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The Researcher, Physicians, Regulator, and Patient in an Age of Personalized Medicine

Clifford A. Hudis, M.D.
Chief, Breast Cancer Medicine Service
Memorial Sloan-Kettering Cancer Center

Dr. Hudis presented by phone from an airplane re-routed in its trip to DC.

Dr. Hudis suggested that the focus of his talk – personalized medicine – is more accurately described as precision medicine. Cancer treatment has always been personalized – by tumor site, cell type, cell profiles, specific targets on the cell, and complex pathways within cells. A more holistic approach is to personalize treatment against the background of the patient.

Analyzing or classifying breast cancer patients as "triple negative" is one way of personalizing breast cancer and in fact has been the conventional means of personalizing breast cancer. A more recent, additional level of analysis has been to consider whether a tumor is also estrogen positive. Analysis of a whole set of genes has identified a subset within the triple negatives where tumors that looked estrogen-positive did not have the receptor. Instead, they had the androgen receptor. This finding led to experiments to look at androgen-positive breast cancer and treat those patients with an anti-androgen receptor drug.

The movement toward personalized, or precision, cancer care presents challenges for conducting clinical trials. Breast cancer is a collection of diseases, and more precise analysis of breast cancer makes it difficult even for large freestanding cancer centers to do trials. Such centers simply will not have enough subjects with the specific type of breast cancer to complete a trial of a personalized therapy.

A multi-center consortium, on the other hand, can accrue the number of patients necessary to complete such a trial. In the case of breast cancer, the Translational Breast Cancer Research Consortium, or TBCRC, has provided the nimble, independent structure for breast cancer trials. TBCRC can adapt to the fact that breast cancer is really an umbrella of phenotypes, trials are biology-driven, and trials are too small and too intensive for cooperative groups but also too large for any single institution. With the infrastructure provided by TBCRC, the challenge was then to take an "ancient" androgen-positive receptor drug into trials. The

research team begged a company for the drug and then had to convince the regulators within institutions that it was acceptable to extrapolate a dose for men to women.

The screening for enrollment in this trial was also daunting. About 10% of triple-negative tumors have this marker, which meant that it was necessary to pre-screen about 400 patients to find the 45 for trial; only a portion of the 45 would be eligible for the study. The screening process yielded 28 patients to enroll in the study.

The challenge is obvious: clinical researchers have to go through lots of tumors and patients to find the appropriate subsets of patients for the most adventurous studies. Only about 2% of breast cancer patients will be helped by the drug tested in this trial.

Dr. Hudis then suggested a different area of inquiry. There are pathways linking obesity with breast cancer, but researchers have not necessarily dug down deep to understand the relationship of obesity to breast cancer.

Obesity is a chronic inflammatory condition, a condition that can be targeted. The macrophages in obese women secrete inflammatory mediators. Simply by being obese, a woman can trigger breast cancer. The map of the United States that indicates rates of obesity also offers some clues about the links between obesity and breast cancer. The maps from the 1990, 2000, and 2010 Behavioral Risk Factor Surveillance System illustrate the obesity trends among adults in the United States.

Why does this matter? The downstream target of this "fat cascade" is aromatase activity. There is a link between obesity and the specific target of ER+ breast cancer. How do we target this inflammatory pathway? Dr. Hudis said that the obvious thing is to diet and lose weight, buy there are also important research topics to be pursued.

Dr. Hudis suggested that there is considerable promise related to the development of targeted therapies and that the challenges associated with their development can be overcome. However, he also ventured a cautionary note. Even if researchers are successful in developing targeted drugs, these drugs may represent only a small and minor step forward. Targeted therapies will represent a delaying tactic and an important option in cancer treatment. However, there will be limits to their impact.

Jamey Skillings, M.D.
Vice President
Medical Affairs
Pfizer

Dr. Skillings said that, as a physician and researcher with years of cancer care experience in Canada, it was a delight to tell the story of crizotinib.

The work on crizotinib was initiated by Japanese investigators, who focused on an ALK mutation known in lymphoma that was also found to be an oncogenic driver in lung cancer.
The ongoing study of crizotinib in lung cancer was quickly modified on the basis of the findings of the Japanese scientists to recruit patients with the ALK mutation. Massachusetts General Hospital ran the

reference lab, a function that was absolutely critical to ensure that the investigators found the right patients for the trial.

The team presented initial data at the 2010 ASCO Annual Meeting; the data were from about 100 patients, with 82 of that total evaluable. Having seen and presented the data on activity in the "right" patients, Pfizer then collaborated with a diagnostic company to develop a test to identify the patients for crizotinib.

Early on, Pfizer initiated discussions with the Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) and the Center for Devices and Radiological Health (CDRH), to plan for the co-development of the drug and diagnostic.

Pfizer invested in two global phase 3 studies; the company was prepared to invest heavily although only 3 to 5% of lung cancer patients have the ALK mutation. The investment was judged a wise one because the problem of lung cancer patients with the ALK mutation was judged to be a global problem.

It is not yet clear why some have the ALK mutation. The mutation occurs often in non-smokers and is likely related to an environmental exposure.

Patients get a tremendous benefit from crizotinib. Progression-free survival has made a difference for survival. It was very clear early on that very ill lung cancer patients who were on death's door were given time –and good time –by crizotinib. However, cancer is very smart and is able to challenge crizotinib by adapting.

The experience with crizotinib is comparable to the experience with Herceptin. The drug would not have been very effective if the company had treated all comers, but Pfizer was able to target the drug to those with ALK mutation. We have no idea what the impact would be on those without the mutation.

Cancer researchers are now in a position where they can demonstrate dramatic benefit and better value proposition by proper targeting of drugs.

In the case of the ALK mutation, we have to test hundreds to identify a few with the mutation. In the case of crizotinib, how did we test? We had many sites around the world and worked with academic centers across the globe. One question we asked is whether there are differences – geographic and otherwise – in the incidence of the ALK mutation. We saw some bias toward higher rates of ALK mutation at Massachusetts General because of the way they selected patients; they chose to select younger and non-smokers.

The drug was launched in July 2011, and the launch was followed by a serious need to educate pathologists about the test. If patients are not tested, we will not identify those who will benefit from crizotinib. There is also the matter of constantly looking for improvements in the diagnostic test. The current test depends on FISH technology, but there are ongoing efforts to develop other kinds of pathology tests. For example, the company is look at other sources of tissue besides biopsy. In this case, pleural fluid might be an option.

There are also ongoing efforts to develop academic collaborations that would identify the mutations among those with adenocarcinoma, so that treatments could be more appropriately targeted. There needs to be a move to more flexible platforms and the use of multiplex tests. Sequential testing is no longer an acceptable

option because it takes time and expense and unacceptable for patients who have little time. For example, testing for EGFR and then ALK is not a good idea; instead, concurrent testing is important.

Researchers have recently discovered that crizotinib targets the ROS1 gene, a mutation found in 1% of lung cancer patients. Would we have to screen 100 patients to fine a single one with the mutation? It will not be possible to do post-marketing studies with such small numbers. In addition, no reliable test for the ROS1 is currently available. As a result, these patients cannot be reliably identified.

Dr. Skillings said that if she were diagnosed with lung cancer now, she would want to be tested for EGFR, ALK, and ROS1 mutations. She indicated that she might have that option, if she went to an academic center. The core question becomes how to diagnose and treat patients earlier.

There were some very positive developments from the development of crizotinib. Dr. Skillings said that she had never seen academics work together as well as they did on crizotinib. They put aside their publication wishes to collaborate and get the drug to market. In addition, the interaction with the FDA on crizotinib was completely positive. In the case of crizotinib, all parties were learning through the process, as this was one of the first cases of concurrent development of the drug and diagnostic.

Dr. Skillings was asked to comment on the implications for the development plan of the fact that Pfizer had the drug before the target, in the case of crizotinib. Dr. Skillings said that the team knew the drug was a C-Met inhibitor and an ALK inhibitor and was initially more interested in C-Met inhibition and the use of the agent in gastric tumor. It was work of those evaluating their refractory patients that helped identify those who might benefit the most, and that in turned moved the plan toward lung cancer.

Dr. Skillings also indicated that, although the company has received some encouragement to assess the action of the group in those outside the target group, there is not a strong motivation to use the drug in non-ALK patients. The fact that the non-ALK patients have so little time to waste is a strong argument against testing crizotinib in this population.

Dr. Skillings commented on the post-marketing studies and said that establishing survival will be complicated because of the decision to permit patients to cross over. The investigators saw such tremendous benefit, according to Dr. Skillings, that they felt they could not deny patients access to the drug. Investigators believe the drug is making a tremendous difference in the lives of lung cancer patients, but proving that the drug is extending survival will be more difficult.

A meeting participant raised the issue of the "trial of one," a concept that companies have raised at Institute of Medicine meetings on genomic medicine and likely have also raised with FDA. Should FDA, asked the participant, consider additions to the labeling of drugs based on data from a "trial of one"?

In response to questions, Dr. Skillings described the development path for pediatric indications of crizotinib. She said that the credit for these studies, which include studies of crizotinib in neuroblastoma and in anaplastic lymphoma that is ALK-driven (called ALCL), rests with the pediatric oncologists of the Children's Oncology Group who pressed for access to the agent. Even with the collaboration between Pfizer and pediatric oncologists, there have been obstacles to development, including the initial insistence on the part of the Pediatric Committee of the Oncologic Drugs Advisory Committee that the pediatric trials be randomized.

According to Dr. Skillings, the company has not yet gotten to the discussion about how the data from the pediatric studies might support changes to labeling.

Meeting participants identified some day-to-day obstacles to use of crizotinib or any of the targeted therapies. Practices are routinely testing for ALK and EGFR, according to meeting participants, but the testing is not covered by a number of payers. Because the diagnostic tests cost $3000 to $3800, the lack of coverage can present a real problem for patients. The issue of access and payment must be addressed soon, meeting participants said, because drugs like crizotinib are the paradigm for many other drugs soon to emerge from the pipeline.

The meeting participants discussed the difficulties of addressing reimbursement for diagnostic tests. Some expressed surprise that there are reimbursement problems, because crizotinib and other targeted therapies are labeled for use only if diagnostic testing is completed. Others suggested that the pharmaceutical companies that develop the drug are not necessarily in the best position to advocate for reimbursement for diagnostic tests. Others suggested that, although some drugs are labeled to be used only in connection with FDA-approved diagnostic tests, health care providers are using CLIA-approved tests. This practice may also create issues related to reimbursement for diagnostic tests.

Dr. Skillings was asked to comment on whether there comes a point where it is impossible to pursue great science and a great drug, if the drug might be used in only 500 people per year, for instance. Dr. Skillings acknowledged that industry does have to prioritize and that industry leaders have to see a value proposition. However, the industry has also demonstrated that it is willing to test novel approaches to development.

Meeting participants suggested that the age of genomic medicine is going to be quite complicated, as complicated tumors will likely require combination therapies. Dr. Skillings said that a problem that industry has not yet dealt with is the serious competition in the field. For example, in the renal cell carcinoma field, the lead compound was quickly followed by a number of additional compounds.

Gregory Reaman, M.D.
Associate Director
Office of Hematology & Oncology Products
Food and Drug Administration

Dr. Reaman started by pointing out the tension that exists for an agency that is charged with protecting the public health and yet is confronted with a number of therapies that are targeted to the individual. This concern, or tension, was at the basis of the whole decision to develop a guidance with respect to companion diagnostics. There is a fundamental concern within the agency about making decisions that will ensure that the right drug gets to the right patient – not only during investigation and review but also after approval. FDA must make sure that the drug is approved for the appropriate and select population.

Crizotinib and zelboraf are the co-poster children of good development. For both drugs, the regulatory process included many meetings between agency and sponsors to support the review of the drug.

Dr. Reaman identified challenges associated with the appropriate diagnostic test to support a targeted therapy. The diagnostic test that is approved today may not be the approved test – or the preferred test – tomorrow.

There is solid communication and collaboration between CDER and CDRH, but the regulatory challenges are developing and shifting at a rapid pace, changes that challenge the current state of collaboration across the centers.

In addition to challenges associated with development and regulatory review of diagnostics, there will be transformations in the regulatory review of targeted therapies. Large randomized phase III trials have always been problematic in children, but they may also be increasingly problematic if we are looking at the development of targeted therapies for small populations of adults. There will need to be changes in the way all trials are designed.

In response to a general question about the involvement advocates in discovery and development, Dr. Skillings commended the willingness of patients to discuss ALK testing and the potential for benefitting from crizotinib. The involvement of patients in the research process ensured rapid accrual.

Fran Visco commented on the power and risks of relying on anecdotes. Patients are typically persuaded that the drug they received has saved their lives. However, relying so heavily on anecdotes can actually create problems. We need to make sure that decisions are not made solely on the basis of anecdotes. One need only look at Iressa and Avastin to see the risks of relying on anecdotal information.

Ms. Visco described the different levels of advocate involvement in the research and regulatory process. Project LEAD is a National Breast Cancer Coalition program that teaches the language of science – including information about the cell cycle, P value, and other elements of research. Over the years, Project LEAD has educated close to 2,000 advocates.

Dr. Reaman agreed that the involvement of advocates in discovery and development is critically important. Advocates can drive science and can question scientific decisions that are being made.

Fran Visco
President and CEO
National Breast Cancer Coalition

Ms. Visco began her remarks with a description of the National Breast Cancer Coalition (NBCC), a grass-roots coalition of organizations and individuals that is science-based and focused on public policy. The advocates who participate in NBCC are not focused solely on their breast cancer – instead, their involvement has to be about ending breast cancer for all. NBCC is now seeking to advance Breast Cancer Deadline 2020, a deadline that was established in order to restore a sense of urgency to breast cancer research.

NBCC sees the ultimate goal of research as saving lives. Patients are willing to endure great toxicities and high financial burden for meaningful clinical outcomes. The role of NBCC is to question everything – the system, motives, and priorities –to guarantee a focus on saving lives.

The NBCC definition of personalized is a non-toxic treatment with minimal long-term side effects and significant clinical benefit.

To date, NBCC sees the successes of personalized medicine as less expensive genome sequencing and the identification of hundreds of biomarkers. We are persuaded that we have set the bar too low; we should be looking at overall survival and not just progression-free survival. We are still stalled in a place where results are incremental and we are seeing small increases in overall survival. Drugs are still given with traditional toxicities and long-term adverse events. We need to be considering the tumor as well as the microenvironment and also considering the impact of resistance de novo and acquired.

On the business side, we have to consider what the business model will be for investment in targeted therapies that provide benefit for smaller and smaller populations.

Ms. Visco described the Herceptin model as one of promise but also one that presents problems. Herceptin was the first significant targeted therapy. NBCC advocates were very involved in the development of Herceptin, from protocol decision-making to DSMB data review to compassionate use and informed consent, to consumer education to promote accrual. The results for NBCC were significant endpoints, the definition of the population that would benefit, and tests available to identify the population.

About half of HER2 positive patients do not respond to Herceptin at all due to a resistance mechanism, and those who do respond often build up resistance in a year or two. Moreover, Herceptin is very expensive. The therapy is a step forward, but we have to be sure that we do not create this model over and over again.

There are some questions that we need to consider. Is the pursuit of biomarkers realistic without valid assays? If tumors are like fingerprints, is individualized personalized therapy viable? Is targeting the tumor a little too focused?

A recent article in *Cell* identified tremendous heterogeneity within tumors. This raises a really important issue in personalized treatment. This heterogeneity can lead to misleading information about targeting of therapies.

There are also problems with defining innovation. Is the second iPhone innovative? Herceptin was innovative; will the second generation of such drugs be innovative? And what is worth fighting for?

We have new ways to treat breast cancer, but we have not done much to prevent breast cancer or prevent metastases. NBCC has developed goals in these two areas. The organization started with a pilot project looking at a preventive vaccine in breast cancer. We have put more and more on the bones of that plan. The work on the preventive vaccine was a pilot test to see if the model that NBCC had in mind was worthwhile. The result is a substantive, strategic plan of action to end breast cancer

Changes in Oncology Practice Models, Payment, and Location: The Impact of Health Reform and Delivery Reform

Kate Goodrich, M.D.
Office of Clinical Standards and Quality
Center for Medicare & Medicaid Services

Dr. Goodrich is a practicing medicine hospitalist who was the chair of hospital medicine and head of an institutional review board. In September 2011, she made a change of career to come to the Center for Medicare & Medicaid Services (CMS), where she serves in the Office of Clinical Standards and Quality.

CMS is the largest purchaser of health care in the world and its expenditures account for one-third of national health care expenditures. Moreover, millions of consumers will receive care through the Affordable Care Act.

The team at CMS still follows the imperative defined by former CMS Administrator Donald Berwick to provide better care for individuals and better health for the U.S. population at a lower cost.

According to Dr. Goodrich, the mission statement of CMS says that the agency is to serve as a trusted partner. This means that employees have to maintain a relentless focus on what is best for the patient. A principal goal for the coverage group at CMS is to improve value in care and ensure the most effective care for beneficiaries.

Dr. Goodrich highlighted an upcoming meeting of the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) to consider the standards for coverage with evidence development. This process is used to cover an item or service while CMS is waiting for additional data. The focus of CED is primarily items and services where original studies did not include Medicare beneficiaries. In other words, the original studies mostly included patients under the age of 65 or did not look at the outcomes that are important to Medicare beneficiaries. CMS has asked for public comments on the CED process, in hopes of designing a process that will shorten the coverage process and spur innovation. The CED process has been used more in the last year than in the last five or six years.

Another innovation highlighted by Dr. Goodrich is a pilot project focusing on parallel review by FDA and CMS. Under the pilot, the agencies hope to conduct one or two parallel reviews a year and they are currently seeking nominations for device technologies. The intent is to reduce the time between FDA marketing and coverage. The process also gives sponsors an insight into CMS needs and demands related to coverage. To date, device manufacturers have been very focused on the FDA process and not on CMS coverage and payment issues. The FDA-CMS process should encourage more involvement in coverage and payment matters.

Dr. Goodrich also highlighted National Coverage Decisions that are oncology-related, including those related to stem cell transplantation, Provenge coverage, and liver transplantation.

The Affordable Care Act broadens pay-for-performance and pay-for-reporting initiatives that will have some impact on cancer care quality. The measures to date are focused significantly on hospitals, with quality reporting for PPS-exempt cancer centers being implemented in 2014. Over time, according to Dr. Goodrich, the efforts of CMS will focus on aligning measures across all programs.

Currently, CMS is focusing on existing measures and paying special attention to National Quality Forum (NQF) measures. However, the agency is also very interested in measures for patient care, including potential cancer-specific measures.

The overall movement for CMS is from fee-for-service toward a system that rewards outcomes and quality. In addition to initiatives to measure quality, CMS is establishing a quality collaborative and learning and action networks, training clinicians and multi-disciplinary teams, and seeking to understand how local context affects results.

Dr. Goodrich was asked to comment on the process that CMS is utilizing to ensure engagement of patients. Dr. Goodrich said that CMS is doing significant work to assess the impact of its measures, with a report assessing the impact of measure out in few weeks. There is a technical expert panel to be convened soon, and one of the directives that CMS gave the panel was to solicit the patient voice and ask what measures the patients care about. In that case, the goal of CMS is to get patient input into the process. Finally, said Dr. Goodrich, CMS is pursuing the work and example of Dr. Berwick in seeking out the patient voice to guide the work of the quality improvement organizations and also asking beneficiaries what they want to see in terms of measures.

Therese M. Mulvey, M.D.
Physician-in-Chief/Medical Oncologist
Southcoast Health Systems
Massachusetts

Dr. Mulvey introduced her remarks with the warning or advice that what is happening to cancer care in Massachusetts is coming soon to other areas of the country.

Dr. Mulvey said that the big success of health reform in Massachusetts is the fact that 98% of the state's citizens have health insurance. The few who do not have insurance are those who fit into religious exemptions or who pay the penalty and forgo coverage. In addition to those who fit into these exemptions, illegal aliens are uninsured in Massachusetts.

A recent Blue Cross Blue Shield report concluded that for those in Massachusetts, routine health care costs are manageable. However, many (and especially young people) say that they have difficulty finding primary care physicians. Fifty percent of diabetics are not receiving preventive care, and about half of all emergency room visits are still classified as preventable. It is also clear that hospital admissions could be reduced by better ambulatory care.

Residents in Massachusetts support the individual mandate, and employers support reform by a 2 to 1 margin.

According to Dr. Mulvey, the increase in costs associated with early implementation of reform in Massachusetts has moderated. However, there has been a significant increase in utilization management, and administrative costs in the state are much greater than prior to reform.

Oral chemotherapy is a serious problem for oncologists in Massachusetts. It can take as long as four hours of time to put someone on chemotherapy, because it requires obtaining prior authorization and also implementation of an adherence plan. In addition to oral chemotherapy, it is impossible to order a PET scan or SAT scan without prior authorization.

There are other problems of health care delivery. For example, there is more so-called cherry-picking of patients, there are fewer primary care physicians accepting Medicaid patients, and there are no consistent quality measures but instead measures that are different across all payers.

The implementation of health reform in Massachusetts has also resulted in other transitions and highlighted other strains in the system. Minimum creditable coverage does not necessarily translate to adequate coverage for cancer patients. As the movement toward accountable care organizations and medical home models accelerates, there are lingering questions about whether oncologists will be part of the medical home. There is also a pressing need for enhanced health information technology, but there are lingering questions about who will pay for such improvements.

Dr. Mulvey also offered a brief preview of American Society of Clinical Oncology (ASCO) cost of care initiatives that focus on the things that oncologists do that bring little value to patients. She suggested that this topic – high-cost care of limited benefit – is getting significant attention in Massachusetts, as well.

Dr. Mulvey said that there is significant venture capital activity in Massachusetts, with at least one company buying practices, visiting nurse associations, hospices, and urgent care providers. She noted that there is profit to be made in the reformed health care system, and venture capital companies see the opportunities for making profits through efficiencies and consolidation.

A meeting participant asked Dr. Mulvey to expand her comment about the difficulties of prescribing and administering oral chemotherapy. She explained that if she made a decision to write an oral chemotherapy prescription, she also asked the patient what insurance she has and therefore what specialty pharmacy she must use. The prescription is filled through the specialty pharmacy, which sends the drug to the patient. Dr. Mulvey's practice is to ask the patient to come back to the office for an appointment that will permit her to review the drug and drug side effects and implement a management and adherence plan. The renewal of that prescription starts the process all over again. In addition, if the patient has a coverage plan with a significant co-insurance requirement, the social worker of the practice will work with the patient to manage the co-insurance or to refer to a patient assistance program.

In response to a comment that the Massachusetts situation, with improved rates of insurance coverage, actually "sounds pretty good," Dr. Mulvey agreed that the current situation is better than one with as many as a million Massachusetts citizens uninsured. However, she said that the new system brings different demons, which she previously described.

In response to a specific question about denials of coverage, Dr. Mulvey indicated that ordering imaging services is definitely accompanied by some hassles.

Ira Klein, M.D., M.B.A., F.A.C.P
Aetna Oncology Solutions
Aetna

Dr. Klein began his remarks with the observation that when the public sector chooses to be an insurer providing comprehensive and solid coverage, it confronts all the issues that a private insurer would confront.

He observed that Massachusetts seems right on target and that what Massachusetts has done is very much a lesson for us all.

Dr Klein said that this is a dynamic time in health care and that we need a new model. We are already moving to hospital-based systems and to early phases of accountable care organizations. Hospitals are under incredible pressure, as they have spent large sums on bricks and mortar and people. They are still building a lot of facilities, at the same time that their traditional models are going out the window.

The transitions in oncology care, which may be accelerated by the reliance on an ASP-based system of drug reimbursement, are rapid and far-reaching. Dr. Klein contended that the geographic shifts in oncology care reduce the quality of care. He suggested that oncology is like politics, in that oncology care is local. It is hard, he suggested, for those with cancer to routinely travel long distances for their cancer care. Instead, they need to receive care in the community.

Large institutions that are purchasing oncology practices have great advertising and clean buildings, but there is not a lot of evidence that the quality of care is better.

Dr. Klein posed a question about the relationship between cost of care and quality of care. He contended that they are not associated. The more that the system spends on specialists, the more the quality of care declines. Dr. Klein said that oversight of critical elements of information about care and poor communication affect cancer care. Incomplete information generates more tests and false positives and then more tests.

Having identified some of the failures of cancer care delivery system and the health delivery system overall, Dr. Klein turned his attention to offering some solutions. Dr. Klein said that a critical key to better quality and care is a benefit design that reduces costs, holds the line on quality, and guarantees access to preventive services. He also stressed that there must be some traffic lights in order to control costs. For the outlier population that would do whatever is allowed, there must be some controls.

What can be done in oncology? The seeds of the solutions are what we have already talked about. There must be more routine use of information technology to improve the coordination of care. There must be health information technology at the office level to coordinate care and reward providers.

Better use of health information technology gives us a win by increasing quality and lowering cost. What the patient gets is more coordination of care, more rational use of drugs, better care coordination, and overall higher quality of care.

Payers are saying to practitioners, "Please pick some solutions you like and we will reward you for sticking to the solutions you like." Payers are also trying to make the solutions consistent across all payers. We are looking at solutions that other payers can use, as a consistent system will allow all practices to be in alignment.

Dr. Klein also suggested that work on pathways approaches, episode bundling, and accountable care organizations will likely yield some solid systems for better quality and control of costs.

Joseph O. Jacobson, M.D.
Chief Quality Officer
Dana-Farber Cancer Institute

Dr. Jacobson said that his remarks would focus on the difficulties that the comprehensive cancer center will face in a reformed health care system. The reimbursement system for certain cancer centers is a fee-for-service system, as the centers are PPS-exempt. To date under this system, clinical income has supported the research enterprise. Cancer centers are largely unprepared to move into the world of bundled payments.

According to Dr. Jacobson, Ezekiel Emanuel imagines that accountable care organizations will replace insurers in the next three years. Where would the comprehensive cancer centers fit into a system of ACOs? The worst case scenario is that Dana-Farber goes away because its unit cost looks high.

Or let's return to the system of reform in Massachusetts. If the payers in Massachusetts create a product that is 12% lower than the lowest cost product currently, these products may exclude Dana-Farber or Children's or may have a system of tiering that is so difficult that the patients at Dana-Farber and Children's are excluded.

Or the comprehensive cancer centers may take care of high wealth individuals or really complex cases with no place else to go. It is hard to see how that is a model for survival.

Comprehensive cancer centers are required to do basic science and research and also clinical care. The core grant from NCI does not encourage the centers to be focused on care delivery, but if the centers are to survive they must become innovators in cancer care delivery.

We believe we must take lessons from Michael Porter and measure the outcomes we achieve per cost incurred. Value must be defined around the patient.

The Quality Oncology Practice Initiative (QOPI) to date has used only process measures. For the future, QOPI has to look at all costs associated with care. The tier one issues for judging value are survival and degree of health recovery; the tier two issues are the length of time to get back to reasonable quality of life and the toxicities of therapy, and the tier three issues are the sustainability of recovery and the long-term consequences of care.

NCI-designated cancer centers have never paid attention to efficiency. They have a complex infrastructure and little incentive to streamline their processes. The centers are fundamentally unprepared to compete in the value-based environment.

John V. Cox, D.O., M.B.A.
Texas Oncology
Dallas, Texas

Dr. Cox explained that he is part of US Oncology, which includes 280 oncology specialists and therefore is not a typical oncology practice. He also has a role at the ASCO's Journal of Oncology Practice (JOP). At the

JOP, said Dr. Cox, there is significant emphasis on the issues of cancer care delivery and payment that are also the focus of the panel.

Dr. Cox said that one of the core issues that must be confronted to reform cancer care delivery is the impulse to buy and bill. The revenue that supports oncologists is the margin on drugs. As the cost of those drugs has grown, payers and patients look at doctors. That is understandable scrutiny, because we are at the end of the supply chain. It is no longer acceptable to offer a philosophical apology about the cost of care as we deliver that care. We have to have a meaningful discussion with patients about the cost of care, a discussion that also addresses the risks and benefits of care.

Oncology practices also have to develop the facility to measure. Dr. Cox said that practices not only have to learn how to use electronic health records and modernize their billing practices. They also have to adopt and learn how to do team-based care. Oncologists must also learn from the primary care world; their goal must be to develop a system of care in which all allied professionals who are part of the oncology care team practice to their highest level of training and expertise.

Dr. Cox said that the current standards for practice result in his schedule, which clearly favors volume of services. If he looks out three months, he is fully scheduled. However, it is not clear that all of those patients need to see him. Instead, said Dr. Cox, we need to identify those at risk, reform how practices are dealing with survivorship, coordinate care through the use of multidisciplinary teams, and measure the benefits of the care we deliver.

Transformational principles must be applied to oncology practice, and patient-centered medical home principles have to be embraced.

Implementation of the Affordable Care Act: Highlights of Recent HHS Activity

Jay Angoff
Senior Advisor and Acting Region VII Director
Department of Health and Human Services

Today is a good time, said Mr. Angoff, for a review of the provisions of the Affordable Care Act that were implemented in the first year and that are in the course of being implemented in the second year since enactment.

The Department of Health and Human Services (HHS) had to meet difficult deadlines in the weeks after the March 23, 2010, enactment date. Three core accomplishments within 90 days of enactment were: 1) implementation of the pre-existing condition insurance plan, or the high-risk pools, in each state, 2) establishment of the early retiree reinsurance program, and 3) launching of www.healthcare.gov.

The implementation of the high-risk polls had to be accomplished in very short order, and the programs will be only temporary. These programs violate the fundamental principle of insurance because the pools accept the sickest individuals and pick up the full tab. The pools are helping 50,000 with no insurance who would otherwise be unable to afford care.

The early retiree insurance program makes payment to employers for coverage of those employees who retire between 55 and 68 whose employers can keep them in health plans with assistance of a subsidy. These are individuals who would otherwise be surcharged for age and any health conditions they have.

The website, www.healthcare.gov, is not a stereotypical website. Substantively, it has lots of information about health insurance and quality. The site is interactive and permits one to enter age and a bit more personal information and get information for those selling insurance in the area. The quotes are not bindable quotes, but they do provide consumers information regarding the operation of the exchanges in 2014.

After completing implementation of these provisions within 90 days, HHS turned its attention to provisions that had to be implemented within 180 days. Those included the Patient's Bill of Rights, lifetime limits, preventive services, the elimination of pre-existing condition limits for children, and the extension of dependent coverage for those up to age 26.

By the end of 2010, HHS had put into place a medical loss ratio rule, which requires insurance companies to spend 80 percent of health dollars on health care expenses and no more than 20 percent on administrative expenses. Beginning in 2014, companies will have to compete on price and quality and not on risk segmenting of the market. Mr. Angoff stated that there are many companies that are lean with low administrative expenses. However, there are also companies that do not manage care or control costs but instead spend much time attracting the youngest and healthiest. Those carriers will have to change their business model or will not survive the market. If administrative expenses exceed the MLR limit, carriers will be required to refund money to policyholders. There are three way to meet the rule: increase benefits to bring up the numerator, lower rates to bring down the denominator, or make refunds to policyholders.

Also implemented is a rate review regulation that for the first time requires insurance companies to get a review by the state insurance commissioner or by the federal government if there is no state review. Also for the first time, companies will have to justify any increase over 10 percent. To the extent that the state or HHS finds the increase unreasonable, the states will have an incentive to look carefully at their rate increases.

The most aggressive deadlines of the Affordable Care Act have been met. There is much still to be done with regard to implementation, but the deadlines going forward are not as hard as the past deadlines.

The bulletin on essential health benefits, published at the end of 2011, was received much more enthusiastically by the states and insurers than by consumer advocates. HHS allowed the states and industry much flexibility in setting essential health benefits.

The rationale for a plan that permits states great flexibility in choosing a plan from ten currently offered in the states is that if a plan is popular it must be a pretty good plan. There is a tacit assumption that at least one of the plan choices will be a solid plan. Mr. Angoff touted not only the flexibility permitted the states but also the ability of insurers to make substitutions within categories. Mr. Angoff said that HHS disagreed with the position of some patient advocates that the department should have been very prescriptive about the design of the health plan.

Mr. Angoff acknowledged that the drug benefit in the essential health benefits package is more restrictive than the plan in Medicare Part D.

Mr. Angoff reminded the audience that the exchanges are the mechanism through which the purchase of insurance will be facilitated. It is only through the exchanges that subsidies will be available. The system will work because the exchanges are effectively the marketplace for subsidies.

Mr. Angoff finished his remarks by reviewing the flexibility reflected in the plan for implementing the Affordable Care Act. There is flexibility as to the states' partnership with the federal government, flexibility as to network adequacy, and flexibility as to the strength of the exchange.

Questions and Discussion

Ms. Visco directed a question to the previous panel, asking them to comment on the earlier statement that for-profit health care entities are worse for patients than not-for-profits. Dr. Mulvey identified some potential problems with for-profit entities in her geographic area. She said that a venture capital firm has recently come into distressed parts of her state to purchase medical practices at 4 to 5 times their market value. There is no clear problem in the short term, but there may be in the long term if these newly purchased practices do not accept Medicare and Medicaid patients. Also, she said, the practices of the venture capital firm feel predatory.

Dr. Link suggested that some of the payment systems that are being implemented seem like capitated care redux. The new systems leave unanswered some critical questions, including who defines quality.

Dr. Jacobson said that the health services and health economics literature would lead one to conclude that accountable care organizations (ACOs) are different from the system of managed care because there is now a means of measuring quality. A system such as the BCBS quality program, with both process and outcome metrics, is one such system. Dr. Jacobson said that he understands that managed care has gotten bad press, but there is no clear evidence that it reduced quality of care.

Dr. Cox said that he has been impressed that the physicians in Texas ACOs are all organized around quality. There has been no financial discussion around the ACO, which is a contrast to the days of managed care, when physicians simply looked at a contract and worried about the strategy to get their 5% back.

A meeting participant asked if anyone was aware of any analysis of the costs associated with the requirement for pre-certification for oral chemotherapy. Dr. Mulvey responded indirectly that the greatest cost-savings are associated with avoided emergency room visits.

Essential Health Benefits: The Impact on Patients and Health Providers

Katherine Hayes, J.D.
Associate Research Professor
Department of Health Policy
School of Public Health and Health Services
George Washington University

Ms. Hayes said that the goal of her remarks would be to put the bulletin on essential health benefits in some policy and political context. She also said that her remarks assume that the Supreme Court upholds the law and that implementation continues.

Ms. Hayes that the entire concept of essential health benefits was motivated by the desire to create parity in benefits. Those who supported action to define essential health benefits were motivated by the desire to create parity in benefits and by a concern that insurers, without a defined package of essential health benefits, would discriminate against those with health conditions. Ms. Hayes did remind the audience that insurers will utilize other ways to manage their losses, including through their use of strict definitions of medical necessity. For example, insurers may seek to define experimental treatment in ways that will limit access and utilization. In addition, insurers may use treatment guidelines to effectively limit coverage.

Ms. Hayes reviewed the basic outline of the approach to essential health benefits, under which the states are permitted to establish a benchmark plan. Under this plan, insurance issuers may adopt the benchmark or may adopt variations to it.

Of particular concern to patient advocates is the prescription drug coverage as outlined in the essential health benefits bulletin. The bulletin proposes standards for prescription drug coverage that are less expansive than those in Medicare Part D. The bulletin provides coverage for only one drug per class (compared to two per class in Part D) and has no protected classes of drugs (in the Medicare program, all or substantially all drugs in certain protected classes must be included on a formulary). Ms. Hayes posed questions about how CMS will be able to guarantee that a plan with a limited formulary meets the non-discrimination provision.

She also framed questions about how the HHS Secretary can assure that the flexibility provided to both states and plans do not undermine federal efforts to limit risk.

Gregory Gierer, M.P.P.
Vice President,
Policy & Regulatory Affairs
America's Health Insurance Plans (AHIP)

Mr. Gierer's remarks provided on overview of the guidance document on essential health benefits as well as the perspective of America's Health Insurance Plans (AHIP) on the guidance.

Mr. Gierer began with a review of the structure of the Affordable Care Act, which he described as a three-legged stool of market reforms, subsidies, and the individual mandate. AHIP maintains that comprehensive insurance market reforms, subsidies for the purchase of coverage, and the mandate to purchase coverage are inextricably linked. As a result, AHIP is very focused on the Supreme Court arguments on the Affordable Care Act and the Court's much-anticipated ruling on the Affordable Care Act.

He described the experience in certain states that confirm that insurance reforms will not work without the mandate. For example, in New Jersey the lack of a universal participation requirement has undermined the effectiveness of the insurance market reforms implemented in the state.

Mr. Gierer reminded the audience that the essential health benefits bulletin released on December 16, 2011, is a pre-rule bulletin. Since the release of the bulletin, HHS has provided additional information about essential health benefits and has indicated that a formal rule will be released.

HHS asked the Institute of Medicine (IOM) to provide advice on essential health benefits, and the report back from the IOM stressed affordability of the benefit package. IOM warned that if cost is not taken into account, the benefit package will become unreasonably expensive and therefore unaffordable. As a result, the fundamental principle of the Affordable Care Act would not be met.

Mr. Gierer also quoted the work of Jonathan Gruber that finds that a 10 percent increase in the cost of the benefit package will increase the federal cost of reform by 14 percent. Higher costs will mean fewer newly insured Americans.

Beyond considering how the essential health benefits package affects the cost of care, the country needs to do more to manage the cost of health care. The nation must pursue innovations in health system and delivery reforms.

Mr. Gierer said that health plans continue to focus on cost and affordability to achieve the goal of expanded coverage. The plans recommend that HHS examine the impact of the cost of the essential health benefit package and also the impact of the cost of the package on the expansion of coverage. AHIP also recommends a rigorous review of mandated benefits.

Timing is a big issue for the health plans. AHIP recommends that the states move ahead with implementation as expeditiously as possible. The bulletin and additional documents from HHS provide useful guidance, but all parties involved in implementation need more complete guidance. Moving forward, AHIP recommends that after a two-year transition period the entire system should move to a value-based system.

AHIP is still working on its comments on the bulletin on actuarial value, but in its comments it will probably stress the need for more flexibility to make decisions within tiers.

Mr. Gierer stressed, as had previous speakers, the need for innovations in health care delivery, including the development of accountable care organizations and a movement away from the inefficient fee-for-service system of payment. Innovations to prevent and better manage chronic conditions are among the reforms that should be implemented. There is also a need for better medication adherence programs to address the serious public health and cost problems created by non-adherence.

Joshua M. Sharfstein, M.D.
Secretary
Department of Health and Mental Hygiene
State of Maryland

Dr. Sharfstein said that his comments were aimed at a very practical level. In the state of Maryland, legislation is pending that would appoint 100 individuals to advise on health reform implementation. In addition, a committee is empowered by the legislation to make decisions about essential health benefits by

September 2012. The questions before this panel include: What benefits are covered, and how much will the benefit package cost? Dr. Sharfstein contended that as much as 98 percent of the benefits in the package choices will be the same. Attention will be directed to the remaining 2 percent that might be different among packages.

Dr. Sharfstein also noted that, if issuers are permitted to swap out benefits in the ten benefit categories, the real issue to focus on is actuarial value and not the benefit package. The pending legislation would authorize the elimination of health mandates, in the event that the state chooses a benefit package that does not cover mandates.

Dr. Sharfstein indicated that he is concerned about the standards for prescription drug coverage, including the limit to one drug per class. His concern echoes that of Ms. Hayes, which is that the single drug in the class might not provide patients the treatment option they need.

The process of health reform implementation is different in each state. In Maryland, leaders made a choice to embrace a non-ideological approach, trying to use the Affordable Care Act for the best of the people of Maryland.

Dr. Sharfstein ended with a comment that echoed the concerns of other speakers, which is that health reform will not be successful if costs are not controlled.

Questions and Discussion

A meeting participant asked the panelists to comment on the non-discrimination language in the ACA and whether there is an opportunity to require a certification of non-discrimination in order to truly protect patients. Ms. Hayes recommended that those concerned about the non-discrimination language talk to the Administration. Dr. Sharfstein pointed out that states may put additional requirements on plans in the exchanges. If problems with the plans are identified, it would be possible for the states to review the plans. He also pointed out that plans have to pay each other for the amount of risk that they have in their pool. That means that an insurer that has avoided cancer patients entirely would be forced to contribute to other issuers for that reduction in risk.

A participant asked Dr. Sharfstein to comment on the contingency plans that states have developed for different possible Supreme Court decisions. Dr. Sharfstein said that, no matter what happens with the Affordable Care Act, the fundamental questions facing the health care system will not go away. However, he said, we think that a rejection of the Affordable Care Act will be an enormous step backward. The state of Maryland has brought together a diverse group of stakeholders to address questions related to reforming the health care system. However, there is no doubt that we should lose a lot if we lost the Affordable Care Act.

Drug Shortages: The Impact on Cancer Patients and Providers and Strategies for Solving the Problem

Scott Gottlieb, M.D.
Resident Scholar
American Enterprise Institute

Dr. Gottlieb, who has testified on the topic of drug shortages before a House committee and a Senate Committee, said that he believes drug shortages have been caused at least in part by the FDA approach. In his opinion, FDA got tougher all at once in its inspections. The agency has the instinct to shut down an entire facility, even if the manufacturing problem is restricted to only one portion of the facility. Most manufacturing facilities don't make one product but make many at the same time. Because there are currently some facilities that are entirely shut down, even if the initial problem was restricted to a single part of the facility, it is possible that the problem of drug shortages could worsen before it improves.

Is the FDA approach appropriate or not? Some actions are appropriate; some may be overreactions. Of course particulate matter should not be there, but we need to compare that risk to the risk of shortages.

Dr. Gottlieb said that it is his observation that the field staff are aggressive in inspections and in making decisions to shut down facilities, and then the FDA central staff have to react to those decisions. Traditionally, intrusions by the central FDA staff into the field force have been poorly received.

One approach to solving the drug shortage problem is to change the review of sterile injectables -- carve these products out of existing review structure and give responsibility to a separate office. Another option, outside FDA jurisdiction, would be to permit a manufacturer to use a code that will provide higher reimbursement. Still another option might be to permit manufacturers to make claims around their manufacturing process, and to allow them to boost their reimbursement on the basis of these claims. In the current situation where there are significant shortages, these ideas should be considered. Dr. Gottlieb said there is no clear FDA impediment to these ideas.

Dr. Gottlieb also suggested that the problems experienced with childhood vaccines are comparable to the problems creating shortages of sterile injectables. He suggested that there is a chance to recreate the atmosphere for bipartisan solutions, as with childhood vaccines.

CAPT Valerie Jensen, R.Ph.
Associate Director
CDER Drug Shortage Program
Food and Drug Administration

CDR Christine Bina, R.Ph., M.P.H.
Senior Program Management Officer
CDER Drug Shortage Program
Food and Drug Administration

Captain Jensen and Commander Bina described the FDA approach to addressing drug shortages as one of balancing risks – maintaining drug availability but at the same time maintaining quality facilities. They said that FDA tries to maintain open lines of communication with industry to develop solutions to shortages. They indicated that it is often the reaction of industry to shut down an entire facility, but that is not the preference of FDA. Instead, FDA tries to prevent firms from shutting down and instead looks at ways to carve out the line or portion of the facility where there is a manufacturing problem.

Drs. Jensen and Bina also addressed the matter of sterility. They said that the risks associated with non-sterile drugs are huge, so FDA obviously cannot accept problems with sterility of products. However, the agency can sometimes isolate the lot that is not sterile and put a hold on or recall the lot that has sterility problems.

Dr. Jensen reviewed the status of drug shortages. She indicated that, as of March 2012, the number of new shortages in 2012 was lower than in 2011. However, many of the shortages from 2011 carried over to 2012. In 2012, most of the issues are product quality issues. Problems with access to raw materials are not as important.

The most significant shortages of cancer drugs are cytarabine, methotrexate, and Doxil.

The FDA continues to work with large pharmaceutical manufacturers to devise strategies to address shortages. There is a fundamental problem with a lack of redundancy at many firms. The lines in some firms are used constantly, so there is little flexibility to put a new product on the line. This means that there is little ability to find manufacturing capacity for drugs in short supply.

Dr. Bina reviewed the steps that FDA takes to try to obtain the earliest possible notice from companies about shortages. With early notice, the agency is in an improved situation to resolve the problem. In some cases, shortages can actually be resolved. In other cases, the shortages are so enormous and the reasons for them so significant that the shortages will last for a substantial period of time.

Dr. Bina identified the presence of particulates in products and problems with crystallization as two specific problems that have occurred and created significant shortages of drugs. She also cited equipment breakdowns as a cause of drug shortages and indicated that in the cases of equipment failures, FDA typically receives little advance notice. Nonetheless, the agency moves to put all hands on deck and address the problem of shortages. When there are equipment failures, the agency tries to be flexible and creative, seeking new sites for manufacturing in some cases.

One tool that the agency can utilize is regulatory discretion. This agency is most likely to use its discretion with minor, or low-risk, issues. For example, in one situation the agency found that a simple filter could be used to remove precipitants in a product. In that situation, the agency was able to send a letter to medical professionals to tell them what could be done for the safe usage of the product.

The agency may also ask other manufacturers to increase their manufacturing of a product to address the shortages created by one manufacturer.

There are also circumstances where FDA has looked outside the United States for product to replace drugs in shortage. That happened in the case of methotrexate and LipoDox.

Dr. Bina noted the pending legislation that would increase the requirements related to reporting of shortages that are imposed on manufacturers.

She ended with a reminder that the FDA website information related to drugs shortages is updated daily; the agency encourages reporting of shortages, as the earliest possible notice helps the agency manage shortages.

Michael Link, M.D.
President
American Society of Clinical Oncology
Professor, Pediatrics – Hematology & Oncology
Stanford University School of Medicine

Dr. Link said that drug shortages are creating a crisis in care. The fundamental problem, he said, is that there are not that many oncology drugs that work, and some of those that do in fact work are in short supply. For chemotherapy drugs, there are rarely work-arounds for drugs in short supply.

He suggested that we need to consider why the problem is shortages is so intense in the case of sterile injectables. There are several factors that contribute to the crisis of drug shortages: 1) there are few firms manufacturing sterile injectables, 2) there is a low margin associated with the manufacturing of sterile injectables, 3) the manufacturing process is complex and subject to interruptions, and 4) overall, the manufacturing of sterile injectables is not an economically viable enterprise.

Dr. Link suggested that policymakers consider why drug shortages are not occurring as frequently in other countries, where the generic drug price is higher and the brand name price is lower than in the United States.

The consequences of drugs shortages are many, including: 1) treatment delays, which in the case of cancer is never a good idea, 2) substitution of treatments, which can increase patient anxiety, 3) time and expense dedicated to finding substitute drug supply, 4) adverse effects on ongoing clinical trials, and 5) mark-ups of the prices of drugs in short supply, resulting in increased cost of care.

Dr. Link identified some steps that are being taken to address drug shortages: 1) ASCO is aggressively publicizing the problem of drug shortages and attempting to keep attention directed to the problem, 2) interested parties have also formed the Citizens Oncology Foundation to import and manufacture off-patent drugs; those parties are seeking support from ASCO and others for this venture, 3) legislation is being considered that would enhance notification of FDA regarding shortages, and 4) research and meetings among experts are underway to understand the economics of drug shortages continue.

Daniel Todd, M.D.
Committee on Finance
United States Senate

Mr. Todd described the work of the Senator Hatch, as the ranking member of the Finance Committee, as complementary to the work of the Senate HELP Committee focusing on changes to FDA practices to improve reporting and management of drug shortages. The Senate Finance Committee, in contrast, is focusing on economic issues. Mr. Todd spoke in general about ideas that are being considered and under development. He identified one proposal as shifting the reimbursement for sterile injectables to a wholesale acquisition cost (WAC) model, as compared to the current average sales price system. He suggested that a WAC system that provides high enough prices and that is perceived as stable might persuade manufacturers to remain in the sterile injectable manufacturing space.

He also suggested that the 340B program, which provides for discounted purchase of drug for certain entities that are providing care to the medically underinsured, may also contribute to the drug shortage problem and should be included in a comprehensive look at the economics of drug shortages.

Finally, Mr. Todd said that the Senate Finance Committee Republicans would consider economic incentives to persuade companies to remain in or return to the sterile injectable market.

Questions and Discussion

There was a back-and-forth among panelists and audience members about whether FDA is imposing a standard for particulates in drugs that is too rigorous and whether FDA has in recent years and months become more aggressive in its standards. Patient advocates in the audience said that they had no quarrel with a stringent standard with regard to particulates and would not want to see a loosening of standards for drugs used in cancer treatment.

There was also discussion about the policy steps that are being taken to address shortages, including enhanced requirements for manufacturer notification and changes in the reimbursement system. Some audience members worried that the steps could actually worsen rather than improve the shortage situation. One audience member suggested that there might be fewer shortages but lengthier shortages for those drugs that are in short supply. The panelists generally maintained that the policy measures, even if inadequate solutions, will not worsen the problem of shortages.

Friday, March 23, 2012

Tell It Like It Is: Improving Access to Better Quality Cancer Care and Better Quality of Life

Thomas J. Smith, M.D., F.A.C.P.
Harry J. Duffey Family Professor of Palliative Medicine
Director of Palliative Medicine, Johns Hopkins Medical Institutions
Professor of Oncology, Sidney Kimmel Comprehensive Cancer Center

Dr. Smith offered a detailed description of gaps in the delivery of cancer care that compromise the overall quality of care. He began with an overview of the process of care. He said that only 43% of patients ever had any "goals of care" documents, 34% died in hospitals, and 23% were discharged to hospice. Dr. Smith also cited the percentage of cancer patients receiving chemotherapy within 2 weeks of death as a marker of poor quality of care. He also acknowledged the data previously shared by Lee Newcomer of United HealthCare that as many as 17% of women receiving Herceptin are not HER2 positive.

These markers of lapses in quality of care are not the only problems experienced by patients. They are also seeing their financial responsibility for their care going up. In terms of premiums, family responsibility can range from $1700 to $4000, which is an amount that is not sustainable for families or for corporations. A sign of the lack of sustainability is the fact that close to one million personal bankruptcies each year are due to medical costs.

It is critical for us to realize that the pattern of care is under our control. Imaging, chemotherapy, surveillance, and integration are all under our control and therefore can be changed.

A significant amount of salaries is from "buy and bill" for chemotherapy. We also know that health care providers who own services use those services more. On the other hand, some services provided by oncologists are poorly reimbursed. All of these things can be fixed.

Dr. Smith suggested that the Choosing Wisely campaign to be introduced in early April by several medical specialty societies – identifying for each specialty five things that physicians and patients should question – is a realistic first step in bending the cost curve.

There are five immediate things that oncologists can do to bend the cost curve: 1) target surveillance procedures, 2) use monotherapy for second- and third-line treatment of metastatic disease, 3) for patients with cancer that has progressed on treatment, limit future active therapy to patients with good performance status, 4) avoid "nth" line chemotherapy for patients not responding to three consecutive regimens; direct those patients to clinical trials, and 5) make a dose reduction to replace use of growth factors.

There are five attitudes that have to change: 1) acknowledge that we drive the cost of care, 2) acknowledge that both doctors and patients need more realistic expectations, 3) realign compensation for quality care, 4) encourage better utilization of end-of-life non-chemotherapy-oriented palliative care, and 5)accept the need for cost-effectiveness analysis and some limits on care.

We also have to have realistic expectations, including that there will be higher copayments, significant movement across plans, and more emphasis on value.

Dr. Smith suggested that there are lots of reasons to integrate palliative and hospice care. Palliative care offers the trifecta of better quality of life, better quality of care, and at a lower cost. Fortunately, in the years from 1990 to 2012, there has been a movement from a few palliative care programs to many more.

Those who talk to doctors about impending death have less worry, less depression, better quality of life, use hospice more and longer, use less CPR, and have better caregiver quality of life.

Dr. Smith debunked a few myths about palliative care:

1. People do not want to know. In fact, the evidence shows that people do in fact want to know their prognosis. Instead, it is doctors who do not want to have the discussion.
2. We can't really predict or prognosticate about a patient and his or her care. In fact, we can predict prognosis (www.eprognosis.org) and on that basis make a plan of care.
3. A discussion about prognosis will make people depressed. In contrast, the evidence suggests that those who make no plan actually have a worse death.
4. Involvement of palliative care or hospice care will reduce survival. There are no data that suggest that palliative care or hospice will result in a shorter survival, and in fact the data from Temel, et al. suggest a longer and better survival with palliative care provided.

5. It is not culturally sensitive to discuss dying and end-of-life choices. All that is necessary is to ask patients what they want to know. Ask, tell, and ask – this is the model of communication.
6. Talking about death will take away hope. Instead, hope is maintained if realistic information is given along with transition prompts. Avoiding the discussion reduces hope and reduces trust in the team.

Dr. Smith expressed approval of the ASCO provisional clinical opinion on palliative care.

He cited a few model programs that are utilizing palliative care and reaping positive effects. In the Kaiser system, the assignment of a palliative care team to a case saves Kaiser $5,000 to $7,000 by avoiding hospitalizations.

In Aetna's Compassionate Care Program, patients do not have to give up anything. In this program, hospice use doubled, but Medicare inpatient days went down and ICU days also declined. Overall, there are significant savings in the program.

There are a number of things we can do without redesigning the whole health care system. Dr. Smith cited as one example his work with the late Chris Desch. In their work, they reworked the medical chart. The revised chart permitted listing of all prior therapies, identification of performance status, listing of code status, and identification of the goal of treatment. In this sort of records system, you can also add prompts for palliative care.

Dr. Smith ended with a review of ways to cut the cost of care and boost the quality of care.

1. Target surveillance procedures to those most likely to benefit. There is no evidence to support the aggressive use of surveillance. A tough conversation is required to convey that surveillance does not work. It is imperative that health care providers leave people with the things that can be done that DO work.
2. Limit active therapy to patients with good performance status. There is a fundamental screening question that should be used but is not: does the patient walk unaided into the clinic?
3. Dose reduction can replace the routine use of white-cell stimulating factors in patients with solid tumors. The United States has 3% of the population and uses 75% of the world supply of white-cell stimulating factors. Is the use of these drugs, which are highly profitable to practices, a conflict of interest?
4. Switch to non-chemotherapy palliative care after cancer grows through 2 or 3 regimens, depending on disease.

Questions and Discussion

Dr. Smith was asked to comment on the appropriate management of rare cancers. He indicated that he was highly sensitive to the problems of management of such diseases because he is married to a geneticist who sees rare diseases, often referred to as "syndrome without a name," or SWAN. He said that there is wide variation in strategies for management of rare cancers, a variation that might be addressed by collaboration among those treating these diseases to develop the best pathways for management.