

MEETING SUMMARY
PRESIDENT’S CANCER PANEL
ACCESS TO AND COST OF CANCER DRUGS IN A CHANGING
HEALTHCARE LANDSCAPE

June 10, 2016
New York, NY

This workshop was the first in the President’s Cancer Panel’s (the Panel) 2016–2017 series on access to and cost of cancer drugs. The workshop brought together participants with diverse expertise and perspectives, including oncologists, health economists, patients and patient advocates, pharmaceutical and biotechnology executives, academic institution representatives, and federal agency stakeholders. Participants discussed challenges related to drug costs and access faced by patients, providers, healthcare systems, and payers, as well as factors that influence drug development and pricing. Participants were encouraged to live-Tweet at [#CancerRxValue](#) during the workshop. This meeting summary was prepared to satisfy requirements established by the Federal Advisory Committee Act. The summary provides an overview of presentations and discussions occurring as part of the workshop and does not necessarily reflect the views of Panel members.

President’s Cancer Panel

Barbara Rimer, DrPH, Chair
Owen Witte, MD

National Cancer Institute, National Institutes of Health

Abby Sandler, PhD, Executive Secretary, President’s Cancer Panel

Meeting Co-Chair

Gary Gilliland, MD, PhD, President and Director, Fred Hutchinson Cancer Research Center

Participants

Julian Adams, PhD, President, Research and Development, Infinity Pharmaceuticals

Peter Bach, MD, Director, Center for Health Policy and Outcomes, Memorial Sloan Kettering Cancer Center

Heather Block, Breast Cancer Patient and Advocate

Frank Clyburn, MBA, President, Global Oncology Business Unit, Global Human Health, Merck & Co.

Stacie Dusetzina, PhD, Assistant Professor, Division of Pharmaceutical Outcomes and Policy, University of North Carolina Eshelman School of Pharmacy; Assistant Professor, Health Policy and Management, University of North Carolina Gillings School of Global Public Health

Ann Geiger, PhD, MPH, Associate Director (Acting), Healthcare Delivery Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute

Clifford Hudis, MD, Chief, Breast Medicine Service, Memorial Sloan Kettering Cancer Center; Chief Executive Officer (Incoming), American Society of Clinical Oncology

Ron Kline, MD, Medical Officer, Patient Care Models Group, Centers for Medicare and Medicaid Services

Paul Kluetz, MD, Associate Director of Clinical Science, Office of Hematology and Oncology Products, Center for Drug Evaluation and Research, U.S. Food and Drug Administration

Sharon Levine, MD, Executive Vice President, The Permanente Federation, Director and Senior Advisor for Public Policy, Pharmacy, and Professional Development, The Permanente Medical Group of Northern California

Steve Miller, MD, Senior Vice President, Chief Medical Officer, Express Scripts

Meg Mooney, MD, Chief, Clinical Investigations Branch, Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute

Jeremy Nobel, MD, Medical Director, Northeast Business Group on Health; Instructor, Department of Global Health and Social Medicine, Harvard Medical School

Loyce Pace, MPH, Executive Advisor, Programs and Policy, LIVESTRONG Foundation

Meredith Rosenthal, PhD, Professor, Health Economics and Policy, Harvard T.H. Chan School of Public Health

Frederic Sax, MD, Senior Vice President, Managing Director, Advisory Services, Quintiles

Andrew Schorr, MS, Founder and President, Patient Power

WELCOME AND INTRODUCTIONS

Dr. Rimer welcomed invited participants and other attendees to the meeting on behalf of the Panel. She introduced Panel members, provided a brief overview of the history and purpose of the Panel, and described the aims of the current series of meetings. Dr. Rimer thanked the workshop co-chair, Dr. Gary Gilliland. She also introduced workshop facilitator Robert Mittman and Panel staff members.

OPENING ROUNDTABLE

The overarching goal of the workshop was to identify a set of topics related to cancer drug prices and access that could serve as an organizing framework for a series of Panel meetings. Participants introduced themselves and were asked to identify issues related to drug access and pricing that lend themselves to solutions. Several participants discussed the need for the prices of oncology drugs to reflect their value, and many acknowledged the need to develop a shared definition of value and identify shared values among stakeholders. Any value framework should be patient centered, and additional clinical trial endpoints that accurately assess the benefits of drugs for patients may need development. Patients and providers must be educated about the costs of various therapeutic options so they can make informed decisions. One strategy for reducing the cost of drug development and accelerating access to effective drugs is to improve clinical trials by expanding eligibility criteria and making trials more accessible to patients and physicians. Fostering competition may help drive down drug prices, and incentives for physicians could be altered to promote treatment selection based on benefit rather than price. Health insurance policies, particularly Medicare, need to be modified to ensure that high-value products are accessible for the patients who need them. It also is important that all clinical trial data be made available so healthcare organizations and physicians can make informed decisions about which drugs should be used when. Access and affordability must be balanced with the need to support future innovative research by the biopharmaceutical industry.

OPENING PRESENTATIONS

DR. GARY GILLILAND

CANCER DRUG DEVELOPMENT COSTS AND PRICING

Background

Dr. Gilliland took the helm as Fred Hutch's President and Director in 2015. Dr. Gilliland, who holds a PhD in microbiology as well as a medical doctorate, spent 20 years on the faculty at Harvard where he

was a professor of medicine at Harvard Medical School and professor of stem cell and regenerative biology at Harvard University. He was also an investigator at the Howard Hughes Medical Institute and Director of the leukemia program at the Dana-Farber/Harvard Cancer Center. Much of his initial work at Harvard focused on the genetic basis of blood cancers. In 2009, Dr. Gilliland left Harvard for Merck Research Laboratories. As the Senior Vice President and global oncology franchise head, he oversaw preclinical and clinical oncology development, as well as clinical oncology licensing. In 2013, he became the Vice Dean and Vice President of Precision Medicine at Perelman School of Medicine at the University of Pennsylvania. He has earned numerous honors for his work, including election to the National Academy of Medicine in 2015 and to the American Academy of Arts and Sciences in 2016.

Key Points

- There has been an exponential increase in the cost of cancer drugs from 1965 to the present. This creates real challenges that, while not unique to cancer, are particularly problematic to cancer because of: (1) the prevalence of cancer, estimated to increase by 75 percent worldwide by 2030, (2) the lengthy duration of many cancer treatments, and (3) the potential for use of combination therapies involving expensive individual drugs.
- Oral branded drugs appear to have a gradual but persistent increase in price following market approval. According to one study looking at inflation-adjusted drug prices from 2007–2013, there is a 5 percent increase each year, and a 10 percent increase each year following U.S. Food and Drug Administration (FDA) approval of supplemental indications. However, there is only a 2 percent decrement in pricing following FDA approval of competitor drugs or related mechanisms. It is not clear why market competition does not drive down pricing further.
- The reasons for the increasing cost of cancer drugs are not understood. One issue relates to Medicare pricing policies and difficulties associated with negotiating pricing with pharmaceutical companies. Mandatory coverage laws adopted by states also present challenges.
- Technological advances, new patient stratification strategies, and other approaches such as “breakthrough status” designation have helped accelerate FDA approval of new drugs and/or use of drugs in combinations. One example is pembrolizumab, which was approved on a Phase 1b expansion study and has strong postmarket commitment.
- Financial toxicity and its impact on patients should be considered when weighing costs. Some studies show that 20–40 percent of cancer patients suffer severe financial impact and that patients who file bankruptcy suffer worse treatment outcomes than patients who do not.
- The cost of drug development may be a significant factor in pricing. A [recent study](#) by researchers at Tufts University indicated that the cost of developing a single cancer drug is approximately \$2.6 billion. This does not take into account companies that attempt, but fail, to register a single drug. Larger pharmaceutical companies that register multiple cancer drugs may have costs per drug of up to \$5 billion, based on their profit and loss statements. That is the budget of the NCI for one year.
- Only 12 percent of cancer drugs reach the point of registration, meaning 88 percent fail to register. There are many reasons why drugs fail, including the lengthy registration process and evolving standards of care that may render a drug obsolete by the time it reaches registration.
- Benefits of cancer drugs also should be considered. Data from PhRMA generated between 1988–2000 estimate that 23 million lives have been saved with an approximately \$1.9 trillion value in terms of increased productivity and lifespan.
- The value of therapies should take into account cost-effectiveness (i.e., how much incremental changes in outcome are worth). Emerging curative approaches to therapy are changing value propositions regarding cancer cost-effectiveness. An expensive drug that cures a disease may have a higher value than a less expensive drug that is not curative.

- Policies around manufacturing and use of generic drugs impact price, and potentially supply, of cancer drugs. Monopolies for some generic drugs exist, providing an opportunity to manipulate pricing. Just-in-time policies create a risk of drug shortages if there is a batch failure with no backup.

DR. STACIE DUSETZINA

ACCESS TO CANCER TREATMENTS: ROLE OF DRUG PRICES AND POLICIES

Background

Dr. Dusetzina is a health services researcher and Assistant Professor at the University of North Carolina at Chapel Hill in the Eshelman School of Pharmacy and the Gillings School of Global Public Health. Her work focuses on measuring and evaluating population-level use and costs of anticancer therapy in the United States. Prescription drug pricing—particularly in oncology—has been a topic of increasing interest in recent years, with very little population-based data available to inform public debates. Dr. Dusetzina’s work has contributed to the evidence base for the role of drug costs in patient access to care. Her research on the topic of prescription drug spending and access has been broadly covered by Reuters, *The Washington Post*, STAT News, and *The Wall Street Journal*.

Key Points

- A [recent study](#) using data from 2000 to 2014 shows a trend of orally administered anticancer medications being launched at increasingly higher monthly price points. This is consistent with the research of Drs. Scott Ramsey and Caroline Bennette, who found that drug prices are increasing about 4.4 percent per year above inflation over time, independent of other factors, such as expanding label indications.
- Out-of-pocket drug costs affect patient access to anticancer medications. One study found that approximately 10 percent of patients do not pick up their prescriptions at the pharmacy and that this percentage increases as the expected out-of-pocket payment goes up. Similarly, Medicare beneficiaries without subsidies may delay treatment.
- Discontinuation of or nonadherence to treatment is another risk of high drug costs. A [study](#) done by Dr. Dusetzina and colleagues has shown that for patients with higher cost sharing, rates of drug discontinuation in the first six months of treatment increased by approximately 70 percent, and approximately 42 percent were nonadherent to anticancer drug regimens.
- Efforts are underway to limit out-of-pocket expenses for patients on commercial health plans. Oral anticancer parity laws requiring parity in medical and pharmacy coverage for drugs (i.e., equal cost sharing between infused and orally administered anticancer medications) have been passed in 40 states and Washington, DC, and a federal bill was introduced in June 2015 to expand parity to other states as well as self-funded health plans. Laws to cap co-pays (i.e., limit out-of-pocket costs to patients) have been adopted by four states, and nine other states are considering adoption. The pharmaceutical industry—in particular, Pfizer—is a strong supporter.
- Early evidence suggests that policies intended to limit patients’ out-of-pocket expenses—such as oral anticancer parity laws and co-pay caps—have had limited impact to date. Some patients in states with oral anticancer parity laws have experienced modest savings, but out-of-pocket spending has increased for others. This may be, in part, because many commercial insurance plans provided relatively generous drug coverage even before parity laws were enacted. Increasing health plan deductibles and coinsurance also may be counteracting the financial benefits of parity laws or other policies. A [Kaiser Family Foundation survey](#) found that 25–35 percent of people do not have the financial assets to meet their health plan deductibles.

- A [recent study](#) conducted by Dr. Dusetzina and a colleague looked at Medicare Part D drug coverage for orally administered anticancer medications and found virtually no differences in benefit design across all available Part D plans, meaning that plan participants have no options to shop around for better pricing on drugs. In addition, nearly 100 percent of anticancer drugs on Medicare Part D plans require coinsurance, which represents out-of-pocket spending for patients. Even after “closing the donut hole” in 2020, the best-case scenario for senior citizens who do not have low-income subsidies involves high out-of-pocket drug costs.
- Legislation proposed by Senators Ron Wyden and Jeff Merkley would cap out-of-pocket spending on Medicare Part D plans by removing the 5 percent coinsurance requirement after the catastrophic phase of the benefit has been reached. This has great potential benefit for oral anticancer medication users on Medicare.
- Participants in the [October 2015 Kaiser Health Tracking Poll](#) named the top two healthcare priorities for the President and Congress as: (1) making high-cost drugs for conditions such as cancer accessible to those who need them and (2) lowering drug prices.
- The high cost of drugs is both an insurance coverage issue and a drug pricing issue. It is important to look at innovative solutions such as value-based insurance payment and paying for outcomes while at the same time continuing to foster and reward innovation.

DR. PAUL KLUETZ

ROLE OF CLINICAL TRIAL ENDPOINTS IN DETERMINING DRUG VALUE

Background

Dr. Kluetz is a board-certified medical oncologist and internist who currently is serving as Associate Director of Clinical Science within the Office of Hematology and Oncology Products at FDA. At FDA, Dr. Kluetz has been engaged actively with the drug development, patient advocacy, and healthcare policy communities, developing a particular interest in several regulatory topics, including defining clinical benefit in oncology trials, the use of expedited programs such as accelerated approval and breakthrough therapy initiatives, and opportunities and challenges associated with patient-reported outcome data. More recently, he has taken a lead role in the FDA oncology effort, creating a cross-disciplinary initiative to review existing practices and identify opportunities to obtain more rigorous and informative patient-focused data in cancer clinical trials. Dr. Kluetz completed a medical oncology fellowship at the National Cancer Institute and remains clinically active, practicing inpatient medicine as a teaching attending at Georgetown University Hospital.

Key Points

- FDA has no knowledge of cost when reviewing investigational new drugs. Consideration of cost is not part of its regulatory mission or function. FDA considers drug benefit and risk; the focus is on understanding endpoints in clinical trials and whether a drug is safe and effective. It is difficult to quantify the risk-benefit determination for consideration in value frameworks. The American Society of Clinical Oncology (ASCO) value framework is a good start and takes into account various factors important for novel therapies.
- Targeted drug therapies with strong antitumor effects have enabled a dramatic increase in the use of accelerated approval over the past five years. However, it remains unclear what this means with respect to value frameworks. One issue is lack of heterogeneity with respect to clinical trial endpoints, which makes it difficult to define a single set of inputs for a value algorithm. For example, whereas randomized clinical trials may look at overall survival, the single-arm trials often used for breakthrough drugs may use objective response rate and duration of response as endpoints. Inserting objective response rate into a value framework does not reflect a complete story. It does not take into

account duration of response, depth of response, number of complete responses, or where the responses occurred, and these subtleties will change the importance of the endpoint.

- It is important in considering the strength of an endpoint to look at both *what* is being measured—survival, progression-free survival, objective response rate, patient-reported outcomes, measures of function—as well as the *fidelity* of the endpoint— measurement characteristics, the ability to be biased, and how much interpretation is required. For example, while patient-reported outcomes are important to patients and a strong endpoint in that regard, they are difficult to measure because of their high variability.
- The ASCO framework takes into account the kinetics of tumor growth, which is an important consideration when assessing the value of a drug. Some drugs, including some of the new immunotherapies, may not yield impressive changes in survival or improvements in progression-free survival but successfully control tumors in some patients. In some cases, 10 to 20 percent of patients are still living with metastatic solid tumors two to four years into treatment.
- Drug safety and tolerability are poorly captured and articulated in clinical trials. The cancer community should do a better job of integrating these factors in a quantitative and scientific manner.
- FDA has identified three measures for assessing health-related quality of life within the context of drug trials: symptoms of disease, symptomatic toxicities, and physical function. Insights into the rates of deterioration of physical function associated with specific cancers could be gained if physical function measurement tools (e.g., NIH PROMIS [Patient-Reported Outcomes Measurement Information System]) were used in real-world settings. It may be possible to integrate objective data on physical activity from wearable biosensors (e.g., Fitbit).
- More effort is needed to determine how to use structured real-world data, such as electronic patient-reported outcomes, to look at tolerability. This could help determine levels of physical activity while on treatment or time to deterioration. FDA and Kaiser Permanente are trying to develop a collaborative research agreement to explore this area.

BRAINSTORM—CANCER DRUG ACCESS AND COST: EFFECTS ON CLINICAL CANCER CARE

Participants were asked to discuss how issues of drug access and drug cost affect clinical cancer care. This includes the impact of the financial burden of cancer on the physical, emotional, and psychosocial health of patients and their families, as well as ways that drug access and cost influence clinicians and healthcare organizations.

- State governments spend significant funds to provide healthcare through state programs (e.g., Medicaid). This diverts funding from other public services. Physicians and others should be concerned about the impact of drug costs on state budgets and public services.
- Market forces have not yielded rational prices for cancer drugs for a number of reasons. A high level of emotion surrounds cancer diagnosis and treatment. Cancer is not a single disease; it is a collection of many diseases. Furthermore, most cancer treatments are very expensive, which means price differences between options are often very small.
- Caps on cost sharing—which limit the amount an individual or family is required pay out-of-pocket for drugs or care—are appropriate. However, the remainder of the cost is shifted to health insurance companies, which leads to increases in insurance premiums. Even when cost-sharing programs are in place, high drug costs reduce the affordability of care by increasing the cost of insurance.
- Patient Power conducted a survey of 1,000 patients on the hardships of cancer care. Approximately one-third of respondents said they had experienced hardships as a result of their care. About 10 percent had experienced foreclosure on their homes or bankruptcy, and many more faced difficult choices about how to prioritize their spending.

- A LIVESTRONG survey of 2,000 cancer survivors revealed that this population experiences great financial burdens as a result of their diagnoses and care. At least half of respondents reported spending \$10,000 or more out-of-pocket for their care. Many cancer patients are not receiving support from charitable programs or other navigation services. About 80 percent of respondents indicated that they did not have conversations with their providers about costs of care. Some providers are concerned that patients who know about the costs of care up front will be less likely to undergo treatment. However, survey respondents indicated that they likely would have made the same treatment decisions if they had known the cost, but they would have preferred to know about cost beforehand so they could make arrangements accordingly.
- Treatment cost may be a critical issue or may be irrelevant to a patient, depending on individual circumstances.
- The financial impact of cancer care is not limited to drug costs. Cancer patients often must stop working during their treatment. In some cases, caregivers also stop working or work reduced hours.
- Many cancer patients are thankful that drugs are available but are highly suspicious of the pharmaceutical industry and, in some cases, their physicians. They often wonder if treatment recommendations reflect what is best for them and are concerned that these recommendations are profit driven. Patients should not be responsible for ensuring that treatment recommendations are appropriate. Drug pricing and financial toxicity should be addressed on the national level.
- In the past, physicians may have viewed high drug prices as a societal problem somewhat dissociated from the individual patients they were treating. However, cancer drug pricing is now creating serious problems both for individual patients and for society. Physicians need to help address this problem and think about how best to be stewards of healthcare resources.
- Oncologists practice in a variety of settings and have varying levels of knowledge about costs and patient financial issues. Some are in community practices, others are in academic centers, and a growing number are affiliated with larger, organized health systems. Many clinics, particularly community oncology clinics, do not have counselors to help patients deal with financial issues. Many clinicians do not know what their patients' out-of-pocket costs will be for a given treatment, in part because of the complicated nature of insurance coverage. In some cases, low-resource populations may experience lower financial burden due to drug costs because they receive generous coverage and/or support through various programs.
- Doctors may have limited knowledge about patients' costs for pharmacy drugs but have extensive knowledge about the prices and costs of drugs administered in the office. In some proportion, doctors' profits from office-administered drugs come from patients' pockets.
- In order to have meaningful discussions about the cost and value of treatment options, clinicians must know the clinical benefits of drugs and understand the preferences of patients and their families.
- Some clinicians are uncomfortable talking with their patients about costs. Others may have moral objections to raising issues related to cost because they do not think financial considerations should play a role in the patient-provider relationship. Physicians have an obligation to be knowledgeable and communicate with patients about costs of care, in part because costs of healthcare have such profound effects on patients. Physicians should accept some responsibility for stewardship of resources and transparency.
- The oncology care model requires that out-of-pocket costs and total costs of care are discussed with patients. Physicians should encourage patients to communicate about difficulties covering costs of drugs or treatments. These difficulties may change over the course of treatment, so communication should be ongoing.

- In some cases, physicians may be more likely to recommend a treatment if they know the cost will be covered by insurance. Physicians should recognize that society pays for these treatments even if patients are not paying for them directly.
- Many clinicians are bound to follow externally developed guidelines developed by third-party payers when dispensing and ordering treatments. If they do not follow these guidelines, they are not reimbursed. Institutions and insurance companies often require clinicians to choose one drug over another for business reasons. Guideline developers should be included in conversations about how to address rising cancer drug costs.
- At Kaiser Permanente, the cost of drugs does not directly influence clinicians' incomes. Kaiser's oncologists collectively develop treatment guidelines based on the best available evidence, but individual clinicians have nearly unlimited freedom to determine what treatment is right for a given patient. As an organization, Kaiser attempts to be a good steward of its resources by recognizing that every dollar spent comes from a health member's pocket. There is a collective accountability to use resources well.
- Physicians are seeing increasing numbers of patients and are asked to perform a growing number of tasks during visits. If physicians are asked to discuss financial issues, it is important that they be provided with tools that allow them to do this in an efficient and effective manner.
- Financial issues are included in the curricula of an increasing number of oncology fellowships each year. The next generation of oncologists likely will be more comfortable discussing financial issues with patients.
- Leukemia survivors who participated in FDA patient advocacy workshops expressed concerns that they were not informed about the side effects and long-term effects of bone marrow transplantation. Patients want to be informed about the toxicities of their treatments so they know what to expect. Similarly, patients want to be informed about the financial toxicities of their treatments.
- Most patients do not know how much their drugs cost. Many of them are more focused on maintaining insurance coverage or managing their insurance costs. There is significant obscurity surrounding drug charges and costs. The same drug at the same dosage can cost significantly different prices in different locations. The cost also may vary depending on the patients' insurance. It is easier to get straightforward information about drug costs in many other countries.
- Oral cancer drugs can help reduce hospital and office visit costs if patients adhere to recommended schedules and doses. Patients should be informed about the potential benefits of their drugs and the importance of adherence.
- The work of Dr. Dan Kahneman, a Nobel Prize-winning psychologist, indicates that people often make emotional decisions, not rational decisions. When patients delay or stop their care, it cannot be assumed that their choices are based on rational, analytic decision making. Patients may have negative emotional barriers toward healthcare that influence their decision making. These may be exacerbated if patients experience guilt or shame associated with their diagnosis (e.g., cancer linked to tobacco use). Clinicians often do not understand the emotional barriers that influence patient decision making, and there are no reliable ways to measure the impact of these barriers on patient engagement with their physicians.
- Lack of transparency is a problem across the healthcare system, not just for drugs. It also is difficult for patients to identify prices for procedures (e.g., MRI).
- Consideration should be given to patients' values. Patients want treatments that will help them survive their cancers, but they also are very interested in maintaining their quality of life, which includes avoiding financial toxicity. Patients want side effects of treatment (e.g., fatigue, sexuality, financial issues) to be addressed.

- The FDA report [*The Voice of the Patient*](#) summarizes findings of discussions with patients that have occurred as part of the Patient-Focused Drug Development initiative. FDA has heard that patients want to be cured or live as long as possible after their diagnoses. If cure is not possible, they want their diseases to be controlled, and they want information about how they will feel and function during treatment. It is important that there is a dialogue between patients and medical professionals with respect to identifying priorities and managing expectations. Both patients' and providers' perspectives must be considered.
- Sensitive measures are needed to generate reproducible data about quality of life to help inform patients about what to expect during treatment. Health-related quality of life is a multidimensional concept and is not a very sensitive measure of all outcomes. For example, it is not a sensitive measure of treatment burden or efficacy; however, it does help assess physical function and tolerability of symptoms. FDA is working to identify effective measures for use in clinical trials.
- Healthcare systems take efficacy, safety, tolerability, and drug pricing into account when making decisions about which treatments will be covered. For example, some healthcare systems will not pay for liposomal doxorubicin even though it is associated with lower incidence of hand-foot syndrome than is doxorubicin without liposomal encapsulation. This is because the liposomal version of the drug is not cost-effective given the relatively low frequency of hand-foot syndrome.
- The various stakeholders in cancer care—including patients, healthcare professionals, payers, and pharmaceutical companies—define value differently. These stakeholders should work together to discuss these value frameworks and develop solutions that work for everyone.
- Patients' preferences and values vary and may depend on a variety of factors, including their stage in life. One patient may be most concerned about preserving quality of life for a short period of time while another may want to extend life as long as possible, sacrificing some quality of life if necessary. There may be some values that all patients share (e.g., maintenance of social roles vis-à-vis family and friends), but healthcare providers should ascertain the values of each patient rather than assume that all patients value the same things.
- Values that are important in healthcare include compassion, transparency, stewardship, and sustainability.
- Drug price should be a product of the value of the drug. Current drug pricing is based on a number of market forces rather than on the benefits provided to the people taking the drugs. Patients are the only stakeholder group that should matter with respect to establishing the value of a drug. The features of drugs that impart value for patients should be identified and used to establish prices. Other countries have found ways to do this, and a solution is needed for the United States.
- Cultural context plays a role in determining how drugs are valued. In the United States, high value is placed on patient autonomy. Some other countries place higher value on broader societal good.
- A number of frameworks for drug value are under development, including the ASCO framework, the DrugAbacus developed by Dr. Peter Bach and colleagues, and others. Dr. John Doyle and colleagues conducted an analysis of these frameworks and found that they each yield different answers with respect to value, indicating that the frameworks need to be further evaluated.
- There is opportunity for patient advocacy organizations to help serve as a bridge between patients and physicians in discussions related to value. However, advocacy organizations need guidance related to factors that influence drug pricing and costs in order to determine how best to support patients.
- Researchers can help define research questions and identify measures for assessing patient values.
- Bundled payment models may incentivize providers to use drugs more efficiently and focus on high-value drugs.

PUBLIC COMMENT

- There was no comment from the public.

BRAINSTORM—BEYOND CLINICAL CARE: MARKET, POLICY, HEALTH SYSTEM, AND REGULATORY EFFECTS ON CANCER DRUG ACCESS AND COST

Participants discussed market, policy, health system, and regulatory factors that influence drug cost and access.

- Precision medicine for oncology is becoming a reality as drugs targeted to specific mutations are developed. Precision medicine has significant implications for drug pricing because many targeted drugs should be tested in and approved for specific, sometimes rare, diseases in relatively small populations of patients. This can make it more expensive to run clinical trials and more difficult to achieve profitability once a drug is on the market.
- As precision medicine continues to define subpopulations for various drugs, many drugs in development may gain “orphan” status. One concern about this is that a given drug may be the only treatment option available for its target population, creating a monopoly of sorts and reducing the likelihood that competition will keep prices low.
- *In vitro* diagnostic tests can help identify patients most likely to respond to a drug, which can facilitate the review and approval process. The benefits of a drug will be more obvious if it is tested in the “right” population. This allows smaller trial sizes and shorter trial times. Matching the right patients to the right drugs also saves money in clinical care because money is not spent giving drugs to patients who will not benefit. However, it will be more difficult for pharmaceutical companies to recoup their investment if only small numbers of patients are eligible to receive certain drugs.
- It is challenging to develop a companion diagnostic test concurrently with a new drug because the regulatory processes and profit margins are different for drugs and devices. Some companion diagnostic tests are included in the indications for their associated drugs, while others may be used to identify patients who may be more likely to benefit from certain drugs. FDA has attempted to address this issue, in part, by ensuring that various centers within the agency have access to oncology-specific expertise. The FDA Office of Hematology and Oncology Products has developed collaborative relationships with the Center for Devices and Radiological Health and the Center for Biologics Evaluation and Research and other Centers within FDA.
- Pricing becomes more complicated when combination targeted therapies are tested and used. Most cancers will not be cured using monotherapies. Combination therapies are needed to avoid or combat resistance. How combination therapies should be priced requires consideration. It will not be sustainable to charge twice as much for two targeted drugs.
- Ideally, next-generation *in vitro* diagnostic tools will allow for simultaneous analysis of multiple biomarkers so there is not a separate diagnostic test for each drug. The FDA Center for Devices and Radiological Health is working to address some of the challenges to this approach, including identifying an appropriate platform and bridging approved diagnostic tests with a next-generation test.
- FDA has approved combination therapies in the past. FDA’s main concern is whether addition of a new drug to an existing treatment adds toxicity without imparting benefit. Combination therapy approvals are considered on a case-by-case basis.
- NIH has a role in evaluating the efficacy of combinations of approved therapies. In general, this is done through comparative effectiveness trials.
- FDA has modified its review processes for oncology drugs over the past several years. Disease experts who are integrated into academic communities now play a prominent role in the review

process, including working with companies on clinical trial designs. More-effective and novel therapies move through FDA review and approval processes more quickly than do other drugs.

- It is important to consider all factors that influence drug development costs, including time to approval, patent processes, and research and development costs.
- There is no rational drug pricing model in the United States. Stakeholders should discuss what factors should be included in such a model. Factors that could be considered include treatment guidelines, clinical and patient-reported outcomes, and transparency of data.
- Processes for developing treatment guidelines should be clear so that patients and providers trust them. Consideration should be given to whether treatment guidelines should be specifically designed to reduce waste.
- Transparency is needed to unmask the data needed to inform rational drug pricing. Some of the factors influencing drug pricing can be modified through market forces; others are more amenable to change through policy. For example, Massachusetts used policy to promote transparency of claims data by implementing regulations requiring all payers to submit their claims to a single database.
- The distinction between drug cost and drug price is important. Expedited regulatory review and lowering of clinical trial costs may reduce the cost of drug development, but there is no evidence that these things translate into lower drug prices.
- Drug prices are not driven by slow FDA review and approval processes or expensive litigation expenses. They also are not necessarily aligned with clinical benefit. Drug prices are established based on the market's willingness to pay. More-effective drugs will be more expensive because the market will be willing to pay more for them. The market willingness to pay is based on patients' willingness to pay but is also determined by drug formularies and other factors. If payers and others are permitted to implement policies that promote high-value care, this could put downward pressure on drug prices that do not reflect the health benefits of the drug. Clinicians should be discouraged from prescribing drugs that are unlikely to benefit patients.
- Rebates and discounts should be considered when analyzing drug prices. Pharmaceutical companies recognize that healthcare costs have been shifting to patients and are concerned about patients' out-of-pocket drug costs.
- Patients and patient advocacy organizations would like to have a clearer understanding of how drug pricing is established so they can help address the problem. For example, patients could advocate to streamline regulatory processes or help identify patients with rare cancers for clinical trials. Patients do not understand why the prices for some drugs (e.g., Gleevec®) have gone up over time, even after yielding significant profits for pharmaceutical companies.
- Most stakeholders are in favor of pay-for-performance models, but questions remain about how performance should be measured, as well as how and when payments should be administered.
- Pharmaceutical companies are exploring alternative mechanisms for drug payment (e.g., based on indication or drug effectiveness). For example, AstraZeneca has developed a program through which health plans are reimbursed if a particular drug does not work for a patient. For certain drugs, if a patient does not refill the prescription a defined number of times, it is assumed to have been ineffective for that patient, and AstraZeneca reimburses the cost of the drug to the health plan.
- There may be regulatory solutions to some aspects of drug pricing, but it is important to consider potential unintended consequences of regulations. For example, the 340B Drug Discount Program has benefitted hospitals more than the low-resource patients it was intended to help.
- The federal government could promote oncology drug development by adequately funding NIH and FDA. NIH is a workforce of innovation in the United States, and NIH-funded discoveries can lead to

the creation of new companies. FDA needs funding to allow it to modernize and do its job more efficiently.

- The federal government should be cautious about providing tax incentives for development of orphan drugs. In the near future, every drug could be an orphan drug.
- Cost-effectiveness studies are critical for developing rational drug pricing models. The Patient-Centered Outcomes Research Institute (PCORI) should be allowed to conduct cost-effectiveness studies, or PCORI funding should be diverted to agencies such as NIH that can support cost-effectiveness studies.
- Funding should be available to support comparative effectiveness and policy-related research. Pharmaceutical companies may be willing to fund these types of studies, but that could create a real or perceived conflict of interest.
- Federal agencies are limited in the ways in which they can use certain funds. For example, some types of economic research cannot be funded through certain initiatives. Researchers interested in doing cost- and policy-related studies should contact staff within the appropriate NIH Institute or Center to obtain guidance on study topics.
- It is possible that science will advance to the point that society will not be able to afford beneficial treatments. This will be a tougher problem to solve than the current drug pricing dilemma.
- Better data are needed to facilitate analysis of oncology drug value. It currently is not possible to do large-scale analysis of clinical outcomes (aside from death) and costs associated with specific treatments. ASCO's CancerLinQ may help compile some of the information needed for these analyses.
- High drug prices make it prohibitively expensive to conduct clinical trials on combinations of approved therapies. Research funding organizations and agencies cannot afford to pay for the drugs.
- Novel drugs are priced highest right after they are approved, before competitor drugs are developed and approved. Accelerating approval of competitor drugs would help drive prices down.
- Healthcare organizations and payers have limited ability to negotiate drug prices because negotiating power is tied to the ability to walk away. Walking away is not an option when negotiating prices for sole-source drugs or drugs that are substantially better than their predecessors.
- Medicare and Medicaid cannot effectively negotiate for lower drug prices because they do not have power to significantly restrict drug formularies or limit pharmacies that can be used. Drug companies and pharmacies are less likely to agree to lower prices because they will not be guaranteed any increase in volume.
- Drug shortages, including those of generic drugs, are caused by a number of factors, and each shortage is different.
- In the past, when the price of a generic drug increased, companies would reactivate their license for the drug and begin manufacturing it, which would drive down prices. Now, because of backlogs at FDA, it can take several years to reactivate a license to manufacture a generic drug, which allows current manufacturers to keep prices high without worrying about competition.
- Some generic drug shortages are caused because many generic drug manufacturers use just-in-time manufacturing processes. If something goes wrong with a batch of a drug that is manufactured by a single company, shortages can occur. Manufacturing plays a critical part in drug safety. Problems with manufacturing can potentially harm many patients.

INPUT INTO FUTURE WORKSHOPS: PRIORITIZATION OF FOCUS AREAS

Participants brainstormed about topics and questions to be addressed at future Panel workshops related to cancer drug access and cost.

- A workshop could be held on rational pricing and payment models for cancer drugs. Discussions could focus on outcome measures, the definition of value, pathways, guidelines, and transparency. The value of a drug will change over time and may increase or decrease after approval, depending on new data on effectiveness, introduction of similar drugs, and other changes.
- The effects of payment systems, such as bundled payment models and fee-for-service, on drug costs should be discussed.
- A workshop on regulatory issues could be convened, including discussion about regulations that facilitate and impede a functioning oncology drug market. The goal should be to achieve appropriate balance between regulation and market forces. Examples of regulations that could be discussed include the Medicaid “best price” rule, the 340B Drug Pricing Program, and “any willing provider” laws. FDA regulations that influence the market also could be discussed. Consideration also should be given to what could be accomplished within existing regulatory structures.
- A workshop could focus on policies for improving patient access to drugs. Discussion could address Medicare and commercial insurance policies and proposed policies related to patient out-of-pocket costs.
- There are ongoing policy efforts related to drug pricing. For example, payers are exploring pay-for-performance, outcomes-based pricing, reference pricing, and other payment models. The Panel should consider what already is being done or considered to address the issue of drug prices.
- The patient voice must be represented at future workshops, either as the focus of a single workshop or as an element of all workshops. Patients’ points of view are heterogeneous but should be considered along with other market forces. Patients’ decisions reflect their perspectives on a drug’s value. When bevacizumab failed to receive full FDA approval for metastatic breast cancer, many patients were angry and disappointed. However, among patients who could have easily afforded the drug, very few were willing to pay for it out-of-pocket.
- Transparency is an important issue for drug pricing. There should be transparency of clinical trial data, and these data should be the property of trial participants, not trial sponsors. In many cases, companies release incomplete summaries of clinical trial outcomes, particularly when drugs are not approved. All clinical trial data should be made available so they can be analyzed by researchers and other drug innovators. There also should be more transparency about the relationships between pharmaceutical companies and prescribing doctors. The Sunshine Act was intended to accomplish this but does not require disclosure of rebates paid by companies to doctors.
- Efforts are needed to facilitate data sharing. Patients should have access to their data and the ability to share those data with researchers and others. Data standards would facilitate integration of data from different sources. Most patients are willing to share their data if doing so could help improve outcomes. Many patient organizations (e.g., LIVESTRONG, Leukemia Research Foundation, Patient Power, American Cancer Society, PatientsLikeMe) have databases of patient data. There could be a national registry of patients, with the data available for research. The federal government could lead this type of initiative.
- A workshop could focus on the future of cancer drugs and treatment. Immunotherapies are showing tremendous promise and may completely change the oncology treatment landscape within three to five years. These therapies may end up being considerably more expensive than oral therapies, but they also may be far more effective. Considerations of the future of cancer treatment should be included in all workshops.
- The cost of drugs should be considered within the broader context of the cost of cancer care, including costs of hospitalization, hospice care, and other things. Patient advocacy organizations need more information about all of the costs associated with cancer care so they can help patients and promote solutions.

- There should be discussion of ways to reduce or eliminate spending on ineffective therapies. The Choosing Wisely campaign provides a model for this. It would be interesting to determine what fraction of cancer drug spending is for ineffective or minimally effective drugs. Part of this conversation would be defining what is meant by “ineffective.” While it may be easy to identify a proportion of ineffective drugs, it is more difficult to identify relatively or marginally ineffective drugs. In some cases, doctors may prescribe drugs with limited efficacy because there are no other options. In addition, it may be difficult to discourage use of ineffective drugs because government payers have limited ability to dictate what drugs providers can and cannot use. Consideration also should be given to the doctor-patient relationship. Patients often push back when their doctors recommend against using certain drugs or tests.
- One potential framework for a series of workshops would be to have one on payment systems and regulatory issues, one on guidelines and pathways for standard of care, one on measurement of outcomes and value, and a final workshop on rational pricing models.
- There may be opportunities to streamline FDA regulatory processes. Academic investigators and companies have expressed frustration with the amount of paperwork that must be completed as part of the drug review process, including for adverse event reporting. It may be beneficial to bring together representatives from industry, contract research organizations, and FDA to discuss possible solutions that may influence drug costs.
- Thought should be given to how to overhaul the clinical trials system. Conducting clinical trials for adults with cancer is an onerous task with extensive paperwork, and many investigators are not willing to do it. Research strategies should be developed that allow data to be collected from more patients at lower cost, particularly as precision medicines are developed.
- The President’s Cancer Panel submits its report to the President of the United States and can recommend action by the Executive Branch. However, the Panel also can recommend action by other organizations and agencies.

INPUT INTO FUTURE WORKSHOPS: TOPICS AND QUESTIONS

Three potential workshop topics were discussed. Participants provided ideas for discussion items for each workshop, as well as potential participants. The patient perspective will be represented at each workshop. The need for transparency also will be discussed in combination with various topics (e.g., need for transparency to determine how drug prices are set and what various stakeholders pay for drugs.)

Workshop 1: Ecosystem of Costs and Prices

- The effects of consolidation and competition at various levels of the market (e.g., anti-trust) on drug prices should be discussed. Dr. Leemore Dafny, who is a health economist, could speak to these issues. Other health economists who may be able to contribute are Drs. Len Nichols from George Mason University and Steve Kafka from Foundation Medicine.
- Intellectual property issues and patent extensions influence drug prices. Jamie Love and Dr. Aaron Kesselheim (Harvard) are experts in this area. A related topic is government investment in research and the rights government voluntarily gives up.
- The workshop should seek to identify cost inputs that potentially can be modified. For example, clinical trial streamlining may help reduce costs.
- Consideration should be given to whether the current drug development model is appropriate. Other models and their potential impact on innovation could be explored.
- Innovative payment systems should be discussed in either Workshop 1 or 3. One potential participant is Dr. Jennifer Malin from Anthem.

- The workshop should include representatives from the pharmaceutical, biotechnology, and generic drug industries.
- Experts in medical innovation should be invited to participate. Examples include Dr. Jedd Wolchok, who is involved in the immunotherapy field; a representative from Roche Molecular Systems, which just received approval for the first-ever liquid biopsy for lung cancer; and representatives from Genomic Health, Oncotype DX, and Myriad Genetics.

Workshop 2: Regulations and Policies

- Policies that facilitate or impede patient access to cancer drugs should be a focus of the workshop. Dr. Patrick Conway, Chief Medical Officer and a Deputy Director at the Centers for Medicare and Medicaid, could speak to these issues. Topics should include Medicaid Best Price, 340B, and rationalization of Medicare policies across various programs (e.g., Part B, Part D, Medicare Advantage).
- Regulatory barriers that prevent payers' ability to implement better payment designs (e.g., value-based payment) should be discussed. Dr. Mike Chernew, who is involved with the Medicare Payment Advisory Commission, is a potential participant.
- Congressional representatives or legislative aides may be helpful participants. For example, Beth Wikler from Senator Al Franken's office could be invited to discuss policy issues. Representatives from congressional offices involved in appropriations may be able to discuss issues related to FDA and NIH funding (e.g., Senators Patty Murray, Lamar Alexander).
- Bonnie Burns from Medicare Health Advocates could speak to issues related to MediGap. Representatives from large health plans (e.g., Aetna) also may have insights on this topic.
- State medical directors from states that are addressing problems with Medicaid should be included. Possibilities include Dr. John Kelly from Pennsylvania and Matt Salo, Executive Director of the National Association of Medicaid Directors.
- Policies that directly affect patient out-of-pocket costs should be discussed (e.g., co-pay caps).
- The impact of FDA expedited approval mechanisms (e.g., breakthrough designation) on competition should be discussed. Drugs that have received accelerated approval are not considered "available therapies" when innovation of new drugs is being considered (i.e., a similar drug also could receive accelerated approval). An FDA representative (e.g., Dr. Rick Pazdur, Dr. Paul Kluetz) could be invited to talk about these issues.
- It may be beneficial to have federal employees rotate through different cancer-related agencies to help each agency gain a better understanding of what other agencies do.
- Other possible participants include Anthony Barrueta from Kaiser Foundation Health Plan; Dr. David Shulkin from the Department of Veterans Affairs; Bill Sage from the University of Texas; and Dr. David Hyman from the University of Illinois, Urbana-Champaign.

Workshop 3: Rational Pricing and Payment Models

- An overview of the various cancer drug value frameworks should be presented at the workshop, including frameworks developed by ASCO, the Institute for Clinical and Economic Review (Dr. Steve Pearson), and the European Society for Medical Oncology, as well as the DrugAbacus. Dr. Deb Schrag presented an overview and comparison of these four models at the ASCO annual meeting. The ASCO framework identifies the relative value of a treatment compared with other treatments; it is not a pricing tool.
- Representatives from pharmaceutical companies should be invited and asked to provide insights on the factors that influence drug prices. Publicized estimates of the cost of drug development range from \$175 million to \$5.5 billion. Possible participants include Dr. Ira Klein, who was at Aetna and is

now at Johnson & Johnson; Gordon Kuntz from Amerisource Bergen, and representatives from Merck and/or Pfizer.

- Standard core measures for determining the value of a drug should be discussed, particularly with respect to patient-reported outcomes. The ASCO framework includes health-related quality of life. Other measures include symptom improvement and symptom palliation. There is confusion within the clinical trial community about how to measure health-related quality of life. Health-related quality of life is being integrated into some European payer systems.
- It would be interesting to hear about innovative payment models, such as value-based insurance, reference-based pricing, the episodes-of-care model, total-cost-of-care contracts, and two-part tariffs. Dr. Patrick Conway from CMS, who is involved with the Part B pilot project, would have insights on this topic. Representatives from major commercial health plans also should be invited. Drs. Jennifer Malin from Anthem, Lee Newcomer from United Healthcare, and Mike Kolodziej from Aetna would be possible participants. Brian Marcotte from the National Business Group on Health, which represents many national employers, also might provide an interesting point of view. ASCO also has a payment model.
- Part of the discussion of payment models should focus on pathways. Physicians' agreement to prescribe certain drugs based on a hierarchy of value allows costs to be managed in different ways compared with plans that allow physicians complete freedom with respect to which drugs are prescribed. Via Oncology, which is linked to the University of Pittsburgh Medical Center, has done interesting work with pathways. Dr. Bob Jesse at the VA also would be able to speak to this issue.
- It might be interesting to have a representative from a European payer speak at a workshop. Dr. Sarah Garner from the National Institute for Health and Care Excellence in the United Kingdom or a representative from the Institute for Quality and Efficiency in Health Care in Germany might provide interesting perspectives.

CLOSING ROUNDTABLE

Participants were asked to consider whether and how the day's discussion had changed their views regarding areas of cancer drug pricing that were most ripe for solution. Most participants reported that their perspectives had not changed considerably, although they had gained deeper understanding of many of the issues surrounding cancer drug costs and pricing and a better appreciation for the complexities of the issue. The changing landscape of cancer treatment was emphasized as an important theme, with the potential for new highly effective and very expensive therapies to significantly alter the cost of care. The need to consider drug prices within the context of the total cost of cancer care was discussed, as was the importance of ensuring that patients have access to the drugs they need. The potential to reduce the cost of drug development by addressing inefficiencies in clinical trial processes and FDA review also was mentioned. Multiple participants noted that patients want to be informed about drug prices and can be valuable partners in advocating for change.

PUBLIC COMMENT

- A member of the public offered her perspective based on her experiences as a lung cancer survivor, a caregiver to a lung cancer patient, a pediatric oncology social worker, and a health educator. She urged Panel members and workshop participants to continue to keep patients' voices in mind as they work to make drugs more affordable and accessible. Many patients worry about the financial toxicity of their cancer treatments and feel forced to choose between taking their medications and paying their mortgages. Many of these patients are not able to express these financial concerns to their physicians. The speaker noted that she has not had to worry about the cost of her care because she has insurance, but she is concerned about the cost of her care to the healthcare system. It is thrilling to think that cures for cancer may be on the horizon. Suggestions for participants at future workshops included

health aides from the offices of Congresswoman Lois Capps and Congressman Frank LoBiondo, who co-chair the Congressional Lung Cancer Caucus.

CLOSING REMARKS

Panel members thanked participants, the co-chair, the facilitator, and the graphic recorder for their contributions to the workshop. They urged participants to send any additional comments to the Panel office and expressed hope that participants will be willing to provide additional information and insights as the series is developed. Dr. Rimer expressed gratitude to the patients who shared their experiences and reiterated the Panel's commitment to ensuring that patients' voices are represented at all of the workshops.

CERTIFICATION OF MEETING SUMMARY

I certify that this summary of the President's Cancer Panel meeting, *Access to and Cost of Cancer Drugs in a Changing Healthcare Landscape*, held June 10, 2016, is accurate and complete.

Certified by: _____

Date: August 23, 2016

Barbara K. Rimer, DrPH
Chair
President's Cancer Panel