Recommendations for the Evaluation and Prioritization of Cost-Effectiveness Analyses (CEA) paired with NCI-Sponsored Treatment Trials and a Funding Mechanism for Supporting CEA

Prepared for CTAC by the NCI Cost-Effectiveness Analysis Working Group
September 21, 2010

Working Group Members

Scott Ramsey, Fred Hutchinson CRC (Chair)
Martin Brown, NCI
David Cella, Northwestern University
Jeffrey S. Hoch, University of Toronto
Deborah Marshall, McMaster University
David Meltzer, University of Chicago
Margaret Mooney, NCI
Daniel Polsky, University of Pennsylvania
Richard L. Schilsky, University of Chicago
Jane Weeks, Dana-Farber Cancer Institute
James L. Wade, Decatur Memorial Hospital

Cost-Effectiveness Analysis Working Group (CEA WG)

The Clinical Trials and Translational Research Advisory Committee (CTAC) has considered the value of including economic analyses in the NCI funding of cancer-related treatment trials. At their July 15, 2009 meeting, CTAC recommended forming a Working Group (WG) to address issues related to Cost-Effectiveness Analysis (CEA) and to provide recommendations to the NCI.

Function/Mission Statement

The purpose of the Cost-Effectiveness Analysis Working Group (CEA WG) is to advise the Clinical Trials and Translational Research Advisory Committee (CTAC) and the NCI on the development of a prioritization process and funding mechanisms to ensure that the most important cost-effectiveness analyses can be conducted in association with NCI-sponsored clinical trials.

Objectives

1. Develop prioritization criteria for determining the most important cost-effectiveness analyses to conduct in conjunction with clinical trials.
2. Recommend possible funding mechanisms for support of high priority cost-effectiveness analyses.

Background

Cost-effectiveness analyses (CEA) provides useful information to help health care payers manage the use of costly medical technologies in order to maximize the health of their patient populations when facing constrained budgets, and to clinicians and patients to help guide treatment decisions based on CEA's unique endpoints, perspectives, and time horizon. To be most useful to decision-makers, CEA of new cancer therapies must be timely and have high internal validity. Conducting a CEA alongside a treatment trial can achieve these goals and also offers the benefit of efficiency by utilizing the existing structure of treatment trials to collect additional data for the economic analysis. To maximize the feasibility, internal validity and timeliness of CEA alongside treatment trials, it is important to incorporate CEA studies during the design phase of treatment trials.

Although pairing cost-effectiveness studies to phase 3 treatment trials offers many advantages, additional funds beyond those needed to conduct the treatment trial itself are needed at the onset to achieve the important goals. It is therefore important to have a process for selecting studies where the timely results of an economic analysis will be maximally useful to the oncology community.

Evaluation, Prioritization and Eligibility Criteria

The proposed CEA evaluation criteria are intended to help guide the selection of cancer treatment trials that warrant additional funds for a CEA. This guidance provides criteria that are commonly used to prioritize studies for CEA. They are not intended to supersede other factors specific to the National Cancer Institute, the trial investigators, or other groups that may be important in making decisions about the inclusion of CEA in clinical trials or the funding of CEA.

Researchers should consider pairing a cost-effectiveness analysis (CEA) proposal to phase 3 treatment trials when the following four conditions are met:

1. The results of a Phase 3 clinical intervention trial are expected to substantially influence clinical practice.
2. The cost-effectiveness study would be of high impact judged by substantial budget implications for health care systems, either in terms of overall cost savings or added costs to the system.
3. It is feasible to conduct a high quality CEA as part of the clinical trial. Specific issues to consider include:
    - The comparator (control arm) should be relevant to current clinical practice.
    - The trial should be of sufficient duration, with respect to follow-up of patient outcomes, that consequences of interest to economic evaluation can be captured either directly or through modeling.
    - There is reasonable statistical power for the key cost-effectiveness analysis.

4. Because of high cost, there is a reasonable degree of uncertainty regarding the outcome of the CEA even if the clinical outcome favors the experimental treatment.

For CEA studies that are projected to be very costly and whose value is uncertain, value of information analysis (VOI) should be considered. Value of information analysis may also be useful when there are questions about study design questions could be addressed by modeling.

Recommended Type of Cost-Effectiveness Analyses (CEA)

Numerous groups, including the US Preventive Services Task Force on Cost-Effectiveness in Health Care recommend that economic analyses should be conducted as cost-utility studies; that is as a specific type of CEA with outcomes measured as quality-adjusted life years. This implies that evaluation of survival and quality of life (expressed as health state utilities) should be included as endpoints in the trial. In addition, the Task Force recommends that studies should take multiple perspectives, with the societal and payer perspectives in addition to patient specific outcomes.

Overview - Evaluation and Funding Mechanism

It is the intent of the National Cancer Institute (NCI) to invite funded Cooperative Groups (CGs) and funded Community Clinical Oncology Program (CCOP) Research Bases to apply on a competitive basis for funding to support CEA studies that are paired to phase 3 treatment and prevention trial concepts. The process for evaluation and funding of CEA proposals will be managed through the Coordinating Center for Clinical Trials (CCCT) in the NCI Office of the Director. The funding of CEA proposals will be based on the scientific merit of both the parent treatment or prevention trial concept and the CEA proposal and each must be approved by the appropriate review bodies.

Eligible Trial Types

Regarding NCI-funded treatment trials, the parent concept in which the CEA proposal is paired must conform to the policies of the Division of Cancer Treatment and Diagnosis (DCTD) and Division of Cancer Prevention, National Cancer Institute (NCI) for Phase 3 treatment and prevention clinical trials. In addition, to be eligible for funding consideration, CEA proposals must meet the following requirements:

- The parent treatment trial must be a randomized Phase 3 trial with a control arm.
- The parent treatment trial and proposed CEA study must be conducted by CG's or CCOP Research Bases.
- The CEA proposal and parent treatment trial in which CEA is paired should meet the CEA Proposal Evaluation Criteria (see above).

Proposal Submission

In the development of recommendations regarding CEA proposal submission, the CEA WG considered the stage(s) of clinical trials in which a CEA proposal should be considered. For Phase 1/2 treatment trial proposals, few expectations exist for clinically useful CEA. This, in combination with NCI funding prioritization, suggests that Phase 3 trials should be the primary focus for CEA funding.

Two pathways for the evaluation of CEA proposals as well as potential funding mechanisms were also discussed. One pathway described the mechanism to be followed if CEA studies were required with, or could be added to, treatment trial concepts submitted to CTEP/DCP. The other described the mechanism for Cooperative Groups (CGs) and Community Clinical Oncology Program (CCOP) Research Bases to optionally include CEA studies with treatment trial concepts submitted to CTEP/DCP. An important element to one of the pathways was that CGs would need to develop their own internal processes to both determine whether CEA should be included in a proposal as well as a mechanism to assemble the resources needed to develop and carry out the CEA portion properly. Generally it was felt that currently there are insufficient CEA experts available to form specialized CEA Groups within each CG. It was also determined that the availability of expertise within NCI to consider whether CEA should be included in treatment trial concepts is limited. As a result, it is recommended that CEA not be mandatory with each treatment trial concept submitted. It was agreed, however, that through discussion, the Task Force (TF) for each Scientific Steering Committee (SSC) may provide their recommendations to CGs and CCOP Research Bases about including CEA in a trial concept. The evaluation of CEA paired with Phase 3 treatment trials submitted will be the responsibility of the disease–specific scientific steering committees for treatment trials and the Symptom Management, Quality of Life Steering Committee for studies having quality of life as their primary endpoint. NCI and external ad hoc CEA experts will be required for the evaluation process.

CEA proposals included in treatment trial concepts should be developed by CGs and CCOP Research Bases through an established process. When CGs and CCOP Research Bases choose to propose a CEA study, this must be submitted with the parent treatment trial concept that has been developed. Guidance is provided by the NCI regarding the funding eligibility of treatment trial concepts that include CEA as well as the criteria commonly used to prioritize CEA proposals being considered for funding (see CEA Proposal Evaluation Criteria above).

Recommended Funding Mechanism

The CEA WG determined that the current Biomarker, Imaging and Quality of Life Studies Program (BIQSFP) funding mechanism and prioritization process provides the best structure upon which a similar mechanism for CEA proposals paired with treatment trials could be based. The BIQSFP processes were established for essential correlative biomarker and imaging studies and quality of life studies that are incorporated into the fundamental design of a clinical trial and are not currently supported by the U10 funding mechanism (For more information, see http://biqsfp.cancer.gov/).

1. Applications for funding of CEA proposals paired to treatment trial concepts are submitted to the Cancer Therapy Evaluation Program (CTEP) or the Division of Cancer Prevent (DCP) Protocol and Information Office (PIO) via the usual process for submitting concepts to CTEP or DCP (see Appendix A - *Evaluation and Funding Mechanism for Cost-Effectiveness Analyses Proposals alongside NCI-sponsored Treatment Trials Flowchart*).

The Principal Investigator (PI) of CGs and CCOP Research Bases may choose to informally submit a parent treatment trial concept with a paired CEA proposal to a Scientific Steering Committee (SSC) Task Force (TF), if available, for discussion prior to submission for evaluation by the Scientific Steering Committee (SSC).

2. Once a concept is completed, it can be is submitted to the appropriate Scientific Steering Committees (SSC) for evaluation.

3. The responsibility of SSCs is to evaluate and prioritize cancer clinical trial concepts and facilitate the sharing of ideas among a broad range of clinical investigators, basic and translational scientists, NCI staff, community oncologists, and patient advocates. SSCs evaluate CEA proposals paired with treatment trial concepts through their concept evaluation and prioritization process. SSCs will make use of ad hoc CEA expert(s), including resources available at the NCI, to evaluate CEA proposals included in clinical trial concepts.

4. Meritorious CEA proposals that are paired with concepts that have been approved by SSCs are recommended by NCI Staff to the Clinical and Translational Research Operations Committee (CTROC). CTROC is an internal NCI advisory committee and includes the Directors of all NCI Divisions, Offices, and Centers that have clinical trials or translational science portfolios. CTROC makes the final recommendation regarding the funding of the CEA proposal.

Clinical Trials and Translational Research Advisory Committee (CTAC)

The Clinical Trials and Translational Research Advisory Committee (CTAC) annually reviews the approved funding portfolio, providing strategic oversight and advice that would include the inclusion of CEA studies within treatment trials approved for funding through the NCI-supported national clinical trials enterprise.

Science Applications International Corporation-Frederick, Incorporated (SAIC-F)

Approved CEA studies are supported through subcontracts established between those institutions receiving the CEA awards and Science Applications International Corporation-Frederick, Incorporated (SAIC-F). Quarterly invoices/progress reports will be submitted to SAIC-F for payment of approved funds. An annual Protocol Progress Report addressing the CEA award is to be submitted with the annual progress report of the parent concept award.

Cost-Effectiveness Analysis Working Group Members

Chair

Scott Ramsey, MD, PhD
Professor in the School of Medicine
University of Washington
Full Member in the Division of Public Health Sciences
Fred Hutchinson Cancer Research Center
Seattle, WA

Members

Martin Brown, PhD
Chief, Health Services and Economics Section
Applied Research Branch, Cancer Surveillance Research Program, DCCPS
National Cancer Institute
Bethesda, MD

David Cella, PhD
Chairman and Professor
Department of Medical Social Sciences
Northwestern University Feinberg School of Medicine
Chicago, IL

Jeffrey S Hoch, PhD
Associate Professor, Associate SGS Member
Centre for Research on Inner City Health
St. Michael's Hospital
Department of Health Policy, Management and Evaluation
University of Toronto
Toronto, ON

Deborah Marshall, PhD
Associate Professor
Department of Clinical Epidemiology & Biostatistics
Centre for Evaluation of Medicines
McMaster University
Hamilton, ON

David Meltzer, MD, PhD
Associate Professor, Department of Medicine
Associated Faculty Member, Harris School and the Department of Economics
The University of Chicago
Chicago, IL

Margaret Mooney, MD
Chief, Clinical Investigations Branch
Cancer Therapy Evaluation Program, CTEP, DCTD
National Cancer Institute
Bethesda, MD

Daniel Polsky, PhD
Professor of Medicine
Director of Research, Leonard Davis Institute of Health Economics
Professor of Health Care Management, The Wharton School
University of Pennsylvania
Philadelphia, PA

Richard L. Schilsky, MD
Professor of Medicine
Chief, Section of Hematology/Oncology
University of Chicago Medical Center
Chicago, IL

Jane Weeks, MD
Professor of Medicine, Harvard Medical School
Professor of Health Policy and Management, Harvard School of Public Health
Dana-Farber Cancer Institute
Boston, MA

James L. Wade, III, MD
Principal Investigator, Central Illinois CCOP
Associate Professor of Clinical Medicine
Feinberg School of Medicine, Northwestern University
210 W. McKinley Ave.; Suite 1
Decatur, Illinois

Executive Secretary
Raymond Petryshyn, Ph.D.
Program Director
Coordinating Center for Clinical Trials
National Cancer Institute
Rockville, MD

Appendix A - Evaluation and Funding Mechanism for Cost-Effectiveness Analyses Proposals alongside NCI-sponsored Treatment Trials Flowchart