ASCO

American Society of Clinical Oncology

February 17, 2009

The Honorable Bettye Davis
Alaska State Senator
District K
Capitol Building Room 30
Juneau, AK 99801-1182

Dear Senator Davis:

The Denali Oncology Group and American Society of Clinical Oncology are pleased to offer support for your legislation to require insurance coverage for people who participate in clinical trials. Our organizations represent physicians specializing in cancer treatment and clinical research, and clinical research is a vital mission of our membership.

Clinical trials are critically important because they offer the promise of new cancer treatments. As you know from personal experience, they also provide an essential, state-of-the-art treatment option for current cancer patients. Therefore, insurance coverage of the routine patient care costs associated with clinical trials is vital for cancer patients.

For many people with cancer, participation in a clinical trial is often their best treatment option. Yet, as you know, many third-party payers take the position that routine patient care costs should be denied to anyone who enrolls in such trials. We believe such policy deprives beneficiaries of the value of their health insurance, wrongly restricts their treatment options, and inhibits medical progress against serious and life-threatening diseases. DOG and ASCO believe that insurers should cover all routine care costs for patients who are enrolled in cancer clinical trials. Your legislation is the key to making this happen.

DOG and ASCO applaud your leadership in pursuing legislation that provides this essential element of quality cancer care. We are eager to work with you to ensure passage. Please do not hesitate to contact Suanna Bruinooge, ASCO's Director of Research Policy, at 571-483-1613 or suanna.bruinooge@asco.org, or Dr. Mary Stewart at mstewartonc@yahoo.com or 907-279-3155.

Sincerely,

Joseph S. Bailes

Mary Stewart, MD
President, Denali Oncology Group

Joseph S. Bailes, MD
Chair, ASCO Government Relations Council

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2318 Mill Road, Suite 800
Alexandria, VA 22314
T: 571-483-1300
F: 571-366-9530
www.asco.org

American Society of Clinical Oncology
Statement In Support of Insurance Coverage for Clinical Trials

With more than 26,000 members worldwide, ASCO is the leading medical society for physicians involved in cancer treatment and research. Engagement in clinical research is a vital mission of ASCO members. Unfortunately, many cancer patients have limited curative treatment options and enrollment in a clinical trial may offer hope for a response to a new drug or other intervention. Oncologists want their patients to consider enrolling in clinical trials, not only because of potential treatment benefits for the individual patient but also because it is through these trials that general progress against cancer is achieved. Patients are usually eager to participate if given the opportunity. ASCO considers the opportunity to participate in cancer clinical trials as an essential element of quality cancer care.

Unfortunately, participation in clinical trials is significantly deterred by the prospect that insurance coverage may be withheld on the ground that treatment provided in trials is "experimental" or "investigational." This position has been effectively discarded by the federal Medicare program, as well as by the Department of Defense health care system, and by many states. ASCO strongly supports state and federal efforts to ensure that patients enrolled in clinical trials receive coverage for the routine health care costs that would be covered if they did not participate on a trial. It is a basic issue of fairness, and it will help ensure that we continue to improve treatment options for cancer patients and learn about this devastating group of diseases.

What is a Clinical Trial?

Clinical trials are research studies involving people. Clinical trials are designed to evaluate whether a new treatment is safe, effective, and better than the current standard of care. These interventions can include new drugs, new combinations of existing therapies, new approaches to radiation therapy or surgery, new methods of treatment, complementary or alternative therapies, and new prevention methods. Cancer clinical trials are designed to compare an investigational therapy with the standard treatment regimen being used at the time. Placebo-controlled clinical trials in cancer research are rare, but are used when there is no effective, standard treatment available.

Cancer clinical trials have led to scientific advances that have increased doctors' understanding of how and why tumors develop and grow. The knowledge gained has helped scientists and doctors develop new ideas on how

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to slow, halt, and even prevent the development of the disease. Clinical trials are the most reliable route to definitive answers and are the only accepted scientific method to determine if a new treatment works better than the current standard of care.

Clinical trials undergo rigorous review prior to opening and involve regular oversight during and after a trial to protect the safety and rights of the participants involved. Each clinical trial follows a set of rules called a protocol. A protocol describes inclusion and exclusion criteria; the schedule of tests, procedures, medications, and doses; and the length of the study. While in a clinical trial, participants are seen regularly by the research staff to monitor their health and determine the safety and effectiveness of the treatment.

Precedents for Clinical Trials Coverage

For more than two decades, the cancer community has expressed its concerns about the negative impact of restrictions on coverage of clinical trials by third-party payers, both public and private. Such restrictions are harmful not only to individual patients but also to overall progress against cancer. In 1999, public authorities began to respond favorably to these arguments and to reform their coverage policies with respect to clinical trials.

Pursuant to a negotiated agreement between the National Cancer Institute (NCI) and the Department of Defense (DoD), the DoD's TRICARE health care plan commenced coverage of NCI-sponsored clinical trials in 1999. The original agreement, began as a pilot project, was made a permanent benefit in March 2008, accompanied by a DoD press release describing it as "a long successful project between the NCI and DoD."

In 2000, the Medicare program took a more expansive approach to clinical trial coverage. In an Executive Memorandum, President Clinton instructed Medicare officials to adopt a clinical trials policy covering not just cancer trials but all diseases and all phases. To implement the policy, the Centers for Medicare & Medicaid Services (then the Health Care Financing Administration) published a National Coverage Determination in September 2000.

State governments have also been active in ensuring coverage of clinical trials by private insurance plans under their control. Almost half of the states throughout the U.S. enjoy coverage of clinical trials, either through legislation

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Alexandria, VA 22314
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or through voluntary consensus agreements with insurers, and more are considering such requirements.

Impact of Policy Changes on Clinical Trial Participation

One of the nation's leading cooperative research groups, the Southwest Oncology Group (SWOG), has conducted studies that underscore the impact of the Medicare coverage policy on clinical trial participation among the elderly. In 1999, SWOG published a study finding significant under-representation of the elderly in cancer clinical trials.[1] The study found that, whereas 63% of cancer patients were Medicare eligible, seniors were only 25% of those patients participating in SWOG clinical trials during the period 1993-1996. Following the Medicare coverage policy in 2000, a second SWOG study found there was a significant increase in participation among Medicare beneficiaries, with seniors representing 38% of SWOG trial participants in the period 2001-2003.[2]

Cost of Clinical Trials Coverage

While there have been no definitive studies of the cost consequences of clinical trial coverage, there have been a series of articles finding that participation in clinical trials "did not result in substantial increases in the direct costs of medical care,"[3] that "[c]linical protocols may add relatively little to that cost,"[4] and that "additional costs of an open reimbursement policy for government-sponsored cancer clinical trials appear minimal."[5] And with almost eight years of experience with the 2000 Medicare coverage policy, there is no evidence of increased cost to the program.

Conclusion

In light of the experience described above, we heartily support efforts to ensure that health plans and all insurers provide coverage for the routine costs

[1] Hutchins et al., "Underrepresentation of Patients 65 Years of Age or Older in Cancer-Treatment Trials," N Engl J Med 341: 2061-2067 (1999).
[2] Unger et al., "Impact of the Year 2000 Medicare Policy Change on Older Patient Enrollment to Cancer Clinical Trials," J Clin Oncol 24:141-144 (2006).
[3] Fireman et al., "Cost of Care for Patients in Cancer Clinical Trials," J Natl Cancer Inst 92:136-142 (2000).
[4] Wager et al., "Incremental Costs of Enrolling Cancer Patients in Clinical Trials: a Population-Based Study," J. Natl. Cancer Inst 91:847-853 (1999).
[5] Goldman et al., "Incremental Treatment Costs in National Cancer Institute-Sponsored Clinical Trials," 289:2970-2977 (2003).

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associated with clinical trials participation. ASCO members strive to ensure access to the best treatment options for their cancer patients, and this requires that health insurers offer clinical trials coverage. We think it is clear that best cancer care and best health care coverage require access to high quality cancer clinical trials.

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American Association for Cancer Research

Association of American Cancer Institutes

American Society of Clinical Oncology

December 1, 2008

Kevin J. Cullen, MD
Director, University of Maryland
Marlene and Stewart Greenebaum Cancer Center
22 South Greene Street
Baltimore, MD 21201

Dear Dr. Cullen:

This letter is written in follow-up to our recent discussions about Medicare coverage of routine patient care costs for beneficiaries participating in phase I cancer clinical trials. As the world's leading professional and scientific organizations representing oncology cancer care professionals, we write to affirm our position that phase 1 cancer clinical trials are the essential gateway for advancement of new cancer treatments—and a vital component of our cancer treatment armamentarium.

It is the view of the undersigned organizations that the current Medicare National Coverage Determination (NCD) (310.1) for Routine Costs in Clinical Trials explicitly includes coverage of phase I cancer clinical trials and that these trials should be covered.

Requirements for Medicare Coverage
The NCD lays out three basic requirements for Medicare coverage:

- The subject or purpose of the trial must be the evaluation of an item or service that falls within a Medicare benefit category (e.g., physicians' service, durable medical equipment, diagnostic test) and is not statutorily excluded from coverage (e.g., cosmetic surgery, hearing aids).
- The trial must not be designed exclusively to test toxicity or disease pathophysiology. It must have therapeutic intent.
- Trials of therapeutic interventions must enroll patients with diagnosed disease rather than healthy volunteers. Trials of diagnostic interventions may enroll healthy patients in order to have a proper control group.

The NCD also requires that clinical trials covered under the policy have seven "desirable characteristics."

1. The principal purpose of the trial is to test whether the intervention potentially improves the participants' health outcomes;
2. The trial is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;

3. The trial does not unjustifiably duplicate existing studies;
4. The trial design is appropriate to answer the research question being asked in the trial;
5. The trial is sponsored by a credible organization or individual capable of executing the proposed trial successfully;
6. The trial is in compliance with Federal regulations relating to the protection of human subjects; and
7. All aspects of the trial are conducted according to the appropriate standards of scientific integrity.

The policy also states that certain trials "are presumed to meet these characteristics and are automatically qualified to receive Medicare coverage." Trials that are automatically deemed include:

1. Trials funded by NIH, CDC, AHRQ, CMS, DOD, and VA;
2. Trials supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD and VA;
3. Trials conducted under an investigational new drug application (IND) reviewed by the FDA; and
4. Drug trials that are exempt from having an IND under 21 CFR 312.2(b)(1) will be deemed automatically qualified until the qualifying criteria are developed and the certification process is in place. At that time the principal investigators of these trials must certify that the trials meet the qualifying criteria in order to maintain Medicare coverage of routine costs. This certification process will only affect the future status of the trial and will not be used to retroactively change the earlier deemed status."

Phase 1 Cancer Clinical Trials Have Therapeutic Intent

The National Cancer Institute's (NCI) Investigator Handbook is instructive as to the therapeutic intent of a Phase I trial. That handbook includes the following information about phase 1 cancer clinical trials (emphasis added):

> Phase 1 trials determine a safe dose for Phase 2 trials and define acute effects on normal tissues. In addition, these trials examine the agent's pharmacology and may reveal evidence of antitumor activity. **Therapeutic intent is always present in Phase 1 trials**; indeed, anticancer agents are not tested in patients unless preclinical activity studies have already demonstrated evidence of significant activity in laboratory models.[1]

The Food and Drug Administration (FDA) has also adopted a definition of phase 1 trials that is consistent with the NCI's definition. FDA states that phase 1 studies "are designed to determine the metabolic and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to **gain early evidence of effectiveness**." This early evidence of effectiveness is the grounding for therapeutic intent – both in the choice of oncologists and patients to enroll in the trial, and as one of the aims of the trial.

Although the scientific goals of a phase 1 trial are to determine the toxic effects, pharmacologic behavior, and recommended doses for future study of a new agent, there is always a strong preclinical

[1] Available on the NCI website at http://ctep.cancer.gov/handbook/index.html

rationale for bringing the drug into the clinic with the expectation of positive clinical outcomes for some patients.[2] In fact, Institutional Review Boards would not permit the administration of potentially toxic treatments to patients unless there was some reasonable prospect of antitumor effect.[3] It is also important to note that phase 1 oncology treatment trials are **never** done in healthy volunteers because of the potential toxicities associated with the treatments under investigation.

Additionally, many of the NCI phase 1 trials involve agents that are already approved for the treatment of one type of cancer and are being studied in a different type of cancer, or in combination with other treatments. As a result, we have some evidence of therapeutic effectiveness that provides solid grounding on which to base therapeutic intent. Indeed, an analysis of 12,000 individuals who participated in 460 NCI-funded phase 1 trials done in 2005 found that 10.6% of patients experienced an objective response. This number increased to 17.8% of patients when one drug included in the trial regimen was already FDA-approved.[4]

Furthermore, our growing knowledge of the molecular basis of cancer is allowing us to increasingly develop treatments that are targeted to particular molecular pathways and personalized to specific patient populations. These types of agents will provide a "high pretreatment probability of achieving both an objective response and more subjective clinical benefit" for the trial participants.[5]

To bring about these exciting new developments in cancer treatment, clinical trials participation is required. It is particularly important in the Medicare-aged population not only because of the increased incidence of cancer in the elderly and but also to develop our understanding of how treatments work in this population. Both the NCI and FDA definitions demonstrate that phase 1 oncology trials meet the requirements for Medicare coverage, including therapeutic intent, and should be covered.

Sincerely,

Raymond N. DuBois, MD, PhD
President
American Association for
Cancer Research

Edward J. Benz, Jr., MD
President
Association of American
Cancer Institutes

Richard L. Schilsky, MD
President
American Society of
Clinical Oncology

[2] ASCO: Critical role of phase 1 clinical trials in cancer treatment. J Clin Oncol 15:853-859, 1997.
[3] Kodish E, Stocking C, Ratain MJ, et al: Ethical issues in phase I oncology research: A comparison of investigators and IRB chairpersons. J Clin Oncol 10:1810-1816, 1992.
[4] Horstmann E, McCabe MS, Grochow L, et al: Risks and benefits of phase 1 oncology trials, 1991 through 2002. New Engl J Med 352:895-905, 2005.
[5] Markman M: Further evidence of clinical benefits associated with participation in phase 1 oncology trials. B J Cancer 98:1021-1022, 2008.

Coverage of Routine Patient Care Costs in Clinical Trials
Position Statement

Approved by the ASCO Board of Directors, March 2005

For people with serious or life-threatening illness, like cancer, completely satisfactory or curative treatment often is not available. Those patients are nevertheless able to receive state-of-the-art therapy through high-quality clinical trials, offering not only an important treatment option but an opportunity to advance medical knowledge.

Cancer patients face a number of obstacles to clinical trials enrollment. One of the barriers is the potential denial of third party payment for the routine patient care costs for those enrolled in clinical trials. Historically, payers have denied coverage for care provided in a clinical trial, arguing that such care is "experimental" and therefore not a covered benefit.

Current Clinical Trials Coverage

The American Society of Clinical Oncology (ASCO) and its partners in the patient advocacy community have sought, over the course of more than a decade, to reform clinical trials payment policy in public and private health plans. These efforts have resulted in reforms in Medicare payment policy and in enactment of legislation to ensure clinical trials coverage in more than 20 states.

In 2000, in response to Congressional pressure and cancer community advocacy, the Clinton Administration issued an Executive Memorandum setting a policy for coverage of the routine patient care costs for Medicare beneficiaries enrolled in clinical trials for all diseases.

In addition to action by Medicare, a number of states have enacted legislation that would ensure coverage of routine patient care costs in clinical trials (coverage ranges from cancer clinical trials only to trials for all diseases) by those health plans that are regulated by the state. Some of those states have adopted, either in statute or in implementing regulations, the coverage standards of the Medicare program. In several states without clinical trials coverage mandates, third party payers have entered into voluntary agreements to cover routine costs in clinical trials. States continue to engage in efforts to improve coverage in state plans.

ASCO Position

These federal, state, and private sector initiatives reflect widespread recognition of clinical trials coverage as a critical element of quality cancer care. However, not all of the initiatives meet the standards for coverage endorsed by ASCO, and a significant number of cancer patients remain beyond the reach of these reimbursement reforms. ASCO recommends that every cancer patient should have access to clinical trials under the criteria defined below.

Standards for Clinical Trials Coverage

The following ASCO standards should remain the standard for Medicare coverage and should serve as the model for state legislative initiatives, including provisions governing coverage under state-funded programs like Medicaid, as well as mandates for private insurance and managed care plans.

The cost of medical care provided when a patient with serious or life-threatening disease is entered on a Phase I, II, III, or IV (post-marketing) clinical trial – including hospital, physician, and other health care items and services as well as the cost of approved drugs for labeled or unlabeled uses which might be part of the regimen[1] – should not be denied coverage when all of the following are demonstrated:

- Treatment is provided with a therapeutic intent[2];
- Treatment is being provided pursuant to a clinical trial approved by one of the National Institutes of Health (NIH), an NIH cooperative group or an NIH center; the Food and Drug Administration (FDA) in the form of an investigational new drug (IND) or new device (IDE) exemption; the Department of Defense; the Department of Veterans Affairs; or a qualified non-governmental research entity as identified in National Cancer Institute guidelines or center support grants;
- The trial is conducted according to a written protocol, which includes the following elements: trial design and scientific justification, criteria for inclusion and exclusion, outcome measures, statistical analysis plan, conflicts and other ethical controls, and publication policy;
- The protocol has undergone scientific review by a group of independent and qualified experts;
- The clinical trial has been reviewed and approved by a qualified institutional review board (IRB);
- The facility and personnel providing the treatment are capable of doing so by virtue of their experience or training;
- There is no non-investigational therapy that is clearly superior to the protocol treatment; and
- The available clinical or preclinical data provide a reasonable expectation that the protocol treatment will be at least as efficacious as non-investigational therapy.[3]

Originally adopted February 1993
As amended June 1994 and March 2005

[1] Items and services required by the design of the trial should be covered, except those items or services normally paid for by other funding sources such as the cost of certain investigational drugs, the costs of any non-health services that might be required for a person to receive the treatment, and the costs of managing the research.

[2] Treatment with therapeutic intent may be aimed at improving patient outcome relative to either survival or quality of life.

[3] While these standards refer to clinical trials involving "treatment" or "therapy", the same principles would apply equally to trials of interventions to prevent, rather than treat, diseases.