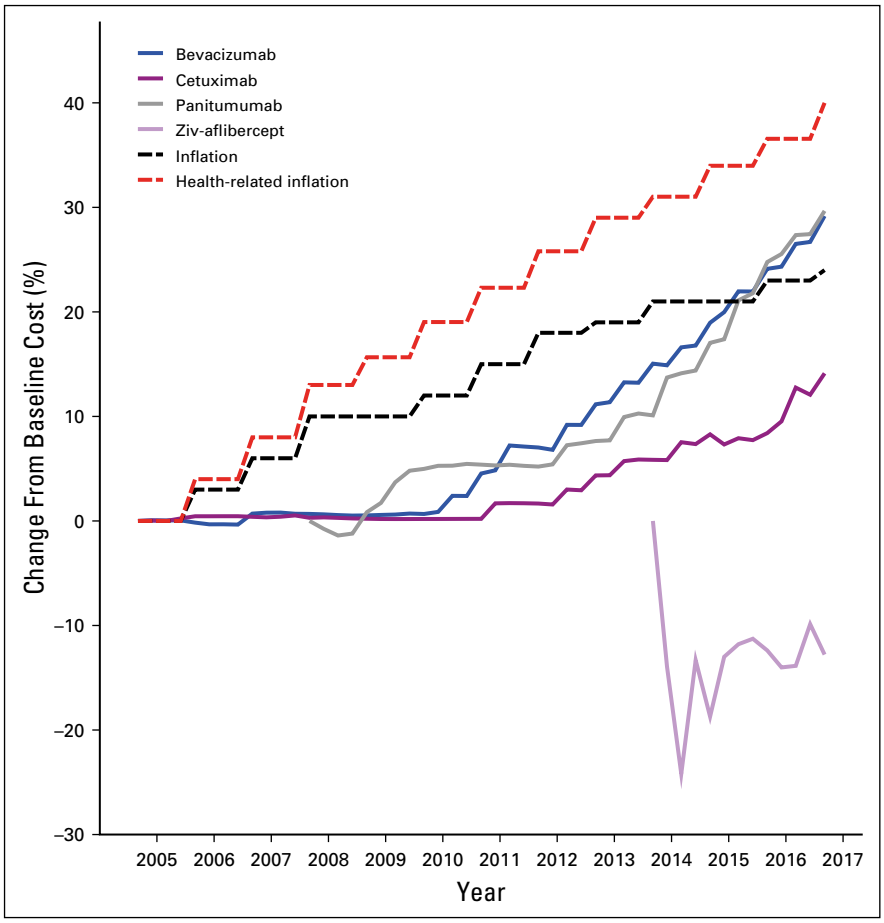

Fig 2. Cost trajectories of targeted therapies for metastatic colon cancer. Cumulative change (%) from baseline mean monthly cost by year. General inflation rates are plotted as black dotted line; health-related inflation is plotted as red dotted line.

cetuximab. The cost of ziv-aflibercept, which was approved in 2012 with a high and controversial price tag, plunged immediately after public outcry led by Memorial Sloan Kettering Cancer Center; by the end of the follow-up period, it had undergone a total decrease in cost of −12.8%. However, our observation of cost increases as a result of the competition between cetuximab and panitimumab and the well-described cost increases for imatinib, nilotinib, and dasatinib may not be the rule. Bennette et al[12] demonstrated in the cohort of drugs they analyzed that in general there are decreases in costs of orally administered anticancer drugs when competition enters the market.

When further examining the influence of market changes on cost trajectories through a more systematic approach, we found that the price increases observed could not be explained by changes in any of the market structure variables examined. Addition of FDA supplemental approvals, addition of compendium off-label indications, and introduction of new competitors into the market did not influence the rates of price change. Our results are inconsistent with the results of Bennette et al,[12] who found that costs rose after FDA approval for supplemental indications and decreased when a competitor entered the market.

Our work has some limitations. The use of quarterly Medicare ASPs has some pitfalls. The first is that CMS publishes ASPs with a time lag of 6 months, and when accounting for inflation, this might slightly distort the results. The more relevant limitation to drawing conclusions from this analysis about the entire anticancer drug market is that by using ASPs, we limited our analysis to the Medicare payer's perspective. The perspectives of other payers may be different, because Medicare is not allowed to negotiate prices with manufacturers.[23,24] Reimbursement for Part B drugs was reduced from ASP plus 6% to ASP plus 4.3% with the US budget sequester of 2012. This fact does not change our results, because we used ASP alone. In 2016, CMS launched six pilot programs in an attempt to lower costs and improve value of treatment in Medicare.[25] Our analysis is valid in the context of these potential reforms because we used the baseline indicators for all Medicare Part B drug prices.

Immunotherapy is a major cancer treatment breakthrough that has emerged in recent years. Our analysis included only one immunotherapy agent, ipilimumab, and the cost has increased by 11% in the 5 years since entering the market. Using the same methods described in this report, we found that in the short follow-up period since FDA approval, nivolumab and pembrolizumab, two other approved immunotherapy agents, had stable costs. It will be interesting to follow the price trajectories of immunotherapy in the coming years, as more agents gain approval, with more supplemental and off-label indications and an increasing market size.

Although in Medicare is not legally permitted to negotiate prices, in other countries prices are controlled and negotiated

before public reimbursement. A recent study showed prices were higher in the United States compared with the United Kingdom at launch and postlaunch.[26] Several laws limit the ability of Medicare to negotiate drug prices.[11] To maintain a sustainable health care system, it is essential to take into account that in addition to rising launch prices of new anticancer drugs, costs often change substantially after launch. Prices may continue to increase regardless of market volume or competition entering the market. Individual price hikes have been the main focus of the public debate over drug prices. Our study reveals that gradual price increases over the years might result is substantial cumulative increases. One potential solution toward managing this problem is to introduce new regulations into the marketplace.[27]

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

AUTHOR CONTRIBUTIONS

Conception and design: All authors
Collection and assembly of data: Noa Gordon, Daniel A. Goldstein
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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Affiliations

Noa Gordon, **Salomon M. Stemmer**, and **Daniel A. Goldstein**, Institute of Oncology, Davidoff Center, Rabin Medical Center, Petah-Tikva; **Noa Gordon** and **Dan Greenberg**, Ben-Gurion University of the Negev, Beer-Sheva; **Salomon M. Stemmer**, Tel Aviv University, Tel Aviv, Israel; and **Daniel A. Goldstein**, Winship Cancer Institute, Emory University, Atlanta, GA.

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Noa Gordon
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Salomon M. Stemmer
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Dan Greenberg
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Daniel A. Goldstein
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Honoraria: AstraZeneca