

PRESIDENT'S CANCER PANEL

**Translational Research
The Interface With Insurance Reimbursement:
A Northeast Perspective**

**October 25, 1996
Providence, Rhode Island**

OVERVIEW

The President's Cancer Panel was chartered to monitor and evaluate the effectiveness of the National Cancer Program and to report to the President on barriers to implementation of the Program. The purpose of this meeting, the third in a series of four, was to explore in-depth the impact of managed care mechanisms and issues on cutting-edge clinical cancer research.

Fifteen speakers representing the government, industry, consumers, and research institutions located in the Northeast described the impact of managed care on translational research that transfers research findings from the bench to the bedside. Participants also addressed the ability of academic medical centers to continue to provide the educational and research capabilities needed to train young investigators in a managed care environment. Various recommendations regarding reimbursement for the patient care costs associated with clinical trial participation were offered.

OPENING REMARKS

Dr. Harold Freeman
Chairman

In opening the meeting, Dr. Freeman stated that:

- The purpose of this meeting, the third in a series of four, was to elicit the views of health care providers, representatives of the pharmaceutical industry, and consumers regarding the impact of managed care reimbursement policies on translational research, which takes new therapies from the bench to the bedside.
- Clinical trials are essential in improving the standard of care for people with cancer. Thus, a critical component of this nation's war against cancer is the ability to maintain and improve the flow of preclinical and clinical research findings into quality care and practice. Yet, only 3 percent of Americans are enrolled currently in clinical trials, and there is evidence that these numbers may be decreasing. Even in areas of the country (such as the Southwest) where patient accrual rates remain steady, researchers report that they are being forced to expend additional resources in order to maintain current levels of participation in clinical protocols.
- Managed care is profoundly changing the way that clinical research is performed, particularly in the northwest region of the country, where it has achieved significant market penetration. Previous speakers highlighted numerous obstacles to conducting clinical trials in managed care settings, including burdensome administrative and management requirements for physicians, voluminous patient rosters, increased reliance on primary care physicians to make treatment decisions that in the past had been reserved for specialists, lengthy preapproval processes, rules limiting referrals to participating physicians and institutions, and otherwise insufficient support of clinical research by managed care plans.
- Another important barrier to clinical trial participation is a growing trend on the part of insurers to apply restrictive policies to deny reimbursement of the associated patient care costs. This problem is particularly acute with regard to

Phase I and II trials; often, insurers classify these protocols as "experimental," arguing that health benefits have not been proven fully at this early stage of development. Perhaps more troubling, there is some evidence that insurers are denying reimbursement for even standard patient care costs, such as PSA screening, if these costs are associated with clinical research.

- Ultimately, the question that must be answered in order to maintain a vigorous National Cancer Program is "Who should pay the costs associated with performing clinical research?" given the undeniably essential role it plays in ensuring quality cancer care for patients both today and in the future.
- The Panel has heard several suggestions for improving the funding of clinical research, including: (1) increasing the funds available to the National Cancer Institute to support promising research initiatives through additional grants; (2) promoting additional Federal initiatives to improve trial participation, such as the recent effort between the NCI and the Department of Defense that will allow CHAMPUS enrollees to access NCI-sponsored Phase II and III trials; (3) mandating third-party payers to contribute to clinical research; and (4) making support for clinical trials an accreditation standard for managed care providers. In addition, it appears that in some areas of the country, the pharmaceutical industry is assuming an increasing portion of clinical trial costs in order to bring promising new therapies to the market quickly.
- Representatives of managed care plans have indicated to the Panel their willingness to support Phase III trials as long as they are intended to answer clinically significant questions and cost considerations are incorporated into their design.
- It remains the Panel's belief, however, that access to quality cancer care and the maintenance of a vigorous clinical research program must take priority over economic considerations and cost efficiencies if we are to continue to improve standard cancer treatment, prevention, and care.

OPENING REMARKS

Dr. Paul Calabresi

Background

In anticipation of the 25th anniversary of the National Cancer Act, the National Cancer Advisory Board, at the request of the Congress, prepared a report entitled *Cancer at a Crossroads: A Report to Congress for the Nation*. This comprehensive overview summarizes the successes of the National Cancer Program, identifies obstacles to eradicating cancer, and suggests strategies to meet the goals of the Act. First, the report recommends that greater effort be made to apply expeditiously the knowledge gained from clinical research to standard medical practice and care. Second, it urges greater funding of, and attention to, translational research, the critical bridge between the laboratory and patients. Third, the report endorses a greater commitment to basic research, with the goal of accelerating progress while maintaining excellence.

Key Points

- This fall marks the 25th anniversary of the passage of the National Cancer Act, the legislation establishing the President's Cancer Panel and charging the Panel to report directly to the President any issues posing an impediment to the efficiency and the effectiveness of the National Cancer Program. Therefore, it is most appropriate that the Panel is evaluating the impact of managed care on cancer research at this time of sweeping changes in our health care delivery system.
- Promising cancer therapeutics typically are tested in a sequential series of steps designed to assess the safety and efficacy of new products. According to speakers at previous Panel meetings, managed care plans and insurers in some parts of the country are providing reimbursement for certain clinical trials, especially if the therapy is in the later stages of development (i.e., Phase III trials--large-scale efficacy trials involving larger populations) or Phase IV trials (postmarketing studies). Reimbursement is usually denied, however, for Phase I and Phase II trials.
- To assess the impact of managed care on clinical research in the Northeast, a number of important questions must be addressed:
 - Has managed care improved or hindered our ability to conduct Phase I, II, III, and IV clinical trials in the Northeast? Screening? Outreach efforts and patient education?
 - Will these trends accelerate or otherwise change as managed care penetrates the health care market in the Northeast?
 - Has managed care changed patient accrual rates in clinical trials in the Northeast, or otherwise affected patients' inclination to participate in clinical trials?
 - Regardless of setting, what are the essential components of quality cancer care? Can these components be separated into categories such as preventive care or standard screening and treatment regimens? Should one

category of quality cancer care include research options for patients for whom no standard treatment exists or who are otherwise incurable?

- Who should pay for the treatment or other interventions in each of these categories of care—the patient, Federal or local governments, private health care corporations, the pharmaceutical and biotechnology companies? Could these parties share the costs? If so, how?
- Does managed care discriminate against those who are socially, economically, or intellectually ill-equipped to fight for their health care rights? If so, could this result in a bias in research results?

WELCOME

Dr. Donald Marsh
Dean
Brown University School of Medicine

Dr. Marsh welcomed the Panel, speakers, and other attendees, adding that:

- Academic medical centers make a unique contribution to our biomedical research program, as they provide a principal venue for the conduct of translational research. Recent changes in our health care delivery system threaten the ability of academic medical centers to remain viable in this age of cost containment.
- In Dr. Marsh's view, payers must be made to understand the larger societal benefits gained from clinical trials and translational research if academic medical centers are to continue to fulfill their mission of bringing new therapies to people with cancer and those at risk.

WELCOME

Mr. Willaim Kreykes
President and CEO
Lifespan

- The collaborative partnership between Lifespan, Brown University School of Medicine, and Rhode Island Hospital has resulted in an immeasurable increase in the depth and breadth of academic service and research capabilities in this geographic area.
- Health care reform should be viewed as an opportunity to address many of the perverse incentives that exist in the U.S. health care delivery system, an industry now driven by production rather than health status enhancement.
- However, in moving toward a more rational system, it must be recognized that academic medical centers previously depended on hidden subsidies from routine patient care to support the advanced tertiary care and research activities that are at the heart of medical advances. Thus, in the evolving economically driven health care delivery system, explicit carve-outs or subsidies will be necessary if academic medical centers are to continue to make their unique contributions to patient care.

- On a systemwide basis, managed care offers many possible benefits, including greater emphasis on prevention, development of better research protocols, greater consistency across the health care delivery system, and improved affordability.
- On an individual basis, however, managed care can present obstacles to receiving quality care, particularly when preapproval, referral, and administrative requirements take precedence over the best interest of the patient. For patients to successfully navigate this new world, they will need to be informed fully about their diagnosis and treatment options as well as the decision-making processes within their particular plan. In addition, perseverance, tenacity, and a willingness to challenge negative decisions sometimes will be necessary.
- If we are to provide quality care in these new settings, a distinction must be made between managed *care* and managed *costs*.

STRATEGIES FOR EVALUATING NEW THERAPEUTIC OPTIONS UNDER MANAGED CARE

Dr. Vincent R. DeVita, Jr.
Yale Comprehensive Cancer Center
Yale University School of Medicine

Background

In 1988, approximately 25,000 patients participated in clinical trials; the comparable number for 1995 was 26,500. Of this number, 15,500 patients participated in trials conducted by NCI or its cooperative group members. The vast majority, or 12,000 patients, were involved in one of 140 Phase III trials. Only 364 patients were enrolled in one of 58 NCI-sponsored Phase I trials, and 3,015 patients participated in one of 210 Phase II trials. This picture contrasts dramatically with the experience of children with cancer, two-thirds of whom receive therapy under a clinical trial protocol. It has been estimated that if 10 percent of adults participated in trials, this would comprise a sufficiently large population to answer most of the major research questions concerning common adult tumors.

In 1984, the NCI established a goal for the year 2000: a 25 percent reduction in cancer mortality. The latest data suggest that mortality from cancer has been falling from 2 to 3 percent per year since 1990, so that the goal of a 25 percent reduction appears to be achievable. Nevertheless, if we could apply all of the knowledge gained about cancer etiology, prevention, detection, and treatment and deliver the resulting interventions in a uniform and equitable manner, it would be possible to reduce cancer mortality by half.

Key Points

- Clinical trials have become even more essential in the current age of molecular biology, in which the opportunities to explore new therapies outstrip our ability to study them. In particular, Phase I and Phase II trials play significant roles, since

they serve as the true gateways for bringing innovative therapies into standard medical practice. Phase I and II trials will become even more important as molecular biology allows us to supplant some animal model research with earlier studies exploring an agent's therapeutic effect on the human body.

- The greatest threat to biomedical research is not any particular mode of reimbursement or payment. The exploding costs of medical care pose the most significant challenge, and have contributed substantially to this country's struggle to remain competitive in a global economy.
- Congressional support for biomedical research tends to fluctuate with the health of the overall U.S. economy, so it is necessary to ensure that funding for NIH remains adequate even in times of an otherwise austere national budget.
- Leading experts estimate that excess costs account for as much as 30 percent of U.S. health care expenditures, or approximately \$300 billion each year. In that context, managed care can be viewed as a welcome trend that will help us to spend our health care dollars more efficiently while still purchasing quality care.
- Experience to date indicates that a phase of intense price competition typically accompanies the entrance of managed care companies into a region. As these companies evolve and managed care begins to penetrate the market, however, consumers begin to demand--through legislation and regulation, if necessary--that quality concerns also be given priority. Therefore, price competition should be followed by quality competition.
- The bridge between the cost and quality phases of managed care competition will be the development of disease-specific clinical guidelines. These standards of care should include clinical trial participation in appropriate circumstances. Payers have expressed willingness to pay for treatment in clinical trials if standards of care are in place. If this is done, access to research protocols could improve under managed care.
- Access to a variety of providers should also improve over time as managed care companies merge and create broader networks of participating providers and institutions. In addition, government efforts like NCI's agreement with the DoD and the agency's discussions with Blue Cross and Blue Shield are aimed at eradicating barriers to accrual into high-priority clinical trials.
- An important, and often overlooked, impediment to clinical trial accrual is the attitude of physicians facing both ethical and administrative issues--for example, the requirement to randomize patients in a double-blind study, or the complex documentation requirements for group protocols. These issues were as much of an obstacle 20 years ago in an era of fee-for-service health care as they are in today's managed care environment. In fact, they may explain why clinical trial participation rates (approximately 3 percent of adults with cancer) have not changed substantially over the years despite far-reaching changes in the health care delivery system.
- Currently, Yale Cancer Center is accruing more patients to its trials than in the past, although considerable effort is expended to secure reimbursement for patients' participation. It is possible that this situation could deteriorate as managed care makes further inroads into the Connecticut marketplace.

- In the long-term, a managed care environment in a free enterprise system could provide the best answer to controlling health care expenditures while providing more uniform quality cancer care to all, including access to clinical trials. To achieve this goal, clinical trial participation must be an established standard of care, not an exception.

Dr. Kirby Bland

**Brown University School of Medicine
Rhode Island Hospital**

Background

The growing clout of managed care has special ramifications for Medicare and Medicaid, the health care programs for the elderly and the poor, respectively, that are administered by HCFA. Currently, 60 million beneficiaries are enrolled in these two programs. Medicare enrollment in health maintenance organizations increased 25 percent in 1995 to total at least 4 million individuals. For Medicaid, the numbers are even larger—enrollment in managed care plans increased 50 percent between 1994 and 1995, so that approximately one-third of Medicaid beneficiaries now are enrolled in managed care plans.

On a practical level, these numbers mean that HCFA is the largest purchaser of managed health care in the country, and its decisions regarding accountability, quality measurement, and outcome data will have far-reaching impacts on managed care in the private sector.

Key Points

- Several factors account for our inability to enroll in clinical trials all patients who potentially could benefit from participation: increasing time commitments and administrative burdens on physicians who are experiencing diminishing financial incentives for their participation; fear and confusion among patients concerned about selecting the most appropriate course of therapy; the inherent tension between opening clinical trials to the greater community and perhaps losing valuable data generated from center-sponsored trials; the shift toward the provision of care by generalists rather than specialists; patient resistance to entering clinical trials; stringent requirements for protocol review by members of the participating medical staff and Institutional Review Board; opposition to the randomization of patients required in Phase III trials; difficulties in securing reimbursement from managed care companies and other third-party payers; and increased patient care costs associated with tertiary care facilities like academic medical centers.
- At the same time, other forces encourage increased participation in clinical trials, including the evolution of well-informed patient advocacy groups modeled on the successes of the AIDS advocacy community, an explosion in cancer information and technology, and increased support on the part of NCI and the pharmaceutical and technology industries for both community and hospital-based cancer research.

- In addition, direct marketing to consumers, expeditious approval times on the part of the Food and Drug Administration, and efforts to secure reimbursement for off-label uses of approved drugs have fostered a greater appreciation among the public of the importance of the drug development process in general and the availability of specific promising new products. The threat of litigation and adverse publicity also are forcing third-party insurers to cover certain cancer therapies such as autologous bone marrow transplantation for breast cancer.
- State legislatures are becoming active on the issue of clinical trials reimbursement; for example, Rhode Island recently enacted a statute requiring coverage for cancer therapies in Phase III or Phase IV clinical studies meeting specified criteria. Efforts are under way to expand this coverage to Phase I and II trials.
- On the national scene, advocacy organizations are urging Congress to require Medicare to cover the patient care costs incurred in clinical trials. As a first step, Senators Mack and Rockefeller plan to reintroduce in the 105th Congress a bill that establishes a demonstration project to study and provide coverage of these costs for Medicare beneficiaries enrolled in certain approved trials (all phases).
- Advocates for both consumers and professional groups have become more active at the agency level as well; for example, they forced the FDA to address bottlenecks in its regulatory review of new products in order to shorten the 10 to 12 years it sometimes takes to bring a product to market. This lengthy process can result in slow patient accruals, unnecessary delays, and reimbursement denials; it also raises ethical questions about the best course of treatment for patients involved in the study.
- The growing availability of new therapeutic agents will challenge the traditional models of cytotoxic agents and result in greater variability in reimbursement policies.
- The American College of Surgeons has established a clinical trials group that will have the potential to accrue a large number of surgical patients to Phase I through IV trials.

Additional Research Needs and Other Recommendations

- Phase I trials should encourage both flexibility and investigator creativity and should maximize the potential benefit to patients. Reasonable—but not exhaustive—preclinical information should support Phase I trials, and they should be designed to incorporate ethical issues and to answer medically important questions. An issue of debate is whether lengthy IRB review and approval of protocols is always necessary, or whether FDA approval might suffice in certain instances.
- As stated by the Washington Cancer Trials Conference, third-party payers should cover the expenses incurred in all phases of study, from Phase I to Phase IV. In addition, managed care organizations should encourage their members to participate in clinical trials that have therapeutic intent. The goal of these proposed policy changes is to speed the development of new agents to treat advanced cancers and to expedite the delivery of available drugs to patients

- potentially deprived of them by capricious and ill-founded reimbursement policies.
- In assessing future clinical trials reimbursement policy, we must acknowledge the current reality, in which much of the chemotherapy being administered consists of off-label uses of multiple agents provided outside of a properly designed trial intended to advance our knowledge of appropriate cancer care. Thus, much of the potential empirical benefit and related data that could be gained from today's care are lost, except for instances in which data on outcomes, disease-free and overall survival, and quality of life are captured by regional cancer registries. In addition, the costs to payers reimbursing for these therapies, which have not been evaluated for therapeutic effectiveness and patient-related outcomes, are significant.
 - Members of the academic community have a responsibility to contribute to the scientific foundation of cancer care by obtaining outcome data in well-designed, peer-reviewed clinical trials. To support this goal, we must encourage patients to participate in appropriate protocols, provide sufficient reimbursement for their providers of care as well as the researchers, and enlarge support systems for the analysis of necessary outcomes research.

Dr. Arvin S. Glicksman
Quality Assurance Review Center

Background

Dr. Glicksman shared with the Panel the results of a national survey of clinical investigators designed to measure the impact of managed care on clinical research. Overall, 25 percent of respondents reported a change in their institution's attitude regarding participation in clinical trials. Approximately 65 percent--particularly respondents in the East--stated that they received subsidies to cover overhead costs such as personnel, travel, and supplies; only 30 percent (primarily in the Northeast) received support for patient care costs incurred in their clinical trials. Subsidies are generated from indirect costs (18 percent) or practice plan funds (47 percent); over one-half of the respondents did not know the source of the subsidies they receive.

Overall, 77 percent of respondents, including 93 percent of medical oncologists, participate in clinical trials other than those sponsored by the national trials groups. Phase I trials garnered lower participation rates (34 percent in NCI-sponsored trials; 39 percent in cancer center trials; 41 percent in industry-sponsored trials) than either Phase II (48 percent in NCI-sponsored trials; 52 percent in cancer center trials; 60 percent in industry-sponsored trials) or Phase III trials (54 percent in NCI-sponsored trials; 45 percent in cancer center trials; 50 percent in industry-sponsored trials). There were no major differences by discipline or geographic region.

One-half of respondents reported a decrease in the availability of patients for Phase II and Phase III trials in the wake of managed care. Frequently cited observations included markedly fewer referrals, more emphasis on cost

containment, an increase in fragmented care, limitations on care rendered outside of a network, and fewer patients available to be evaluated for recently approved therapies. Only 22 percent of respondents, however, indicated that the decreased availability of patients affected which trials they participate in as investigators. Additionally, only 22 percent felt that patient willingness to participate had been impacted by managed care, although concerns about reimbursement and randomization are voiced frequently. Financial anxieties were most prevalent in the West, where managed care has achieved significant market penetration.

Key Points

- To combat rising health care expenditures that exceeded 12 percent of the gross national product, several cost containment measures gained acceptance in the 1980s: limiting tests and procedures; transferring more care to the outpatient setting; relying on nonmedically trained gatekeepers to control access to specialists; and promoting the use of generic drugs. Although these steps may have slowed increases in health care spending, the transition from traditional fee-for-service medical care to managed care has been particularly difficult for the elderly, the chronically ill, and others with minimal influences or resources to adapt to this new environment.
- Despite the demonstrated value of clinical trials in achieving progressive advances against cancer, managed care severely threatens the continued existence of clinical research because of an emphasis on the short term and excessive concern with the bottom line over responsibility to patients and researchers.
- The cancer community in Rhode Island was successful in convincing the State legislature of the merits of clinical trials; a statute mandating coverage of new cancer therapies in specified Phase III and Phase IV trials was passed. After 2 years, two major HMOs in Rhode Island reported no adverse financial impact of the legislation. Legislators may consider amending the current law to cover Phase II trials, a move that is supported by 88 percent of Rhode Island oncologists who were surveyed on this issue.
- Clinical investigators have a clear responsibility to ensure that the trials in which they participate are designed both economically and to advance scientific knowledge. At the same time, the managed care industry has an obligation to operate in the interests of the communities it serves. If necessary, local and national legislation to address the current lack of oversight should be enacted so that continuing advances in the cure and care of cancer are possible.

Drs. DeVita, Blank, and Glicksman
Discussion Period

Key Points

- Criteria are needed to establish which clinical trials should be reimbursed; the Medicare legislation to be reintroduced in the next Congress by Senators Rockefeller and Mack, for example, would cover trials of anticancer agents approved by NIH, NCI, FDA, DoD, and the VA. The Rhode Island legislation

- requires that trials are NCI-approved or NCI-designated cancer center approved, and IRB approved by the participating institution. Once managed care organizations begin competing on the basis of quality as well as price, it should be possible to negotiate capitated rates that incorporate the cost of including clinical trials as standard care in appropriate cases.
- Although the number of individuals participating in clinical trials may not have changed significantly in recent years, there is evidence to suggest that the research questions being pursued may be changing. Dr. DeVita believes the establishment of human investigations committees has largely quashed adventurous clinical research and resulted in a trend toward conservative trials. He also noted that the effects of certain anti-clinical trial myths (e.g., reluctance of certain patient populations to be randomized) may be inappropriately blamed on changes in the health care system.
 - The typical slowness of disseminating research results to practice was cited—frequently, it takes 5 years after positive studies are published to get the new treatment into practice, and another 5 to 10 years before an impact on national mortality can be observed. The pediatric cancer model offers important lessons for achieving more immediate patient benefit from clinical research.
 - Concern was expressed regarding potential negative effects of industry's growing role in the clinical research process—for example, greater emphasis on applied rather than basic research. Participants acknowledged that financial incentives and the quest to secure FDA approval drive the research objectives of companies in the private sector; on the other hand, the commercial new product pipeline has contributed many exciting therapeutic advances, especially in the recent past. Industry is also becoming more involved in basic research, and the NCI is taking the lead in developing industry partnerships in readiness for research opportunities that will become available when the entire human genome has been sequenced.
 - It was suggested that managed care evolved at least in part because the physician community did not act to trim excess costs from the system. As the managed care industry has shifted from primarily not-for-profit to for-profit entities, however, the legitimate profits that were being returned to the system to support research, infrastructure, and training are being redirected to corporate shareholders.
 - In addition to expressing concerns about the continued viability of clinical research, participants questioned whether graduate medical programs will survive under managed care. Managed care organizations must either be persuaded or forced (through taxation of some kind) to make long-term investments in infrastructure, and only those organizations willing to replenish the system's resources should receive approval under the prevailing regulatory mechanisms.
 - The unwillingness of MCOs to support tobacco control interventions such as physician counseling of patients who smoke (an intervention known to be effective but not unduly time consuming) demonstrates MCOs' reluctance to invest in benefits that may not be realized in the current fiscal year. In Rhode Island, HMOs have declined to respond to Requests for Proposals to establish smoking cessation interventions even for pregnant and postnatal women.

STRATEGIES FOR EVALUATING NEW THERAPEUTIC OPTIONS UNDER MANAGED CARE

Dr. Bruce Chabner

Massachusetts General Hospital Cancer Center

Key Points

- In addition to the rapidly evolving changes in our health care delivery system, we are experiencing a paradigm shift in the drug development process as biotechnology and cancer biology research yield such products as cell cycle inhibitors, antiangiogenic compounds, and antimetastatic compounds. These innovative agents differ markedly from the drugs currently available, most of which inhibit DNA synthesis or otherwise affect the integrity of DNA. These emerging therapies will require different, and often longer, Phase I and Phase II testing because: their effects likely will be cytostatic rather than cytotoxic; they will require continuous rather than cyclical administration; their clinical endpoints will include parameters of tumor growth, biochemical parameters, and time to development of metastases rather than tumor size regression; and they likely will be tested in slower-growing solid tumors that have proven more resistant to existing chemotherapy.
- Many of these new agents are emerging from the biotechnology industry, which raises issues that are distinct from those associated with the funding of trials by the NCI or traditional pharmaceutical firms. For example, most biotechnology firms are small companies with limited resources, so they may not have the requisite staff, laboratory infrastructure, or regulatory knowledge to support clinical testing of these promising agents or the ability to rigorously analyze the resulting data. Partnerships with academia and/or the government are necessary to bring this additional expertise to bear on the development of these new products. In particular, careful analysis of early clinical data by senior oncology investigators is critical to avoid inappropriate and overoptimistic evaluations of Phase I results.
- Diminishing institutional resources, fewer NIH grants for Phase I and Phase II trials, decreasing third-party support for trials, and the rise of clinical research organizations (CROs) present massive challenges to the future of academic medical centers. Yet academic centers often are the most appropriate place to test the newer drugs because their specialized nature demands biologically trained investigators who understand the drugs' origins and mechanisms of action and can therefore work effectively with basic scientists to design sound clinical trials with appropriate endpoints. Individuals with this training are seldom found in community practices.
- Massachusetts General does not suffer from significant reimbursement problems (it sustains outright denials for only approximately 5 percent of patients enrolled in trials). However, the effects of a new cost consciousness, and corresponding disincentives to perform research, are nonetheless apparent. For example, the hospital now tracks the revenues generated by each of its physicians, so that physicians who participate in trials must either work longer hours or see fewer

revenue-generating patients in order to meet the demands of their clinical research. In addition, as more patients are seen on a capitated basis, the risk of meeting the extra costs of clinical trials--blood tests, extra visits, possible complications--lies exclusively with the hospital.

Additional Research Needs and Other Recommendations

- There must be support to develop laboratory-trained, clinically competent investigators who understand cancer biology, clinical trials methodology, pharmacokinetics, and regulatory issues. Traditionally, this support came from institutions early in the investigator's career, but the pressure to become bottom-line oriented is diminishing the assistance that hospitals and academic medical centers can give to young investigators. Support that the large, well-endowed companies provided in the past cannot be matched by the smaller biotechnology firms. Specific awards to support postfellowship training in clinical trials methodology and clinical pharmacology (including diagnosis-related activities), perhaps modeled on the KO8 award program, could be established to close this gap, allowing young investigators to make the transition from training to a faculty role.
- Academic medical centers must begin to meet the needs of the emerging biotechnology industry, particularly in the areas of technology transfer, information management systems, regulatory affairs, and clinical trials management and design. These are capacities now found at the CROs but not at most academic medical centers. To expedite the development of this expertise and technologic capacity, the Small Business Innovative Research (SBIR) program could be revamped to support early clinical trials undertaken collaboratively between academic institutions and biotechnology firms.
- Negotiations to secure clinical trial reimbursement from managed care organizations and other third-party payers should include not only Phase III, but also Phase I and Phase II trials. These early trials, which typically are limited in scope, number of patients, and corresponding expenses, serve as the gateway to later Phase III and Phase IV trials.
- NCI should proactively facilitate early clinical trials by adding more staff to monitor ongoing trials, expeditiously securing investigational new drug approvals, and expanding early trials of promising drugs and making them available to more institutions.
- Standards are needed to force managed care companies to contribute to improved health care in the future rather than merely generating today's profits.

Dr. Chabner--Discussion Period

Key Points

- In the past, government grants supported the laboratory training of young scientists while hospitals funded fellowship positions for the first 12 to 18 months of training. Medicare also contributes to fellowship training support, but is now

requiring duplicative paperwork that is especially troublesome in an environment pressured by cost and efficiency concerns and creates a strong disincentive to retain fellows. Institutions are finding, however, that they can no longer provide this support, due mainly to the impact of managed care in a number of key areas. First, for-profit managed care companies typically have not reinvested their profits in participating institutions as was the practice of not-for-profit academic centers. Second, managed care's emphasis on primary care has forced academic medical centers to cut fellowship positions, which means that competition for the few available fellowships is intense. This trend, in turn, is forcing junior staff members to go into primary care (where it is perceived the most viable career path lies) rather than specialty medicine. This dynamic will lead to a declining cadre of clinical researchers in the future.

- Dr. Chabner noted capitation has achieved only 10 to 15 percent market penetration in the Boston market. However, he expects that significant changes will occur as the number of Medicare patients in capitated plans increases in the area.
- Dr. Chabner clarified his position that third-party payers and managed care organizations should pay for the patient care costs associated with all phases of clinical trials, including Phase I. Other types of research expenses, such as costs for data management, clinical pharmacology, and extra nursing, should be covered by grants from NCI or other government agencies. He also reiterated his view that managed care plans should either be taxed to provide reasonable support for clinical research or should be required to provide it as part of the benefit package.

Dr. Emil Frei
Harvard Medical School
Dana-Farber Cancer Institute

Key Points

- Key Points
 - Phase I studies, which are the critical gateway for all progress in cancer therapy, address both toxicity and dosage and often are not covered by third-party payers. This emphasis on establishing dose tolerances rather than therapeutic effect presents ethical dilemmas for the investigator, since it has been shown that patients in Phase I trials often do not understand that they are receiving subtherapeutic doses. Moreover, most patients have indicated that they would refuse to enter a Phase I study if its only goal was to establish toxicity, a finding that clearly raises informed consent issues.
 - Many factors, including FDA requirements, IRB reviews, and sponsor and physician attitudes account for the traditionally conservative, safety-oriented design of Phase I studies. One of the limits of classical dose escalation schema in Phase I studies--such as the modified Fibonacci technique--is that often a relatively large number of patients is needed over substantial periods of time to reach full therapeutic dose. This

drawback will become especially limiting when these classical techniques are applied to the new biologic agents under development.

- Efforts to make Phase I trials more efficient and to incorporate therapeutic intent as well as toxicologic parameters should be undertaken by the research community in appropriate circumstances. This effort is important because the response of a drug in these early stages of testing often has a great impact on the vigor with which its further development is undertaken. In addition, pursuing therapeutic effect would negate third-party payers' contention that Phase I studies constitute pure research, and therefore should not be covered because of their investigational or experimental nature.
- Pre-NDA Phase II studies that are positive and confirmed should be sufficient to support an NDA. Phase IV trials conducted after NDA approval are a more desirable environment for exploring exactly how a new agent compares with standard treatment.
- These types of modifications to classical clinical trial design should improve the outlook for reimbursement, since even Phase I trials would be pursued with therapeutic intent and the number of patients needed for these studies would decline. If the patient's insurer will not pay, trial costs should be borne by the sponsor.

Additional Research Needs and Other Recommendations

- The new agents appearing in the pipeline as a result of basic science advances argue for adopting flexible experimental designs tailored to the specific agents under review.
- Phase I studies should be designed with therapeutic as well as toxicological intent, and physicians and patients should collaborate in making risk/benefit calculations at each dose adjustment by using the continuous reassessment method modeled on the bayesian approach. In addition, researchers could employ a geometric, twofold dose increase rather than the modified Fibonacci method in cases where there is absolutely no evidence of toxicity at the previous dosage.
- Phase I studies also could be made more efficient by allowing inpatient dose escalation, a step that should be taken now that preclinical toxicity studies are subacute and chronic, and therefore can establish evidence of cumulative or delayed toxicity. (It should be noted that cumulative dose-limiting toxicity was found to be present in only three or four of 43 active chemotherapy agents tested). These steps could pave the way for Phase II studies that are conducted fairly quickly as part of a continuous process; in addition, most patients in Phase I studies would then experience the therapeutic range predicted by preclinical models. In exploring these proposed outer limits of dosing, pharmacokinetics will play an essential role.
- Phase II trials should be designed to maximize the possibility of a positive result, since false positives will be discovered in extended trials, while

false negatives likely will result in the agent being dropped from further study. Impressive results can be achieved in sequential Phase II studies in which only one variable is changed at a time, and a tracking system for prognostic and demographic factors is employed.

Dr. Peter Quesenberry
University of Massachusetts Medical Center

Key Points

- Although managed care has achieved approximately 40 percent market penetration in the Northeast, thus far its impact on accrual to protocols has been minimal; in fact, the University of Massachusetts is experiencing growth in its clinical trials program.
- Managed care presents opportunities for improvement over the current health care delivery system. However, managed care at this time is in fact managed cost, a perspective that can detrimentally affect patients. Managed care can impact patient care negatively if timely diagnosis and treatment are delayed, if cancer patients are forced to use primary care physicians instead of oncologists, and if key elements of care are shifted to nonphysicians.
- Declining levels of total institutional resources under managed care have led to fewer fellowship and residency positions. Record-keeping and monitoring requirements have increased dramatically for attending staff, making it more difficult for them to participate in clinical research. Ever-increasing focus on the bottom line also discourages participation in clinical research. In addition, insufficient resources to support academic or clinical research careers is making it difficult to recruit and retain promising young talent.
- In the long term, protocol research is cost-effective, but managed care administrators may not appreciate this fact because they typically focus on generating current-year profits. However, relying on primary care to treat complicated diseases can prove quite expensive, especially if costly mistakes are made in diagnosis and treatment. Enrollment in research protocols offers the added advantage of gathering data about the new agent; no new knowledge and questionable patient benefits are gained from second- and third-line treatments known to generate infrequent responses in advanced disease.

Additional Research Needs and Other Recommendations

- Delivery of care should be made revenue-neutral for physicians to eliminate disincentives to provide care or to refer to specialists in appropriate circumstances. This step is politically positive and would decrease physicians' risk of malpractice.
- Fully capitated plans pose a potentially greater threat to research than many existing managed care arrangements, since research may be unable to compete within the institution for shrinking revenues. Conversely, in a fully capitated arrangement, the institution at risk can choose to allocate funds for research and

enroll patients in studies it believes are more cost-effective and potentially more efficacious than standard care.

- Managed care plans and other insurers should be required to reimburse peer-reviewed clinical trial research. Such support should be mandated by law before the current economic dynamics have disastrous effects on the clinical research community.

Drs. Frei and Quesenberry
Discussion Period

Key Points

- Defining effective therapy can be very difficult, especially when particular treatments (e.g., autologous bone marrow transplants for breast cancer) gain widespread use before carefully controlled trials establish their effectiveness or otherwise compare them with standard therapy. Under these circumstances, it becomes difficult to accrue patients in randomized trials because media hype and proactive sponsorship can drive demand for the unproven therapy outside of a trial. Whether managed care plans or other insurers should be required to cover treatment in this situation is an open question, although it could be argued that payment is appropriate as long as investigators believe the new treatment has a definite advantage over standard therapy.
- Panel members and participants agreed that Phase I studies always should be viewed as having therapeutic intent since the toxic nature of cancer drugs requires that they be tested on patients instead of healthy subjects. Because cancer is such a devastating disease, the safety concerns of patients enrolled in Phase I trials of new chemotherapy agents differ substantively from those of subjects testing other types of agents, such as decongestants or pain relievers. The oncology community should increase efforts to promote the view that Phase I and II cancer drug studies together comprise a short continuum that should be viewed as a cohesive study of therapeutic benefit, rather than separate studies of toxicology and therapeutic response.
- Taking a new therapy through the drug approval process is a complex and lengthy undertaking that now averages from 8 to 10 years and can involve 5,000 to 6,000 patients in up to 80 different trials. Although there are steps that could be taken to shorten the Phase I/Phase II stages of drug development, the real hurdle occurs at Phase III, where it can take 5 years to implement and carry out a comparison study. In some cases, it can take up to 10 or 15 years to obtain Phase III results and, often, they are irrelevant by the time the data are analyzed. This argues for very careful design and selection of Phase III pre-NDA trials that are tailored to produce data needed for NDA approval. Phase II studies, if positive and confirmed, may be sufficient for NDA approval. Once NDA approval has been achieved for the initially identified indication, broader testing is much more easily accomplished.
- Although health care systems such as those in Great Britain and Canada provide universal care, they traditionally have not supported clinical research on the scale practiced in the United States. Thus, any reduction in this country's commitment

to clinical research could have far-reaching ramifications for the many other nations that depend on U.S.-sponsored trials to evaluate new therapies.

Dr. David W. Yandell
Vermont Cancer Center
University of Vermont

Background

The Vermont Cancer Center, which is an NCI-designated comprehensive cancer center, serves a mostly rural population of 800,000 in Vermont and upstate New York. Approximately 15 percent of all adult patients, and practically all of the Center's pediatric patients, are treated on protocols. At this time, about 35 percent of the Center's patient base is covered by some type of managed care plan, although only a small percentage of these individuals is covered by true capitated plans.

Two translational research themes have emerged at the Center over the past few years. The first emphasizes a bench-to-bedside approach, from synthetic chemistry and preclinical pharmacology studies to Phase I studies in the clinic. The second type focuses on translating what we know about genes and cancer, and also genes and the environment, into the population. As an example of this second type of research, the Center, along with several other institutions including Dartmouth and Roswell Park, has developed a program to identify families at high risk for developing cancer and to then intervene with testing, counseling, and surveillance. Interestingly, only about one-half of those in the high-risk category wish to participate initially, and a significant portion of these individuals refuse to be tested after receiving counseling; many of those refusing intervention cite concerns about insurability if a genetic abnormality is detected. If this type of program is to survive in the current cost-cutting environment, it will be necessary to validate these interventions with hard data establishing their effectiveness.

A recent re-engineering project provided the following information about the hours spent by the Center's staff: (1) 1.8 full-time equivalents for clinical fee-for-service testing; (2) 1 FTE for research grant projects; (3) 0.8 FTE for research and development; and (4) 1.2 FTEs for teaching medical school students, residents, and allied health sciences technologists.

Key Points

- Although he does not have hard data to support his observations, Dr. Yandell does not believe that managed care has had a significant impact on Phase I accruals. However, follow-up care has suffered, as preferred provider requirements limit patients' ability to return to the Center and may lead them to drop out of long-term trials. Managed care plans also have refused to cover certain studies (including the Breast Cancer Prevention Trial) and rigorous referral and preapproval requirements can impede participation in clinical trials.

- Perhaps more significantly from a long-term perspective, market forces have compelled the Center to limit severely its teaching of medical school students and residents. This change in the traditional role of academic medical centers has profound implications for the development of future clinical researchers. Although the Center has cutting-edge capacities in DNA testing and molecular biologic technologies, residents are no longer exposed to these technologies in the course of their training. Eliminating this component of training was necessary to preserve the research function. This aspect of the threat of managed care is often not fully recognized.

Additional Research Needs and Other Recommendations

- NCI should consider revamping its rules on the funding of designated cancer centers so these institutions are able to quickly redirect resources to promptly address changes in the evolving health care structure.
- Incentives at academic medical centers must be structured to provide researchers with enough resources and time to commit themselves fully to promising clinical studies. Currently, even investigators with funded projects find they have no time for research.
- The effectiveness of interventions in high-risk patients, including prevention techniques, should be evaluated through studies designed to establish positive cost/benefit ratios or improvements in quality of life. Additional steps that could be taken include updating patient registration systems to provide reasons for nonregistration, instituting an outreach program to facilitate community participation in clinical trials, and establishing electronic data networks and videoconferencing to link providers and make it easier for them to enter patients on trials.
- Consideration should be given to focusing the general clinical research centers more specifically on cancer research.

Amy Stansfield, R.N., M.B.A.
Norris Cotton Cancer Center
Dartmouth-Hitchcock Medical Center

Key Points

- The Norris Cotton Cancer Center enrolls 10 to 15 percent of its patients on protocols; only 10 percent of ambulatory care patients are covered by true managed care plans. In the inpatient population, reimbursement is governed by negotiated fixed payments in about 80 percent of cases.
- Insurance problems take many forms and can include such payer practices as narrowly defining the word "experimental," restrictively applying FDA information on approved indications for cancer drugs, and limiting access to particular institutions in patients' communities. These problems and, often, lengthy treatment delays pending preapproval all occur at a time when patients face highly stressful circumstances.

- From a providers' viewpoint, dwindling economic support means that physicians are being asked to do more with less, and this limits their ability to conduct clinical trials, especially when considering the lengthy learning curve that is necessary for patients and their payers to become familiar with the research process and the specific protocol. Restrictive reimbursement policies make physicians hesitate to enter patients in studies to evaluate complex therapies that may require extensive inpatient admissions or expensive medications for which securing reimbursement may be difficult.
- Small community hospitals face even greater hurdles in supporting a clinical research program, given their tight operating budgets, limited staff, lack of communication resources such as e-mail, small patient volumes, and often, an older-than-average patient population. While the shift to outpatient cancer care has the potential to reduce costs, many outpatient ambulatory settings are not equipped to provide complex therapies; attempting to do so places undue burden on the physicians and support staff caring for these patients.
- Innovations resulting from clinical research has the potential to decrease health care costs and must be encouraged. As beneficiaries of these advances, third-party payers to contribute to the costs of these studies.
- Although managed care has had some negative impact on clinical research, its emphasis on cost-effectiveness has forced providers to eliminate unnecessary testing and treatments and encouraged the development of outcome data--both positive developments. Norris Cotton Cancer Center has responded to managed care pressures by implementing accelerated clinical improvement programs to enhance quality of care. It has also established a charity fund to help support patients' care on trials when insurers will not provide reimbursement.

Additional Research Needs and Other Recommendations

- Institutions should take a proactive approach to changes in health financing and delivery by meeting with third-party payers and educating them both about the importance of supporting clinical trials and the unique role played by academic medical centers. This type of collaborative effort will help all players understand the others' position and create a level playing field for deciding who should pay for clinical research.
- The risks and associated costs of conducting clinical trials should be shared by participating institutions, patients, and third-party payers, including managed care organizations.

Dr. Yardell and Ms. Stansfield
Discussion Period

Key Points

- Feedback from callers to the Cancer Information Service suggests that physicians and institutions running clinical trials may never see or hear from the many patients who cannot enroll because of health plan restrictions that foreclose the possibility of participation at the outset of the process. If a patient is in a managed

- care plan and none of the plan physicians or institutions are conducting clinical trials, it is highly unlikely that the patient will have an opportunity to be included in a clinical study. It is also unlikely that his or her desire to participate in a trial will come to the attention of those actually conducting appropriate studies.
- When questioned regarding recommendations to change medical residency programs, Dr. Freeman and Dr. Calabresi indicated that in its report, the Panel would offer suggestions and express its concerns in this area, but that these would be of a general nature. Organizations like the Association of Professors of Medicine, the American College of Physicians, and ASIM are currently working on new guidelines and revised curricula; these organizations are the best suited to address these issues in detail and are equipped to assess the need for new guidelines and curricula specifically tailored to reflect the evolving health care delivery system.
 - Dr. Rabson indicated that he would discuss with the Director, NCCR, the possibility of increasing GCRC budgets to permit greater access to these resources by cancer centers and cancer patients. Dr. Calabresi suggested that the NCI, industry, and managed care companies could all contribute to the budget that would be needed to support cancer clinical research at the GCRCs, particularly Phase I/II studies.

INDUSTRY PERSPECTIVE ON CLINICAL TRIALS

Dr. Philip S. Schein
U.S. Bioscience, Inc.

Background

NCI contributes to the development of promising new anticancer drugs through both its intramural and extramural programs. Before a new drug is accepted into the Cancer Therapy Evaluation Program (CTEP), it must be shown to have sufficient scientific and medical merit to warrant the use of government funds to support its investigation. Currently, CTEP conducts Phase I studies at 17 institutions located mainly in major cancer centers; in addition, the NCI holds over 200 active investigational new drug applications for new anticancer therapies and actively supports the primary development of a diverse array of cancer therapeutics.

NCI typically works with the pharmaceutical and biotechnology industries to develop these promising agents through Cooperative Research and Development Agreements (CRADAs). These agreements normally contain cost-sharing provisions so that the drug's sponsor provides financial and other compensation to reimburse the government for the opportunity to utilize NCI resources. CRADAs should be tailored to fit each particular situation, so that larger, more established drug companies assume a proportionately greater share of Phase I costs than smaller firms that typically have less capital. These smaller firms, many of which are in the biotechnology industry, are facing increasing pressure from the capital

markets and managed care; in fact, of the 1,300 small biotechnology companies in the United States, less than 10 are profitable.

Another potentially important resource for Phase I studies, particularly for investigator-initiated RO1 trials, are the academically based GCRCs supported by the NCRR. Although private drug sponsors can utilize GCRCs to conduct their studies, many prefer to use CROs or community-based hospitals because they are often less expensive. These other institutions, however, usually cannot offer the expertise that exists within an academically based GCRC whose principal mission is to translate basic research discoveries into clinical application.

Key Points

- Preclinical data supporting a new therapy's efficacy must be very compelling before a pharmaceutical company is willing to commit the time and resources needed to undergo the complex drug development process, which involves chemical scale-up, formulation development, preclinical toxicology, and pharmacologic evaluation.
- The primary goal of Phase I trials is to define a safe dose for further studies of therapeutic activity and to study the drug's qualitative organ system toxicities. An essential part of Phase I testing involves clinical pharmacology, including pharmacokinetics, i.e., drug absorption, metabolism, excretion, organ distribution, routes of administration, and possible interactions with other drugs.
- Unlike other classes of pharmaceuticals, Phase I studies of anticancer therapies are always conducted on patients with active (and typically advanced) cancer, and usually include basic pharmacodynamic measurements such as tumor response. It is important to appreciate that only patients with a malignant disease that is no longer amenable to established forms of treatment are selected for Phase I studies of anticancer drugs. Moreover, new anticancer agents are selected for testing in humans only after a substantial database of preclinical results suggests the new agent offers a reasonable probability of therapeutic benefit. These facts should be recognized by third-party payers and Medicare in setting their reimbursement policies, since enrollment in a clinical trial may represent the best and only available therapeutic option for some patients with cancer.
- Nonetheless, insurers and Medicare often deny reimbursement for Phase I trials of anticancer drugs on the basis of their "experimental" nature. Both economics and the failure of insurers to understand their obligation to allow, if not to encourage, patients with advanced cancer to enter these trials explain their historic refusal to reimburse such participation.
- The true financial risks of covering early clinical trials are not overwhelming, however, given that Phase I studies typically involve only a small number of patients, and are usually conducted at designated cancer centers by highly qualified physicians. In addition, it is important to note that insurers are already obligated to pay for the cost of routine patient care, including access to physicians and other health care providers and supportive care; industry sponsors usually provide the investigational agents at no cost. Also, most Phase I protocols have

undergone rigorous review by an IRB, the FDA, and sometimes the NCI, so that numerous entry and exclusionary criteria limit the number of eligible patients. Finally, even if a patient was not enrolled in a Phase I trial, in all likelihood an alternative standard treatment would be provided and reimbursed even though it offered little hope of therapeutic value.

- Thus, the financial exposure to insurers for reimbursing Phase I trials is quite limited, especially when compared with the greater societal benefit that research offers in the form of advances in cancer treatment. Managed care organizations have an ethical obligation to make a commitment to improving treatment by supporting clinical trials if they expect to play a major role in determining how patients are cared for in this country.
- This viewpoint on the ethical responsibility of MCOs concerning clinical research is beginning to be accepted by government legislatures and the public at large. The Rhode Island legislation requiring reimbursement for Phase III and Phase IV trials is one example of this trend, although it should be expanded to cover Phase I and Phase II trials. California recently enacted a bill that creates an automatic appeals process for terminally ill patients who are denied experimental treatment; if a panel of three experts determines that the experimental treatment would provide more benefit to a patient than standard treatment, third-party payers must cover it.
- Although the California legislation is a first step in ensuring that people are not denied access to appropriate care, we must realize that costly and time-consuming appeals processes and litigation should not consume patients' lives. In time, an informed public and a responsible government will not allow the denial of an important medical option to patients for whom no real alternative therapy exists.

Additional Research Needs and Other Recommendations

- To equitably apportion the costs of Phase I development, third-party payers could be required to reimburse those costs associated with routine management of the patient (i.e., access to a physician and other health care personnel, basic medications, and monitoring of the patient's condition through blood tests, x-rays, and CT scans in appropriate circumstances). Other additional tests designed to monitor the new agent's effect on the patient, such as pharmacokinetic and pharmacodynamic studies, should be the responsibility of the drug's sponsor.
- The CRADA mechanism is an essential component of the National Cancer Program, as it allows private industry, including small innovative firms, to work in cooperation with the NCI's national resource base for Phase I clinical development. It is in the public interest to support and build upon the past successes of the CRADA program.
- The GCRC system should be evaluated to explore whether new cost-sharing arrangements could be implemented to promote greater utilization of the GCRCs by pharmaceutical and biotechnology firms.

Dr. Schein--Discussion Period

Key Points

- Dr. Schein reemphasized that reimbursement for Phase I trials should not be a major issue of concern for third-party payers given the stringent protocol criteria that restrict the number of eligible patients and the normally limited scope and duration of these trials. At the same time, since Phase I activity drives the decision as to whether to continue the development process, any roadblocks to these trials should be eliminated since they can translate into major delay, or even failure, in bringing potentially important new therapeutics to patients. Thus, it is worth the considerable investment of time and persuasive effort needed to convince third-party payers to cover Phase I testing in patients for whom no alternative therapy exists.
- Because anticancer agents must be studied in patients with active tumors as opposed to normal, healthy volunteers, third-party payers and the Medicare program should reimburse Phase I patient care costs. It may be useful to establish the frequency with which therapeutic benefit is realized in Phase I studies by conducting a review of the existing clinical database and finding those patients who benefited from a Phase I agent after exhausting other available therapeutic options.
- Panel members and participants acknowledged that to require third party payers to cover Phase I costs, it probably will be necessary to define standard care for any given cancer. At this time, however, there is considerable debate about what constitutes standard care for many tumors, since no uniformly effective treatment exists for many types of cancer. Developing standards for cancer treatment could prove to be enormously time consuming and frustrating given the dynamic world of cancer care in which therapies evolve quickly and treatment regimens are individualized to suit each particular patient.
- Given the inherent difficulties in setting guidelines for standard cancer care, it may be more appropriate to tax third-party payers and/or industry across the board so that funds could be collected and distributed to support clinical trials. This approach would recognize that these players must make contributions to the fundamental development of new therapies that may turn out to be safer, more effective, and less costly than existing treatments.
- Efforts to educate the public and government officials about the need to support clinical trials should be undertaken by all affected parties, including the Panel itself in its final report, the NCI, the American Cancer Society, and organizations representing both consumers and health care professionals. Addressing the barriers that keep us from translating basic research gains to the benefit of cancer patients and others at risk for the disease is particularly timely given the 25th anniversary of the National Cancer Act.
- Greater effort should be made to review cost-sharing mechanisms at GCRCs so that the pharmaceutical industry can better utilize this promising resource. Even though GCRCs are not dedicated exclusively to cancer research, their staff are

- experts in conducting translational research and so are in a position to help advance the cancer therapeutics knowledge base.
- Dr. Schein noted that under the criterion outlined in his presentation (whether the new agent is tested in patients with active disease rather than healthy volunteers), there are other diseases, such as AIDS, for which third-party reimbursement of early clinical trials would be appropriate.

Dr. Seth A. Rudnick
CytoTherapeutics

Discussion

The biotechnology industry is a relatively new business that consists of more than 1,300 firms--200 of which are dedicated to cancer research--employing over 100,000 individuals. In the two decades since its founding, the biotechnology industry has produced 43 therapeutic agents at a cost of more than \$350 million for each approved product. The equivalent cost in the pharmaceutical industry is estimated at nearly \$500 million per product. The typical small, entrepreneurial biotechnology company simply is not in a position to assume additional costs for new product development, particularly with regard to routine patient care costs.

The importance of ensuring access to clinical trials has not escaped the notice of Congress; for example, as early as 1990 the House Ways and Means Committee recommended a demonstration project to assess the impact of covering patient care costs. As noted, the Rockefeller-Mack legislation introduced during the last Congress would have established a demonstration project under which HCFA would cover the patient care costs of Medicare beneficiaries enrolled in specific chemotherapeutic clinical trials. Although the legislation did not pass, its sponsors hoped that it would demonstrate to private payers the feasibility of covering these types of costs.

Private voluntary organizations also have recognized the importance of supporting clinical research. For example, the Leukemia Society inaugurated the Translational Research Award Program in 1994 to facilitate transferring clinical gains from the bench to the bedside. This program, which allocates 30 percent of the Society's research dollars, has funded 45 of the 325 grant applications received to date.

Key Points

- The discovery and development of new cancer therapies is a moral and public health imperative that ultimately leads to reduced health care costs and increases in survival rates. However, arbitrary decisions by third-party payers concerning their reimbursement of routine patient care costs associated with clinical trials threatens the \$25 billion cancer research investment this country has made in its health care system.

- Historically, all parties involved in clinical research--patients, drug sponsors, and third-party payers--allocated fairly both the financial and personal risks involved in clinical trials. Society benefited from this arrangement whereby patients bore the personal risk of exposing themselves to a new therapeutic agent, third-party payers covered routine patient care costs, and drug sponsors were responsible for the additional research costs involved in running a clinical trial.
- Unfortunately, recent trends show that this collaborative effort is no longer occurring at the same level as in the past. In 1970, third-party payers covered 80 percent of the routine patient care costs associated with clinical trials; by 1990, the figure had dropped to approximately 70 percent, and recent data suggest that it is now down to between 50 and 65 percent.
- At the same time, global cure rates for cancer have risen to 50 percent, largely due to diagnostic and therapeutic advances attributable to clinical research. To put these figures in perspective, if each year 1 million Americans are diagnosed with cancer, a 15 percent improvement in cure rates means that 150,000 additional lives are saved in each subsequent year.
- Despite widespread support for clinical research within the cancer community and advances in information technologies, the percentage of patients on clinical protocols has not changed significantly over the years. In fact, only 2 to 3 percent of the adult population with cancer (20,000 to 25,000 patients) are entered in NCI-sponsored trials. An approximately equivalent number participate in industry-sponsored studies.
- These low accrual rates are due in part to managed care's fixation on the short-term bottom line. This emphasis on profit margins drives MCOs to deny payment even for minor costs associated with clinical research. Over time, however, research can lower health care costs and improve quality of life by producing more effective and less costly therapies.
- While industry normally contributes to research costs through overhead contributions to participating institutions, it cannot be expected to cover routine patient care costs; such a requirement will cause fewer patients to be enrolled in protocols, with extremely detrimental implications for advancing patient care.

Additional Research Needs and Other Recommendations

- All phases of anticancer studies should be covered by third-party payers. It is illogical for third-party payers to deny reimbursement for Phase I studies, which typically involve few patients and are of short duration, while agreeing to cover more extensive (and expensive) Phase III trials.
- Data should be gathered from HCFA and other third-party payers, including managed care companies, regarding payment of patient care costs associated with clinical trials to assess the extent to which payers are covering legitimate routine costs of care of patients on trials.

Dr. Michael D. Loberg
Bristol-Myers Squibb

Background

Clinical trials are at the heart of a pharmaceutical company's core business; accordingly, Bristol-Myers Squibb invests 16 percent of sales in research and development to determine why people get sick and how to intervene pharmacologically to make them well. At this time, Bristol-Myers Squibb is conducting over 200 clinical trials of oncologic therapies, including biotechnology products. Over the years, the company has worked with the NCI on more than 200 trials.

Bristol-Myers Squibb developed taxol through a CRADA with NCI; this agent faced daunting supply obstacles and toxicity issues. Working collaboratively with the NCI, Bristol-Myers Squibb was able to obtain FDA approval within 2 years of the signing of the CRADA, an example of how obstacles can be overcome through successful public/private partnerships. Although taxol is currently approved for use in ovarian and breast cancer, Bristol-Myers Squibb is sponsoring a number of long-term multimodality combination studies of its use in treating other cancers.

To date, Bristol-Myers Squibb has not experienced impediments in its drug development process due to declining patient enrollment in clinical trials. However, it is becoming much more expensive to conduct the requisite studies because additional sites are now required to secure sufficient patient accrual, resulting in tremendous additional fixed costs.

Key Points

- Clinical trials are particularly important in oncology, in which they often represent the best option available to a patient and are the only means to advance cancer treatment and care in a field where innovation is of paramount importance. Several problems exist with regard to clinical trials, however, not least of which are inadequate funding and a lack of understanding about the true value of clinical research. A third, and related, problem is the tendency of third-party payers to deny reimbursement for clinical trial participation. Most of these issues arise from frequently held misconceptions about clinical research (e.g., it offers no treatment benefit to patients, it is more costly than standard therapy, reimbursement of patient care costs are not the payer's responsibility).
- Managed care is impacting the health care delivery system in a number of fundamental ways, including putting financial pressure on physicians to see more patients for less compensation. In addition, academic medical centers have been hit especially hard, because decreasing discretionary funds make it impossible to provide low-cost care while conducting research and educating residents and fellows. Finally, managed care has the potential to reduce patient access to

- clinical protocols, particularly Phase I trials offering therapeutic benefit to patients with active disease.
- Several solutions are possible, including increased public/private collaborations between the pharmaceutical industry and NCI, academic institutions, and research boutiques. Mandated reimbursement for clinical trial patient care costs may be an appropriate near-term strategy. Finally, enhanced efforts to educate decision makers about the importance of clinical trials, and increased incentives (i.e., product exclusivity) to invest in long-term clinical research could help ameliorate the impact of managed care.
 - Managed care companies should embrace clinical trials, since in the long-term they can save money and result in advances in patient care; health care is expensive only when pharmaceuticals fail, and the way to improve available therapies is through clinical trials. Therefore, clinical research should be seen as part of the culture and ethics of this Nation.
 - To sustain a vigorous biomedical research program, we need additional dollars invested in research; the recent 6.9 percent increase in NIH's budget is a vote of confidence in the quality of NCI's current activities.
 - Private companies will invest the enormous amount of time and resources necessary to take a promising agent through the drug development process only if sufficient incentives exist to warrant that investment. Typically, product exclusivity is the incentive that drives this decision. However, the new types of therapies under development will require extensive testing. As a result, companies will lose a significant portion of the new agents' revenue-generating life cycle to additional studies; thus, it may be appropriate to consider extending current exclusivity periods in this type of situation. Although a drug's cost typically drops by 50 percent once generic versions enter the market, it is important to realize that any incentive to conduct additional research on that product also disappears, so society must weigh the costs and benefits of promoting this competition.
 - The fact that only 3 percent of cancer patients in this country are enrolled in clinical protocols indicates the need for a change in current reimbursement policies. Bristol-Myers Squibb fully supports the National Breast Cancer Coalition, the National Coalition for Cancer Survivorship, the American Cancer Society, and the many other organizations that are striving to ensure that patients have access to specialists and to promising new products.

Additional Research Needs and Other Recommendations

- A model of shared responsibility is most appropriate in determining who should pay the costs of clinical research. Basically, the agent's sponsor (whether a pharmaceutical company or the NCI) should cover research costs and the cost of the investigational agent, while third-party payers should reimburse the costs of routine patient care.
- Although Dr. Loberg normally favors free market solutions, he believes it may be necessary to mandate coverage of the costs of routine patient care incurred in clinical trials. An example of successful legislation that was used to impact private payers' reimbursement policies was contained in the Omnibus Budget

Reconciliation Act (OBRA) of 1993, that directed HCFA to reimburse certain off-label uses of anticancer drugs by Medicare beneficiaries. The Rockefeller-Mack legislation would have created a Medicare demonstration project to cover costs associated with anticancer trials approved by NIH, FDA, the VA, the DoD, or other peer-reviewed mechanisms. This type of legislation is needed because managed care's current focus on short-term profits (due in large measure to high enrollment turnover rates) instead of quality and value prevents the industry from taking a long-term view.

- Efforts should be undertaken to obtain cost-effectiveness and pharmacoeconomic data demonstrating that effective pharmaceuticals and the clinical trials in which they are studied can save millions of health care dollars.
- Additional public/private collaborations should be encouraged through CRADAs.
- Given the longer investigational phase that many of the new anticancer agents will require, it may be appropriate to revisit the issue of how we should balance maintaining sufficient research incentives through exclusivity versus encouraging access to low-cost drugs. Conceivably, sponsors could receive increased exclusivity for providing additional research dollars for new uses of approved products.

Drs. Rudnick and Loberg
Discussion Period

Key Points

- Dr. Calabresi reported that managed care representatives adamantly opposed broadening the Rhode Island bill to include Phase I trials on principle rather than financial considerations. His impression was that managed care companies view Phase I trials as strictly research, and they believe it is not their role to support such research. Moreover, they may fear that by reimbursing Phase I trials, they will be headed down a slippery slope from which they will next be asked to cover basic science and preclinical research.
- Given these attitudes and concerns, a tax or voluntary fund that is set aside to provide general support for clinical research may be a better solution.
- Dr. Loberg reiterated his position that managed care companies must understand they are being asked to reimburse clinical trial costs only in cases where routine patient care was already needed, rather than in studies involving healthy volunteers. Participants also pointed out that third-party payers should be educated about the greater societal benefits attendant to clinical trials, and the very real disincentives to participation resulting from restrictive reimbursement policies. In addition, it is possible that therapy rendered under a clinical protocol may prove less expensive in some cases than standard therapy known to offer little therapeutic benefit. When it is understood that the financial risk of covering Phase I trials is quite limited, and that the sponsors of new therapies will be responsible for covering research costs, it should be possible for all parties to reach a mutually acceptable resolution of this issue. Retrospective chart review may be necessary to develop the data to demonstrate the cost-effectiveness of trial

participation given the subsidy provided by pharmaceutical companies or other sponsors.

- In explaining industry's need for extended exclusivity, Dr. Loberg pointed out that a pharmaceutical company must see a return on its investment in new therapies in order to remain in business. In cases where there is a short period of exclusivity due to a lengthy development process, the company is forced to charge higher prices for the new drug in order to secure this return. Once this exclusivity expires, there is no incentive to conduct additional research on the drug even though important questions may remain (as in the case of taxol).
- Concerning the criteria by which clinical trials will be judged eligible for reimbursement (and by whom) in the Rockefeller-Mack legislation, Dr. Loberg suggested that while the list of accrediting authorities might not be all-inclusive, it was certainly credible. He believes, however, that there is no advantage to being overly restrictive with regard to accrediting authorities, particularly since he believes that community-based trials conducted in physicians' offices will become more important as managed care companies demand pharmacoeconomic data. Dr. Rudnick seconded this opinion, and noted that the goal should be to have a broad vetting process so that the study cohort is representative of the population that will ultimately be treated. He also pointed out that only 50 percent of clinical trials are conducted within the NCI system, so a large number of studies are reviewed outside of the agency's purview.
- Participants agreed that managed care erects economic disincentives to discourage physicians from enrolling their patients in clinical trials; physicians in these plans no longer have the time to teach or conduct research, especially in private practice and community settings. They also agreed that, thus far, managed care's impact seems to be most evident in a decline in the number and quality of staff at research institutions rather than deterioration of the physical infrastructure. It was noted, however, that the explosion in information sharing and data manipulation capabilities has kept infrastructure costs lower than they otherwise might be.
- Although managed care has affected the overall profitability of the pharmaceutical industry, companies have yet to cut back substantially on R&D. Instead, they have pursued other cost-cutting avenues, such as restructuring and mergers, to regain profitability while keeping support for their core business of R&D at consistent levels. It was suggested that managed care has more directly affected the R&D decisions of smaller biotechnology firms compared with large pharmaceutical companies.
- Bristol-Myers Squibb is collaborating with the NCI, the Office of Minority Populations, and the National Asian Women's Breast Cancer Association to ensure that more Asian women have access to clinical trials for breast cancer. The company is creating a network of physicians who treat a significant number of Asians and equipping their offices with electronic data entry capabilities so that they can operate as research centers.
- Participants indicated that research should be conducted irrespective of its ability to reduce costs. Therapies that take a patient out of his/her health care plan (e.g., bone marrow transplant for leukemia) may be less expensive in the long run than several rounds of less effective treatment. In addition, quality of life and longevity

may improve on the more expensive agent. Not all research will result in lower costs; however, the purpose of a clinical investigation is to compare different therapies, and the outcome and related costs may not be known until the data are analyzed. For this reason, it is critical that we return to a model in which all of the interested parties are required to share equitably the risks and costs of conducting clinical research.

- An audience member expressed the opinion that protocols reviewed by the Comprehensive Cancer Centers are carefully evaluated for scientific merit and, thus, usually provide good results once they are undertaken. Conversely, protocols reviewed by other bodies--FDA, IRBs, or industry--do not always receive the same type of rigorous review for scientific merit. It may not be prudent to equate all of these types of protocols for purposes of reimbursement.

Dr. Thomas Mays
Office of Technology Development

Background

The primary focus of the Office of Technology Development (OTD) is to provide access to new candidate drugs both by bringing new materials into NCI and transferring materials and information outside to the private sector. To accomplish this mission, OTD enters into clinical trial agreements (CTAs) and CRADAs that are individually drawn to fit the circumstances of each collaborative effort. In these documents, the private-sector partner typically is required to provide funding, expertise, drugs, or other materials to the NCI to support the research project. As a result of these efforts, in fiscal year (FY) 1997, NCI will receive more than \$15 million in royalties, a figure that surpasses all other Federal agencies combined. The clinical trial CRADA program will bring in approximately \$7 million in FY 1997.

NCI plays a significant role in developing new oncologic agents, primarily through CTEP, which interfaces, conducts, and oversees many of the clinical trials supported by the agency. CTEP awards \$75 million per year in Cooperative Group grants that support more than 500 protocols enrolling 30,000 patients. This effort is carried out through 16 Cooperative Groups involving 500 institutions and 5,000 investigators. All of these protocols undergo rigorous review by the NCI, and investigators must adhere to stringent protocol requirements.

CTEP reviews all active INDs to determine required actions, reviews data management software for adverse event reactions, and facilitates IND filing through an Intramural Liaison Office. In addition to the development of more conventional cytotoxic and biologic agents, CTEP has designated the following scientific initiatives as high priority: angiogenesis inhibitors/antimetastatic agents; signal transduction modulators; cancer vaccines; differentiation/gene expression; modulators of drug resistance; and gene therapy.

Currently, the Division of Cancer Treatment, Diagnosis and Centers (DCTDC) is sponsoring 205 INDs, and has eight active CRADAs and 47 CTAs with various pharmaceutical companies. As of January 1, 1995, NCI had sponsored 50 of the requisite INDs supporting a total of 72 FDA-approved anticancer drugs.

Key Points

- NCI's Office of Technology Development and NIH's Office of Technology Transfer (OTT) serve valuable roles in the technology transfer process. OTD usually gets involved in the very early stages of the process by conducting patent searches and negotiating CTAs, CRADAs, material transfer agreements, and confidential disclosure agreements. OTT takes over once a patent or invention is ready to be filed or a license needs to be negotiated.
- OTD is undertaking several new initiatives to streamline the CRADA process: (1) NCI CRADAs to develop technology transfer informatics; (2) research workshops; (3) cooperative group guidelines; and (4) clinical trials metrics.
- Under the first initiative, OTD will enter into a CRADA with a private technology development entity; the goals of the CRADA will be to improve OTD's ability to identify undeveloped and unlicensed products, assess potential industry partners, create a multimedia informatics environment at OTD, more effectively communicate NIH CRADA opportunities to the industrial community, and ensure that NCI selects the most qualified collaborator for each CRADA.
- The second initiative will allow NCI scientists to facilitate research collaborations by meeting with industry representatives at workshops spanning five different technologies--cellular regulation and control; diagnostics and gene-based therapies; chemopreventive agents and vaccine development; molecular targeting, drug screening and pharmaceutical development; and service center technologies.
- The third initiative centers on CTEP's efforts to draft guidelines to enhance the NCI cooperative group/pharmaceutical industry relationship. The guidelines will cover such issues as indemnification by NCI, confidentiality, proprietary and intellectual property rights, publication rights, and other topics in an effort to expedite these NCI-funded trials by providing consistent ground rules to guide these collaborative efforts.
- The fourth initiative involves developing clinical trials metrics to assess the impact of technology transfer and NCI-sponsored clinical research on public health. In addition to evaluating information about the number and size of research grants, this initiative will also assess CTEP's role in facilitating clinical trials, FDA approval times for new products, the number of new products available to patients, how industry has commercialized and marketed these therapies, the impact of various standards of care enumerated by providers, and certain case studies. A second phase of the initiative will consist of identifying process sites, including cancers with decreasing mortality rates and applicable treatment guidelines, and NCI's contributions, with a specific focus on OTD's contributions to these technologies. This information will then be correlated with data such as number of lives saved and changes in survival and morbidity rates.

- OTD links the research efforts of NCI, industry, and academia and encourages collaborative efforts between these parties. This cooperation allows each sector to bring its particular strength to bear on the goal of ensuring that promising therapies are available to patients as soon as possible. A recent amendment to the Federal Technology Transfer Act will facilitate this process because it allows federal agencies to use royalties to support mission-related research; in addition, agencies can hire temporary full-time staffers who will be exempt from FTE restrictions under CRADAs. NCI already has benefited from these provisions as it has used royalty funds to recruit talented professionals to serve as Technology Transfer Fellows (TTFs).
- OTD is striving to address some of the cost-sharing concerns raised by earlier participants by implementing CRADAs that are flexible and tailored to each collaborative effort. In addition, the agency is using some of its CRADA funds to offset the costs of conducting clinical trials; in fact, a large portion of the \$7 million which NCI will receive this year from CRADA funds will be distributed to the cooperative groups to support clinical trials. However, NCI does not require CRADA collaborators to provide funds under all CRADAs. Many small businesses can serve as very helpful partners in providing expertise and proprietary research materials, but not be able to provide funding under CRADAs.

Dr. Mays--Discussion Period

Key Points

- Asked whether OTD planned to tie royalty payments to additional incentives for industry, Dr. Mays noted that NCI uses the patent mechanism to provide a period of exclusivity in appropriate cases. In cases such as taxol, the agency provided exclusive access to the raw data needed to support an NDA to afford its private sector partner a degree of exclusivity. Dr. Mays pointed out that the law allowing the use of royalties to support training programs, clinical trials, and other mission-related activities is relatively new, so NCI has not yet decided the precise disposition of these funds. He does not believe, however, that royalties could be used to provide a degree of exclusivity. He also clarified that in negotiating a license with industry, OTT normally requires a lower royalty rate than typically found in private-sector licenses because it does not want the ultimate consumers of the product (i.e. patients) to pay a higher price for therapeutic agents.

CONSUMER POINT OF VIEW IN TRANSLATIONAL RESEARCH

Ms. Marlene McCarthy
Rhode Island Breast Cancer Coalition

Key Points

- In the 25 years since the passage of the National Cancer Act, the science of cancer has improved largely due to partnerships between the government and the private industry; a good example of a successful consumer-driven effort is the DoD peer-

reviewed breast cancer research program. On the other hand, cancer also has a history that includes large institutions, a deeply entrenched bureaucracy, expenditures totaling billions of dollars, a longstanding public information campaign promoting specific conceptions and responses to the disease, and millions of deaths.

- The goal of a national initiative against cancer should be to implement a program in which all Americans are able to receive appropriate treatment for their disease. Because clinical trials often offer patients the best treatment option, and they are the only means we have to expand our knowledge of cancer, they should be considered standard therapy in appropriate cases. However, it may be necessary to provide incentive-based financial support to physicians, research support to scientists, and incentives to managed care organizations to encourage all of these parties to participate in clinical trials.
- Unfortunately, several barriers limit clinical trial participation, including a lack of information on the part of both patients and physicians. Also, patient attitudes can pose a disincentive to participation in clinical studies, since the terms "trial," "experimental," and "investigational" often have negative connotations for patients. Furthermore, restrictive insurance policies inhibit clinical trial participation; too often, consumers learn of these limitations only after a diagnosis of cancer. Finally, physicians frequently are asked to demonstrate the cost-effectiveness of a proposed Phase I or Phase II therapy, which proves difficult (if not impossible) if they do not have sufficient numbers of patients on the protocol to secure these data.
- Managed care plans are proving particularly problematic because the long-term health of their enrollees is not a driving factor in an industry that views its relationships with patients as a 12-month renewable partnership. The reliance of managed care on primary care gatekeepers to administer screening and diagnostic tests, recommend treatment, and make referrals to specialists poses grave threats to cancer patients, who need the expertise of an oncologist to provide quality medical care. The cost-driven decisions of managed care companies can result in rationed services. The costs of care of patients enrolled in clinical trials are denied; these patient care costs, including those arising from unexpected reactions, should be covered by managed care plans.
- In the evolving health care delivery system, the government must be in the forefront of efforts to ensure sound scientific research, total parity and access to care, a user-friendly reporting system, innovative technology, and better communications between researchers, health care providers, and patients. This need is particularly acute given that the roles and relationships of hospitals, health care professionals and institutions, insurers, and consumers are being reshaped.
- These sweeping changes present daunting challenges to medical consumers who are already burdened with a diagnosis of cancer. To ask them to spend time and energy struggling to access the best care, which in many cases is available only through a clinical protocol, is not appropriate in a country dedicated to the eradication of this disease. There is no doubt that the current system discriminates against the uninsured, the underinsured, the elderly, the disabled, and the poor. However, patients are beginning to recognize they will have to demand

appropriate care in this environment, so we should expect to see an increase in advocacy groups comprised of informed medical consumers.

- All parties share responsibility for seeing that quality health care is available to all. The Federal Government is responsible for improving our health care delivery system. State governments are responsible for supervising the delivery of health care. Providers are responsible for giving the best care possible to their patients. And consumers are responsible for understanding their options for care, making informed decisions about that care, and becoming advocates for ongoing improvements in the health care delivery system.

Additional Research Needs and Other Recommendations

- Clinical trial enrollment would improve if physicians were better informed about research opportunities and if they could clearly explain the benefits of research to their patients. In addition, a public information campaign explaining the importance of evaluating promising new therapies through clinical trials would be helpful. Informed physicians are confident care providers, and informed patients are proactive consumers.
- Government should examine its investment in private companies deriving market benefit from the research and development of oncologic products, and then require these companies to reinvest these profits in additional research and training. Appropriate incentives should be developed to encourage continued collaboration between the public and private sectors. Finally, equitable cost-sharing arrangements should exist to fund the costs of routine patient care in clinical trials, research costs, and the costs of educating and training necessary professionals.
- Guidelines establishing standard cancer care, including ranges showing minimal and excessive costs, should be developed and published. It should be recognized that quality cancer care also includes meeting patients' psychosocial needs.
- A national action plan on cancer health care should be developed to ensure that equality in health care delivery is guaranteed for all individuals in this country. Profits should not drive the quality of available health care, nor should the poor, the elderly, the disabled, the underinsured, and the uninsured be denied access to quality cancer care. The need for a consumer-focused, universal health care system will become more apparent as corporations continue to downsize, medical institutions merge, and managed care organizations and for-profit hospitals continue to proliferate.

Ms. McCarthy--Discussion Period

Key Points

- Ms. McCarthy clarified her position that third-party payers should pay for all patient care costs arising out of clinical trials, including those associated with unforeseen events.

- Consumers must be well-informed if they are to access clinical trials in appropriate circumstances; in this regard, the public information line at 1-800-FOR-CANCER is a valuable resource.
- The growing patient movement is a potent force that is helping policy makers to understand the very real consequences of their decisions. Often, the public demands solutions to problems once they are personalized through individuals telling their individual stories--the recent legislation mandating minimum hospital days for childbirth exemplifies the power that consumers can tap. However, approaching these issues on a piecemeal basis is time consuming and frustrating. It may be most useful to focus public attention on the drawbacks associated with managed care, so that elected officials hear the public's demand for complete quality care at affordable prices.

CLOSING REMARKS

Dr. Harold Freeman

In his closing remarks, Dr. Freeman noted that:

- Managed care's growth was fueled by the escalating health care costs this country experienced in the last decade as well as the Administration's unsuccessful attempt to utilize managed care in part to create a universal health care system in 1994. Testimony presented to the Panel establishes the profound effect that managed care is having on the health care delivery system, particularly in the West, where it has achieved 75 to 80 percent market penetration.
- Managed care appears to present a particularly grave threat to our continued ability to train young investigators, and this problem must be addressed if we are to remain in the forefront of cancer care.
- Patient advocates will play a very prominent role in articulating the need to ensure quality cancer care even as we control costs.
- Creating standards of cancer care implicates a number of difficult issues, not the least of which is the proposition that the managed care industry defines standard care by what it chooses to reimburse, and at this time patient care costs associated with clinical trials are not covered. However, if we are to pursue the idea of mandated cost-sharing, it will be necessary to separate traditional or routine care from the extra costs associated with participating in a research protocol.
- With regard to Phase I trials of anticancer agents, we must emphasize that they have therapeutic intent and may well represent the best option available to people for whom standard therapies have failed.