Researchers Dissect the Cost of Targeted Agents

By Caroline Helwick

It comes as no surprise: targeted therapies now dominate anticancer drug spending in the United States, according to a team of researchers from several major cancer centers.

In the United States alone, sales of targeted therapies exceed $10 billion annually. Insurance design plays an important role in cost containment, including what patients pay out of pocket, and these strategies differ for oral versus intravenous (IV) chemotherapies. At ASCO 2015, researchers described payer trends, utilization, and out-of-pocket costs for privately insured patients receiving oral and IV chemotherapy.

"We found that the average insurance payment per month for targeted oral therapies has skyrocketed, from just over $3000 a month to $7000 in a 10-year period," said Fabrice Smieliauskas, PhD, MA, of the University of Chicago, IL, who presented the results of his poster.

"It's not one single drug," Dr Smieliauskas emphasized. "The price of Gleevec rose from $30,000 to $92,000 over 10 years. That's a high-selling drug and may be a main driver, but on average, all the drugs we sampled displayed this tendency."

Insurance payments for targeted IV drugs, on the other hand, "started high," at nearly $7000 monthly, but remained steady at this price through 2010.

The out-of-pocket costs of oral drugs were the lowest among all chemotherapy types. "Targeted IV drugs have a much higher out-of-pocket cost, because, at least in this sample, they were likely to involve coinsurance (usually, 20%). Oral drugs were covered under a fixed copay," Dr Smieliauskas explained.

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Because of this, he maintained, "the notion of oral drug parity laws is misguided for this patient population…. Oral drug parity could actually make the financial toxicity worse for patients."

As hospitals purchase physician practices—increasing billing rates for targeted IV anticancer medications—oral versus IV differences in out-of-pocket spending will continue to grow, the researchers noted.

Table Distribution of Insurance Payments for Cancer Therapies, 2001-2011

Year	Nontargeted drugs, %	Targeted oral drugs, %	Targeted intravenous drugs, %
2001	78	2	20
2005	59	5	36
2008	42	13	45
2011	37	25	38

Study Details

The study population was drawn from the LifeLink Health Plan Claims Database, representing approximately 70 million individuals from more than 80 US health plans, many of them employer-sponsored. The analysis included 200,168 nonelderly patients with cancer (mean age, 52 years) who received treatment between 2001 and 2011 with targeted oral anticancer medications, targeted IV medications, and others.

The costs were presented as cancer drug expenditures per patient per month, normalized to 2013 US dollars.

The study showed a steady growth in the use of targeted oral agents, rapid growth and then leveling off for targeted IV agents, and a consistent decline in the use of nontargeted agents until 2008, followed by a plateauing (**Table**).

The investigators found that the total cost for chemotherapy of any kind, per patient, increased by $7765 between 2001 and 2005, and by $6846 between 2005 and 2010, primarily as a result of the heavy use of new drugs. For the more recent time period, the launch price of new agents increased by $1016, and this accounted for 15% of the increased cost of treatment. The prices of drugs also increased by more than $700 after their launch.

"The targeted agents cost more when they launch, but also, the price goes up further after they launch," Dr Smieliauskas noted.

The analysis did not include immunotherapies. "Things will go bonkers when we include those," Dr Smieliauskas suggested. ■

Bevacizumab Wins Cost-Effectiveness Contest in First-Line Metastatic Colorectal Cancer

An economic analysis of the landmark Cancer and Leukemia Group B (CALGB)/Southwest Oncology Group (SWOG) 80405 trial, which compared bevacizumab and cetuximab in patients with metastatic colorectal cancer, declares bevacizumab the clear winner, because its total cost is $39,000 less than cetuximab.

"Chemotherapy plus bevacizumab costs less and achieves very similar survival and quality-adjusted survival as chemotherapy plus cetuximab for first-line treatment of *KRAS* wild-type metastatic colorectal cancer," according to Deborah Schrag, MD, MPH, Chief of the Division of Population Sciences, Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, who presented the analysis at ASCO 2015.

Photo by © ASCO/Max Gersh 2015

"Chemotherapy plus bevacizumab costs less and achieves very similar survival and quality-adjusted survival as chemotherapy plus cetuximab for first-line treatment of *KRAS* wild-type metastatic colorectal cancer."

—Deborah Schrag, MD, MPH

At a median follow-up of 24 months, no significant differences were observed in median overall survival or progression-free survival between the treatment groups, which was 29 months and 10.8 months, respectively, with bevacizumab plus chemotherapy and 29.9 months and 10.4 months, respectively, with cetuximab plus chemotherapy.

"Our study objective was to determine the most cost-effective treatment strategy for first-line metastatic colorectal cancer," said Dr Schrag. "The cost-effectiveness analysis was prospectively planned for CALGB/SWOG 80405, given the high costs of all the study arms."

The 2014 cost for 1 cycle (8 weeks) of these treatments in the average patient was $9324 for bevacizumab and $20,856 for cetuximab. This was based on an average selling price of $66.60 per 10 mg for bevacizumab given at 5 mg/kg every 2 weeks, and $53.30 per 10 mg for cetuximab, given at 250 mg/m^2 every 2 weeks (400 mg/m^2 for the first dose).

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Dr Schrag and her colleagues calculated the incremental cost-effectiveness and cost-utility ratios for the 2 treatment strategies. Their analysis took into account the utilization and cost of chemotherapy and the major care episodes related to treatment.

They assumed the use of vial sharing and the efficient use of every milligram of drug, that the end-of-life costs were similar between the arms, that the postprogression treatment intensity was identical between the arms, that all hospital regular bed days and intensive care unit days were "created equal," that the genomic testing costs were identical, and that the arms were similar in terms of provider visits and chair intensity.

The efficacy of the regimens was similar, as were the quality-adjusted life-years (QALYs), Dr Schrag noted; she pointed out that the 2 drugs differ in toxicities but are generally well-tolerated.

The life-years and QALYs, based on the EQ-5D measurements of health outcomes, were 2.88 and 2.75, respectively, for bevacizumab and 3.03 and 2.90, respectively, for cetuximab. The only difference in a subjective measurement was greater "skin satisfaction" with bevacizumab, as was expected.

"There were no meaningful differences" in subjective outcome measures between the arms, Dr Schrag indicated.

The analysis did, however, reveal large cost differences between the treatment arms, which stemmed from differences in the cost of the biologics.

Dr Schrag indicated that if the average selling price of cetuximab was reduced by 45%, the cost would be neutral.

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> —Peter B. Bach, MD, MAPP

Dr Bach Comments

Peter B. Bach, MD, MAPP, Director of the Center for Health Policy and Outcomes, Memorial Sloan Kettering Cancer Center, NY, commented on Dr Schrag's study.

"We are in an era when we have decided on a hierarchy of comparative decision-making in cancer that begins with efficacy, then is followed by toxicity and then cost," Dr Bach said.

"Dr Schrag's analysis could have been 'back-of-the-envelope,' but she spent a lot of effort to lay this out. And she found no statistically significant difference, whether in life-years or QALYs, with 2 drugs that cost considerably different against dealer's choice backbone chemotherapy," he said.

"Benefits to some extent are constrained by biology, as are harms. But prices and costs? We accept these prices, put them into our cost-effectiveness analysis….Why not close this loop? If drugs are equal except for cost, why not just say no to the higher-cost agent?"

In fact, that is just what Dr Schrag does. "There's a good argument" for bevacizumab first line, "and that is what I use," she said.—*CH* ■

UnitedHealthcare's Episode-Based Payment... Continued from page 11

income" and to provide a learning system that offers data (feedback) to physician groups, Dr Newcomer explained.

To date, the program has focused on breast, colon, and lung cancers, and its key components include:

- Selecting preferred chemotherapy regimens for 19 episodes (payment conditions) in breast, lung, and colon cancers
- Calculating drug profits from those margins
- Drawing a "line in the sand"
- Paying fees for service: drugs are paid at average sales price, and episode payments are unchanged with drug changes
- Measuring performance annually
- Changing episode payments only when the total cost is lowered or outcomes are improved.

Elaborating on these points, Dr Newcomer said that each medical group was asked to settle on a best treatment strategy within the 19 conditions. UnitedHealthcare then looked at the group's existing fee schedule, calculated what their payments would have been (ie, drug profits from those regimens), and made this amount their episode-of-care payment.

"We said, 'We will pay this to you the first day you see a patient, but then it's frozen. We won't increase this until we get enough patients to measure results. Then, if you get better outcomes, we will share this [the gains] with you. If not, your payment stays the same," Dr Newcomer explained.

Emerging drugs can be incorporated; however, the episode payment will not increase until better results are demonstrated. Physicians bill the payer as they always have, "but we take drugs and prices down to ASP [average sales price], because we have paid the profits the first day," Dr Newcomer pointed out.

UnitedHealthcare developed 64 outcome measures, and met with physicians annually for performance reviews. The payer takes responsibility for collecting the data on the patients, which eliminates an administrative burden for the oncology practice.

Using stage II HER2-negative, estrogen receptor/progesterone receptor–positive breast cancer as an example, Dr Newcomer noted that the reference sample, or "target" (based on fee-for-service claims data), had a total cost of $65,000. This cost includes chemotherapy drugs (ASP), chemotherapy drug margins, hospitalizations, physician care, ancillary care, and other things related to caring for this patient subset. The program participants are measured against this benchmark.

Participating oncology groups, so far, have shown a good amount of variability in their average total costs of care per episode. Of note, although all the programs committed to using the same chemotherapy regimen for the patient with stage II disease described above, one group's chemotherapy cost was only $9000, whereas another group topped $23,000.

"Either their patients were a lot more obese, or we had a problem. There was a 2-fold difference in cost for the same regimen and fee schedule," Dr Newcomer noted.

A review revealed that only 50% of the patients in the higher-cost practice were receiving the protocol regimen; the other 50% were treated off protocol. "Controls were not in place," Dr Newcomer said. "These were the kind of discussions we had as we worked through this."

Ultimately, compared with the fee-for-service database for the same time period, the episode-based program delivered equivalent patient care for 34% less cost. Much of these cost-savings "went back into the next set of episode fees, for better performance," Dr Newcomer said. "Because they came through on performance, some gains were shared."

UnitedHealthcare will add 6 additional groups in 2015 to the episode-based program, quadrupling the number of patients in the project.—*CH* ■

KEY POINTS

- Episode-based programs reward physicians for actual results, not work performed
- Oncology groups have shown a good amount of variability; one group's chemotherapy cost was only $9000, whereas another group topped $23,000
- Only 50% of the patients in the higher-cost practice were receiving the protocol regimen; the other 50% were treated off protocol
- Compared with a fee-for-service database for the same time period, the episode-based program delivered comparable patient care for 34% less cost
- UnitedHealthcare is expanding its episode-based payment program to 12 practices in 2015, thus quadrupling the number of participants in the program